

BMJ Best Practice

Coronavirus disease 2019 (COVID-19)

Straight to the point of care



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Summary

Coronavirus disease 2019 (COVID-19) is an infectious acute respiratory disease caused by a novel coronavirus. The World Health Organization (WHO) was informed of cases of pneumonia of unknown microbial etiology associated with Wuhan City, Hubei Province, China on 31 December 2019. The WHO later announced that a novel coronavirus had been detected in samples taken from these patients. Since then, the epidemic has escalated and rapidly spread around the world, with the WHO first declaring a public health emergency of international concern on 30 January 2020, and then formally declaring it a pandemic on 11 March 2020. Clinical trials and investigations to learn more about the virus, its origin, how it affects humans, and its management are ongoing. This topic is based on the best evidence currently available, but as this is a rapidly evolving situation, evidence is limited in some areas and some recommendations may be based on observational studies and retrospective analyses, as well as randomized controlled trials and guidelines.

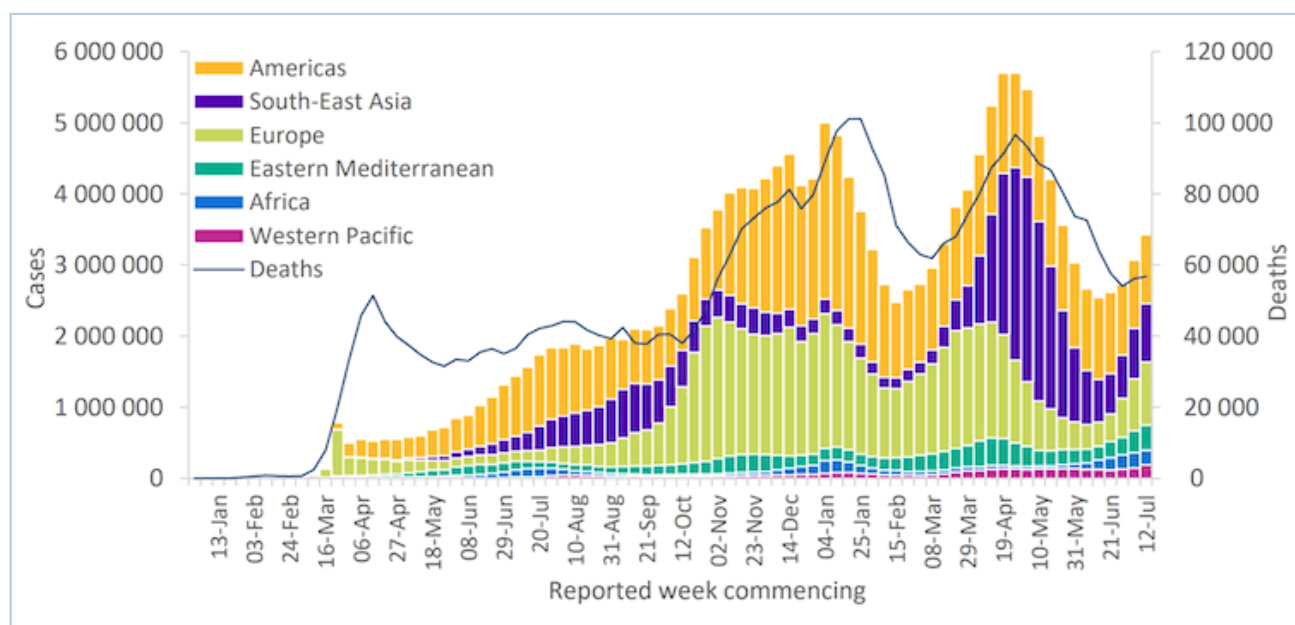
Definition

A potentially severe acute respiratory infection caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).^[1] The clinical presentation is generally that of a respiratory infection with a symptom severity ranging from a mild common cold-like illness, to a severe viral pneumonia leading to acute respiratory distress syndrome that is potentially fatal. Characteristic symptoms include fever, cough, dyspnea, and loss of taste/smell, although some patients may be asymptomatic. Complications of severe disease include, but are not limited to, multi-organ failure, septic shock, and venous thromboembolism. Symptoms may be persistent and continue for more than 12 weeks in some patients.

Epidemiology

Over 191.1 million cases have been reported globally, with approximately 4.1 million deaths according to the World Health Organization. The US has the highest number of reported infections and deaths in the world. India, Brazil, Russia, and France have the highest number of infections after the US. Brazil, India, Mexico, and Peru have the highest number of deaths after the US.

[WHO: coronavirus disease (COVID-19) dashboard] (<https://who.sprinklr.com>)



Number of COVID-19 cases reported weekly by WHO Region, and global deaths, as of 18 July 2021

World Health Organization

Current detailed data for the US situation is available.

- [CDC: COVID data tracker weekly review] (<https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview.html>)

Adults

- In China, 87% of confirmed cases were ages 30 to 79 years and 3% were ages 80 years or older in the first wave of the pandemic. Approximately 51% of patients were male.[4]
- In the UK, the median age of patients was 73 years and males accounted for 60% of admissions in a prospective observational cohort study of more than 20,000 hospitalized patients in the first wave.[5]
- In the US, older patients (ages ≥ 65 years) accounted for 31% of all cases, 45% of hospitalizations, 53% of intensive care unit admissions, and 80% of deaths in the first wave, with the highest incidence of severe outcomes in patients ages ≥ 85 years.[6]

Adolescents

- Adolescents appear to have similar susceptibility to infection as adults.[7]
- In the US, hospitalizations in adolescents peaked at 2.1 per 100,000 in early January 2021, declined to 0.6 per 100,000 in March, and rose to 1.3 per 100,000 in April. Among hospitalized adolescents, approximately one third required admission to the intensive care unit and 5% required mechanical ventilation. This data was based on 204 adolescents who were likely hospitalized primarily for

COVID-19 during January 1 to March 31 2021.[8] The cumulative number of hospitalizations in the 5 to 17 year old age bracket from March 2020 to June 2021 was 1909 cases.[9]

Children

- Evidence suggests that children have a lower susceptibility to infection compared with adults, with an odds ratio of 0.56 for being an infected contact compared with adults.[7] Most cases in children are from familial clusters, or children who have a history of close contact with an infected patient. It is rare for children to be the index case in household transmission clusters.[10] Infection rates vary according to geographic location.[4] [11] [12] [13] [14] [15] [16] The mean age of children with infection was 6.5 years in the first wave.[17] Unlike adults, children do not seem to be at higher risk for severe illness based on age or sex.[18]
- In the UK, a prospective observational cohort study found that children and young adults represented 0.9% of all hospitalized patients at the time. The median age of children admitted to hospital was 4.6 years, 56% were male, 35% were under 12 months of age, and 42% had at least one comorbidity. In terms of ethnicity, 57% were White, 12% were South Asian, and 10% were Black. Age under 1 month, age 10 to 14 years, and Black race were risk factors for admission to critical care.[19]
- In the US, a retrospective cohort study of over 135,000 children found that the mean age of infected children was 8.8 years, and 53% were male. In terms of ethnicity, 59% were White, 15% were Black, 11% were Hispanic, and 3% were Asian. Only 4% of children tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in this population, and clinical manifestations were typically mild.[20] Cases in children, adolescents, and young adults increased between October to December 2020; however, hospitalizations, intensive care unit admissions, and deaths remain low for these groups (2.5%, 0.8%, and <0.1% respectively, based on available data).[21]
- Globally, the case fatality rate in children appears to be higher in low- and middle-income countries compared with high-income countries.[22]
- [American Academy of Pediatrics: children and COVID-19 – state-level data report] (<https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report>)

Pregnant women

- The overall prevalence in pregnant and recently pregnant women attending or admitted to hospital for any reason has been estimated to be 10%; however, the rate varies across studies and countries.[23] [24] A meta-analysis of over 2500 pregnant women with confirmed disease found that 73.9% of women were in the third trimester; 50.8% were from Black, Asian, or minority ethnic groups; 38.2% were obese; and 32.5% had chronic comorbidities.[25]
- In the UK, the estimated incidence of admission to hospital with confirmed infection in pregnancy is 4.9 per 1000 maternities. Most women were in the second or third trimester. Of these patients, 41% were ages 35 years or older, 56% were from Black or other ethnic minority groups, 69% were overweight or obese, and 34% had preexisting comorbidities.[26]
- In the US, 101,710 cases have been reported in pregnant women (as of 19 July 2021), with 17,380 hospitalizations and 114 deaths.[27] According to an analysis of approximately 400,000 women ages 15 to 44 years with symptomatic disease, Hispanic and non-Hispanic Black pregnant women appear to be disproportionately affected during pregnancy.[28]

Healthcare workers

- Approximately 14% of the cases reported to the World Health Organization are in healthcare workers (range 2% to 35%).[29]

- The incidence of infection in healthcare workers ranged from 0% to 49.6% (by polymerase chain reaction), and the prevalence of SARS-CoV-2 seropositivity ranged from 1.6% to 31.6%. The wide ranges are likely related to differences in settings, exposures, rates of community transmission, symptom status, use of infection control measures, and other factors. There was no consistent association between sex, age, or healthcare worker role (i.e., nurse versus physician) and risk for infection or seropositivity. However, Black or Hispanic ethnicity was significantly associated with an increased risk of infection compared with White people. Working in a hospital unit with COVID-19 patients, being a frontline worker, and direct or prolonged patient contact were also associated with an increased risk for infection. The presence of immunoglobulin G antibodies was associated with a decreased risk for reinfection.[30] [31]
- The majority of healthcare workers reported contact in the healthcare setting. In a study of over 9000 cases reported in healthcare workers in the US, 55% had contact only in a healthcare setting, 27% only in a household, 13% only in the community, and 5% in more than one setting.[32]

Etiology

Virology

- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a previously unknown betacoronavirus that was discovered in bronchoalveolar lavage samples taken from clusters of patients who presented with pneumonia of unknown cause in Wuhan City, Hubei Province, China, in December 2019.[33]
- Coronaviruses are a large family of enveloped RNA viruses, some of which cause illness in people (e.g., common cold, severe acute respiratory syndrome [SARS], Middle East respiratory syndrome [MERS]), and others that circulate among mammals and birds. Rarely, animal coronaviruses can spread to humans and subsequently spread between people, as was the case with SARS and MERS.
- SARS-CoV-2 belongs to the *Sarbecovirus* subgenus of the *Coronaviridae* family, and is the seventh coronavirus known to infect humans. The virus has been found to be similar to SARS-like coronaviruses from bats, but it is distinct from SARS-CoV and MERS-CoV.[34] [35] The full genome has been determined and published in GenBank. [GenBank] (<https://www.ncbi.nlm.nih.gov/genbank>)

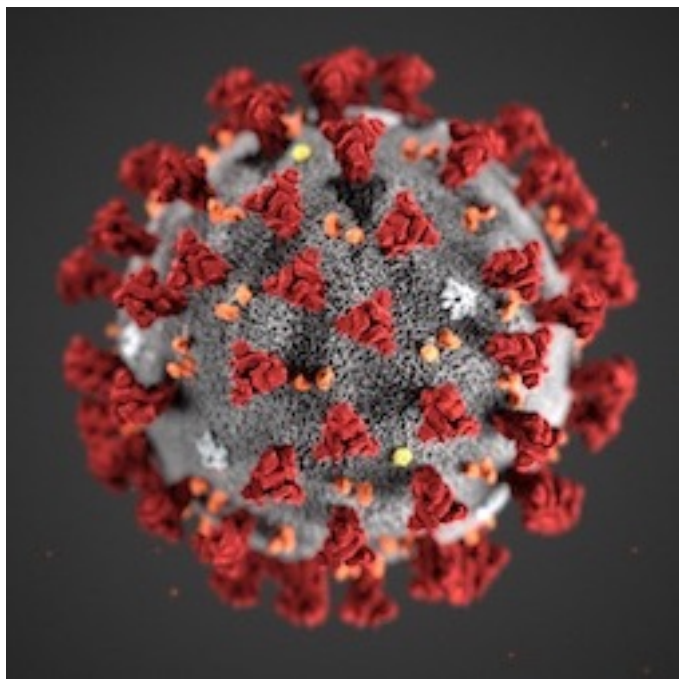


Illustration revealing ultrastructural morphology exhibited by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) when viewed with electron microscopically

Centers for Disease Control and Prevention

SARS-CoV-2 variants

- All viruses, including SARS-CoV-2, change over time. Over 665,000 variants of the virus have been sequenced by the COVID-19 Genomics UK Consortium (COG-UK) as of 20 July 2021. [COG-UK: data] (<https://www.cogconsortium.uk>)
- The World Health Organization has introduced new easy-to-pronounce and nonstigmatizing labels for SARS-CoV-2 variants based on the Greek alphabet. [WHO: tracking SARS-CoV-2 variants] (<https://www.who.int/en/activities/tracking-SARS-CoV-2-variants>)
- SARS-CoV-2 variants of concern (VOC) include the following.
 - Alpha (VOC-20DEC-01; B.1.1.7 lineage): first identified in Kent, South East of England in September 2020, and reported to the World Health Organization in December 2020. The origin is unclear. The variant has been reported in at least 137 countries, and community transmission has been reported in 35 of these countries (as of 19 April 2021). There is evidence that suggests this variant may be more transmissible. Secondary attack rates have been reported to be higher if the index case has this variant. The reported secondary attack rate is 10.2% in household contacts of people with the variant (who have not traveled). However, secondary attack rates for nonvariant forms are known to vary quite widely (see Secondary attack rate below). The variant appears to be associated with an increased risk of hospitalization and intensive care unit admission (suggesting more severe disease), but not mortality, compared with the wild-type virus, although data are conflicting.[36] [37] [38] The variant was not associated with changes in symptoms reported or their duration.[39] There is consistent evidence of cross-neutralizing activity in convalescent sera (i.e., sera from individuals who have been infected with B.1.1.7 shows neutralizing activity against viruses from other lineages, and the converse is also true). There is evidence that there is no increase in reinfection rate,

and that vaccine performance is preserved against this variant.[40] [41] [42] The variant has mutations that have been associated with attenuation in other variants.[43]

- Beta (VOC-20DEC-02; B.1.351 lineage): first detected in Nelson Mandela Bay, South Africa in October 2020. The variant has been reported in at least 97 countries, including the UK (as of 19 April 2021). The variant has similar spike protein mutations to the B.1.1.7 lineage. Sequence analysis reveals that the N501Y mutation reported in the UK and South Africa originated independently. These mutations may affect its transmissibility and antigenic profile.[40]
- Gamma (VOC-21JAN-02; P.1 lineage): a descendant of the B.1.1.28 lineage first detected in Japan in travelers from Brazil. The variant has been reported in at least 55 countries (as of 19 April 2021), including the UK. Based on modeling and laboratory data, it is plausible that there is some degree of immune escape, or increased transmissibility, or both with this variant. However, the magnitude and clinical significance of these effects are yet to be determined.[40]
- Delta (VOC-21APR-02; B.1.617.2): first identified in India in April 2021. It is now the dominant variant in the UK. There are also a small number of cases of the Delta variant with a K417N mutation (AY.1 lineage). Preliminary evidence suggests that this variant is likely to be more transmissible than the B.1.1.7 variant based on available data. The secondary attack rate among household contacts of cases that have not traveled is 10.9% (as of 5 July 2021), and the rate has been decreasing. This is slightly higher compared with the B.1.1.7 variant, which is currently 10.2% among household contacts of cases that have not traveled (see above). An increase in cases has not been associated with a similar proportional increase in hospitalizations or deaths in the UK. This variant has been reported in many countries around the world. The crude case fatality rate is estimated to be 0.2%, with the majority of deaths occurring in people 50 years and older (as of 5 July 2021).[40] Emerging evidence suggests that current vaccines may be effective against the variant after two doses, but with reduced efficacy after one dose. Efficacy is comparable to vaccine efficacy against hospitalization from the Alpha variant, but may be less effective against infection compared with the alpha variant.[44] [45] [46] [47] Data on this variant are still evolving.
- Epsilon (B.1.427 and B.1.429 lineages): first detected in California in the US, these variants have been classified as variants of concern by the Centers for Disease Control and Prevention, but not the World Health Organization or Public Health England. They may have an increased risk of transmission, may cause more severe disease, and may not be as responsive to certain treatments; however, data are limited.[48] [49]
- Further investigations are required to more fully understand the impact of these variants. There are many other variants under investigation.

Origin of virus

- A majority of patients in the initial stages of this outbreak reported a link to the Huanan South China Seafood Market, a live animal or "wet" market, suggesting a zoonotic origin of the virus.[50] [51] [52] An initial assessment of the transmission dynamics in the first 425 confirmed cases found that 55% of cases before 1 January 2020 were linked to the market, whereas only 8.6% of cases after this date were linked to the market. This suggests that person-to-person spread was occurring among close contacts since the middle of December 2019.[52]
- Some studies suggest that SARS-CoV-2 may be a recombinant virus between a bat coronavirus and an origin-unknown coronavirus.[34] [35] [53] [54] Pangolins and minks have been suggested as possible intermediate hosts.[55] [56] [57] [58] However, there is currently no evidence to demonstrate the possible route of transmission from a bat reservoir to human through one or several intermediary animal species.[59] Further research is required to determine the origin of SARS-CoV-2.

- More recent studies suggest that the virus may have emerged earlier than previously thought.[60]

Transmission dynamics

- Respiratory transmission is the dominant mode of transmission, with proximity and ventilation being the key determinants of transmission risk.[61] Available evidence suggests that transmission between people occurs primarily through direct, indirect, or close contact with infected people through infected secretions such as saliva and respiratory secretions, or through their respiratory droplets, which are expelled when an infected person coughs, sneezes, talks, or sings.[62]
- Airborne transmission can occur in healthcare settings during aerosol-generating procedures. There are also some outbreak reports that suggest aerosol transmission is possible in the community under certain conditions; however, these reports relate to enclosed indoor crowded spaces with poor ventilation where the infected person may have been breathing heavily (e.g., restaurants, choir practice, fitness classes). A detailed investigation of these clusters suggests that droplet and fomite transmission could also explain the transmission in these reports.[62] [63] While the air close to, and distant from, patients has been found to frequently be contaminated with SARS-CoV-2 RNA, few of these samples contained viable virus.[64] The risk of transmission is much lower outdoors compared with indoors, with a limited number of studies estimating a transmission rate of <1%.[65] Evidence that nebulizer treatments increase the risk of transmission of coronaviruses similar to SARS-CoV-2 is inconclusive, and there is minimal direct evidence about the risk for transmission of SARS-CoV-2.[66]
- Fomite transmission (from direct contact with fomites) may be possible, but there is currently no conclusive evidence for this mode of transmission. In the few cases where fomite transmission has been presumed, respiratory transmission has not been completely excluded.[61] While the majority of studies report identification of the virus on inanimate surfaces, there is a lack of evidence to demonstrate recovery of viable virus.[67] The virus has been found to be more stable on plastic and stainless steel (up to 72 hours) compared with copper (up to 4 hours) and cardboard (up to 24 hours) under experimental conditions, but this does not reflect real-life conditions.[68]
- Fecal-oral transmission (or respiratory transmission through aerosolized feces) may be possible, but there is only limited circumstantial evidence to support this mode of transmission.[61] The pooled detection rate of fecal SARS-CoV-2 RNA in patients with COVID-19 is approximately 51%, with 64% of samples remaining positive for a mean of 12.5 days (up to 33 days maximum) after respiratory samples became negative.[69]
- Transmission via other body fluids (including sexual transmission or bloodborne transmission) has not been reported.[61] While the virus has been detected in blood, cerebrospinal fluid, pericardial fluid, pleural fluid, urine, semen, saliva, ocular tissue including the cornea, tears, and conjunctival secretions, as well as in the middle ear and mastoid, the presence of virus or viral components does not equate with infectivity.[70] [71] [72] [73] [74] [75] [76] [77] [78] [79] [80] [81] [82] While SARS-CoV-2 is not sexually transmitted, it may have an effect on male fertility, although this is yet to be confirmed.[83]
- Vertical transmission occurs rarely and transplacental transmission has been documented. There is limited evidence on the extent of vertical transmission and its timing.[84] Overall, 6.3% of infants born to mothers with COVID-19 tested positive for SARS-CoV-2 at birth. Transmission was reported in both preterm and full-term infants. There is also evidence for antibodies against SARS-CoV-2 among infants born to mothers with COVID-19 who tested negative for SARS-CoV-2.[85] The rate of infection appears to be no greater when the baby is born vaginally, breastfed, or allowed contact with the mother.[86] Viral fragments have been detected in breast milk; however, this finding is uncommon and, when it occurs, has been associated with mild symptoms in infants. Anti-SARS-CoV-2 antibodies

are more prevalent in breast milk compared with viral fragments.[87] Vertical transmission is unlikely to occur if correct hygiene precautions are taken.[88]

- Nosocomial transmission was reported in 44% of patients in one systematic review; however, this review was limited to case series conducted early in the outbreak in Wuhan before the institution of appropriate infection prevention and control measures.[89] Hospital-acquired infections (defined as patients diagnosed more than 7 days after hospital admission) accounted for approximately 17% of infections in the NHS England as of 26 October 2020, and rates have been as high as 25% in some areas.[90] Studies of healthcare workers exposed to index cases (not in the presence of aerosol-generating procedures) found little to no nosocomial transmission when contact and droplet precautions were used.[62] [91]

Transmission dynamics in relation to symptoms

- Symptomatic transmission
 - Transmission appears to mainly be spread via droplets and close contact with infected symptomatic cases. Transmissibility depends on the amount of viable virus being shed and expelled by a person (viral load is highest just before or around the time of symptom onset and during the first 5-7 days of illness), the type of contact, the setting, and what infection prevention and control measures are in place.[62] [92]
- Presymptomatic transmission
 - Transmission may occur during the incubation period, usually 1 to 3 days before symptom onset.[92]
 - Presymptomatic transmission was reported in 12.6% of cases in China, and 6.4% of cases in Singapore.[93] [94]
 - People without symptoms may be presymptomatic, or they may remain persistently asymptomatic.
- Asymptomatic transmission
 - Transmission from asymptomatic cases (laboratory-confirmed cases who never develop symptoms) has been reported; however, most of the evidence is based on early data from China and has limitations (e.g., small number of cases, cases may have been presymptomatic).[95] [96] [97] [98] [99] [100] [101] The World Health Organization states that asymptomatic cases are not the major driver of the overall epidemic dynamics.[102] Numerous studies have reported no evidence of asymptomatic transmission from carriers of SARS-CoV-2.[103] [104] [105] In a post-lockdown screening study in nearly 10 million residents in Wuhan, there were no positive tests among 1174 close contacts of asymptomatic cases. In addition to this, virus culture was carried out on samples from asymptomatic positive cases and all cultures were negative, indicating that asymptomatic positive cases in the study were not infectious.[106]
 - Estimating the prevalence of asymptomatic cases in the population is difficult. A meta-analysis of over 50,000 people found that 15.6% of confirmed cases were asymptomatic at the time of testing (range 2% to 75%), and nearly half developed symptoms later.[107] The overall estimate of the proportion of people who become infected and remain asymptomatic throughout infection has been estimated to be 17% to 33%.[108] [109] [110] [111]
 - Healthcare workers may play a role in asymptomatic transmission. About 7.6% of healthcare workers who worked in hospital units with infected patients tested positive for SARS-CoV-2 antibodies; however, only 58% of these workers reported prior symptoms.[112] A cross-sectional

study of nearly 2800 healthcare workers found that 5.4% of COVID-19-facing asymptomatic healthcare workers tested positive, compared with 0.6% of non-COVID-19-facing asymptomatic healthcare workers.^[113]

- Children are more likely to be asymptomatic.^[107] The pooled proportion of asymptomatic cases in children was thought to be significant (around 40%).^{[114] [115]} However, recent studies have found that the rate of asymptomatic infection in children was very low (1% compared with 9% in adults in one study, and 0.6% compared with 1.8% in adults in another study), indicating that children appear not to be particular drivers of the pandemic.^{[116] [117]}

Superspreading events

- Superspreading events have been reported. These events are associated with explosive growth early in an outbreak and sustained transmission in later stages.^[118]
- Reported events include church/religious gatherings, family or social gatherings, weddings, choir practices, overnight youth camps or high school retreats, fitness classes, indoor recreational sporting activities, business conferences, and working in call centers.^{[61] [119] [120] [121] [122]} Widespread transmission has also been reported in long-term care facilities, homeless shelters, prisons, immigration detention centers, and meat and poultry processing facilities, as well as on board cruise ships.^{[123] [124] [125] [126] [127] [128] [129] [130] [131]}
- Limited transmission has been reported in childcare, school, and university settings, and infected cases may transmit the infection to their household members.^{[132] [133] [134]} There is limited high-quality evidence to quantify the extent of transmission in schools, or to compare it with community transmission. However, emerging evidence suggests a lower overall infection attack rate in students (0.15%) compared with school staff (0.7%).^[135]
- Some individuals are supershedders of virus, but the reasons underlying superspreader events are often more complex than just excess virus shedding and can include a variety of behavioral, host, and environmental factors.^[136]

Viral transmission factors

- Incubation period
 - The incubation period is estimated to be between 1 and 14 days, with a median of 5 to 7 days.^{[2] [137]} Viable virus is relatively short lived; infectiousness peaks around 1 day before symptom onset and declines within 7 days.^[61]
 - The pooled mean incubation period is 9.6 days in children.^[17]
- Reproduction number (R_0)
 - Reports suggest that the reproduction number, the number of people who acquire the infection from an infected person, is estimated to be 2.2 to 3.3. However, there is very high heterogeneity across studies and the number varies between countries.^{[52] [138] [139] [140] [141]} The Centers for Disease Control and Prevention gives a current best estimate of 2.5 (as of 19 March 2021).^[142]
 - The R_0 decreases when public health measures (e.g., social distancing) are put in place.^[143]
- Serial interval

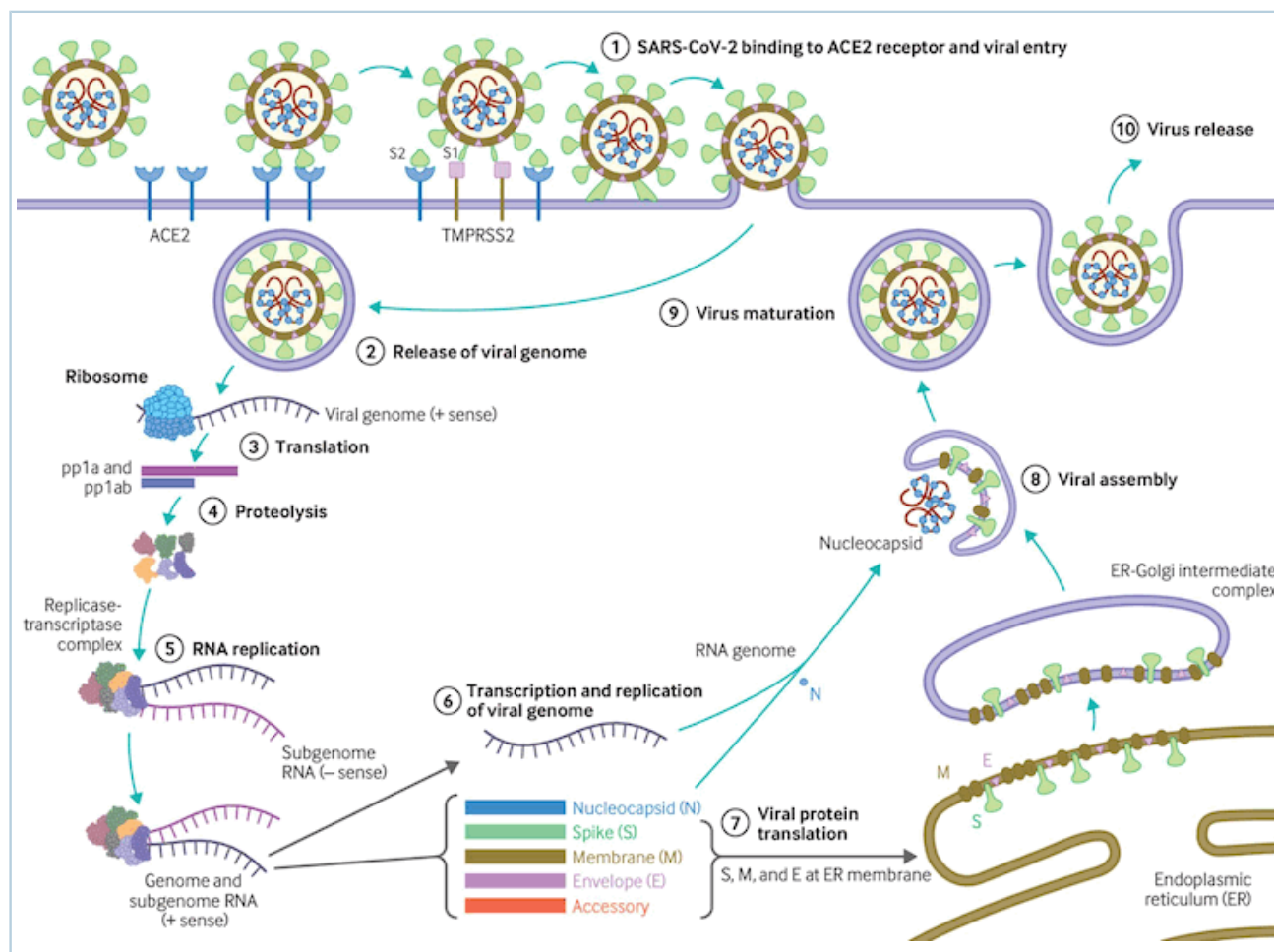
- The time between the start of symptoms in the primary patient and the onset of symptoms in the patient being infected in a chain of transmission has been estimated to be approximately 5.45 days (range 4.2 to 6.7 days).[\[144\]](#)
- Secondary attack rate
 - The secondary attack rate is the proportion of people exposed to an index (or primary) case that go on to develop the disease as a result of the exposure.
 - The pooled secondary attack rate among all close contacts of an index case has been estimated to be 7%.[\[145\]](#)
 - The secondary attack rate differs between contact settings. More familiar prolonged contact increases the potential for transmission. Pooled estimates of the secondary attack rate range from 1.2% to 5.9% in social settings (depending on level of contact and whether contact is with strangers or family and friends), 1.9% in workplaces (based on limited data), 3.6% in healthcare facilities, and 21.1% for household settings (increases with exposure >5 days).[\[146\]](#)
 - Another systematic review and meta-analysis of household transmission estimates the pooled household secondary attack rate to be slightly lower at 16.6%. The rate is higher for symptomatic index cases (18%) compared with asymptomatic cases (0.7%), and adults have a higher susceptibility to infection compared with children. Spouses of the index case are more likely to be infected compared with other household members.[\[147\]](#)
 - The secondary attack rate increases with the severity of the index case (i.e., 0.3% for asymptomatic cases to 6.2% for severe/critical cases) according to a study of 3410 close contacts of 391 index cases.[\[102\]](#)
 - The secondary attack rate for close contacts of presymptomatic people has been estimated to be approximately 7%, compared with 1% in asymptomatic people and 6% in symptomatic people.[\[148\]](#)
 - Children ages <5 years had lower secondary attack rates compared with older children, and the risk of infection was higher if the household index case was the mother.[\[149\]](#) The secondary attack rate was 1.2% in children in a childcare setting or school.[\[150\]](#)
 - Secondary attack rates for SARS-CoV-2 variants may differ (see Emerging SARS-CoV-2 variants above).
- Viral load
 - Viral load is highest in the upper respiratory tract (nasopharynx and oropharynx) early in the course of infection (usually peaks in the first week of illness), and then increases in the lower respiratory tract (sputum). Viral load decreases after symptom onset. Patients with severe disease have higher viral loads compared with those with mild disease. Viral load in the upper respiratory tract is comparable in asymptomatic and symptomatic patients; however, most studies demonstrate faster viral clearance among asymptomatic people compared with symptomatic people.[\[151\]](#)
 - Viral load appears to be a leading driver of virus transmission. In one cohort study, the secondary attack rate was 17% among 753 contacts of index cases, with a variation from 12% when the index case had a viral load lower than 1×10^6 copies/mL to 24% when the index case had a viral load of 1×10^{10} copies/mL or higher (in nasopharyngeal swabs). Higher viral loads in swabs of asymptomatic contacts were associated with a higher risk of developing symptomatic disease, and these contacts had shorter incubation periods than those with a lower viral load.[\[152\]](#)

- Viral shedding
 - The mean duration of shedding was 17 days in the upper respiratory tract, 14.6 days in the lower respiratory tract, 17.2 days in stool, and 16.6 days in serum samples. The maximum duration of shedding was 83 days in the upper respiratory tract, 59 days in the lower respiratory tract, 126 days in stool, and 60 days in serum samples. However, no live virus was detected beyond day 9 of symptoms, despite persistently high viral loads. Duration of viral shedding was longer in symptomatic patients compared with asymptomatic patients, and in patients with severe illness compared with those with nonsevere illness.[\[151\]](#)
 - The period of infectiousness is far shorter than the duration of detectable viral shedding. No viable virus has been isolated in patients with mild or moderate disease after 10 days of symptoms, or after 20 days in those with severe or critical disease, despite ongoing viral shedding. Data about the dynamics of viral shedding in people with persistent asymptomatic infection are inconsistent.[\[61\]](#) There is no convincing evidence that duration of viral shedding correlates with duration of infectivity.[\[153\]](#)
 - Factors associated with prolonged viral shedding include male sex, older age, comorbid hypertension, delayed admission to hospital after symptom onset or severe illness on admission, and use of invasive mechanical ventilation or corticosteroids.[\[154\]](#) Immunocompromised patients may shed for at least 2 months.[\[155\]](#)

Pathophysiology

The pathophysiology resembles that of other coronavirus infections. However, emerging evidence indicates that COVID-19 has distinctive pathophysiological features that set it apart from respiratory failure of other origins.[\[156\]](#)

SARS-CoV-2 attaches to the angiotensin-converting enzyme-2 (ACE2) receptor on target host cells, followed by internalization and replication of the virus. ACE2 receptors are highly expressed in the upper and lower respiratory tract cells, but are also expressed in myocardial cells, renal epithelial cells, enterocytes, and endothelial cells in multiple organs, which may explain the extrapulmonary manifestations associated with the disease.[\[157\]](#) The virus uses host transmembrane protease serine 2 (TMPRSS2) for viral spike protein priming and fusion of viral and host cell membranes.[\[158\]](#) The SARS-CoV-2 spike protein plays a key role in the recognition of the ACE2 receptor and cell membrane fusion process. A unique structural feature of the spike glycoprotein receptor-binding domain confers potentially higher binding affinity for ACE2 on host cells compared with SARS-CoV-1.[\[159\]](#) This furin-like cleavage site does not appear to exist in other coronaviruses.[\[160\]](#) The binding energy between the spike protein and ACE2 was highest for humans out of all species tested in one study, suggesting that the spike protein is uniquely evolved to bind to and infect human cells expressing ACE2.[\[161\]](#) Emerging evidence suggests that the spike protein alone may damage endothelial cells by downregulating ACE2 and consequently inhibiting mitochondrial function. Further research is required on whether the spike protein can by itself trigger cell signaling that could lead to various biologic processes.[\[162\]](#) [\[163\]](#) SARS-CoV-2 variants may be more transmissible, at least in part, due to enhanced spike protein binding affinity for the ACE2 receptor.[\[164\]](#)



Virus replication cycle

BMJ. 2020;371:m3862

In addition to direct cytopathic viral injury, severe disease is frequently complicated by an infection-induced microangiopathy or hypercoagulable state that causes capillary, venous, and/or arterial thrombosis, which may lead to end-organ damage due to distant thrombotic or embolic disease. The predominant pathologic findings in fatal cases were diffuse alveolar damage, coagulopathy, and hemodynamic compromise. Involvement of nonpulmonary organs was limited to mild parenchymal inflammation (e.g., myocarditis, hepatitis, encephalitis). Direct viral cytopathic injury of extrapulmonary organs in general was not regarded as the cause of organ failure.^[157] SARS-CoV-2-induced endotheliitis may play a role in both the respiratory and nonrespiratory manifestations.^[165]

Classification

World Health Organization: COVID-19 disease severity^[2]

Mild illness

- Symptomatic patients meeting the case definition for COVID-19 without evidence of hypoxia or pneumonia.
- Common symptoms include fever, cough, fatigue, anorexia, dyspnea, and myalgia. Other nonspecific symptoms include sore throat, nasal congestion, headache, diarrhea, nausea/vomiting, and loss of

smell/taste. Additional neurologic manifestations reported include dizziness, agitation, weakness, seizures, or findings suggestive of stroke. Children may not report fever or cough as frequently as adults.

- Older people and immunosuppressed people may present with atypical symptoms (e.g., fatigue, reduced alertness, reduced mobility, diarrhea, loss of appetite, delirium, absence of fever).
- Symptoms due to physiologic adaptations of pregnancy or adverse pregnancy events (e.g., dyspnea, fever, gastrointestinal symptoms, fatigue) or other diseases (e.g., malaria) may overlap with COVID-19 symptoms.

Moderate disease

- Adolescent or adult: clinical signs of pneumonia (i.e., fever, cough, dyspnea, fast breathing) but no signs of severe pneumonia, including blood oxygen saturation levels (SpO_2) $\geq 90\%$ on room air.
- Children: clinical signs of nonsevere pneumonia (i.e., cough or difficulty breathing plus fast breathing and/or chest indrawing) and no signs of severe pneumonia. Fast breathing is defined as:
 - <2 months of age: ≥ 60 breaths/minute
 - 2-11 months of age: ≥ 50 breaths/minute
 - 1-5 years of age: ≥ 40 breaths/minute.
- While the diagnosis can be made on clinical grounds, chest imaging may assist in diagnosis and identify or exclude pulmonary complications.

Severe disease

- Adolescent or adult: clinical signs of pneumonia (i.e., fever, cough, dyspnea, fast breathing) plus one of the following:
 - Respiratory rate > 30 breaths/minute
 - Severe respiratory distress
 - $\text{SpO}_2 < 90\%$ on room air.
- Children: clinical signs of pneumonia (i.e., cough or difficulty in breathing) plus at least one of the following:
 - Central cyanosis or $\text{SpO}_2 < 90\%$
 - Severe respiratory distress (e.g., fast breathing, grunting, very severe chest indrawing)
 - General danger signs: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions
 - Fast breathing (<2 months: ≥ 60 breaths per minute; 2-11 months: ≥ 50 breaths per minute; 1-5 years: ≥ 40 breaths per minute).
- While the diagnosis can be made on clinical grounds, chest imaging may assist in diagnosis and identify or exclude pulmonary complications.

Critical disease

- Presence of acute respiratory distress syndrome (ARDS), sepsis, septic shock, acute thrombosis, or multisystem inflammatory syndrome in children.

National Institutes of Health: clinical classification of COVID-19^[3]

Asymptomatic or presymptomatic infection

- People who test positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using a virologic test but have no symptoms consistent with COVID-19.

Mild illness

- People who have any of various signs and symptoms (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) without shortness of breath, dyspnea, or abnormal chest imaging.

Moderate illness

- People who have evidence of lower respiratory disease by clinical assessment or imaging and an oxygen saturation (SpO_2) $\geq 94\%$ on room air at sea level.

Severe illness

- People who have respiratory frequency >30 breaths per minute, $\text{SpO}_2 < 94\%$ on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen ($\text{PaO}_2/\text{FiO}_2$) < 300 mmHg, or lung infiltrates $> 50\%$.

Critical illness

- People who have respiratory failure, septic shock, and/or multiple organ dysfunction.

Persistent symptoms or organ dysfunction after acute COVID-19

- People who experience persistent symptoms and/or organ dysfunction after acute disease. Also known as post-acute COVID-19 syndrome or long COVID. See the Complications section for more information.

Case history

Case history #1

A 61-year-old man presents to the hospital with fever, dry cough, and difficulty breathing. He also reports feeling very tired and unwell. He has a history of hypertension, which is controlled with enalapril. On exam, his pulse is 120 bpm, his temperature is 101.6°F (38.7°C), and his oxygen saturation is 88%. He appears acutely ill. He is admitted to hospital in an isolation room and is started on oxygen, intravenous fluids, and venous thromboembolism prophylaxis. Blood and sputum cultures are ordered. Chest x-ray shows bilateral lung infiltrates, and computed tomography of the chest reveals multiple bilateral lobular and subsegmental areas of ground-glass opacity. A nasopharyngeal swab is sent for real-time reverse transcriptase polymerase chain reaction testing, and the result comes back positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) a few hours later. The patient is started on dexamethasone.

Case history #2

A 26-year-old woman presents at her local COVID-19 testing clinic with symptoms of a sore throat and loss of taste. She denies having a fever, and has not knowingly been in contact with a confirmed case of COVID-19. After being tested, she is advised to go home, self-isolate until her test results are sent to her via text message, and call her doctor if her symptoms get worse. She receives a text message later that day confirming that her test is positive for SARS-CoV-2, and that she must self-isolate according to her local public health recommendations.

Other presentations

See the Diagnosis section for more information on other presentations.

Approach

COVID-19 is a notifiable disease. Report all suspected or confirmed cases to your local health authorities.

Early recognition and rapid diagnosis are essential to prevent transmission and provide supportive care in a timely manner. Have a high index of clinical suspicion for COVID-19 in all patients who present with fever and/or acute respiratory illness; however, be aware that some patients may not present with signs or symptoms of a febrile respiratory illness.

COVID-19 care pathways should be established at local, regional, and national levels for people with suspected or confirmed COVID-19. Screen patients at the first point of contact within the health system based on case definitions and an assessment of symptoms, and enter suspected or confirmed cases into the pathway. Suspected cases should remain in the pathway until proven negative. Immediately isolate all suspected and confirmed cases and implement local infection prevention and control procedures. Triage patients with a standardized triage tool and evaluate the patient to assess the severity of disease. Use clinical judgment, including consideration of the patient's values and preferences and local and national policy if available, to guide management decisions including admission to hospital and to the intensive care unit, rather than currently available prediction models for prognosis.^[2]

Best Practice has published a separate topic on the management of coexisting conditions in the context of COVID-19. [\[BMJ Best Practice: Management of coexisting conditions in the context of COVID-19\] \(https://bestpractice.bmj.com/topics/en-us/3000190#important-update\)](https://bestpractice.bmj.com/topics/en-us/3000190#important-update)

Key recommendations

- Isolate all suspected or confirmed cases immediately. Triage patients with a standardized triage tool and evaluate the severity of disease. Follow local infection prevention and control guidelines.^[2]
- Have a high index of clinical suspicion in all patients who present with fever and/or acute respiratory illness. People with a history of residence/work/travel in a location with a high risk of transmission or community transmission and contacts of probable and confirmed cases are at higher risk of infection.^[166]
- Suspect the diagnosis in patients with a new continuous cough, fever, or altered sense of taste or smell.^[534] Patients may also present with symptoms including dyspnea, fatigue, myalgia/arthralgia, sore throat, headache, nasal congestion or rhinorrhea, sputum production, chest tightness, or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).^[535]
- Order a real-time reverse transcription polymerase chain reaction (RT-PCR) to confirm the diagnosis. Upper and lower respiratory specimens are preferred. Serologic testing may be useful in some settings.^[536] Results should be interpreted in the context of the pretest probability of disease.
- Be on high alert for children and adolescents with acute gastrointestinal symptoms and signs of cardiac inflammation. Evidence so far suggests a milder or asymptomatic course of disease in children.^[537] However, a rare multisystem inflammatory condition with some features similar to those of Kawasaki disease and toxic shock syndrome has been temporally associated with COVID-19 in children and adolescents.^[538]
- Order the following laboratory investigations in hospitalized patients: complete blood count, comprehensive metabolic panel, arterial blood gas, blood glucose level, coagulation screen, inflammatory markers, cardiac biomarkers, serum creatine kinase, and blood and sputum cultures for other pathogens. Pulse oximetry may reveal low oxygen saturation.

- Prioritize a chest x-ray in patients who are seriously ill with suspected pneumonia. Consider a computed tomography (CT) scan of the chest if chest x-ray is uncertain or normal.^[539] Consult local guidelines.
- For full details and guidance see information below.

History

Take a detailed history to ascertain the level of risk for COVID-19 and assess the possibility of other causes, including a travel history and an assessment of risk factors.

Suspect the diagnosis in:^[166]

- People residing or working in an area with a high risk of transmission (e.g., closed residential settings, humanitarian setting), people residing in or traveling to an area with community transmission, and people working in a health setting (including within health facilities and households) at any time within the 14 days prior to symptom onset
- People who have had contact with a probable or confirmed case. A contact is a person who has experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case:
 - Face-to-face contact with a probable or confirmed case within 3 feet (1 meter) and for at least 15 minutes
 - Direct physical contact with a probable or confirmed case
 - Direct care for a patient with probable or confirmed COVID-19 without using recommended personal protective equipment
 - Other situations as indicated by local risk assessments.

The Centers for Disease Control and Prevention defines a close contact as someone who has been within 6 feet (2 meters) of an infected person for at least 15 minutes over a 24-hour period, beginning 2 days before symptom onset (or 2 days before testing in asymptomatic patients).^[167]

Ask anyone seeking routine or emergency care, regardless of whether they have symptoms, about recent travel to countries where there is transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern (consult local guidance for current list of countries), or whether they are a contact of a returning traveler from these countries.^[168]

Clinical presentation in adults

Approximately 15% of patients present with the symptom triad of fever, cough, and dyspnea, and 90% present with more than one symptom.^[51] Some patients may be minimally symptomatic or asymptomatic, while others may present with severe pneumonia or complications such as acute respiratory syndrome, septic shock, acute myocardial infarction, venous thromboembolism, or multi-organ failure. According to a UK study, approximately 25% of people who had evidence of past infection were asymptomatic, and 40% did not have one of the three classic symptoms (i.e., fever, persistent dry cough, altered sense of taste/smell).^[540]

The most common symptoms are:

- Fever
- Cough

- Dyspnea
- Altered sense of taste/smell.

Less common symptoms include:

- Myalgia or arthralgia
- Fatigue
- Sputum production
- Chest tightness
- Gastrointestinal symptoms
- Sore throat
- Headache
- Dizziness
- Neurologic symptoms
- Ocular symptoms
- Audio-vestibular symptoms
- Cutaneous symptoms
- Rhinorrhea/nasal congestion
- Chest pain
- Hemoptysis.

Signs and symptoms of febrile respiratory illness may not possess the necessary sensitivity for early diagnostic suspicion.[541] A Cochrane review found that at least half of patients had a cough, sore throat, fever, myalgia/arthralgia, fatigue, or headache. Anosmia and/or ageusia was also common. The presence of fever, myalgia/arthralgia, fatigue, and headache substantially increased the likelihood of COVID-19 when present. Cough and sore throat were common in people without COVID-19, so these symptoms alone were less helpful for diagnosis. No single symptom or sign included in the review could accurately diagnose COVID-19 and the authors concluded that neither the absence or presence of signs or symptoms are accurate enough to rule in or rule out disease. However, the presence of anosmia and/or ageusia may be useful as a red flag for diagnosis. The presence of fever or cough may also be useful to identify people for further testing.[535] Nonrespiratory symptoms may appear before the onset of fever and lower respiratory tract symptoms.[542] Lower urinary tract symptoms have also been reported rarely.

The clinical presentation has varied slightly across geographic locations. Initial impressions from the US note that the clinical presentation may be broader than that observed in China and Italy, with chest pain, headaches, altered mental status, and gastrointestinal symptoms all observed on initial presentation. Severe hepatic and renal dysfunction that spares the lungs has also been observed.[543] Data from the first hospitalized patients in New York found that while the most common presenting symptoms were fever, cough, dyspnea, and myalgia, gastrointestinal symptoms appeared to be more common than in China.[544]

Severity

- 80% of adults present with mild to moderate illness
- 14% of adults present with severe illness
- 5% of adults present with critical illness
- 1% of adults present with asymptomatic illness.[4]

The most prevalent symptoms in patients with mild to moderate illness, according to one European study, are headache, loss of smell, nasal congestion, cough, asthenia, myalgia, rhinorrhea, gustatory

dysfunction, and sore throat. Fever was reported less commonly. The mean duration of symptoms was 11.5 days. The presentation varied according to age, with younger patients generally having ear, nose, and throat complaints, and older patients generally having fever, fatigue, and loss of appetite.[545] More common symptoms in patients with severe disease include fever, dyspnea, and anorexia.[139]

Symptoms of COVID-19 may differ in patients who have been vaccinated. Data from the UK COVID Symptom Study report that the most common symptoms of COVID-19 after full vaccination are headache, runny nose, sneezing, and sore throat. The previous traditional symptoms such as anosmia, shortness of breath, fever, and cough rank further down the list and are no longer top indicators of having COVID-19 in vaccinated people, according to this data. In patients who are unvaccinated, headache, sore throat, runny nose, fever, and persistent cough are the most common symptoms, which differs from when COVID-19 appeared over a year ago.[546]

Pregnant women

- The clinical characteristics in pregnant women are similar to those reported for nonpregnant adults.[547] The most common symptoms in pregnant women are fever and cough. However, pregnant women are less likely to report fever, dyspnea, and myalgia compared with nonpregnant women of reproductive age. Pregnant and recently pregnant women were more likely to be asymptomatic than nonpregnant women of reproductive age.[23] [24]
- It is important to note that symptoms such as fever, dyspnea, gastrointestinal symptoms, and fatigue may overlap with symptoms due to physiologic adaptations of pregnancy or adverse pregnancy events.[2]

Atypical presentations

- Atypical presentations may occur, especially in older patients and patients who are immunocompromised (e.g., falls, delirium/confusion, functional decline, reduced mobility, syncope, persistent hiccups, absence of fever). Older patients and those with comorbidities may present with mild symptoms, but have a high risk of deterioration.[2]
- There have been case reports of parotitis (possibly related to intraparotid lymphadenitis), oral vesiculobullous lesions, retinal lesions, and androgenetic alopecia in patients with COVID-19; however, it is unknown whether these findings are associated with SARS-CoV-2 infection as yet.[548] [549] [550] [551]

Coinfections and superinfections

- The pooled prevalence of coinfection in SARS-CoV-2-positive patients was 19%, and the pooled prevalence of superinfection was 24%. The highest prevalence of superinfection was in intensive care unit patients. Pooled prevalence stratified by pathogen type was: viral coinfections 10%; viral superinfections 4%; bacterial coinfections 8%; bacterial superinfections 20%; fungal coinfections 4%; and fungal superinfections 8%. The most frequently identified bacteria were *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, and *Staphylococcus aureus*. The most frequent bacteria identified in superinfected patients was *Acinetobacter* species, which is common in ventilated patients. The most frequently identified viruses were influenza type A, influenza type B, and respiratory syncytial virus. The most frequently identified fungi was *Aspergillus*. Patients with a coinfection or superinfection had higher risk of mortality compared with those who only had SARS-CoV-2 infection. Patients with superinfections had a higher prevalence of mechanical ventilation compared with those with coinfections.[552]

- Be alert for the development of mucormycosis.[\[553\]](#) Diagnose and manage urgently - see the Complications section for more information.

Clinical presentation in children

Signs and symptoms may be similar to other common viral respiratory infections and other childhood illnesses, so a high index of suspicion for COVID-19 is required in children.

Evidence suggests a milder, or asymptomatic, disease course in the majority of children, with low rates of severe disease and mortality. Infants under 1 year of age and adolescents 10 to 14 years of age have a higher risk for developing severe disease. Risk factors for severe disease include the presence of comorbidities and higher viral load. The clinical presentation in children is heterogeneous and includes a wide spectrum of clinical features. The most common presenting symptoms in children are fever and cough. Gastrointestinal symptoms (nausea, vomiting, diarrhea) are also common in children. Other less common symptoms include dyspnea, nasal congestion, rhinorrhea, rash, conjunctivitis, fatigue, abdominal pain, and neurologic symptoms. A higher prevalence of gastrointestinal symptoms has been reported in children >5 years of age compared with children ≤5 years of age.[\[537\]](#) Fever, cough, appetite loss, and dyspnea are less common in children compared with adults.[\[554\]](#) The presence of diarrhea has been associated with a severe clinical course in children.[\[555\]](#)

The most common symptoms in neonates include fever, inability to feed, lethargy, irritability, feeding difficulties, dyspnea, silent hypoxia, and neurologic symptoms. Cases of late-onset neonatal sepsis and encephalitis have been reported rarely.[\[537\]](#) [\[556\]](#) [\[557\]](#) [\[558\]](#)

Be alert for signs and symptoms of pediatric inflammatory multisystem syndrome (PIMS), also known as multisystem inflammatory syndrome in children (MIS-C). Consider PIMS/MIS-C in children presenting with fever and abdominal symptoms, particularly if they develop conjunctivitis or a rash. Refer to a pediatric emergency department for evaluation.[\[559\]](#) See the Complications section for more information.

Coinfections may be more common in children.[\[560\]](#) Coinfection was documented in 6% of children in US and Italian studies, with the most common pathogens being respiratory syncytial virus, rhinoviruses, Epstein-Barr virus, enteroviruses, influenza A, non-SARS coronaviruses, and *Streptococcus pneumoniae*.[\[12\]](#) [\[561\]](#)

Physical exam

Perform a physical exam. Avoid use of a stethoscope if possible due to risk of viral contamination. Patients may be febrile (with or without chills/rigors) and have obvious cough and/or difficulty breathing. Auscultation of the chest may reveal inspiratory crackles, rales, and/or bronchial breathing in patients with pneumonia or respiratory distress. Patients with respiratory distress may have tachycardia, tachypnea, or cyanosis accompanying hypoxia. Bradycardia has been noted in a small cohort of patients with mild to moderate disease.[\[562\]](#)

Pulse oximetry

Pulse oximetry may reveal low oxygen saturation (SpO₂ <90%). Clinicians should be aware that patients with COVID-19 can develop "silent hypoxia": their oxygen saturations can drop to low levels and precipitate acute respiratory failure without the presence of obvious symptoms of respiratory distress.[\[563\]](#)

The UK National Institute for Health and Care Excellence recommends using oxygen saturation levels below 94% for adults (or below 88% for adults with known type 2 respiratory failure) and below 91% for children in room air at rest to identify people who are seriously ill.[564]

Pulse oximeters may exhibit suboptimal accuracy in certain populations. Limited data from studies with small numbers of participants suggest that skin pigmentation can affect pulse oximeter accuracy. In one study, occult hypoxemia (defined in the study as arterial oxygen saturation <88% by arterial blood gas despite oxygen saturation of 92% to 96% on pulse oximetry) was not detected by pulse oximetry nearly three times more frequently in Black patients compared with White patients.[565] The US Food and Drug Administration (FDA) has warned that multiple factors can affect the accuracy of a pulse oximeter reading (e.g., poor circulation, skin pigmentation, skin thickness, skin temperature, current tobacco use, use of fingernail polish). The FDA recommends considering accuracy limitations when using a pulse oximeter to assist in diagnosis and treatment decisions, and to use trends in readings over time rather than absolute cut-offs if possible.[566]

Only a small proportion of patients have other organ dysfunction, meaning that after the initial phase of acute deterioration, traditional methods of recognizing further deterioration (e.g., National Early Warning Score 2 [NEWS2] scores) may not help predict those patients who go on to develop respiratory failure.[563]

While NEWS2 is still recommended for use in patients with COVID-19, the UK Royal College of Physicians now advises that any increase in oxygen requirements in these patients should trigger an escalation call to a competent clinical decision maker, and prompt an initial increase in observations to at least hourly until a clinical review happens.[567]

Pulse oximeters can be used at home to detect hypoxia. Home pulse oximetry requires clinical support (e.g., regular phone contact from a health professional in a virtual ward setting).

[BMJ Practice Pointer: remote management of covid-19 using home pulse oximetry and virtual ward support] (<https://www.bmj.com/content/372/bmj.n677>)

Initial laboratory investigations

Order the following laboratory investigations in all patients with severe illness:

- ABG
- CBC
- Comprehensive metabolic panel
- Blood glucose level
- Coagulation screen
- Inflammatory markers (e.g., serum C-reactive protein, erythrocyte sedimentation rate, interleukin-6, lactate dehydrogenase, procalcitonin, amyloid A, and ferritin)
- Cardiac biomarkers
- Serum creatine kinase and myoglobin.

The most common laboratory abnormalities are lymphopenia, leukocytosis, leukopenia, thrombocytopenia, hypoalbuminemia, elevated cardiac biomarkers, elevated inflammatory markers, elevated D-dimer, and abnormal liver and renal function.[544] [568] [569] [570] Laboratory abnormalities – in particular, lymphopenia, leukocyte abnormalities, and other markers of systemic inflammation – are less common in children.[571] [572] Most patients (62%) with asymptomatic disease present with normal

laboratory parameters. Of those with laboratory abnormalities, leukopenia, lymphopenia, elevated lactate dehydrogenase, and elevated C-reactive protein were the most common findings.[573]

Collect blood and sputum specimens for culture in patients with severe or critical disease to rule out other causes of lower respiratory tract infection and sepsis, especially patients with an atypical epidemiologic history. Specimens should be collected prior to starting empiric antimicrobials if possible.[2]

Ongoing investigations

- Regularly monitor the following in hospitalized patients to facilitate early recognition of deterioration and monitor for complications:[2] [574]
 - Vital signs (temperature, respiratory rate, heart rate, blood pressure, oxygen saturation)
 - Hematologic and biochemistry parameters
 - Coagulation parameters (D-dimer, fibrinogen, platelet count, prothrombin time)
 - ECG
 - Chest imaging
 - Signs and symptoms of venous or arterial thromboembolism.
- Patients may develop bacterial or fungal coinfections; therefore, it is important to ensure appropriate imaging is ordered and microbiologic specimens are taken when this is suspected.

Molecular testing

Testing strategies vary widely between countries.[575]

Molecular testing is required to confirm the diagnosis. Molecular testing is an aid to diagnosis only. The World Health Organization (WHO) recommends that healthcare providers consider a positive or negative result in combination with specimen type, clinical observations, patient history, and epidemiologic information. Where a test result does not correspond with the clinical presentation, a new specimen should be taken and retested using the same or a different molecular test (see Limitations of molecular testing below).[576]

Order a nucleic acid amplification test, such as real-time reverse-transcription polymerase chain reaction (RT-PCR), for SARS-CoV-2 in patients with suspected infection whenever possible (see the Criteria section).[536] Tests should be performed according to guidance issued by local health authorities and adhere to appropriate biosafety practices.

Commonly used assays are expected to be able to detect SARS-CoV-2 variants.[168] However, some tests may be impacted by variants.[577]

Who to test

- Base decisions about who to test on clinical and epidemiologic factors.[536]
- The World Health Organization recommends testing all people who meet the suspected case definition of COVID-19, regardless of vaccination status or disease history. When resources are constrained, people who are at risk of developing severe disease, healthcare workers, inpatients, and the first symptomatic individuals in the setting of a suspected outbreak should be prioritized. Testing of asymptomatic individuals is currently recommended only for specific groups including contacts of confirmed or probable cases and frequently exposed groups such as healthcare workers and long-term care facility workers.[578]

- In the UK, testing is recommended in:[\[579\]](#)
 - People with symptoms of new continuous cough, high temperature, or altered sense of smell/taste
 - People with acute respiratory infection, influenza-like illness, clinical or radiologic evidence of pneumonia, or acute worsening of underlying respiratory illness, or fever without another cause (whether presenting in primary or secondary care).
- In the US, testing is recommended in:[\[580\]](#)
 - Anyone with signs or symptoms consistent with COVID-19
 - Asymptomatic unvaccinated people identified through contact tracing efforts
 - Asymptomatic unvaccinated people with recent known or suspected exposure to SARS-CoV-2, including those who have been in close contact (less than 6 feet [2 meters] for a total of 15 minutes or more over a 24-hour period) with a person with documented infection
 - Asymptomatic unvaccinated people without recent known or suspected exposure to SARS-CoV-2 for early identification, isolation, and disease prevention (only when screening testing is recommended by public health officials).
- The American Academy of Pediatrics recommends testing children with symptoms consistent with COVID-19, children in close contact with an individual with probable or confirmed infection, and children who require screening based on recommendations from public health authorities or other situations (e.g., prior to a medical procedure such as elective surgery or as a school or workplace requirement). The decision to test does not differ by the age of the child. Testing is not recommended for other illnesses that lack shared symptoms (e.g., urinary tract infection, cellulitis), or for children exposed to close contacts of infected individuals unless those contacts are symptomatic or other criteria are met.[\[581\]](#)
- Consult local health authorities for guidance as testing priorities depend on local recommendations and available resources.

Specimens

- The optimal specimen for testing depends on the clinical presentation and the time since symptom onset. The WHO recommends the following.[\[536\]](#)
 - Upper respiratory specimens: recommended for early-stage infections, especially asymptomatic or mild cases. Nasopharyngeal swabs yield a more reliable result than oropharyngeal swabs; combined nasopharyngeal and oropharyngeal swabs further improve reliability.
 - Lower respiratory specimens: recommended for later-stage infections, or patients in whom there is a strong suspicion for infection and their upper respiratory tract specimen test was negative. Suitable specimens are sputum and/or endotracheal aspirate or bronchoalveolar lavage in patients with more severe respiratory disease. However, consider the high risk of aerosol transmission when collecting lower respiratory specimens – an induced sputum specimen is not recommended as it may increase the risk of aerosol transmission.
 - Other respiratory specimens: studies on combined oropharyngeal and nares/nasal swabs, mid-turbinate or lower nasal or nares swabs, or tongue swabs have been conducted; however, further assessment and validation is required. Oral fluid collection may be suitable in some circumstances (e.g., young children, older patients with dementia). A systematic review and meta-analysis found that pooled nasal and throat swabs offered the best

diagnostic performance of alternative sampling approaches compared with nasopharyngeal swabs for diagnosis in an ambulatory care setting. The sensitivity was 97%, the specificity was 99%, the positive predictive value was 97%, and the negative predictive value was 99%. Throat swabs gave a much lower sensitivity and positive predictive value. Self-collection was not associated with any impairment of diagnostic accuracy.[\[582\]](#)

- Saliva: meta-analyses of paired saliva samples and nasopharyngeal swabs found no statistically significant difference in sensitivity or specificity between these specimens for SARS-CoV-2 detection, especially in the ambulatory setting. Sensitivity was not significantly different among asymptomatic people and outpatients. Methods of saliva collection may affect sensitivity. Meta-analyses demonstrate that saliva is as valid as nasopharyngeal sampling for the detection of SARS-CoV-2 infections in symptomatic and asymptomatic patients. Saliva sampling is simple, fast, noninvasive, inexpensive, and painless.[\[583\]](#) [\[584\]](#) [\[585\]](#) [\[586\]](#) [\[587\]](#) [\[588\]](#) The WHO does not currently recommend the use of saliva as the sole specimen type for routine clinical diagnostics.
- Fecal specimens: consider when upper or lower respiratory specimens are negative and the clinical suspicion for infection remains (may be used from the second week after symptom onset).
- Recommended specimen types may differ between countries. For example, in the US, the Centers for Disease Control and Prevention (CDC) recommends the following upper respiratory specimens: nasopharyngeal or oropharyngeal swab; nasal mid-turbinate swab; anterior nares swab; or nasopharyngeal/nasal wash/aspirate. Recommended lower respiratory tract specimens include: sputum, bronchoalveolar lavage, tracheal aspirate, pleural fluid, and lung biopsy. Nasal mid-turbinate swab is an acceptable specimen for home or onsite self-collection. The CDC does not recommend using oral specimens (e.g., saliva) for confirmatory testing.[\[589\]](#) [\[590\]](#) In contrast, the Infectious Diseases Society of America recommends saliva as a suitable option for molecular testing in symptomatic people.[\[591\]](#)
 - Anterior nasal swabs appear to be less sensitive (82% to 88%) compared with nasopharyngeal swabs (98%). Mid-turbinate and anterior nares swabs perform similarly.[\[592\]](#)
- Collect specimens under appropriate infection prevention and control procedures.

Test result

- A positive RT-PCR result confirms SARS-CoV-2 infection (in the context of the limitations associated with RT-PCR testing). If the result is negative, and there is still a clinical suspicion of infection (e.g., an epidemiologic link, typical x-ray findings, absence of another etiology), resample the patient and repeat the test. A positive result confirms infection. If the second test is negative, consider serologic testing (see below).[\[536\]](#)
- Genomic sequencing is not routinely recommended, but may be useful to investigate the dynamics of an outbreak, including changes in the size of an epidemic over time, its spatiotemporal spread, and testing hypotheses about transmission routes.[\[536\]](#)

Complications of nasal swab testing

- Complications associated with nasal swab testing are not well characterized and data is scarce. Complications were extremely low in one study (1.24 complications per 100,000 tests). Adverse effects may include epistaxis, nasal discomfort, headache, ear discomfort, rhinorrhea, and broken

swabs being stuck (and requiring removal via nasal endoscopy). Bleeding may be life-threatening. Correct sampling techniques are crucial.[\[593\]](#) [\[594\]](#)

- A case of iatrogenic cerebrospinal fluid leak has been reported after nasal testing for COVID-19 in a woman with an undiagnosed skull base defect at the fovea ethmoidalis.[\[595\]](#)

Testing for other infections

- Collect nasopharyngeal swabs for testing to rule out infection with other respiratory pathogens (e.g., influenza, atypical pathogens) when clinically indicated according to local guidance. Depending on local epidemiology and clinical symptoms, test for other potential causes including malaria, dengue fever, and typhoid fever as appropriate. It is important to note that coinfections can occur, and a positive test for a non-COVID-19 pathogen does not rule out COVID-19.[\[2\]](#) [\[596\]](#)
- When SARS-CoV-2 and influenza viruses are cocirculating, test for both viruses in all hospitalized patients with acute respiratory illness, and only test for influenza virus in outpatients with acute respiratory illness if the results will change clinical management of the patient.[\[533\]](#)

Limitations of molecular testing

Molecular testing is an aid to diagnosis only. The WHO recommends that healthcare providers consider a positive or negative result in combination with specimen type, clinical observations, patient history, and epidemiologic information. It also recommends that laboratories ensure that specimens with high cycle threshold values are not incorrectly assigned a positive result due to background noise, and that they provide the cycle threshold value in the report to the healthcare provider. Disease prevalence alters the predictive value of test results. As disease prevalence decreases, the risk of a false positive increases. This means that the probability that a person who has a positive result is truly infected decreases as prevalence decreases, irrespective of the claimed specificity of the test. Careful interpretation of weak positive results is needed.[\[576\]](#)

Interpret RT-PCR test results with caution.

- The evidence for the use of RT-PCR in the diagnosis of COVID-19 is still emerging, and uncertainties about its efficacy and accuracy remain. Estimates of diagnostic accuracy need to be interpreted with caution in the absence of a definitive reference standard to diagnose or rule out COVID-19. Also, more evidence is needed about the efficacy of testing outside of hospital settings and in asymptomatic or mild cases.[\[597\]](#)
- Few studies have attempted to culture live SARS-CoV-2 virus from human samples. This is an issue because viral culture is regarded as a gold standard test against which any diagnostic index test for viruses must be measured and calibrated, to understand the predictive properties of that test.[\[598\]](#) Prospective routine testing of reference and viral culture specimens is necessary to establish the usefulness and reliability of RT-PCR to diagnose COVID-19, and its relation to patients factors such as date of onset of symptoms and copy threshold, in order to help predict infectivity.[\[599\]](#)
- As there is no clear-cut "gold standard" for COVID-19 testing, evaluating test results can be challenging. Clinical adjudication may be the best available 'gold standard' based on repeat swabs, history, clinical presentation, and chest imaging.[\[600\]](#)

It is not clear whether a positive result always indicates the presence of infectious virus.

- RT-PCR detects viral RNA, but it is not fully understood how that represents infectious virus. Complete live viruses are necessary for transmission, not the fragments identified by PCR.[\[601\]](#)

This could ultimately lead to restrictions for people who do not present an infection risk. Because inactivated RNA degrades slowly over time, it may still be detected many weeks after the patient is no longer infectious.[598]

- One study found that only 28.9% of positive RT-PCR SARS-CoV-2 samples demonstrated viral growth when incubated on Vero cells. There was no growth in samples with an RT-PCR cycle threshold >24, or when the symptom onset to test time was >8 days. Therefore, infectivity of patients with a cycle threshold >24 and duration of symptoms >8 days may be low.[602] Another study found that patients with a cycle threshold of 34 or above do not excrete infectious virus.[603] A systematic review found that cycle threshold values were significantly lower and log copies higher in specimens that produce live virus culture. Those with high cycle threshold are unlikely to have infectious potential.[601]
- [Centre for Evidence-Based Medicine: are you infectious if you have a positive PCR test result for COVID-19?] (<https://www.cebm.net/covid-19/infectious-positive-pcr-test-result-covid-19>)

Interpreting test results depends on the accuracy of the test itself, and the pre- and post-test probabilities of disease. The accuracy of the result depends on various factors including the site and quality of sampling, stage of disease, degree of viral multiplication or clearance, and disease prevalence.[600]

- Sensitivity and specificity: the pooled sensitivity has been estimated to be 87.8%, with the specificity estimated to be in the range of 87.7% to 100%.[597]
- Pretest probability: the pretest probability estimate should be made using knowledge of local rates of infection from national and regional data, as well as the patient's symptoms, potential exposure to cases, a previous medical history of COVID-19 or the presence of antibodies, and the likelihood of an alternative diagnosis.[600] When the pretest probability is low, positive results should be interpreted with caution, and ideally a second specimen tested for confirmation.[604]
- Post-test probability: the lower the prevalence of disease in a given population, the lower the post-test probability.[605] For example, if a test with a specificity of 99% is used to test a high-risk symptomatic population where the likelihood of infection is 50%, the positive predictive value is 99%. This means that for every 100 people with a positive test result, 99 people will have SARS-CoV-2 infection but 1 person without infection will have a false-positive result. Conversely, in a low-risk asymptomatic population where the likelihood of infection is low (e.g., 0.05%), the positive predictive value is around 4.3%. This means that for every 100 people with a positive test result, 4 to 5 people will have SARS-CoV-2 infection, but 95 to 96 people without infection will have a false-positive result.[606]
- [BMJ Practice Pointer: interpreting a covid-19 test result] (<https://www.bmj.com/content/369/bmj.m1808>)

False-positive results

- False-positive results can be caused by a laboratory error or a cross-reaction with antibodies formed by current and past exposure to seasonal human coronavirus infections (e.g., common cold).[607] False-positive results are more likely when the prevalence of SARS-COV-2 is moderate to low.[608]
- There is a lack of data on the rate of false-positive tests. However, preliminary estimates in the UK are in the range of 0.8% to 4%.[609] This rate could translate into a significant proportion of daily false-positive results due to the current low prevalence of the virus in the UK population, adversely affecting the positive predictive value of the test.[604]
- Examples of the potential consequences of false-positive test results include:[604]

- Unnecessarily postponing or canceling elective procedures or treatments
- Potential exposure to infection following a wrong pathway in hospital settings during urgent hospital admissions
- Financial losses due to self-isolation, income losses, and canceled travel
- Psychological damage due to misdiagnosis including fear of infecting others or stigmatization
- Increased depression or domestic violence due to lockdown and isolation
- Overestimating the incidence and extent of asymptomatic infection in the population.

False-negative results

- False-negative rates of between 2% and 29% have been reported.^[600] A systematic review found that the false-negative rate varied across studies from 1.8% to 58% (median 11%); however, there was substantial and largely unexplained heterogeneity across studies.^[610]
- The probability of a false-negative result in an infected person decreases from 100% on day 1 of infection to 67% on day 4. The median false-negative rate drops to 38% on the day of symptom onset, decreases to 20% on day 8, and then starts to increase again from day 9.^[611]
- Examples of the potential consequences of false-negative test results include:^[600]
 - Patients may be moved into non-COVID-19 wards leading to spread of hospital-acquired infection
 - Caregivers could spread infection to vulnerable dependents
 - Healthcare workers risk spreading the infection to multiple vulnerable individuals.

Serologic testing

Serology cannot be used as a standalone diagnostic test for acute SARS-CoV-2 infections. However, it may be useful in various settings (e.g, negative molecular testing, diagnosing patients with late presentation or prolonged symptoms, serosurveillance studies).^[536] ^[612]

[\[BMJ practice pointer: testing for SARS-CoV-2 antibodies\]](https://www.bmj.com/content/370/bmj.m3325) (<https://www.bmj.com/content/370/bmj.m3325>)

The WHO recommends collecting a paired serum sample, one specimen in the acute phase and one in the convalescent phase 2 to 4 weeks later, in patients where infection is strongly suspected and the RT-PCR result is negative.^[536]

- Seroconversion or a rise in antibody titers in paired sera help to confirm whether the infection is recent and/or acute. If the initial sample tests positive, this could be due to a past infection that is not related to the current illness.
- Seroconversion may be faster and more robust in patients with severe disease compared with those with mild disease or asymptomatic infection.

The CDC recommends serologic testing as a method to support the diagnosis of illness or complications in the following situations:^[613]

- A positive antibody test at least 7 days following acute illness onset in people with a previous negative antibody test (i.e., seroconversion) and who did not receive a positive viral test may indicate SARS-CoV-2 infection between the dates of the negative and positive antibody tests

- A positive antibody test can help support a diagnosis when patients present with complications of COVID-19 illness, such as multisystem inflammatory syndrome and other post-acute sequelae of COVID-19.

Assays with FDA emergency-use authorization are recommended. Serologic tests with very high sensitivity and specificity are preferred because they are more likely to exhibit high expected predictive values when administered at least 3 weeks following onset of illness.

The Infectious Diseases Society of America recommends serologic testing in the following circumstances:[614]

- Evaluation of patients with a high clinical suspicion for infection when molecular diagnostic testing is negative and at least 2 weeks have passed since symptom onset
- Evaluation of pediatric inflammatory multisystem syndrome in children
- Serosurveillance studies.

Antibody responses to SARS-CoV-2 typically occur during the first 1 to 3 weeks of illness, with the seroconversion time of IgG antibodies often being earlier than that of IgM antibodies.[615] [616]

A Cochrane review found that antibody tests for IgG/IgM only detected 30% of people with COVID-19 when the test was performed 1 week after the onset of symptoms, but accuracy increased in week 2 with 70% detected and week 3 with over 90% detected. Data beyond 3 weeks were limited. Tests gave false-positive results in 2% of patients without COVID-19. The review found that the sensitivity of antibody tests is too low in the first week since symptom onset to have a primary role in the diagnosis of COVID-19, but tests are likely to have a useful role in detecting previous infection if used 15 or more days after symptom onset (although there were very little data beyond 35 days).[617]

Limitations of serologic testing

The evidence for the use of antibody tests in the diagnosis of COVID-19 is still emerging, and uncertainties about their efficacy and accuracy remain. Estimates of diagnostic accuracy need to be interpreted with caution in the absence of a definitive reference standard to diagnose or rule out COVID-19. More evidence is needed about the efficacy of testing outside of hospital settings and in asymptomatic or mild cases. The estimated sensitivity of antibody tests ranged from 18.4% to 96.1% (the lowest reported sensitivity was from a point-of-care test, although a sensitivity <50% was reported for one laboratory test), and specificity ranged from 88.9% to 100%.[597]

Understanding of the antibody response to SARS-CoV-2 is still emerging; therefore, antibody detection tests must be used with caution, and not used to determine acute infections.[536]

- Results do not indicate the presence or absence of current or previous infection with certainty as IgM and IgG antibodies may take 1 to 3 weeks to develop after infection.[613] A reliable diagnosis is often only possible in the recovery phase when opportunities for management or interruption of transmission have passed.[536]
- The duration of the persistence of antibodies produced in response to SARS-CoV-2 is still under investigation. The presence of antibodies that bind to SARS-CoV-2 does not guarantee that they are neutralizing antibodies, or that they offer protective immunity.[536]
- Although an antibody test may employ a specific antigen(s), antibodies developed in response to different proteins may cross-react (i.e., the antigen may detect antibodies it is not intended to detect). Therefore, it may not provide sufficient information on the presence of antigen-specific antibodies.[613]

- Vaccination may cause false-positive results for tests that utilize the S antigen or subunits like receptor-binding domains, but not for tests that use the N antigen.[\[613\]](#)

Rapid diagnostic tests

Antibody detection

- While rapid antibody detection kits have been approved for the qualitative detection of SARS-CoV-2 IgG/IgM antibodies in serum, plasma, or whole blood, the WHO does not recommend the use of these tests outside of research settings as they have not been validated as yet.[\[618\]](#)
- Evidence is particularly weak for point-of-care serologic tests. A meta-analysis found that the overall sensitivity of chemiluminescent immunoassays (CLIAs) for IgG or IgM was approximately 98%, and the sensitivity of enzyme-linked immunosorbent assays (ELISAs) was 84%; however, lateral flow immunoassays (LFIAs), which have been developed as point-of-care tests, had the lowest sensitivity at 66%. Test sensitivity was highest 3 or more weeks after onset of symptoms. Available evidence does not support the use of existing point-of-care serologic tests.[\[619\]](#)

Antigen detection

- Antigen testing relies on direct detection of SARS-CoV-2 viral proteins in nasal swabs and other respiratory specimens using a lateral flow immunoassay. Results are usually available in less than 30 minutes. While antigen tests are substantially less sensitive than RT-PCR, they offer the possibility of rapid, inexpensive, and early detection of the most infectious cases in appropriate settings. If used, testing should occur within the first 5 to 7 days following the onset of symptoms.[\[620\]](#)
- The WHO recommends antigen testing only in certain scenarios where RT-PCR is unavailable or where prolonged turnaround times preclude clinical utility, provided that the test meets the minimum performance requirements of $\geq 80\%$ sensitivity and $\geq 97\%$ specificity compared with an RT-PCR reference assay.[\[620\]](#)
- The Infectious Diseases Society of America recommends antigen testing in some individuals only when molecular testing is not readily available or is logistically infeasible, noting that the overall quality of available evidence supporting its use was graded as very low to moderate.[\[621\]](#)
- The CDC recommends that antigen tests may be used in congregate and community settings; however, confirmatory molecular testing may be needed.[\[622\]](#)
- The FDA has warned that false-positive results can occur with antigen tests, including when users do not follow the instructions for use, and that the number of false-positive tests increases as disease prevalence decreases.[\[623\]](#)
 - A Cochrane review found that rapid antigen tests vary in sensitivity. Sensitivity was higher in the first week after symptom onset in symptomatic people (78.3%), compared with the second week of symptoms (51%). Sensitivity was higher in those with RT-PCR cycle threshold values ≤ 25 (94.5%), compared with those with cycle threshold values > 25 (40.7%). Sensitivity was higher in symptomatic people (72%), compared with asymptomatic people (58.1%). Sensitivity also varied between brands of tests. Positive predictive values suggest that confirmatory testing of those with positive results may be considered in low prevalence settings. Evidence for testing in asymptomatic cohorts was limited, and no studies assessed the accuracy of repeated lateral flow testing or self-testing.[\[624\]](#)
 - An observational cohort study that assessed the performance of rapid antigen lateral flow testing against RT-PCR in an asymptomatic general population in the UK found that

the lateral flow test can be useful for detecting infections among asymptomatic adults, particularly those with a high viral load who are likely to be infectious. Lateral flow tests showed a sensitivity of 40%, specificity of 99.9%, positive predictive value of 90.3%, and negative predictive value of 99.2% in this population. Approximately 10% of people with a higher viral load detected by RT-PCR were missed by lateral flow tests.[625]

- Rapid antigen testing appears to be a reliable diagnostic tool to quickly detect people with a high viral load, and can help to detect and isolate potential superspreaders before RT-PCR results are available. However, testing is unsuccessful in detecting people with lower viral load and asymptomatic patients.[626]
- Laboratory-based (nonrapid) antigen tests are also available in some countries.

Molecular testing

- Rapid molecular tests are available. Some rapid molecular tests show accuracy levels similar to laboratory-based RT-PCR tests with high sensitivity and specificity. However, there is limited evidence available to support their use in symptomatic people, and there is no evidence for their use in asymptomatic populations. Resource implications of their use at scale are potentially high. Rapid molecular tests may be suitable for some testing scenarios (e.g., where obtaining test results within 2 hours will enable appropriate decision-making).[624]

Chest imaging

All imaging procedures should be performed according to local infection prevention and control procedures to prevent transmission. Chest imaging is considered safe in pregnant women.[627]

Order a chest x-ray in all patients with suspected pneumonia.

- Unilateral lung infiltrates are found in 25% of patients, and bilateral lung infiltrates are found in 75% of patients.[50] [51] [628]
- Chest x-ray is moderately sensitive and moderately specific for the diagnosis of COVID-19. Pooled results found that chest x-ray correctly diagnosed COVID-19 in 80.6% of people who had the disease. However, it incorrectly identified COVID-19 in 28.5% of people who did not have the disease.[629]
- Although chest x-ray appears to have a lower sensitivity compared with chest CT, it has the advantages of being less resource-intensive, associated with lower radiation doses, easier to repeat sequentially, and portable.[630]

Consider ordering a CT scan of the chest.

- Chest CT may play a role in diagnosis in a limited number of hospitalized patients, particularly when initial molecular testing has been inconclusive, or when an alternative diagnosis is being considered.[631] However, it is not diagnostic for COVID-19 and local guidance should be consulted on whether to perform a CT scan.
- The British Society of Thoracic Imaging (BSTI) recommends CT imaging in patients with clinically suspected COVID-19 who are seriously ill if chest x-ray is uncertain or normal. Without the suspicion of COVID-19, the radiology is nonspecific and could represent many other disease processes. The BSTI in collaboration with NHS England have produced a radiology decision support tool to help clinicians

- decide whether or not chest imaging should be ordered.[539] [BSTI: radiology decision tool for suspected COVID-19] (https://www.bsti.org.uk/media/resources/files/NHSE_BSTI_APPROVED_Radiology_on_CoVid19_v6_modified1_-_Read-Only.pdf)
- Some institutions in the UK recommend a more pragmatic approach for patients with high clinical suspicion of COVID-19, with chest CT recommended only after two indeterminate or normal chest x-rays in combination with a negative RT-PCR test.[632]
 - The American College of Radiology recommends reserving CT for hospitalized, symptomatic patients with specific clinical indications for CT, and emphasizes that a normal chest CT does not mean that a patient does not have COVID-19 and that an abnormal chest CT is not specific for COVID-19 diagnosis.[633]
 - Chest CT is sensitive and moderately specific for the diagnosis of COVID-19. Pooled results found that chest CT correctly diagnosed COVID-19 in 87.9% of people who had the disease. However, it incorrectly identified COVID-19 in 20% of people who did not have the disease. Therefore, chest CT may have more utility for excluding COVID-19 than for differentiating it from other causes of respiratory illness.[629] Accuracy appears to be lower among children; however, there are limited data in this population.[631]
 - Evidence of pneumonia on CT may precede a positive RT-PCR result for SARS-CoV-2 in some patients.[634] Some patients may present with a normal chest finding despite a positive RT-PCR.[635] Results of RT-PCR testing may be false-negative, so patients with typical CT findings should have repeat RT-PCR testing to confirm the diagnosis.[636]
 - CT imaging abnormalities may be present in asymptomatic patients. The pooled estimate of the rate of positive chest CT findings in asymptomatic cases was 47.6% (mainly ground-glass opacity).[637]
 - Pregnant women appear to present more commonly with more advanced CT findings compared with the general adult population; however, results are similar to those in the general adult population.[638]

Typical features of chest CT

- Abnormal chest CT findings have been reported in up to 97% of COVID-19 patients in one meta-analysis of 50,466 hospitalized patients.[639]
- The most common findings are ground-glass opacity, either in isolation or coexisting with other findings such as consolidation, interlobular septal thickening, or crazy-paving pattern. The most common distribution pattern is bilateral, peripheral/subpleural, posterior distribution of the opacities, with a lower lobe predominance. Extensive/multilobar involvement with consolidations is more common in older patients and those with severe disease.[640]
- Ground-glass opacity has the highest diagnostic performance for COVID-19 pneumonia, followed by ground-glass opacity plus consolidation, and consolidation only.[641] The simultaneous presence of ground-glass opacity and other features of viral pneumonia had optimum performance in the detection of COVID-19 (sensitivity 90% and specificity 89%).[642]
- CT scan generally shows an increase in the size, number, and density of ground-glass opacities in the early follow-up period, with a progression to mixed areas of ground-glass opacities, consolidations, and crazy paving peaking at day 10 to 11, before gradually resolving or persisting as patchy fibrosis.[640]
- A small comparative study found that patients with COVID-19 are more likely to have bilateral involvement with multiple mottling and ground-glass opacity compared with other types of pneumonia.[643]

- Children frequently have normal or mild CT chest findings. The most common signs in children are patchy ground-glass opacity and, less frequently, nonspecific patchy shadows, areas of consolidation, and a halo sign. Abnormalities are more common in the lower lobes and are predominantly unilateral. Pleural effusion is rare. Children may have signs of pneumonia on chest imaging despite having minimal or no symptoms.[\[644\]](#) Ground-glass opacity and peribronchial thickening were the most prevalent findings in infants younger than 1 year of age.[\[645\]](#)

Atypical features of chest CT

- Pulmonary vascular enlargement, interlobular or intralobular septal thickening, adjacent pleural thickening, air bronchograms, subpleural lines, crazy-paving pattern, bronchus distortion, bronchiectasis, vacuolar retraction sign, and halo sign are atypical features. Pleural effusion, pericardial effusion, cavitation, pneumothorax, and mediastinal lymphadenopathy have also been reported rarely.[\[640\]](#)

The WHO recommends chest imaging in the following scenarios:[\[630\]](#)

- Symptomatic patients with suspected COVID-19 when RT-PCR is not available, RT-PCR test results are delayed, or initial RT-PCR testing is negative but there is a high clinical suspicion for COVID-19 (for diagnosis)
- Patients with suspected or confirmed COVID-19 who are not currently hospitalized and have mild symptoms (to decide on hospital admission versus home discharge)
- Patients with suspected or confirmed COVID-19 who are not currently hospitalized and have moderate to severe symptoms (to help decide on regular ward admission versus intensive care unit admission)
- Patients with suspected or confirmed COVID-19 who are currently hospitalized and have moderate to severe symptoms (to inform therapeutic management).

Emerging tests

Reverse transcription loop-mediated isothermal amplification

- Reverse transcription loop-mediated isothermal amplification (RT-LAMP) assays are an emerging test to detect SARS-CoV-2 viral RNA. While assays are simple and quick, there is less evidence for their use. Assays for SARS-CoV-2 have been developed and are being evaluated.[\[646\]](#) [\[647\]](#) [\[648\]](#) A sensitivity of 95.5% and specificity of 99.5% has been reported.[\[649\]](#)

Lung ultrasound

- Lung ultrasound is used as a diagnostic tool in some centers as an alternative to chest x-ray and chest CT. Although there is only very low-certainty evidence supporting its diagnostic accuracy, it might be helpful as a supplemental or alternate imaging modality.[\[630\]](#)
- Ultrasound is sensitive but not specific for the diagnosis of COVID-19. Pooled results found that lung ultrasound correctly diagnosed COVID-19 in 86.4% of people with the disease. However, it incorrectly diagnosed COVID-19 in 45% of people who did not have the disease. Therefore, ultrasound may have more utility for excluding COVID-19 than for differentiating it from other causes of respiratory illness.[\[629\]](#)
- B-lines are the prominent pattern in patients with COVID-19, occurring with a pooled frequency of 97%. Pleural line abnormalities are also common, with a pooled frequency of 70%. While these findings are not specific for COVID-19, they increase the likelihood of disease in the context of a

characteristic clinical presentation. Other findings include consolidations, pleural thickening, and pleural effusion.[650]

- It has the advantages of portability, bedside evaluation, reduced healthcare worker exposure, easier sterilization process, absence of ionizing radiation exposure, and repeatability during follow-up. It may also be more readily available in resource-limited settings. However, it also has some limitations (e.g., it is unable to discern chronicity of a lesion) and other imaging modalities may be required. Ultrasound may be used in pregnant women and children.[651] [652]
- Possible roles for ultrasound include: reducing nosocomial transmission; monitoring progress of patients; and a possible role in subpopulations who are vulnerable but are not suitable for CT (e.g., pregnant women).[653] Lung ultrasound score may play a role in prognosis.[654]
- [BSTI: lung ultrasound (LUS) for COVID-19 patients in critical care areas] (https://www.bsti.org.uk/media/resources/files/Lung_US_print_out_and_scoring_proforma.pdf)

Viral isolation

- Viral isolation is not recommended as a routine diagnostic procedure. All procedures involving viral isolation in cell culture require trained staff and biosafety level 3 (BSL-3) facilities.[536]

Calprotectin

- Calprotectin is an emerging biomarker of interest. Calprotectin levels often increase following infection or trauma, and in inflammatory disease. Serum/fecal calprotectin levels have been demonstrated to be significantly elevated in COVID-19 patients with severe disease, and it may have prognostic significance.[655]

History and exam

Key diagnostic factors

fever (common)

- Reported in approximately 77% of patients.[139] In one case series, only 44% of patients had a fever on presentation, but it developed in 89% of patients after hospitalization.[656] The course may be prolonged and intermittent, and some patients may have chills/rigors. The prevalence of fever is higher in adults compared with children; approximately 54% of children do not exhibit fever as an initial presenting symptom.[657] In children, fever may be absent or brief and rapidly resolving.[658]

cough (common)

- Reported in approximately 68% of patients.[139] The cough is usually dry; however, a productive cough has been reported in some patients. Can persist for weeks or months after infection.[659]

dyspnea (common)

- Reported in approximately 38% of patients.[139] Median time from onset of symptoms to development of dyspnea is 5 to 8 days.[50] [51] [660] May last weeks after initial onset of symptoms. Wheeze has been reported in 17% of patients.[661]

altered sense of smell/taste (common)

- Presence of anosmia and/or ageusia may be useful as a red flag for diagnosis.[535] Olfactory dysfunction (anosmia/hyposmia) has been reported in approximately 41% of patients, and gustatory

dysfunction (ageusia/dysgeusia) has been reported in approximately 35% of patients.[139] Prevalence appears to be higher in European studies.[662] May be an early symptom before the onset of other symptoms, or may be the only symptom in patients with mild to moderate illness.[663] Prevalence of anosmia/ageusia presenting before other symptoms was 13% to 73%, at the same time as other symptoms was 14% to 39%, and after other symptoms was 27% to 49%.[664] Persistent anosmia has an excellent prognosis with nearly complete recovery at 1 year.[665] Anosmia or hyposmia is significantly associated with an enhanced risk of testing positive for COVID-19, and is a good predictor of infection.[666] Many drugs are associated with taste and smell changes (e.g., antibiotics, ACE inhibitors) and should be considered in the differential diagnosis.[667]

Other diagnostic factors

fatigue (common)

- Reported in approximately 30% of patients.[139] Patients may also report malaise. Fatigue and exhaustion may be extreme and protracted, even in patients with mild disease.

myalgia or arthralgia (common)

- Reported in approximately 17% (myalgia) and 11% (arthralgia) of patients.[661] Arthritis has been reported rarely.[668]

sputum production/expectoration (common)

- Reported in approximately 18% of patients.[139]

chest tightness (common)

- Reported in approximately 22.9% of patients.[569]

gastrointestinal symptoms (common)

- Reported in 20% of patients. The weighted pooled prevalence of specific symptoms is as follows: loss of appetite 22.3%; diarrhea 2.4%; nausea/vomiting 9%; and abdominal pain 6.2%. Gastrointestinal symptoms appear to be more prevalent outside of China, although this may be due to increased awareness and reporting of these symptoms as the pandemic progressed.[669] Gastrointestinal symptoms are not associated with an increased likelihood for testing positive for COVID-19; however, anorexia and diarrhea, when combined with loss of smell/taste and fever, were 99% specific for COVID-19 infection in one prospective case-control study.[670] The presence of gastrointestinal symptoms may be a predictor of progression to severe disease.[671] [672] However, the presence of these symptoms does not appear to affect intensive care unit admission rate or mortality.[673] The presence of diarrhea has been associated with a severe clinical course in children.[555] Hematochezia has been reported.[674]

sore throat (common)

- Reported in approximately 16% of patients.[139] Usually presents early in the clinical course.

headache (common)

- Reported in approximately 25% of patients. Headache is twice as prevalent in COVID-19 patients compared with patients with non-COVID-19 viral respiratory tract infections.[675]

dizziness (common)

- Reported in approximately 11% of patients.[661]

neurologic symptoms (common)

- Confusion has been reported in approximately 11% of patients.[661]
- The overall prevalence of delirium is 24.3%, with an increased prevalence in adults >65 years of age (28%). Delirium has been associated with a 3-fold increase in mortality.[676] Benzodiazepine use and the lack of family visitation (virtual or in-person) have been identified as risk factors for delirium.[677] The pooled prevalence of anxiety, depression, and insomnia is 15.2%, 16%, and 23.9%, respectively.[678] Altered mental status was as common in younger hospitalized patients (<60 years) as it was in older patients in one study.[679] [680]

ocular symptoms (common)

- Reported in 11% of patients. The most common ocular symptoms include dry eye or foreign body sensation (16%), redness (13.3%), tearing (12.8%), itching (12.6%), eye pain (9.6%), and discharge (8.8%). Conjunctivitis was the most common ocular disease in patients with ocular manifestations (88.8%).[681] Most symptoms are mild and last for 4 to 14 days with no complications. Prodromal symptoms occur in 12.5% of patients.[682] Mild ocular symptoms (e.g., conjunctival discharge, eye rubbing, conjunctival congestion) were reported in 22.7% of children in one cross-sectional study. Children with systemic symptoms were more likely to develop ocular symptoms.[683]

rhinorrhea/nasal congestion (uncommon)

- Rhinorrhea has been reported in approximately 8% of patients, and nasal congestion has been reported in approximately 5% of patients.[661]

audio-vestibular symptoms (uncommon)

- Sudden sensorineural hearing loss, tinnitus, and rotatory vertigo have been reported in 7.6%, 14.8%, and 7.2% of patients, respectively. Otalgia has also been reported.[684]

chest pain (uncommon)

- Reported in approximately 7% of patients.[661] May indicate pneumonia.

cutaneous symptoms (uncommon)

- The pooled prevalence of overall cutaneous lesions is 5.7%. The most common symptoms are a viral exanthem-like presentation (4.2%), maculopapular rash (3.8%), and vesiculobullous lesions (1.7%). Other manifestations include urticaria, chilblain-like lesions, livedo reticularis, and finger/toe gangrene.[685] [686] In the UK COVID Symptom Study, 17% of respondents reported rash as the first symptom of disease, and 21% of respondents reported rash as the only clinical sign.[687] Cutaneous signs may be the only, or the first, presenting sign.[688] Cutaneous symptoms have been reported in children.[689] It is unclear whether skin lesions are from viral infection, systemic consequences of the infection, or drugs the patient may be on. Further data is required to better understand cutaneous involvement and whether there is a causal relationship. A prospective case series in adolescents found that chilblain-like lesions are not associated with systemic or localized SARS-CoV-2 infection.[690]
- [British Association of Dermatologists: Covid-19 skin patterns] (<https://covidskinsigns.com>)

lower urinary tract symptoms (uncommon)

- There is emerging evidence that patients may rarely have signs, symptoms, and radiologic and laboratory features indicative of involvement of the lower urinary tract and male genital system. This may include scrotal discomfort, swelling, or pain (acute orchitis, epididymitis, or epididymo-orchitis), low-flow priapism, impaired spermatogenesis, bladder hemorrhage, acute urinary retention,

and worsening of existing lower urinary tract symptoms (including exacerbation of benign prostatic hyperplasia). Further research is required.^[691] ^[692]

hemoptysis (uncommon)

- Reported in approximately 2% of patients.^[661] May be a symptom of pulmonary embolism.^[693]

bronchial breath sounds (uncommon)

- May indicate pneumonia.

tachypnea (uncommon)

- May be present in patients with acute respiratory distress.

tachycardia (uncommon)

- May be present in patients with acute respiratory distress.

cyanosis (uncommon)

- May be present in patients with acute respiratory distress.

crackles/rales on auscultation (uncommon)

- May be present in patients with acute respiratory distress.

Risk factors

Strong

contact with probable or confirmed case

- People who have been in contact with a probable or confirmed case are at increased risk of infection.
- The World Health Organization defines a contact as a person who has experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case: face-to-face contact with a probable or confirmed case within 3 feet (1 meter) and for at least 15 minutes; direct physical contact with a probable or confirmed case; direct care for a patient with probable or confirmed COVID-19 without using recommended personal protective equipment; or other situations as indicated by local risk assessments.^[166]
- The Centers for Disease Control and Prevention defines a close contact as someone who has been within 6 feet (2 meters) of an infected person for at least 15 minutes over a 24-hour period, beginning 2 days before symptom onset (or 2 days before testing in asymptomatic patients).^[167]

residence/work/travel in location with high risk of transmission

- People who live or work in, or travel to, a location with a high risk of transmission are at increased risk of infection.
- People residing or working in an area with a high risk of transmission (e.g., closed residential settings, humanitarian setting), people residing in or traveling to an area with community transmission, and people working in a health setting (including within health facilities and households) at any time within the 14 days prior to symptom onset are at higher risk of infection.^[166]
- People at risk of infection from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern include: those who have been in, or transited through, any countries with transmission of variants of concern (consult local guidance for lists of affected countries) and

who develop symptoms within 10 days of departure or transit (or date of sampling for a positive SARS-CoV-2 test if asymptomatic); those known to be infected with a variant of concern based on sequencing results, regardless of travel history; contacts of these individuals.[168]

older age

- Older people are at increased risk for infection and severe disease.[169]
- The risk of hospitalization and death increases with age. For example, in people ages 85 years and older, the risk of hospitalization is 15 times higher and the risk of death is 610 times higher compared with 18- to 29-year-olds according to US data.[170]

	0-4 years	5-17 years	18-29 years	30-39 years	40-49 years	50-64 years	65-74 years	75-84 years	85+ years
Hospitalization	<1 x	<1 x	Reference group	2x	2x	4x	6x	9x	15x
Death	<1 x	<1 x		4x	10x	35x	95x	230x	610x

Risk for hospitalization and death by age group (rate ratios compared with 18- to 29-year-olds)

Table based on data from the CDC

- In the UK, data from a cross-sectional study indicated that people ages 40 to 64 years are at greatest risk of infection, followed by patients 75 years and older, and then people ages 65 to 74 years.[171] The highest mortality rate was observed in patients 80 years and older.[172]
- In the US, patients ≥65 years accounted for 31% of all cases, 45% of hospitalizations, 53% of intensive care unit admissions, and 80% of deaths early in the pandemic, with the highest incidence of severe outcomes in patients ages ≥85 years.[6]
- Observational studies in older adults ages ≥60 years across multiple countries found that approximately 51% of older patients had severe infection, while 22% were critically ill.[173]
- While age is an independent risk factor, the risk in older people is also partly related to the likelihood that older adults are more likely to have comorbidities. The higher prevalence of malnutrition in older patients may also contribute to poor outcomes.[174]

male sex

- Males are at increased risk for infection and severe disease.[169]
- In the UK, data from a cross-sectional study found that the adjusted odds of a positive test were greater in males (18.4%) compared with females (13.3%).[171]
- It has been hypothesized that this may be due to the presence of androgens, a lower level of SARS-CoV-2 antibodies compared with females, women mounting a stronger immune response compared with men, genetic factors, or a higher prevalence of alcohol consumption and smoking; however, further research is required.[175] [176]

ethnicity

- People who belong to Black, Asian, and minority ethnic (BAME) groups are at increased risk of infection and severe disease.[177] [178]
- In the UK, data indicate that South Asian, Black, and mixed ethnicity populations have an increased risk for testing positive and of adverse outcomes (i.e., hospitalization, intensive care unit admission, death) compared with the White population, even after accounting for differences in sociodemographic, clinical, and household characteristics.[179] Race may play an important role in adverse outcomes in children as well as adults.[180]
- In the US, the proportion of hospitalized patients was highest for Hispanic or Latino patients, and these racial and ethnic disparities were largest during May–July 2020 and became less pronounced as the

pandemic spread throughout the country.[181] Cumulative age-adjusted data from the Centers for Disease Control and Prevention (as of 16 July 2021) indicate that Hispanic or Latino people, non-Hispanic American Indian or Alaska Native people, and non-Hispanic Black people have approximately 2.8, 3.4, and 2.8 times the rate of hospitalizations and 2.3, 2.4, and 2 times the rate of deaths of non-Hispanic White people, respectively.[182] However, cohort studies in the US have found no difference in outcomes between non-Hispanic Black and Hispanic patients compared with White patients after adjusting for sociodemographic factors (e.g., age, sex, insurance) and comorbidities. These patients may have an increased risk of mortality and morbidity due to their disproportionate representation among hospitalizations.[183] [184] [185]

- Racial disparities in outcomes may be partially attributed to higher rates of comorbidities in certain ethnic groups.[186]

residence in a long-term care facility

- People in a long-term care facility are at increased risk for infection and severe disease.[123] [187]
- In the UK, care home residents represented approximately one third of the total number of deaths in England and Wales during the first wave of the pandemic; other countries reported a similar experience. This was likely due to shortages in personal protective equipment, a vulnerable population, and a lack of testing.[188] A study across four nursing homes found that 26% of residents died over a 2-month period, with all-cause mortality increasing by 203% compared with previous years. Approximately 40% of residents tested positive for SARS-CoV-2, and of these, 43% were asymptomatic and 18% had atypical symptoms.[189]
- In the US, the 30-day all-cause mortality rate was 21% in a cohort study of more than 5000 nursing home residents. Older age, male sex, and impaired cognitive and physical function were independently associated with mortality.[190]

presence of comorbidities

- People with comorbidities are at increased risk for severe disease, and the more comorbidities, the greater the risk.[191] [192]
- In the UK, the most common comorbidities reported in a cohort study of more than 20,000 hospitalized patients were cardiac disease (31%), uncomplicated diabetes (21%), nonasthmatic chronic pulmonary disease (18%), and chronic kidney disease (16%).[5]
- In the US, approximately 95% of hospitalized adults had at least one reported underlying medical condition, with the most common being hypertension, disorders of lipid metabolism, and obesity. Approximately 99% of patients who died had at least one underlying health condition. The strongest risk factors for death were obesity, anxiety and fear-related disorders, and diabetes, as well as the total number of underlying conditions.[193] It has been estimated that approximately 56% of adults, and 32% of young adults (ages 18-25 years), are at risk for severe disease because of the presence of at least one comorbidity.[194] [195]
- Globally, hypertension (21%), obesity (18%), and diabetes (18%) were the most prevalent comorbidities. Cancer, chronic kidney disease, diabetes, and hypertension were independently associated with mortality. Chronic kidney disease was statistically the most prominent comorbidity leading to death.[196]

obesity

- People with obesity are at increased risk for infection and severe disease.[197]
- Of the 2.5 million deaths reported globally by the end of February 2021, 2.2 million were in countries where more than half the population is classified as overweight. In countries where less than half the

adult population is classified as overweight, the likelihood of death is around one tenth of the level seen in countries where more than half the population is classified as overweight.[198]

- People with obesity (≥ 30 kg/m²) and people who are overweight (25-30 kg/m²) are at increased risk of severe disease.[192] Evidence from a meta-analysis suggests a linear dose-response association between body mass index and disease severity and mortality.[199] However, another meta-analysis demonstrated a J-curve relationship between body mass index and mortality, indicating that both underweight and obese patients had a higher risk of mortality compared with those of normal weight.[200]
- A cohort study in the UK found that the risk of severe outcomes (i.e., hospitalization, intensive care unit admission, death) increased progressively above a body mass index ≥ 23 kg/m², independent of the excess risks of related diseases (e.g., diabetes). The relative risk was particularly notable in people <40 years of age and those with Black ethnicity.[201]
- A cohort study in the US found a nonlinear relationship between body mass index and disease severity, with the lowest risk at body mass indexes near the threshold between healthy weight and overweight, then increasing with higher body mass index.[202]
- Obesity is associated with an increased risk for disease progression, hospitalization, intensive care unit admission, need for invasive mechanical ventilation, complications (e.g., venous thromboembolism and renal failure), and in-hospital mortality, especially among younger patients.[197] [203] [204]

cardiovascular disease

- People with cardiovascular disease are at increased risk for severe disease.[192]
- Arrhythmias, coronary artery disease, and cardiovascular disease are significantly associated with intensive care unit admission. Heart failure, arrhythmias, coronary artery disease, and cardiovascular disease are also significantly associated with an increased risk of mortality.[205] Preexisting atrial fibrillation was associated with a higher risk of short-term death.[206] Coronary heart disease has also been associated with disease progression and severe/critical disease. The association is affected by the presence of hypertension; patients with coronary heart disease and hypertension had an increased risk of poor prognosis compared with those without hypertension.[207]
- People with risk factors for cardiovascular disease (e.g., hypertension, diabetes) are also at increased risk for severe disease and mortality (see below).[208] [209]

diabetes

- People with type 1 or type 2 diabetes are at increased risk for severe disease.[192]
- Diabetes is associated with an increased risk for disease progression, intensive care admission, acute respiratory distress syndrome, need for invasive mechanical ventilation, and mortality.[210] [211]
- In the UK, one third of all deaths in hospitalized patients occurred in patients with diabetes.[212] An analysis of more than 19,000 patients admitted to critical care over the entire first wave of the pandemic found that type 2 diabetes is associated with a 20% increase in mortality in patients with severe disease, independent of age, sex, ethnicity, obesity, or other major comorbidity.[213]
- Risk factors for poor prognosis and higher mortality in patients with type 1 or type 2 diabetes include older age, male sex, non-White ethnicity, socioeconomic deprivation, renal impairment/acute kidney injury, history of stroke or heart failure, poor glycemic control prior to infection, higher glycosylated hemoglobin levels, higher body mass index, elevated C-reactive protein, diabetic ketoacidosis, hyperglycemic hyperosmolar state, and insulin use.[214] [215] [216] [217] [218] The higher risk of intensive care unit admission and mechanical ventilation in patients with type 1 diabetes may be accounted for by the presence of diabetic ketoacidosis.[219] Patients with newly diagnosed diabetes

have a higher risk of all-cause mortality compared with patients with known diabetes, hyperglycemia, or normal glucose.[220]

- Use of metformin, sodium–glucose cotransporter-2 inhibitors, glucagon-like peptide-1 receptor agonists, or dipeptidyl peptidase-4 inhibitors may be associated with lower mortality.[221] [222] [223]
- The poor prognosis in these patients is likely due to the syndromic nature of diabetes, with factors such as hyperglycemia, older age, and the presence of comorbidities (e.g., obesity, hypertension, cardiovascular disease) all contributing to the increased risk.[224]

chronic respiratory disease

- People with chronic obstructive pulmonary disease COPD, including emphysema and chronic bronchitis, are at increased risk for severe disease. People with moderate to severe asthma, or other chronic lung diseases (e.g., interstitial lung disease, cystic fibrosis, idiopathic pulmonary fibrosis, pulmonary hypertension) may be at increased risk for severe disease; however, evidence is limited.[192] There is no clear evidence that people with asthma or COPD are at higher risk of infection.[225] [226]
- COPD is associated with an increased risk of hospitalization, intensive care unit admission, and mortality.[227] A national, multicenter prospective cohort study in the UK (75,463 patients from 258 healthcare facilities) found that patients with COPD were less likely to receive critical care than patients without an underlying respiratory condition.[228]
- It is unclear whether asthma increases the risk of infection or severe outcomes (i.e., hospitalization, intensive care unit admission, mortality). Systematic reviews do not detect a clear increase in risk, and high-quality primary studies report conflicting results. People with asthma who have comorbid COPD, and people with nonallergic asthma, appear to have worse outcomes.[229] According to meta-analyses, asthma is not associated with an increased risk for infection, severe disease, worse prognosis, mortality, or a higher risk of intubation or mechanical ventilation. Clinical outcomes were similar between patients with asthma and patients without asthma. Patients with asthma may have a lower risk of death compared with nonasthmatic patients.[230] [231] [232] [233] However, a national, multicenter prospective cohort study in the UK (75,463 patients from 258 healthcare facilities) found that patients with asthma were more likely to receive critical care than patients without an underlying respiratory condition. Severe asthma was associated with increased mortality compared with patients with nonsevere asthma in patients ages 16 years and older. Inhaled corticosteroid use in patients with asthma was associated with lower mortality compared with patients without an underlying respiratory condition in patients ages 50 years and older.[228]
- People with obstructive sleep apnea may be at increased risk for severe disease, intensive care admission, mechanical ventilation, and mortality; however, evidence is limited.[234] Obstructive sleep apnea has not been associated with an increased risk of infection.[235]
- People with cystic fibrosis do not appear to be at increased risk of infection; however, there is evidence that some patients may experience a more severe clinical course (e.g., post-transplantation).[236]
- People with tuberculosis appear to be at an increased risk of severe disease and mortality.[237]
- There are no data on whether pediatric respiratory diseases (including childhood asthma) are risk factors for infection or severity.[238]

chronic kidney disease

- People with chronic kidney disease are at increased risk for severe disease, and may be at higher risk for infection.[171] [192]
- Patients with chronic kidney disease had a significantly higher risk of hospitalization and all-cause mortality compared with people without chronic kidney disease. Patients with chronic kidney disease

also had a higher risk of progressing to critical illness in the pooled analysis of included studies and subgroup analyses of studies with multivariable adjustment, although neither result achieved statistical significance.[\[239\]](#)

- Patients with end-stage renal disease who were on renal replacement therapy had an increased risk of intensive care unit admission, need for mechanical ventilation, and mortality.[\[240\]](#)
- In the UK, data from a cross-sectional study found that the adjusted odds of a positive test were greater in patients with chronic kidney disease (32.9%) compared with those without (14.4%).[\[171\]](#)
- Preexisting chronic kidney disease is an independent risk factor for developing acute kidney injury as a complication.[\[241\]](#)

pregnancy

- Pregnant women are at increased risk for severe disease.[\[192\]](#)
- According to an analysis of approximately 400,000 women ages 15 to 44 years with symptomatic disease, pregnant women were more likely to be hospitalized, be admitted to the intensive care unit, receive invasive mechanical ventilation or extracorporeal membrane oxygenation, and die compared with nonpregnant women.[\[28\]](#)
- Pregnant women and neonates are more vulnerable to adverse outcomes in low- to middle-income countries compared with high-income countries.[\[242\]](#)
- See the Complications section for more information on pregnancy-related complications.

smoking

- People who are current or former smokers are at increased risk for severe disease.[\[192\]](#)
- Smoking is associated with severe or critical outcomes, and an increased risk of intensive care unit admission and mortality. The association appears to be more significant in former smokers compared with current smokers. Current smokers are at higher risk of developing severe disease compared with nonsmokers.[\[243\]](#) Smokers have double the mortality risk compared with nonsmokers.[\[244\]](#) This may be due to increased airway expression of the angiotensin-converting enzyme-2 receptor in smokers.[\[245\]](#)
- The World Health Organization has reviewed the available evidence and concluded that smoking is associated with increased severity of disease and death in hospitalized patients.[\[246\]](#)

malignancy

- People with cancer are at increased risk for infection and severe disease.[\[192\]](#) [\[247\]](#)
- Patients with cancer have an increased risk of severe disease, increased ventilatory requirements, and mortality compared with the general population. Intensive care unit admission rates were not statistically significant between the two groups. Hematologic malignancies were associated with the highest risk of mortality (possibly explained by the greater degree of immunosuppression used in the treatment of these patients), followed by lung cancer. There is no clear association between treatment modality and mortality. A higher risk of infection is likely due to immunosuppressive treatments and/or recurrent hospital visits.[\[248\]](#) The pooled in-hospital mortality risk in patients with cancer is 14.1%.[\[249\]](#)
- Mortality in cancer patients is affected by preexisting noncancer comorbidities, and is significantly higher in people with hypertension, cardiovascular disease, chronic obstructive pulmonary disease, and diabetes.[\[250\]](#)
- Children with cancer may be no more vulnerable to infection compared with children without cancer. Limited data show that the overall morbidity in pediatric patients with cancer is low, with only 5% requiring hospitalization for symptoms.[\[251\]](#) Overall survival in children with cancer is very high

(99.4%), and there was no significant difference in the risk of hospitalization or intensive care unit admission between hematologic malignancies and solid tumors in children.[\[252\]](#)

cerebrovascular disease

- People with cerebrovascular disease are at increased risk for severe disease.[\[192\]](#)
- Patients with a history of cerebrovascular disease were more likely to progress to adverse outcomes compared with patients without a history of cerebrovascular disease.[\[253\]](#) Patients with preexisting cerebrovascular disease had 2.67-fold higher odds of poor outcomes including intensive care admission, mechanical ventilation, and mortality.[\[254\]](#)

solid organ or blood stem cell transplant

- People with an immunocompromised state from solid organ or blood stem cell transplant may be at increased risk for severe disease; however, evidence is limited.[\[192\]](#)
- Solid organ transplant recipients are at increased risk for hospitalization, intensive care unit admission, and mortality. However, the increased rate of hospitalization may reflect a preferred management strategy of closer inpatient monitoring in these patients rather than being an indicator of disease severity. Overall mortality in solid organ transplant recipients was 20%.[\[255\]](#) Solid organ transplant recipients had a 1.4-fold increased odds of mortality compared with the general population.[\[256\]](#)

Down syndrome or learning disability

- People with Down syndrome or learning disability may be at increased risk for severe disease; however, evidence is limited.[\[192\]](#)
- In the UK, a cohort study found a 4-fold increased risk for hospitalization and a 10-fold increased risk for mortality in people with Down syndrome.[\[257\]](#) This may possibly be due to the presence of immune dysfunction, congenital heart disease, and pulmonary pathology.
- Another study in the UK found that adults with learning disability and those with Down syndrome or cerebral palsy have markedly increased risks of hospital admission and death over and above the risks observed for non-COVID-19 causes of death.[\[258\]](#)

hemoglobin disorders

- People with sickle cell disease or thalassemia may be at increased risk for severe disease; however, evidence is limited.[\[192\]](#)
- In the UK, patients with sickle cell disease were found to have a 4-fold increased risk for hospitalization and a 2.6-fold increased risk for death. Sickle cell trait was also associated with increased risks for both outcomes, albeit to a lesser extent.[\[259\]](#)
- In the US, among 178 patients with sickle cell disease (mean patient age <40 years), 69% were hospitalized, 11% were admitted to intensive care, and 7% died.[\[260\]](#) Infection can cause acute chest syndrome in patients with sickle cell disease.[\[261\]](#) [\[262\]](#)

hypertension

- People with hypertension may be at increased risk for severe disease; however, evidence is limited.[\[192\]](#)
- Almost all available evidence suggests that hypertension increases the risk of severe disease or mortality, although it was sometimes unclear whether this was independent of other risk factors. There were no systematic reviews or meta-analyses studying whether people with hypertension were at greater risk of infection.[\[263\]](#)

- Hypertension has been associated with increased poor composite outcome, including mortality, severe disease, acute respiratory distress syndrome, need for intensive care admission, and disease progression.[\[264\]](#) Patients with hypertension have a 2.98-fold higher risk of severe disease, a 1.82-fold higher risk of critical disease, and a 2.17 to 2.88-fold higher risk of fatality compared with patients without hypertension.[\[265\]](#) [\[266\]](#)
- Initially, there was a concern that people on ACE inhibitors or angiotensin-II receptor antagonists may be at increased risk for infection or severe disease due to upregulation of ACE2 receptor expression.[\[267\]](#) However, high-certainty evidence suggests that use of these drugs is not associated with severe disease, and there is no association between the use of these medications and a positive SARS-CoV-2 test result among symptomatic patients.[\[268\]](#) [\[269\]](#)

dementia

- People with dementia may be at increased risk for infection and severe disease; however, evidence is limited.[\[192\]](#) [\[270\]](#)
- Older adults with dementia are at a higher risk of mortality in the short term. Dementia patients are more likely to be vulnerable to having diseases such as hypertension, diabetes, and pneumonia, and be immunocompromised. The pooled mortality rate of patients with dementia was 39% compared with 20% in older adults without dementia.[\[271\]](#)
- In the UK, over one quarter of people who died with COVID-19 from March to June 2020 had dementia. Dementia and Alzheimer disease was the most common main preexisting health condition in deaths involving COVID-19 between March and June 2020.[\[272\]](#)
- A retrospective case-control study of electronic patient health records in the US found that patients with dementia were at increased risk of infection compared with patients without dementia. They also had significantly worse outcomes (6-month hospitalization risk and mortality risk) compared with patients with dementia but no COVID-19 and patients with COVID-19 but no dementia. The highest risk was seen in patients with vascular dementia.[\[273\]](#)

immunosuppression

- People who are immunocompromised may be at increased risk for severe disease; however, evidence is limited.[\[192\]](#)
- This includes people with a history of primary immune deficiencies or prolonged use of corticosteroids or other immunosuppressant medications.
- Glucocorticoid exposure of ≥ 10 mg/day (prednisone) has been associated with a higher odds of hospitalization in patients with rheumatologic disease.[\[274\]](#) Patients treated with cyclosporine/tacrolimus also had an increased risk for hospitalization; however, it was not clear whether the increased risk is related to the drug itself, the underlying condition for which the patient is treated, or other factors.[\[275\]](#)
- Immunosuppressed patients are not at significantly increased risk of infection compared with the general population.[\[276\]](#)
- Also see HIV infection and Autoimmune disease below.

HIV infection

- People living with HIV may be at increased risk for severe disease; however, evidence is limited.[\[192\]](#)
- It is still unclear whether HIV infection influences infection and disease course. Observational studies report conflicting results. A retrospective cohort study in the UK found that people with HIV appear to be at increased risk for mortality.[\[277\]](#) A retrospective cohort study in New York found that while people with HIV do not appear to be at increased risk of infection, they are at increased risk for poor

outcomes (mainly higher rates of severe disease requiring hospitalization) compared with people living without diagnosed HIV infection. Hospitalization risk increased with progression of HIV disease stage.[278] HIV infection was not independently associated with poor outcomes among hospitalized patients in Zambia; however, patients with severe HIV disease were more likely to develop severe disease or die compared with those with controlled HIV disease.[279]

- Evidence from meta-analyses is also conflicting. One meta-analysis found that HIV infection was not associated with composite poor outcome.[280] However, other meta-analyses have found that people living with HIV infection have an increased risk for infection and mortality compared with people without HIV. People on tenofovir disoproxil-based regimens may have a lower risk of infection and poor outcomes; however, evidence is inconclusive.[281] [282] [283]
- Despite the conflicting evidence, the World Health Organization states that HIV infection appears to be a significant independent risk factor for severe or critical disease at hospital admission and in-hospital mortality. HIV infection was independently associated with a higher risk of mortality compared with the HIV-negative population after adjusting for age, sex, disease severity, and underlying conditions. Age >65 years, male sex, and the presence of diabetes or hypertension were risk factors for severe or critical illness at hospital admission, as well as in-hospital mortality. Data were predominantly from South Africa, which may limit the generalizability of the results.[284]

substance use disorders

- People with substance use disorders may be at increased risk for severe disease; however, evidence is limited.[192] This includes alcohol, opioid, or cocaine use disorder.
- People with substance abuse disorders, especially those using drugs that affect the respiratory and cardiovascular systems, may be vulnerable to the adverse respiratory effects of COVID-19. Cohort studies have found substance use disorders were associated with increased hospitalization, intensive care unit admission, ventilator use, and mortality.[285] [286]
- People with opioid use disorder had higher odds of hospitalization, maximum length of hospital stay, and invasive mechanical ventilation compared with those without an opioid use disorder. However, patients did not appear to have an increased risk of mortality. Patients treated with methadone or buprenorphine appeared to have worse outcomes in terms of hospitalization and length of hospital stay, but better outcomes in terms of mortality risk and need for invasive mechanical ventilation compared with patients not receiving opioid agonist treatment.[287]

children with certain underlying conditions

- Children with certain underlying conditions may be at increased risk for severe disease; however, evidence is limited.[192]
- These conditions include obesity, diabetes, asthma and chronic lung disease, immunosuppression, and sickle cell disease. Children may also be at risk if they are medically complex; have serious genetic, neurologic, or metabolic disorders; or have congenital heart disease.[192]
- A cross-sectional study of over 43,000 children in the US found that the most commonly documented underlying conditions were obesity, asthma, neurodevelopmental disorders, anxiety and fear-related disorders, and depressive disorders. Children with type 1 diabetes, cardiac and circulatory congenital anomalies, obesity, hypertension, epilepsy, neuropsychiatric disorders, and asthma as well as children with chronic disease had higher risk of hospitalization and severe disease. Limited data suggest that children with congenital heart disease might be at increased risk of severe disease.[288]

Weak

chronic liver disease

- People with chronic liver disease, especially cirrhosis, may be at increased risk for severe disease; however, evidence is limited.[\[192\]](#)
- Chronic liver disease has been associated with an increased risk for severe disease and mortality.[\[289\]](#) The 30-day mortality rate is higher in patients with cirrhosis, with the main causes of death being respiratory complications and sudden worsening of liver function leading to end-stage liver disease.[\[290\]](#)
- People with metabolic dysfunction-associated fatty liver disease (nonalcoholic fatty liver disease) are at increased risk for severe disease.[\[291\]](#) [\[292\]](#) Disease severity has been associated with age <60 years and intermediate or high fibrosis-4 (FIB-4) scores.[\[293\]](#) [\[294\]](#)

vitamin D deficiency

- People with vitamin D deficiency may be at higher risk for infection and severe disease; however, evidence is limited.[\[295\]](#) [\[296\]](#)
- Meta-analyses have found that low serum vitamin D level is significantly associated with a higher risk of infection (people with vitamin D deficiency were 80% more likely to be infected), and increased risk for severe disease, hospitalization, and mortality.[\[297\]](#) [\[298\]](#) [\[299\]](#) [\[300\]](#) [\[301\]](#) However, it is unclear whether these associations were statistically significant and the certainty of evidence is very low.[\[302\]](#) [\[303\]](#)

proton-pump inhibitor use

- People taking proton-pump inhibitors (PPIs) may be at increased risk for severe disease; however, evidence is limited.[\[304\]](#)
- Data on whether PPI use increases the risk for infection is conflicting. The largest meta-analysis to date found that PPI use was not associated with an increased risk for infection.[\[305\]](#)
- Patients taking PPIs may be at increased risk for secondary infections, severe clinical outcomes, and death.[\[306\]](#) [\[307\]](#) [\[308\]](#) Current or regular users of PPIs were more likely to have severe outcomes compared with non-PPI users. Also, current PPI users were more likely to be hospitalized for longer compared with non-PPI users, although this was not statistically significant. Past use of PPIs is not associated with increased susceptibility to infection or severe outcomes.[\[309\]](#)
- A nationwide meta-analysis of over 80,000 cases in Denmark found that while current use of a proton-pump inhibitor may be associated with an increased risk of hospital admission, it was not associated with an increased risk for infection or severe outcomes. The authors concluded that conflicting results from previous studies may be more likely due to differences in study design and population.[\[310\]](#)

autoimmune disease

- People with autoimmune disease may be at higher risk for infection and severe disease; however, evidence is limited.[\[311\]](#)
- Autoimmune disease has been associated with an increased risk of infection. However, clinical outcomes were not considerably worse when compared with people without autoimmune disease. Use of corticosteroids increased the risk of infection and severe outcomes, and use of combination disease-modifying antirheumatic drugs (DMARDs) increased the risk of severe outcomes. DMARD monotherapy, particularly tumor necrosis factor inhibitors, reduced the risk of severe disease and mortality. Other factors associated with severe disease in this population include older age and the presence of comorbidities.[\[311\]](#)
- The overall seroprevalence and severity of infection in patients with immune-mediated inflammatory diseases (rheumatoid arthritis, axial spondyloarthritis, systemic lupus erythematosus, Sjogren

syndrome, and giant cell arteritis) across six European countries resembled that of the general population. Increased systemic inflammation may play a role in the occurrence of symptomatic disease in these patients, whereas biologic and targeted synthetic DMARDs appeared to be protective.[\[312\]](#) Most patients with systemic lupus erythematosus produced and maintained a serologic response beyond 30 weeks despite the use of a variety of immunosuppressants.[\[313\]](#)

- In patients with systemic autoimmune rheumatic diseases, patients may be at a higher risk of hospitalization, intensive care unit admission, kidney injury or acute renal failure, hyperinflammation, mechanical ventilation, and venous thromboembolism when compared with patients without systemic autoimmune rheumatic diseases.[\[314\]](#) [\[315\]](#) In patients with inflammatory rheumatic and musculoskeletal diseases, use of rituximab was associated with more severe disease but not an increased risk of mortality.[\[316\]](#)
- In patients with multiple sclerosis, neurologic disability, older age, Black race, cardiovascular comorbidities, recent treatment with corticosteroids, and obesity were risk factors for severe disease and mortality.[\[317\]](#) [\[318\]](#) Current evidence does not suggest that multiple sclerosis significantly increases the mortality rate. Highest hospitalization and mortality rates were in patients who were not on disease-modifying therapies, followed by those who were on B cell-depleting therapies (e.g., rituximab, ocrelizumab).[\[319\]](#)
- In patients with inflammatory bowel disease, infection risk was comparable to the general population, and patient outcomes (hospitalization, intensive care unit admission, and mortality) were worse in ulcerative colitis and patients on corticosteroids, thiopurines, aminosalicylates, or combination therapy. Outcomes were better in patients on biologic agents.[\[320\]](#) [\[321\]](#) [\[322\]](#) Seroprevalence, seroconversion, and the magnitude of anti-SARS-CoV-2 antibody reactivity was significantly attenuated in infliximab-treated patients compared with vedolizumab-treated patients in one study. This may increase the patient's susceptibility to reinfection.[\[323\]](#)

Parkinson disease

- People with Parkinson disease may be at higher risk for infection or severe disease; however, evidence is limited.[\[324\]](#) [\[325\]](#)
- Risk factors for infection may include obesity, pulmonary disease, and hospitalization. Vitamin D supplementation was associated with a lower risk of infection.[\[325\]](#)
- Parkinson disease was associated with severe disease, poor in-hospital outcomes, and mortality in one meta-analysis. However, the evidence for an association is still unclear. The association was influenced by age, but not by sex or the presence of dementia, hypertension, or diabetes.[\[324\]](#)

physical inactivity

- Physical inactivity may be associated with a higher risk for severe disease; however, evidence is limited.
- A retrospective observational study in nearly 50,000 patients found that patients with COVID-19 who were consistently inactive during the 2 years before the pandemic had a greater risk of hospitalization, intensive care unit admission, and death compared with patients who were consistently meeting physical activity guidelines or who were doing some level of physical activity. Other than older age and a history of organ transplant, physical inactivity was the strongest risk factor for severe disease outcomes in this study.[\[326\]](#)

dyslipidemia

- Dyslipidemia appears to be associated with an increased risk for severe disease and mortality; however, evidence is limited.[\[327\]](#) [\[328\]](#) [\[329\]](#)

- The association was stronger in males, older age, and those with hypertension.[330]
- Initially there was a concern that people on statins may be at increased risk of infection or more severe disease, as statins have been shown to increase ACE2 expression in animals and may promote the activation of the inflammatory pathway in acute respiratory distress syndrome.[267] However, so far, studies do not support this hypothesis, and studies have shown a protective effect (lower risk of mortality or severe disease).[331]

surgery

- Surgical mortality and complications may be higher in patients with COVID-19 compared with patients without COVID-19.[332]
- A retrospective study of 34 patients in China who underwent elective surgeries during the incubation period of COVID-19 found that all patients developed pneumonia after surgery. Approximately 44% of these patients required admission to the intensive care unit, and 20% died.[333]
- Postoperative pulmonary complications occur in half of patients with perioperative SARS-CoV-2 infection, and are associated with higher mortality, particularly in men and those ages 70 years and over.[334]

blood groups A and B

- People with blood group A may be at increased risk for infection and mortality, and people with blood group B may be at increased risk for infection; however, evidence is limited.[335]
- There is no evidence for an association between blood group AB and the risk of infection. Blood group O appears to be protective against infection; however, evidence is of low/very low quality. People who are Rh-positive were more vulnerable to infection compared with those who were Rh-negative.[335] [336]
- A genome-wide association study found that patients with blood group A are at 45% increased risk of respiratory failure compared with other blood groups. It also found a protective effect in blood group O. Two chromosomal loci were associated with respiratory failure, and one of these coincided with the ABO blood group locus.[337] The SARS-CoV-2 receptor-binding domain directly binds the blood group A antigen expressed on respiratory epithelial cells, directly linking blood group A and SARS-CoV-2.[338]

gut dysbiosis

- There is limited evidence that gut and lung microbiota dysfunction may be implicated in the pathogenesis of COVID-19.[339]
- Patients appear to have a depletion of beneficial commensals (e.g., *Eubacterium ventriosum*, *Eubacterium rectale*, *Faecalibacterium prausnitzii*, *Roseburia* and Lachnospiraceae taxa) and an overgrowth of opportunistic pathogens (e.g., *Clostridium hathewayi*, *Actinomyces viscosus*, *Bacteroides nordii*) during hospitalization.[340] [341] [342] Associations between gut microbiota composition, levels of cytokines, and inflammatory markers in patients with COVID-19 suggest that the gut microbiome is involved in disease severity, possibly via modulating host immune responses. Gut dysbiosis after disease resolution may contribute to persistent symptoms.[343]

environmental factors

- Climate and latitude: limited evidence suggests that cold and dry conditions and higher latitude may increase transmission, and warm and humid conditions may reduce the rate of infections; however, evidence is conflicting and is not sufficient to prove causation.[344] [345] [346] [347] [348] [349] [350]

- Air pollution: limited evidence suggests an association between exposure to ambient air pollution and COVID-19; however, evidence is not sufficient to prove causation.[\[351\]](#) [\[352\]](#) [\[353\]](#) [\[354\]](#)
- Residence in urban or deprived areas: limited evidence suggests that the prevalence was greater in people living in urban areas compared with people living in rural areas, and in people living in more deprived areas compared with people living in less deprived areas.[\[171\]](#) [\[355\]](#)

Investigations

1st test to order

Test	Result
<p>real-time reverse transcription polymerase chain reaction (RT-PCR)</p> <ul style="list-style-type: none"> Order an RT-PCR for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in patients with suspected infection whenever possible (see the Criteria section).^[536] Commonly used assays are expected to be able to detect SARS-CoV-2 variants.^[168] However, some tests may be impacted by variants.^[577] The US Food and Drug Administration has warned that false-negative results may occur with any molecular test for the detection of SARS-CoV-2 if a mutation occurs in the part of the virus' genome assessed by that test. Multiple genetic targets to determine a final result are less likely to be impacted by increased prevalence of genetic variants. Consider negative results in combination with clinical observations, patient history, and epidemiologic information.^[694] Molecular testing is an aid to diagnosis only. The World Health Organization recommends that healthcare providers consider a positive or negative result in combination with specimen type, clinical observations, patient history, and epidemiologic information. Where a test result does not correspond with the clinical presentation, a new specimen should be taken and retested using the same or a different molecular test.^[576] Base decisions about who to test on clinical and epidemiologic factors.^[536] Consult local health authorities for guidance as testing priorities depend on local recommendations and available resources. The World Health Organization recommends testing all people who meet the suspected case definition of COVID-19, regardless of vaccination status or disease history. When resources are constrained, people who are at risk of developing severe disease, healthcare workers, inpatients, and the first symptomatic individuals in the setting of a suspected outbreak should be prioritized. Testing of asymptomatic individuals is currently recommended only for specific groups including contacts of confirmed or probable cases and frequently exposed groups such as healthcare workers and long-term care facility workers.^[578] In the UK, testing is recommended in: (1) people with symptoms of new continuous cough, high temperature, or altered sense of smell/taste; (2) people with acute respiratory infection, influenza-like illness, clinical or radiologic evidence of pneumonia, or acute worsening of underlying respiratory illness, or fever without another cause (whether presenting in primary or secondary care).^[579] In the US, testing is recommended in: (1) anyone with signs or symptoms consistent with COVID-19; (2) asymptomatic unvaccinated people identified through contact tracing efforts; (3) asymptomatic unvaccinated people with recent known or suspected exposure to SARS-CoV-2, including those who have been in close contact (less than 6 feet [2 meters] for a total of 15 minutes or more over a 24-hour period) with a person with documented infection; (4) asymptomatic unvaccinated people without recent known or suspected exposure to SARS-CoV-2 for early identification, isolation, and disease prevention 	<p>positive for SARS-CoV-2 viral RNA; may be positive for influenza A and B viruses and other respiratory pathogens</p>

Test	Result
<p>(only when screening testing is recommended by public health officials).[580]</p> <ul style="list-style-type: none"> • The American Academy of Pediatrics recommends testing children with symptoms consistent with COVID-19, children in close contact with an individual with probable or confirmed infection, and children who require screening based on recommendations from public health authorities or other situations (e.g., prior to a medical procedure such as elective surgery or as a school or workplace requirement). The decision to test does not differ by the age of the child. Testing is not recommended for other illnesses that lack shared symptoms (e.g., urinary tract infection, cellulitis), or for children exposed to close contacts of infected individuals unless those contacts are symptomatic or other criteria are met.[581] • The optimal specimen for testing depends on the clinical presentation and the time since symptom onset. The World Health Organization recommends upper respiratory specimens (nasopharyngeal and/or oropharyngeal swabs) for early-stage infections, especially asymptomatic or mild cases, and lower respiratory specimens (sputum and/or endotracheal aspirate or bronchoalveolar lavage in patients with more severe respiratory disease) for later-stage infections or patients in whom there is a strong suspicion for infection and their upper respiratory tract specimen test was negative. Other specimens (e.g., nasal mid-turbinate swab, anterior nares swab, nasopharyngeal/nasal wash/aspirate, saliva, fecal) may be recommended in some circumstances; consult local guidance.[536] [591] [589] Meta-analyses of paired saliva samples and nasopharyngeal swabs found no statistically significant difference in sensitivity or specificity between these specimens for SARS-CoV-2 detection, especially in the ambulatory setting. Sensitivity was not significantly different among asymptomatic people and outpatients. Methods of saliva collection may affect sensitivity. Meta-analyses demonstrate that saliva is as valid as nasopharyngeal sampling for the detection of SARS-CoV-2 infections in symptomatic and asymptomatic patients. Saliva sampling is simple, fast, noninvasive, inexpensive, and painless.[583] [584] [585] [586] [587] [588] • A positive RT-PCR result confirms SARS-CoV-2 infection (in the context of the limitations associated with RT-PCR testing). If the result is negative, and there is still a clinical suspicion of infection (e.g., an epidemiologic link, typical x-ray findings, absence of another etiology), resample the patient and repeat the test. A positive result confirms infection. If the second test is negative, consider serologic testing (see below).[536] • The pooled sensitivity has been estimated to be 87.8%, with the specificity estimated to be in the range of 87.7% to 100%.[597] • Interpret test results with caution. Evidence for the use of RT-PCR in the diagnosis of COVID-19 is still emerging, and uncertainties about its efficacy and accuracy remain.[597] It is not fully understood whether a positive result always represents infectious virus, especially at high cycle thresholds.[598] [601] [602] [603] Interpreting the result depends on the accuracy of the test itself, and the pre- and post-test probabilities of disease.[600] When the pretest probability is low, positive results should be interpreted with caution, and ideally a second specimen tested for confirmation.[604] The lower the prevalence of disease in a given population, the lower the post-test probability.[605] False-positive results can be caused by a laboratory error or a cross-reaction with antibodies formed by current 	

Test	Result
<p>and past exposure to seasonal human coronavirus infections (e.g., common cold), and are more likely when the prevalence of disease is moderate to low.[607] [608] Preliminary estimates of the false-positive rate in the UK are in the range of 0.8% to 4%.[609] False-negative rates of between 2% and 29% have been reported.[600] A systematic review found that the false-negative rate varied across studies from 1.8% to 58% (median 11%); however, there was substantial and largely unexplained heterogeneity across studies.[610]</p> <ul style="list-style-type: none"> • Rapid molecular tests are available. They may be suitable for some testing scenarios (e.g., where obtaining test results within 2 hours will enable appropriate decision-making); however, evidence is limited.[624] • Also collect nasopharyngeal swabs to rule out influenza and other respiratory infections according to local guidance. It is important to note that coinfections can occur, and a positive test for a non-COVID-19 pathogen does not rule out COVID-19.[2] [596] When SARS-CoV-2 and influenza viruses are cocirculating, test for both viruses in all hospitalized patients with acute respiratory illness, and only test for influenza virus in outpatients with acute respiratory illness if the results will change clinical management of the patient.[533] Single-test multiplex assays to diagnose infection caused by influenza A, influenza B, and SARS-CoV-2 are available in some countries. 	
<p>pulse oximetry</p> <ul style="list-style-type: none"> • Clinicians should be aware that patients with COVID-19 can develop "silent hypoxia": their oxygen saturations can drop to low levels and precipitate acute respiratory failure without the presence of obvious symptoms of respiratory distress.[563] • Pulse oximetry may be available as part of remote monitoring in the community. Evidence suggests that patients who may benefit most from monitoring are those who are symptomatic and are either over 65 years of age, or are under 65 years of age and are extremely clinically vulnerable to COVID-19. [NHS England: pulse oximetry to detect early deterioration of patients with COVID-19 in primary and community care settings] (https://www.england.nhs.uk/coronavirus/publication/pulse-oximetry-to-detect-early-deterioration-of-patients-with-covid-19-in-primary-and-community-care-settings) • The UK National Institute for Health and Care Excellence recommends using oxygen saturation levels below 94% for adults (or below 88% for adults with known type 2 respiratory failure) and below 91% for children in room air at rest to identify people who are seriously ill.[564] • Pulse oximeters may exhibit suboptimal accuracy in certain populations. Limited data from studies with small numbers of participants suggest that skin pigmentation can affect pulse oximeter accuracy. In one study, occult hypoxemia (defined in the study as arterial oxygen saturation <88% by arterial blood gas despite oxygen saturation of 92% to 96% on pulse oximetry) was not detected by pulse oximetry nearly three times more frequently in Black patients compared with White patients.[565] The US Food and Drug Administration (FDA) has warned that multiple factors can affect the accuracy of a pulse oximeter reading (e.g., poor circulation, skin pigmentation, skin thickness, skin temperature, current tobacco use, use of fingernail polish). The FDA recommends considering accuracy limitations when using a pulse oximeter to assist in diagnosis and 	<p>may show low oxygen saturation (cut-off depends on local guidelines)</p>

Test	Result
<p>treatment decisions, and to use trends in readings over time rather than absolute cut-offs if possible.[566]</p> <ul style="list-style-type: none"> Only a small proportion of patients have other organ dysfunction, meaning that after the initial phase of acute deterioration, traditional methods of recognizing further deterioration (e.g., National Early Warning Score 2 [NEWS2] scores) may not help predict those patients who go on to develop respiratory failure.[563] Pulse oximeters can be used at home to detect hypoxia. Home pulse oximetry requires clinical support (e.g., regular phone contact from a health professional in a virtual ward setting). [BMJ Practice Pointer: remote management of covid-19 using home pulse oximetry and virtual ward support] (https://www.bmj.com/content/372/bmj.n677) 	
<p>ABG</p> <ul style="list-style-type: none"> Order in patients with severe illness as indicated to detect hypercarbia or acidosis. Recommended in patients with respiratory distress and cyanosis who have low oxygen saturation ($\text{SpO}_2 < 90\%$). 	<p>may show low partial oxygen pressure</p>
<p>CBC</p> <ul style="list-style-type: none"> Order in patients with severe illness. Lymphopenia, leukocytosis, thrombocytopenia, decreased eosinophils, decreased hemoglobin, and high neutrophil-to-lymphocyte ratio are significantly associated with severe disease, and may be useful for predicting disease progression. Severe cases are more likely to present with lymphopenia and thrombocytopenia, but not leukopenia.[695] Elevated red blood cell distribution width (at admission and increasing during hospitalization) has been associated with a significantly increased risk of mortality in hospitalized patients.[696] Absolute counts of major lymphocyte subsets, particularly CD4+ and CD8+ T-cell counts, are significantly decreased in patients with severe disease.[697] Late-phase thrombocytopenia (i.e., occurring 3 weeks or more after symptom onset) has been reported but is uncommon.[698] 	<p>lymphopenia; leukocytosis; leukopenia; thrombocytopenia; decreased eosinophils; decreased hemoglobin</p>
<p>comprehensive metabolic panel</p> <ul style="list-style-type: none"> Order in patients with severe illness. Elevated liver enzymes, total bilirubin, creatinine, and blood urea nitrogen, and hypoalbuminemia are significantly associated with severe disease, and may be useful for predicting disease progression.[695] Hypokalemia has been reported in 54% of patients.[699] Hypocalcemia has been reported in 63% of patients, and is associated with poor outcomes.[700] [701] Hyponatremia has been reported in 24% of patients, and is associated with poor outcomes.[702] Other electrolyte derangements may be present. 	<p>elevated liver enzymes; elevated total bilirubin; renal impairment; hypoalbuminemia; electrolyte derangements</p>
<p>blood glucose level</p> <ul style="list-style-type: none"> Order in patients with severe illness. Fasting hyperglycemia independently predicts poor prognosis and is associated with an increased risk of mortality, regardless of whether or not the patient has diabetes.[703] [704] Hypoglycemia has also been associated with increased mortality in a retrospective cohort study.[705] 	<p>variable</p>

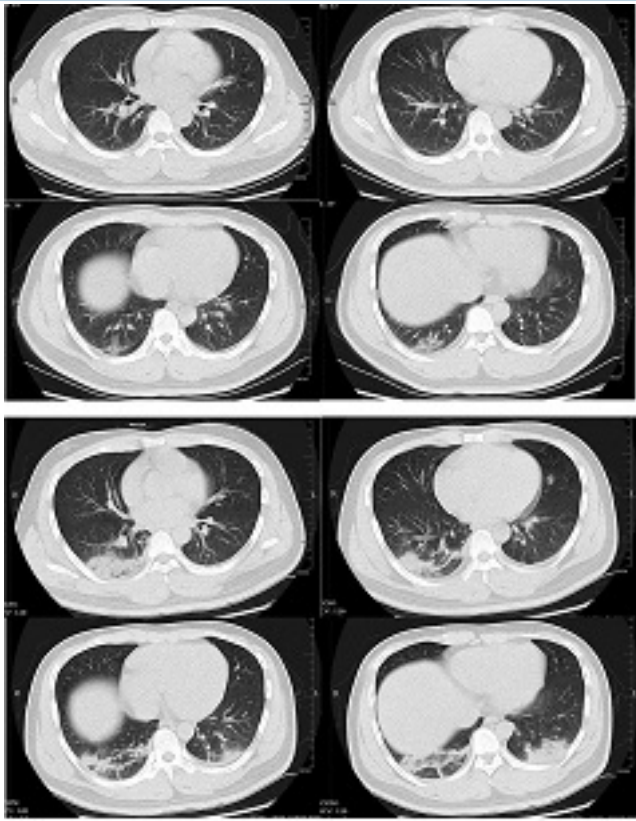
Test	Result
coagulation screen <ul style="list-style-type: none"> Order in patients with severe illness. Elevated D-dimer, elevated fibrinogen (and fibrin degradation product), and prolonged prothrombin time are significantly associated with severe disease, and may be useful for predicting disease progression.[695] [706] The risk of severe disease and mortality is 2-fold and 4-fold higher, respectively, in patients with elevated D-dimer levels.[707] Patients with very high D-dimer levels have an increased risk of thrombosis.[708] [709] 	elevated D-dimer; prolonged prothrombin time; elevated fibrinogen
cardiac biomarkers <ul style="list-style-type: none"> Order in patients with severe illness. Elevated creatine kinase-myocardial band (CK-MB), B-type natriuretic peptide (BNP), N-terminal proBNP (NT-proBNP), and troponin are associated with severe disease and mortality, and may be useful for predicting disease progression or survival.[710] CK-MB has been found to be elevated in mild disease in children. The significance of this is unknown.[572] 	may be elevated
serum C-reactive protein <ul style="list-style-type: none"> Order in patients with severe illness. Elevated C-reactive protein is significantly associated with severe disease, and may be useful for predicting disease progression.[695] Patients with elevated C-reactive protein at the time of initial presentation were more likely to have acute kidney injury, venous thromboembolism, critical illness, and in-hospital mortality during their hospital stay compared with patients with lower levels.[711] 	may be elevated
serum erythrocyte sedimentation rate <ul style="list-style-type: none"> Order in patients with severe illness. Commonly elevated in patients with COVID-19.[570] 	may be elevated
serum lactate dehydrogenase <ul style="list-style-type: none"> Order in patients with severe illness. Elevated serum lactate dehydrogenase is significantly associated with severe disease, and may be useful for predicting disease progression.[695] 	may be elevated
serum interleukin-6 level <ul style="list-style-type: none"> Order in patients with severe illness. Elevated interleukin-6 level is significantly associated with severe disease, and may be useful for predicting disease progression.[695] Less likely to be elevated in children.[712] 	may be elevated
serum procalcitonin <ul style="list-style-type: none"> Order in patients with severe illness. Elevated serum procalcitonin is significantly associated with severe disease, and may be useful for predicting disease progression.[695] Elevated serum procalcitonin may be more common in children.[560] May be elevated in patients with secondary bacterial infection.[50] [51] There is insufficient evidence to recommend routine procalcitonin testing to guide decisions about the use of antibiotics. However, it may be helpful in identifying whether there is a bacterial 	may be elevated

Test	Result
infection, although the most appropriate procalcitonin threshold is uncertain. [564]	
serum ferritin level <ul style="list-style-type: none"> Order in patients with severe illness. Elevated ferritin is significantly associated with severe disease, and may be useful for predicting disease progression.[713] May indicate development of cytokine release syndrome.[714] 	may be elevated
serum amyloid A level <ul style="list-style-type: none"> Order in patients with severe illness. Levels increase in severe disease; therefore, it may be useful as a biomarker for predicting disease progression.[715] 	may be elevated
serum creatine kinase and myoglobin <ul style="list-style-type: none"> Order in patients with severe illness. Elevated serum creatine kinase and myoglobin are significantly associated with severe disease, and may be useful for predicting disease progression.[695] 	may be elevated
blood and sputum cultures <ul style="list-style-type: none"> Collect blood and sputum specimens for culture in patients with severe or critical disease to rule out other causes of lower respiratory tract infection and sepsis, especially patients with an atypical epidemiologic history.[2] Specimens should be collected prior to starting empiric antimicrobials if possible. 	negative for bacterial infection
chest x-ray <ul style="list-style-type: none"> Order in all patients with suspected pneumonia. Unilateral lung infiltrates are found in 25% of patients, and bilateral lung infiltrates are found in 75% of patients.[50] [51] [628] Chest x-ray is moderately sensitive and moderately specific for the diagnosis of COVID-19. Pooled results found that chest x-ray correctly diagnosed COVID-19 in 80.6% of people who had the disease. However, it incorrectly identified COVID-19 in 28.5% of people who did not have the disease.[629] Although chest x-ray appears to have a lower sensitivity compared with chest CT, it has the advantages of being less resource-intensive, associated with lower radiation doses, easier to repeat sequentially, and portable.[630] 	unilateral or bilateral lung infiltrates

Other tests to consider

Test	Result
<p>computed tomography (CT) chest</p> <ul style="list-style-type: none"> Consider a CT scan of the chest. Consult local guidance on whether to perform a CT scan. The British Society of Thoracic Imaging (BSTI) recommends CT imaging in patients with clinically suspected COVID-19 who are seriously ill if chest x-ray is uncertain or normal. [BSTI: radiology decision tool for suspected COVID-19] (https://www.bsti.org.uk/media/resources/files/NHSE_BSTI_APPROVED_Radiology_on_CoVid19_v6_modified1_Read-Only.pdf) Some institutions in the UK recommend a more pragmatic approach for patients with high clinical suspicion of COVID-19, with chest CT recommended only after two indeterminate or normal chest x-rays in combination with a negative RT-PCR test.[632] The American College of Radiology recommends reserving CT for hospitalized, symptomatic patients with specific clinical indications for CT, and emphasizes that a normal chest CT does not mean that a patient does not have COVID-19 and that an abnormal chest CT is not specific for COVID-19 diagnosis.[633] Chest CT is sensitive and moderately specific for the diagnosis of COVID-19. Pooled results found that chest CT correctly diagnosed COVID-19 in 87.9% of people who had the disease. However, it incorrectly identified COVID-19 in 20% of people who did not have the disease. Therefore, chest CT may have more utility for excluding COVID-19 than for differentiating it from other causes of respiratory illness.[629] Accuracy appears to be lower among children; however, there are limited data in this population.[631] Evidence of pneumonia on CT may precede a positive RT-PCR result for SARS-CoV-2 in some patients.[634] Some patients may present with a normal chest finding despite a positive RT-PCR.[635] Results of RT-PCR testing may be false-negative, so patients with typical CT findings should have repeat RT-PCR testing to confirm the diagnosis.[636] CT imaging abnormalities may be present in asymptomatic patients. The pooled estimate of the rate of positive chest CT findings in asymptomatic cases was 47.6% (mainly ground-glass opacity).[637] Abnormal chest CT findings have been reported in up to 97% of hospitalized patients.[639] The most common findings are ground-glass opacity, either in isolation or coexisting with other findings such as consolidation, interlobular septal thickening, or crazy-paving pattern. The most common distribution pattern is bilateral, peripheral/subpleural, posterior distribution of the opacities, with a lower lobe predominance. Extensive/multilobar involvement with consolidations is more common in older patients and those with severe disease. Pulmonary vascular enlargement, interlobular or intralobular septal thickening, adjacent pleural thickening, air bronchograms, subpleural lines, crazy-paving pattern, bronchus distortion, bronchiectasis, vacuolar retraction sign, and halo sign are atypical features. Pleural effusion, pericardial effusion, cavitation, pneumothorax, and mediastinal lymphadenopathy have also been reported rarely.[640] Ground-glass opacity has the highest diagnostic performance for COVID-19 pneumonia, followed by ground-glass opacity plus consolidation, and consolidation only.[641] Children frequently have normal or mild CT chest findings. The most common signs in children are patchy ground-glass opacity and, less frequently, nonspecific patchy shadows, areas of consolidation, and a 	<p>ground-glass opacity in isolation or coexisting with other findings (e.g., consolidation, interlobular septal thickening, crazy-paving pattern); bilateral, peripheral/subpleural, posterior distribution with a lower lobe predominance</p>

Test	Result
<p>halo sign. Abnormalities are more common in the lower lobes and are predominantly unilateral. Pleural effusion is rare.[644] Ground-glass opacity and peribronchial thickening were the most prevalent findings in infants younger than 1 year of age.[645]</p> <ul style="list-style-type: none"> • CT scan generally shows an increase in the size, number, and density of ground-glass opacities in the early follow-up period, with a progression to mixed areas of ground-glass opacities, consolidations, and crazy paving peaking at day 10 to 11, before gradually resolving or persisting as patchy fibrosis.[640] • The positive predictive value was low (1.5% to 30.7%) in low-prevalence regions, and the negative predictive value ranged from 95.4% to 99.8% in one meta-analysis. Pooled sensitivity and specificity were 94% to 96% and 37%, respectively.[716] [717] The simultaneous presence of ground-glass opacity and other features of viral pneumonia had optimum performance in the detection of COVID-19 (sensitivity 90% and specificity 89%).[642] • CT is more sensitive than RT-PCR in detecting COVID-19, but has a very low specificity.[718] In a cohort of over 1000 patients in a hyperendemic area in China, chest CT had a higher sensitivity for diagnosis of COVID-19 compared with initial RT-PCR from swab samples (88% versus 59%). Improvement of abnormal CT findings also preceded change from RT-PCR positivity to negativity in this cohort during recovery. The sensitivity of chest CT was 97% in patients who ultimately had positive RT-PCR results. However, in this setting, 75% of patients with negative RT-PCR results also had positive chest CT findings. Of these patients, 48% were considered highly likely cases, while 33% were considered probable cases.[719] 	

Test	Result
 <p><i>Transverse CT scans from a 32-year-old man, showing ground-glass opacity and consolidation of lower lobe of right lung near the pleura on day 1 after symptom onset (top panel), and bilateral ground-glass opacity and consolidation on day 7 after symptom onset</i> <i>Xu XW et al. BMJ. 2020;368:m606</i></p>	
<p>serology</p> <ul style="list-style-type: none"> • Important: a positive test for spike protein IgM or IgG could indicate either prior infection or prior vaccination with a COVID-19 vaccine. To evaluate for evidence of prior infection in an individual who has received a vaccine, a test that specifically evaluates IgM or IgG to the nucleocapsid protein should be used. A positive nucleocapsid protein-based assay indicates prior infection. Antibody testing is not currently recommended to assess immunity following vaccination.[356] [720] [721] [359] • Cannot be used as a standalone diagnostic for acute infections; however, may be useful in various settings (e.g, negative molecular testing, diagnosing patients with late presentation or prolonged symptoms, serosurveillance studies).[536] [612] • [BMJ practice pointer: testing for SARS-CoV-2 antibodies] (https://www.bmj.com/content/370/bmj.m3325) • The World Health Organization (WHO) recommends collecting a paired serum sample, one specimen in the acute phase and one in the convalescent phase 2 to 4 weeks later, in patients where infection is strongly suspected and the RT-PCR result is negative. Seroconversion or a rise in antibody titers in paired sera help to confirm whether the infection is recent and/or acute. If the initial sample tests positive, this could be due to a past infection that is not related to the current illness. Seroconversion may be faster and more robust in patients with severe disease compared with those with mild disease or asymptomatic infection.[536] 	<p>positive for SARS-CoV-2 virus antibodies; seroconversion or a rise in antibody titers in paired sera</p>

Test	Result
<ul style="list-style-type: none"> • The Centers for Disease Control and Prevention recommends serologic testing as a method to support the diagnosis of illness or complications in the following situations: a positive antibody test at least 7 days following acute illness onset in people with a previous negative antibody test (i.e., seroconversion) and who did not receive a positive viral test may indicate SARS-CoV-2 infection between the dates of the negative and positive antibody tests; a positive antibody test can help support a diagnosis when patients present with complications of COVID-19 illness, such as multisystem inflammatory syndrome and other post-acute sequelae of COVID-19.[613] • The Infectious Diseases Society of America recommends serologic testing in the following circumstances: evaluation of patients with a high clinical suspicion for infection when molecular diagnostic testing is negative and at least 2 weeks have passed since symptom onset; evaluation of pediatric inflammatory multisystem syndrome in children; and serosurveillance studies.[614] • Antibody responses to SARS-CoV-2 typically occur during the first 1 to 3 weeks of illness, with the seroconversion time of IgG antibodies often being earlier than that of IgM antibodies.[615] [616] • The estimated sensitivity of antibody tests ranged from 18.4% to 96.1% (the lowest reported sensitivity was from a point-of-care test, although a sensitivity <50% was reported for one laboratory test), and specificity ranged from 88.9% to 100%. Estimates of diagnostic accuracy need to be interpreted with caution in the absence of a definitive reference standard to diagnose or rule out COVID-19.[597] • Limitations of testing: serologic testing cannot be used to determine acute infection; results do not indicate the presence or absence of current or previous infection with certainty; reliable diagnosis is often only possible in the recovery phase when opportunities for management or interruption of transmission have passed; cross-reactivity with other coronaviruses, which can result in false-positive results.[536] [613] • While rapid antibody detection kits have been approved for the qualitative detection of SARS-CoV-2 IgG/IgM antibodies in serum, plasma, or whole blood, the WHO does not recommend the use of these tests outside of research settings as they have not been validated as yet.[618] 	
<p>antigen test</p> <ul style="list-style-type: none"> • Rapid diagnostic test. Relies on direct detection of SARS-CoV-2 viral proteins in nasal swabs and other respiratory specimens using a lateral flow immunoassay. Results are usually available in less than 30 minutes. While antigen tests are substantially less sensitive than RT-PCR, they offer the possibility of rapid, inexpensive, and early detection of the most infectious cases in appropriate settings. If used, testing should occur within the first 5 to 7 days following the onset of symptoms. The World Health Organization recommends antigen testing only in certain scenarios where RT-PCR is unavailable or where prolonged turnaround times preclude clinical utility, provided that the test meets the minimum performance requirements of ≥80% sensitivity and ≥97% specificity compared with an RT-PCR reference assay.[620] • The Infectious Diseases Society of America recommends antigen testing in some individuals only when molecular testing is not readily available or is logistically infeasible, noting that the overall quality of available evidence supporting its use was graded as very low to moderate.[621] 	<p>positive for SARS-CoV-2 virus antigen</p>

Test	Result
<ul style="list-style-type: none"> • The Centers for Disease Control and Prevention recommends antigen tests may be used in congregate and community settings; however, confirmatory molecular testing may be needed.^[622] • The US Food and Drug Administration has warned that false-positive results can occur with antigen tests, including when users do not follow the instructions for use, and that the number of false-positive tests increases as disease prevalence decreases.^[623] The agency has also recommended not using certain tests due to performance issues.^[722] • A Cochrane review found that rapid antigen tests vary in sensitivity. Sensitivity was higher in the first week after symptom onset in symptomatic people (78.3%), compared with the second week of symptoms (51%). Sensitivity was higher in those with RT-PCR cycle threshold values ≤ 25 (94.5%), compared with those with cycle threshold values > 25 (40.7%). Sensitivity was higher in symptomatic people (72%), compared with asymptomatic people (58.1%). Sensitivity also varied between brands of tests. Positive predictive values suggest that confirmatory testing of those with positive results may be considered in low prevalence settings. Evidence for testing in asymptomatic cohorts was limited, and no studies assessed the accuracy of repeated lateral flow testing or self-testing.^[624] • An observational cohort study that assessed the performance of rapid antigen lateral flow testing against RT-PCR in an asymptomatic general population in the UK found that the lateral flow test can be useful for detecting infections among asymptomatic adults, particularly those with a high viral load who are likely to be infectious. Lateral flow tests showed a sensitivity of 40%, specificity of 99.9%, positive predictive value of 90.3%, and negative predictive value of 99.2% in this population. Approximately 10% of people with a higher viral load detected by RT-PCR were missed by lateral flow tests.^[625] • Rapid antigen testing appears to be a reliable diagnostic tool to quickly detect persons with a high viral load, and can help to detect and isolate potential superspreaders before RT-PCR results are available. However, testing is unsuccessful in detecting persons with lower viral load and asymptomatic patients.^[626] • Rapid, lateral flow antigen tests for home use are available over-the-counter in some countries.^[723] • Laboratory-based (nonrapid) antigen tests are also available in some countries. • Recommendations for the use of lateral flow tests differ between countries. For example, in the UK, lateral flow tests are only currently recommended for patients without symptoms.^[724] Consult local guidance for more information. • [BMJ: interpreting a lateral flow SARS-CoV-2 antigen test] (https://www.bmj.com/content/373/bmj.n1411) 	

Emerging tests

Test	Result
reverse transcription loop-mediated isothermal amplification (RT-LAMP) <ul style="list-style-type: none"> A similar process to RT-PCR, but uses constant temperatures and produces more viral DNA compared with RT-PCR. While simple and quick, it is a newer technology and there is less evidence for its use. Assays for SARS-CoV-2 have been developed and are being evaluated.[646] [647] [648] A sensitivity of 95.5% and specificity of 99.5% has been reported.[649] An at-home test kit that provides rapid results within 30 minutes has been approved in the US under an emergency-use authorization for self-testing at home that provides rapid results.[725] 	positive for SARS-CoV-2 viral RNA
lung ultrasound <ul style="list-style-type: none"> Lung ultrasound is used as a diagnostic tool in some centers as an alternative to chest x-ray and chest CT. Although there is only very low-certainty evidence supporting its diagnostic accuracy, it might be helpful as a supplemental or alternate imaging modality.[630] Ultrasound is sensitive but not specific for the diagnosis of COVID-19. Pooled results found that lung ultrasound correctly diagnosed COVID-19 in 86.4% of people with the disease. However, it incorrectly diagnosed COVID-19 in 45% of people who did not have the disease. Therefore, ultrasound may have more utility for excluding COVID-19 than for differentiating it from other causes of respiratory illness.[629] B-lines are the prominent pattern in patients with COVID-19, occurring with a pooled frequency of 97%. Pleural line abnormalities are also common with a pooled frequency of 70%. While these findings are not specific for COVID-19, they increase the likelihood of disease in the context of a characteristic clinical presentation. Other findings include consolidations, pleural thickening, and pleural effusion.[650] Has the advantages of portability, bedside evaluation, reduced healthcare worker exposure, easier sterilization process, absence of ionizing radiation exposure, and repeatability during follow-up. It may also be more readily available in resource-limited settings. However, it also has some limitations (e.g., it is unable to discern chronicity of a lesion) and other imaging modalities may be required.[650] May be used in pregnant women and children.[651] [652] Possible roles include: reducing nosocomial transmission; monitoring progress of patients; and a possible role in subpopulations who are vulnerable but are not suitable for CT (e.g., pregnant women).[653] Lung ultrasound score may play a role in prognosis.[654] [BSTI: lung ultrasound (LUS) for COVID-19 patients in critical care areas] (https://www.bsti.org.uk/media/resources/files/Lung_US_print_out_and_scoring_proforma.pdf) 	B-lines; pleural line abnormalities
calprotectin <ul style="list-style-type: none"> Calprotectin is an emerging biomarker of interest. Calprotectin levels often increase following infection or trauma, and in inflammatory disease. Serum/fecal calprotectin levels have been demonstrated to be significantly elevated in COVID-19 patients with severe disease, and it may have prognostic significance.[655] 	elevated

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Community-acquired pneumonia	<ul style="list-style-type: none"> • Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset. • Differentiating COVID-19 from community-acquired bacterial pneumonia is not usually possible from signs and symptoms. However, patients with bacterial pneumonia are more likely to have rapid development of symptoms and purulent sputum. They are less likely to have myalgia, anosmia, or pleuritic pain.[726] 	<ul style="list-style-type: none"> • Blood or sputum culture or molecular testing: positive for causative organism. • RT-PCR: negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral RNA (coinfections are possible). • CT chest: centrilobular nodules, mucoid impactions.[727]
Influenza infection	<ul style="list-style-type: none"> • Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset. • Differentiating COVID-19 from community-acquired respiratory tract infections is not possible from signs and symptoms. • Incubation period is shorter.[728] Symptoms typically peak during the first 3 to 7 days of illness with influenza, compared with week 2 or 3 of illness with COVID-19.[729] • More common in children.[729] Children with COVID-19 tend to be older, and are more likely to have comorbidities, fever, gastrointestinal symptoms, headache, and chest pain compared with those with influenza.[730] • Fever is less common. Rhinorrhea, sore throat, myalgia, headache, and dyspnea are more 	<ul style="list-style-type: none"> • Only testing can distinguish between influenza infection and COVID-19 and identify coinfection. When SARS-CoV-2 and influenza viruses are cocirculating, test for both viruses in all hospitalized patients with acute respiratory illness, and only test for influenza virus in outpatients with acute respiratory illness if the results will change clinical management of the patient.[733] • RT-PCR: positive for influenza A or B viral RNA; negative for SARS-CoV-2 viral RNA (coinfections are possible). • Chest x-ray: less likely to be abnormal.[728] • CT chest: there is emerging evidence that CT can be used for differentiating between influenza and COVID-19. COVID-19 patients are more likely to have rounded or linear opacities, crazy-paving sign, vascular enlargement, and interlobular septal

Condition	Differentiating signs / symptoms	Differentiating tests
	common.[728] [731] New-onset smell and/or taste disorders were less common in a case-control study.[732]	<ul style="list-style-type: none"> thickening, but less likely to have nodules, tree-in-bud sign, bronchiectasis, and pleural effusion.[734] [735] Inflammatory markers and coagulation screen: there is emerging evidence that inflammatory markers (lactate dehydrogenase, erythrocyte sedimentation rate, C-reactive protein) and coagulation parameters are not as high in patients with influenza compared with COVID-19.[736]
Common cold	<ul style="list-style-type: none"> Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset. Differentiating COVID-19 from community-acquired respiratory tract infections is not possible from signs and symptoms. However, fever is less common, and headache, rhinorrhea, myalgia, and sore throat are more common. Patients may have a greater number of general symptoms.[731] 	<ul style="list-style-type: none"> RT-PCR: positive for causative organism; negative for SARS-CoV-2 viral RNA (coinfections are possible).
Other viral or bacterial respiratory infections	<ul style="list-style-type: none"> Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset. Differentiating COVID-19 from community-acquired respiratory tract infections is not possible from signs and symptoms. Adenovirus and <i>Mycoplasma</i> should be considered in clusters of pneumonia patients, especially in closed settings such as military camps and schools. 	<ul style="list-style-type: none"> Blood or sputum culture of molecular testing: positive for causative organism. RT-PCR: negative for SARS-CoV-2 viral RNA (coinfections are possible).

Condition	Differentiating signs / symptoms	Differentiating tests
Aspiration pneumonia	<ul style="list-style-type: none"> • Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset. • Differentiating COVID-19 from aspiration pneumonia is not usually possible from signs and symptoms. 	<ul style="list-style-type: none"> • RT-PCR: negative for SARS-CoV-2 viral RNA (coinfections are possible). • CT chest: difficult to distinguish on CT; however, anterior lung involvement may be more suggestive of COVID-19 pneumonia.[737]
Pneumocystis jirovecii pneumonia	<ul style="list-style-type: none"> • Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset. • Differentiating COVID-19 from pneumocystis jirovecii pneumonia is not usually possible from signs and symptoms. • Patients are usually immunocompromised (e.g., HIV positive) and duration of symptoms may be longer. 	<ul style="list-style-type: none"> • Sputum culture: positive for <i>Pneumocystis</i>. • RT-PCR: negative for SARS-CoV-2 viral RNA (coinfections are possible). • CT chest: ground-glass opacity is usually more diffusely distributed with a tendency to spare the subpleural regions.[727]
Middle East respiratory syndrome (MERS)	<ul style="list-style-type: none"> • Travel history to the Middle East or contact with a confirmed case of MERS. • Differentiating COVID-19 from MERS is not possible from signs and symptoms. • Initial data suggest that the clinical course of COVID-19 is less severe and the case fatality rate is lower compared with MERS. 	<ul style="list-style-type: none"> • Reverse-transcriptase polymerase chain reaction (RT-PCR): positive for MERS-CoV viral RNA.
Severe acute respiratory syndrome (SARS)	<ul style="list-style-type: none"> • There have been no cases of SARS reported since 2004. 	<ul style="list-style-type: none"> • RT-PCR: positive for severe acute respiratory syndrome coronavirus (SARS-CoV) viral RNA.
Avian influenza A (H7N9) virus infection	<ul style="list-style-type: none"> • May be difficult to differentiate based on epidemiologic history as avian influenza H7N9 is endemic in China. • Close contact with infected birds (e.g., farmer or visitor to a live market in endemic areas), or living in an area 	<ul style="list-style-type: none"> • RT-PCR: positive for H7-specific viral RNA.

Condition	Differentiating signs / symptoms	Differentiating tests
	when avian influenza is endemic.	
Avian influenza A (H5N1) virus infection	<ul style="list-style-type: none"> Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset. Close contact with infected birds (e.g., farmer or visitor to a live market in endemic areas), or living in an area when avian influenza is endemic. 	<ul style="list-style-type: none"> RT-PCR: positive for H5N1 viral RNA.
Pulmonary tuberculosis	<ul style="list-style-type: none"> Consider diagnosis in endemic areas, especially in patients who are immunocompromised. History of symptoms is usually longer. Presence of night sweats and weight loss may help to differentiate. 	<ul style="list-style-type: none"> Chest x-ray: fibronodular opacities in upper lobes with or without cavitation; atypical pattern includes opacities in middle or lower lobes, or hilar or paratracheal lymphadenopathy, and/or pleural effusion. Sputum acid-fast bacilli smear and sputum culture: positive. Molecular testing: positive for <i>Mycobacterium tuberculosis</i>.
Febrile neutropenia	<ul style="list-style-type: none"> Suspect neutropenic sepsis in patients with a history of recent systemic anticancer treatment who present with fever (with or without respiratory symptoms) as this can be rapid and life-threatening.^[738] Symptoms of COVID-19 and neutropenic sepsis may be difficult to differentiate at initial presentation. 	<ul style="list-style-type: none"> CBC: neutropenia. RT-PCR: negative for SARS-CoV-2 viral RNA.

Criteria

Case definitions

Various case definitions are available:

- [WHO: public health surveillance for COVID-19 – interim guidance] (<https://www.who.int/publications/item/who-2019-nCoV-surveillanceguidance-2020.7>)
- [CDC: coronavirus disease 2019 (COVID-19) 2020 interim case definition] (<https://wwwn.cdc.gov/nndss/conditions/coronavirus-disease-2019-covid-19/case-definition/2020>)

- [PHE: COVID-19 – investigation and initial clinical management of possible cases] (<https://www.gov.uk/government/publications/wuhan-novel-coronavirus-initial-investigation-of-possible-cases/investigation-and-initial-clinical-management-of-possible-cases-of-wuhan-novel-coronavirus-wn-cov-infection>)
- [ECDC: case definition for coronavirus disease 2019 (COVID-19)] (<https://www.ecdc.europa.eu/en/covid-19/surveillance/case-definition>)

Screening

Management of contacts

Definition

- The World Health Organization defines a contact as a person who has experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case:[739]
 - Face-to-face contact with a probable or confirmed case within 3 feet (1 meter) and for more than 15 minutes
 - Direct physical contact with a probable or confirmed case
 - Direct care for a patient with probable or confirmed COVID-19 without using recommended personal protective equipment
 - Other situations as indicated by local risk assessments.
- The Centers for Disease Control and Prevention (CDC) defines a close contact as someone who has been within 6 feet (2 meters) of an infected person for at least 15 minutes over a 24-hour period, beginning 2 days before symptom onset (or 2 days before testing in asymptomatic patients).[167]
- Consult local guidance as definitions of a contact may vary depending on local public health advice.

Quarantine periods

- The World Health Organization recommends that asymptomatic contacts of confirmed or probable cases, including healthcare workers, be quarantined in a designated facility or in a separate room in the household for 14 days from the last contact with the case. Any person in quarantine who develops symptoms should be treated and managed as a suspected case and tested according to national testing strategies and guidelines. Laboratory testing is not a requirement for leaving quarantine after 14 days for contacts who do not develop symptoms.[739]
- In the UK, Public Health England recommends a 10-day quarantine (or self-isolation) period after a potential exposure (it was reduced from 14 days to 10 days on 14 December 2020).[740] From 16 August 2021, fully vaccinated people will no longer need to self-isolate if they are identified as a close contact.[741]
- The CDC has shortened the minimum quarantine time after a potential exposure from 14 days to 7-10 days. Quarantine can end after day 7 if the patient tests negative and no symptoms have been reported during the quarantine period. Quarantine can end after day 10 without testing and if no symptoms have been reported during the quarantine period. Additional criteria (e.g., symptom monitoring, mask wearing) should continue until day 14 in both cases.[742]
- Consult local guidance for recommended quarantine locations and timeframes as recommendations vary depending on local public health advice.

Screening of asymptomatic populations

The World Health Organization does not currently recommend widespread screening of asymptomatic individuals due to the significant costs associated with it and the lack of data on its operational effectiveness. Testing of asymptomatic individuals is currently recommended only for specific groups including contacts of confirmed or probable cases and frequently exposed groups such as healthcare workers and long-term care facility workers.[578]

Screening of travelers

Exit and entry screening may be recommended in countries where borders are still open, particularly when repatriating nationals from affected areas. Travelers returning from affected areas should self-monitor for symptoms for 14 days and follow local protocols of the receiving country. Some countries may require travelers to enter mandatory quarantine in a designated location (e.g., a hotel). Travelers who develop symptoms are advised to contact their local healthcare provider, preferably by phone.^[743] One study of 566 repatriated Japanese nationals from Wuhan City found that symptom-based screening performed poorly and missed presymptomatic and asymptomatic cases. This highlights the need for testing and follow-up.^[744]

Drive-through screening centers

Drive-through screening centers have been set up in some countries for safer and more efficient screening. The testee does not leave their car throughout the entire process, which includes registration and questionnaire, exam, specimen collection, and instructions on what to do after. This method has the advantage of increased testing capacity and prevention of cross-infection between testees in the waiting space.^[745]

Temperature screening

There is little scientific evidence to support temperature screening with thermal cameras or temperature screening products as a reliable method for the detection of COVID-19 or any other febrile illness, especially if used as the main method of testing.^[746]

Noncontact infrared thermometers generally have reasonable sensitivity and specificity for detecting fever; however, their performance varies in different settings. Environmental factors (e.g., absolute temperature, variation in temperature, relative humidity) play an important role in the accuracy of the result. False negatives may be seen in people wearing make-up on the target area or who are significantly perspiring. False positives may be seen in people who are pregnant, menstruating, or on hormone replacement therapy, or those who have recently consumed alcohol or hot beverages, or done strenuous physical activity. Also, fever is not present in asymptomatic or presymptomatic people, and may not be present in symptomatic people, which means infected individuals could be missed.^[747]

While the forehead is the most feasible site for scanning, it is thought to be more prone to physiologic and environmental variations, and the wrist may be a better option as it may give more stable measurements under different circumstances.^[748]

Noncontact infrared thermometers demonstrated variable accuracy levels across populations and had a low sensitivity for temperatures $>99.5^{\circ}\text{F}$ ($>37.5^{\circ}\text{C}$) in adults compared with temporal artery thermometers. Therefore, they may not be the most accurate device for the mass screening of fever during a pandemic.^[749]

Approach

Management predominantly depends on disease severity, and focuses on the following principles: isolation at a suitable location; infection prevention and control measures; symptom management; optimized supportive care; and organ support in severe or critical illness.

Best Practice has published a separate topic on the management of coexisting conditions in the context of COVID-19. [BMJ Best Practice: Management of coexisting conditions in the context of COVID-19] (<https://bestpractice.bmj.com/topics/en-us/3000190#important-update>)

Key recommendations

- Consider whether the patient can be managed at home. Generally, patients with asymptomatic or mild disease can be managed at home or in a community facility.[2]
- Admit patients with moderate or severe disease to an appropriate healthcare facility. Assess adults for frailty on admission. Patients with critical disease require intensive care; involve the critical care team in discussions about admission to critical care when necessary. Monitor patients closely for signs of disease progression.[2] [564]
- Provide symptom relief as necessary. This may include treatments for fever, cough, breathlessness, anxiety, delirium, or agitation.[2] [564]
- Start supportive care according to the clinical presentation. This might include oxygen therapy, intravenous fluids, venous thromboembolism prophylaxis, high-flow nasal oxygen, noninvasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation. Sepsis and septic shock should be managed according to local protocols.[2]
- Consider empiric antibiotics if there is clinical suspicion of a secondary bacterial infection. Antibiotics may be required in patients with moderate, severe, or critical disease. Give within 1 hour of initial assessment for patients with suspected sepsis or if the patient meets high-risk criteria. Base the regimen on the clinical diagnosis, local epidemiology and susceptibility data, and local treatment guidelines.[2] [564]
- Consider systemic corticosteroid therapy for 7 to 10 days in patients with severe or critical disease. Moderate-quality evidence suggests that systemic corticosteroids probably reduce 28-day mortality in patients with severe and critical disease, and probably reduce the need for invasive ventilation.[533] [762]
- Consider an interleukin-6 inhibitor (tocilizumab or sarilumab) in patients with severe or critical disease. High-certainty evidence suggests that interleukin-6 inhibitors reduce mortality and the need for mechanical ventilation.[762] [763] [764]
- Assess whether the patient requires any rehabilitation or follow-up after discharge. Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.[2]
- For full details and guidance see information below.

Location of care

The decision about location of care depends on various factors including clinical presentation, disease severity, need for supportive care, presence of risk factors for severe disease, and conditions at home (including the presence of vulnerable people). Make the decision on a case-by-case basis using the following general principles.[2]

- Mild disease: manage in a healthcare facility, in a community facility, or at home. Home isolation can be considered in most patients, including asymptomatic patients.
- Moderate disease: manage in a healthcare facility, in a community facility, or at home. Home isolation can be considered in low-risk patients (i.e., patients who are not at high risk of deterioration).
- Severe disease: manage in an appropriate healthcare facility.
- Critical disease: manage in an intensive/critical care unit.

The location of care will also depend on guidance from local health authorities and available resources. Forced quarantine orders are being used in some countries.

Manage people who require hospitalization and who are at risk of being infected with a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant of concern in a single room with en-suite bathroom facilities and appropriate infection control procedures for the duration of their isolation period. In those who test positive, discuss further risk assessment and appropriate case management with the local/regional specialist infectious diseases center.[\[168\]](#)

The strongest risk factors for hospital admission are older age (odds ratio of >2 for all age groups older than 44 years, and odds ratio of 37.9 for people ages 75 years and over), heart failure, male sex, chronic kidney disease, and increased body mass index (BMI).[\[765\]](#) The median time from onset of symptoms to hospital admission is around 7 days.[\[50\]](#) [\[660\]](#)

Children are less likely to require hospitalization, but, if admitted, generally only require supportive care.[\[18\]](#) [\[766\]](#) Risk factors for intensive care admission in children include age <1 month, male sex, preexisting medical conditions, and presence of lower respiratory tract infection signs or symptoms at presentation.[\[767\]](#) The majority of children who require ventilation have underlying comorbidities, most commonly cardiac disease.[\[768\]](#) Children with COVID-19 are reported to have similar hospitalization rates, intensive care admission rates, and mechanical ventilator use compared with those with seasonal influenza.[\[730\]](#)

Overall, 19% of hospitalized patients require noninvasive ventilation, 17% require intensive care, 9% require invasive ventilation, and 2% require extracorporeal membrane oxygenation.[\[661\]](#) The rate of intensive care admission varies between studies; however, a meta-analysis of nearly 25,000 patients found that the admission rate was 32%, and the pooled prevalence of mortality in patients in the intensive care unit was 39%.[\[769\]](#) Another more recent meta-analysis found the mortality rate in patients in the intensive care unit to be 35.5%.[\[770\]](#) The most common reasons for intensive care unit admission are hypoxemic respiratory failure leading to mechanical ventilation and hypotension.[\[771\]](#) Patients admitted to intensive care units were older, were predominantly male, and had a median length of stay of 23 days (range 12 to 32 days).[\[772\]](#) The strongest risk factors for critical illness are oxygen saturation <88%; elevated serum troponin, C-reactive protein, and D-dimer; and, to a lesser extent, older age, BMI >40, heart failure, and male sex.[\[765\]](#) The most common risk factors for intensive care unit mortality were invasive mechanical ventilation, acute kidney injury, and acute respiratory distress syndrome.[\[773\]](#)

Management of mild COVID-19

Patients with suspected or confirmed mild disease (i.e., symptomatic patients meeting the case definition for COVID-19 without evidence of hypoxia or pneumonia) and asymptomatic patients should be isolated to contain virus transmission.[\[2\]](#)

Location of care

- Manage patients in a healthcare facility, in a community facility, or at home. Home isolation can be considered in most patients, with telemedicine or remote visits as appropriate.[2] [533] This decision requires careful clinical judgment and should be informed by an assessment of the patient's home environment to ensure that: infection prevention and control measures and other requirements can be met (e.g., basic hygiene, adequate ventilation); the caregiver is able to provide care and recognize when the patient may be deteriorating; the caregiver has adequate support (e.g., food, supplies, psychological support); the support of a trained health worker is available in the community.[774]
- There is some evidence to suggest that implementation of an early home treatment algorithm reduced the risk of hospitalization and related treatment costs in a small cohort of patients.[775]

Isolation period

- Discontinue transmission-based precautions (including isolation) and release patients from the care pathway: 10 days after positive test (asymptomatic patients); 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms (symptomatic patients).[2]
- The Centers for Disease Control and Prevention (CDC) recommends discontinuing home isolation once at least 10 days (or up to 20 days in patients who are severely immunocompromised) have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. In asymptomatic people, the CDC recommends discontinuing home isolation once at least 10 days have passed since the date of a positive test. For severely immunocompromised patients who are asymptomatic, isolation may be discontinued when at least 10 days and up to 20 days have passed since the date of a positive test; consider consultation with infectious diseases specialists and infection control experts. Alternatively, the CDC recommends at least two negative reverse-transcription polymerase chain reaction (RT-PCR) tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used. A symptom-based strategy is preferred; however, a test-based strategy can be considered in severely immunocompromised patients.[776] If the patient is hospitalized, the CDC guidance for discontinuing isolation is the same as for moderate disease (see below).
- Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the self-isolation period is 10 days in patients with milder disease who are managed in the community.[777]

Infection prevention and control

- For patients in home isolation, advise patients and household members to follow appropriate infection prevention and control measures:
 - [WHO: home care for patients with suspected or confirmed COVID-19 and management of their contacts] ([https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-\(ncov\)-infection-presenting-with-mild-symptoms-and-management-of-contacts](https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and-management-of-contacts))
 - [CDC: interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 (COVID-19)] (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-home-care.html>)

Symptom management

- Fever and pain: acetaminophen or ibuprofen are recommended.[2] [564] There is no evidence at present of severe adverse events in COVID-19 patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, or of effects as a result of the use of NSAIDs on acute healthcare utilization, long-term survival, or quality of life in patients with COVID-19.[778] [779] [780] [781] [782] [783] [784] Ibuprofen should only be taken at the lowest effective dose for the shortest period needed to control symptoms.
- Cough: advise patients to avoid lying on their back as this makes coughing ineffective. Use simple measures first (e.g., a teaspoon of honey in patients ages 1 year and older) to help cough.[564] A meta-analysis found that honey is superior to usual care (e.g., antitussives) for the improvement of upper respiratory tract infection symptoms, particularly cough frequency and severity.[785]
- Olfactory dysfunction: consider treatment (e.g., olfactory training) if olfactory dysfunction persists beyond 2 weeks. Often it improves spontaneously and does not require specific treatment. There is no evidence to support the use of treatments in patients with COVID-19.[786]

Supportive care

- Advise patients about adequate nutrition and appropriate rehydration. Advise patients to drink fluids regularly to avoid dehydration. Fluid intake needs can be higher than usual because of fever. However, too much fluid can worsen oxygenation.[2] [564]
- Advise patients to improve air circulation by opening a window or door.[564]
- Provide basic mental health and psychosocial support for all patients, and manage any symptoms of insomnia, depression, or anxiety as appropriate.[2]
- Most children with mild disease can be managed with supportive care alone and will not require any specific therapy.[533]

Monitor

- Closely monitor patients with risk factors for severe illness, and counsel patients about signs and symptoms of deterioration or complications that require prompt urgent care (e.g., difficulty breathing, chest pain).[2] [533]
- Pulse oximetry monitoring at home is recommended in symptomatic patients with risk factors for progression to severe disease who are not hospitalized. Patient education and appropriate follow-up are required.[2]

Corticosteroids

- The World Health Organization (WHO) does not recommend systemic corticosteroids in patients with nonsevere disease as they may increase the risk of mortality in these patients.[762]
- In the UK, the National Institute for Health and Care Excellence does not recommend routinely using systemic corticosteroids in people who do not need supplemental oxygen, unless there is another medical indication to do so.[564]
- In the US, the National Institutes of Health guidelines panel recommends against the use of systemic corticosteroids in nonhospitalized patients with mild to moderate disease in the absence of another indication.[533]

Management of moderate COVID-19

Patients with suspected or confirmed moderate disease (i.e., clinical signs of pneumonia but no signs of severe pneumonia) should be isolated to contain virus transmission.[2]

Location of care

- Manage patients in a healthcare facility, in a community facility, or at home. Home isolation, with telemedicine or remote visits as appropriate, can be considered in low-risk patients. Manage patients at high risk of deterioration in a healthcare facility.[2] [533]

Isolation period

- Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.[2]
- The CDC recommends discontinuing isolation once at least 10 days (not severely immunocompromised) or up to 20 days (severely immunocompromised) have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. In asymptomatic people, the CDC recommends discontinuing isolation once at least 10 days (not severely immunocompromised) or up to 20 days (severely immunocompromised) have passed since the date of a positive test. Severely immunocompromised patients may produce replication-competent virus beyond 20 days and require additional testing and consultation with infectious diseases specialists and infection control experts before discontinuing isolation. Alternatively, the CDC recommends at least two negative RT-PCR tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used. A symptom-based strategy is preferred; however, a test-based strategy can be considered in severely immunocompromised patients.[787] If the patient is isolated at home, the CDC guidance for discontinuing isolation is the same as for mild disease (see above).
- Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 14 days from a positive test in hospitalized patients, and 10 days in patients with milder disease who are managed in the community. Immunocompetent patients who tested positive on RT-PCR and have completed their 14-day isolation period are exempt from testing prior to hospital discharge if they are within 90 days from their initial illness onset or test, unless they develop new symptoms.[777]

Infection prevention and control

- Implement local infection prevention and control procedures when managing patients with COVID-19. For patients in home isolation, advise patients and household members to follow appropriate infection prevention and control measures (see above).

Symptom management and supportive care

- Manage symptoms and provide supportive care as appropriate (see above).
- Most children with moderate disease can be managed with supportive care alone and will not require any specific therapy.[533]

Antibiotics

- Do not offer an antibiotic for preventing secondary bacterial pneumonia in people with COVID-19.[564]
- Consider empiric antibiotics only if there is clinical suspicion of secondary bacterial infection. Start treatment as soon as possible, and refer to local guidelines for choice of regimen.[2] [533] [564]

- Antibiotics may also be considered in older people (particularly those in long-term care facilities) and children <5 years of age to provide empiric antibiotic treatment for possible pneumonia.[2]
- Advise patients to seek medical help without delay if their symptoms do not improve, or worsen rapidly or significantly. Reconsider whether the person has signs and symptoms of more severe disease on reassessment, and whether to refer them to hospital, other acute community support services, or palliative care services.[564]

Monitor

- Closely monitor patients for signs or symptoms of disease progression.
- If the patient is being managed at home, counsel them about signs and symptoms of deterioration or complications that require prompt urgent care (e.g., difficulty breathing, chest pain). Pulse oximetry monitoring at home is recommended in symptomatic patients with risk factors for progression to severe disease who are not hospitalized. Patient education and appropriate follow-up are required.[2]
- If the patient is being managed in hospital, monitor patients closely for signs of clinical deterioration using medical early warning scores (e.g., National Early Warning Score 2 [NEWS2]), and respond immediately with appropriate supportive care interventions.[2]

Corticosteroids

- The WHO does not recommend systemic corticosteroids in patients with nonsevere disease as they may increase the risk of mortality in these patients.[762]
- In the UK, the National Institute for Health and Care Excellence does not recommend routinely using systemic corticosteroids in people who do not need supplemental oxygen, unless there is another medical indication to do so.[564]
- In the US, the National Institutes of Health guidelines panel recommends against the use of corticosteroids in nonhospitalized patients with mild to moderate disease in the absence of another indication. However, the guideline panel recommends oral dexamethasone in patients who are discharged from the emergency department despite new or increased need for supplemental oxygen (for the duration of supplemental oxygen and not to exceed 10 days), when hospital resources are limited, inpatient admission is not possible, and close follow-up is ensured.[533]

Management of severe COVID-19

Patients with suspected or confirmed severe disease are at risk of rapid clinical deterioration.[2]

- Severe disease in adults is defined as having clinical signs of pneumonia plus at least one of the following:
 - Respiratory rate >30 breaths/minute
 - Severe respiratory distress
 - SpO₂ <90% on room air
- Severe disease in children is defined as having clinical signs of pneumonia plus at least one of the following:
 - Central cyanosis or SpO₂ <90%
 - Severe respiratory distress

- General danger signs: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions
- Fast breathing (<2 months: ≥ 60 breaths per minute; 2-11 months: ≥ 50 breaths per minute; 1-5 years: ≥ 40 breaths per minute).

Location of care

- Manage patients in an appropriate healthcare facility under the guidance of a specialist team.[2]
- Use the Clinical Frailty Scale (CFS) to assess baseline health and inform discussions on treatment expectations when appropriate and within an individualised assessment of frailty. [Clinical Frailty Scale] (<https://www.scfn.org.uk/clinical-frailty-scale>) Do not use the CFS for younger people, or for people with stable long-term disabilities (e.g., cerebral palsy), learning disabilities, or autism. Make an individualized assessment of frailty in these people, using clinical assessment and alternative scoring methods.[564]
- A meta-analysis found that an increase in CFS was associated with an increase in mortality (each 1-point increase in CFS was associated with a 12% increase in mortality).[788]
- Patients with a score between 6-9 or 4-5 had significantly increased mortality compared with those with a score of 1-3. In the context of COVID-19, a score of 1-3 may be considered a lower risk of mortality, a score of 4-5 moderate risk, and a score of 6-9 high risk.[789]
- However, some studies suggest that a more nuanced understanding of frailty and outcomes is needed, and you should exercise caution in placing too much emphasis on the influence of frailty alone when discussing prognosis in older people.[790]

Isolation period

- Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.[2]
- The CDC recommends discontinuing isolation once at least 10 days and up to 20 days have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. Consider consultation with infection control experts before discontinuing isolation. Severely immunocompromised patients may produce replication-competent virus beyond 20 days and require additional testing and consultation with infectious diseases specialists and infection control experts before discontinuing isolation. Alternatively, the CDC recommends at least two negative RT-PCR tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used. A symptom-based strategy is preferred; however, a test-based strategy can be considered in severely immunocompromised patients.[787]
- Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 14 days from a positive test in hospitalized patients. Immunocompetent patients who tested positive on RT-PCR and have completed their 14-day isolation period are exempt from testing prior to hospital discharge if they are within 90 days from their initial illness onset or test, unless they develop new symptoms.[777]

Infection prevention and control

- Implement local infection prevention and control procedures when managing patients with COVID-19.

Oxygen

- Start supplemental oxygen therapy immediately in any patient with emergency signs (i.e., obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma and/or convulsions), or any patient without emergency signs and $\text{SpO}_2 < 90\%$.^[2] ^[533] There is no evidence of benefit for oxygen therapy in patients with COVID-19 in the absence of hypoxemia.^[791]
- Target SpO_2 to $\geq 94\%$ during resuscitation in adults and children with emergency signs who require emergency airway management and oxygen therapy. Once the patient is stable, a target $\text{SpO}_2 > 90\%$ in children and nonpregnant adults, and $\geq 92\%$ to 95% in pregnant women is recommended. Nasal prongs or a nasal cannula are preferred in young children.^[2] Some guidelines recommend that SpO_2 should be maintained no higher than 96% .^[792]
- Some centers may recommend different SpO_2 targets in order to support prioritization of oxygen flow for the most severely ill patients in hospital. NHS England recommends a target of 92% to 96% (or 90% to 94% if clinically appropriate), for example.^[793]
- Consider positioning techniques (e.g., high supported sitting), and airway clearance management to optimize oxygenation and assist with secretion clearance in adults. Consider awake prone positioning (for 8-12 hours/day, broken into shorter periods over the day) in severely ill patients who require supplemental oxygen.^[2] ^[533]
 - Awake prone positioning of nonintubated patients was associated with improvement in oxygen variables ($\text{PaO}_2/\text{FiO}_2$, PaO_2 , and SpO_2), respiratory rate, and mortality, but no significant difference was noted in the rate of intubation. However, evidence is limited.^[794] ^[795]
- Monitor patients closely for signs of progressive acute hypoxemic respiratory failure. Patients who continue to deteriorate despite standard oxygen therapy require advanced oxygen/ventilatory support.^[2] ^[533]

Symptom management and supportive care

- Fluids and electrolytes: use cautious fluid management in adults and children without tissue hypoperfusion and fluid responsiveness as aggressive fluid resuscitation may worsen oxygenation.^[2] Correct any electrolyte or metabolic abnormalities, such as hyperglycemia or metabolic acidosis, according to local protocols.^[796]
- Fever and pain: acetaminophen or ibuprofen are recommended.^[2] ^[564] There is no evidence at present of severe adverse events in COVID-19 patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, or of effects as a result of the use of NSAIDs on acute healthcare utilization, long-term survival, or quality of life in patients with COVID-19.^[778] ^[779] ^[780] ^[781] ^[782] ^[783] ^[784] Ibuprofen should only be taken at the lowest effective dose for the shortest period needed to control symptoms.
- Cough: advise patients to avoid lying on their back as this makes coughing ineffective. Use simple measures first (e.g., a teaspoon of honey in patients ages 1 year and older) to help cough. Short-term use of a cough suppressant may be considered in select patients (e.g., if the cough is distressing to the patient) provided there are no contraindications.^[564] A meta-analysis found that honey is superior to usual care (e.g., antitussives) for the improvement of upper respiratory tract infection symptoms, particularly cough frequency and severity.^[785]

- Breathlessness: keep the room cool, and encourage relaxation, breathing techniques, and changing body positions. Identify and treat any reversible causes of breathlessness (e.g., pulmonary edema, pulmonary embolism, COPD, asthma).[564]
- Anxiety, delirium, and agitation: identify and treat any underlying or reversible causes (e.g., offer reassurance, treat hypoxia, correct metabolic or endocrine abnormalities, address coinfections, minimize use of drugs that may cause or worsen delirium, treat substance withdrawal, maintain normal sleep cycles, treat pain or breathlessness).[2] [564] Low doses of haloperidol (or another suitable antipsychotic) can also be considered for agitation.[2] Nonpharmacologic interventions are the mainstay for the management of delirium when possible, and prevention is key.[797]
- Mouth care: an important part of overall patient care in hospitalized patients who are ventilated or nonventilated and those undergoing step-down or end-of-life care.[798]
- Provide basic mental health and psychosocial support for all patients, and manage any symptoms of insomnia or depression as appropriate.[2]

Venous thromboembolism prophylaxis

- Assess the risk of bleeding as soon as possible after admission, or by the time of the first consultant review, using a suitable risk assessment tool.[564]
- Start venous thromboembolism (VTE) prophylaxis in acutely ill hospitalized adults and adolescents, provided there are no contraindications.[2] [533] [799] [800]
 - The National Institute for Health and Care Excellence in the UK recommends starting as soon as possible and within 14 hours of admission, and continuing for a minimum of 14 days or until discharge.[564]
 - For hospitalized children, indications for VTE prophylaxis should be the same as those for children without COVID-19.[533]
- Low molecular weight heparin, unfractionated heparin, or fondaparinux are the recommended options for standard thromboprophylaxis.[2]
 - The National Institute for Health and Care Excellence in the UK recommends low molecular weight heparin first-line, with fondaparinux or unfractionated heparin reserved for patients who cannot have low molecular weight heparin.[564]
 - A retrospective observational study found that enoxaparin is associated with lower 28-day mortality, lower rates of bleeding events, lower intensive care admission rates, and shorter hospital stays compared with unfractionated heparin; however, the study had important limitations and further research is required.[801]
 - Unfractionated heparin is contraindicated in patients with severe thrombocytopenia. Fondaparinux is recommended in patients with a history of heparin-induced thrombocytopenia. Mechanical thromboprophylaxis (e.g., intermittent pneumatic compression devices) is recommended if anticoagulation is contraindicated or not available.[800] [802]
 - Avoid direct oral anticoagulants in the absence of an evidence-based indication for oral anticoagulation. An open-label, multicenter, randomized controlled trial found that in-hospital therapeutic anticoagulation with rivaroxaban or enoxaparin followed by rivaroxaban until day 30 did not improve clinical outcomes and increased bleeding compared with prophylactic anticoagulation among hospitalized patients with an elevated D-dimer level.[803]
- The optimal dose is yet to be determined. Standard prophylaxis doses are generally recommended over intermediate- or full treatment-dose regimens in patients without an established indication for

higher-dose anticoagulation. However, this recommendation varies and you should consult your local guidelines.

- The World Health Organization recommends standard thromboprophylaxis dosing of anticoagulation rather than therapeutic or intermediate dosing in patients without an established indication for higher-dose anticoagulation.[2]
- The National Institute for Health and Care Excellence in the UK recommends clinicians consider a treatment dose of a low molecular weight heparin in young people and adults who are likely to be in hospital for at least 3 days and need supplemental oxygen (but who are not yet receiving high-flow oxygen, continuous positive airway pressure, noninvasive ventilation, or invasive mechanical ventilation), unless contraindicated. This is because of fewer deaths and less likelihood of needing intensive care with this dose compared with a standard prophylaxis dose without a notable increase in major bleeding, although the evidence for this recommendation is weak. Treatment should be for a minimum of 14 days or until discharge, and the dose may need to be reduced if the clinical circumstances change (such as a need for advanced respiratory support). For those who do not need supplemental oxygen, follow standard VTE prophylaxis guidelines.[564]
- The National Institutes of Health guidelines panel recommends prophylactic-dose anticoagulation, and states that there are insufficient data to recommend increased anticoagulant doses for VTE prophylaxis in COVID-19 patients outside the setting of a clinical trial.[533]
- A large multicenter cohort of hospitalized patients found that prophylactic-dose strategies were associated with lower 60-day mortality compared with treatment-dose strategies, suggesting that prophylactic-dose strategies may be optimal in hospitalized patients.[804]
- Dose adjustments may be required in patients with extremes of body weight or renal impairment.[564]
- For patients who are already on an anticoagulant for another condition, continue the patient's current therapeutic dose unless contraindicated by a change in clinical circumstances. Consider switching to low molecular weight heparin if the patient's clinical condition is deteriorating and the patient is not currently on low molecular weight heparin.[564]
- Monitor patients for signs and symptoms suggestive of thromboembolism and proceed with appropriate diagnostic and management pathways if clinically suspected.[2] If the patient's clinical condition changes, assess the risk of VTE, reassess the bleeding risk, and review VTE prophylaxis.[564]
- Continue until hospital discharge.[2] Routine post-discharge VTE prophylaxis is not generally recommended, except in certain high-risk patients.[533] [799] [800] Ensure patients who require VTE prophylaxis after discharge are able to use it correctly or have arrangements made for someone to help them.[564]
- There is currently insufficient evidence to determine the risks and benefits of prophylactic anticoagulation in hospitalized patients with COVID-19.[805]
- A systematic review and meta-analysis found that the pooled odds of mortality between anticoagulated and nonanticoagulated hospitalized patients were similar, but lower in the standard prophylactic-dose group. Prophylactic-dose anticoagulation significantly decreased the odds of in-hospital death by 17% compared with no anticoagulation. Mortality increased in the intermediate- to therapeutic-dose group with an increased risk of major bleeding.[806]

- Clinicians should rely on pre-COVID-19 evidence-based principles of anticoagulation management combined with rational approaches to address clinical challenges.[\[799\]](#)

Antimicrobials

- Do not offer antibiotics for preventing or treating pneumonia if SARS-CoV-2, another virus, or a fungal infection is likely to be the cause.[\[564\]](#) There is insufficient evidence to recommend empiric broad-spectrum antibiotics in the absence of another indication.[\[533\]](#)
- Consider empiric antibiotics if there is clinical suspicion of secondary bacterial infection. Give within 1 hour of initial assessment for patients with suspected sepsis or if the patient meets high-risk criteria (or within 4 hours of establishing a diagnosis of secondary bacterial pneumonia); do not wait for microbiology results. Base the regimen on the clinical diagnosis (e.g., community-acquired pneumonia, hospital-acquired pneumonia, sepsis), local epidemiology and susceptibility data, and local treatment guidelines.[\[2\]](#) [\[533\]](#) [\[564\]](#)
- Consider seeking specialist advice for people who: are immunocompromised; have a history of infection with resistant organisms; have a history of repeated infective exacerbations of lung disease; are pregnant; or are receiving advanced respiratory or organ support. Seek specialist advice if there is a suspicion that the person has an infection with multidrug-resistant bacteria and may need a different antibiotic, or there is clinical or microbiologic evidence of infection and the person's condition does not improve as expected after 48 to 72 hours of antibiotic treatment.[\[564\]](#)
- Reassess antibiotic use daily. De-escalate empiric therapy on the basis of microbiology results and clinical judgment. Regularly review the possibility of switching from intravenous to oral therapy. Duration of treatment should be as short as possible (e.g., 5 to 7 days). Antibiotic stewardship programs should be in place.[\[2\]](#) A meta-analysis found that the prevalence of antibiotic prescribing in patients with COVID-19 was 75%, which is significantly higher than the estimated prevalence of bacterial coinfection. Therefore, unnecessary antibiotic use is likely to be high in these patients.[\[807\]](#)
- Treat laboratory-confirmed coinfections (e.g., malaria, tuberculosis, influenza) as appropriate according to local protocols.[\[2\]](#) The treatment of influenza is the same in all patients regardless of SARS-CoV-2 coinfection. Start empiric treatment with oseltamivir in hospitalized patients who are suspected of having either or both infections as soon as possible without waiting for influenza test results. Antiviral therapy can be stopped once influenza has been ruled out.[\[533\]](#)

Corticosteroids

- The WHO strongly recommends systemic corticosteroid therapy (low-dose intravenous or oral dexamethasone or hydrocortisone) for 7 to 10 days in adults with severe disease. This recommendation is based on two meta-analyses that pooled data from eight randomized trials (over 7000 patients), including the UK RECOVERY trial. Moderate-quality evidence suggests that systemic corticosteroids probably reduce 28-day mortality in patients with severe disease. There is no evidence directly comparing dexamethasone and hydrocortisone. The harms of treatment in this context are considered to be minor. It is unclear whether these recommendations can be applied to children or those who are immunocompromised.[\[762\]](#) [\[763\]](#) [\[764\]](#) [\[808\]](#) [\[809\]](#)
- In the UK, the National Institute for Health and Care Excellence recommends offering dexamethasone (or an alternative such as hydrocortisone or prednisone when dexamethasone cannot be used or is unavailable) to people who need supplemental oxygen to meet their prescribed oxygen saturation levels, or who have a level of hypoxia that needs supplemental

oxygen but who are unable to have or tolerate it. Treatment is for up to 10 days unless there is a clear indication to stop early.[\[564\]](#)

- In the US, the National Institutes of Health guidelines panel recommends dexamethasone, either alone or in combination with remdesivir (see the Emerging section for information on remdesivir), in hospitalized adults who require supplemental oxygen. Alternative corticosteroids may be used in situations where dexamethasone is not available. It is not routinely recommended for pediatric patients who require only low levels of oxygen support (i.e., via a nasal cannula only). Use of dexamethasone for the treatment of severe disease in children who are profoundly immunocompromised has not been evaluated, may be harmful, and therefore should be considered only on a case-by-case basis.[\[533\]](#) The Infectious Diseases Society of America supports the use of dexamethasone in hospitalized patients with severe disease.[\[810\]](#)
- Monitor patients for adverse effects (e.g., hyperglycemia, secondary infections, psychiatric effects, reactivation of latent infections) and assess for drug-drug interactions.[\[533\]](#)

Interleukin-6 (IL-6) inhibitors

- The WHO strongly recommends an IL-6 inhibitor (tocilizumab or sarilumab), in combination with a systemic corticosteroid and initiated at the same time, in patients with severe disease. IL-6 inhibitors are typically administered as a single intravenous dose; however, a second dose may be administered 12 to 48 hours after the first dose if the clinical response is inadequate. This recommendation is based on high-certainty evidence that shows IL-6 inhibitors reduce mortality and the need for mechanical ventilation, and low-certainty evidence that suggests that IL-6 inhibitors may also reduce the duration of mechanical ventilation and hospitalization. The evidence regarding the risk of severe adverse events is uncertain. The applicability of this recommendation to children is currently uncertain.[\[762\]](#) [\[763\]](#) [\[764\]](#) This recommendation is based on data from the UK RECOVERY and REMAP-CAP trials.[\[811\]](#) [\[812\]](#)
- In the UK, the National Institute for Health and Care Excellence recommends a single dose of tocilizumab in hospitalized adults if all of the following conditions apply: they are having or have completed a course of corticosteroids such as dexamethasone (unless they cannot have corticosteroids); they have not had another IL-6 inhibitor during this admission; there is no evidence of a bacterial or viral infection (other than SARS-CoV-2) that might be worsened by tocilizumab; AND they either need supplemental oxygen and have a C-reactive protein level of ≥ 75 mg/L, OR they are within 48 hours of starting high-flow nasal oxygen, continuous positive airway pressure, noninvasive ventilation, or invasive mechanical ventilation. Consider tocilizumab for children and young people who have severe disease or pediatric inflammatory multisystem syndrome only if they are ages 1 year and over, and only in the context of a clinical trial. Sarilumab may be considered an alternative option in adults only if tocilizumab cannot be used or is unavailable (use the same eligibility criteria as those for tocilizumab).[\[564\]](#) Tocilizumab has not been granted a conditional marketing authorization for this indication in the UK as yet.
- In the US, the Infectious Diseases Society of America recommends considering tocilizumab in hospitalized adults with progressive severe disease who have elevated markers of systemic inflammation, in addition to standard of care (i.e., corticosteroids), rather than standard of care alone.[\[810\]](#) Tocilizumab has been granted an emergency-use authorization in the US for the treatment of hospitalized adults and pediatric patients 2 years of age and older who are receiving systemic corticosteroids and require supplemental oxygen.[\[813\]](#)
- Evidence supports the use of these drugs.

- A Cochrane review found that tocilizumab reduced all-cause mortality at day 28, and probably resulted in slightly fewer serious adverse events compared with standard care alone or placebo. The evidence suggests uncertainty around the effect on mortality after day 60. However, tocilizumab probably results in little or no increase in clinical improvement at day 28 (i.e., hospital discharge or improvement measured by trialist-defined scales). The impact of tocilizumab on other outcomes is uncertain. Evidence for an effect of sarilumab is uncertain.[\[814\]](#)
- A living systematic review and network meta-analysis found that IL-6 inhibitors are likely to reduce the need for mechanical ventilation (moderate-certainty evidence) and may reduce the duration of hospitalization (low-certainty evidence) compared with standard care.[\[815\]](#)
[\[816\]](#)
- The largest and most recent meta-analysis of over 10,000 hospitalized patients from 27 randomized controlled trials found that IL-6 antagonists were associated with lower all-cause mortality 28 days after randomization compared with usual care or placebo. There was no clear association between administration of IL-6 inhibitors and all-cause mortality at 90 days; however, data were limited.[\[817\]](#)

Monitor

- Monitor patients closely for signs of clinical deterioration, and respond immediately with appropriate supportive care interventions.[\[2\]](#)

Discharge and rehabilitation

- Routinely assess older patients for mobility, functional swallow, cognitive impairment, and mental health concerns, and based on that assessment determine whether the patient is ready for discharge, and whether the patient has any rehabilitation and follow-up requirements.[\[2\]](#)

Palliative care

- Palliative care interventions should be made accessible at each institution that provides care for patients with COVID-19. Identify whether the patient has an advance care plan and respect the patient's priorities and preferences when formulating the patient's care plan.[\[2\]](#)
- There is a lack of data on palliative care in patients with COVID-19. However, a rapid systematic review of pharmacologic strategies used for palliative care in these patients, the first international review of its kind, found that a higher proportion of patients required continuous subcutaneous infusions for medication delivery than is typically seen in the palliative care population. Modest doses of commonly used end-of-life medications were required for symptom control. However, these findings should be interpreted with caution due to the lack of data available.[\[818\]](#)
- Follow local palliative care guidelines.

Management of critical COVID-19

Patients with critical disease (i.e., presence of acute respiratory distress syndrome, sepsis, or septic shock) should be admitted or transferred to an intensive/critical care unit. Use existing care bundles (i.e., three or more evidence-informed practices delivered together and consistently to improve care), chosen locally by the hospital or intensive care unit and adapted as necessary for local circumstances.[\[2\]](#)

Location of care

- Manage patients in an intensive/critical care unit under the guidance of a specialist team.[2]
- Discuss the risks, benefits, and potential outcomes of treatment options with patients and their families, and allow them to express preferences about their management. Take their wishes and expectations into account when considering the ceiling of treatment. Use decision support tools if available. Put treatment escalation plans in place, and discuss any existing advance care plans or advance decisions to refuse treatment with patients who have preexisting advanced comorbidities.[564]

Isolation period

- Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.[2]
- The CDC recommends discontinuing isolation once at least 10 days and up to 20 days have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. Consider consultation with infection control experts before discontinuing isolation. Severely immunocompromised patients may produce replication-competent virus beyond 20 days and require additional testing and consultation with infectious diseases specialists and infection control experts before discontinuing isolation. Alternatively, the CDC recommends at least two negative RT-PCR tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used. A symptom-based strategy is preferred; however, a test-based strategy can be considered in severely immunocompromised patients.[787]
- Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 14 days from a positive test in hospitalized patients. Immunocompetent patients who tested positive on RT-PCR and have completed their 14-day isolation period are exempt from testing prior to hospital discharge if they are within 90 days from their initial illness onset or test, unless they develop new symptoms.[777]

Infection prevention and control

- Implement local infection prevention and control procedures when managing patients with COVID-19.

High-flow nasal oxygen or noninvasive ventilation

- Consider a trial of high-flow nasal oxygen (HFNO) or noninvasive ventilation (e.g., continuous positive airway pressure [CPAP] or bilevel positive airway pressure [BiPAP]) in selected patients with mild acute respiratory distress syndrome (ARDS). Consider awake prone positioning (for 8-12 hours/day, broken into shorter periods over the day) in severely ill patients who require HFNO or noninvasive ventilation.[2]
- Indirect and low-certainty evidence suggests that noninvasive ventilation probably reduces mortality in patients with COVID-19, similar to mechanical ventilation, but may increase the risk of viral transmission.[819] [820]
- Awake prone positioning of nonintubated patients was associated with improvement in oxygen variables ($\text{PaO}_2/\text{FiO}_2$, PaO_2 , and SpO_2), respiratory rate, and mortality, but no significant difference was noted in the rate of intubation. However, evidence is limited.[794] [795]

- Airborne precautions are recommended for these interventions (including bubble CPAP) due to uncertainty about the potential for aerosolization.^[2] Novel methods to protect clinicians without access to standard personal protective equipment during aerosol-generating procedures have been suggested.^{[821] [822] [823] [824]}
- Patients with hypercapnia, hemodynamic instability, multi-organ failure, or abnormal mental status should generally not receive HFNO, although emerging data suggests that it may be safe in patients with mild to moderate and nonworsening hypercapnia. Patients with hypoxemic respiratory failure and hemodynamic instability, multi-organ failure, or abnormal mental status should not receive these treatments in place of other options such as invasive ventilation.^[2]
- There is ongoing debate about the optimal mode of respiratory support before mechanical ventilation.^[825]
 - NHS England recommends CPAP as the preferred form of noninvasive ventilation in patients with hypoxemic (type 1) respiratory failure. It doesn't advocate the use of HFNO based on a lack of efficacy, oxygen use (HFNO can place a strain on oxygen supplies with the risk of site supply failure), and infection spread.^[826]
 - Other guidelines recommend HFNO over noninvasive ventilation, unless HFNO is not available.^{[533] [792]}
 - Despite the trend to avoid HFNO, it has been shown to have a similar risk of aerosol generation to standard oxygen masks.^[827]
- Early CPAP may provide a bridge to invasive mechanical ventilation. Reserve the use of BiPAP for patients with hypercapnic acute on chronic ventilatory failure (type 2 respiratory failure).^[826]
- Monitor patients closely for acute deterioration. If patients do not improve after a short trial of these interventions they require urgent endotracheal intubation.^{[2] [792]}
- More detailed guidance on the management of ARDS in COVID-19 is beyond the scope of this topic; consult a specialist for further guidance.

Mechanical ventilation

- Consider endotracheal intubation and invasive mechanical ventilation in patients who are acutely deteriorating despite advanced oxygen/noninvasive ventilatory support measures.^{[2] [533]}
 - Use of mechanical ventilation in COVID-19 patients carries a high risk of mortality. Mortality is highly variable across studies, ranging between 21% and 100%. An overall in-hospital mortality risk ratio of 0.70 has been reported based on random-effect pooled estimates. However, it is important to note that outcomes appear to have improved as the pandemic has progressed.^[828]
- Endotracheal intubation should be performed by an experienced provider using airborne precautions.^[2] Intubation by video laryngoscopy is recommended if possible.^[533] Young children, or adults who are obese or pregnant, may desaturate quickly during intubation and therefore require preoxygenation with 100% FiO₂ for 5 minutes.^[2]
- Mechanically ventilated patients with ARDS should receive a lung-protective, low tidal volume/low inspiratory pressure ventilation strategy (lower targets are recommended in children). A higher positive end-expiratory pressure (PEEP) strategy is preferred over a lower PEEP strategy in moderate to severe ARDS. However, individualization of PEEP, where the patient is monitored for beneficial or harmful effects and driving pressure during titration with consideration of the risks and benefits of PEEP titration, is recommended.^{[2] [533] [792]} NHS England recommends a low PEEP strategy in patients with normal compliance where recruitment may not be required.^[829]

- Although some patients with COVID-19 pneumonia meet the criteria for ARDS, there is some discussion about whether COVID-19 pneumonia is its own specific disease with atypical phenotypes. Anecdotal evidence suggests that the main characteristic of the atypical presentation is the dissociation between well-preserved lung mechanics and the severity of hypoxemia.[\[830\]](#) [\[831\]](#) [\[832\]](#) [\[833\]](#) [\[834\]](#) [\[835\]](#) However, this approach has been criticized.[\[836\]](#) [\[837\]](#)
- It has been argued that an evidence-based approach extrapolating data from ARDS not related to COVID-19 is the most reasonable approach for intensive care of COVID-19 patients.[\[838\]](#) As a consequence of this, some clinicians have warned that protocol-driven ventilator use may be causing lung injury in some patients, and that ventilator settings should be based on physiologic findings rather than using standard protocols. High PEEP may have a detrimental effect on patients with normal compliance.[\[830\]](#)
- PEEP should always be carefully titrated.[\[839\]](#)
- Consider prone ventilation in patients with severe ARDS for 12 to 16 hours per day. Pregnant women in the third trimester may benefit from being placed in the lateral decubitus position. Caution is required in children.[\[2\]](#) [\[533\]](#) [\[792\]](#) Longer durations may be feasible in some patients.[\[840\]](#)
- Lung recruitment maneuvers are suggested, but staircase recruitment maneuvers are not recommended.[\[533\]](#) [\[792\]](#)
- More detailed guidance on the management of ARDS in COVID-19, including sedation and the use of neuromuscular blockade during ventilation, is beyond the scope of this topic; consult a specialist for further guidance.

Inhaled pulmonary vasodilator

- Consider a trial of an inhaled pulmonary vasodilator in adults who have severe ARDS and hypoxemia despite optimizing ventilation. Taper off if there is no rapid improvement in oxygenation.[\[533\]](#) [\[792\]](#)

Extracorporeal membrane oxygenation

- Consider extracorporeal membrane oxygenation (ECMO) according to availability and expertise if the above methods fail.[\[2\]](#) [\[792\]](#) [\[841\]](#) ECMO is not suitable for all patients, and only those who meet certain inclusion criteria may be considered for ECMO.[\[842\]](#)
- There is insufficient evidence to recommend either for or against the routine use of ECMO.[\[533\]](#)
 - A systematic review and meta-analysis found that in-hospital mortality in adults receiving ECMO was 37.1% during the first year of the pandemic, similar to those with non-COVID-19-related acute respiratory distress syndrome. Increasing age was a risk factor for death. The duration of treatment appears to be prolonged in COVID-19 patients; however, a prolonged treatment course was not a predictor of mortality.[\[843\]](#)
 - Single-access, dual-stage venovenous ECMO with early extubation appears to be safe and effective in patients with COVID-19 respiratory failure.[\[844\]](#)

Management of septic shock/sepsis

- The management of sepsis and septic shock in patients with COVID-19 is beyond the scope of this topic. See the Complications section.

Symptom management and supportive care

- Consider fluid and electrolyte management, antimicrobial treatment, VTE prophylaxis, and symptom management as appropriate (see Management of severe COVID-19 above).
- For VTE prophylaxis, unfractionated heparin is preferred over fondaparinux in critically ill patients if low molecular weight heparin cannot be used.[\[800\]](#)
 - The UK National Institute for Health and Care Excellence (NICE) does not recommend treatment-dose low molecular weight heparin for VTE prophylaxis for patients receiving advanced respiratory support unless the patient is part of a nationally approved clinical trial because it is likely to cause harm in this group. NICE recommends reducing the dose to a locally agreed intermediate or standard dose and reassessing VTE and bleeding risks daily in patients who progress to needing high-flow oxygen, continuous positive airway pressure, noninvasive or invasive mechanical ventilation, or palliative care.[\[564\]](#)
 - NHS England recommends that therapeutic doses should not be offered unless there is a standard indication for therapeutic anticoagulation, as trials show that therapeutic doses do not improve clinical outcome of severe disease in the critical care setting.[\[845\]](#)
 - Some guidelines recommend that escalated doses can be considered in critically ill patients.[\[799\]](#) [\[574\]](#)
 - A multicenter randomized controlled trial found that intermediate-dose prophylactic anticoagulation did not result in a significant difference in the primary outcome of a composite of adjudicated venous or arterial thrombosis, treatment with extracorporeal membrane oxygenation, or 30-day mortality compared with standard-dose prophylactic anticoagulation among patients admitted to the intensive care unit. These results do not support the routine empiric use of intermediate-dose prophylactic anticoagulation in unselected patients admitted to the intensive care unit.[\[846\]](#)

Corticosteroids

- The WHO strongly recommends systemic corticosteroid therapy (low-dose intravenous or oral dexamethasone or hydrocortisone) for 7 to 10 days in adults with critical disease. Moderate-quality evidence suggests that systemic corticosteroids probably reduce 28-day mortality in patients with critical disease. They also probably reduce the need for invasive ventilation.[\[762\]](#) There is also evidence that corticosteroids probably increase ventilator-free days (moderate certainty).[\[815\]](#) [\[816\]](#)
- In the US, the National Institutes of Health guidelines panel recommends dexamethasone (or a suitable alternative corticosteroid), either alone or in combination with remdesivir (see the Emerging section for information on remdesivir), in hospitalized patients who require high-flow oxygen or noninvasive ventilation. In patients who are on mechanical ventilation or ECMO, the panel recommends dexamethasone alone or in combination with tocilizumab for patients who are within 24 hours of admission to the intensive care unit. The panel recommends using dexamethasone in hospitalized children who require high-flow oxygen, noninvasive ventilation, invasive mechanical ventilation, or extracorporeal membrane oxygenation.[\[533\]](#)
 - A meta-analysis found an increased risk of VTE with corticosteroid administration in patients with critical disease. However, no definite findings were available due to the differing corticosteroid regimens and the heterogeneity of the studies.[\[847\]](#)
- See the corticosteroids section under Management of severe COVID-19 above for more information.

IL-6 inhibitors

- The WHO strongly recommends an IL-6 inhibitor, in combination with a systemic corticosteroid and initiated at the same time, in patients with critical disease.[\[762\]](#)
- In the US, the National Institutes of Health guidelines panel recommends adding tocilizumab to dexamethasone (or a suitable alternative corticosteroid) or dexamethasone plus remdesivir in patients who require noninvasive mechanical ventilation or high-flow nasal oxygen and have been recently hospitalized (e.g., within 3 days) with rapidly increasing oxygen needs and systemic inflammation. In patients who are on mechanical ventilation or ECMO, the panel recommends adding tocilizumab to dexamethasone for patients who are within 24 hours of admission to the intensive care unit. There is insufficient evidence for the panel to recommend either for or against the use of tocilizumab in hospitalized children.[\[533\]](#) Tocilizumab has been granted an emergency-use authorization in the US for the treatment of hospitalized adults and pediatric patients 2 years of age and older who are receiving systemic corticosteroids and require noninvasive or invasive mechanical ventilation, or ECMO.[\[813\]](#)
- See the IL-6 inhibitors section under Management of severe COVID-19 above for more information.

Discharge and rehabilitation

- Routinely assess intensive care patients for mobility, functional swallow, cognitive impairment, and mental health concerns, and based on that assessment determine whether the patient is ready for discharge, and whether the patient has any rehabilitation and follow-up requirements.[\[2\]](#)

Palliative care

- Palliative care interventions should be made accessible at each institution that provides care for patients with COVID-19. Identify whether the patient has an advance care plan and respect the patient's priorities and preferences when formulating the patient's care plan.[\[2\]](#)
 - There is a lack of data on palliative care in patients with COVID-19. However, a rapid systematic review of pharmacologic strategies used for palliative care in these patients, the first international review of its kind, found that a higher proportion of patients required continuous subcutaneous infusions for medication delivery than is typically seen in the palliative care population. Modest doses of commonly used end-of-life medications were required for symptom control. However, these findings should be interpreted with caution due to the lack of data available.[\[818\]](#)
- Follow local palliative care guidelines.

Management of pregnant women

Pregnant women should be managed by a multidisciplinary team, including obstetric, perinatal, neonatal, and intensive care specialists, as well as midwifery and mental health and psychosocial support. A woman-centered, respectful, skilled approach to care is recommended.[\[2\]](#) In women with severe or critical disease, the multidisciplinary team should be organized as soon as possible after maternal hypoxemia occurs in order to assess fetal maturity, disease progression, and the best options for delivery.[\[848\]](#)

There are limited data available on the management of pregnant women with COVID-19; however, pregnant women can generally be treated with the same supportive therapies detailed above, taking into account the physiologic changes that occur with pregnancy.[\[2\]](#)

The prevalence of asymptomatic SARS-CoV-2-positive pregnant women admitted for delivery appears to be low (<3% in a cohort in Connecticut, and 0.43% in a cohort in California).[849] [850] Screening women and their delivery partners before admission may not be helpful. More than 15% of asymptomatic maternity patients tested positive for SARS-CoV-2 infection despite having been screened negative using a telephone screening tool in one small observational study in New York. In addition to this, 58% of their asymptomatic support persons tested positive despite being screened negative.[851] Another study in a New York obstetric population found that 88% of women who tested positive for SARS-CoV-2 at admission were asymptomatic at presentation.[852]

Location of care

- Manage pregnant women in a healthcare facility, in a community facility, or at home. Women with suspected or confirmed mild disease may not require acute care in a hospital unless there is concern for rapid deterioration or an inability to return to hospital promptly.[2] Follow local infection prevention and control procedures as for nonpregnant people.
- Consider home care in women with asymptomatic or mild illness, provided the patient has no signs of potentially severe illness (e.g., breathlessness, hemoptysis, new chest pain/pressure, anorexia, dehydration, confusion), no comorbidities, and no obstetric issues; the patient is able to care for herself; and monitoring and follow-up is possible. Otherwise, manage pregnant women in a hospital setting with appropriate maternal and fetal monitoring whenever possible.[627] [853] [854]
- Postpone routine prenatal or postpartum health visits for women who are in home isolation and reschedule them after the isolation period is completed. Delivery of counseling and care should be conducted via telemedicine whenever possible. Counsel women about healthy diet, mobility and exercise, intake of micronutrients, smoking, and alcohol and substance use. Advise women to seek urgent care if they develop any worsening of illness or danger signs, or danger signs of pregnancy.[2]
- The American College of Obstetricians and Gynecologists has published an algorithm to help decide whether hospital admission or home care is more appropriate. [ACOG: outpatient assessment and management for pregnant women with suspected or confirmed novel coronavirus (COVID-19)] (<https://www.acog.org/-/media/project/acog/acogorg/files/pdfs/clinical-guidance/practice-advisory/covid-19-algorithm.pdf?la=en&hash=2D9E7F62C97F8231561616FFDCA3B1A6>)

Prenatal corticosteroids

- Consider prenatal corticosteroids for fetal lung maturation in women who are at risk of preterm birth (24 to 37 weeks' gestation). Caution is advised because corticosteroids could potentially worsen the maternal clinical condition, and the decision should be made in conjunction with the multidisciplinary team.[627] [854] [855] The WHO recommends prenatal corticosteroids only when there is no clinical evidence of maternal infection and adequate childbirth and newborn care is available, and in women with mild COVID-19 after assessing the risks and benefits.[2]
- There is no evidence that corticosteroids in the doses prescribed for fetal lung maturation cause any harm in the context of COVID-19, but there is also no evidence of safety. The unknown effect on maternal outcome should be weighed against the neonatal benefit, particularly at later preterm gestations.[856]

Treatments

- In general, the therapeutic management should be the same for pregnant women as for nonpregnant patients. Most clinical trials to date have excluded pregnant women. However,

potentially effective treatments should not be withheld from pregnant women due to theoretical concerns about the safety of these therapeutic agents in pregnancy. Decisions should be made with a shared decision-making process between the patient and the clinical team.[533]

VTE prophylaxis

- The National Institutes of Health recommends prophylactic dose anticoagulation in pregnant women who are hospitalized with severe disease, provided there are no contraindications to its use. Anticoagulation during labor and delivery requires specialized care and planning, and should be managed in a similar way to pregnant women with other conditions that require anticoagulation. VTE prophylaxis after discharge is not recommended.[533]
- The Royal College of Obstetricians and Gynaecologists (RCOG) has also published guidance on the prevention of VTE in pregnant women.[856]

Labor and delivery

- Implement local infection prevention and control measures during labor and delivery. Screen birth partners for COVID-19 infection using the standard case definition.[2]
- Individualize mode of birth based on obstetric indications and the woman's preferences. Vaginal delivery is preferred in women with confirmed infection to avoid unnecessary surgical complications. Induction of labor, interventions to accelerate labor and delivery, and cesarean delivery are generally only recommended when medically justified based on maternal and fetal condition. COVID-19 positive status alone is not an indication for cesarean section.[2] [627] [854]
- Delayed umbilical cord clamping (not earlier than 1 minute after birth) is recommended for improved maternal and infant health and nutrition outcomes. The risk of transmission via blood is thought to be minimal, and there is no evidence that delayed cord clamping increases the risk of viral transmission from the mother to the newborn.[2]
- Consider babies born to mothers with suspected or confirmed infection to be a person under investigation and isolate them from healthy newborns. Test them for infection 24 hours after birth, and again 48 hours after birth.[857]

Newborn care

- Experts are divided on separating mother and baby after delivery; make decisions on a case-by-case basis using shared-decision making.
- A retrospective cohort analysis, the largest series to date, found no clinical evidence of vertical transmission in 101 newborns born to mothers with suspected or confirmed SARS-CoV-2 infection, despite most newborns rooming-in and direct breastfeeding practices. This suggests that separation may not be warranted and breastfeeding appears to be safe.[858]
- The WHO recommends that mothers and infants should remain together unless the mother is too sick to care for her baby. Breastfeeding should be encouraged while applying appropriate infection prevention and control measures (e.g., performing hand hygiene before and after contact with the baby, wearing a mask while breastfeeding).[2] The WHO advises that the benefits of breastfeeding outweigh the potential risks for transmission.[859] Mother-to-infant transmission appears to be rare during rooming-in, provided that adequate droplet and contact precautions are taken.[860]
- The CDC recommends that temporary separation of a newborn from a mother with confirmed or suspected COVID-19 may be considered after weighing the risks and benefits as current evidence suggests the risk of a neonate acquiring infection from its mother is low; healthcare providers should respect maternal autonomy in the medical decision-making process. If separation is not undertaken, measures to minimize the risk of transmission should be implemented.[861] A mother

with confirmed infection should be counseled to take all possible precautions to avoid transmission to the infant during breastfeeding (e.g., hand hygiene, wearing a cloth face covering). Expressed milk should be fed to the newborn by a healthy caregiver.^[862]

- The RCOG recommends that mothers with confirmed infection and healthy babies are kept together in the immediate postpartum period. It is recommended that the risks and benefits are discussed with neonatologists and families in order to individualize care in babies who may be more susceptible to infection. The RCOG advises that the benefits of breastfeeding outweigh any potential risks of transmission of the virus through breast milk, and recommends appropriate preventive precautions to limit transmission to the baby.^[856]
- The American Academy of Pediatrics (AAP) recommends that mothers and newborns may room-in, with appropriate infection prevention and control precautions, according to usual center practice. However, it may be appropriate to temporarily separate the mother and newborn (or to have the newborn cared for by noninfected caregivers in the mother's room) when the mother is acutely ill with COVID-19 and cannot care for the infant in a safe way. The AAP strongly supports breastfeeding as the best choice for feeding. Breast milk can be expressed after appropriate hygiene measures and fed by an uninfected caregiver. If the mother chooses to breastfeed the infant themselves, appropriate prevention measures are recommended. After discharge, advise mothers with COVID-19 to practice prevention measures (e.g., hand hygiene, respiratory hygiene/mask) for newborn care until: they are afebrile for 24 hours without the use of antipyretics; at least 10 days have passed since symptoms first appeared (or 10 days since a positive test in asymptomatic women); and symptoms have improved. A newborn with documented infection but no symptoms requires close outpatient follow-up after discharge for 14 days after birth.^[857]

Management of people living with HIV

Recommendations for the triage, management, and treatment of COVID-19 in people with HIV are the same as those for the general population. Continue antiretroviral therapy and prophylaxis for opportunistic infections whenever possible, including patients who require hospitalization. Consult with a HIV specialist before adjusting or switching antiretroviral medications, and pay attention to potential drug-drug interactions and overlapping toxicities with COVID-19 treatments.^[533]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

Acute (summary)		
mild COVID-19		
	1st	consider home isolation
	plus	monitoring
	plus	symptom management and supportive care
	adjunct	antipyretic/analgesic
	adjunct	experimental therapies
moderate COVID-19		
	1st	consider home isolation or hospital admission
	plus	monitoring
	plus	symptom management and supportive care
	adjunct	antibiotics
	adjunct	antipyretic/analgesic
	adjunct	experimental therapies
severe COVID-19		
	1st	hospital admission
	plus	consider oxygen therapy
	plus	symptom management and supportive care
	plus	venous thromboembolism prophylaxis
	plus	monitoring
	adjunct	antibiotics
	adjunct	corticosteroid
	adjunct	interleukin-6 (IL-6) inhibitor
	adjunct	treatment of coinfections
	adjunct	antipyretic/analgesic
	adjunct	experimental therapies
	adjunct	plan for discharge and rehabilitation
	adjunct	palliative care
critical COVID-19		
	1st	intensive/critical care unit admission

Acute**(summary)**

- plus symptom management and supportive care**
- plus venous thromboembolism prophylaxis**
- plus consider high-flow nasal oxygen or noninvasive ventilation**
- plus consider invasive mechanical ventilation**
- adjunct inhaled pulmonary vasodilator**
- adjunct extracorporeal membrane oxygenation**
- adjunct management of sepsis/septic shock**
- adjunct corticosteroid**
- adjunct interleukin-6 (IL-6) inhibitor**
- adjunct treatment of coinfections**
- adjunct experimental therapies**
- adjunct plan for discharge and rehabilitation**
- adjunct palliative care**

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

Acute

mild COVID-19

1st

consider home isolation

» Isolate patients with suspected or confirmed mild disease (i.e., symptomatic patients meeting the case definition for COVID-19 without evidence of hypoxia or pneumonia) and asymptomatic patients to contain virus transmission.[2]

» Manage patients in a healthcare facility, in a community facility, or at home. Home isolation can be considered in most patients, with telemedicine or remote visits as appropriate.[2] [533] This decision requires careful clinical judgment and should be informed by an assessment of the patient's home environment to ensure that: infection prevention and control measures and other requirements can be met (e.g., basic hygiene, adequate ventilation); the caregiver is able to provide care and recognize when the patient may be deteriorating; the caregiver has adequate support (e.g., food, supplies, psychological support); the support of a trained health worker is available in the community.[774] The location of care will depend on guidance from local health authorities and available resources.

» Pregnant women with suspected or confirmed mild disease may not require acute care in a hospital unless there is concern for rapid deterioration or an inability to return to hospital promptly.[2]

» Advise patients and household members to follow appropriate infection prevention and control measures:

» [WHO: home care for patients with suspected or confirmed COVID-19 and management of their contacts] ([https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-\(ncov\)-infection-presenting-with-mild-symptoms-and-management-of-contacts](https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and-management-of-contacts))

» [CDC: interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 (COVID-19)] (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-home-care.html>)

» Discontinue transmission-based precautions (including isolation) and release patients from the care pathway: 10 days after positive test (asymptomatic patients); 10 days after

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symptom onset plus at least 3 days without fever and respiratory symptoms (symptomatic patients).[2] The Centers for Disease Control and Prevention (CDC) recommends discontinuing home isolation once at least 10 days (or up to 20 days in patients who are severely immunocompromised) have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. In asymptomatic people, the CDC recommends discontinuing home isolation once at least 10 days have passed since the date of a positive test. For severely immunocompromised patients who are asymptomatic, isolation may be discontinued when at least 10 days and up to 20 days have passed since the date of a positive test; consider consultation with infectious diseases specialists and infection control experts. Alternatively, the CDC recommends at least two negative reverse-transcription polymerase chain reaction (RT-PCR) tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used. A symptom-based strategy is preferred; however, a test-based strategy can be considered in severely immunocompromised patients.[776] If the patient is hospitalized, CDC guidance for discontinuing isolation is the same as for moderate disease (see below). Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 10 days in patients with milder disease who are managed in the community.[777]

plus monitoring

Treatment recommended for ALL patients in selected patient group

» Closely monitor patients with risk factors for severe illness and counsel patients about signs and symptoms of deterioration or complications that require prompt urgent care (e.g., difficulty breathing, chest pain).[2] [533]

» Pulse oximetry monitoring at home is recommended in symptomatic patients with risk factors for progression to severe disease who are not hospitalized. Patient education and appropriate follow-up are required.[2]

plus symptom management and supportive care

Treatment recommended for ALL patients in selected patient group

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» Advise patients to avoid lying on their back as this makes coughing ineffective. Use simple measures first (e.g., a teaspoon of honey in patients ages 1 year and older) to help cough.[564] A meta-analysis found that honey is superior to usual care (e.g., antitussives) for the improvement of upper respiratory tract infection symptoms, particularly cough frequency and severity.[785]

» Advise patients about adequate nutrition and appropriate rehydration. Advise patients to drink fluids regularly to avoid dehydration. Fluid intake needs can be higher than usual because of fever. However, too much fluid can worsen oxygenation.[2] [564]

» Advise patients to improve air circulation by opening a window or door.[564]

» Provide basic mental health and psychosocial support for all patients, and manage any symptoms of insomnia, depression, or anxiety as appropriate.[2]

» Consider treatment for olfactory dysfunction (e.g., olfactory training) if it persists beyond 2 weeks. There is no evidence to support the use of these treatments in patients with COVID-19.[786]

» Most children with mild disease can be managed with supportive care alone.[533]

adjunct

antipyretic/analgesic

Treatment recommended for SOME patients in selected patient group

Primary options

» **acetaminophen**: children: 10-15 mg/kg orally every 4-6 hours when required, maximum 75 mg/kg/day; adults: 325-1000 mg orally (immediate-release) every 4-6 hours when required, maximum 4000 mg/day

OR

» **ibuprofen**: children 6 months to 11 years of age: 5-10 mg/kg orally every 6-8 hours when required, maximum 40 mg/kg/day; children ≥12 years of age and adults: 200-400 mg orally every 4-6 hours when required, maximum 2400 mg/day

» Acetaminophen or ibuprofen are recommended.[2] [564] There is no evidence at present of severe adverse events in COVID-19

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patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, or of effects as a result of the use of NSAIDs on acute healthcare utilization, long-term survival, or quality of life in patients with COVID-19.[778] [779] [780] [781] [782] [783] [784]

» Ibuprofen should only be taken at the lowest effective dose for the shortest period needed to control symptoms. It is not recommended in pregnant women (especially in the third trimester) or children <6 months of age (age cut-offs vary by country).

adjunct experimental therapies

Treatment recommended for SOME patients in selected patient group

» Consider any appropriate experimental or emerging therapies.

» Antiviral therapies will have a greater effect early in the course of the disease, whereas immunosuppressive/anti-inflammatory therapies are likely to have a greater effect later in the course of the disease.[533]

» See the Emerging section for more information.

moderate COVID-19

1st consider home isolation or hospital admission

» Isolate patients with suspected or confirmed moderate disease (i.e., clinical signs of pneumonia but no signs of severe pneumonia) to contain virus transmission.[2]

» Manage patients in a healthcare facility, in a community facility, or at home. Home isolation, with telemedicine or remote visits as appropriate, can be considered in low-risk patients. Manage patients at high risk of deterioration and pregnant women in a healthcare facility.[2] [533]

» Implement local infection prevention and control procedures when managing patients with COVID-19. For patients in home isolation, advise patients and household members to follow appropriate infection prevention and control measures:

» [WHO: home care for patients with suspected or confirmed COVID-19 and management of their contacts] ([https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-\(ncov\)-infection-presenting-](https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-)

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with-mild-symptoms-and-management-of-contacts)

» [CDC: interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 (COVID-19)] (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-home-care.html>)

» Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.[2] The Centers for Disease Control and Prevention (CDC) recommends discontinuing isolation once at least 10 days (not severely immunocompromised) or up to 20 days (severely immunocompromised) have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. In asymptomatic people, the CDC recommends discontinuing isolation once at least 10 days (not severely immunocompromised) or up to 20 days (severely immunocompromised) have passed since the date of a positive test. Severely immunocompromised patients may produce replication-competent virus beyond 20 days and require additional testing and consultation with infectious diseases specialists and infection control experts before discontinuing isolation. Alternatively, the CDC recommends at least two negative reverse-transcription polymerase chain reaction (RT-PCR) tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used. A symptom-based strategy is preferred; however, a test-based strategy can be considered in severely immunocompromised patients.[787] If the patient is isolated at home, CDC guidance for discontinuing isolation is the same as for mild disease (see above). Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 14 days from a positive test in hospitalized patients, and 10 days in patients with milder disease who are managed in the community. Immunocompetent patients who tested positive on RT-PCR and have completed their 14-day isolation period are exempt from testing prior to hospital discharge if they are within 90 days from their initial illness onset or test, unless they develop new symptoms.[777]

plus monitoring

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Treatment recommended for ALL patients in selected patient group

» Closely monitor patients for signs or symptoms of disease progression. If the patient is being managed at home, counsel them about signs and symptoms of deterioration or complications that require prompt urgent care (e.g., difficulty breathing, chest pain).[863] [533] Pulse oximetry monitoring at home is recommended in symptomatic patients with risk factors for progression to severe disease who are not hospitalized. Patient education and appropriate follow-up are required.[863] If the patient is being managed in hospital, monitor patients closely for signs of clinical deterioration using medical early warning scores (e.g., National Early Warning Score 2 [NEWS2]), and respond immediately with appropriate supportive care interventions.[2]

plus

symptom management and supportive care

Treatment recommended for ALL patients in selected patient group

» Advise patients to avoid lying on their back as this makes coughing ineffective. Use simple measures first (e.g., a teaspoon of honey in patients ages 1 year and older) to help cough.[564] A meta-analysis found that honey is superior to usual care (e.g., antitussives) for the improvement of upper respiratory tract infection symptoms, particularly cough frequency and severity.[785]

» Advise patients about adequate nutrition and appropriate rehydration. Advise patients to drink fluids regularly to avoid dehydration. Fluid intake needs can be higher than usual because of fever. However, too much fluid can worsen oxygenation.[2] [564]

» Advise patients to improve air circulation by opening a window or door.[564]

» Provide basic mental health and psychosocial support for all patients, and manage any symptoms of insomnia, depression, or anxiety as appropriate.[2]

» Consider treatment for olfactory dysfunction (e.g., olfactory training) if it persists beyond 2 weeks. There is no evidence to support the use of these treatments in patients with COVID-19.[786]

» Most children with moderate disease can be managed with supportive care alone.[533]

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adjunct antibiotics

Treatment recommended for SOME patients in selected patient group

» Consider empiric antibiotics only if there is clinical suspicion of secondary bacterial infection. Start treatment as soon as possible, and refer to local guidelines for choice of regimen.[2] [533] [564] The regimen should be based on the clinical diagnosis, local epidemiology and susceptibility data, and local treatment guidelines.

» Antibiotics may also be considered in older people (particularly those in long-term care facilities) and children <5 years of age to provide empiric antibiotic treatment for possible pneumonia.[2]

» Do not offer an antibiotic for preventing secondary bacterial pneumonia in people with COVID-19.[564]

» Advise patients to seek medical help without delay if their symptoms do not improve, or worsen rapidly or significantly. Reconsider whether the person has signs and symptoms of more severe disease on reassessment, and whether to refer them to hospital, other acute community support services, or palliative care services.[564]

adjunct antipyretic/analgesic

Treatment recommended for SOME patients in selected patient group

Primary options

» **acetaminophen**: children: 10-15 mg/kg orally every 4-6 hours when required, maximum 75 mg/kg/day; adults: 325-1000 mg orally (immediate-release) every 4-6 hours when required, maximum 4000 mg/day

OR

» **ibuprofen**: children 6 months to 11 years of age: 5-10 mg/kg orally every 6-8 hours when required, maximum 40 mg/kg/day; children ≥12 years of age and adults: 200-400 mg orally every 4-6 hours when required, maximum 2400 mg/day

» Acetaminophen or ibuprofen are recommended.[2] [564] There is no evidence at present of severe adverse events in COVID-19 patients taking nonsteroidal anti-inflammatory

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drugs (NSAIDs) such as ibuprofen, or of effects as a result of the use of NSAIDs on acute healthcare utilization, long-term survival, or quality of life in patients with COVID-19.[778] [779] [780] [781] [782] [783] [784]

» Ibuprofen should only be taken at the lowest effective dose for the shortest period needed to control symptoms. It is not recommended in pregnant women (especially in the third trimester) or children <6 months of age (age cut-offs vary by country).

adjunct experimental therapies

Treatment recommended for SOME patients in selected patient group

» Consider any appropriate experimental or emerging therapies.

» Antiviral therapies will have a greater effect early in the course of the disease, whereas immunosuppressive/anti-inflammatory therapies are likely to have a greater effect later in the course of the disease.[533]

» See the Emerging section for more information.

severe COVID-19

1st hospital admission

» Admit patients with suspected or confirmed severe disease to an appropriate healthcare facility under the guidance of a specialist team as these patients are at risk of rapid clinical deterioration.

» Severe disease in adults is defined as having clinical signs of pneumonia plus at least one of the following: respiratory rate >30 breaths/minute, severe respiratory distress, or SpO₂ <90% on room air. Severe disease in children is defined as having clinical signs of pneumonia plus at least one of the following: central cyanosis or SpO₂ <90%, severe respiratory distress, general danger signs (inability to breastfeed or drink, lethargy or unconsciousness, or convulsions), or fast breathing (<2 months: ≥60 breaths per minute; 2-11 months: ≥50 breaths per minute; 1-5 years: ≥40 breaths per minute).[2]

» Pregnant women should be managed by a multidisciplinary team, including obstetric, perinatal, neonatal, and intensive care specialists, as well as midwifery and mental health and psychosocial support. A woman-

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centered, respectful, skilled approach to care is recommended.[2] The multidisciplinary team should be organized as soon as possible after maternal hypoxemia occurs in order to assess fetal maturity, disease progression, and the best options for delivery.[848]

» Implement local infection prevention and control procedures when managing patients with COVID-19.

» Use the Clinical Frailty Scale (CFS) to assess baseline health and inform discussions on treatment expectations when appropriate and within an individualised assessment of frailty. [Clinical Frailty Scale] (<https://www.scfn.org.uk/clinical-frailty-scale>) Do not use the CFS for younger people, people with stable long-term disabilities (e.g., cerebral palsy), learning disabilities, or autism. Make an individualized assessment of frailty in these people, using clinical assessment and alternative scoring methods.[564] A meta-analysis found that an increase in CFS was associated with an increase in mortality (each 1-point increase in CFS was associated with a 12% increase in mortality).[788] However, some studies suggest that a more nuanced understanding of frailty and outcomes is needed, and you should exercise caution in placing too much emphasis on the influence of frailty alone when discussing prognosis in older people.[790]

» Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.[2] The Centers for Disease Control and Prevention (CDC) recommends discontinuing isolation once at least 10 days and up to 20 days have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. Consider consultation with infection control experts before discontinuing isolation. Severely immunocompromised patients may produce replication-competent virus beyond 20 days and require additional testing and consultation with infectious diseases specialists and infection control experts before discontinuing isolation. Alternatively, the CDC recommends at least two negative reverse-transcription polymerase chain reaction (RT-PCR) tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used.

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A symptom-based strategy is preferred; however, a test-based strategy can be considered in severely immunocompromised patients.^[787] Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 14 days from a positive test in hospitalized patients. Immunocompetent patients who tested positive on RT-PCR and have completed their 14-day isolation period are exempt from testing prior to hospital discharge if they are within 90 days from their initial illness onset or test, unless they develop new symptoms.^[777]

plus

consider oxygen therapy

Treatment recommended for ALL patients in selected patient group

» Start supplemental oxygen therapy immediately in any patient with emergency signs (i.e., obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma and/or convulsions), or any patient without emergency signs and $\text{SpO}_2 < 90\%$.^{[2] [533]}

» Target SpO_2 to $\geq 94\%$ during resuscitation in adults and children with emergency signs who require emergency airway management and oxygen therapy. Once the patient is stable, a target $\text{SpO}_2 > 90\%$ in children and nonpregnant adults, and $\geq 92\%$ to 95% in pregnant women, is recommended. Nasal prongs or a nasal cannula are preferred in young children.^[2] Some guidelines recommend that SpO_2 should be maintained no higher than 96% .^[792]

» Some centers may recommend different SpO_2 targets in order to support prioritization of oxygen flow for the most severely ill patients in hospital. NHS England recommends a target of 92% to 96% (or 90% if clinically appropriate), for example.^[793]

» Consider positioning techniques (e.g., high supported sitting), and airway clearance management to optimize oxygenation and assist with secretion clearance in adults. Consider awake prone positioning (for 8-12 hours/day, broken into shorter periods over the day) in severely ill patients who require supplemental oxygen.^{[2] [533]} Awake prone positioning of nonintubated patients was associated with improvement in oxygen variables ($\text{PaO}_2/\text{FiO}_2$, PaO_2 , and SpO_2), respiratory rate, and mortality, but no significant difference was noted in the rate of intubation. However, evidence is limited.^{[794] [795]}

Acute

plus

» Monitor patients closely for signs of progressive acute hypoxemic respiratory failure.[\[2\]](#) [\[533\]](#)

symptom management and supportive care

Treatment recommended for ALL patients in selected patient group

» Fluids and electrolytes: use cautious fluid management in adults and children without tissue hypoperfusion and fluid responsiveness as aggressive fluid resuscitation may worsen oxygenation.[\[2\]](#) Correct any electrolyte or metabolic abnormalities, such as hyperglycemia or metabolic acidosis, according to local protocols.[\[796\]](#)

» Cough: advise patients to avoid lying on their back as this makes coughing ineffective. Use simple measures first (e.g., a teaspoon of honey in patients ages 1 year and older) to help cough. Short-term use of a cough suppressant may be considered in select patients (e.g., if the cough is distressing to the patient) provided there are no contraindications.[\[564\]](#) A meta-analysis found that honey is superior to usual care (e.g., antitussives) for the improvement of upper respiratory tract infection symptoms, particularly cough frequency and severity.[\[785\]](#)

» Breathlessness: keep the room cool, and encourage relaxation, breathing techniques, and changing body positions. Identify and treat any reversible causes of breathlessness (e.g., pulmonary edema, pulmonary embolism, COPD, asthma). Consider a trial of oxygen, if available.[\[564\]](#)

» Anxiety, delirium, and agitation: identify and treat any underlying or reversible causes (e.g., offer reassurance, treat hypoxia, correct metabolic or endocrine abnormalities, address coinfections, minimize use of drugs that may cause or worsen delirium, treat substance withdrawal, maintain normal sleep cycles, treat pain or breathlessness).[\[2\]](#) [\[564\]](#) Low doses of haloperidol (or another suitable antipsychotic) can be considered for agitation.[\[2\]](#) Nonpharmacologic interventions are the mainstay for the management of delirium when possible, and prevention is key.[\[797\]](#)

» Mouth care: an important part of overall patient care in hospitalized patients who are ventilated or nonventilated and those undergoing step-down or end-of-life care.[\[798\]](#)

Acute

plus

» Mental health symptoms: provide basic mental health and psychosocial support for all patients, and manage any symptoms of insomnia or depression as appropriate.[2]

venous thromboembolism prophylaxis

Treatment recommended for ALL patients in selected patient group

Primary options

» **enoxaparin**: consult specialist for guidance on dose

OR

» **dalteparin**: consult specialist for guidance on dose

Secondary options

» **fondaparinux**: consult specialist for guidance on dose

OR

» **heparin**: consult specialist for guidance on dose

» Assess the risk of bleeding as soon as possible after admission, or by the time of the first consultant review, using a suitable risk assessment tool.[564]

» Start venous thromboembolism (VTE) prophylaxis in acutely ill hospitalized adults and adolescents, provided there are no contraindications.[2] [533] [799] [800] The UK National Institute for Health and Care Excellence (NICE) recommends starting as soon as possible and within 14 hours of admission, and continuing for a minimum of 14 days or until discharge.[564] For hospitalized children, indications for VTE prophylaxis should be the same as those for children without COVID-19.[533]

» Low molecular weight heparin, unfractionated heparin, or fondaparinux are the recommended options for standard thromboprophylaxis.[2] NICE recommends low molecular weight heparin first-line, with fondaparinux or unfractionated heparin reserved for patients who cannot have low molecular weight heparin.[564] Unfractionated heparin is contraindicated in patients with severe thrombocytopenia. Fondaparinux is recommended in patients with

Acute

a history of heparin-induced thrombocytopenia. Mechanical thromboprophylaxis (e.g., intermittent pneumatic compression devices) is recommended if anticoagulation is contraindicated or not available.[800] [802]

» The optimal dose is yet to be determined. Standard prophylaxis doses are generally recommended over intermediate- or full treatment-dose regimens in patients without an established indication for higher-dose anticoagulation. However, this recommendation varies and you should consult your local guidelines. The World Health Organization recommends standard thromboprophylaxis dosing of anticoagulation rather than therapeutic or intermediate dosing in patients without an established indication for higher-dose anticoagulation.[2] NICE recommends clinicians consider a treatment dose of a low molecular weight heparin in young people and adults who are likely to be in hospital for at least 3 days and need supplemental oxygen (but who are not yet receiving high-flow oxygen, continuous positive airway pressure, noninvasive ventilation, or invasive mechanical ventilation), unless contraindicated. This is because of fewer deaths and less likelihood of needing intensive care with this dose compared with a standard prophylaxis dose without a notable increase in major bleeding, although the evidence for this recommendation is weak. Treatment should be for a minimum of 14 days or until discharge, and the dose may need to be reduced if the clinical circumstances change (such as a need for advanced respiratory support). For those who do not need supplemental oxygen, follow standard VTE prophylaxis guidelines.[564] The National Institutes of Health guidelines panel recommends prophylactic-dose anticoagulation, and states that there are insufficient data to recommend increased anticoagulant doses for VTE prophylaxis in COVID-19 patients outside the setting of a clinical trial.[533]

» Dose adjustments may be required in patients with extremes of body weight or renal impairment.[564]

» For patients who are already on an anticoagulant for another condition, continue the patient's current therapeutic dose unless contraindicated by a change in clinical circumstances. Consider switching to low molecular weight heparin as the preferred option for venous thromboembolism prophylaxis if the patient's clinical condition is deteriorating and

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the patient is not currently on low molecular weight heparin.[564]

» Monitor patients for signs and symptoms suggestive of thromboembolism and proceed with appropriate diagnostic and management pathways if clinically suspected.[2] If the patient's clinical condition changes, assess the risk of VTE, reassess the bleeding risk, and review VTE prophylaxis.[564]

» Continue until hospital discharge.[2] Routine post-discharge VTE prophylaxis is not generally recommended, except in certain high-risk patients.[533] [799] [800] Ensure patients who require VTE prophylaxis after discharge are able to use it correctly or have arrangements made for someone to help them.[564]

» There is currently insufficient evidence to determine the risks and benefits of prophylactic anticoagulation in hospitalized patients with COVID-19.[805] A systematic review and meta-analysis found that the pooled odds of mortality between anticoagulated and nonanticoagulated hospitalized patients were similar, but lower in the standard prophylactic-dose group. Prophylactic-dose anticoagulation significantly decreased the odds of in-hospital death by 17% compared with no anticoagulation. Mortality increased in the intermediate- to therapeutic-dose group with an increased risk of major bleeding.[806] Clinicians should rely on pre-COVID-19 evidence-based principles of anticoagulation management combined with rational approaches to address clinical challenges.[799]

plus **monitoring**

Treatment recommended for ALL patients in selected patient group

» Monitor patients closely for signs of clinical deterioration, and respond immediately with appropriate supportive care interventions.[2]

adjunct **antibiotics**

Treatment recommended for SOME patients in selected patient group

» Consider empiric antibiotics if there is clinical suspicion of secondary bacterial infection. Give within 1 hour of initial assessment for patients with suspected sepsis or if the patient meets high-risk criteria (or within 4 hours of establishing a diagnosis of secondary bacterial pneumonia); do not wait for microbiology results. Base the regimen on the clinical diagnosis

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(e.g., community-acquired pneumonia, hospital-acquired pneumonia, sepsis), local epidemiology and susceptibility data, and local treatment guidelines.[2] [533] [564]

» Do not offer antibiotics for preventing or treating pneumonia if SARS-CoV-2, another virus, or a fungal infection is likely to be the cause.[564] There is insufficient evidence to recommend empiric broad-spectrum antibiotics in the absence of another indication.[533]

» Consider seeking specialist advice for people who: are immunocompromised; have a history of infection with resistant organisms; have a history of repeated infective exacerbations of lung disease; are pregnant; or are receiving advanced respiratory or organ support.[564] Seek specialist advice if there is a suspicion that the person has an infection with multidrug-resistant bacteria and may need a different antibiotic, or there is clinical or microbiologic evidence of infection and the person's condition does not improve as expected after 48 to 72 hours of antibiotic treatment.[564]

» Reassess antibiotic use daily. De-escalate empiric therapy on the basis of microbiology results and clinical judgment. Regularly review the possibility of switching from intravenous to oral therapy. Duration of treatment should be as short as possible (e.g., 5 to 7 days). Antibiotic stewardship programs should be in place.[2]

adjunct corticosteroid

Treatment recommended for SOME patients in selected patient group

Primary options

» **dexamethasone**: children: consult specialist for guidance on dose; adults: 6 mg orally/ intravenously once daily for 7-10 days

OR

» **hydrocortisone**: children: consult specialist for guidance on dose; adults: 50 mg orally/ intravenously every 8 hours for 7-10 days

Secondary options

» **prednisone**: children: consult specialist for guidance on dose; adults: 40 mg/day orally given in 1-2 divided doses for 7-10 days

OR

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» **methylprednisolone**: children: consult specialist for guidance on dose; adults: 32 mg/day orally/intravenously given in 1-2 divided doses for 7-10 days

» Consider a systemic corticosteroid. Guideline recommendations vary.

» The World Health Organization strongly recommends systemic corticosteroid therapy (low-dose intravenous or oral dexamethasone or hydrocortisone) for 7 to 10 days in adults with severe disease. This recommendation is based on two meta-analyses that pooled data from eight randomized trials (over 7000 patients), including the UK RECOVERY trial. Moderate-quality evidence suggests that systemic corticosteroids probably reduce 28-day mortality in patients with severe disease. There is no evidence directly comparing dexamethasone and hydrocortisone. The harms of treatment in this context are considered to be minor. It is unclear whether these recommendations can be applied to children or those who are immunocompromised.[762] [763] [764] [808] [809]

» [BMJ rapid recommendations: a living WHO guideline on drugs for COVID-19] (<https://www.bmj.com/content/370/bmj.m3379>)

» In the UK, the National Institute for Health and Care Excellence recommends offering dexamethasone (or an alternative such as hydrocortisone or prednisone when dexamethasone cannot be used or is unavailable) to people who need supplemental oxygen to meet their prescribed oxygen saturation levels, or who have a level of hypoxia that needs supplemental oxygen but who are unable to have or tolerate it. Treatment is for up to 10 days unless there is a clear indication to stop early.[564]

» In the US, the National Institutes of Health guidelines panel recommends dexamethasone, either alone or in combination with remdesivir (see the Emerging section for information on remdesivir), in hospitalized adults who require supplemental oxygen. Alternative corticosteroids may be used in situations where dexamethasone is not available. It is not routinely recommended for pediatric patients who require only low levels of oxygen support (i.e., via a nasal cannula only). Use of dexamethasone for the treatment of severe disease in children who are profoundly immunocompromised has not been evaluated, may be harmful, and therefore

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should be considered only on a case-by-case basis.[533] The Infectious Diseases Society of America supports the use of dexamethasone in hospitalized patients with severe disease.[810]

» Monitor patients for adverse effects (e.g., hyperglycemia, secondary infections, psychiatric effects, reactivation of latent infections) and assess for drug-drug interactions.[533]

adjunct interleukin-6 (IL-6) inhibitor

Treatment recommended for SOME patients in selected patient group

Primary options

» **tocilizumab**: children: consult specialist for guidance on dose; adults: 8 mg/kg intravenously as a single dose, maximum 800 mg/dose

Typically administered as a single intravenous dose; however, a second dose may be administered 12 to 48 hours after the first dose if the clinical response is inadequate. World Health Organization. Therapeutics and COVID-19: living guideline. 2021 [internet publication]. <https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.2>

OR

» **sarilumab**: children: consult specialist for guidance on dose; adults: 400 mg intravenously as a single dose

Typically administered as a single intravenous dose; however, a second dose may be administered 12 to 48 hours after the first dose if the clinical response is inadequate. World Health Organization. Therapeutics and COVID-19: living guideline. 2021 [internet publication]. <https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.2>

» Consider an IL-6 inhibitor. Guideline recommendations vary.

» The World Health Organization strongly recommends an IL-6 inhibitor (tocilizumab or sarilumab), in combination with a systemic corticosteroid and initiated at the same time, in patients with severe disease. This recommendation is based on high-certainty evidence that shows IL-6 inhibitors reduce mortality and the need for mechanical ventilation, and low-certainty evidence that suggests that IL-6 inhibitors may also reduce the duration of mechanical ventilation and hospitalization. The evidence regarding the

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risk of severe adverse events is uncertain. The applicability of this recommendation to children is currently uncertain.[762] [763] [764] This recommendation is based on data from the UK RECOVERY and REMAP-CAP trials.[811] [812]

» [BMJ rapid recommendations: a living WHO guideline on drugs for COVID-19] (<https://www.bmj.com/content/370/bmj.m3379>)

» In the UK, the National Institute for Health and Care Excellence recommends a single dose of tocilizumab in hospitalized adults if all of the following conditions apply: they are having or have completed a course of corticosteroids such as dexamethasone (unless they cannot have corticosteroids); they have not had another IL-6 inhibitor during this admission; there is no evidence of a bacterial or viral infection (other than SARS-CoV-2) that might be worsened by tocilizumab; AND they either need supplemental oxygen and have a C-reactive protein level of ≥ 75 mg/L, OR they are within 48 hours of starting high-flow nasal oxygen, continuous positive airway pressure, noninvasive ventilation, or invasive mechanical ventilation. Consider tocilizumab for children and young people who have severe disease or pediatric inflammatory multisystem syndrome only if they are ages 1 year and over, and only in the context of a clinical trial. Sarilumab may be considered an alternative option in adults only if tocilizumab cannot be used or is unavailable (use the same eligibility criteria as those for tocilizumab).[564] Tocilizumab has not been granted a conditional marketing authorization for this indication in the UK as yet.

» In the US, the Infectious Diseases Society of America recommends considering tocilizumab in hospitalized adults with progressive severe disease who have elevated markers of systemic inflammation, in addition to standard of care (i.e., corticosteroids), rather than standard of care alone.[810] Tocilizumab has been granted an emergency-use authorization in the US for the treatment of hospitalized adults and pediatric patients 2 years of age and older who are receiving systemic corticosteroids and require supplemental oxygen.[813]

» Patients on IL-6 inhibitors are at increased risk of infection including active tuberculosis, invasive fungal infections, and opportunistic pathogens.

» Routine blood work including neutrophil count, platelets, transaminases, and total bilirubin should be checked prior to initiation of therapy.

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All patients should be monitored for signs and symptoms of infection given the increased risk of immunosuppression in addition to systemic corticosteroids.[762]

» These drugs should be avoided in patients who are significantly immunocompromised.[533]

adjunct treatment of coinfections

Treatment recommended for SOME patients in selected patient group

» Treat laboratory-confirmed coinfections (e.g., malaria, tuberculosis, influenza) as appropriate according to local protocols.[2] The treatment of influenza is the same in all patients regardless of SARS-CoV-2 coinfection. Start empiric treatment with oseltamivir in hospitalized patients who are suspected of having either or both infections as soon as possible without waiting for influenza test results. Antiviral therapy can be stopped once influenza has been ruled out.[533]

adjunct antipyretic/analgesic

Treatment recommended for SOME patients in selected patient group

Primary options

» **acetaminophen**: children: 10-15 mg/kg orally every 4-6 hours when required, maximum 75 mg/kg/day; adults: 325-1000 mg orally (immediate-release) every 4-6 hours when required, maximum 4000 mg/day

OR

» **ibuprofen**: children 6 months to 11 years of age: 5-10 mg/kg orally every 6-8 hours when required, maximum 40 mg/kg/day; children ≥12 years of age and adults: 200-400 mg orally every 4-6 hours when required, maximum 2400 mg/day

» Acetaminophen or ibuprofen are recommended.[2] [564] There is no evidence at present of severe adverse events in COVID-19 patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, or of effects as a result of the use of NSAIDs on acute healthcare utilization, long-term survival, or quality of life in patients with COVID-19.[778] [779] [780] [781] [782] [783] [784]

» Ibuprofen should only be taken at the lowest effective dose for the shortest period needed to control symptoms. It is not recommended in pregnant women (especially in the third

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- trimester) or children <6 months of age (age cut-offs vary by country).
- adjunct experimental therapies**
- Treatment recommended for SOME patients in selected patient group
- » Consider any appropriate experimental or emerging therapies.
 - » Antiviral therapies will have a greater effect early in the course of the disease, whereas immunosuppressive/anti-inflammatory therapies are likely to have a greater effect later in the course of the disease.[533]
 - » See the Emerging section for more information.
- adjunct plan for discharge and rehabilitation**
- Treatment recommended for SOME patients in selected patient group
- » Routinely assess older patients for mobility, functional swallow, cognitive impairment, and mental health concerns. Based on that assessment determine whether the patient is ready for discharge, and whether the patient has any rehabilitation and follow-up requirements.[2]
- adjunct palliative care**
- Treatment recommended for SOME patients in selected patient group
- » Palliative care interventions should be made accessible at each institution that provides care for patients with COVID-19. Identify whether the patient has an advance care plan and respect the patient's priorities and preferences when formulating the patient's care plan.[2] Follow local palliative care guidelines.
 - » There is a lack of data on palliative care in patients with COVID-19. A rapid systematic review of pharmacologic strategies used for palliative care in these patients, the first international review of its kind, found that a higher proportion of patients required continuous subcutaneous infusions for medication delivery than is typically seen in the palliative care population. Modest doses of commonly used end-of-life medications were required for symptom control. However, these findings should be interpreted with caution due to the lack of data available.[818]

critical COVID-19

1st intensive/critical care unit admission

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- » Admit or transfer patients with critical disease (i.e., presence of acute respiratory distress syndrome, sepsis, or septic shock) to an intensive/critical care unit under the guidance of a specialist team.[2]
- » Discuss the risks, benefits, and potential outcomes of treatment options with patients and their families, and allow them to express preferences about their management. Take their wishes and expectations into account when considering the ceiling of treatment. Use decision support tools if available. Put treatment escalation plans in place, and discuss any existing advance care plans or advance decisions to refuse treatment with patients who have preexisting advanced comorbidities.[564]
- » Implement local infection prevention and control procedures when managing patients with COVID-19.
- » Pregnant women should be managed by a multidisciplinary team, including obstetric, perinatal, neonatal, and intensive care specialists, as well as midwifery and mental health and psychosocial support. A woman-centered, respectful, skilled approach to care is recommended.[2] The multidisciplinary team should be organized as soon as possible after maternal hypoxemia occurs in order to assess fetal maturity, disease progression, and the best options for delivery.[848]
- » Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.[2] The Centers for Disease Control and Prevention (CDC) recommends discontinuing isolation once at least 10 days and up to 20 days have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. Consider consultation with infection control experts before discontinuing isolation. Severely immunocompromised patients may produce replication-competent virus beyond 20 days and require additional testing and consultation with infectious diseases specialists and infection control experts before discontinuing isolation. Alternatively, the CDC recommends at least two negative reverse-transcription polymerase chain reaction (RT-PCR) tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used.

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A symptom-based strategy is preferred; however, a test-based strategy can be considered in severely immunocompromised patients.^[787] Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 14 days from a positive test in hospitalized patients. Immunocompetent patients who tested positive on RT-PCR and have completed their 14-day isolation period are exempt from testing prior to hospital discharge if they are within 90 days from their initial illness onset or test, unless they develop new symptoms.^[777]

plus symptom management and supportive care

Treatment recommended for ALL patients in selected patient group

» Consider fluid and electrolyte management, antimicrobial treatment, and symptom management as appropriate. See Severe COVID-19 above for more detailed information.

» Follow local guidelines for the management of pain, sedation, and delirium.^[533]

» Implement standard interventions to prevent complications associated with critical illness.^[2]

plus venous thromboembolism prophylaxis

Treatment recommended for ALL patients in selected patient group

Primary options

» **enoxaparin**: consult specialist for guidance on dose

OR

» **dalteparin**: consult specialist for guidance on dose

Secondary options

» **heparin**: consult specialist for guidance on dose

OR

» **fondaparinux**: consult specialist for guidance on dose

» Start venous thromboembolism (VTE) prophylaxis in acutely ill hospitalized adults

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and adolescents, provided there are no contraindications.[863] [533] [799] [800]

» Unfractionated heparin is preferred over fondaparinux in critically ill patients if low molecular weight heparin, as the preferred option for venous thromboembolism prophylaxis, cannot be used.[800]

» The UK National Institute for Health and Care Excellence (NICE) does not recommend treatment-dose low molecular weight heparin for VTE prophylaxis for patients receiving advanced respiratory support unless the patient is part of a nationally approved clinical trial because it is likely to cause harm in this group. NICE recommends reducing the dose to a locally agreed intermediate or standard dose and reassessing VTE and bleeding risks daily in patients who progress to needing high-flow oxygen, continuous positive airway pressure, noninvasive or invasive mechanical ventilation, or palliative care.[564]

» NHS England recommends that therapeutic doses should not be offered unless there is a standard indication for therapeutic anticoagulation, as trials show that therapeutic doses do not improve clinical outcome of severe disease in the critical care setting.[845]

» Some guidelines recommend that escalated doses can be considered in critically ill patients.[799] [574]

» Dose adjustments may be required in patients with extremes of body weight or renal impairment.[564]

» Evidence is limited in patients with critical disease.

» A multicenter randomized controlled trial found that intermediate-dose prophylactic anticoagulation did not result in a significant difference in the primary outcome of a composite of adjudicated venous or arterial thrombosis, treatment with extracorporeal membrane oxygenation, or 30-day mortality compared with standard-dose prophylactic anticoagulation among patients admitted to the intensive care unit. These results do not support the routine empiric use of intermediate-dose prophylactic anticoagulation in unselected patients admitted to the intensive care unit.[846]

» See Severe COVID-19 above for more detailed information on VTE prophylaxis.

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plus

consider high-flow nasal oxygen or noninvasive ventilation

Treatment recommended for ALL patients in selected patient group

» Consider a trial of high-flow nasal oxygen (HFNO) or noninvasive ventilation (e.g., continuous positive airway pressure [CPAP] or bilevel positive airway pressure [BiPAP]) in selected patients with mild acute respiratory distress syndrome.

» Patients with hypercapnia, hemodynamic instability, multi-organ failure, or abnormal mental status should generally not receive HFNO, although emerging data suggest that it may be safe in patients with mild to moderate and nonworsening hypercapnia. Patients with hypoxemic respiratory failure and hemodynamic instability, multi-organ failure, or abnormal mental status should not receive these treatments in place of other options such as invasive ventilation.[2]

» Airborne precautions are recommended for these interventions (including bubble CPAP) due to uncertainty about the potential for aerosolization.[2]

» Consider awake prone positioning (for 8-12 hours/day, broken into shorter periods over the day) in severely ill patients who require HFNO or noninvasive ventilation.[2] Awake prone positioning of nonintubated patients was associated with improvement in oxygen variables ($\text{PaO}_2/\text{FiO}_2$, PaO_2 , and SpO_2), respiratory rate, and mortality, but no significant difference was noted in the rate of intubation. However, evidence is limited.[794] [795]

» There is ongoing debate about the optimal mode of respiratory support before mechanical ventilation.[825] NHS England recommends CPAP as the preferred form of noninvasive ventilation in patients with hypoxemic (type 1) respiratory failure. It doesn't advocate the use of HFNO based on a lack of efficacy, oxygen use (HFNO can place a strain on oxygen supplies with the risk of site supply failure), and infection spread.[826] Other guidelines recommend HFNO over noninvasive ventilation, unless HFNO is not available.[533] [792] Despite the trend to avoid HFNO, it has been shown to have a similar risk of aerosol generation to standard oxygen masks.[827]

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» Early CPAP may provide a bridge to invasive mechanical ventilation. Reserve the use of BiPAP for patients with hypercapnic acute on chronic ventilatory failure (type 2 respiratory failure).[826]

» Monitor patients closely for acute deterioration. If patients do not improve after a short trial of these interventions, they require urgent endotracheal intubation.[2] [792]

plus consider invasive mechanical ventilation

Treatment recommended for ALL patients in selected patient group

» Consider endotracheal intubation and mechanical ventilation in patients who are acutely deteriorating despite advanced oxygen/noninvasive ventilatory support measures.[2] [533]

» Endotracheal intubation should be performed by an experienced provider using airborne precautions.[2] Intubation by video laryngoscopy is recommended if possible.[533] Young children, or adults who are obese or pregnant, may desaturate quickly during intubation and therefore require preoxygenation with 100% fraction of inspired oxygen (FiO₂) for 5 minutes.[2]

» Mechanically ventilated patients with acute respiratory distress syndrome (ARDS) should receive a lung-protective, low tidal volume/low inspiratory pressure ventilation strategy (lower targets are recommended in children). A higher positive end-expiratory pressure (PEEP) strategy is preferred over a lower PEEP strategy in moderate to severe ARDS. However, individualization of PEEP, where the patient is monitored for beneficial or harmful effects and driving pressure during titration with consideration of the risks and benefits of PEEP titration, is recommended.[2] [533] [792] NHS England recommends a low PEEP strategy in patients with normal compliance where recruitment may not be required.[829]

» Although some patients with COVID-19 pneumonia meet the criteria for ARDS, there is some discussion about whether COVID-19 pneumonia is its own specific disease with atypical phenotypes. Anecdotal evidence suggests that the main characteristic of the atypical presentation is the dissociation between well-preserved lung mechanics and the severity of hypoxemia.[830] [831] [832] [833] [834] [835] However, this approach has been criticized.[836]

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[837] It has been argued that an evidence-based approach extrapolating data from ARDS not related to COVID-19 is the most reasonable approach for intensive care of COVID-19 patients.[838] As a consequence of this, some clinicians have warned that protocol-driven ventilator use may be causing lung injury in some patients, and that ventilator settings should be based on physiologic findings rather than using standard protocols. High PEEP may have a detrimental effect on patients with normal compliance.[830] PEEP should always be carefully titrated.[839]

» Consider prone ventilation in patients with severe ARDS for 12 to 16 hours per day. Pregnant women in the third trimester may benefit from being placed in the lateral decubitus position. Caution is required in children.[2] [533] [792] Longer durations may be feasible in some patients.[840]

» Lung recruitment maneuvers are suggested, but staircase recruitment maneuvers are not recommended.[533] [792]

adjunct inhaled pulmonary vasodilator

Treatment recommended for SOME patients in selected patient group

» Consider a trial of an inhaled pulmonary vasodilator in adults who have severe acute respiratory distress syndrome and hypoxemia despite optimizing ventilation. Taper off if there is no rapid improvement in oxygenation.[533] [792]

adjunct extracorporeal membrane oxygenation

Treatment recommended for SOME patients in selected patient group

» Consider extracorporeal membrane oxygenation (ECMO) according to availability and expertise if the above methods fail.[2] [792] [841] ECMO is not suitable for all patients, and only those who meet certain inclusion criteria may be considered for ECMO.[842]

» There is insufficient evidence to recommend either for or against the routine use of ECMO.[533]

» A systematic review and meta-analysis found that in-hospital mortality in adults receiving ECMO was 37.1% during the first year of the pandemic, similar to those with non-COVID-19-related acute respiratory distress syndrome. Increasing age was a risk factor for death. The duration of treatment appears to be

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prolonged in COVID-19 patients; however, a prolonged treatment course was not a predictor of mortality.[843]

» Single-access, dual-stage venovenous ECMO with early extubation appears to be safe and effective in patients with COVID-19 respiratory failure.[844]

adjunct management of sepsis/septic shock

Treatment recommended for SOME patients in selected patient group

» The management of sepsis and septic shock in patients with COVID-19 is beyond the scope of this topic. See the Complications section.

adjunct corticosteroid

Treatment recommended for SOME patients in selected patient group

Primary options

» [dexamethasone](#): children: consult specialist for guidance on dose; adults: 6 mg orally/intravenously once daily for 7-10 days

OR

» [hydrocortisone](#): children: consult specialist for guidance on dose; adults: 50 mg orally/intravenously every 8 hours for 7-10 days

Secondary options

» [prednisone](#): children: consult specialist for guidance on dose; adults: 40 mg/day orally given in 1-2 divided doses for 7-10 days

OR

» [methylprednisolone](#): children: consult specialist for guidance on dose; adults: 32 mg/day orally/intravenously given in 1-2 divided doses for 7-10 days

» Consider a systemic corticosteroid. Guideline recommendations vary.

» The World Health Organization (WHO) strongly recommends systemic corticosteroid therapy (low-dose intravenous or oral dexamethasone or hydrocortisone) for 7 to 10 days in adults with critical disease. This recommendation is based on two meta-analyses that pooled data from eight randomized trials (over 7000 patients), including the UK RECOVERY trial. Moderate-quality evidence suggests that systemic

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corticosteroids probably reduce 28-day mortality in patients with critical disease. They also probably reduce the need for invasive ventilation. There is no evidence directly comparing dexamethasone and hydrocortisone. The harms of treatment in this context are considered to be minor. It is unclear whether these recommendations can be applied to children or those who are immunocompromised.[762] [763] [764] [808] [809] There is also evidence that corticosteroids probably increase ventilator-free days (moderate certainty).[815] [816]

» [BMJ rapid recommendations: a living WHO guideline on drugs for COVID-19] (<https://www.bmj.com/content/370/bmj.m3379>)

» In the UK, the National Institute for Health and Care Excellence recommends offering dexamethasone (or an alternative such as hydrocortisone or prednisone when dexamethasone cannot be used or is unavailable) to people who need supplemental oxygen to meet their prescribed oxygen saturation levels, or who have a level of hypoxia that needs supplemental oxygen but who are unable to have or tolerate it. Treatment is for up to 10 days unless there is a clear indication to stop early.[564]

» In the US, the National Institutes of Health guidelines panel recommends using dexamethasone, either alone or in combination with remdesivir (see the Emerging section for information on remdesivir), in hospitalized patients who require high-flow oxygen or noninvasive ventilation. In patients who are on mechanical ventilation or extracorporeal membrane oxygenation, the panel recommends dexamethasone alone or in combination with tocilizumab for patients who are within 24 hours of admission to the intensive care unit. Alternative corticosteroids may be used in situations where dexamethasone is not available. The panel recommends using dexamethasone in hospitalized children who require high-flow oxygen, noninvasive ventilation, invasive mechanical ventilation, or extracorporeal membrane oxygenation.[533]

» Monitor patients for adverse effects (e.g., hyperglycemia, secondary infections, psychiatric effects, reactivation of latent infections) and assess for drug-drug interactions.[533]

» A meta-analysis found an increased risk of venous thromboembolism with corticosteroid administration in patients with critical disease.

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However, no definite findings were available due to the differing corticosteroid regimens and the heterogeneity of the studies.[847]

adjunct interleukin-6 (IL-6) inhibitor

Treatment recommended for SOME patients in selected patient group

Primary options

» **tocilizumab**: children: consult specialist for guidance on dose; adults: 8 mg/kg intravenously as a single dose, maximum 800 mg/dose

Typically administered as a single intravenous dose; however, a second dose may be administered 12 to 48 hours after the first dose if the clinical response is inadequate. World Health Organization. Therapeutics and COVID-19: living guideline. 2021 [internet publication]. <https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.2>

OR

» **sarilumab**: children: consult specialist for guidance on dose; adults: 400 mg intravenously as a single dose
Typically administered as a single intravenous dose; however, a second dose may be administered 12 to 48 hours after the first dose if the clinical response is inadequate. World Health Organization. Therapeutics and COVID-19: living guideline. 2021 [internet publication]. <https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.2>

» Consider an IL-6 inhibitor. Guideline recommendations vary.

» The World Health Organization strongly recommends an IL-6 inhibitor (tocilizumab or sarilumab), in combination with a systemic corticosteroid and initiated at the same time, in patients with critical disease. This recommendation is based on high-certainty evidence that shows IL-6 inhibitors reduce mortality and the need for mechanical ventilation, and low-certainty evidence that suggests that IL-6 inhibitors may also reduce the duration of mechanical ventilation and hospitalization. The evidence regarding the risk of severe adverse events is uncertain. The applicability of this recommendation to children is currently uncertain.[762] [763] [764] This recommendation is based on data from the UK RECOVERY and REMAP-CAP trials.[811] [812]

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» [BMJ rapid recommendations: a living WHO guideline on drugs for COVID-19] (<https://www.bmj.com/content/370/bmj.m3379>)

» In the US, the National Institutes of Health guidelines panel recommends adding tocilizumab to dexamethasone (or a suitable alternative corticosteroid) or dexamethasone plus remdesivir in patients who require noninvasive mechanical ventilation or high-flow nasal oxygen and have been recently hospitalized (e.g., within 3 days) with rapidly increasing oxygen needs and systemic inflammation. In patients who are on mechanical ventilation or extracorporeal membrane oxygenation, the panel recommends adding tocilizumab to dexamethasone for patients who are within 24 hours of admission to the intensive care unit. There is insufficient evidence for the panel to recommend either for or against the use of tocilizumab in hospitalized children.[533] Tocilizumab has been granted an emergency-use authorization in the US for the treatment of hospitalized adults and pediatric patients 2 years of age and older who are receiving systemic corticosteroids and require noninvasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation.[813]

» Patients on IL-6 inhibitors are at increased risk of infection including active tuberculosis, invasive fungal infections, and opportunistic pathogens.

» Routine blood work including neutrophil count, platelets, transaminases, and total bilirubin should be checked prior to initiation of therapy. All patients should be monitored for signs and symptoms of infection given the increased risk of immunosuppression in addition to systemic corticosteroids.[762]

» These drugs should be avoided in patients who are significantly immunocompromised.[533]

adjunct treatment of coinfections

Treatment recommended for SOME patients in selected patient group

» Treat laboratory-confirmed coinfections (e.g., malaria, tuberculosis, influenza) as appropriate according to local protocols.[2] The treatment of influenza is the same in all patients regardless of SARS-CoV-2 coinfection. Start empiric treatment with oseltamivir in hospitalized patients who are suspected of having either or both infections as soon as possible without waiting for influenza test results. Antiviral therapy can be stopped once influenza has been ruled out.[533]

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adjunct experimental therapies

Treatment recommended for SOME patients in selected patient group

» Consider any appropriate experimental or emerging therapies.

» Antiviral therapies will have a greater effect early in the course of the disease, whereas immunosuppressive/anti-inflammatory therapies are likely to have a greater effect later in the course of the disease.[533]

» See the Emerging section for more information.

adjunct plan for discharge and rehabilitation

Treatment recommended for SOME patients in selected patient group

» Routinely assess intensive care patients for mobility, functional swallow, cognitive impairment, and mental health concerns. Based on that assessment determine whether the patient is ready for discharge, and whether the patient has any rehabilitation and follow-up requirements.[2]

adjunct palliative care

Treatment recommended for SOME patients in selected patient group

» Palliative care interventions should be made accessible at each institution that provides care for patients with COVID-19. Identify whether the patient has an advance care plan and respect the patient's priorities and preferences when formulating the patient's care plan.[2] Follow local palliative care guidelines.

» There is a lack of data on palliative care in patients with COVID-19. A rapid systematic review of pharmacologic strategies used for palliative care in these patients, the first international review of its kind, found that a higher proportion of patients required continuous subcutaneous infusions for medication delivery than is typically seen in the palliative care population. Modest doses of commonly used end-of-life medications were required for symptom control. However, these findings should be interpreted with caution due to the lack of data available.[818]

Emerging

Remdesivir

Remdesivir is an investigational broad-spectrum antiviral agent that inhibits RNA-dependent RNA polymerase. It is approved in many countries for the treatment of COVID-19. In the UK and Europe, remdesivir has been conditionally approved in adolescents (≥ 12 years of age who weigh at least 40 kg) and adults with pneumonia who require supplemental oxygen (low- or high-flow oxygen or other noninvasive ventilation at start of treatment).^[864] In the US, remdesivir has been approved for the treatment of adolescents (≥ 12 years of age who weigh at least 40 kg) and adults who require hospitalization, and has emergency-use authorization for use in children.^[865] The World Health Organization recommends against the use of remdesivir in hospitalized patients in addition to standard care, regardless of disease severity.^{[762] [763] [764]} This weak or conditional recommendation is based on a systematic review and network meta-analysis of four randomized trials with 7333 hospitalized patients, and included the NIAID-ACTT-1 trial (on which the original US approval of remdesivir was based) and the WHO Solidarity trial. There is currently no evidence that remdesivir improves patient outcomes such as time to clinical improvement, the need for mechanical ventilation, or mortality. However, the meta-analysis did not prove that remdesivir has no benefit.^{[763] [764]} The WHO Solidarity trial found that remdesivir appears to have little or no effect on hospitalized patients, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay.^[866] Another living systematic review and network meta-analysis found that remdesivir may reduce the need for mechanical ventilation (low-certainty evidence) compared with standard of care.^{[815] [816]} The UK National Institute for Health and Care Excellence recommends considering remdesivir for up to 5 days in adults and children ≥ 12 years of age and ≥ 40 kg who are in hospital and needing low-flow supplemental oxygen.^[564] Do not use remdesivir in adults, young people, and children in hospital and on high-flow nasal oxygen, continuous positive airway pressure, noninvasive mechanical ventilation, or invasive mechanical ventilation, except as part of a clinical trial. There is limited evidence suggesting that remdesivir probably reduces the risk of death in hospitalized patients who need low-flow supplemental oxygen. However, evidence shows that remdesivir may increase the risk of death in people who are on high-flow nasal oxygen, continuous positive airway pressure, noninvasive ventilation, or invasive mechanical ventilation. Evidence does not suggest any greater benefit with a 10-day course of remdesivir compared with a 5-day course, but suggests an increased risk of harm. There may also be no benefit in completing the full course of remdesivir if the patient progresses to needing high-flow oxygen, noninvasive ventilation, or invasive mechanical ventilation during treatment. Evidence for remdesivir in children and young people is limited. The US National Institutes of Health guidelines panel recommends remdesivir in hospitalized adults who require supplemental oxygen.^[533] It may be given alone (e.g., for patients who require minimal supplemental oxygen) or in combination with dexamethasone (e.g., for patients who require increasing amounts of supplemental oxygen). The panel also recommends remdesivir, in combination with dexamethasone, in hospitalized patients who require high-flow oxygen or noninvasive ventilation. It does not recommend remdesivir in patients who require invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO). The panel acknowledges that remdesivir may also be appropriate in hospitalized patients who do not require oxygen, but who are at high risk of disease progression. The recommended treatment course is 5 days or until hospital discharge, whichever comes first. Some experts recommend a 10-day course in patients who have not shown substantial clinical improvement by day 5. In children, the panel recommends remdesivir in those who are hospitalized, are ages ≥ 12 years, have risk factors for severe disease, and have an emergent or increasing need for supplemental oxygen. The panel recommends remdesivir in hospitalized children ages ≥ 16 years who have an emergent or increasing need for supplemental oxygen, regardless of whether they have risk factors for severe disease. The panel recommends considering remdesivir in hospitalized children of all ages who have an emergent or increasing need for supplemental oxygen, in consultation with a pediatric infectious disease specialist. The Infectious Diseases Society of America recommends remdesivir in hospitalized patients with severe disease over no antiviral treatment, based on moderate-certainty evidence.^[810] The recommended treatment course is 5 days in patients on oxygen, and 10 days in patients on mechanical ventilation or ECMO. The panel suggests against the routine use of remdesivir in hospitalized patients who do not require oxygen and have an oxygen saturation $>94\%$ on room air, based on very low-certainty evidence. There are conflicting recommendations across international guidelines about the use of remdesivir, so it is important that you check local guidance and protocols. Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing this drug.

Casirivimab/imdevimab

Casirivimab and imdevimab are intravenous investigational neutralizing human immunoglobulin G-1 monoclonal antibodies with activity against SARS-CoV-2. The two antibodies bind to nonoverlapping epitopes of the receptor-binding domain of the spike protein to block virus entry into host cells. Casirivimab/imdevimab (formerly known as REGN-COV2) has been granted an emergency-use authorization in the US for the treatment of mild to moderate disease in children and adults.^[867] The US emergency-use authorization covers patients with positive results of direct viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe disease and/or hospitalization. This includes patients who are 65 years of age or older, or who have certain chronic medical conditions. The European Medicines Agency has issued advice that casirivimab/imdevimab may be used in patients ages 12 years and older who do not require supplemental oxygen and who are at high risk of progressing to severe disease; however, the agency is yet to issue a marketing authorization.^[868] The US National Institutes of Health guidelines panel recommends casirivimab/imdevimab for the treatment of nonhospitalized patients with mild to moderate disease who are at high risk of clinical progression, as defined by the emergency-use authorization criteria.^[533] Treatment should be started as soon as possible after the patient receives a positive test result and within 10 days of symptom onset. The panel recommends against the use of monoclonal antibodies in hospitalized patients, except in the context of a clinical trial. However, their use may be considered in patients with mild to moderate disease who are hospitalized for a reason other than COVID-19 but who otherwise meet the emergency-use authorization criteria. In children, there are insufficient data to recommend either for or against the use of monoclonal antibody products in those who are not hospitalized but have risk factors for severe disease. However, they may be considered on a case-by-case basis for nonhospitalized children who meet emergency-use authorization criteria for high risk of severe disease (especially those who meet more than one criterion or are ages ≥ 16 years) in consultation with a pediatric infectious disease specialist. The Infectious Diseases Society of America suggests casirivimab/imdevimab in ambulatory patients with mild to moderate disease who are at high risk for progression to severe disease rather than no neutralizing antibodies, based on low-certainty evidence.^[810] Patients with mild to moderate disease who are at high risk of progression to severe disease admitted to the hospital for reasons other than COVID-19 may also receive casirivimab/imdevimab. There are limited data on efficacy in high-risk patients between 12 and 18 years of age. Evidence is emerging. Emergency-use authorization was based on a randomized, double-blind, placebo-controlled trial in nonhospitalized adults with mild to moderate symptoms that found that casirivimab/imdevimab reduced hospitalization or emergency department visits in patients at high risk for disease progression within 28 days after treatment, when compared with placebo. This study is yet to be published.^[867] The UK RECOVERY trial found that among hospitalized patients who were seronegative at baseline, casirivimab/imdevimab significantly reduced the primary outcome of 28-day mortality by one fifth compared with usual care alone. There was clear evidence that the effect of treatment in seronegative patients differed from that in seropositive patients. Results are yet to be published.^[869] An interim analysis of an ongoing, randomized, double-blind, phase 1-3 trial in nonhospitalized patients found that casirivimab/imdevimab reduced viral load from baseline through to day 7, with a greater effect in patients whose immune response had not yet been initiated or who had a high viral load at baseline.^[870] Casirivimab/imdevimab is not authorized for use in hospitalized patients or those who require oxygen as it has not shown benefit in these patients. Further enrollment of patients requiring high-flow oxygen or mechanical ventilation has been placed on hold due to a potential safety signal and an unfavorable risk/benefit profile at this time. However, enrollment of hospitalized patients requiring either no or low-flow oxygen is being continued.^[871] Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing this drug. Casirivimab/imdevimab is given as an intravenous infusion; however, subcutaneous administration has also been authorized in the US as an alternative route of administration when intravenous administration is not feasible and would lead to delay in treatment. Circulating SARS-CoV-2 variants may be associated with resistance to monoclonal antibodies. Consult local guidance for details regarding specific variants and resistance.

Sotrovimab

Sotrovimab (formerly known as VIR-7831) is an investigational monoclonal antibody with activity against SARS-CoV-2. It is designed to attach to the spike protein of the virus. The US emergency-use authorization covers patients with positive results of direct viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe disease and/or hospitalization. This includes patients who are 65 years of age or older, or who have certain chronic medical conditions.^[872] The European Medicines Agency has issued advice that sotrovimab may be used in patients ages 12

years and older (weighing at least 40 kg) who do not require supplemental oxygen and who are at high risk of progressing to severe disease; however, the agency is yet to issue a marketing authorization.[873] The US National Institutes of Health guidelines panel recommends sotrovimab for the treatment of nonhospitalized patients with mild to moderate disease who are at high risk of clinical progression, as defined by the emergency-use authorization criteria.[533] The panel's recommendations are based on preliminary results from clinical trials. Treatment should be started as soon as possible after the patient receives a positive test result and within 10 days of symptom onset. The panel recommends against the use of monoclonal antibodies in hospitalized patients, except in the context of a clinical trial. However, their use may be considered in patients with mild to moderate disease who are hospitalized for a reason other than COVID-19 but who otherwise meet the emergency-use authorization criteria. In children, there are insufficient data to recommend either for or against the use of monoclonal antibody products in those who are not hospitalized but have risk factors for severe disease. However, monoclonal antibody products may be considered on a case-by-case basis for nonhospitalized children who meet emergency-use authorization criteria for high risk of severe disease (especially those who meet more than one criterion or are ages ≥ 16 years) in consultation with a pediatric infectious disease specialist. The Infectious Diseases Society of America suggests sotrovimab in ambulatory patients with mild to moderate disease who are at high risk for progression to severe disease rather than no neutralizing antibodies, based on low-certainty evidence.[810] Patients with mild to moderate disease who are at high risk of progression to severe disease admitted to the hospital for reasons other than COVID-19 may also receive sotrovimab. There are limited data on efficacy in high-risk patients between 12 and 18 years of age. Evidence is limited. Authorization was based on an interim analysis from a phase 1/2/3 randomized controlled trial in 583 nonhospitalized adults with mild to moderate disease that reported an 85% reduction in hospitalization or death compared with placebo.[872] While the manufacturer has published press releases about interim results from clinical trials, these trials have not been published as yet. Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing this drug. Sotrovimab is given as an intravenous infusion. Circulating SARS-CoV-2 variants may be associated with resistance to monoclonal antibodies. Consult local guidance for details regarding specific variants and resistance.

Bamlanivimab/etesevimab

Bamlanivimab (formerly known as LY-CoV555) and etesevimab (formerly known as LY-CoV016) are intravenous investigational neutralizing human immunoglobulin G-1 monoclonal antibodies with activity against SARS-CoV-2. The two antibodies bind to different, but overlapping, epitopes of the receptor-binding domain of the spike protein to block virus entry into host cells. Bamlanivimab/etesevimab has been granted an emergency-use authorization in the US for the treatment of mild to moderate disease in children and adults.[867] The US emergency-use authorization covers patients with positive results of direct viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe disease and/or hospitalization. This includes patients who are 65 years of age or older, or who have certain chronic medical conditions. The European Medicines Agency has issued advice that bamlanivimab/etesevimab may be used in patients ages 12 years and older who do not require supplemental oxygen and who are at high risk of progressing to severe disease. The agency is yet to issue a marketing authorization, but has started a rolling review of the data. The agency also concluded that despite uncertainties around the benefits of bamlanivimab monotherapy, it can be considered a treatment option for this indication.[874] The US National Institutes of Health guidelines panel currently recommends against the use of bamlanivimab/etesevimab at this time due to circulation of variants of concern, which have reduced susceptibility to this treatment.[533] The Infectious Diseases Society of America suggests bamlanivimab/etesevimab in ambulatory patients with mild to moderate disease who are at high risk for progression to severe disease rather than no neutralizing antibodies, based on low-certainty evidence.[810] Patients with mild to moderate disease who are at high risk of progression to severe disease admitted to the hospital for reasons other than COVID-19 may also receive bamlanivimab/etesevimab. There are limited data on efficacy in high-risk patients between 12 and 18 years of age. The panel recommends against the use of bamlanivimab monotherapy in hospitalized patients with severe disease, based on moderate-certainty evidence. Evidence is emerging. Among patients with mild to moderate disease, treatment with bamlanivimab/etesevimab was associated with a significant reduction in viral load at day 11 compared with placebo; however, no significant difference in viral load reduction was observed with bamlanivimab monotherapy.[875] Among residents and staff in skilled nursing and assisted living facilities, treatment with bamlanivimab monotherapy reduced the incidence of infection compared with placebo.[876] Among high-risk ambulatory patients, treatment with bamlanivimab/etesevimab reduced the risk of hospitalization and death compared with placebo and accelerated the reduction in viral load.[877] Immune escape variants have been reported in

immunocompromised patients treated with bamlanivimab monotherapy.[878] Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing this drug. Bamlanivimab/etesevimab is given as an intravenous infusion. Circulating SARS-CoV-2 variants may be associated with resistance to monoclonal antibodies. Consult local guidance for details regarding specific variants and resistance.

Convalescent plasma

Convalescent plasma is a blood product that contains antibodies to SARS-CoV-2 from patients who have recovered. High-titer convalescent plasma (i.e., plasma with high SARS-CoV-2 antibody titers) has been granted an emergency-use authorization in the US for the treatment of hospitalized patients early in the disease course, and to those hospitalized patients who have impaired humoral immunity and cannot produce an adequate antibody response. Low-titer convalescent plasma is no longer authorized.[879] It has not been authorized for this indication in the UK or Europe. UK guidance recommends that convalescent plasma should not be used in the management of hospitalized patients with suspected or confirmed infection.[880] This recommendation is based on data from the UK RECOVERY and REMAP-CAP trials. Preliminary data (yet to be peer reviewed) from the UK RECOVERY trial found that high-titer convalescent plasma did not improve survival or other prespecified clinical outcomes among hospitalized patients.[881] The US National Institutes of Health guidelines panel recommends against the use of low-titer convalescent plasma.[533] There are insufficient data for the panel to recommend either for or against the use of high-titer convalescent plasma in hospitalized patients with impaired immunity. The panel recommends against the use of high-titer convalescent plasma in hospitalized patients who do not have impaired immunity and who do not require mechanical ventilation, except in the context of a clinical trial. The panel recommends against the use of convalescent plasma in hospitalized patients who do not have impaired immunity and who require mechanical ventilation. There are insufficient data for the panel to recommend either for or against the use of high-titer convalescent plasma in nonhospitalized patients, except in the context of a clinical trial. In children, the panel recommends against the use of convalescent plasma in those who are mechanically ventilated. The panel recommends against the use of convalescent plasma in hospitalized children who do not require mechanical ventilation, except in the context of a clinical trial. High-titer convalescent plasma may be considered on a case-by-case basis for hospitalized children who meet the emergency-use authorization criteria for its use, in consultation with a pediatric infectious disease specialist. The Infectious Diseases Society of America suggests against the use of convalescent plasma in hospitalized patients, based on low-certainty evidence.[810] The guideline panel recommends convalescent plasma in ambulatory patients with mild to moderate disease only in the context of a clinical trial. Evidence is emerging. Emergency-use authorization was based on the preprint (not peer reviewed) publication of an open-label, multicenter, expanded access program study of over 35,000 patients that found convalescent plasma lowered 7-day mortality by 9% in hospitalized patients when given within 3 days of diagnosis, and by 12% when given 4 or more days later.[882] Evidence from meta-analyses appears to be conflicting. A meta-analysis and systematic review of four peer-reviewed randomized controlled trials and six unpublished randomized controlled trials, and a meta-analysis and systematic review of 12 randomized controlled trials, found that treatment with convalescent plasma was not significantly associated with a decrease in all-cause mortality (or any benefit for other outcomes) compared with placebo or standard of care, based on low- to moderate-certainty evidence.[883] [884] However, while another meta-analysis of ten randomized controlled trials also found no association between convalescent plasma therapy and a reduction in mortality, when one of the trials was excluded due to a large proportion of patients in the convalescent plasma arm receiving plasma with low levels of SARS-CoV-2 antibodies, additional analyses found that patients treated with convalescent plasma exhibited a lower mortality rate compared with patients who did not receive convalescent plasma (11% versus 16%). Therefore, early transfusion of high-titer plasma appears to reduce mortality.[885] A meta-analysis that included three randomized controlled trials and nine observational studies found that convalescent plasma reduced mortality when used as an adjunctive therapy.[886] A Cochrane review found high-certainty evidence that convalescent plasma does not reduce mortality and has little to no impact on measures of clinical improvement for the treatment of moderate to severe disease.[887] The UK RECOVERY trial found that high-titer convalescent plasma did not improve 28-day mortality or other prespecified outcomes (hospital discharge within 28 days, progression to invasive mechanical ventilation) in hospitalized patients compared with usual care.[888] A randomized, double-blind, placebo-controlled trial in older patients with mild disease who received convalescent plasma within 72 hours after the onset of symptoms found that early administration reduced the progression to severe disease.[889] However, a National Institutes of Health clinical trial evaluating the safety and efficacy of convalescent plasma in treating emergency department patients who developed mild to moderate symptoms has been halted. An interim analysis of the

trial data determined that while convalescent plasma caused no harm, it was unlikely to benefit this group of patients.[890] A cohort study found a potential survival benefit in patients with hematologic cancers.[891]

Baricitinib

Baricitinib is an oral Janus kinase inhibitor. It is thought to prevent the dysregulated production of proinflammatory cytokines in patients with severe or critical disease. Baricitinib is already approved in some countries for certain conditions. It has been granted an emergency-use authorization for the treatment of COVID-19 in the US, in combination with remdesivir, for the treatment of suspected or confirmed disease in hospitalized children ages 2 years and older and adults who require supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation.[892] It has not been authorized for this indication in the UK or Europe; however, the European Medicines Agency is currently evaluating its use in hospitalized patients from 10 years of age who require supplemental oxygen.[893] The US National Institutes of Health guidelines panel recommends baricitinib, in combination with dexamethasone alone or dexamethasone plus remdesivir, in recently hospitalized patients on high-flow oxygen or noninvasive ventilation with rapidly increasing oxygen needs and systemic inflammation.[533] The panel recommends against the use of baricitinib in combination with tocilizumab except in the context of a clinical trial. There is potential for an additive risk of infection. There is insufficient evidence to recommend either for or against the use of baricitinib in children. The panel recommends against the use of other Janus kinase inhibitors except in a clinical trial. The Infectious Diseases Society of America recommends baricitinib with remdesivir in hospitalized patients with severe disease who cannot receive corticosteroids because of a contraindication, rather than remdesivir alone.[810] The combination should only be given with a corticosteroid in the context of a clinical trial. Evidence is emerging. Emergency-use authorization was based on a randomized, double-blind, placebo-controlled trial that found baricitinib plus remdesivir reduced time to recovery (defined as either being discharged from the hospital, or being hospitalized but not requiring supplemental oxygen and no longer requiring ongoing medical care) within 29 days after initiating treatment compared with patients who received placebo plus remdesivir. The median time to recovery was 7 days for baricitinib plus remdesivir and 8 days for placebo plus remdesivir.[894] A living systematic review and network meta-analysis found that Janus kinase inhibitors may reduce the need for mechanical ventilation (low-certainty evidence) and probably reduce the duration of mechanical ventilation (moderate-certainty evidence) compared with standard care.[815] [816] Another systematic review and network meta-analysis found that Janus kinase inhibitors are also associated with a reduced risk of mortality, and clinical improvement in hospitalized patients.[895] A meta-analysis that included six cohort studies and five clinical trials involving over 2000 participants treated with either baricitinib or ruxolitinib found that use of Janus kinase inhibitors reduced the need for invasive mechanical ventilation and increased survival, but did not reduce the length of hospitalization. The evidence was most convincing for baricitinib. Timing of treatment may be important in determining the impact on outcomes.[896] There is a lack of evidence for other drugs within this drug class (e.g., tofacitinib, fedratinib, ruxolitinib); however, clinical trials are ongoing. Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing this drug.

Ivermectin

Ivermectin is a broad-spectrum antiparasitic agent. It has been shown to be effective against SARS-CoV-2 in vitro.[897] Ivermectin is already approved in some countries for parasitic infections, but is off-label for this indication. The European Medicines Agency does not recommend ivermectin for the treatment or prevention of COVID-19 outside of clinical trials.[898] The World Health Organization does not recommend ivermectin except in the context of a clinical trial.[762] This recommendation applies to patients with any disease severity and any duration of symptoms. There is insufficient evidence to be clear to what extent, if any, ivermectin is helpful or harmful in treating COVID-19.[763] [764] For most key outcomes, including mortality, mechanical ventilation, hospital admission, duration of hospitalization, and viral clearance, the evidence is of very low certainty. The US National Institutes of Health guidelines panel states that there is currently insufficient evidence to recommend either for or against the use of ivermectin.[533] The Infectious Diseases Society of America recommends against the use of ivermectin in outpatients and hospitalized patients outside of the context of a clinical trial, adding that more trials of sufficient design are needed.[810] Other international guidelines may recommend ivermectin in select patient groups. Indian guidelines recommend that ivermectin may be considered as an option in patients with mild disease, although acknowledge that this recommendation is based on low-certainty evidence.[899] Evidence is emerging. A meta-analysis of 18 randomized controlled trials found statistically significant reductions in mortality, time to clinical recovery, and time to viral clearance with use of ivermectin.[900] A meta-analysis of nine randomized controlled trials found

that ivermectin was associated with decreased mortality compared with standard of care or placebo, with a low certainty of evidence.[901] Another meta-analysis found that ivermectin reduced the risk of death based on moderate-certainty evidence. Low-certainty evidence found that ivermectin prophylaxis reduced infection by an average of 86%. Secondary outcomes provided less-certain evidence.[902] Another meta-analysis of six randomized controlled trials found a preliminary positive effect on mortality associated with use in hospitalized patients. The authors concluded that this effect warrants further appropriately designed, large-scale randomized controlled trials. The meta-analysis was limited by a small number of patients included with a significant risk of biases in the majority of included trials.[903] A systematic review and meta-analysis found that adding ivermectin to usual care led to significant clinical improvement and a significant reduction in all-cause mortality compared with usual care; however, the quality of evidence was very low.[904] A living systematic review and network meta-analysis found that studies on ivermectin for prophylaxis have been small and it remains very uncertain whether ivermectin reduces the risk of infection. Evidence for the effects of ivermectin on mortality is of very low certainty.[905] A randomized controlled trial in patients with mild to moderate disease found that those treated with ivermectin plus doxycycline recovered 2 days earlier and were less likely to progress to severe disease compared with placebo.[906] The PRINCIPLE trial in the UK is currently investigating the use of ivermectin.[907] Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing this drug.

Anakinra

Anakinra is an intravenous/subcutaneous interleukin-1 inhibitor. It is being trialed in patients for the treatment of SARS-CoV-2-induced cytokine release syndrome. Anakinra is already approved in some countries for certain conditions, but is off-label for this indication. The European Medicines Agency has started to evaluate an application to extend the use of anakinra to include the treatment of COVID-19 in adults with pneumonia who are at risk of developing severe respiratory failure.[908] The US National Institutes of Health guidelines panel states that there is currently insufficient evidence to recommend either for or against the use of anakinra.[533] The UK National Institute for Health and Care Excellence states that there is no evidence available to determine whether anakinra is effective, safe, or cost-effective for treating adults and children with secondary hemophagocytic lymphohistiocytosis triggered by SARS-CoV-2 or a similar coronavirus.[909] Evidence is limited. A systematic review and meta-analysis of nine observational studies found that anakinra reduced the need for invasive mechanical ventilation and mortality risk in hospitalized nonintubated patients compared with standard of care. However, confirmation of safety and efficacy requires randomized controlled trials.[910] A systematic review and meta-analysis of 15 studies (five observational studies, five case series, four case reports, and one randomized controlled trial) also found that anakinra significantly reduced the need for invasive mechanical ventilation and mortality risk compared with standard care alone.[911] Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing this drug.

Regdanvimab

Regdanvimab (formerly known as CT-P59) is an investigational neutralizing monoclonal antibody with activity against SARS-CoV-2. Regdanvimab has been granted a conditional marketing authorization in South Korea for the treatment of adults with mild symptoms who are ages ≥ 60 years or have at least one underlying medical condition, and all adults with moderate symptoms. The European Medicines Agency recommends that regdanvimab can be used for the treatment of confirmed COVID-19 in adult patients who do not require supplemental oxygen therapy and who are at high risk of progressing to severe disease.[912] Evidence is limited. According to press releases from the manufacturer, regdanvimab reduced progression from mild-moderate to severe disease by 50%, and from moderate to severe disease by 68%, and reduced the risk of hospitalization or death by 72% in patients at high risk of progressing to severe disease. However, results from the phase 2/3 trials are yet to be published.[913] [914] Regdanvimab has also demonstrated neutralizing capability against key emerging mutations, including the B.1.1.7 variant.[915]

Intravenous immune globulin

Intravenous immune globulin (IVIG) is a blood product prepared from serum pooled from healthy donors. It has an immunomodulatory effect that suppresses a hyperactive immune response. IVIG is already approved in some countries for certain conditions, but is off-label for this indication. The US National Institutes of Health guidelines panel states that there are insufficient data to recommend either for or against the use of anti-SARS-CoV-2 specific immune globulin.[533] Evidence is limited. A meta-analysis of four clinical

trials and three cohort studies with 825 hospitalized patients found that IVIG reduced mortality in patients with critical disease; however, there was no significant difference between the severe and nonsevere subgroups.[916] Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing this drug.

Stem cell therapy

Mesenchymal stem cells are an investigational product and have been studied for their immunomodulatory properties. It is thought that they can reduce the pathologic changes that occur in the lungs, and inhibit the cell-mediated immune inflammatory response.[917] Mesenchymal stem cells are not approved for this indication. The US National Institutes of Health guidelines panel recommends against the use of mesenchymal stem cells except in the context of a clinical trial.[533] Evidence is limited. Remestemcel-L (ex vivo cultured adult human mesenchymal stem cells from the bone marrow of healthy adult donors) is currently in phase 3 trials for the treatment of moderate to severe acute respiratory distress syndrome in ventilator-dependent patients. An interim analysis of data found that the trial is not likely to meet its 30-day mortality reduction end point and has stopped enrollment, although the trial will be completed with the patients currently enrolled, with follow-up as planned.[918]

Interferons

Interferons are a family of cytokines with antiviral properties. Interferons are already approved in some countries for certain conditions, but are off-label for this indication. The US National Institutes of Health guidelines panel recommends against the use of interferons for the treatment of severe or critically ill patients except in the context of a clinical trial.[533] Evidence is limited. The WHO Solidarity trial found that interferon beta-1a appears to have little or no effect on hospitalized patients, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay.[866] A randomized, placebo-controlled, phase 2 trial found that nebulized interferon beta-1a was associated with a higher odds of clinical improvement and more rapid recovery.[919] A phase 2 trial found that peginterferon lambda reduced viral load and increased the number of participants with a negative nasopharyngeal swab at day 7 in outpatients with mild to moderate disease compared with placebo.[920] [921] Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing these drugs.

Vitamin D

Vitamin D supplementation has been associated with a reduced risk of acute respiratory infections such as influenza.[922] [923] [924] [925] The US National Institutes of Health guidelines panel states that there are insufficient data to recommend either for or against vitamin D for the treatment or prevention of COVID-19.[533] The UK National Institute for Health and Care Excellence recommends vitamin D supplementation in adults (including pregnant and breastfeeding women), young people, and children over 4 years of age between October and early March (and at other times of the year if at risk of vitamin D deficiency) to maintain bone and muscle health. However, it does not recommend supplementation to solely prevent or treat COVID-19, except as part of a clinical trial.[926] Evidence is limited. A Cochrane review found there is currently insufficient evidence to determine the benefits and harms of vitamin D supplementation. The evidence is very uncertain. There was substantial clinical and methodological heterogeneity of included studies, mainly due to different supplementation strategies, formulations, vitamin D status of participants, and reported outcomes.[927] Meta-analyses found that vitamin D might be associated with improved clinical outcomes and that there may be a potential role for vitamin D supplementation in reducing disease severity, but noted that additional evidence is required.[928] [929] A pilot randomized controlled trial found that high-dose calcifediol significantly reduced the need for intensive care unit treatment in hospitalized patients, and may improve clinical outcomes.[930]

Vitamin C

Vitamin C supplementation has shown promise in the treatment of viral infections.[931] High-dose intravenous vitamin C is being trialed in some centers for the treatment of severe disease.[932] The US National Institutes of Health guidelines panel states that there are insufficient data to recommend either for or against vitamin C for the treatment of noncritically ill or critically ill patients.[533] Evidence is limited. There is no evidence to support or refute the use of vitamin C in the treatment of patients with COVID-19; however,

several trials are ongoing.[933] A pilot randomized controlled trial found high-dose intravenous vitamin C may show potential benefit in improving oxygenation and reducing mortality in critically ill patients; however, the trial was underpowered.[934]

Colchicine

Colchicine is an anti-inflammatory agent that downregulates multiple pro-inflammatory pathways. It is thought that its inhibitory effects on neutrophil activity, cytokine generation, and the inflammation/thrombosis interface, along with an overall lack of evidence for systemic immunosuppression, make it a useful treatment.[935] Colchicine is already approved in some countries for indications such as gout and familial Mediterranean fever, but is off-label for this indication. The UK National Institute for Health and Care Excellence does not recommend colchicine in hospitalized patients.[564] The guideline also recommends against its use in community settings. The US National Institutes of Health guidelines panel states that there is currently insufficient evidence to recommend either for or against the use of colchicine in nonhospitalized patients.[533] The panel recommends against its use in hospitalized patients. The UK Medicines and Healthcare products Regulatory Agency states that colchicine should not be used except in the context of a clinical trial, or unless there is an additional licensed indication for its use.[936] Evidence is limited. A living systematic review and network meta-analysis found that colchicine may reduce mortality (low-certainty evidence) and probably reduces the duration of hospitalization (low-certainty evidence) compared with standard care.[815] [816] A systematic review and meta-analysis found that colchicine was associated with a reduction in disease severity and mortality, especially when given early in the course of disease (within 3-6 days from the onset of symptoms or hospital admission). However, the analysis was largely based on observational studies and only included three randomized clinical trials.[937] Another systematic review and meta-analysis supports the reduction in mortality; however, meta-regression analysis found that the benefit was reduced as age increased.[938] A double-blind, placebo-controlled, randomized trial of over 4400 nonhospitalized patients found that colchicine led to a lower rate of the composite of death or hospital admission compared with placebo among patients with polymerase chain reaction (PCR)-confirmed disease; however, the effect was not statistically significant when participants without a PCR-confirmed diagnosis were included.[939] More randomized controlled trials are required. Colchicine was being studied in the RECOVERY trial; however, recruitment has now closed as an interim analysis of the trial data found no convincing evidence that further recruitment would provide conclusive proof of mortality benefit.[940] Studies are inconclusive in patients with mild to moderate disease, and adverse effects are significant.[941] Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing this drug.

Fluvoxamine

Fluvoxamine is a selective serotonin-reuptake inhibitor that has anti-inflammatory effects.[942] Fluvoxamine is already approved in some countries for indications such as depression and obsessive compulsive disorder, but is off-label for this indication. The US National Institutes of Health guidelines panel states that there is currently insufficient evidence to recommend either for or against the use of fluvoxamine.[533] Evidence is limited. A preliminary double-blind, randomized controlled trial found that adult outpatients had a lower likelihood of clinical deterioration over 15 days compared with placebo; however, the study was limited by a small sample size and short follow-up duration.[943] A prospective cohort study in the setting of a mass outbreak found that fluvoxamine may prevent clinical deterioration requiring hospitalization and symptoms persisting beyond 2 weeks.[944] Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing this drug.

Nitazoxanide

Nitazoxanide is a broad-spectrum antiparasitic agent with in vitro activity against SARS-CoV-2 that is already approved in some countries for indications such as cryptosporidiosis and giardiasis, but is off-label for this indication. The US National Institutes of Health guidelines panel recommends against the use of nitazoxanide except in the context of a clinical trial.[533] Evidence is limited. A randomized, double-blind pilot trial found an evident decrease in the time for hospital discharge, faster evolution to reverse transcription polymerase chain reaction negativity, and a higher reduction of inflammatory markers among patients treated with nitazoxanide compared with placebo. However, this was a small, proof-of-concept trial.[945] A multicenter, randomized, double-blind, placebo-controlled trial in adults with mild disease found that nitazoxanide was associated with reduced viral load but not reduced time to symptom

resolution.[946] Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing this drug.

Granulocyte-macrophage colony-stimulating factor (GM-CSF) inhibitors

GM-CSF inhibitors (e.g., lenzilumab, mavrilimumab, otilimab) may mitigate lung inflammation in severe and critical disease by minimizing downstream production of numerous pro-inflammatory mediators involved in the pathogenesis of disease. These agents are currently investigational. The US National Institutes of Health guidelines panel states that there is currently insufficient evidence to recommend either for or against the use of GM-CSF inhibitors.[533] Evidence is limited. A phase 3 randomized, double-blind, placebo-controlled trial (preprint) found that lenzilumab significantly improved survival without ventilation in hospitalized, hypoxic patients COMPARED with remdesivir and/or corticosteroids. Subjects with a C-reactive protein level <150 mg/L and age <85 years had the greatest benefit.[947] A small multicenter, double-blind, randomized, placebo-controlled trial found that there was no significant difference in the proportion of patients with severe disease, hypoxemia, and systemic hyperinflammation who were free of supplemental oxygen at day 14 after treatment with mavrilimumab compared with placebo.[948]

Inhaled corticosteroids

Inhaled budesonide is undergoing clinical trials and shows promise.[949] It is already approved in some countries for indications such as asthma and COPD, but is off-label for this indication. The UK Medicines and Healthcare products Regulatory Agency states that inhaled budesonide can be considered on a case-by-case basis in eligible patients who meet all of the following criteria (and who do not meet specific exclusion criteria): patients with onset of symptoms within the past 14 days, and symptoms are ongoing; confirmation of diagnosis by molecular testing within the past 14 days; age 65 years and over, or age 50 to 64 years with a comorbidity consistent with a long-term health condition.[950] The European Medicines Agency advises that there is currently insufficient evidence that inhaled corticosteroids are beneficial.[951] Evidence is limited. The PRINCIPLE trial has reported a 3-day median benefit in self-reported recovery for patients in the community setting who received inhaled budesonide.[952] The impact on hospitalization rates or mortality has not been established. Results are yet to be published. Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing this drug.

Antibiotics

Azithromycin is a macrolide antibiotic, and doxycycline is a tetracycline antibiotic. Both are approved for use in various bacterial infections. The UK National Institute for Health and Care Excellence does not recommend the use of azithromycin.[564] The guideline panel considered that the results from studies of azithromycin for moderate to critical disease in the hospital setting and mild to moderate disease in the community setting showed no meaningful benefit in any of the critical outcomes. The UK Medicines and Healthcare products Regulatory Agency recommends that azithromycin and doxycycline should not be used within primary care (or hospitalized patients for azithromycin) unless there are additional indications for which their use remains appropriate.[953] The US National Institutes of Health guidelines panel recommends against the use of antibacterial therapy (e.g., azithromycin, doxycycline) in the absence of another indication.[533] Evidence does not support the use of these drugs. A systematic review and meta-analysis found that azithromycin was not associated with an improvement in hospitalization rate, intensive care unit admission, need for respiratory support, or mortality rate compared with control.[954] The overall quality of evidence was low to very low. The UK RECOVERY trial found that azithromycin showed no significant clinical benefit (i.e., length of hospital stay, need for invasive mechanical ventilation, 28-day mortality) in hospitalized patients compared with usual standard care alone.[955] The UK PRINCIPLE trial is currently evaluating three treatment strategies in older people (people ages over 65 years, or people ages over 50 years with an underlying health condition): usual care alone; usual care plus azithromycin; and usual care plus doxycycline.[956] The ATOMIC2 open-label randomized trial found that adding azithromycin to standard of care treatment in nonhospitalized patients with mild to moderate disease did not reduce the risk of subsequent hospital admission or death.[957] An interim analysis of the trial concluded that azithromycin and doxycycline offered no meaningful beneficial effect, in terms of time to recovery, hospitalization, or death compared with standard of care in patients ages 50 years and over who were treated at home in the early stages of infection.[953] [958] Consult local drug formulary

for information about contraindications, cautions, adverse effects, and drug interactions before prescribing these drugs.

Lopinavir/ritonavir

Lopinavir/ritonavir is an oral protease inhibitor. It is approved for the treatment of HIV infection, but is off-label for this indication. The World Health Organization strongly recommends against the use of lopinavir/ritonavir, regardless of disease severity. This recommendation is based on low- to moderate-certainty evidence.^{[762] [763] [764]} The US National Institutes of Health guidelines panel recommends against the use of lopinavir/ritonavir except in the context of a clinical trial.^[533] The Infectious Diseases Society of America also recommends against the use of lopinavir/ritonavir based on moderate-certainty evidence.^[810] Evidence does not support the use of this drug. The WHO Solidarity trial found that lopinavir/ritonavir appears to have little or no effect on hospitalized patients, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay.^[866] The UK RECOVERY trial found that there is no beneficial effect of lopinavir/ritonavir in hospitalized patients, with no significant difference in 28-day mortality, risk of progression to mechanical ventilation or death, or duration of hospital stay between the two treatment arms (lopinavir/ritonavir versus usual care alone).^[959] A systematic review and meta-analysis found that lopinavir/ritonavir had no significant advantage in efficacy over standard care, no antivirals, or other antiviral treatments.^[960] Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing this drug.

Hydroxychloroquine/chloroquine

Hydroxychloroquine and chloroquine are oral disease-modifying antirheumatic drugs with anti-inflammatory and immunomodulatory effects. These drugs have been shown to be effective against SARS-CoV-2 in vitro.^{[961] [962]} Hydroxychloroquine and chloroquine are already approved in some countries for certain conditions, but are off-label for this indication. The World Health Organization (WHO) strongly recommends against the use of hydroxychloroquine or chloroquine, regardless of disease severity, based on low- to moderate-certainty evidence.^{[762] [763] [764]} The WHO also strongly recommends against the use of hydroxychloroquine for prevention of COVID-19. A systematic review and network meta-analysis found that hydroxychloroquine had a small or no effect on mortality and admission to hospital. There was a small or no effect on laboratory-confirmed infection, but probably increased adverse events leading to discontinuation.^{[963] [964]} The US National Institutes of Health guidelines panel recommends the use of hydroxychloroquine or chloroquine (with or without azithromycin) in hospitalised or nonhospitalized patients.^[533] The panel recommends against the use of hydroxychloroquine for postexposure prophylaxis. The Infectious Diseases Society of America strongly recommends against the use of hydroxychloroquine or chloroquine in hospitalized patients based on moderate-certainty evidence.^[810] Evidence does not support the use of these drugs for treatment. A Cochrane review found that hydroxychloroquine has no clinical benefit in hospitalized patients, with moderate- to high-certainty evidence from several randomized trials, and a probable increase in adverse events associated with its use. Evidence for prevention of hospital admission in outpatients is very uncertain. Evidence for pre- or postexposure prophylaxis is limited.^[965] A living systematic review concluded that there is low-strength evidence from trials and cohort studies that hydroxychloroquine has no positive effect on all-cause mortality or the need for mechanical ventilation. Trials show low strength of evidence for no positive effect on intubation or death and discharge from the hospital, whereas evidence from cohort studies about these outcomes remains insufficient. Data are insufficiently strong to support a treatment benefit of hydroxychloroquine for other outcomes (e.g., intensive care unit admission, symptom resolution). In trials where hydroxychloroquine is initiated in the outpatient setting, there is low strength of evidence that it reduces hospitalization; however, there is insufficient evidence from cohort studies.^{[966] [967]} The WHO Solidarity trial found that hydroxychloroquine appears to have little or no effect on hospitalized patients, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay.^[866] The UK RECOVERY trial found that hydroxychloroquine does not reduce the risk of death at 28 days compared with usual care.^[968] A living systematic review and network meta-analysis found that hydroxychloroquine did not reduce the rate of infection, admission to hospital, or mortality compared with standard care or placebo when used for prophylaxis. More patients discontinued hydroxychloroquine because of adverse events.^[905] Consult local drug formulary for information about contraindications, cautions, adverse effects, and drug interactions before prescribing these drugs.

Clinical trials

Various other treatments are in clinical trials around the world. [Global coronavirus COVID-19 clinical trial tracker] (<https://www.covid-trials.org>) International trials to identify treatments that may be beneficial, such as the World Health Organization's Solidarity trial, and the UK's randomized evaluation of COVID-19 therapy (RECOVERY) trial, are ongoing. The RECOVERY Trial is currently testing these treatments: baricitinib; dimethyl fumarate; and casirivimab/imdevimab. [RECOVERY trial] (<https://www.recoverytrial.net>) [WHO: "Solidarity" clinical trial for COVID-19 treatments] (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments>)

Primary prevention

Vaccines

- Vaccines are available under emergency-use or conditional marketing authorizations.
 - This is not a full marketing authorization or approval.
- The World Health Organization (WHO) has authorized the use of the following six vaccines for global use below.[356] [357] [358] [359] [360] [361] Other vaccines have also been authorized in specific countries (e.g., Sputnik V® in Russia, Covaxin® in India).[362] [363]
 - Pfizer/BioNTech (mRNA)
 - Moderna (mRNA)
 - AstraZeneca (adenovirus vector)
 - Janssen (adenovirus vector)
 - Sinopharm's Covilo® (inactivated SARS-CoV-2 virus)
 - Sinovac's CoronaVac® (inactivated SARS-CoV-2 virus)
 - [WHO: COVID-19 vaccines technical documents] (<https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials>)
- Vaccine availability and immunization programs differ between countries.
 - Consult your local guidance for information.
- Patients must give informed consent prior to vaccination.
 - For consent to immunization to be valid, it must be given freely, voluntarily, and without coercion by an appropriately informed person.[364]
- Protection starts around 14 days after full vaccination.
 - Vaccination may not protect all vaccine recipients. Breakthrough infections that have resulted in hospitalization or death, as well as asymptomatic infections, have been reported in fully vaccinated people.[365] [366] [367] [368]
 - Have a high level of suspicion of reported symptoms post-vaccination, and avoid dismissing complaints as vaccine-related until vaccine recipients are tested and true infection is ruled out.[369]
 - Duration of protection after vaccination is unknown and is still being assessed in ongoing clinical trials. There is emerging evidence of a durable humoral and cellular immune response for at least 8 months after vaccination with a viral vector vaccine.[370]
- Vaccinated people should continue to follow local public health recommendations.
 - There is insufficient evidence on the extent of vaccine impact on virus transmission.[356] [357] [358] [359] [360] [361]
 - Evidence of efficacy in the real world is emerging (see Vaccines: real world efficacy data below).

PFIZER/BIONTECH COVID-19 VACCINE*mRNA vaccine*

Efficacy*	95%	Age	≥12 years
Dose	0.3 mL (30 mcg) IM; second dose at least 3 weeks after		
Contraindications	Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine		
Precautions	History of anaphylaxis/allergic reactions Immunocompromised Pregnancy and breastfeeding History of myocarditis and pericarditis		
Adverse events	Common injection-site reactions; fatigue; headache; myalgia; chills; arthralgia; fever Uncommon nausea; malaise; lymphadenopathy; anaphylaxis; hypersensitivity; myocarditis and pericarditis; diarrhea; vomiting; pain in extremity; acute peripheral facial paralysis; syncope		
Interactions	Interactions with other vaccines/drugs have not been studied. The FDA recommends that COVID-19 vaccines and other vaccines may be administered without regard to timing.		

*Information for the Pfizer/BioNTech COVID-19 vaccine is based on the US prescribing information. Consult your local drug formulary or guidelines for more detailed information. *Efficacy in preventing symptomatic infection in people ages 16 years and older according to clinical trials. Last updated: 8 July 2021*
BMJ Best Practice editorial team; compiled using data from the US product information

MODERNA COVID-19 VACCINE <i>mRNA vaccine</i>			
Efficacy*	94.1%	Age	≥18 years
Dose	0.5 mL (100 mcg) IM; second dose at least 28 days after		
Contraindications	Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine		
Precautions	History of anaphylaxis/allergic reactions Immunocompromised Pregnancy and breastfeeding History of myocarditis and pericarditis		
Adverse events	Common injection-site reactions; fatigue; headache; myalgia; chills; arthralgia; nausea; vomiting; axillary swelling/tenderness; fever Uncommon lymphadenopathy; anaphylaxis; hypersensitivity; myocarditis and pericarditis; acute peripheral facial paralysis; face swelling (if dermatologic fillers present)		
Interactions	Interactions with other vaccines/drugs have not been studied. The FDA recommends that COVID-19 vaccines and other vaccines may be administered without regard to timing.		

*Information for the Moderna COVID-19 vaccine is based on the US prescribing information. Consult your local drug formulary or guidelines for more detailed information. *Efficacy in preventing symptomatic infection in people ages 18 years and older according to clinical trials. Last updated: 8 July 2021*
BMJ Best Practice editorial team; compiled using data from the US product information

JANSSEN COVID-19 VACCINE <i>Viral vector vaccine</i>			
Efficacy*	66.9%	Age	≥18 years
Dose	0.5 mL IM (5×10^{10} viral particles) as a single dose		
Contraindications	Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine		
Precautions	History of anaphylaxis/allergic reactions Immunocompromised Pregnancy and breastfeeding		
Adverse events	Common injection-site reactions; headache; fatigue; myalgia; nausea; fever Uncommon severe allergic reactions; anaphylaxis; urticaria; hypersensitivity; pain in extremity; generalized weakness; thrombosis with thrombocytopenia syndrome		
Interactions	Interactions with other vaccines/drugs have not been studied. The FDA recommends that COVID-19 vaccines and other vaccines may be administered without regard to timing.		

*Information for the Janssen COVID-19 vaccine is based on the US prescribing information. Consult your local drug formulary or guidelines for more detailed information. *Efficacy in preventing symptomatic infection in people ages 18 years and older according to clinical trials. Last updated: 8 July 2021*

BMJ Best Practice editorial team; compiled using data from the Us product information

Vaccines: dose schedules

- Dose schedules may differ between countries depending on vaccine coverage rates and supply constraints.
- The WHO recommends that countries that have not yet achieved high vaccine coverage rates in high-priority groups and who are experiencing a high incidence of cases combined with vaccine supply constraints should focus on achieving a high first-dose coverage in the high-priority groups by extending the interdose interval of mRNA vaccines by up to 12 weeks.^{[356] [357]} The WHO recommends an interval of 8 to 12 weeks between the two doses of the AstraZeneca vaccine (rather than 4 to 12 weeks as the manufacturer recommends) as two-dose efficacy and immunogenicity increase with a longer interdose interval.^[358]

- In the UK, the Joint Committee on Vaccination and Immunisation (JCVI) recommends that the second dose of a vaccine should be routinely scheduled between 8 and 12 weeks after the first dose for all available vaccines. The main exception to the 8-week lower interval would be those about to commence immunosuppressive treatment. Evidence shows that delaying the second dose to 12 weeks after the first improves the boosting effect.
- [Public Health England: COVID-19 vaccination information for healthcare practitioners] (<https://www.gov.uk/government/publications/covid-19-vaccination-programme-guidance-for-healthcare-practitioners>)
- In the US, the Centers for Disease Control and Prevention recommends that the second dose of an mRNA vaccine can be scheduled for up to 6 weeks after the first dose if the recommended dosing interval cannot be met. The agency continues to emphasize that the second dose should be given as close to the recommended interval as possible, and states that the two mRNA vaccines that are available in the US may be considered interchangeable in exceptional circumstances.
- [CDC: interim clinical considerations for use of COVID-19 vaccines currently authorized in the United States] (<https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>)
- Use the same vaccine product for both doses.
- There is a lack of data on using two different vaccines to complete a two-dose schedule. However, recommendations will be updated as further information becomes available on interchangeability between vaccines.[356] [357] [358] [359] [360] [361]
- Heterologous vaccination schedules have been found to induce a robust humoral and cellular immune response after a second dose of an mRNA vaccine in people primed with the AstraZeneca vaccine 8 to 12 weeks earlier, and were associated with an acceptable and manageable reactogenicity profile in small cohort studies.[371] [372] However, an interim analysis of a UK multicenter, participant-masked, randomized heterologous prime-boost vaccination study found an increase in systemic reactogenicity after the boost dose in heterologous vaccine schedules in comparison to homologous vaccine schedules in participants ages 50 years and older.[373] The difference between studies may be explained, in part, by the difference in administration intervals used between the studies (i.e., 28 days versus 8 to 12 weeks).
- Further safety and efficacy data are required before heterologous schedules can be recommended.

Vaccines: safety signals

- Thrombosis with thrombocytopenia syndrome (TTS)
 - TTS has been reported after vaccination with the AstraZeneca and Janssen vaccines.[374] [375] Regulatory agencies have confirmed that a causal relationship is plausible.[376] [377] [378] [379] [380] [381] There has been no safety signal for TTS following receipt of mRNA vaccines, although a small number of cases have been reported.[382]
 - In the UK, monitoring of the Yellow Card reporting system has detected 405 reports of TSS after administration of the AstraZeneca vaccine, including 147 cases of cerebral venous sinus thrombosis and 258 cases of thrombosis in other major veins, with 74 deaths, an overall case fatality rate of 18% (as of 7 July 2021). Most cases occurred after the first dose; however, 39 cases have been reported after the second dose. The overall risk has been estimated to be 14.8 cases per million people who receive the vaccine.[383]
 - In the US, a total of 17 cases have been reported with the Janssen vaccine (as of 21 April 2021). All of these cases occurred in women between the ages of 18 and 59, with a symptom onset between 6 and 15 days after vaccination. The overall risk has currently been estimated to be 0.9 cases per million people who receive the vaccine, with the risk increasing to 7 per million in women ages 18 to 49 years.[384] [385] [386]

- Some countries have permanently stopped the use of these vaccines in their immunization program.[\[387\]](#) [\[388\]](#) Other countries have implemented age-related prescribing restrictions. For example, in the UK, the JCVI advises that it is preferable for adults ages <40 years without underlying health conditions that put them at higher risk of severe disease to receive an alternative to the AstraZeneca vaccine, where available.[\[389\]](#) [\[390\]](#) Age cut-offs vary widely between countries so it is important to consult your local guidance.
- The US Centers for Disease Control and Prevention recommends that people with a history of an episode of an immune-mediated syndrome characterized by thrombosis and thrombocytopenia, such as heparin-induced thrombocytopenia, should be offered an mRNA vaccine instead of the Janssen vaccine (the AstraZeneca vaccine is not currently available in the US) if it has been ≤90 days since their illness resolved. After 90 days, patients may be vaccinated with any authorized vaccine.[\[391\]](#)
- Pregnancy predisposes to thrombosis; therefore, women should discuss with their healthcare professional whether the benefits of having these vaccines outweigh the risks.[\[377\]](#)
- Regulatory agencies state that the benefits of these vaccines continue to outweigh the risks.[\[376\]](#) [\[377\]](#) [\[378\]](#) [\[381\]](#) [\[384\]](#)
- See the Complications section for more information on this condition, including diagnosis and management.
- Myocarditis and pericarditis
 - Myocarditis and pericarditis have been reported after vaccination.[\[392\]](#) [\[393\]](#) [\[394\]](#) [\[395\]](#) Regulatory agencies have concluded that myocarditis and pericarditis can occur in very rare cases following vaccination with mRNA vaccines and have updated the prescribing information for these vaccines.[\[396\]](#) [\[397\]](#) [\[398\]](#)
 - Cases occurred predominantly in adolescents and young adults 12 to 29 years of age, more often in males than in females, more often following dose 2 than dose 1, and typically within 7 days after vaccination.[\[399\]](#)
 - In a case series of 23 previously healthy male military members, myocarditis was identified within 4 days of vaccination. For most patients, the diagnosis was made after the second dose of an mRNA vaccine.[\[400\]](#)
 - In the UK, monitoring of the Yellow Card reporting system has detected 81 cases of myocarditis and 63 reports of pericarditis with the Pfizer/BioNTech vaccine, 69 cases of myocarditis and 107 reports of pericarditis with the AstraZeneca vaccine, and 9 cases of myocarditis and 9 reports of pericarditis with the Moderna vaccine (as of 7 July 2021).[\[383\]](#)
 - In the US, monitoring by the Vaccine Adverse Event Reporting System (VAERS) detected 1226 reports of myocarditis after vaccination with an mRNA vaccine. This equates to 40.6 cases per million second doses of vaccine in males ages 12 to 29 years, and 2.4 per million in males ages ≥30 years.[\[399\]](#)
 - The Centers for Disease Control and Prevention recommends that people with a history of myocarditis or pericarditis may receive any vaccine after the episode has completely resolved. People with a history of myocarditis or pericarditis after their first dose of an mRNA vaccine should defer receiving their second dose, or may consider it under certain circumstances provided the episode has fully resolved.[\[391\]](#)
 - Consider myocarditis and pericarditis in adolescents or young adults with acute chest pain, shortness of breath, or palpitations.[\[401\]](#)
- Anaphylaxis
 - Severe allergic reactions, including anaphylaxis, have been reported after vaccination. Reactions may be due to the presence of lipid pegylated ethylene glycol (PEG), or PEG derivatives such as polysorbates.[\[402\]](#)
 - In the UK, monitoring of the Yellow Card reporting system has detected 428 cases of anaphylaxis with the Pfizer/BioNTech vaccine, 781 cases with the AstraZeneca vaccine, and 26 cases with the Moderna vaccine (as of 7 July 2021).[\[383\]](#)
 - In the US, monitoring by VAERS detected 4.7 cases of anaphylaxis per million doses of the Pfizer/BioNTech vaccine, and 2.5 cases per million doses of the Moderna vaccine as of 18 January 2021.[\[403\]](#)

- Globally, the incidence of anaphylaxis post-vaccination has been reported to be 7.91 cases per million based on available data.[\[404\]](#)
- A history of anaphylaxis to any component of the vaccine is a contraindication to vaccination. People who have an anaphylactic reaction following the first dose of the vaccine should not receive a second dose of the same vaccine. Observe people for 15 to 30 minutes after vaccination in healthcare settings where anaphylaxis can be immediately treated.[\[356\]](#) [\[357\]](#) [\[358\]](#) [\[359\]](#) [\[360\]](#) [\[361\]](#) Consult local guidelines for recommendations on vaccinating people with a history of allergies or anaphylaxis as guidance may differ across locations.
- Capillary leak syndrome
 - Capillary leak syndrome has been reported after vaccination with the AstraZeneca vaccine. Most cases occurred in women within 4 days of vaccination, and half of the patients had a history of capillary leak syndrome.[\[405\]](#)
 - The European Medicines Agency advises that the AstraZeneca and Janssen vaccines are contraindicated in people with a history of capillary leak syndrome.[\[405\]](#) [\[406\]](#)
 - Severe, life-threatening flares have also been reported with mRNA vaccines.[\[407\]](#) Cases of capillary leak syndrome have also been reported in patients with COVID-19.[\[408\]](#)
 - In the UK, monitoring of the Yellow Card reporting system has detected 8 cases of capillary leak syndrome with the AstraZeneca vaccine (as of 7 July 2021).[\[383\]](#)
- Bell palsy
 - Clinical trials of the mRNA vaccines showed an imbalance in the incidence of Bell palsy following vaccination compared with the placebo arm of each trial, suggesting vaccination may be associated with Bell palsy.[\[409\]](#)
 - Analysis of data from the World Health Organization's pharmacovigilance database up until early March 2021 failed to identify a higher risk of facial paralysis after vaccination.[\[410\]](#)
 - A case-control study also failed to identify a higher risk after recent vaccination with the Pfizer/BioNTech vaccine.[\[411\]](#)
 - EudraVigilance data indicate a much higher frequency of facial paralysis after the Pfizer/BioNTech vaccine (13.6 cases per million doses) compared with the AstraZeneca vaccine (4.1 cases per million doses), indicating that the risk may be higher with mRNA vaccines.[\[412\]](#)
 - In the UK, the Yellow Card system has found that the number of reports of facial paralysis received so far is similar to the expected natural rate and does not currently suggest an increased risk following vaccination.[\[383\]](#)
- Lymphadenopathy
 - Ipsilateral axillary/supraclavicular lymphadenopathy has been reported within 2 to 4 days after vaccination. It occurs more commonly after the second dose, and more commonly with the Moderna vaccine compared with the Pfizer/BioNTech vaccine.[\[413\]](#)
 - Although UK guidelines currently recommend a 2-week suspected-cancer referral for unexplained axillary lymphadenopathy in those ages >30 years, a watchful wait approach may be appropriate in patients who have been vaccinated in the past week, provided that they have a normal breast exam and no history of breast cancer. Further examination up to 2 weeks later is recommended, with referral to secondary care for those with nonresolving lymphadenopathy. An urgent referral to the breast clinic is advisable in patients with current or previous history of breast cancer.[\[414\]](#)
- Guillain-Barre syndrome
 - Guillain-Barre syndrome has been reported after vaccination.[\[415\]](#) [\[416\]](#)
 - The European Medicines Agency has recommended adding a warning to the prescribing information of the AstraZeneca vaccine as available data neither confirm nor rule out a possible association with the vaccine.[\[417\]](#)
 - In the UK, monitoring of the Yellow Card reporting system has detected 344 cases of Guillain-Barre syndrome and 20 cases of Miller Fisher syndrome with the AstraZeneca vaccine, 41 cases of Guillain-Barre syndrome with the Pfizer/BioNTech vaccine, and 2 reports of Guillain-Barre syndrome with the Moderna vaccine (as of 7 July 2021). The UK Medicines

and Healthcare products Regulatory Agency is reviewing these cases to assess whether there is an increased risk of Guillain-Barre syndrome after vaccination. Based on the available evidence at this stage, the agency is not able to confirm or rule out a causal relationship with the vaccine.[383]

- Vaccines and menstrual disorders/unexpected vaginal bleeding
 - Menstrual disorders including heavier than usual periods, delayed periods, and unexpected vaginal bleeding have been reported after vaccination (22,981 reports as of 7 July 2021).[383]
 - Current evidence does not suggest an increased risk of either menstrual disorders or unexpected vaginal bleeding following the vaccines; however, the UK Medicines and Healthcare products Regulatory Agency is closely monitoring the situation.[383]
- Immune thrombocytopenic purpura
 - Immune thrombocytopenic purpura has been reported after vaccination with the AstraZeneca vaccine.[418]
- Facial swelling
 - People with a history of receiving dermal fillers may develop swelling at or near the site of filler injection (e.g., lips, face) following administration of an mRNA vaccine. This appears to be temporary and may be treated with corticosteroids. The European Medicines Agency found that there is at least a reasonable possibility of a causal association between the vaccine and the reported cases of facial swelling.[419]
- Delayed-onset local reactions
 - Delayed-onset local reactions around the injection site have been reported with the Moderna vaccine (median 7-8 days after first vaccination), and are sometimes quite large (e.g., at least 10 cm in diameter). Most people who had a reaction to the first dose also developed a similar reaction to the second dose, and developed it much sooner compared with the first dose.[420] [421]
- Vasovagal reactions
 - Anxiety-related reactions, including vasovagal reactions and hyperventilation, have been reported after vaccination. Ensure precautions are in place to avoid injury from fainting.[422]
- Report all suspected adverse reactions after vaccination via your local reporting system. This is mandatory in some countries.
 - UK: [Yellow Card: coronavirus (COVID-19)] (<https://coronavirus-yellowcard.mhra.gov.uk>)
 - US: [Vaccine Adverse Event Reporting System (VAERS)] (<https://vaers.hhs.gov>)
 - Europe: [EudraVigilance] (<https://www.ema.europa.eu/en/human-regulatory/research-development/pharmacovigilance/eudravigilance>)
 - International: [WHO: Adverse Event Following Immunization (AEFI) form] (<http://investigation.gvsi-aefi-tools.org/#step-1>)
- Surveillance of adverse events is extremely important, and may reveal additional, less frequent serious adverse events not detected in clinical trials. The mRNA vaccines have not been authorized for use in humans previously, so there is no long-term safety and efficacy data available for these types of vaccines.

Vaccines: special patient populations

- There are limited or no data available from clinical trials about the use of vaccines in specific patient populations.
- Pregnancy

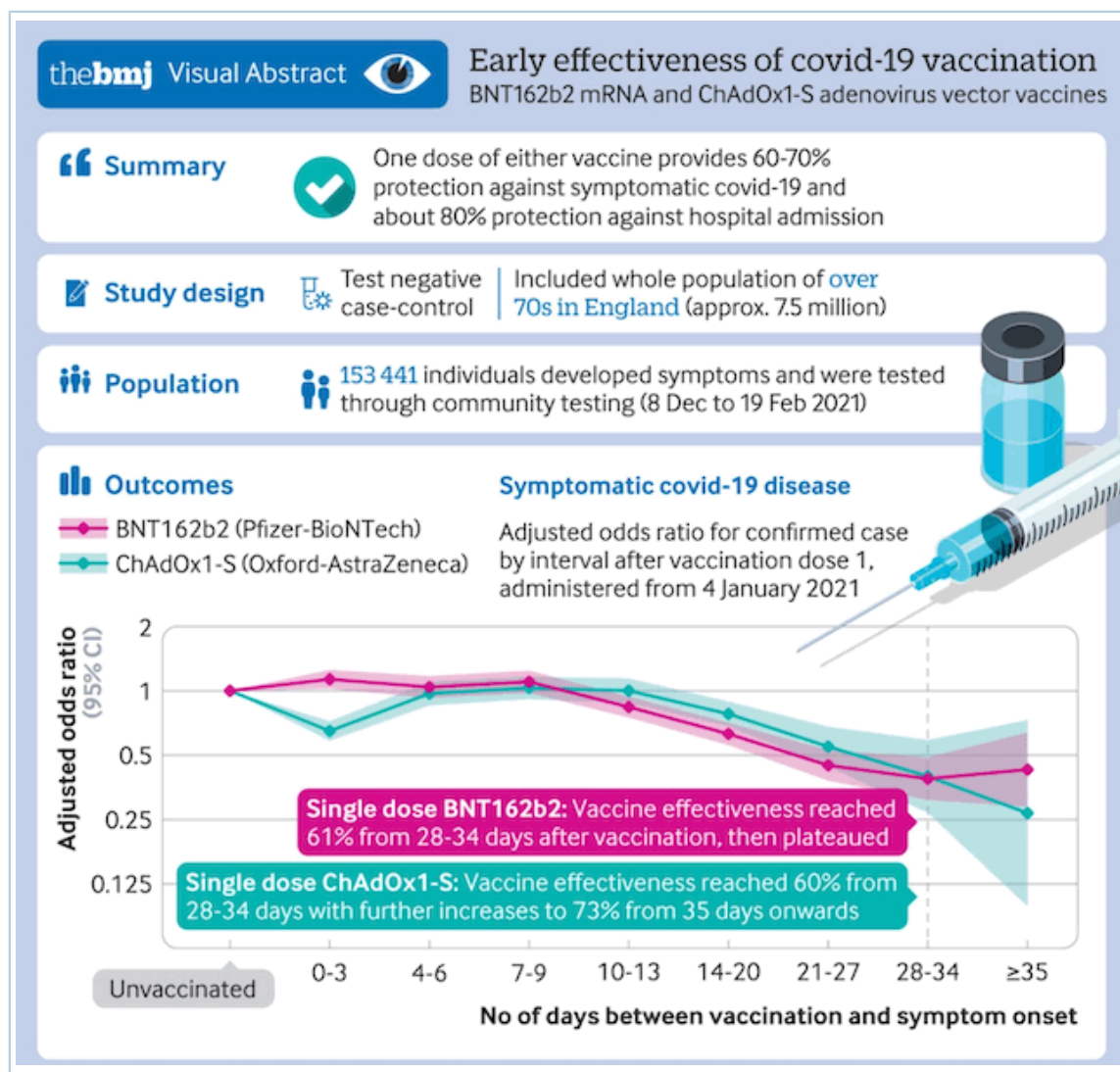
- Use caution in pregnant women as there are limited safety and efficacy data available. Preliminary data from the v-safe pregnancy registry and VAERS in the US did not show any obvious safety signals among pregnant women who received mRNA vaccines. These data have many limitations, and continued monitoring is needed to further assess the risk. Among 221 pregnancy-related adverse events reported to VAERS, the most frequently reported event was spontaneous abortion (46 cases), followed by stillbirth, premature rupture of membranes, and vaginal bleeding (3 reports for each). No congenital anomalies were reported to VAERS.[423]
- The WHO recommends vaccines in pregnant women when the benefits outweigh the potential risks. The WHO does not recommend pregnancy testing prior to vaccination, or delaying pregnancy or terminating a pregnancy because of vaccination.[356] [357] [358] [359] [360] [361]
- The UK Joint Committee on Vaccination and Immunisation (JCVI) advises that pregnant women should be offered the vaccine, preferably an mRNA vaccine, at the same time as the rest of the population, based on their age and clinical risk group. However, the JCVI acknowledges that more research is needed, and advises pregnant women to discuss the risk and benefits with their clinician.[424] [425]
- The US Centers for Disease Control and Prevention recommends that pregnant women are eligible for and can receive a vaccine. Pregnant women who choose to receive a vaccine are encouraged to enroll in the v-safe program. [CDC: v-safe COVID-19 vaccine pregnancy registry] (<https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafepregnancyregistry.html>) The agency also recommends that women who are trying to become pregnant can receive a vaccine, although it acknowledges that there are no safety data available.[391]
- The American College of Obstetricians and Gynecologists recommends that pregnant women have access to vaccines. Women should have access to available information about the safety and efficacy of the vaccine, including information about data that are not available. A conversation between the patient and the clinical team may assist with the decision. Pregnant women who decline vaccination should be supported in their decision.[426]
- Breastfeeding
 - Use caution in breastfeeding women as there are limited safety and efficacy data available. A small prospective study found robust secretion of SARS-CoV-2 specific immunoglobulin A (IgA) and IgG antibodies in breast milk for 6 weeks after vaccination.[427] Vaccine-associated mRNA was not detected in 13 milk samples collected 4 to 48 hours after vaccination from 7 breastfeeding individuals.[428] However, further research is required.
 - The WHO recommends that vaccines may be used in lactating women as in other adults. The WHO does not recommend discontinuing breastfeeding because of vaccination.[356] [357] [358] [359] [360] [361]
 - The US Centers for Disease Control and Prevention recommends that lactating women can receive a vaccine, although it acknowledges that there are no safety data available.[391]
 - The American College of Obstetricians and Gynecologists recommends that vaccines should be offered to lactating individuals similar to nonlactating individuals.[426]
- Children and adolescents
 - The Pfizer/BioNTech vaccine has been authorized for use in young people ages 12 to 15 years in many countries, including the UK, Europe, and the US.[429] [430] [431] [432] Authorization was based on an ongoing randomized, placebo-controlled clinical trial in the US of over 2000 participants that reports 100% efficacy from 7 days after the second dose.[433] Due to the limited number of children included in the study, the trial could not have detected rare adverse effects.
 - The WHO recommends considering use of the Pfizer/BioNTech vaccine in children ages 12 to 15 years only when high vaccine coverage with 2 doses has been achieved in high-priority groups. Children ages 12 to 15 years with comorbidities that put them at significantly higher risk of serious disease, alongside other high-risk groups, may be offered vaccination.[356]
 - The UK's JCVI recommends that children who are at increased risk of serious disease are offered the Pfizer/BioNTech vaccine, including children ages 12 to 15 years with severe neurodisabilities, Down syndrome, immunosuppression, and multiple or severe learning

- disabilities. The JCVI also recommends that children ages 12 to 17 years who live with an immunosuppressed person should be offered the vaccine. Routine vaccination of children outside of these groups is not recommended, based on the current evidence.[\[434\]](#)
- The European Medicines Agency and the US Food and Drug Administration are evaluating an application to extend the use of the Moderna vaccine to include young people ages 12 to 17 years.[\[435\]](#)
- There are currently no efficacy or safety data for children <12 years of age.
- Older people and people with comorbidities
 - The WHO recommends that older people (without an upper age limit) and people with comorbidities that have been identified as increasing the risk for severe disease may be vaccinated.[\[356\]](#) [\[357\]](#) [\[358\]](#) [\[359\]](#) [\[360\]](#) [\[361\]](#)
- Current or previous SARS-CoV-2 infection
 - Delayed vaccination is recommended in people with current acute COVID-19 (or any other acute febrile illness) until they have recovered from the acute illness and the criteria for discontinuation of isolation have been met.[\[356\]](#) [\[357\]](#) [\[358\]](#) [\[359\]](#) [\[360\]](#) [\[361\]](#)
 - Delayed vaccination is recommended in people who previously received passive antibody therapy for COVID-19 (for at least 90 days).[\[356\]](#) [\[357\]](#) [\[358\]](#) [\[359\]](#) [\[360\]](#) [\[361\]](#)
 - Delayed vaccination may be considered in people who have had confirmed SARS-CoV-2 infection in the preceding 6 months (until near the end of this period) if, for example, there is limited vaccine supply. Emerging data indicate that symptomatic reinfection after natural infection may occur in settings where variants of concerns with evidence of immune escape are circulating. In these settings, earlier immunization after infection may be advisable.[\[356\]](#) [\[357\]](#) [\[358\]](#) [\[359\]](#) [\[360\]](#) [\[361\]](#)
 - Emerging evidence suggests that one dose of the vaccine may be sufficient for people who have already been infected with SARS-CoV-2.[\[436\]](#) [\[437\]](#) [\[438\]](#) [\[439\]](#) People who have had previous SARS-CoV-2 infection are unlikely to become reinfected whether or not they receive the vaccine.[\[440\]](#)
- Immunocompromised
 - The WHO recommends that immunocompromised people, people living with HIV, and people with autoimmune conditions who have no contraindications to vaccination may be vaccinated if they are part of a group recommended for vaccination.[\[356\]](#) [\[357\]](#) [\[358\]](#) [\[359\]](#) [\[360\]](#) [\[361\]](#)
 - Emerging preprint data from the UK indicate that the Pfizer/BioNTech and AstraZeneca vaccines are effective at preventing symptomatic disease in the majority of people with underlying health conditions who are clinically vulnerable. Efficacy was reduced in immunocompromised patients after one dose; however, after a second dose there was only a small and nonsignificant reduction in vaccine efficacy. Further research is needed to understand vaccine efficacy against severe disease among immunosuppressed groups.[\[441\]](#)
 - A small study found that the AstraZeneca vaccine was safe and immunogenic in people with HIV infection with well-suppressed viremia and good CD4 cell counts. Further data are required to test the durability of this response and in those who are viremic or have low CD4 cell counts.[\[442\]](#)
- Autoimmune disease
 - It is uncertain whether vaccines may cause an exacerbation of preexisting autoimmune diseases.
 - A case of reactivation of IgA vasculitis has been reported.[\[443\]](#)
 - In patients with psoriasis, seroconversion rates after vaccination were lower in patients receiving immunosuppressants, with the lowest rate in those receiving methotrexate. Neutralizing activity was preserved in those receiving targeted biologic agents.[\[444\]](#)
- Malignancy and solid organ or stem cell transplant recipients

- Emerging data suggest that vaccine efficacy may be lower in cancer patients and solid organ transplant recipients.[\[445\]](#) [\[446\]](#) [\[447\]](#) [\[448\]](#) [\[449\]](#) [\[450\]](#) [\[451\]](#) [\[452\]](#) [\[453\]](#) [\[454\]](#)
- Frequent and high levels of humoral responses have been identified in allogeneic hematopoietic stem cell transplant recipients after two vaccine doses.[\[455\]](#)
- Patients with lymphoma can develop a robust serologic response as early as 6 months after treatment.[\[456\]](#)
- Patients with hematologic malignancies mount blunted and heterogeneous antibody responses. People treated with Bruton tyrosine kinase inhibitors, ruxolitinib, venetoclax, and anti-CD20 antibody therapies appear to be most affected.[\[457\]](#)
- A third dose of the Pfizer/BioNTech vaccine significantly improved the immunogenicity of the vaccine in a small group of solid organ transplant recipients.[\[458\]](#)

Vaccines: real world efficacy data

- Initial authorization of vaccines was based on interim analyses of ongoing phase 3 clinical trials with a median follow-up of 2 months.[\[459\]](#) [\[460\]](#) [\[461\]](#) [\[462\]](#) [\[463\]](#)
- Emerging observational evidence suggests real-world efficacy in reducing the rate of symptomatic or asymptomatic infection, disease severity, hospitalization, and death; however, further research is required.
 - The interim results of a living systematic review in Europe found a vaccine efficacy of 80% to 90% in preventing infection (including asymptomatic infection) for vaccines approved in Europe.[\[464\]](#)
 - A meta-analysis of 19 observational studies found that the Pfizer/BioNTech vaccine provided a significant protective effect against testing positive on reverse transcription polymerase chain reaction (regardless of the presence of symptoms) 14 days or more after the first dose (vaccine efficacy 53%), and 7 days or more after the second dose (vaccine efficacy 95%).[\[465\]](#)
 - A case control study of over 150,000 adults ages ≥ 70 years who were vaccinated with either the Pfizer/BioNTech or AstraZeneca vaccines and who reported symptoms between 8 December 2020 and 19 February 2021 found that vaccination with one dose of either vaccine was associated with a 60% to 70% protection against symptomatic disease, an 80% protection against hospital admission, and an 85% protection against death. Protection was maintained for at least 6 weeks, and vaccines were effective against the B.1.1.7 variant.[\[466\]](#)



Early effectiveness of covid-19 vaccination

BMJ. 2021 May 13;373:n1088

- A prospective cohort study (preprint) in the UK found that people ages ≥ 70 years who received a single dose of either the Pfizer/BioNTech or AstraZeneca vaccine had a 44% and 55% reduced risk of death, respectively, compared with unvaccinated people. There was a 69% reduced risk of death after the second dose of the Pfizer/BioNTech vaccine.[467]
- A prospective cohort study (preprint) in the UK found that effectiveness in preventing hospitalization was high in people ages ≥ 70 years who received a single dose of either the AstraZeneca or Pfizer/BioNTech vaccines (73% and 81%, respectively, in patients ≥ 80 years; 84% and 81%, respectively, in patients 70-79 years), and especially after two doses of the Pfizer/BioNTech vaccine (93% in patients ≥ 80 years) compared with unvaccinated people.[468] A study in Scotland found that the first dose of the Pfizer/BioNTech vaccine was associated with a 91% reduction in hospital admissions at 28 to 34 days post-vaccination (an 88% reduction for the AstraZeneca vaccine).[469]
- A prospective cohort study (preprint) in the UK found that odds of new infection were reduced by 65% after the first dose of either the Pfizer/BioNTech or AstraZeneca vaccine compared with unvaccinated people without prior evidence of infection. A larger reduction in odds of infection was seen after the second dose (70%). There was no evidence that the benefits varied between the two vaccines.[470]
- A prospective cohort study in UK healthcare workers found that a single dose of the Pfizer/BioNTech vaccine showed effectiveness at preventing both symptomatic and asymptomatic infection of 70% at 21 days after the first dose and 85% at 7 days after two doses compared with an unvaccinated cohort. The study population was exposed to the B.1.1.7 variant.[471]

- A prospective cohort study (preprint) in the UK found that the Pfizer/BioNTech and AstraZeneca vaccines are associated with reduced likelihood of household transmission from individuals diagnosed with COVID-19 after vaccination. The secondary attack rate was reduced from 10.1% when the index case was an unvaccinated person, to 5.7% to 6.25% (depending on the vaccine) when the contact was vaccinated.[472]
- A prospective cohort study in the over 10,000 older adults living in long-term care facilities in the UK found that the Pfizer/BioNTech and AstraZeneca vaccines are associated with a substantially reduced risk of infection from 28 days after a single dose, and this effect was maintained for at least 7 weeks.[473]
- A prospective test-negative case-control study in adults aged at least 80 years who were admitted to hospital in the UK found that one dose of either the Pfizer/BioNTech and AstraZeneca vaccines resulted in a substantial risk reduction in hospitalization.[474]
- Observational studies from Israel have found that the Pfizer/BioNTech vaccine was highly effective in preventing symptomatic and asymptomatic infection, as well as hospitalizations, severe disease, need for mechanical ventilation, and death, including those caused by the B.1.1.7 variant.[475] [476] [477] [478] [479] [480] However, concerns have been raised about the studies.[481]
- Observational studies from the US have found that the Pfizer/BioNTech and Moderna vaccines were highly effective in preventing symptomatic and asymptomatic infection, as well as hospitalizations.[482] [483] [484] [485] [486] [487]
- Current data on the real world effectiveness and the impact of vaccines is published each week in the UK. As of 15 July 2021, vaccine effectiveness has been estimated as follows (evidence varies from low to high depending on the outcome and the vaccine):
 - Symptomatic disease: 85% to 95% (after 2 doses of Pfizer/BioNTech); 70% to 85% (after 2 doses of AstraZeneca)
 - Hospitalization: 90% to 99% (after 2 doses of Pfizer/BioNTech); 80% to 99% (after 2 doses of AstraZeneca)
 - Mortality: 95% to 99% (after 2 doses of Pfizer/BioNTech); 75% to 99% (after 2 doses of AstraZeneca)
 - Infection: 70% to 90% (after 2 doses of Pfizer/BioNTech); 65% to 90% (after 2 doses of AstraZeneca)
 - Transmission: no data available as yet.
 - [Public Health England: COVID-19 vaccine surveillance reports] (<https://www.gov.uk/government/publications/covid-19-vaccine-surveillance-report>)
- Previous trials of coronavirus vaccines identified cellular immunopathology and antibody-dependent enhancement as potential safety issues.[488] [489]
- Available data do not indicate a risk of vaccine-enhanced disease with the mRNA vaccines; however, data are limited and the risk over time, potentially associated with waning immunity, remains unknown and needs to be evaluated further.[459] [460]

Vaccines: efficacy against SARS-CoV-2 variants

- Pfizer/BioNTech: preliminary studies suggest that the Pfizer/BioNTech vaccine may be effective against the following variants, although the neutralization effect may be reduced compared with the wild-type virus:[44] [45] [46] [47] [490] [491] [492] [493] [494] [495] [496] [497]
 - B.1.1.7 (and B.1.1.7 + E484K)
 - B.1.351
 - B.1.526
 - B.1.429
 - B.1.617.1 and B.1.617.2.

- Moderna: preliminary studies suggest that the Moderna vaccine may be effective against the following variants, although the neutralization effect may be reduced compared with the wild-type virus:[44] [493] [498] [499] [500]
 - B.1.1.7
 - B.1.351
 - B.1.617.1 and B.1.617.2.
- AstraZeneca: preliminary studies suggest that the AstraZeneca vaccine may be effective against the following variants, although the neutralization effect may be reduced compared with the wild-type virus:[44] [47] [46] [501]
 - B.1.1.7
 - B.1.617.2.
- Manufacturers are currently testing booster doses against emerging variants.[497] [502] [503]

Infection prevention and control for healthcare professionals

- Consult local infection prevention and control protocols; only basic principles from the World Health Organization guidelines are detailed here.[504]
- Screen all people, including patients, visitors, and others entering the facility, for COVID-19 at the first point of contact with the health facility to allow for early recognition.
- Immediately isolate all suspected or confirmed cases in a well-ventilated area that is separate from other patients. Place patients in adequately ventilated single rooms if possible. When single rooms are not available, place all cases together in the same adequately ventilated room and ensure there is at least 3 feet (1 meter) between patients.
- Implement standard precautions at all times:
 - Practice hand and respiratory hygiene
 - Give patients a medical mask to wear
 - Wear appropriate personal protective equipment
 - Practice safe waste management and environmental cleaning.
- Implement additional contact and droplet precautions before entering a room where cases are admitted:
 - Wear a medical mask, gloves, an appropriate gown, and eye/facial protection (e.g., goggles or a face shield)
 - Use single-use or disposable equipment.
- Implement airborne precautions when performing aerosol-generating procedures, including placing patients in a negative pressure room.
 - Some countries and organizations recommend airborne precautions for any situation involving the care of a COVID-19 patient.
- All specimens collected for laboratory investigations should be regarded as potentially infectious.
- Appropriate personal protective equipment gives healthcare workers a high level of protection.
 - A cross-sectional study of 420 healthcare workers deployed to Wuhan with appropriate personal protective equipment tested negative for SARS-CoV-2 on molecular and serologic testing when they returned home, despite all participants having direct contact with COVID-19 patients and performing at least one aerosol-generating procedure.[505]

- Standard surgical masks are as effective as respirator masks for preventing infection of healthcare workers in outbreaks of viral respiratory illnesses such as influenza, but it is unknown whether this applies to COVID-19.[506]
- Avoid in-person assessment of patients with suspected COVID-19 in primary care when possible to avoid infection. Most patients can be managed remotely by telephone or video consultations.[507]
 - [BMJ: covid-19 in primary care (UK)] (https://sandpit.bmj.com/graphics/2020/covid19_v3.0_web.pdf)
 - [BMJ: covid-19 – a remote assessment in primary care] (<https://www.bmj.com/content/368/bmj.m1182>)
- Detailed infection prevention and control guidance is available:
 - [WHO: infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed] (<https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC-2021.1>)
 - [CDC: interim infection prevention and control recommendations for healthcare personnel during the coronavirus disease 2019 (COVID-19) pandemic] (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html>)
 - [BMJ: covid-19 – PPE guidance] (<https://www.bmj.com/sites/default/files/attachments/resources/2020/04/cv19-ppe-v1.0-web.pdf>)

Infection prevention and control for the general public

- Public health recommendations vary between countries and you should consult your local guidance. It is generally recommended that people stay at least 3 to 6 feet (1-2 meters) away from others (recommendations vary between countries), wash their hands often with soap and water (or hand sanitizer that contains at least 60% alcohol), cover coughs and sneezes, wear a mask, avoid crowds and poorly ventilated spaces, clean and disinfect high touch surfaces, monitor their health and self-isolate or seek medical attention if necessary, and get vaccinated.[508] [509]
 - [WHO: coronavirus disease (COVID-19) advice for the public] (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public>)
- Alcohol-based hand sanitizer: may be recommended in situations where it is not possible to use soap and water; however, adverse events have been reported including:[510] [511] [512] [513]
 - Headache, nausea, and dizziness due to inhalation of vapors, especially in enclosed or poorly ventilated spaces
 - Methanol poisoning (including cases of permanent blindness and death) due to ingestion or frequent repeated topical use
 - Accidental ingestion and unintentional ocular exposures, especially by children
 - Antimicrobial resistance.
- Face masks: the WHO advises that in areas of known or suspected community or cluster transmission, people should wear a nonmedical mask in the following circumstances: indoor or outdoor settings where physical distancing cannot be maintained; indoor settings with inadequate ventilation, regardless of whether physical distancing can be maintained; in situations when physical distancing cannot be maintained and the person has a higher risk of severe complications (e.g., older age, underlying condition); caregivers and those living with suspected or confirmed cases when in the same room, regardless of whether the case has symptoms. Children ages up to 5 years should not wear masks for source control, while a risk-based approach is recommended for children ages 6 to 11 years. Special considerations are required for immunocompromised children, or children with certain diseases, developmental disorders, or disabilities. The WHO advises that people should not wear masks during vigorous-intensity physical activity.[92]

- There is no high-quality or direct scientific evidence to support the widespread use of masks by healthy people in the community setting. Data on effectiveness is based on limited and inconsistent observational and epidemiologic studies.[92]
- The only randomized controlled trial to investigate the efficacy of masks in the community found that the recommendation to wear surgical masks when outside the home did not reduce infection compared with a no mask recommendation. However, the study did not assess whether masks could decrease disease transmission from mask wearers to others (source control).[514] Evidence from randomized controlled trials for other respiratory viral illnesses shows no significant benefit of masks in limiting transmission but is of poor-quality and not SARS-CoV-2-specific.[515]
- A Cochrane review found that wearing a mask may make little to no difference in how many people caught influenza-like illnesses. However, this was based on low-certainty evidence, and does not include results of studies from the current pandemic.[516]
- A living rapid review found that the evidence for mask effectiveness for respiratory tract infection prevention is stronger in healthcare settings compared with community settings; however, direct evidence on comparative effectiveness in SARS-CoV-2 infection is insufficient. The strength of evidence for any mask use versus nonuse in community settings is low.[517] [518]
- Cloth masks have limited efficacy in preventing viral transmission compared with medical-grade masks and the efficacy is dependent on numerous factors (e.g., material type, number of layers, fitting, moisture level), and may result in increased risk of infection.[519] [520]
- There are harms and disadvantages of wearing masks (e.g., headache, breathing difficulties, facial skin lesions, psychological issues, difficulty communicating, increased viral load).[92] There are insufficient data to quantify all of the adverse effects that might reduce the acceptability, adherence, and effectiveness of face masks.[521] [522]
- [BMJ: mask related acne ("maskne") and other facial dermatoses] (<https://www.bmj.com/content/373/bmj.n1304>)
- Nonpharmaceutical interventions: many countries have implemented nonpharmaceutical interventions in order to reduce and delay viral transmission (e.g., social distancing, city lockdowns, stay-at-home orders, curfews, nonessential business closures, bans on gatherings, school and university closures, remote working, quarantine of exposed people).
 - Implementing any nonpharmaceutical interventions was associated with a significant reduction in case growth when comparing countries with more restrictive nonpharmaceutical interventions to countries with less restrictive nonpharmaceutical interventions. However, there was no clear, significant beneficial effect of more restrictive nonpharmaceutical interventions compared with less restrictive nonpharmaceutical interventions in any of the countries studied.[523]
 - Negative consequences of community-based mass quarantine include psychological distress, food insecurity, economic challenges, diminished healthcare access, heightened communication inequalities, alternative delivery of education, and gender-based violence.[524]
- Shielding extremely vulnerable people: shielding is a measure used to protect vulnerable people (including children) who are at very high risk of severe illness from COVID-19 because they have an underlying health condition (e.g., cancer, severe respiratory condition, chronic kidney disease, immunosuppression). Shielding involves minimizing all interactions between those who are extremely vulnerable and other people to protect them from coming into contact with the virus.
 - Shielding is currently paused in the UK, and the government recommends that clinically extremely vulnerable people follow national restrictions for the general population, and continue to take extra precautions to protect themselves.[525]
 - Shielding advice may be available in other countries; consult local public health guidance.
- Travel-related control measures: many countries have implemented measures including complete or partial closure of borders, entry or exit screening, and/or quarantine of travelers.

- Low- to very low-certainty evidence suggests that travel-related control measures may help to limit the spread of infection across national borders. Cross-border travel restrictions are likely to be more effective than entry and exit screening, and screening is likely to be more effective in combination with other measures (e.g., quarantine, observation).^[526]
- Low-certainty evidence suggests that screening at travel hubs may slightly slow the importation of infected cases; however, the evidence base comes from two mathematical model studies and is limited by their assumptions. Evidence suggests that one-time screening in apparently healthy people may miss between 40% and 100% of people who are infected, although the certainty of this ranges from very low to moderate. In very low-prevalence settings, screening for symptoms or temperature may result in few false negatives and many true negatives, despite low overall accuracy. Repeated screenings may result in more cases being identified eventually and reduced harm from false reassurance.^[527] Entry screening at three major US airports found a low yield of laboratory-diagnosed cases (one case per 85,000 travelers) between January and September 2020.^[528]
- A Cochrane review found quarantine to be important in reducing the number of people infected and deaths, especially when started earlier and when used in combination with other prevention and control measures. However, the current evidence is limited because most studies are based on mathematical modeling studies that make assumptions on important model parameters.^[529]
- The psychosocial effects of enforced quarantine may have long-lasting repercussions.^[530]^[531]
- [\[Public Health England: travel abroad - step by step\]](https://www.gov.uk/travel-abroad) (<https://www.gov.uk/travel-abroad>)

Lifestyle modifications

- Lifestyle modifications (e.g., smoking cessation, weight loss) may help to reduce the risk of infection, and may be a useful adjunct to other interventions.^[532]
- The WHO recommends that tobacco users stop using tobacco given the well-established harms associated with tobacco use and second-hand smoke exposure.^[246] Public Health England also recommends stopping smoking.
- [\[Public Health England: COVID-19 – advice for smokers and vapers\]](https://www.gov.uk/government/publications/covid-19-advice-for-smokers-and-vapers/covid-19-advice-for-smokers-and-vapers) (<https://www.gov.uk/government/publications/covid-19-advice-for-smokers-and-vapers/covid-19-advice-for-smokers-and-vapers>)

Pre-exposure or postexposure prophylaxis

- There are no treatments recommended for pre-exposure prophylaxis or postexposure prophylaxis, except in the context of a clinical trial.^[533] See the Emerging section for more information.

Patient discussions

General discussions

- Communicate with patients and their families and caregivers, and support their mental wellbeing to help alleviate any anxiety and fear they may have. Signpost to charities and support groups.^[564]
- Explain that symptoms may include cough, fever, and loss of sense of smell or taste. Patients may also experience breathlessness (which may cause anxiety), delirium (which may cause agitation), fatigue, headache, myalgia, sore throat, drowsiness (particularly in older people), poor appetite, and chest discomfort/pain. Additional symptoms in children may include grunting, nasal flare, nasal congestion, poor appetite, gastrointestinal symptoms, skin rash, and conjunctivitis. The presence of fever, rash, abdominal pain, diarrhea, or vomiting in children may indicate pediatric inflammatory multisystem syndrome (PIMS). Reassure the patient that they are likely to feel much better in a week if their symptoms are mild.^[564]
- Discuss who to contact if their symptoms get worse, or if PIMS is suspected. Offer telephone or video consultations as appropriate.^[564]

- Discuss the benefits and risks of hospital admission or other acute care delivery services. Explain that people may deteriorate rapidly, and discuss future care preferences at the first assessment to give people who do not have existing advance care plans an opportunity to express their preferences.^[564]

Pulse oximetry

- Patients may be required to use a pulse oximeter in the home setting. Patient education and appropriate follow-up are required.
- [\[Health Education England: adult pulse oximetry monitoring video\]](https://www.youtube.com/watch?v=ifnYjD4IKus&t=141s) (<https://www.youtube.com/watch?v=ifnYjD4IKus&t=141s>)

Travel advice

- Many countries have implemented international travel bans/closed their borders, have issued advice for domestic travel. Some countries are restricting entry to foreign nationals who have been to affected areas in the preceding 14 days, or are enforcing quarantine periods (e.g., at home or in a designated facility such as a medi-hotel) where the person's health and infection status are closely monitored. Some countries are requiring a negative test before departure and after arrival, and are implementing travel measures to protect against new international variants of the virus. Masks may be mandatory on flights.
- Consult local guidance for specific travel restriction recommendations in your country:
 - [\[WHO: coronavirus disease \(COVID-19\) travel advice\]](https://www.who.int/emergencies/diseases/novel-coronavirus-2019/travel-advice) (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/travel-advice>)
 - [\[CDC: COVID-19 – travel\]](https://www.cdc.gov/coronavirus/2019-ncov/travelers/index.html) (<https://www.cdc.gov/coronavirus/2019-ncov/travelers/index.html>)
 - [\[NaTHNaC: travel health pro\]](https://travelhealthpro.org.uk) (<https://travelhealthpro.org.uk>)
 - [\[Public Health England: travel advice – coronavirus \(COVID-19\)\]](https://www.gov.uk/guidance/travel-advice-novel-coronavirus) (<https://www.gov.uk/guidance/travel-advice-novel-coronavirus>)
 - [\[UK Department for Transport\]](https://www.gov.uk/government/organisations/department-for-transport) (<https://www.gov.uk/government/organisations/department-for-transport>)
 - [\[Smartraveller Australia: COVID-19\]](https://www.smartraveller.gov.au/news-and-updates/coronavirus-covid-19) (<https://www.smartraveller.gov.au/news-and-updates/coronavirus-covid-19>)
 - [\[Government of Canada: coronavirus disease \(COVID-19\) – travel, testing, quarantine and borders\]](https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/latest-travel-health-advice.html) (<https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/latest-travel-health-advice.html>)
 - [\[Ministry of Manpower Singapore: advisories on COVID-19\]](https://www.mom.gov.sg/covid-19) (<https://www.mom.gov.sg/covid-19>)

Pets and animals

- At this time, there is no evidence that companion animals (including pets and other animals) play a significant role in the spread of COVID-19, and the risk of animals spreading COVID-19 to people is considered to be very low. There is no evidence that the virus can spread to people from the skin or fur of companion animals.^[1258]
- A very small number of pets have been reported to be infected with the virus after close contact with people with confirmed COVID-19; however, thousands of pets have been tested in the US with none testing positive. There is evidence that cats and ferrets may be more susceptible to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, while dogs and other livestock have no or low susceptibility. Nonhuman primates (gorillas) and large cats in captivity (lions, tigers, pumas, cougars, snow leopards) and domestic pet cats have tested positive after contact with symptomatic humans. Transmission between cats has also been reported. The virus has been reported in mink on farms, and once the virus is introduced on a farm, can spread between mink, and between mink and other animals on the farm. There is also the possibility that mink may transmit the infection to humans in these environments.^{[1259] [1260] [1261] [1262] [1263]}

- Advise people to not let pets interact with people or animals outside the household, and if a member of the household becomes unwell to isolate them from everyone else, including pets.[1264]
- [CDC: coronavirus disease 2019 (COVID-19) – pets and other animals] (<https://www.cdc.gov/coronavirus/2019-ncov/animals/pets-other-animals.html>)

Return to physical activity

- Recommend a phased return to exercise only when the patient has been symptom-free for at least 7 days. Advise patients to begin with at least 2 weeks of minimal exertion, and to use daily self-monitoring to track progress and decide whether to move up or drop back a phase. Patients who have a history of severe disease, cardiac involvement, ongoing symptoms, or adverse psychological symptoms require further clinical assessment before returning to physical activity.[1265]
- Guidance on return to sports after COVID-19 in children is available from the American Academy of Pediatrics:
 - [AAP: COVID-19 interim guidance – return to sports and physical activity] (<https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/covid-19-interim-guidance-return-to-sports>)
- Clinical or subclinical myocarditis has been reported in competitive athletes with recent infection that restricts them from training and competitive play.[1266]

Resources

- [WHO: coronavirus disease (COVID-19) pandemic] (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019>)
- [CDC: COVID-19] (<https://www.cdc.gov/coronavirus/2019-nCoV/index.html>)
- [NHS England: coronavirus (COVID-19)] (<https://www.nhs.uk/conditions/coronavirus-covid-19>)
- [NHS England: COVID-19 patient rehabilitation booklet] (<http://flipbooks.leedsth.nhs.uk/LN004864.pdf>)
- [NHS England: your COVID recovery] (<https://www.yourcovidrecovery.nhs.uk>)

Monitoring

Monitoring

Regularly monitor the following in hospitalized patients to facilitate early recognition of deterioration and monitor for complications:[\[2\]](#) [\[574\]](#)

- Vital signs (temperature, respiratory rate, heart rate, blood pressure, oxygen saturation)
- Hematologic and biochemistry parameters
- Coagulation parameters (D-dimer, fibrinogen, platelet count, prothrombin time)
- ECG
- Chest imaging
- Signs and symptoms of venous or arterial thromboembolism.

Medical early warning scores

- Utilize medical early warning scores that facilitate early recognition and escalation of treatment of deteriorating patients (e.g., National Early Warning Score 2 [NEWS2], Pediatric Early Warning Signs [PEWS]) where possible.[\[2\]](#)
- There are no data on the value of using these scores in patients with COVID-19 in the primary care setting.[\[1239\]](#)
- The sequential organ failure assessment (SOFA) score does not possess adequate discriminant accuracy for mortality prediction in patients prior to intubation for COVID-19 pneumonia.[\[1240\]](#)

Pregnant women

- Monitor vital signs three to four times daily and fetal heart rate in pregnant women with confirmed infection who are symptomatic and admitted to hospital. Perform fetal growth ultrasounds and Doppler assessments to monitor for potential intrauterine growth restriction in pregnant women with confirmed infection who are asymptomatic.[\[854\]](#) Perform fetal growth ultrasound 14 days after resolution of symptoms.[\[856\]](#)

Post-discharge follow-up

- Patients who have had suspected or confirmed COVID-19 (of any disease severity) who have persistent, new, or changing symptoms should have access to follow-up care.[\[2\]](#)
- Guidelines for the respiratory follow-up of patients with COVID-19 pneumonia have been published. Follow-up algorithms depend on the severity of pneumonia, and may include clinical consultation and review (face-to-face or telephone) by a doctor or nurse, chest imaging, pulmonary function tests, echocardiogram, sputum sampling, walk test, and assessment of oxygen saturation.[\[1241\]](#)
- More than half of patients discharged from hospital had lung function and chest imaging abnormalities 12 weeks after symptom onset.[\[1242\]](#) Pulmonary function tests may reveal altered diffusion capacity, a restrictive pattern, or an obstructive pattern.[\[1243\]](#)

Prognostic scores in development

- Various prognostic and clinical risk scores are being researched or developed for COVID-19; however, further external validation across various populations is needed before their use can be recommended. The World Health Organization recommends using clinical judgment, including consideration of the patient's values and preferences and local and national policy if available, to guide management decisions including admission to hospital and to the intensive care unit, rather than currently available prediction models for prognosis.[\[2\]](#)
- A-DROP: a modified version of CURB-65 that showed better accuracy of in-hospital death prediction on admission in patients with COVID-19 pneumonia compared with other widely used community-acquired pneumonia scores.[\[1244\]](#)

- APACHE II: an effective clinical tool to predict hospital mortality that performed better than SOFA and CURB-65 scores in patients with COVID-19. A score of 17 or more is an early indicator of death and may help provide guidance to make further clinical decisions.[1245]
- CALL: a risk factor scoring system that scores patients based on four factors: comorbidities, age, lymphocyte count, and lactate dehydrogenase level. One study found that 96% of patients with low CALL scores did not progress to severe disease.[1246]
- COVID-GRAM: a web-based calculator that estimates the probability that a patient will develop critical illness and relies on the following 10 variables at admission: chest radiographic abnormality, age, hemoptysis, dyspnea, unconsciousness, number of comorbidities, cancer history, neutrophil-to-lymphocyte ratio, lactate dehydrogenase, and direct bilirubin. Additional validation studies, especially outside of China, are required.[1247] A retrospective cohort study was unable to fully validate the tool for predicting critical illness among hospitalized patients in Europe as it overestimated the risk in the highest-risk patients.[1248]
- COVID-19MRS: a rapid, operator-independent clinical tool that was found to objectively predict mortality in one retrospective cohort study.[1249]
- COVID-19 SEIMC: a mortality prediction score for predicting 30-day mortality of patients attending hospital emergency departments, based on age, low age-adjusted SaO₂, neutrophil-to-lymphocyte ratio, estimated glomerular filtration rate, dyspnea, and sex. It has been externally validated with two large datasets from patients hospitalized with laboratory-confirmed disease and shows a high degree of accuracy.[1250]
- QCOVID: a novel clinical risk prediction algorithm to estimate the risk of hospital admission and mortality based on age, ethnicity, deprivation, body mass index, and a range of comorbidities. Population-based cohort studies found that the algorithm performed well, showing very high levels of discrimination for deaths and hospital admissions.[1251] [1252] The risk model is being used in the UK to help clinicians identify adults with multiple risk factors that make them more vulnerable to COVID-19, and inform decisions about vaccination cohorts and shielding.[1253]
- SCARP: a novel risk calculator that provides clinically meaningful predictions of whether hospitalized patients will progress to severe illness or death based on variables that are readily available (e.g., pulse oximetry, oxygen supplementation, respiratory rate, pulse). The calculator has undergone internal and temporal validation, but further studies are required.[1254]
- SOARS: a five-predictor risk prediction score based on demographic and clinical characteristics (i.e., SpO₂, obesity, age, respiratory rate, stroke history). May be useful to identify patients who have a low probability of mortality for outpatient monitoring and management, and could potentially be used to inform clinical triage in preadmission settings. Further validation is required.[1255]
- 3F: a mortality prediction model based on three clinical features: age, minimum oxygen saturation, and type of patient encounter (i.e., inpatient vs outpatient and telehealth encounters). One study found that the model showed high accuracy when applied to retrospective and prospective data sets of COVID-19 patients.[1256]
- 4C: a score developed and validated in a UK prospective cohort study of adults admitted to hospital with COVID-19. The score uses patient demographics, clinical observations, and blood parameters commonly available at the time of hospital admission, and can accurately characterize patients as being at low, intermediate, high, or very high risk of death. The score outperformed other risk stratification tools, showed clinical decision-making utility, and had similar performance to more complex models.[1257]
- [The BMJ 10-minute consultation: what is my covid risk?] (<https://www.bmj.com/content/372/bmj.n637>)

Complications

Complications	Timeframe	Likelihood
post-intensive care syndrome	variable	high
<p>Early reports suggest that COVID-19 patients treated in the intensive care unit can present with post-intensive care syndrome, a spectrum of psychiatric, cognitive, and/or physical disability (e.g., muscle weakness, cognitive dysfunction, insomnia, depression, anxiety, post-traumatic stress disorder, delirium, encephalopathy) that affects survivors of critical illness, and persists after the patient has been discharged from the intensive care unit. Weakness affects 33% of patients who receive mechanical ventilation, 50% of patients with sepsis, and <50% of patients who remain in the intensive care unit for more than 1 week. Cognitive dysfunction affects 30% to 80% of patients. The risk can be minimized with medication management, physical rehabilitation, family support, and follow-up clinics.[533]</p>		
venous thromboembolism	variable	high
<p>The pooled incidence of venous thromboembolism, deep vein thrombosis, and pulmonary embolism among hospitalized patients was 14.7, 11.2%, and 7.8%, respectively. The prevalence was significantly higher in patients admitted to the intensive care unit, despite thromboprophylaxis.[1072] While venous thromboembolism appears to be frequent in hospitalized COVID-19 patients, one systematic review and meta-analysis found that the overall risk of venous thromboembolism did not significantly differ between COVID-19 and non-COVID-19 cohorts with similar disease severity, except for patients admitted to the intensive care unit. This suggests that severe disease that requires intensive care unit admission may be a risk factor for developing venous thromboembolism.[1073] Pulmonary embolism is rare in patients presenting to the emergency department, but the incidence is approximately 9-fold higher than in the general non-COVID-19 population.[1074] COVID-19 patients with thromboembolic events have 1.93 times the odds of dying compared with patients without venous thromboembolism.[1075]</p> <p>Coagulopathy in COVID-19 has a prothrombotic character, which may explain reports of thromboembolic complications.[1076] Patients may be predisposed to venous thromboembolism due to the direct effects of COVID-19, or the indirect effects of infection (e.g., severe inflammatory response, critical illness, traditional risk factors).[1077] Thrombotic events may be due to cytokine storm, hypoxic injury, endothelial dysfunction, hypercoagulability, and/or increased platelet activity.[1078]</p> <p>The risk factors with the most evidence for being predictive of venous thromboembolism are older age and elevated D-dimer levels.[1079] Patients with very high D-dimer levels have the greatest risk of thrombosis and may benefit from active monitoring.[708] [709]</p> <p>If venous thromboembolism is suspected, perform a computed tomographic angiography or ultrasound of the venous system of the lower extremities.[1080]</p> <p>Treat patients with a thromboembolic event (or who are highly suspected to have thromboembolic disease if imaging is not possible) with therapeutic doses of anticoagulant therapy as per the standard of care for patients without COVID-19. There are currently insufficient data to recommend either for or against using therapeutic doses of antithrombotic or thrombolytic agents for COVID-19. Patients who require extracorporeal membrane oxygenation or continuous renal replacement therapy, or who have thrombosis of catheters or extracorporeal filters, should be treated with antithrombotic therapy as per the standard institutional protocols for those without COVID-19.[533]</p> <p>Initial parenteral anticoagulation with a low molecular weight heparin or unfractionated heparin is preferred in acutely ill hospitalized patients; however, direct oral anticoagulants may be used provided there is no potential for drug-drug interactions (lead-in therapy with a parenteral anticoagulant is required for dabigatran and edoxaban). Warfarin can be used after overlap with initial parenteral anticoagulation. Parenteral anticoagulation with a low molecular weight heparin or fondaparinux is preferred over unfractionated heparin in critically ill patients. Direct oral anticoagulants are the preferred option in outpatients provided there is no potential for drug-drug interactions, with warfarin considered a suitable</p>		

Complications	Timeframe	Likelihood
<p>alternative. Anticoagulation therapy is recommended for a minimum of 3 months. Thrombolytic therapy is recommended in select patients with pulmonary embolism.[800]</p> <p>The American Society of Hematology has published draft guideline recommendations on the use of anticoagulation in patients with COVID-19.[1081]</p> <p>A high incidence (14.7%) of asymptomatic deep vein thrombosis was reported in a cohort of patients with COVID-19 pneumonia.[1082] An autopsy study of 12 patients revealed deep vein thrombosis in 58% of patients in whom venous thromboembolism was not suspected before death.[1083] These studies highlight the importance of having a high suspicion for venous thromboembolism in patients who have signs of coagulopathy, including elevated D-dimer level.</p> <p>While these patients are at higher risk of thrombotic events, they may also be at an elevated risk for bleeding. In a small retrospective study, 11% of patients at high risk of venous thromboembolism also had a high risk of bleeding.[1084]</p> <p>Antiphospholipid antibodies (mainly lupus anticoagulant) were detected in nearly half of patients in one meta-analysis and systematic review, with an increased prevalence in patients with severe and critical disease. However, there does not currently appear to be any association between this finding and disease outcomes (e.g., thrombosis, invasive ventilation, mortality). Further research on whether antiphospholipid antibodies play a role in the pathogenesis of disease is required.[1085]</p> <p>It has been suggested that a new term (e.g., COVID-19-associated pulmonary thrombosis, diffuse pulmonary intravascular coagulopathy, or microvascular COVID-19 lung vessels obstructive thrombo-inflammatory syndrome [MicroCLOTS]) be used rather than the term pulmonary embolism as it has been hypothesized that the pathophysiology is different; local thrombi are formed in the lung vessels due to a local inflammatory process rather than the classical emboli coming from elsewhere in the body.[1086] [1087] [1088] However, this has not become accepted practice.</p> <p>Cases of arterial thrombosis, cerebral venous thrombosis, splanchnic vein thrombosis, and acute limb ischemia secondary to thrombosis have been reported.[1089] [1090] [1091] [1092] [1093] [1094] The prevalence of arterial thromboembolism appears to be substantial at 3.9%; however, evidence is limited.[1072]</p>		
cardiovascular complications	variable	high
<p>COVID-19 is associated with a high inflammatory burden that can result in cardiovascular complications with a variety of clinical presentations. Inflammation in the myocardium can result in myocarditis, heart failure, arrhythmias, acute coronary syndrome, rapid deterioration, and sudden death.[1095] [1096] These complications can occur on presentation or develop as the severity of illness worsens.[1097] It is uncertain to what extent acute systolic heart failure is mediated by myocarditis, cytokine storm, small vessel thrombotic complications, microvascular dysfunction, or a variant of stress-induced cardiomyopathy.[1098]</p> <p>Cardiovascular complications have been reported in 14.1% of patients during hospitalization, with an overall case fatality rate of 9.6%. Patients with preexisting cardiovascular comorbidities or risk factors are at higher risk for cardiovascular complications and mortality. Complications include arrhythmias or palpitations (18.4%), myocardial injury (10.3%), angina (10.2%), acute myocardial infarction (3.5%), and acute heart failure (2%).[1099] Cases of fulminant myocarditis, cardiac tamponade, cor pulmonale, takotsubo syndrome, and pericarditis have also been reported.[1100] [1101] [1102] [1103] [1104] A Cochrane review found that the most common cardiovascular complications were cardiac arrhythmias, heart failure, and arterial and venous occlusive events.[209] The most common arrhythmias reported during hospitalization were supraventricular and ventricular arrhythmias. QT interval changes and ST-segment deviation have been reported.[1105] QT interval prolongation has been reported independent of whether the patient is taking drugs that prolong the QT interval.[1106]</p> <p>Laboratory biomarkers may help identify those at greater risk of developing cardiovascular complications and of death.[209] Elevated cardiac biomarkers and emerging arrhythmia are associated with the development of severe disease and the need for intensive care admission.[1107]</p>		

Complications	Timeframe	Likelihood
<p>Prevalence of cardiac disease is high among patients who are severely or critically ill, and these patients usually require intensive care and have a poor prognosis and higher rate of in-hospital mortality. These patients are more likely to require noninvasive or invasive ventilation, and have a higher risk of thromboembolic events and septic shock compared with patients without a history of cardiac disease.[1097] [1108] [1109] [1110] [1111]</p> <p>Perform an ECG and order high-sensitivity troponin I (hs-cTnI) or T (hs-cTnT) and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels in patients with symptoms or signs that suggest acute myocardial injury in order to make a diagnosis. The following test results may help inform the diagnosis: evolving ECG changes suggesting myocardial ischemia; NT-proBNP level >400 nanograms/L; high levels of hs-cTnI or hs-cTnT, particularly levels increasing over time. Elevated troponin levels may reflect cardiac inflammatory response to severe disease rather than acute coronary syndrome. Seek specialist cardiology advice on further tests and imaging.[564]</p> <p>Monitor blood pressure, heart rate, and fluid balance, and perform continuous ECG monitoring in all patients with suspected or confirmed acute myocardial injury. Monitor in a setting where cardiac or respiratory deterioration can be rapidly identified.[564]</p> <p>Seek specialist cardiology advice on treatment and follow local treatment protocols. There are limited data to recommend any specific drug treatments for these patients. Management should involve a multidisciplinary team including intensive care specialists, cardiologists, and infectious disease specialists.[1098] It is important to consider that some drugs may prolong the QT interval and lead to arrhythmias. Guidelines for the management of COVID-19-related myocarditis are available.[1112]</p> <p>Infection may have longer-term implications for overall cardiovascular health; however, further research is required.[1113] A study of 100 patients who had recently recovered from COVID-19 found that cardiovascular magnetic resonance imaging revealed ongoing myocardial inflammation in 60% of patients, independent of preexisting conditions, severity and overall course of the acute illness, and time from the original diagnosis.[1114]</p>		
acute kidney injury	variable	high
<p>The pooled incidence of acute kidney injury is 10.6%, which is higher than the incidence in hospitalized patients without COVID-19.[1115] Incidence varies widely across studies, with estimates of approximately 20% reported in some meta-analyses.[1116] [1117] Patients with acute kidney injury have a significantly increased risk of in-hospital mortality (odds ratio of 11.05). The mortality rate and incidence in patients in China was significantly lower than those in patients outside of China. Risk factors include older age ≥60 years, male sex, and severe infection.[1115] Presence of diabetes, hypertension, chronic kidney disease, and tumor history was associated with increased incidence of acute kidney injury at population level across different settings. Patients with a history of kidney transplant had a higher incidence of acute kidney injury; however, their risk of death was lower.[1116] Use of renin-angiotensin-aldosterone system blockade drugs is also significantly associated with an increased risk of acute kidney injury in hospitalized patients.[1118]</p> <p>In a small UK cohort, 29% of hospitalized children met the diagnostic criteria for acute kidney injury, with most cases occurring in children admitted to the intensive care unit and in those with pediatric inflammatory multisystem syndrome.[1119]</p> <p>Can develop at any time before, during, or after hospital admission. Causes include hemodynamic changes, hypovolemia, viral infection leading directly to kidney tubular injury, thrombotic vascular processes, glomerular pathology, or rhabdomyolysis. May be associated with hematuria, proteinuria, and abnormal serum electrolyte levels (e.g., potassium, sodium).[564] Direct kidney infection has been confirmed in an autopsy study of a single patient.[1120]</p> <p>Follow local guidelines for assessing and managing acute kidney injury. Continuous renal replacement therapy (CRRT) is recommended in critically ill patients with acute kidney injury who develop indications for renal replacement therapy; prolonged intermittent renal replacement therapy is recommended over hemodialysis if CRRT is not available or possible.[533]</p>		

Complications	Timeframe	Likelihood
Monitor patients with chronic kidney disease for at least 2 years after acute kidney injury. ^[564]		
Cases of nephritis and collapsing glomerulopathy have been reported. ^{[1121] [1122]}		
acute liver injury	variable	medium
<p>Liver injury may be associated with preexisting liver disease, viral infection, drug toxicity, systemic inflammation, hypoxia, or hemodynamic issues; however, the underlying mechanism is unclear. The overall prevalence has been reported as 25%, although there is no uniform definition of liver injury in these patients and prevalence depends on the definition used in studies. The overall prevalence may be as low as 9% when strict criteria for diagnosis are used. The prevalence of elevated alanine aminotransferase and aspartate aminotransferase was 19% and 22%, respectively. The prevalence of hypertransaminasemia was higher in patients with severe disease compared with patients with nonsevere disease.^[1123] Another meta-analysis concluded that findings from the available evidence to date from observational studies and case reports indicate that transaminases and total bilirubin levels appear not to significantly change in patients with COVID-19.^[1124]</p> <p>Risk factors associated with severe liver injury include older age, preexisting liver disease, and severe COVID-19.^[1125]</p> <p>Medications used in the treatment of COVID-19 (e.g., lopinavir/ritonavir) may have a detrimental effect on liver injury.^[1125]</p> <p>Guidelines on the management of liver derangement in patients with COVID-19 have been published.^[1126]</p>		
neurologic complications	variable	medium
<p>Patients commonly have central or peripheral neurologic complications, possibly due to viral invasion of the central nervous system, inflammatory response, or immune dysregulation.^[1127]</p> <p>Neurologic manifestations have been reported in 22% to 35% of patients across studies. Central nervous system manifestations were more common than peripheral nervous system manifestations.^[1128] A retrospective electronic health records study of nearly 240,000 patients found that approximately one third of patients received a neurologic or psychiatric diagnosis in the 6 months after diagnosis, and 13% received such a diagnosis for the first time. The risk was greater in patients with severe disease.^[1129]</p> <p>Neurologic complications include, but are not limited to, acute cerebrovascular disease, impairment of consciousness, ataxia, seizures, corticospinal tract signs, meningoencephalitis, encephalopathy, encephalomyelitis, peripheral demyelinating lesions, peripheral neuropathies, cerebral venous sinus thrombosis, myopathy, acute transverse myelitis, myasthenia gravis, Guillain-Barre syndrome and other neuropathies, status epilepticus, dementia, catatonia, parkinsonian syndromes, mood/anxiety/psychotic/substance use disorders, and abnormal findings on brain magnetic resonance imaging.^{[1128] [1130] [1131] [1132]}</p> <p>Patients may present with these manifestations, or they may develop them during the course of the disease. Neurologic complications tend to develop 1 to 2 weeks after the onset of respiratory disease.^[1133]</p> <p>Acute cerebrovascular disease (including ischemic stroke, hemorrhagic stroke, cerebral venous thrombosis, and transient ischemic attack) has been reported in 0.5% to 5.9% of patients. The most common type was ischemic stroke (0.4% to 4.9%).^[1127] Patients with severe disease are at an increased risk of ischemic stroke compared with patients with nonsevere disease.^[1134] Stroke is relatively frequent among hospitalized COVID-19 patients relative to other viral respiratory infections, and has a high risk of in-hospital mortality. Risk factors include older age and male sex. Median time from onset of COVID-19 symptoms to stroke was 8 days.^{[1135] [1136]} Stroke presents later in severe disease, and earlier in mild to moderate disease.^[1137] Patients may present with ischemic stroke during the convalescent phase of infection, including younger people <50 years of age with asymptomatic or pauci-symptomatic</p>		

Complications	Timeframe	Likelihood
<p>COVID-19.[1138] Ischemic stroke appears to be more severe and result in worse outcomes (severe disability) in patients with COVID-19, with the median NIH Stroke Scale score being higher among those with COVID-19 compared with those without.[1139] Guidelines for the management of acute ischemic stroke in patients with COVID-19 infection have been published.[1140]</p> <p>Guillain-Barre syndrome has been reported. Both post-infectious and pre-infectious patterns have been reported.[1127] The pooled prevalence among hospitalized and nonhospitalized patients was 0.15%.[1141] The mean age of patients was 55 years with a male predominance. Most patients had respiratory and/or severe symptoms of COVID-19, although it has also been reported in asymptomatic patients. A higher prevalence of the classic sensorimotor form and acute inflammatory demyelinating polyneuropathy have been reported, although rare variants have also been noted.[1142] Patients had an increased odds for demyelinating subtypes. Clinical outcomes were comparable to those for contemporary or historical controls not infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1141]</p> <p>Encephalitis has been reported in <1% of patients, but increases up to 6.7% in critically ill patients. Encephalitis is associated with poorer outcomes including admission to the intensive care unit, need for mechanical ventilation, and increased mortality rate (13.4%) compared with the general population of COVID-19 patients.[1143]</p> <p>Patients with preexisting neurologic disorders may develop an exacerbation of their neurologic symptoms and severe COVID-19.[1144]</p> <p>Patients may show cerebral changes on magnetic resonance imaging months after recovery, suggesting that long-term consequences may be possible.[1145]</p> <p>Neurologic involvement is common in children and adolescents. In a case series of 1695 patients <21 years of age, 22% of patients had documented neurologic involvement. Those with neurologic involvement were more likely to have an underlying neurologic disorder compared with those without, but a similar number were previously healthy. In the majority of cases, symptoms were transient. However, approximately 12% had life-threatening conditions including severe encephalopathy, central nervous system infection/demyelination, Guillain-Barre syndrome/variants, and acute fulminant cerebral edema.[1146]</p>		
post-COVID-19 syndrome (long COVID)	variable	medium
<p>Also known as post-acute COVID-19, post-acute COVID-19 syndrome, chronic COVID, long-haul COVID, post-acute sequelae of SARS-CoV-2 infection (PASC), and post-COVID conditions.</p> <p>Definition: signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks, and are not explained by an alternative diagnosis. Ongoing symptomatic COVID-19 is defined as signs and symptoms from 4 weeks up to 12 weeks. The syndrome is not thought to be linked to disease severity or specific signs and symptoms during the acute phase of illness.[991] There is no standardized case definition and case definitions vary. For example, the Centers for Disease Control and Prevention defines post-COVID conditions as an umbrella term for the wide range of health consequences that are present more than 4 weeks after infection with SARS-CoV-2.[1147] Protracted symptoms are common in many viral and bacterial infections. The neurologic symptoms are similar to symptoms of other neurologic conditions such as chronic fatigue syndrome and functional neurologic disorder.[1148]</p> <p>Epidemiology: frequency ranges from 4.7% to 80% across observational studies, and occurs between 3 to 24 weeks after the acute phase or hospital discharge. Potential risk factors include older age, age 40 to 49 years, female sex, obesity, severe clinical status, higher number of comorbidities, higher symptom load, hospital admission, and oxygen supplementation in the acute phase, although data is lacking.[1149] [1150] [1151] A study in the UK found that 38% of patients reported at least one persistent symptom, and 15% reported three or more persistent symptoms, lasting 12 weeks or more (a weighted population prevalence of persistent symptoms of 5.8% for one and 2.2% for three or more symptoms).[1152] Approximately 63%</p>		

Complications	Timeframe	Likelihood
<p>of patients report at least one symptom at 30 days after symptom onset/hospitalization, with 71% reporting at least one symptom after 60 days, and 46% at 90 days or more in a systematic review and meta-analysis. The most commonly reported persistent symptoms were dyspnea and fatigue.[1153] Persistent symptoms have been reported up to 12 months after discharge.[1154] Prolonged illness can occur among young adults with no underlying comorbidities, and in patients who had mild disease. Approximately 12% to 15% of patients who had mild symptoms still had symptoms up to 8 months later.[1155] [1156] The number of symptoms at follow-up was associated with the symptom load during the acute phase of infection and the number of comorbidities in nonhospitalized patients.[1157] Persistent symptoms have been reported in pregnant women and children, but appear to be less common in children compared with adults.[533] [1158] [1159]</p> <p>Diagnosis: use a holistic, person-centered approach that includes a comprehensive clinical history (including history of suspected or confirmed acute COVID-19, nature and severity of previous and current symptoms, timing and duration of symptoms since the start of acute illness, and a history of other health conditions), and appropriate examination that involves assessing physical, cognitive, psychological, and psychiatric symptoms, as well as functional abilities. Refer patients with signs or symptoms that could be caused by an acute or life-threatening complication (e.g., severe hypoxemia, signs of severe lung disease, cardiac chest pain, multisystem inflammatory syndrome in children) urgently to the relevant acute services.[991]</p> <p>Signs and symptoms: symptoms vary widely, may relapse and remit or fluctuate, can change unpredictably, and can occur in those with mild disease only. Common long-term symptoms include persistent cough, low-grade fever, breathlessness, fatigue, pain, chest pain/tightness, palpitations, myalgia, arthralgia, headaches, vision changes, hearing loss, earache, tinnitus, sore throat, loss of taste/smell, impaired mobility, numbness in extremities, dizziness, tremors, memory loss, mood changes, skin rashes, gastrointestinal symptoms, neurocognitive difficulties, sleep disturbances, delirium (older people), and mental health conditions (e.g., anxiety, depression).[533] [991] [1160] Gastrointestinal sequelae including loss of appetite, nausea, acid reflux, and diarrhea are common in patients 3 months after discharge.[1161] Some of the symptoms may overlap with post-intensive care syndrome (see above).[533] The inability to return to normal activities, emotional and mental health outcomes, and financial loss are common.[1162]</p> <p>Investigations: tailor investigations to the clinical presentation, and to rule out any acute or life-threatening complications and alternative diagnoses. Investigations may include blood tests (e.g., complete blood count, kidney and liver function tests, C-reactive protein, ferritin, thyroid function), oxygen saturation, blood pressure and heart rate measurements, exercise tolerance test, chest imaging, electrocardiogram, and psychiatric assessment.[533] [991] [1160] Approximately 50% of patients had residual abnormalities on chest CT and pulmonary function tests at 3 months.[1163] Around 9% of patients had deteriorating chest x-ray appearances at follow-up, which may indicate lung fibrosis. Persistently elevated D-dimer and C-reactive protein have also been reported.[1164]</p> <p>Management: give advice and information on self-management including ways to self-manage symptoms (e.g., set realistic goals, antipyretic for fever, breathing techniques for chronic cough, home pulse oximetry for monitoring breathlessness, pulmonary rehabilitation, staged return to exercise); who to contact if there is concern about symptoms or if there is need for support; sources of support (e.g., support groups, online forums); and how to get support from other services (e.g., social care, housing, financial support). A personalized, multidisciplinary rehabilitation plan that covers physical, psychological, and psychiatric aspects of rehabilitation is an important part of management. Many patients recover spontaneously with holistic support, rest, symptomatic treatment, and a gradual increase in activity. Referral to a specialist may be required in patients where there is clinical concern along with respiratory, cardiac, or neurologic symptoms that are new, persistent, or progressive.[991] [1160]</p> <p>Follow-up: agree with the patient how often follow-up and monitoring are needed (either in person or remotely), and which healthcare professionals should be involved. Take into account the patient's level of need and the services involved. Tailor monitoring to the patient's symptoms, and consider supported self-monitoring at home (e.g., heart rate, blood pressure, pulse oximetry). Be alert to symptoms that could require referral or investigation.[991]</p>		

Complications	Timeframe	Likelihood
<p>[NICE COVID-19 rapid guideline: managing the long-term effects of COVID-19] (https://www.nice.org.uk/guidance/ng188)</p> <p>[BMJ webinar: long COVID – how to define it and how to manage it] (https://www.bmj.com/content/370/bmj.m3489)</p> <p>[BMJ: management of post-acute covid-19 in primary care] (https://www.bmj.com/content/370/bmj.m3026)</p>		
cardiac arrest	variable	medium
<p>In-hospital cardiac arrest is common in critically ill patients with COVID-19, and is associated with poor survival, particularly among older patients. Among 5019 critically ill patients with COVID-19, 14% had an in-hospital cardiac arrest. Risk factors included older age, male sex, presence of comorbidities, and admission to a hospital with a smaller number of intensive care unit beds. Approximately 57% of patients received cardiopulmonary resuscitation. The most common rhythms at the time of resuscitation were pulseless electrical activity (49.8%) and asystole (23.8%). Of those who received resuscitation, 12% survived to hospital discharge with most of these patients being younger than 45 years of age.[1165]</p>		
sepsis/septic shock	variable	low
<p>Sepsis (diagnosed according to Sepsis-3 or according to the presence of infection-related organ dysfunction necessitating organ support/replacement) has been reported in 78% of intensive care unit patients and 33% of hospitalized patients.[1166]</p> <p>Guidelines for the management of shock in critically ill patients with COVID-19 recommend a conservative fluid strategy (crystalloids preferred over colloids, buffered/balanced crystalloids preferred over unbalanced crystalloids) and a vasoactive agent. Norepinephrine (noradrenaline) is the preferred first-line agent. Vasopressin or epinephrine (adrenaline) can be added to norepinephrine if target mean arterial pressure cannot be achieved with norepinephrine alone.[533] [792] Low-dose corticosteroid therapy is recommended for refractory shock.[533]</p>		
disseminated intravascular coagulation	variable	low
<p>Disseminated intravascular coagulation (DIC) is a manifestation of coagulation failure, and an intermediate link in the development of multi-organ failure. Patients may be at high risk of bleeding/hemorrhage or venous thromboembolism.[1167] The pooled incidence of DIC is 3%, and it is associated with poor prognosis. The incidence was higher in patients with severe disease and those admitted to the intensive care unit, and in nonsurvivors compared with survivors.[1168]</p> <p>Coagulopathy manifests as elevated fibrinogen, elevated D-dimer, and minimal change in prothrombin time, partial thromboplastin time, and platelet count in the early stages of infection. Increasing interleukin-6 levels correlate with increasing fibrinogen levels. Coagulopathy appears to be related to severity of illness and the resultant thromboinflammation. Monitor D-dimer level closely.[1169]</p> <p>Anticoagulant therapy with a low molecular weight heparin or unfractionated heparin has been associated with a better prognosis in patients with severe COVID-19 who have a sepsis-induced coagulopathy (SIC) score of ≥ 4 or a markedly elevated D-dimer level.[1170] In patients with heparin-induced thrombocytopenia (or a history of it), argatroban or bivalirudin are recommended.[1167]</p> <p>Standard guidance for the management of bleeding manifestations associated with DIC or septic coagulopathy should be followed if bleeding occurs; however, bleeding manifestations without other associated factors is rare.[574] [1169]</p>		
acute respiratory failure	variable	low
<p>Reported in 8% of patients in case series.[51]</p>		

Complications	Timeframe	Likelihood
<p>Leading cause of mortality in patients with COVID-19.[995]</p> <p>Children can quickly progress to respiratory failure.[11]</p> <p>Patients with COVID-19 may have a higher risk of developing ventilator-associated pneumonia compared with patients without COVID-19.[1171]</p>		
cytokine release syndrome	variable	low
<p>Cytokine release syndrome may cause ARDS or multiple-organ dysfunction, which may lead to death.[1172] Elevated serum proinflammatory cytokines (e.g., tumor necrosis factor alpha, interleukin-2, interleukin-6, interleukin-8, interleukin-10, granulocyte-colony stimulating factor, monocyte chemoattractant protein 1) and inflammatory markers (e.g., C-reactive protein, serum ferritin) have been commonly reported in patients with severe COVID-19. This likely represents a type of virus-induced secondary hemophagocytic lymphohistiocytosis, which may be fatal.[50] [714] [1173] [1174] Interleukin-6, in particular, has been associated with severe COVID-19 and increased mortality.[1175]</p> <p>One study found that patients who require admission to the intensive care unit have significantly higher levels of interleukin-6, interleukin-10, and tumor necrosis factor alpha, and fewer CD4+ and CD8+ T cells.[1176]</p> <p>However, the pooled mean serum interleukin-6 level was markedly less in patients with severe or critical COVID-19 compared with patients with other disorders associated with elevated cytokines such as cytokine release syndrome, sepsis, and non-COVID-19-related ARDS. These findings question the role of cytokine storm in COVID-19-induced organ dysfunction, and further research is required.[1177]</p> <p>Cytokine release syndrome has been reported in children, although cases appear to be rare.[1178] See the section below on pediatric inflammatory multisystem syndrome.</p>		
pediatric inflammatory multisystem syndrome	variable	low
<p>A rare, but severe condition, reported in children and adolescents approximately 2 to 4 weeks after the onset of COVID-19, likely due to a postinfectious inflammatory process. The syndrome has a strong temporal association with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[1179] [1180] [1181] The syndrome appears to be the result of a delayed immune response to SARS-CoV-2 infection with disease peaks following pandemic peaks by 2 to 5 weeks.[1182] Also known as PIMS, multisystem inflammatory syndrome in children (MIS-C), pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS), as well as other variations.</p> <p>The syndrome shares common features with Kawasaki disease and toxic shock syndrome, but case definitions vary.[538] [1181] [1183] [1184] Most patients have fever, as well as features of shock, cardiac involvement (e.g., elevated cardiac markers, congestive heart failure, cardiac dysfunction, myocarditis, coronary artery dilatation or aneurysm, hypotension, pericardial effusion, mitral regurgitation), gastrointestinal symptoms (e.g., abdominal pain, vomiting, diarrhea), and significantly elevated inflammatory markers.[1179] [1180] Additional clinical and laboratory characteristics including thrombocytopenia, fatigue, headache, myalgia, sore throat, and lymphadenopathy have been suggested to refine the case definition.[19] Mucocutaneous findings may be present, many of which overlap with Kawasaki disease.[1185]</p> <p>Three types of clinical manifestations have been recognized: persistent fever and gastrointestinal symptoms (the most common type); shock with heart dysfunction; and symptoms coincident with the diagnostic criteria for Kawasaki disease.[1186]</p> <p>A systematic review of 27 studies (913 cases) globally found that the median age of patients was 9.3 years of age, and 57% of patients were male. At least one comorbidity was reported in 31% of cases, most commonly obesity, asthma, and chronic lung disease. The most common manifestations were fever (99%), gastrointestinal symptoms (87%), and cardiovascular symptoms such as myocardial dysfunction (55%), coronary artery aneurysms (22%), and shock (66%). The pooled prevalence of respiratory symptoms was</p>		

Complications	Timeframe	Likelihood
<p>41%, and neurologic symptoms was 36%. Other symptoms included conjunctivitis (57%), rash (59%), and oral mucosal changes (42%). Inflammatory and cardiac markers were elevated in the majority of patients, and 38% had abnormal findings on chest x-ray. Approximately 79% of patients required intensive care admission, 63% required inotropic support, 57% required anticoagulation, and 33% required mechanical ventilation. The mortality rate was 1.9%.^[1187]</p> <p>In the UK, 78 cases were reported across 21 pediatric intensive care units in a multicenter observational study. The median age was 11 years and 67% were male. Children from minority ethnic backgrounds accounted for 78% of cases. Fever, shock, abdominal pain, vomiting, and diarrhea were the common presenting features. Around 36% had evidence of coronary artery abnormalities. In terms of treatment, 46% required invasive ventilation and 83% required vasopressor support.^[1188]</p> <p>In the US, 4196 cases have been reported, with 37 deaths (as of 28 June 2021).^[1189] In a US case series of 1116 patients diagnosed with MIS-C, those with MIS-C were more likely to have the following characteristics compared with patients with severe COVID-19: age 6 to 12 years; non-Hispanic Black ethnicity; cardiorespiratory involvement; cardiovascular without respiratory involvement; mucocutaneous without cardiorespiratory involvement; higher neutrophil-to-lymphocyte ratio; higher C-reactive protein level; and lower platelet count. These patterns may help differentiate between MIS-C and COVID-19.^[1190] Factors associated with more severe outcomes (e.g., intensive care unit admission, decreased cardiac function, shock, myocarditis) include: age >5 years; non-Hispanic Black ethnicity; symptoms of dyspnea or abdominal pain; elevated C-reactive protein, troponin, ferritin, D-dimer, brain natriuretic peptide, or interleukin-6; and reduced lymphocyte or platelet counts.^[1191]</p> <p>The most common cardiovascular complications include shock, cardiac arrhythmias, pericardial effusion, and coronary artery dilatation.^[1192] The pooled prevalence of cardiac abnormalities due to MIS-C is as follows: significant left ventricular dysfunction 38%; coronary aneurysm or dilatation 20%; ECG abnormalities or cardiac arrhythmias 28%; raised serum troponin level 33%; and raised proBNP/BNP level 44%.^[1193]</p> <p>Management is mainly supportive and involves a multidisciplinary team (pediatric infectious disease, cardiology, rheumatology, critical care). Patients are commonly managed with intravenous immune globulin, vasopressor support, corticosteroids, immune modulators, anticoagulation, antiplatelet therapy, and respiratory support.^{[1179] [1180]} A national consensus management pathway from the UK is available.^[1194] The optimal choice and combination of immunomodulating therapies have not been definitively established, but intravenous immune globulin and/or corticosteroids are generally considered first-line treatment, with interleukin-1 antagonists reserved for refractory cases.^[533] Initial treatment with intravenous immune globulin plus a corticosteroid was associated with a lower risk of new or persistent cardiovascular dysfunction compared with intravenous immune globulin alone in one cohort study.^[1195] However, another cohort study found no evidence of substantial differences in two primary outcomes (inotropic support or mechanical ventilation by day 2 or later or death; and reduction in disease severity on an ordinal scale by day 2) among children who received the three most common treatments for this disorder (i.e., intravenous immune globulin alone, intravenous immune globulin plus a corticosteroid, and corticosteroids alone).^[1196] The American College of Rheumatology has published guidelines on the diagnosis and management of MIS-C.^[1197]</p> <p>Follow-up of patients at 6 months found that while cardiac, gastrointestinal, renal, hematologic, and otolaryngology outcomes largely resolved at 6 months, muscular fatigue and emotional lability were common.^[1198]</p> <p>While an association between this syndrome and COVID-19 seems plausible based on current evidence, the association is not definitive and further research is required. It is not clear yet whether this syndrome is Kawasaki disease with SARS-CoV-2 as the triggering agent, or whether this is a different syndrome, although increasing evidence suggests that they are two separate syndromes. The syndrome appears to occur in children who have not manifested the early stages of COVID-19, but appears similar to the later phase of COVID-19 in adults.^[1199] Immunologically, PIMS appears to be a distinct clinical entity from Kawasaki disease as neutrophilia and raised monocyte counts, features of Kawasaki disease, were not observed in one cohort.^[1200]</p>		

Complications	Timeframe	Likelihood
Cases of MIS-C have been reported in neonates and temporally associated with prenatal exposure. [1201] [1202]		
Cases of multisystem inflammatory syndrome have been reported in adults. [1203] [1204]		
thrombosis with thrombocytopenia syndrome (TTS), vaccine-induced	variable	low
<p>Also known as vaccine-induced prothrombotic immune thrombocytopenia (VIPIT), vaccine-induced immune thrombotic thrombocytopenia (VITT), and vaccine-induced thrombosis and thrombocytopenia (VITT).</p> <p>Definition: thromboembolic events with thrombocytopenia after vaccination with adenovirus vector-based COVID-19 vaccines (e.g., AstraZeneca, Janssen).[374] [375] The vaccines may trigger the development of an immune thrombotic thrombocytopenia mediated by platelet-activating antibodies against PF4, which clinically mimics autoimmune heparin-induced thrombocytopenia.[375] [1205] [1206] The blood clots occur in unusual sites and include cerebral venous sinus thrombosis, splanchnic vein thrombosis, and arterial thrombosis, together with thrombocytopenia and sometimes bleeding. Multifocal venous and arterial thromboses have also been reported in serious cases. These events can rapidly progress and may be life-threatening or fatal.[376] [377] [381] A causal relationship is plausible based on current information. Evidence to date does not suggest that these vaccines cause venous thromboembolism without thrombocytopenia.[376] [377] [378] [379] [380] [381] There has been no safety signal for TTS following receipt of mRNA vaccines, although a small number of cases have been reported.</p> <p>Epidemiology: TTS is very rare. A study in Denmark and Norway reported 11 excess venous thromboembolic events per 100,000 vaccinations, including 2.5 excess cerebral venous thrombosis events per 100,000 vaccinations with the AstraZeneca vaccine.[1207] Data suggest that there is a slightly higher incidence reported in younger adult age groups.[377] Most of the cases reported occurred in women under 60 years of age within 2 to 3 weeks of receiving their first dose.[376] [381] Cases have also been reported after this period.[461] Risk factors have not been identified, and there is limited experience with the second dose.</p> <p>Diagnosis: advise vaccine recipients who experience any severe symptoms (e.g., dyspnea, chest pain, leg swelling, persistent abdominal pain, neurologic symptoms such as severe and persistent headaches or blurred vision, tiny blood spots under the skin beyond the site of the injection) from around 4 to 20 days after vaccination to seek urgent medical attention.[378] Report all cases to local health authorities.</p> <p>Investigations: order a complete blood count (with platelets), coagulation screen (including fibrinogen and D-dimer), blood film/peripheral smear, and platelet factor 4 enzyme-linked immunosorbent assay for any patient presenting with acute thrombosis or new-onset thrombocytopenia within 28 to 30 days of receiving a COVID-19 vaccination. Typical laboratory features include thrombocytopenia, raised D-dimer levels above the level expected for venous thromboembolism, and low fibrinogen. Antibodies to platelet factor 4 have also been identified. Order imaging studies to confirm thromboembolism based on symptom presentation.[1208] [1209] [1210] [1211] [1212]</p> <p>Management: promptly treat patients who develop TTS. Consult a hematologist. There is limited information about the optimal treatment of this condition; however, management is similar to heparin-induced thrombocytopenia. First-line treatment is urgent administration of intravenous immune globulin. Some experts also recommend the use of corticosteroids. Anticoagulate with a nonheparin-based therapy such as a direct oral anticoagulant, fondaparinux, danaparoid, or argatroban, depending on the clinical picture. Avoid platelet transfusions, heparin, low molecular weight heparin, and vitamin K antagonists (e.g., warfarin). Consider plasma exchange and fibrinogen replacement in select patients.[1208] [1209] [1210] [1211] [1212] The management of TTS is evolving and there are differences between the guidelines available. Consult the most current local guidelines for more detailed information on the diagnosis and management of this condition.</p>		

Complications	Timeframe	Likelihood
<p>[Public Health England: information for healthcare professionals on blood clotting following COVID-19 vaccination] (https://www.gov.uk/government/publications/covid-19-vaccination-blood-clotting-information-for-healthcare-professionals)</p> <p>[Examples of learned societies with treatment recommendations] (https://www.ema.europa.eu/en/news/ema-raises-awareness-clinical-care-recommendations-manage-suspected-thrombosis-thrombocytopenia)</p>		
pregnancy-related complications	variable	low
<p>Pregnancy outcome is usually good, although there are little data on exposure during early pregnancy.[25]</p> <p>The odds of admission to the intensive care unit, invasive ventilation, and need for extracorporeal membrane oxygenation were higher in pregnant and recently pregnant women compared with nonpregnant reproductive-aged women. Pregnant women may also be at an increased risk of maternal death. Risk factors for serious complications include preexisting comorbidities (e.g., chronic hypertension, diabetes), high maternal age, non-White ethnicity, presence of pregnancy-specific conditions (e.g., gestational diabetes, preeclampsia), and high body mass index.[23] [24]</p> <p>Preterm birth was more common in pregnant women with COVID-19 compared with pregnant women without the disease. However, the overall rates of spontaneous preterm births in pregnant women with COVID-19 was broadly similar to those observed in the prepandemic period, so these preterm births could have been medically indicated.[23] [24]</p> <p>The overall rates of stillbirths and neonatal deaths do not seem to be higher than the background rates.[23] [24] [1213] In England, there is no evidence of an increase in stillbirths regionally or nationally during the pandemic when compared with the same months in the previous year and despite variable community infection rates in different regions.[1214]</p> <p>Limited low-quality evidence suggests that the risk of infection in neonates is extremely low. Most infections are acquired in the postpartum period, although congenitally acquired infection has been reported. Unlike children who generally have asymptomatic infection, two-thirds of neonatal cases are symptomatic and a significant proportion require intensive care, although the overall prognosis appears to be excellent.[23] [24] [1215]</p>		
aspergillosis	variable	low
<p>Invasive pulmonary aspergillosis has been reported in critically ill patients with moderate to severe ARDS.[1216] [1217] [1218] Aspergillosis has been reported in 10.2% of patients admitted to the intensive care unit. The mortality rate was high at 54.9%.[1219]</p> <p>Intubation for more than 7 days may be a risk factor. Other potential risk factors include older age, chronic obstructive pulmonary disease, immunosuppression, critical illness, or use of high-dose corticosteroids. Consider aspergillosis in patients who deteriorate despite optimal supportive care or have other suspicious radiologic or clinical features.[829] [1220]</p> <p>Prescribe appropriate antifungal therapy according to local guidelines.[1221] Voriconazole levels may need monitoring more frequently in COVID-19 patients due to increased toxicity in these patients.[1222] Guidance on the diagnosis and management of COVID-19-associated pulmonary aspergillosis has been published.[1223]</p>		
mucormycosis	variable	low
<p>Mucormycosis (also known as "black fungus") has been reported rarely.[553] [1224] [1225] The number of cases in India increased significantly during its second wave.[1226]</p> <p>The main risk factors are male sex, uncontrolled diabetes, and immunosuppression (e.g., due to corticosteroid therapy).[553] [1227] [1228]</p>		

Complications	Timeframe	Likelihood
<p>Have a low threshold of suspicion for the diagnosis. It is important not to miss warning signs and symptoms (e.g., nasal congestion; blackish/bloody nasal discharge; sinus or facial pain; toothache or loosening of teeth; vision disturbances; hemoptysis; necrotic eschar on skin, palate, or nasal turbinates). Do not hesitate to order appropriate investigations.[1229] The median time to interval between diagnosis of COVID-19 and evidence of mucormycosis was 15 days. Rhino-orbital mucormycosis was most common (42%), followed by rhino-orbito-cerebral mucormycosis (24%), and pulmonary mucormycosis (10%).[1227]</p> <p>Management strategies in the context of COVID-19 include, but are not limited to: controlling hyperglycemia, diabetes, or diabetic ketoacidosis; reducing corticosteroid dose with the aim to rapidly discontinue; discontinuing immunomodulating drugs; extensive surgical debridement to remove all necrotic material; antifungal therapy (e.g., amphotericin-B) for 4 to 6 weeks; and appropriate supportive care and monitoring.[1229]</p> <p>Patients should be under the care of a multidisciplinary team that includes an infectious disease specialist; an intensivist; a neurologist; a dentist; an ophthalmologist; an ear, nose, and throat specialist; and a surgeon.[1229]</p> <p>Prevention involves controlling hyperglycemia; monitoring blood glucose level in COVID-19 patients after discharge (whether or not they are diabetic); and judicious use of corticosteroids, antibiotics, and antifungals.[1229]</p> <p>The overall mortality rate is 31% to 34%; surgery was associated with better clinical outcomes.[1227][1228]</p>		
pancreatic injury	variable	low
<p>Mild pancreatic injury (defined as elevated serum amylase or lipase levels) has been reported in 17% of patients in one case series.[1230] It is unknown whether this is a direct viral effect or due to the harmful immune response that occurs in some patients. Cases of acute pancreatitis have been reported; however, pancreatic necrosis is rare.[1231] Prior history of pancreatitis does not appear to be a risk factor for pancreatic inflammation in patients with COVID-19.[1232]</p>		
autoimmune hemolytic anemia	variable	low
<p>Warm or cold autoimmune hemolytic anemia (first episode) has been reported in 7 patients after the onset of COVID-19 symptoms and within the timeframe compatible with cytokine release syndrome. Four patients had indolent B lymphoid malignancy. It is unknown whether the hemolytic anemia is related to COVID-19 infection.[1233]</p>		
immune thrombocytopenia	variable	low
<p>Immune thrombocytopenia has been reported rarely. The majority of cases were in patients >50 years of age, with only 7% of cases reported in children. The majority of cases were in patients with moderate to severe COVID-19; however, 7% of cases were in asymptomatic COVID-19 patients. Onset occurred in 20% of cases 3 weeks after the onset of COVID-19 symptoms, with most cases reported after clinical recovery. Severe life-threatening bleeding was uncommon. Treatment involved the use of corticosteroids, intravenous immune globulin, and thrombopoietin-receptor agonists.[1234]</p>		
subacute thyroiditis	variable	low
<p>Subacute thyroiditis is a thyroid disease of viral or post-viral origin. Emerging evidence suggests that infection with SARS-CoV-2 may trigger subacute thyroiditis. A review of 21 cases found a female predominance, with the mean number of days between the start of COVID-19 illness and the appearance of symptoms of subacute thyroiditis being 25 days. Infection had resolved in the majority of patients before the onset of subacute thyroiditis symptoms. Fever and neck pain were the most common presenting complaints. Symptoms resolved in all patients after treatment; however, 5 patients reported having hypothyroid illness on follow-up.[1235]</p>		

Complications	Timeframe	Likelihood
Thyroid dysfunction (defined as abnormal thyroid function tests) in patients with COVID-19 varies across studies (13% to 64%). Assessment of thyroid function may be considered in symptomatic COVID-19 patients to have a baseline before treatment, particularly those who require high-intensity care. [1236]		
gastrointestinal complications	variable	low
Critically ill patients may develop gastrointestinal complications; however, it is unclear whether this is a manifestation of critical illness in general, or whether it is specific to COVID-19. One study found that patients with COVID-19 were more likely to develop gastrointestinal complications compared with those without COVID-19, specifically transaminitis, severe ileus, and mesenteric ischemia. [1237] Macrovascular arterial/venous thrombosis has been identified in almost 50% of patients with bowel ischemia. Overall mortality in COVID-19 patients with gastrointestinal ischemia and radiologically evident mesenteric thrombotic occlusion was 38.7% and 40%, retrospectively. [1238]		

Prognosis

Mortality

The leading cause of death is respiratory failure from acute respiratory distress syndrome (ARDS).[\[995\]](#)

- The overall pooled mortality rate from ARDS in COVID-19 patients is 39%; however, this varies significantly between countries (e.g., China 69%, Iran 28%, France 19%, Germany 13%).[\[996\]](#)
- There is no evidence to suggest worse outcomes (i.e., mechanical ventilator-free days, length of stay in intensive care unit or hospital, or mortality) for patients with COVID-19-related ARDS compared with the general ARDS population.[\[997\]](#)
- Risk factors for respiratory failure include older age, male sex, cardiovascular disease, laboratory markers (such as lactate dehydrogenase, lymphocyte count, and C-reactive protein), and high viral load on admission.[\[998\]](#)
- Other common causes of death include sepsis or septic shock, sepsis-related multiorgan failure, bacterial or viral coinfections, venous thromboembolism, and cardiac failure.[\[999\]](#)

Mortality rate depends on age and the presence of underlying medical conditions.

- People <65 years of age have a very small risk of death even in pandemic epicenters, and deaths in people <65 years of age without any underlying conditions is rare.[\[1000\]](#)
- Deaths in children and young people are rare. During the first pandemic year in England, 25 children and young people died, equivalent to an infection fatality rate of 5 per 100,000 and a mortality rate of 2 per million. This indicates that >99.995% of children recover from infection. The children who died were mainly >10 years of age and of Asian and Black ethnicity.[\[1001\]](#)
- Approximately 99% of patients who died of COVID-19 had at least one underlying health condition in a US cohort study. The strongest risk factors for death were obesity, anxiety and fear-related disorders, and diabetes, as well as the total number of underlying conditions.[\[193\]](#)

Mortality rates have decreased over time despite stable patient characteristics.

- In-hospital mortality decreased from 32.3% to 16.4% between March and August 2020 in a UK cohort study of over 80,000 patients. Mortality declined in all age groups, in all ethnic groups, in men and women, and in patients with and without comorbidities, over and above contributions from declining illness severity.[\[1002\]](#)
- Mortality rates decreased sharply in the US over the first 6 months of the pandemic.[\[1003\]](#) [\[1004\]](#) In-hospital mortality decreased from 10.6% to 9.3% between March and November 2020 in one US cohort study of over 500,000 patients across 209 acute care hospitals.[\[1005\]](#) Among patients with

critical illness admitted to an intensive care unit at an academic health system in the US, the mortality rate decreased from 43.5% to 19.2% over the study period.[1006]

- This may reflect the impact of changes in hospital strategy and clinical processes, and better adherence to evidence-based standard of care therapies for critical illness over time, such as use of corticosteroids, high-flow nasal oxygen to avert intubation, prone positioning, and decreased use of mechanical ventilation. Further studies are needed to confirm these results and investigate causal mechanisms.

Infection fatality rate (IFR)

- Defined as the proportion of deaths among all infected individuals including confirmed cases, undiagnosed cases (e.g., asymptomatic or mildly symptomatic cases), and unreported cases. The IFR gives a more accurate picture of the lethality of a disease compared with the case fatality rate.
- It has been estimated that approximately 1.5 to 2 billion infections have occurred globally as of February 2021, with an estimated overall IFR of 0.15%. There are substantial differences in IFR and infection spread across continents, countries, and locations.[1007]
- The US Centers for Disease Control and Prevention's current best estimate of the IFR, according to age (as of 19 March 2021):[142]
 - 0 to 17 years – 0.002%
 - 18 to 49 years – 0.05%
 - 50 to 64 years – 0.6%
 - ≥65 years – 9%.
- Based on these figures, the overall IFR for people <65 years of age is approximately 0.2%.
- The IFR can vary across locations. A meta-analysis reports the point estimate of the IFR to be 0.68% across populations, with high heterogeneity (as of July 2020). The rate varied across locations from 0.17% to 1.7%.[1008]
- Among people on board the Diamond Princess cruise ship, a unique situation where an accurate assessment of the IFR in a quarantined population can be made, the IFR was 0.85%. However, all deaths occurred in patients >70 years of age, and the rate in a younger, healthier population would be much lower.[1009]
- These estimates have limitations and are likely to change as more data emerge over the course of the pandemic.

Seroprevalence studies

- Estimates of the IFR can be inferred from seroprevalence studies.
 - Worldwide seroprevalence estimates vary. Seroprevalence in the general population has been estimated to be approximately 8%, with higher rates reported in close contacts (18%) and high-risk healthcare workers (17.1%). Pooled estimates of seroprevalence in the general population were highest in the South-East Asian (19.6%), African (16.3%), and Eastern Mediterranean (13.4%) regions. Lower estimates were reported in the Americas (6.8%), European (4.7%), and Western Pacific (1.7%) regions.[1010]
 - Current seroprevalence estimates for 10 sites in the US are available. [CDC: commercial laboratory seroprevalence survey data] (<https://covid.cdc.gov/covid-data-tracker/#serology-surveillance>)
- These studies suggest that the prevalence of infections is much higher than the official case counts suggest, and therefore the virus is much less lethal than initially thought.

Case fatality rate (CFR)

- Defined as the total number of deaths reported divided by the total number of detected cases reported. CFR is subject to selection bias as more severe/hospitalised cases are likely to be tested.

- The World Health Organization's current estimate of the global CFR is 2.1% (as of 18 July 2021).^[1011] This is much lower than the reported CFR of severe acute respiratory syndrome coronavirus (SARS), which was 10%, and Middle East respiratory syndrome (MERS), which was 37%.^[50]
- CFR varies considerably between countries.
 - In China, the overall CFR has been reported to be between 1.4% and 2.3% (0.9% in patients without comorbidities).^[4] ^[1012]
- CFR increases with age.
 - In the US, the majority of deaths were in patients ages ≥ 65 years. The CFR was highest among patients ages ≥ 85 years (10% to 27%), followed by those ages 65 to 84 years (3% to 11%), then those ages 55 to 64 years (1% to 3%), and finally those ages 20 to 54 years ($<1\%$).^[6]
 - In China, the majority of deaths were in patients ages ≥ 60 years.^[4] The CFR was highest among patients ages ≥ 80 years (13.4%), followed by those ages 60 to 79 years (6.4%), and then those ages <60 years (0.32%).^[1012]
 - In Italy, the CFR was highest among patients ages ≥ 80 years (52.5%), followed by those ages 70 to 79 years (35.5%), and then those ages 60 to 69 years (8.5%).^[1013]
 - Deaths are rare in children.^[6] ^[18] In one study, 70% of deaths occurred in those ages 10 to 20 years, 20% in those ages 1 to 9 years, and 10% in children under 1 year of age.^[1014]
- CFR increases with the presence of comorbidities.
 - In China, the majority of deaths were in patients who had preexisting underlying health conditions (10.5% for cardiovascular disease, 7.3% for diabetes, 6.3% for chronic respiratory disease, 6% for hypertension, and 5.6% for cancer).^[4]
- CFR increases with disease severity.
 - The CFR is highest in patients with critical disease, ranging from 26% to 67% in studies.^[4] ^[1015] ^[1016]

Limitations of IFR/CFR

- Estimating the IFR and CFR in the early stages of a pandemic is subject to considerable uncertainties and estimates are likely to change as more data emerges. Rates tend to be high at the start of a pandemic and then trend downwards as more data becomes available.^[1017]
- There is currently no set case definition of a confirmed case, and case definitions vary. A positive polymerase chain reaction (PCR) result is sometimes the only criterion for a case to be recognized; however, a positive PCR test does not necessarily equal a diagnosis of COVID-19, or mean that a person is infected or infectious.^[1018] ^[1019]
- The number of deaths reported on a particular day may not accurately reflect the number of deaths from the previous day due to delays associated with reporting deaths. This makes it difficult to know whether deaths are falling over time in the short term.^[1020]
- Patients who die "with" COVID-19 and patients who die "from" COVID-19 may be counted towards the death toll in some countries. For example, in Italy only 12% of death certificates reported direct causality from COVID-19, while 88% of patients who died had at least one comorbidity.^[1017] ^[1021]

Mortality rate by country

- The number of deaths (per 100,000 population) for different countries varies:^[1022]
 - South Korea – 0.7
 - Japan – 1.2
 - Australia – 3.3
 - Germany – 11.3
 - Canada – 24.6

- France – 46.6
- Sweden – 57.4
- Italy – 59.1
- US – 60.3
- UK – 62.6
- Spain – 65.0
- Belgium – 86.8.

Prognostic factors

Prognostic factors that have been associated with increased risk of severe disease, hospitalization or intensive care unit admission, poor outcomes, and mortality include:[\[1023\]](#) [\[1024\]](#) [\[1025\]](#) [\[1026\]](#) [\[1027\]](#) [\[1028\]](#) [\[1029\]](#)

- Patient factors
 - Increasing age
 - Male sex
 - Obesity
 - Smoking history
 - Blood type A
 - Frailty
- Presence of comorbidities
 - Hypertension
 - Cardiovascular disease
 - Cerebrovascular disease
 - Peripheral artery disease
 - Dementia
 - Diabetes
 - Chronic respiratory disease (e.g., COPD, obstructive sleep apnea) disease
 - Active malignancy
 - Immunosuppression
 - Chronic kidney or liver disease
 - Rheumatologic disease
 - Bacterial or fungal coinfection
- Symptoms/signs
 - Myalgia
 - Pharyngalgia
 - Sputum production
 - Chills
 - Nausea
 - Dyspnea
 - Chest tightness
 - Dizziness
 - Headache
 - Hemoptysis

- Tachypnea
- Hypoxemia
- Respiratory failure
- Hypotension
- Tachycardia
- Complications
 - Shock
 - Acute infection or sepsis
 - Acute kidney, liver, or cardiac injury
 - Acute respiratory distress syndrome
 - Venous thromboembolism
 - Arrhythmias
 - Heart failure
- Investigations
 - Lymphopenia
 - Leukocytosis
 - Neutrophilia
 - Thrombocytopenia
 - Hypoalbuminemia
 - Liver or kidney impairment
 - Elevated inflammatory markers (C-reactive protein, procalcitonin, ferritin, erythrocyte sedimentation rate)
 - Elevated lactate dehydrogenase
 - Elevated creatine kinase
 - Elevated cardiac markers
 - Elevated D-dimer
 - Elevated interleukin-6
 - $\text{PaO}_2/\text{FiO}_2 \leq 200$ mmHg
 - Bilateral pneumonia on chest imaging
 - Consolidative infiltrate or pleural effusion on chest imaging
 - High sequential organ failure assessment (SOFA) score.

The most common underlying diseases in deceased patients were hypertension, diabetes, and cardiovascular diseases.^[1030]

Hospital readmission

People discharged from hospital after acute infection had an increased risk of readmission, multi-organ dysfunction, and mortality compared with the general population. The relative increase in risk was not confined to older people and was not uniform across ethnic groups. Researchers matched approximately 50,000 patients in England who were hospitalized and discharged with COVID-19 to members of the general population; 29% of COVID-19 patients were readmitted during a mean 140 days of follow-up, while 12% died after discharge. Patients with COVID-19 were more frequently diagnosed with cardiovascular events, chronic kidney or liver disease, and diabetes compared with their matched controls.^[1031]

Approximately 9% of over 106,000 patients were readmitted to the same hospital within 2 months of discharge from the initial hospitalization. Multiple readmissions occurred in 1.6% of patients. The median time from discharge to the first readmission was 8 days. Less than 0.1% of patients died during readmission. Risk factors for readmission include:^[1032]

- Age ≥ 65 years
- Presence of chronic conditions (COPD, heart failure, diabetes, chronic kidney disease, obesity)
- Hospitalization within the 3 months preceding the first COVID-19 hospitalization
- Discharge to a skilled nursing facility or with home health care.

The risk of severe post-acute complications in patients who were not admitted to hospital for the primary infection appears to be low. However, they may be at slightly increased risk of venous thromboembolism, dyspnea, and initiating bronchodilator or triptan therapy compared with people who tested negative for SARS-CoV-2. These patients visited their general practitioner and outpatient hospital clinics more often after the primary infection than those who tested negative, which may indicate persistent symptoms that do not lead to specific drug treatment or hospital admission.[\[1033\]](#)

Reinfection

Reinfection refers to a new infection following previous confirmed infection (i.e., severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] real-time reverse transcription polymerase chain reaction [RT-PCR] positive), and is distinct from persistent infection and relapse. There is currently no standard case definition for SARS-CoV-2 reinfection.[\[756\]](#)

There is limited information about reinfection.

- Recurrent RT-PCR positivity in patients 1 to 60 days after recovery ranges between 7% to 23% in studies, with an estimated pooled rate of 12%.[\[1034\]](#) Patients with longer initial illness and younger age were more likely to experience recurrent RT-PCR positivity, while those with severe disease, diabetes, and a low lymphocyte count were less likely.[\[1035\]](#) It is currently unclear whether this is due to reinfection; whether it is due to factors such as the type of specimen collection and technical errors associated with swab testing, infection by mutated SARS-CoV-2, or persistent viral shedding; or whether the test result was a false-negative at the time of discharge.[\[1036\]](#)
- Studies have repeatedly reported positive RT-PCR tests for up to 90 days after initial infection; therefore, it is most likely that these cases are actually protracted initial infections. It is important to note that although persistent viral shedding has been reported for up to 90 days after the onset of infection, replication-competent virus has not been identified 10 to 20 days after the onset of symptoms (depending on disease severity).[\[1037\]](#) A cohort study of 200 patients with past infection found that despite persistent pharyngeal RT-PCR positivity for up to 90 days after recovery, transmission to close contacts was not observed, indicating that these patients are not contagious at the post-symptomatic stage of infection.[\[1038\]](#)

Cases of reinfection are rare.

- Cases of possible reinfections have been estimated to be approximately 0.4% in the UK (as of 30 May 2021). However, only 53 cases were confirmed out of the 15,893 possible reinfections. Current evidence suggests that most reinfections will not cause symptoms. There is currently no evidence that variants of concern are more likely to cause reinfection than others.[\[1039\]](#)
- Cases of possible reinfection have been reported in many countries including China, India, Ecuador, the US, the Netherlands, Qatar, and Belgium. Overall, 68.8% had similar severity, 18.8% had worse symptoms, and 12.5% had milder symptoms with the second episode.[\[1040\]](#)
- Cases of reinfection with SARS-CoV-2 variants have been reported in Brazil, the UK, and South Africa.[\[1041\]](#) [\[1042\]](#) [\[1043\]](#) [\[1044\]](#)

Consider reinfection in the following circumstances:[\[756\]](#)

- A repeat positive RT-PCR test 90 days or more after a previous positive RT-PCR test
- New symptoms in a patient with previous RT-PCR-positive infection after apparent full recovery (i.e., resolution of previous symptoms) and a repeat positive RT-PCR test (including within 90 days after a previous positive RT-PCR test).

Diagnosis

- A compatible clinical presentation together with diagnostic evidence (such as a low RT-PCR cycle threshold value) may be sufficient to diagnose reinfection. However, the diagnosis should be made in conjunction with an infectious disease specialist following a risk assessment that involves reviewing available clinical, diagnostic, and epidemiologic information to inform whether reinfection is likely. Confirmation of reinfection should be obtained through whole genome sequencing of paired specimens, if available.[756]

Management

- Manage patients with suspected reinfection as if they are infectious, as for a new or first infection. Advise the patient to self-isolate pending further investigation and clinical risk assessment. It is important to note that illness due to reinfection may not necessarily follow the same clinical course as the previous episode.[756]

Immunity

The immune response to SARS-CoV-2 is not yet fully understood, but involves both cell-mediated and antibody-mediated immunity. This is an area of rapidly emerging new evidence.

Adaptive immunity is thought to occur within the first 7 to 10 days of infection. A robust memory B-cell and plasmablast response is detected early in infection, with secretion of immunoglobulin A (IgA) and IgM antibodies by day 5 to 7, and IgG by day 7 to 10 from the onset of symptoms. T cells are simultaneously activated in the first week of infection and SARS-CoV-2-specific memory CD4+ and CD8+ T cells peak within 2 weeks. Antibody and T-cell response differ among individuals, and depend on age and disease severity.[1045]

Antibody-mediated immunity

- Current evidence is uncertain to predict the presence, level, or durability of natural immunity conferred by SARS-CoV-2 antibodies against reinfection.[1046]
- Approximately 85% to 99% of infected people develop detectable neutralizing antibodies within 4 weeks following natural infection. However, this varies depending on disease severity, study setting, time since infection, and method used to measure antibodies.[1047] [1048]
- Moderate-strength evidence suggests that most adults develop detectable levels of IgM and IgG antibodies after infection. IgM levels peak early in the disease course at approximately 20 days and then decline. IgG levels peak later at approximately 25 days after symptom onset and may remain detectable for at least 120 days. Most adults generate neutralizing antibodies, which may persist for several months. Some adults do not develop antibodies after infection; the reasons for this are unclear.[1049]
- Maternal IgG antibodies to SARS-CoV-2 have been found to transfer across the placenta after infection in pregnant women.[1050]
- Extreme-aged (some over 100 years), frail residents of a long-term care facility have been found to elicit a robust immune response that was capable of neutralizing the SARS-CoV-2 virus.[1051]
- There were some early studies that suggested asymptomatic people may have a weaker antibody response to infection; however, this has not been confirmed.[1052]
- Current evidence suggests that the immune responses remain robust and protective against reinfection in most people for at least 6 to 10 months after infection (the longest follow-up data is currently only 10 months).[1047] [1053]
- Some SARS-CoV-2 variants with key changes in the spike protein have a reduced susceptibility to neutralization by antibodies. However, cellular immunity elicited by natural infection also targets other viral proteins, which tend to be more conserved across variants than the spike protein.[1047]

Cell-mediated immunity

- The majority of people develop a strong and broad T-cell response with both CD4+ and CD8+ T cells, and some have a memory phenotype.[1054]
- CD4+ and CD8+ T cells declined with a half-life of 3 to 5 months in adults who recovered, and are likely to be present in most adults at least 6 to 8 months after primary infection.[1055] [1056]

- Emerging data suggest that T-cell responses are largely unaffected by SARS-CoV-2 variants.[\[1057\]](#)[\[1058\]](#)

Evidence suggests that infection with SARS-CoV-2 is likely to confer protective immunity against reinfection.[\[1059\]](#) [\[1060\]](#) [\[1061\]](#) [\[1062\]](#)

- A Public Health England study found that naturally acquired immunity, as a result of past infection, provides 84% protection against reinfection compared with people who have not had the disease previously, and protection appeared to last for at least 7 months.[\[1063\]](#)
- Similarly, a population-level observational study among 4 million PCR-tested people in Denmark found protection against repeat infection in the population to be 80% or higher in those younger than 65 years of age, and 47% in those older than 65 years of age. There was no evidence of waning protection over time.[\[1064\]](#)
- An observational study from Lombardy, Italy, found that natural immunity appears to confer a protective effect for at least one year; however, the study ended before SARS-CoV-2 variants began to spread, and it is unknown how well natural immunity to the wild-type virus will protect against these variants.[\[1065\]](#)
- A prospective study in 3000 mostly young male Marine recruits found that around 10% of seropositive participants tested positive for the virus at least once in the 6-week follow-up period compared with 48% of seronegative participants, an 82% reduced incidence rate of infection.[\[1066\]](#)
- According to a large, retrospective study, people who were seropositive for SARS-CoV-2 appeared to be at lower risk for future infection, for at least several months.[\[1067\]](#)
- A study in over 12,000 healthcare workers found that prior SARS-CoV-2 infection that generated antibody responses offered protection from reinfection for most people in the 6 months following infection.[\[1068\]](#)
- A study in over 2000 staff and residents across 100 long-term care facilities in England found that antibodies provided high levels of protection against reinfection for up to 10 months in both staff and residents. Previous infection reduced the risk of reinfection by approximately 85% in residents and 60% in staff members.[\[1069\]](#)

Preexisting immunity to SARS-CoV-2

- Testing of blood samples taken before the COVID-19 pandemic has shown that some people already have immune cells that recognize SARS-CoV-2. Studies have reported T-cell reactivity against SARS-CoV-2 in 20% to 50% of people with no known exposure to the virus.[\[1070\]](#) Approximately 5% of uninfected adults and 62% of uninfected children aged 6 to 16 years had antibodies that recognize SARS-CoV-2 in one study.[\[1071\]](#)
- This may be a consequence of true immune memory derived in part from previous infection with common cold coronaviruses, or from other unknown animal coronaviruses. However, further research into whether there is preexisting immunity to SARS-CoV-2 in the human population is required.

Diagnostic guidelines

International

Interim guidelines for collecting and handling of clinical specimens for COVID-19 testing (<https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html>) [589]

Published by: Centers for Disease Control and Prevention

Last published: 2021

Interim infection prevention and control recommendations for healthcare personnel during the coronavirus disease 2019 (COVID-19) pandemic (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html>) [750]

Published by: Centers for Disease Control and Prevention

Last published: 2021

Overview of testing for SARS-CoV-2 (COVID-19) (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html>) [580]

Published by: Centers for Disease Control and Prevention

Last published: 2021

Interim guidelines for COVID-19 antibody testing (<https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html>) [613]

Published by: Centers for Disease Control and Prevention

Last published: 2021

COVID-19 real-time learning network (<https://www.idsociety.org/public-health/COVID-19-Resource-Center>) [751]

Published by: Infectious Diseases Society of America

Last published: 2021

Infectious Diseases Society of America guidelines on the diagnosis of COVID-19: antigen testing (<https://www.idsociety.org/practice-guideline/covid-19-guideline-antigen-testing>) [621]

Published by: Infectious Diseases Society of America

Last published: 2021

COVID-19 interim guidance (<https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance>) [752]

Published by: American Academy of Pediatrics

Last published: 2021

COVID-19 testing guidance (<https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/covid-19-testing-guidance>) [581]

Published by: American Academy of Pediatrics

Last published: 2021

Infectious Diseases Society of America guidelines on the diagnosis of COVID-19: molecular diagnostic testing (<https://www.idsociety.org/practice-guideline/alphabetical-guidelines>) [591]

Published by: Infectious Diseases Society of America

Last published: 2020

International

Infectious Diseases Society of America guidelines on the diagnosis of COVID-19: serologic testing (<https://www.idsociety.org/practice-guideline/alphabetical-guidelines>) [614]

Published by: Infectious Diseases Society of America

Last published: 2020

Infectious Diseases Society of America guidelines on infection prevention in patients with suspected or known COVID-19 (<https://www.idsociety.org/practice-guideline/alphabetical-guidelines>) [753]

Published by: Infectious Diseases Society of America

Last published: 2020

Country & technical guidance - coronavirus disease (COVID-19) (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance-publications>) [754]

Published by: World Health Organization

Last published: 2021

Recommendations for national SARS-CoV-2 testing strategies and diagnostic capacities (<https://www.who.int/publications/i/item/WHO-2019-nCoV-lab-testing-2021.1-eng>) [578]

Published by: World Health Organization

Last published: 2021

Infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed: interim guidance (<https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC-2021.1>) [504]

Published by: World Health Organization

Last published: 2021

Diagnostic testing for SARS-CoV-2: interim guidance (<https://www.who.int/publications/i/item/diagnostic-testing-for-sars-cov-2>) [536]

Published by: World Health Organization

Last published: 2020

Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays: interim guidance (<https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays>) [620]

Published by: World Health Organization

Last published: 2020

Public health surveillance for COVID-19: interim guidance (<https://www.who.int/publications/i/item/who-2019-nCoV-surveillanceguidance-2020.7>) [166]

Published by: World Health Organization

Last published: 2020

Prevention, identification and management of health worker infection in the context of COVID-19 (<https://www.who.int/publications/i/item/10665-336265>) [29]

Published by: World Health Organization

Last published: 2020

International

Use of chest imaging in COVID-19: a rapid advice guide (<https://www.who.int/publications/i/item/use-of-chest-imaging-in-covid-19>) [630]

Published by: World Health Organization

Last published: 2020

COVID-19: guidance for health professionals (<https://www.gov.uk/government/collections/wuhan-novel-coronavirus>) [755]

Published by: Public Health England

Last published: 2021

COVID-19: investigation and management of suspected SARS-CoV-2 reinfections (<https://www.gov.uk/government/publications/covid-19-investigation-and-management-of-suspected-sars-cov-2-reinfections>) [756]

Published by: Public Health England

Last published: 2021

COVID-19 (<https://www.ecdc.europa.eu/en/novel-coronavirus-china>) [757]

Published by: European Centre for Disease Prevention and Control

Last published: 2021

Assessment of COVID-19 in primary care (<https://www.sign.ac.uk/our-guidelines>) [758]

Published by: Scottish Intercollegiate Guidelines Network

Last published: 2021

COVID-19 position statement: presentations and management of COVID-19 in older people in acute care (<https://www.sign.ac.uk/media/1826/presentations-and-management-of-covid-19-in-older-people-v2-final.pdf>) [759]

Published by: Scottish Intercollegiate Guidelines Network

Last published: 2021

A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (<https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-020-0233-6>) [760]

Published by: Zhongnan Hospital of Wuhan University Novel Coronavirus Management and Research Team; Evidence-Based Medicine Chapter of China International Exchange and Promotive Association for Medical and Health Care

Last published: 2020

Diagnosis and clinical management of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (<https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1735265>) [761]

Published by: Peking Union Medical College Hospital

Last published: 2020

Treatment guidelines

International

Coronavirus disease 2019 (COVID-19) treatment guidelines (<https://covid19treatmentguidelines.nih.gov>) [533]

Published by: National Institutes of Health

Last published: 2021

COVID-19 real-time learning network (<https://www.idsociety.org/covid-19-real-time-learning-network>) [751]

Published by: Infectious Diseases Society of America

Last published: 2021

Infectious Diseases Society of America guidelines on the treatment and management of patients with COVID-19 (<https://www.idsociety.org/practice-guideline/alphabetical-guidelines>) [810]

Published by: Infectious Diseases Society of America

Last published: 2021

Interim clinical guidance for management of patients with confirmed coronavirus disease (COVID-19) (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>) [565]

Published by: Centers for Disease Control and Prevention

Last published: 2021

Healthcare workers: information on COVID-19 (<https://www.cdc.gov/coronavirus/2019-nCoV/hcp/index.html>) [969]

Published by: Centers for Disease Control and Prevention

Last published: 2021

Interim clinical considerations for use of COVID-19 vaccines currently authorized in the United States (<https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>) [391]

Published by: Centers for Disease Control and Prevention

Last published: 2021

Interim U.S. guidance for risk assessment and work restrictions for healthcare personnel with potential exposure to SARS-CoV-2 (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assesment-hcp.html>) [970]

Published by: Centers for Disease Control and Prevention

Last published: 2021

Discontinuation of transmission-based precautions and disposition of patients with SARS-CoV-2 infection in healthcare settings (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html>) [787]

Published by: Centers for Disease Control and Prevention

Last published: 2021

Ending home isolation for persons with COVID-19 not in healthcare settings (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-in-home-patients.html>) [776]

Published by: Centers for Disease Control and Prevention

Last published: 2021

International

COVID-19 interim guidance (<https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance>) [752]

Published by: American Academy of Pediatrics

Last published: 2021

Caring for children and youth with special health care needs during the COVID-19 pandemic (<https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/caring-for-children-and-youth-with-special-health-care-needs-during-the-covid-19-pandemic>) [971]

Published by: American Academy of Pediatrics

Last published: 2021

Coronavirus disease (COVID-19): outbreak update (<https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection.html>) [972]

Published by: Government of Canada

Last published: 2021

Management of infants born to mothers with suspected or confirmed COVID-19 (<https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/faqs-management-of-infants-born-to-covid-19-mothers>) [857]

Published by: American Academy of Pediatrics

Last published: 2021

Interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 (COVID-19) (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-home-care.html>) [973]

Published by: Centers for Disease Control and Prevention

Last published: 2020

Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the Anticoagulation Forum (<https://link.springer.com/article/10.1007/s11239-020-02138-z>) [799]

Published by: Anticoagulation Forum

Last published: 2020

Evaluation and management considerations for neonates at risk for COVID-19 (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/caring-for-newborns.html>) [861]

Published by: Centers for Disease Control and Prevention

Last published: 2020

Novel coronavirus 2019 (COVID-19) (<https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/03/novel-coronavirus-2019>) [853]

Published by: American College of Obstetricians and Gynecologists

Last published: 2020

Country & technical guidance - coronavirus disease (COVID-19) (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance-publications>) [754]

Published by: World Health Organization

Last published: 2021

International

COVID-19 clinical management: living guidance (<https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1>) [2]

Published by: World Health Organization

Last published: 2021

Therapeutics and COVID-19: living guideline (<https://www.who.int/publications/i/item/therapeutics-and-covid-19-living-guideline>) [762]

Published by: World Health Organization

Last published: 2021

Drugs to prevent COVID-19: WHO living guideline (<https://www.who.int/publications/i/item/WHO-2019-nCoV-prophylaxes-2021-1>) [963]

Published by: World Health Organization

Last published: 2021

Surviving Sepsis Campaign guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19) in the ICU (<https://www.sccm.org/SurvivingSepsisCampaign/Guidelines/COVID-19>) [792]

Published by: Surviving Sepsis Campaign

Last published: 2021

COVID-19 guidance and the latest research in the Americas (<https://covid19-evidence.paho.org>) [974]

Published by: Pan American Health Organization

Last published: 2021

Home care for patients with suspected or confirmed COVID-19 and management of their contacts: interim guidance ([https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-\(ncov\)-infection-presenting-with-mild-symptoms-and-management-of-contacts](https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and-management-of-contacts)) [774]

Published by: World Health Organization

Last published: 2020

Criteria for releasing COVID-19 patients from isolation: scientific brief (<https://www.who.int/publications/i/item/criteria-for-releasing-covid-19-patients-from-isolation>) [975]

Published by: World Health Organization

Last published: 2020

Mask use in the context of COVID-19: interim guidance ([https://www.who.int/publications-detail/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-\(2019-ncov\)-outbreak](https://www.who.int/publications-detail/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak)) [92]

Published by: World Health Organization

Last published: 2020

Rapid advice guidelines for management of children with COVID-19 (<http://atm.amegroups.com/article/view/43612/html>) [976]

Published by: International multidisciplinary working group

Last published: 2020

International

ISTH interim guidance on recognition and management of coagulopathy in COVID-19 (<https://onlinelibrary.wiley.com/doi/full/10.1111/jth.14810>) [574]

Published by: International Society of Thrombosis and Haemostasis

Last published: 2020

Global interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium from FIGO and allied partners: information for healthcare professionals (<https://obgyn.onlinelibrary.wiley.com/doi/epdf/10.1002/ijgo.13156>) [627]

Published by: International Federation of Gynecology and Obstetrics

Last published: 2020

ISUOG interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium: information for healthcare professionals – an update (<https://www.isuog.org/clinical-resources/isuog-guidelines.html>) [977]

Published by: International Society of Ultrasound in Obstetrics and Gynecology

Last published: 2020

BMJ's coronavirus (covid-19) hub (<https://www.bmj.com/coronavirus>) [978]

Published by: BMJ

Last published: 2021

COVID-19 rapid guideline: managing COVID-19 (<https://www.nice.org.uk/guidance/ng191>) [564]

Published by: National Institute for Health and Care Excellence (UK)

Last published: 2021

Coronavirus (COVID-19) (<https://www.nice.org.uk/covid-19>) [979]

Published by: National Institute for Health and Care Excellence (UK)

Last published: 2021

COVID-19: guidance for health professionals (<https://www.gov.uk/government/collections/wuhan-novel-coronavirus>) [755]

Published by: Public Health England

Last published: 2021

Coronavirus specialty guides (<https://www.nice.org.uk/covid-19/specialty-guides>) [980]

Published by: NHS England

Last published: 2021

COVID-19: the green book, chapter 14a (<https://www.gov.uk/government/publications/covid-19-the-green-book-chapter-14a>) [981]

Published by: Public Health England

Last published: 2021

COVID-19: investigation and management of suspected SARS-CoV-2 reinfections (<https://www.gov.uk/government/publications/covid-19-investigation-and-management-of-suspected-sars-cov-2-reinfections>) [756]

Published by: Public Health England

Last published: 2021

International

Community palliative, end of life and bereavement care in the COVID-19 pandemic (<https://elearning.rcgp.org.uk/mod/page/view.php?id=10537>) [982]

Published by: Royal College of General Practitioners; Association for Palliative Medicine

Last published: 2021

Management of hospitalised adults with coronavirus disease-19 (COVID-19) (<https://www.ersnet.org/guidelines>) [983]

Published by: European Respiratory Society

Last published: 2021

COVID-19 (<https://www.ecdc.europa.eu/en/novel-coronavirus-china>) [757]

Published by: European Centre for Disease Prevention and Control

Last published: 2021

Coronavirus (COVID-19) infection in pregnancy (<https://www.rcog.org.uk/en/guidelines-research-services/guidelines/coronavirus-pregnancy>) [856]

Published by: Royal College of Obstetricians and Gynaecologists (UK)

Last published: 2021

COVID-19: information for the respiratory community (<https://www.brit-thoracic.org.uk/about-us/covid-19-information-for-the-respiratory-community>) [984]

Published by: British Thoracic Society

Last published: 2021

COVID-19 position statement: presentations and management of COVID-19 in older people in acute care (<https://www.sign.ac.uk/media/1826/presentations-and-management-of-covid-19-in-older-people-v2-final.pdf>) [759]

Published by: Scottish Intercollegiate Guidelines Network

Last published: 2021

Clinical guidance for management of adult COVID-19 patients (<https://covid.aiims.edu/clinical-guidance-for-management-of-adult-covid-19-patients>) [985]

Published by: All India Institute Of Medical Sciences; Indian Council of Medical Research

Last published: 2021

Technical documents and advisory (<https://www.icmr.gov.in/ctechdocad.html>) [899]

Published by: Indian Council of Medical Research

Last published: 2021

Updates on COVID-19 (coronavirus disease 2019) local situation (<https://www.moh.gov.sg/covid-19>) [986]

Published by: Ministry of Health Singapore

Last published: 2021

Coronavirus disease (http://www.chinacdc.cn/jkzt/crb/zt/szkb_11803) [987]

Published by: Chinese Center for Disease Control and Prevention

Last published: 2021

International

New coronavirus infectious disease (COVID-19) related information page (<https://www.niid.go.jp/niid/ja/diseases/ka/corona-virus/2019-ncov.html>) [988]

Published by: National Institute of Infectious Diseases Japan

Last published: 2021

COVID-19 infection (https://www.kansensho.or.jp/modules/topics/index.php?content_id=31) [989]

Published by: Japanese Association for Infectious Diseases

Last published: 2021

Coronavirus disease 2019 (COVID-19) (<https://www1.health.gov.au/internet/main/publishing.nsf/Content/cdna-song-novel-coronavirus.htm>) [990]

Published by: Department of Health Australia

Last published: 2021

COVID-19 rapid guideline: managing the long-term effects of COVID-19 (<https://www.nice.org.uk/guidance/ng188>) [991]

Published by: National Institute for Health and Care Excellence (UK)

Last published: 2020

Management of critically ill patients with COVID-19 in ICU: statement from front-line intensive care experts in Wuhan, China (<https://annalsofintensivecare.springeropen.com/articles/10.1186/s13613-020-00689-1>) [992]

Published by: Chinese expert working panel

Last published: 2020

Handbook of COVID-19 prevention and treatment (<https://video-intl.alicdn.com/Handbook%20of%20COVID-19%20Prevention%20and%20Treatment.pdf>) [993]

Published by: First Affiliated Hospital, Zhejiang University School of Medicine

Last published: 2020

Diagnosis and treatment protocol for novel coronavirus pneumonia (trial version 7) (https://journals.lww.com/cmj/fulltext/2020/05050/diagnosis_and_treatment_protocol_for_novel.13.aspx) [994]

Published by: National Health Commission of the People's Republic of China; National Administration of Traditional Chinese Medicine of the People's Republic of China

Last published: 2020

Diagnosis and clinical management of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (<https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1735265>) [761]

Published by: Peking Union Medical College Hospital

Last published: 2020

Online resources

1. WHO: coronavirus disease (COVID-19) dashboard (<https://who.sprinklr.com>) (*external link*)
2. CDC: COVID data tracker weekly review (<https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview.html>) (*external link*)
3. American Academy of Pediatrics: children and COVID-19 – state-level data report (<https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report>) (*external link*)
4. GenBank (<https://www.ncbi.nlm.nih.gov/genbank>) (*external link*)
5. COG-UK: data (<https://www.cogconsortium.uk>) (*external link*)
6. WHO: tracking SARS-CoV-2 variants (<https://www.who.int/en/activities/tracking-SARS-CoV-2-variants>) (*external link*)
7. WHO: COVID-19 vaccines technical documents (<https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials>) (*external link*)
8. Public Health England: COVID-19 vaccination information for healthcare practitioners (<https://www.gov.uk/government/publications/covid-19-vaccination-programme-guidance-for-healthcare-practitioners>) (*external link*)
9. CDC: interim clinical considerations for use of COVID-19 vaccines currently authorized in the United States (<https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>) (*external link*)
10. Yellow Card: coronavirus (COVID-19) (<https://coronavirus-yellowcard.mhra.gov.uk>) (*external link*)
11. Vaccine Adverse Event Reporting System (VAERS) (<https://vaers.hhs.gov>) (*external link*)
12. EudraVigilance (<https://www.ema.europa.eu/en/human-regulatory/research-development/pharmacovigilance/eudravigilance>) (*external link*)
13. WHO: Adverse Event Following Immunization (AEFI) form (<http://investigation.gvsi-aefi-tools.org/#step-1>) (*external link*)
14. CDC: v-safe COVID-19 vaccine pregnancy registry (<https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafepregnancyregistry.html>) (*external link*)
15. Public Health England: COVID-19 vaccine surveillance reports (<https://www.gov.uk/government/publications/covid-19-vaccine-surveillance-report>) (*external link*)
16. BMJ: covid-19 in primary care (UK) (https://sandpit.bmj.com/graphics/2020/covid19_v3.0_web.pdf) (*external link*)

17. BMJ: covid-19 – a remote assessment in primary care (<https://www.bmj.com/content/368/bmj.m1182>) (*external link*)
18. WHO: infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed (<https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC-2021.1>) (*external link*)
19. CDC: interim infection prevention and control recommendations for healthcare personnel during the coronavirus disease 2019 (COVID-19) pandemic (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html>) (*external link*)
20. BMJ: covid-19 – PPE guidance (<https://www.bmj.com/sites/default/files/attachments/resources/2020/04/cv19-ppe-v1.0-web.pdf>) (*external link*)
21. WHO: coronavirus disease (COVID-19) advice for the public (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public>) (*external link*)
22. BMJ: mask related acne (“maskne”) and other facial dermatoses (<https://www.bmj.com/content/373/bmj.n1304>) (*external link*)
23. Public Health England: travel abroad - step by step (<https://www.gov.uk/travel-abroad>) (*external link*)
24. Public Health England: COVID-19 – advice for smokers and vapers (<https://www.gov.uk/government/publications/covid-19-advice-for-smokers-and-vapers/covid-19-advice-for-smokers-and-vapers>) (*external link*)
25. BMJ Best Practice: Management of coexisting conditions in the context of COVID-19 (<https://bestpractice.bmj.com/topics/en-us/3000190#important-update>) (*external link*)
26. BMJ Practice Pointer: remote management of covid-19 using home pulse oximetry and virtual ward support (<https://www.bmj.com/content/372/bmj.n677>) (*external link*)
27. Centre for Evidence-Based Medicine: are you infectious if you have a positive PCR test result for COVID-19? (<https://www.cebm.net/covid-19/infectious-positive-pcr-test-result-covid-19>) (*external link*)
28. BMJ Practice Pointer: interpreting a covid-19 test result (<https://www.bmj.com/content/369/bmj.m1808>) (*external link*)
29. BMJ practice pointer: testing for SARS-CoV-2 antibodies (<https://www.bmj.com/content/370/bmj.m3325>) (*external link*)
30. BSTI: radiology decision tool for suspected COVID-19 (https://www.bsti.org.uk/media/resources/files/NHSE_BSTI_APPROVED_Radiology_on_CoVid19_v6_modified1_-_Read-Only.pdf) (*external link*)
31. BSTI: lung ultrasound (LUS) for COVID-19 patients in critical care areas (https://www.bsti.org.uk/media/resources/files/Lung_US_print_out_and_scoring_proforma.pdf) (*external link*)

32. British Association of Dermatologists: Covid-19 skin patterns (<https://covidskinsigns.com>) (*external link*)
33. NHS England: pulse oximetry to detect early deterioration of patients with COVID-19 in primary and community care settings (<https://www.england.nhs.uk/coronavirus/publication/pulse-oximetry-to-detect-early-deterioration-of-patients-with-covid-19-in-primary-and-community-care-settings>) (*external link*)
34. BMJ: interpreting a lateral flow SARS-CoV-2 antigen test (<https://www.bmj.com/content/373/bmj.n1411>) (*external link*)
35. WHO: public health surveillance for COVID-19 – interim guidance (<https://www.who.int/publications/i/item/who-2019-nCoV-surveillanceguidance-2020.7>) (*external link*)
36. CDC: coronavirus disease 2019 (COVID-19) 2020 interim case definition (<https://wwwn.cdc.gov/nndss/conditions/coronavirus-disease-2019-covid-19/case-definition/2020>) (*external link*)
37. PHE: COVID-19 – investigation and initial clinical management of possible cases (<https://www.gov.uk/government/publications/wuhan-novel-coronavirus-initial-investigation-of-possible-cases/investigation-and-initial-clinical-management-of-possible-cases-of-wuhan-novel-coronavirus-wn-cov-infection>) (*external link*)
38. ECDC: case definition for coronavirus disease 2019 (COVID-19) (<https://www.ecdc.europa.eu/en/covid-19/surveillance/case-definition>) (*external link*)
39. WHO: home care for patients with suspected or confirmed COVID-19 and management of their contacts ([https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-\(ncov\)-infection-presenting-with-mild-symptoms-and-management-of-contacts](https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and-management-of-contacts)) (*external link*)
40. CDC: interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 (COVID-19) (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-home-care.html>) (*external link*)
41. Clinical Frailty Scale (<https://www.scfn.org.uk/clinical-frailty-scale>) (*external link*)
42. ACOG: outpatient assessment and management for pregnant women with suspected or confirmed novel coronavirus (COVID-19) (<https://www.acog.org/-/media/project/acog/acogorg/files/pdfs/clinical-guidance/practice-advisory/covid-19-algorithm.pdf?la=en&hash=2D9E7F62C97F8231561616FFDCA3B1A6>) (*external link*)
43. BMJ rapid recommendations: a living WHO guideline on drugs for COVID-19 (<https://www.bmj.com/content/370/bmj.m3379>) (*external link*)
44. Global coronavirus COVID-19 clinical trial tracker (<https://www.covid-trials.org>) (*external link*)
45. RECOVERY trial (<https://www.recoverytrial.net>) (*external link*)

46. WHO: "Solidarity" clinical trial for COVID-19 treatments (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments>) (*external link*)
47. CDC: commercial laboratory seroprevalence survey data (<https://covid.cdc.gov/covid-data-tracker/#serology-surveillance>) (*external link*)
48. NICE COVID-19 rapid guideline: managing the long-term effects of COVID-19 (<https://www.nice.org.uk/guidance/ng188>) (*external link*)
49. BMJ webinar: long COVID – how to define it and how to manage it (<https://www.bmj.com/content/370/bmj.m3489>) (*external link*)
50. BMJ: management of post-acute covid-19 in primary care (<https://www.bmj.com/content/370/bmj.m3026>) (*external link*)
51. Public Health England: information for healthcare professionals on blood clotting following COVID-19 vaccination (<https://www.gov.uk/government/publications/covid-19-vaccination-blood-clotting-information-for-healthcare-professionals>) (*external link*)
52. Examples of learned societies with treatment recommendations (<https://www.ema.europa.eu/en/news/ema-raises-awareness-clinical-care-recommendations-manage-suspected-thrombosis-thrombocytopenia>) (*external link*)
53. The BMJ 10-minute consultation: what is my covid risk? (<https://www.bmj.com/content/372/bmj.n637>) (*external link*)
54. Health Education England: adult pulse oximetry monitoring video (<https://www.youtube.com/watch?v=ifnYjD4IKus&t=141s>) (*external link*)
55. WHO: coronavirus disease (COVID-19) travel advice (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/travel-advice>) (*external link*)
56. CDC: COVID-19 – travel (<https://www.cdc.gov/coronavirus/2019-ncov/travelers/index.html>) (*external link*)
57. NaTHNaC: travel health pro (<https://travelhealthpro.org.uk>) (*external link*)
58. Public Health England: travel advice – coronavirus (COVID-19) (<https://www.gov.uk/guidance/travel-advice-novel-coronavirus>) (*external link*)
59. UK Department for Transport (<https://www.gov.uk/government/organisations/department-for-transport>) (*external link*)
60. Smartraveller Australia: COVID-19 (<https://www.smartraveller.gov.au/news-and-updates/coronavirus-covid-19>) (*external link*)

61. Government of Canada: coronavirus disease (COVID-19) – travel, testing, quarantine and borders (<https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/latest-travel-health-advice.html>) (*external link*)
62. Ministry of Manpower Singapore: advisories on COVID-19 (<https://www.mom.gov.sg/covid-19>) (*external link*)
63. CDC: coronavirus disease 2019 (COVID-19) – pets and other animals (<https://www.cdc.gov/coronavirus/2019-ncov/animals/pets-other-animals.html>) (*external link*)
64. AAP: COVID-19 interim guidance – return to sports and physical activity (<https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/covid-19-interim-guidance-return-to-sports>) (*external link*)
65. WHO: coronavirus disease (COVID-19) pandemic (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019>) (*external link*)
66. CDC: COVID-19 (<https://www.cdc.gov/coronavirus/2019-nCoV/index.html>) (*external link*)
67. NHS England: coronavirus (COVID-19) (<https://www.nhs.uk/conditions/coronavirus-covid-19>) (*external link*)
68. NHS England: COVID-19 patient rehabilitation booklet (<http://flipbooks.leedsth.nhs.uk/LN004864.pdf>) (*external link*)
69. NHS England: your COVID recovery (<https://www.yourcovidrecovery.nhs.uk>) (*external link*)

Key articles

References

1. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol.* 2020 Apr;5(4):536-44. [Full text \(https://www.nature.com/articles/s41564-020-0695-z\)](https://www.nature.com/articles/s41564-020-0695-z) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32123347?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32123347?tool=bestpractice.bmj.com)
2. World Health Organization. COVID-19 clinical management: living guidance. 2021 [internet publication]. [Full text \(https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1\)](https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1)
3. National Institutes of Health. Coronavirus disease 2019 (COVID-19) treatment guidelines. 2021 [internet publication]. [Full text \(https://covid19treatmentguidelines.nih.gov\)](https://covid19treatmentguidelines.nih.gov)
4. Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China [in Chinese]. *Zhonghua Liu Xing Bing Xue Za Zhi.* 2020 Feb 17;41(2):145-51. [Full text \(http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51\)](http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32064853?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32064853?tool=bestpractice.bmj.com)
5. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO clinical characterisation protocol: prospective observational cohort study. *BMJ.* 2020 May 22;369:m1985. [Full text \(https://www.bmj.com/content/369/bmj.m1985\)](https://www.bmj.com/content/369/bmj.m1985) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32444460?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32444460?tool=bestpractice.bmj.com)
6. CDC COVID-19 Response Team. Severe outcomes among patients with coronavirus disease 2019 (COVID-19): United States, February 12 - March 16, 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Mar 27;69(12):343-6. [Full text \(https://www.cdc.gov/mmwr/volumes/69/wr/mm6912e2.htm?s_cid=mm6912e2_w\)](https://www.cdc.gov/mmwr/volumes/69/wr/mm6912e2.htm?s_cid=mm6912e2_w) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32214079?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32214079?tool=bestpractice.bmj.com)
7. Viner RM, Mytton OT, Bonell C, et al. Susceptibility to SARS-CoV-2 infection among children and adolescents compared with adults: a systematic review and meta-analysis. *JAMA Pediatr.* 2021 Feb 1;175(2):143-56. [Full text \(https://jamanetwork.com/journals/jamapediatrics/fullarticle/2771181\)](https://jamanetwork.com/journals/jamapediatrics/fullarticle/2771181) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32975552?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32975552?tool=bestpractice.bmj.com)
8. Havers FP, Whitaker M, Self JL, et al. Hospitalization of adolescents aged 12–17 years with laboratory-confirmed COVID-19: COVID-NET, 14 States, March 1, 2020–April 24, 2021. *MMWR Morb Mortal Wkly Rep.* 2021 Jun 4 [Epub ahead of print]. [Full text \(https://www.cdc.gov/mmwr/volumes/70/wr/mm7023e1.htm\)](https://www.cdc.gov/mmwr/volumes/70/wr/mm7023e1.htm)
9. Centers for Disease Control and Prevention. COVID-NET laboratory-confirmed COVID-19 hospitalizations. 2021 [internet publication]. [Full text \(https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalization-network\)](https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalization-network)

10. Zhu Y, Bloxham CJ, Hulme KD, et al. A meta-analysis on the role of children in SARS-CoV-2 in household transmission clusters. *Clin Infect Dis*. 2020 Dec 6 [Epub ahead of print]. [Full text \(https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1825/6024998\)](https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1825/6024998) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33283240?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33283240?tool=bestpractice.bmj.com)
11. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. *Pediatrics*. 2020 Jun;145(6):e20200702. [Full text \(https://pediatrics.aappublications.org/content/145/6/e20200702.long\)](https://pediatrics.aappublications.org/content/145/6/e20200702.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32179660?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32179660?tool=bestpractice.bmj.com)
12. Garazzino S, Montagnani C, Donà D, et al. Multicentre Italian study of SARS-CoV-2 infection in children and adolescents, preliminary data as at 10 April 2020. *Euro Surveill*. 2020 May;25(18). [Full text \(https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.18.2000600\)](https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.18.2000600) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32400362?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32400362?tool=bestpractice.bmj.com)
13. Brambilla I, Castagnoli R, Caimmi S, et al. COVID-19 in the pediatric population admitted to a tertiary referral hospital in Northern Italy: preliminary clinical data. *Pediatr Infect Dis J*. 2020 Jul;39(7):e160. [Full text \(https://journals.lww.com/pidj/Citation/9000/COVID_19_in_the_Pediatric_Population_Admitted_to_a.96177.aspx\)](https://journals.lww.com/pidj/Citation/9000/COVID_19_in_the_Pediatric_Population_Admitted_to_a.96177.aspx) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32404791?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32404791?tool=bestpractice.bmj.com)
14. Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. *JAMA*. 2020 Apr 14;323(14):1335. [Full text \(https://jamanetwork.com/journals/jama/fullarticle/2763401\)](https://jamanetwork.com/journals/jama/fullarticle/2763401) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32181795?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32181795?tool=bestpractice.bmj.com)
15. Tagarro A, Epalza C, Santos M, et al. Screening and severity of coronavirus disease 2019 (COVID-19) in children in Madrid, Spain. *JAMA Pediatr*. 2020 Apr 8 [Epub ahead of print]. [Full text \(https://jamanetwork.com/journals/jamapediatrics/fullarticle/2764394\)](https://jamanetwork.com/journals/jamapediatrics/fullarticle/2764394) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32267485?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32267485?tool=bestpractice.bmj.com)
16. American Academy of Pediatrics. Children and COVID-19: state-level data report. 2021 [internet publication]. [Full text \(https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report\)](https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report)
17. Li B, Zhang S, Zhang R, et al. Epidemiological and clinical characteristics of COVID-19 in children: a systematic review and meta-analysis. *Front Pediatr*. 2020 Nov 2;8:591132. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7667131\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7667131) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33224909?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33224909?tool=bestpractice.bmj.com)
18. Castagnoli R, Votto M, Licari A, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. *JAMA Pediatr*. 2020 Sep 1;174(9):882-9. [Full text \(https://jamanetwork.com/journals/jamapediatrics/fullarticle/2765169\)](https://jamanetwork.com/journals/jamapediatrics/fullarticle/2765169) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32320004?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32320004?tool=bestpractice.bmj.com)
19. Swann OV, Holden KA, Turtle L, et al. Clinical characteristics of children and young people admitted to hospital with covid-19 in United Kingdom: prospective multicentre observational cohort study. *BMJ*. 2020 Aug 27;370:m3249. [Full text \(https://www.bmj.com/content/370/bmj.m3249\)](https://www.bmj.com/content/370/bmj.m3249) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32960186?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32960186?tool=bestpractice.bmj.com)

20. Bailey LC, Razzaghi H, Burrows EK, et al. Assessment of 135,794 pediatric patients tested for severe acute respiratory syndrome coronavirus 2 across the United States. *JAMA Pediatr.* 2021 Feb 1;175(2):176-84. [Full text \(https://jamanetwork.com/journals/jamapediatrics/fullarticle/2773298\)](https://jamanetwork.com/journals/jamapediatrics/fullarticle/2773298) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33226415?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33226415?tool=bestpractice.bmj.com)
21. Leidman E, Duca LM, Omura JD, et al. COVID-19 trends among persons aged 0-24 years: United States, March 1-December 12, 2020. *MMWR Morb Mortal Wkly Rep.* 2021 Jan 22;70(3):88-94. [Full text \(https://www.cdc.gov/mmwr/volumes/70/wr/mm7003e1.htm?s_cid=mm7003e1_w\)](https://www.cdc.gov/mmwr/volumes/70/wr/mm7003e1.htm?s_cid=mm7003e1_w) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33476314?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33476314?tool=bestpractice.bmj.com)
22. Kitano T, Kitano M, Krueger C, et al. The differential impact of pediatric COVID-19 between high-income countries and low- and middle-income countries: a systematic review of fatality and ICU admission in children worldwide. *PLoS One.* 2021 Jan 29;16(1):e0246326. [Full text \(https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0246326\)](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0246326) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33513204?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33513204?tool=bestpractice.bmj.com)
23. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ.* 2020 Sep 1;370:m3320. [Full text \(https://www.bmj.com/content/370/bmj.m3320\)](https://www.bmj.com/content/370/bmj.m3320) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32873575?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32873575?tool=bestpractice.bmj.com)
24. Allotey J, Stallings E, Bonet M, et al. Update to living systematic review on covid-19 in pregnancy. *BMJ.* 2021 Mar 10;372:n615. [Full text \(https://www.bmj.com/content/372/bmj.n615\)](https://www.bmj.com/content/372/bmj.n615) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33692025?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33692025?tool=bestpractice.bmj.com)
25. Khalil A, Kalafat E, Benlioglu C, et al. SARS-CoV-2 infection in pregnancy: a systematic review and meta-analysis of clinical features and pregnancy outcomes. *EClinicalMedicine.* 2020 Aug;25:100446. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7334039\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7334039) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32838230?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32838230?tool=bestpractice.bmj.com)
26. Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. *BMJ.* 2020 Jun 8;369:m2107. [Full text \(https://www.bmj.com/content/369/bmj.m2107\)](https://www.bmj.com/content/369/bmj.m2107) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32513659?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32513659?tool=bestpractice.bmj.com)
27. Centers for Disease Control and Prevention. Data on COVID-19 during pregnancy. 2021 [internet publication]. [Full text \(https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/special-populations/pregnancy-data-on-covid-19.html\)](https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/special-populations/pregnancy-data-on-covid-19.html)
28. Zambrano LD, Ellington S, Strid P, et al. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status: United States, January 22–October 3, 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Nov 6;69(44):1641-7. [Full text \(https://www.cdc.gov/mmwr/volumes/69/wr/mm6944e3.htm\)](https://www.cdc.gov/mmwr/volumes/69/wr/mm6944e3.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33151921?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33151921?tool=bestpractice.bmj.com)
29. World Health Organization. Prevention, identification and management of health worker infection in the context of COVID-19. 2020 [internet publication]. [Full text \(https://www.who.int/publications/i/item/10665-336265\)](https://www.who.int/publications/i/item/10665-336265)

30. Chou R, Dana T, Buckley DI, et al. Epidemiology of and risk factors for coronavirus infection in health care workers: a living rapid review. *Ann Intern Med*. 2020 Jul 21;173(2):120-36. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7240841\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7240841) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32369541?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32369541?tool=bestpractice.bmj.com)
31. Chou R, Dana T, Buckley DI, et al. Update alert 9: epidemiology of and risk factors for coronavirus infection in health care workers. *Ann Intern Med*. 2021 Jun 1 [Epub ahead of print]. [Full text \(https://www.acpjournals.org/doi/10.7326/L21-0302\)](https://www.acpjournals.org/doi/10.7326/L21-0302) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34058107?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34058107?tool=bestpractice.bmj.com)
32. CDC COVID-19 Response Team. Characteristics of health care personnel with COVID-19: United States, February 12 –April 9, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Apr 17;69(15):477-81. [Full text \(https://www.doi.org/10.15585/mmwr.mm6915e6\)](https://www.doi.org/10.15585/mmwr.mm6915e6) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32298247?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32298247?tool=bestpractice.bmj.com)
33. Ren LL, Wang YM, Wu ZQ, et al. Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study. *Chin Med J (Engl)*. 2020 May 5;133(9):1015-24. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7147275\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7147275) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32004165?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32004165?tool=bestpractice.bmj.com)
34. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020 Feb 20;382(8):727-33. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2001017\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2001017) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/31978945?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/31978945?tool=bestpractice.bmj.com)
35. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*. 2020 Feb 22;395(10224):565-74. [Full text \(https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30251-8/fulltext\)](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30251-8/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32007145?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32007145?tool=bestpractice.bmj.com)
36. Nyberg T, Twohig KA, Harris RJ, et al. Risk of hospital admission for patients with SARS-CoV-2 variant B.1.1.7: cohort analysis. *BMJ*. 2021 Jun 15;373:n1412. [Full text \(https://www.bmj.com/content/373/bmj.n1412\)](https://www.bmj.com/content/373/bmj.n1412) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34130987?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34130987?tool=bestpractice.bmj.com)
37. Bager P, Wohlfahrt J, Fonager J, et al. Risk of hospitalisation associated with infection with SARS-CoV-2 lineage B.1.1.7 in Denmark: an observational cohort study. *Lancet Infect Dis*. 2021 Jun 22 [Epub ahead of print]. [Full text \(https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00290-5/fulltext\)](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00290-5/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34171231?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34171231?tool=bestpractice.bmj.com)
38. Patone M, Thomas K, Hatch R, et al. Mortality and critical care unit admission associated with the SARS-CoV-2 lineage B.1.1.7 in England: an observational cohort study. *Lancet Infect Dis*. 2021 Jun 22 [Epub ahead of print]. [Full text \(https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00318-2/fulltext\)](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00318-2/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34171232?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34171232?tool=bestpractice.bmj.com)
39. Graham MS, Sudre CH, May A, et al. Changes in symptomatology, reinfection, and transmissibility associated with the SARS-CoV-2 variant B.1.1.7: an ecological study. *Lancet Public Health*. 2021

- May;6(5):e335-45. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8041365>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33857453?tool=bestpractice.bmj.com>)
40. Public Health England. Investigation of novel SARS-CoV-2 variants of concern. 2021 [internet publication]. Full text (<https://www.gov.uk/government/publications/investigation-of-novel-sars-cov-2-variant-variant-of-concern-20201201>)
 41. Scientific Advisory Group for Emergencies. NERVTAG: update note on B.1.1.7 severity, 11 February 2021. 2021 [internet publication]. Full text (<https://www.gov.uk/government/publications/nervtag-update-note-on-b117-severity-11-february-2021>)
 42. Challen R, Brooks-Pollock E, Read JM, et al. Risk of mortality in patients infected with SARS-CoV-2 variant of concern 202012/1: matched cohort study. BMJ. 2021 Mar 9;372:n579. Full text (<https://www.bmj.com/content/372/bmj.n579>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33687922?tool=bestpractice.bmj.com>)
 43. GISAID. UK reports new variant, termed VUI 202012/01. 2021 [internet publication]. Full text (<https://www.gisaid.org/references/gisaid-in-the-news/uk-reports-new-variant-termed-vui-20201201>)
 44. Edara VV, Lai L, Sahoo MK, et al. Infection and vaccine-induced neutralizing antibody responses to the SARS-CoV-2 B.1.617.1 variant. bioRxiv. 2021 May 10 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8132229>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34013272?tool=bestpractice.bmj.com>)
 45. Lopez Bernal J, Andrews N, Gower C, et al; medRxiv. Effectiveness of COVID-19 vaccines against the B.1.617.2 variant. 2021 [internet publication]. Full text (<https://www.medrxiv.org/content/10.1101/2021.05.22.21257658v1>)
 46. Stowe J, Andrews N, Gower C, et al; Public Health England. Effectiveness of COVID-19 vaccines against hospital admission with the Delta (B.1.617.2) variant. 2021 [internet publication]. Full text (https://khub.net/web/phe-national/public-library/-/document_library/v2WsRK3ZIEig/view_file/479607329)
 47. Sheikh A, McMenamin J, Taylor B, et al. SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. Lancet. 2021 Jun 14 [Epub ahead of print]. Full text ([https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)01358-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01358-1/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34139198?tool=bestpractice.bmj.com>)
 48. Centers for Disease Control and Prevention. SARS-CoV-2 variant classifications and definitions. 2021 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance/variant-info.html>)
 49. Martin Webb L, Matzinger S, Grano C, et al. Identification of and surveillance for the SARS-CoV-2 variants B.1.427 and B.1.429: Colorado, January–March 2021. MMWR Morb Mortal Wkly Rep. 2021 May 14;70(19):717-8. Full text (<https://www.cdc.gov/mmwr/volumes/70/wr/mm7019e2.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33988184?tool=bestpractice.bmj.com>)
 50. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb 15;395(10223):497-506. Full text (<https://www.thelancet.com/>)

- journals/lancet/article/PIIS0140-6736(20)30183-5/fulltext) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/31986264?tool=bestpractice.bmj.com>)
51. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020 Feb 15;395(10223):507-13. Full text ([https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30211-7/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30211-7/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32007143?tool=bestpractice.bmj.com>)
 52. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. 2020 Mar 26;382(13):1199-207. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMoa2001316>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/31995857?tool=bestpractice.bmj.com>)
 53. Paraskevis D, Kostaki EG, Magiorkinis G, et al. Full-genome evolutionary analysis of the novel coronavirus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event. *Infect Genet Evol*. 2020 Jan 29;79:104212. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32004758?tool=bestpractice.bmj.com>)
 54. Ji W, Wang W, Zhao X, et al. Cross-species transmission of the newly identified coronavirus 2019-nCoV. *J Med Virol*. 2020 Apr;92(4):433-40. Full text (<https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.25682>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/31967321?tool=bestpractice.bmj.com>)
 55. Zhang T, Wu Q, Zhang Z. Probable pangolin origin of SARS-CoV-2 associated with the COVID-19 outbreak. *Curr Biol*. 2020 Apr 6;30(7):1346-51. Full text ([https://www.cell.com/current-biology/fulltext/S0960-9822\(20\)30360-2?_returnURL](https://www.cell.com/current-biology/fulltext/S0960-9822(20)30360-2?_returnURL)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32197085?tool=bestpractice.bmj.com>)
 56. Lam TT, Shum MH, Zhu HC, et al. Identifying SARS-CoV-2 related coronaviruses in Malayan pangolins. *Nature*. 2020 Jul;583(7815):282-5. Full text (https://www.nature.com/articles/s41586-020-2169-0_reference.pdf) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32218527?tool=bestpractice.bmj.com>)
 57. Mallapaty S. Animal source of the coronavirus continues to elude scientists. *Nature*. 2020 May 18 [Epub ahead of print]. Full text (<https://www.nature.com/articles/d41586-020-01449-8>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32427902?tool=bestpractice.bmj.com>)
 58. Oreshkova N, Molenaar RJ, Vreman S, et al. SARS-CoV-2 infection in farmed minks, the Netherlands, April and May 2020. *Euro Surveill*. 2020 Jun;25(23):32553059. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7403642>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32553059?tool=bestpractice.bmj.com>)
 59. World Health Organization. WHO-convened global study of the origins of SARS-CoV-2. 2020 [internet publication]. Full text (<https://www.who.int/publications/m/item/who-convened-global-study-of-the-origins-of-sars-cov-2>)
 60. Roberts DL, Rossman JS, Jarić I. Dating first cases of COVID-19. *PLoS Pathog*. 2021 Jun;17(6):e1009620. Full text (<https://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1009620>)

journal.ppat.1009620) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34166465?tool=bestpractice.bmj.com>)

61. Meyerowitz EA, Richterman A, Gandhi RT, et al. Transmission of SARS-CoV-2: a review of viral, host, and environmental factors. *Ann Intern Med*. 2021 Jan;174(1):69-79. Full text (<https://www.acpjournals.org/doi/10.7326/M20-5008>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32941052?tool=bestpractice.bmj.com>)
62. World Health Organization. Transmission of SARS-CoV-2: implications for infection prevention precautions – scientific brief. 2020 [internet publication]. Full text (<https://www.who.int/publications/i/item/modes-of-transmission-of-virus-causing-covid-19-implications-for-ipc-precaution-recommendations>)
63. Centers for Disease Control and Prevention. How COVID-19 spreads. 2020 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covid-spreads.html>)
64. Birgand G, Peiffer-Smadja N, Fournier S, et al. Assessment of air contamination by SARS-CoV-2 in hospital settings. *JAMA Netw Open*. 2020 Dec 1;3(12):e2033232. Full text (<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2774463>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33355679?tool=bestpractice.bmj.com>)
65. Razani N, Malekinejad M, Rutherford GW. Clarification regarding outdoor transmission of SARS-CoV-2 and other respiratory viruses, a systematic review. *J Infect Dis*. 2021 Jun 4 [Epub ahead of print]. Full text (<https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab298/6291889>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34086941?tool=bestpractice.bmj.com>)
66. Goldstein KM, Ghadimi K, Mystakelis H, et al. Risk of transmitting coronavirus disease 2019 during nebulizer treatment: a systematic review. *J Aerosol Med Pulm Drug Deliv*. 2021 Apr 21 [Epub ahead of print]. Full text (<https://www.liebertpub.com/doi/10.1089/jamp.2020.1659?url>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33887156?tool=bestpractice.bmj.com>)
67. Onakpoya IJ, Heneghan CJ, Spencer EA, et al. SARS-CoV-2 and the role of fomite transmission: a systematic review. *F1000Res*. 2021 Mar 24;10:233. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8176266>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34136133?tool=bestpractice.bmj.com>)
68. van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N Engl J Med*. 2020 Apr 16;382(16):1564-7. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMc2004973>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32182409?tool=bestpractice.bmj.com>)
69. van Doorn AS, Meijer B, Frampton CMA, et al. Systematic review with meta-analysis: SARS-CoV-2 stool testing and the potential for faecal-oral transmission. *Aliment Pharmacol Ther*. 2020 Oct;52(8):1276-88. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7461227>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32852082?tool=bestpractice.bmj.com>)
70. Zhang W, Du RH, Li B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerg Microbes Infect*. 2020 Dec;9(1):386-9.

- Full text (<https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1729071>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32065057?tool=bestpractice.bmj.com>)
71. To KK, Tsang OT, Chik-Yan Yip C, et al. Consistent detection of 2019 novel coronavirus in saliva. *Clin Infect Dis*. 2020 Jul 28;71(15):841-3. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7108139>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32047895?tool=bestpractice.bmj.com>)
 72. Centre for Evidence-Based Medicine; Ferner RE, Murray PI, Aronson JK. Spreading SARS-CoV-2 through ocular fluids. 2020 [internet publication]. Full text (<https://www.cebm.net/spreading-sars-cov-2-through-ocular-fluids>)
 73. Lewis A, Frontera J, Placantonakis DG, et al. Cerebrospinal fluid in COVID-19: a systematic review of the literature. *J Neurol Sci*. 2021 Jan 10;421:117316. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7833669>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33561753?tool=bestpractice.bmj.com>)
 74. Seah IYJ, Anderson DE, Kang AEZ, et al. Assessing viral shedding and infectivity of tears in coronavirus disease 2019 (COVID-19) patients. *Ophthalmology*. 2020 Jul;127(7):977-9. Full text ([https://www.aaojournal.org/article/S0161-6420\(20\)30311-0/pdf](https://www.aaojournal.org/article/S0161-6420(20)30311-0/pdf)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32291098?tool=bestpractice.bmj.com>)
 75. Farina A, Uccello G, Spreafico M, et al. SARS-CoV-2 detection in the pericardial fluid of a patient with cardiac tamponade. *Eur J Intern Med*. 2020 Jun;76:100-1. Full text ([https://www.ejinme.com/article/S0953-6205\(20\)30166-7/pdf](https://www.ejinme.com/article/S0953-6205(20)30166-7/pdf)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32359887?tool=bestpractice.bmj.com>)
 76. Algarroba GN, Rekawek P, Vahanian SA, et al. Visualization of severe acute respiratory syndrome coronavirus 2 invading the human placenta using electron microscopy. *Am J Obstet Gynecol*. 2020 Aug;223(2):275-8. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7219376>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32405074?tool=bestpractice.bmj.com>)
 77. Mei F, Bonifazi M, Menzo S, et al. First detection of SARS-CoV-2 by real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay in pleural fluid. *Chest*. 2020 Oct;158(4):e143-6. Full text ([https://journal.chestnet.org/article/S0012-3692\(20\)31660-3/pdf](https://journal.chestnet.org/article/S0012-3692(20)31660-3/pdf)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32534909?tool=bestpractice.bmj.com>)
 78. Kashi AH, De la Rosette J, Amini E, et al. Urinary viral shedding of COVID-19 and its clinical associations: a systematic review and meta-analysis of observational studies. *Urol J*. 2020 Sep 5;17(5):433-41. Full text (<https://journals.sbmu.ac.ir/urolj/index.php/uj/article/view/6248/3994>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32888186?tool=bestpractice.bmj.com>)
 79. Frazier KM, Hooper JE, Mostafa HH, et al. SARS-CoV-2 virus isolated from the mastoid and middle ear: implications for COVID-19 precautions during ear surgery. *JAMA Otolaryngol Head Neck Surg*. 2020 Jul 23;146(10):964-6. Full text (<https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2768621>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32701126?tool=bestpractice.bmj.com>)
 80. Yan Y, Diao B, Liu Y, et al. Severe acute respiratory syndrome coronavirus 2 nucleocapsid protein in the ocular tissues of a patient previously infected with coronavirus disease 2019.

JAMA Ophthalmol. 2020 Oct 8;138(11):1-4. Full text (<https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2771320>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33034620?tool=bestpractice.bmj.com>)

81. Gonzalez DC, Khodamoradi K, Pai R, et al. A systematic review on the investigation of SARS-CoV-2 in semen. Res Rep Urol. 2020 Dec 1;12:615-21. Full text (<https://www.dovepress.com/a-systematic-review-on-the-investigation-of-sars-cov-2-in-semen-peer-reviewed-fulltext-article-RRU>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33294423?tool=bestpractice.bmj.com>)
82. Casagrande M, Fitzek A, Spitzer MS, et al. Presence of SARS-CoV-2 RNA in the cornea of viremic patients with COVID-19. JAMA Ophthalmol. 2021 Apr 1;139(4):383-8. Full text (<https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2775161>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33475692?tool=bestpractice.bmj.com>)
83. Tur-Kaspa I, Tur-Kaspa T, Hildebrand G, et al. COVID-19 may affect male fertility but is not sexually transmitted: a systematic review. F S Rev. 2021 Apr;2(2):140-9. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7857030>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33558864?tool=bestpractice.bmj.com>)
84. World Health Organization. Definition and categorization of the timing of mother-to-child transmission of SARS-CoV-2: scientific brief. 2021 [internet publication]. Full text (<https://www.who.int/publications/item/WHO-2019-nCoV-mother-to-child-transmission-2021.1>)
85. Bwire GM, Njiro BJ, Mwakawanga DL, et al. Possible vertical transmission and antibodies against SARS-CoV-2 among infants born to mothers with COVID-19: a living systematic review. J Med Virol. 2021 Mar;93(3):1361-9. Full text (<https://onlinelibrary.wiley.com/doi/10.1002/jmv.26622>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33090535?tool=bestpractice.bmj.com>)
86. Walker KF, O'Donoghue K, Grace N, et al. Maternal transmission of SARS-COV-2 to the neonate, and possible routes for such transmission: a systematic review and critical analysis. BJOG. 2020 Oct;127(11):1324-36. Full text (<https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1111/1471-0528.16362>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32531146?tool=bestpractice.bmj.com>)
87. Zhu F, Zozaya C, Zhou Q, et al. SARS-CoV-2 genome and antibodies in breastmilk: a systematic review and meta-analysis. Arch Dis Child Fetal Neonatal Ed. 2021 Feb 10 [Epub ahead of print]. Full text (<https://fn.bmj.com/content/early/2021/02/09/archdischild-2020-321074.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33568494?tool=bestpractice.bmj.com>)
88. Salvatore CM, Han JY, Acker KP, et al. Neonatal management and outcomes during the COVID-19 pandemic: an observation cohort study. Lancet Child Adolesc Health. 2020 Oct;4(10):721-7. Full text ([https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(20\)30235-2/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30235-2/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32711687?tool=bestpractice.bmj.com>)
89. Zhou Q, Gao Y, Wang X, et al. Nosocomial infections among patients with COVID-19, SARS and MERS: a rapid review and meta-analysis. Ann Transl Med. 2020 May;8(10):629. Full text (<http://atm.amegroups.com/article/view/42877/html>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32566566?tool=bestpractice.bmj.com>)

90. Centre for Evidence-Based Medicine; Heneghan C, Howdon D, Oke J, et al. The ongoing problem of UK hospital acquired infections. 2020 [internet publication]. [Full text \(https://www.cebm.net/covid-19/the-ongoing-problem-of-hospital-acquired-infections-across-the-uk\)](https://www.cebm.net/covid-19/the-ongoing-problem-of-hospital-acquired-infections-across-the-uk)
91. Rhee C, Baker M, Vaidya V, et al. Incidence of nosocomial COVID-19 in patients hospitalized at a large US academic medical center. *JAMA Netw Open*. 2020 Sep 1;3(9):e2020498. [Full text \(https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770287\)](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770287) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32902653?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32902653?tool=bestpractice.bmj.com)
92. World Health Organization. Mask use in the context of COVID-19: interim guidance. 2020 [internet publication]. [Full text \(https://www.who.int/publications-detail/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-\(2019-ncov\)-outbreak\)](https://www.who.int/publications-detail/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak)
93. Tong ZD, Tang A, Li KF, et al. Potential presymptomatic transmission of SARS-CoV-2, Zhejiang province, China, 2020. *Emerg Infect Dis*. 2020 May 17;26(5). [Full text \(https://wwwnc.cdc.gov/eid/article/26/5/20-0198_article\)](https://wwwnc.cdc.gov/eid/article/26/5/20-0198_article) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32091386?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32091386?tool=bestpractice.bmj.com)
94. Wei WE, Li Z, Chiew CJ, et al. Presymptomatic transmission of SARS-CoV-2: Singapore, January 23 - March 16, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Apr 10;69(14):411-5. [Full text \(https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e1.htm?s_cid=mm6914e1_w\)](https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e1.htm?s_cid=mm6914e1_w) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32271722?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32271722?tool=bestpractice.bmj.com)
95. Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *N Engl J Med*. 2020 Mar 5;382(10):970-71. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMc2001468\)](https://www.nejm.org/doi/full/10.1056/NEJMc2001468) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32003551?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32003551?tool=bestpractice.bmj.com)
96. Hu Z, Song C, Xu C, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. *Sci China Life Sci*. 2020 May;63(5):706-11. [Full text \(https://link.springer.com/content/pdf/10.1007/s11427-020-1661-4.pdf\)](https://link.springer.com/content/pdf/10.1007/s11427-020-1661-4.pdf) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32146694?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32146694?tool=bestpractice.bmj.com)
97. Luo SH, Liu W, Liu ZJ, et al. A confirmed asymptomatic carrier of 2019 novel coronavirus (SARS-CoV-2). *Chin Med J (Engl)*. 2020 May 5;133(9):1123-5. [Full text \(https://journals.lww.com/cmj/Citation/publishahead/A_confirmed_asymptomatic_carrier_of_2019_novel.99353.aspx\)](https://journals.lww.com/cmj/Citation/publishahead/A_confirmed_asymptomatic_carrier_of_2019_novel.99353.aspx) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32149768?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32149768?tool=bestpractice.bmj.com)
98. Lu S, Lin J, Zhang Z, et al. Alert for non-respiratory symptoms of coronavirus disease 2019 patients in epidemic period: a case report of familial cluster with three asymptomatic COVID-19 patients. *J Med Virol*. 2021 Jan;93(1):518-21. [Full text \(https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.25776\)](https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.25776) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32190904?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32190904?tool=bestpractice.bmj.com)
99. Li C, Ji F, Wang L, et al. Asymptomatic and human-to-human transmission of SARS-CoV-2 in a 2-family cluster, Xuzhou, China. *Emerg Infect Dis*. 2020 Mar 31;26(7). [Full text \(https://wwwnc.cdc.gov/eid/article/26/7/20-0718_article\)](https://wwwnc.cdc.gov/eid/article/26/7/20-0718_article) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32228809?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32228809?tool=bestpractice.bmj.com)

100. Liu J, Huang J, Xiang D. Large SARS-CoV-2 outbreak caused by asymptomatic traveler, China. *Emerg Infect Dis*. 2020 Jun 30;29(9). [Full text \(https://wwwnc.cdc.gov/eid/article/26/9/20-1798_article\)](https://wwwnc.cdc.gov/eid/article/26/9/20-1798_article) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32603652?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32603652?tool=bestpractice.bmj.com)
101. Jiang XL, Zhang XL, Zhao XN, et al. Transmission potential of asymptomatic and paucisymptomatic severe acute respiratory syndrome coronavirus 2 infections: a three-family cluster study in China. 2020 Jun 11;221(12):1948-52. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7188140\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7188140) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32319519?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32319519?tool=bestpractice.bmj.com)
102. Luo L, Liu D, Liao X, et al. Contact settings and risk for transmission in 3410 close contacts of patients with COVID-19 in Guangzhou, China: a prospective cohort study. *Ann Intern Med*. 2020 Dec 1;173(11):879-87. [Full text \(https://www.acpjournals.org/doi/10.7326/M20-2671\)](https://www.acpjournals.org/doi/10.7326/M20-2671) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32790510?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32790510?tool=bestpractice.bmj.com)
103. Gao M, Yang L, Chen X, et al. A study on infectivity of asymptomatic SARS-CoV-2 carriers. *Respir Med*. 2020 May 13;169:106026. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7219423\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7219423) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32405162?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32405162?tool=bestpractice.bmj.com)
104. Chen F, Fu D, Yang Q, et al. Low transmission risk of 9 asymptomatic carriers tested positive for both SARS-CoV-2 nucleic acid and serum IgG. *J Infect*. 2020 Sep;81(3):452-82. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7299860\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7299860) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32562791?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32562791?tool=bestpractice.bmj.com)
105. Danis K, Epaulard O, Bénet T, et al. Cluster of coronavirus disease 2019 (Covid-19) in the French Alps, 2020. *Clin Infect Dis*. 2020 Jul 28;71(15):825-32. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7184384\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7184384) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32277759?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32277759?tool=bestpractice.bmj.com)
106. Cao S, Gan Y, Wang C, et al. Post-lockdown SARS-CoV-2 nucleic acid screening in nearly ten million residents of Wuhan, China. *Nat Commun*. 2020 Nov 20;11(1):5917. [Full text \(https://www.nature.com/articles/s41467-020-19802-w\)](https://www.nature.com/articles/s41467-020-19802-w) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33219229?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33219229?tool=bestpractice.bmj.com)
107. He J, Guo Y, Mao R, et al. Proportion of asymptomatic coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *J Med Virol*. 2021 Feb;93(2):820-30. [Full text \(https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.26326\)](https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.26326) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32691881?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32691881?tool=bestpractice.bmj.com)
108. Buitrago-Garcia D, Egli-Gany D, Counotte MJ, et al. Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: a living systematic review and meta-analysis. *PLoS Med*. 2020 Sep;17(9):e1003346. [Full text \(https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003346\)](https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003346) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32960881?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32960881?tool=bestpractice.bmj.com)
109. Byambasuren O, Cardona M, Bell K, et al. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis. *JAMMI*. 2020 Dec;5(4):223-34. [Full text \(https://jammi.utpjournals.press/doi/10.3138/jammi-2020-0030\)](https://jammi.utpjournals.press/doi/10.3138/jammi-2020-0030)

110. Oran DP, Topol EJ. The proportion of SARS-CoV-2 infections that are asymptomatic: a systematic review. *Ann Intern Med.* 2021 May;174(5):655-62. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7839426\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7839426) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33481642?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33481642?tool=bestpractice.bmj.com)
111. Alene M, Yismaw L, Assemie MA, et al. Magnitude of asymptomatic COVID-19 cases throughout the course of infection: A systematic review and meta-analysis. *PLoS One.* 2021;16(3):e0249090. [Full text \(https://www.doi.org/10.1371/journal.pone.0249090\)](https://www.doi.org/10.1371/journal.pone.0249090) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33755688?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33755688?tool=bestpractice.bmj.com)
112. Stubblefield WB, Talbot HK, Feldstein L, et al. Seroprevalence of SARS-CoV-2 among frontline healthcare personnel during the first month of caring for patients with COVID-19: Nashville, Tennessee. *Clin Infect Dis.* 2021 May 4;72(9):1645-8. [Full text \(https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa936/5868028\)](https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa936/5868028) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32628750?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32628750?tool=bestpractice.bmj.com)
113. Vahidy FS, Bernard DW, Boom ML, et al. Prevalence of SARS-CoV-2 infection among asymptomatic health care workers in the Greater Houston, Texas, area. *JAMA Netw Open.* 2020 Jul 1;3(7):e2016451. [Full text \(https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2768707\)](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2768707) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32716512?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32716512?tool=bestpractice.bmj.com)
114. Qiu H, Wu J, Hong L, et al. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. *Lancet Infect Dis.* 2020 Jun;20(6):689-96. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7158906\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7158906) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32220650?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32220650?tool=bestpractice.bmj.com)
115. Zheng B, Wang H, Yu C. An increasing public health burden arising from children infected with SARS-CoV2: a systematic review and meta-analysis. *Pediatr Pulmonol.* 2020 Dec;55(12):3487-96. [Full text \(https://onlinelibrary.wiley.com/doi/10.1002/ppul.25008\)](https://onlinelibrary.wiley.com/doi/10.1002/ppul.25008) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32757374?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32757374?tool=bestpractice.bmj.com)
116. Milani GP, Bottino I, Rocchi A, et al. Frequency of children vs adults carrying severe acute respiratory syndrome coronavirus 2 asymptomatically. *JAMA Pediatr.* 2021 Feb 1;175(2):193-4. [Full text \(https://jamanetwork.com/journals/jamapediatrics/fullarticle/2770117\)](https://jamanetwork.com/journals/jamapediatrics/fullarticle/2770117) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32926119?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32926119?tool=bestpractice.bmj.com)
117. Tönshoff B, Müller B, Elling R, et al. Prevalence of SARS-CoV-2 infection in children and their parents in Southwest Germany. *JAMA Pediatr.* 2021 Jan 22 [Epub ahead of print]. [Full text \(https://jamanetwork.com/journals/jamapediatrics/fullarticle/2775656\)](https://jamanetwork.com/journals/jamapediatrics/fullarticle/2775656) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33480966?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33480966?tool=bestpractice.bmj.com)
118. Frieden TR, Lee CT. Identifying and interrupting superspreading events: implications for control of severe acute respiratory syndrome coronavirus 2. *Emerg Infect Dis.* 2020 Jun;26(6):1059-66. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7258476\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7258476) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32187007?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32187007?tool=bestpractice.bmj.com)
119. Schwartz NG, Moorman AC, Makaretz A, et al. Adolescent with COVID-19 as the source of an outbreak at a 3-week family gathering: four states, June–July 2020. *MMWR Morb Mortal Wkly Rep.*

2020 Oct 9;69(40):1457-59. [Full text \(https://www.cdc.gov/mmwr/volumes/69/wr/mm6940e2.htm\)](https://www.cdc.gov/mmwr/volumes/69/wr/mm6940e2.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33031365?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33031365?tool=bestpractice.bmj.com)

120. Atrubin D, Wiese M, Bohinc B. An outbreak of COVID-19 associated with a recreational hockey game: Florida, June 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Oct 16;69(41):1492-3. [Full text \(https://www.cdc.gov/mmwr/volumes/69/wr/mm6941a4.htm\)](https://www.cdc.gov/mmwr/volumes/69/wr/mm6941a4.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33056952?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33056952?tool=bestpractice.bmj.com)
121. Pray IW, Gibbons-Burgener SN, Rosenberg AZ, et al. COVID-19 outbreak at an overnight summer school retreat: Wisconsin, July-August 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Oct 30;69(43):1600-4. [Full text \(https://www.cdc.gov/mmwr/volumes/69/wr/mm6943a4.htm\)](https://www.cdc.gov/mmwr/volumes/69/wr/mm6943a4.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33119558?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33119558?tool=bestpractice.bmj.com)
122. Ali H, Kondapally K, Pordell P, et al. COVID-19 outbreak in an Amish community: Ohio, May 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Nov 13;69(45):1671-4. [Full text \(https://www.cdc.gov/mmwr/volumes/69/wr/mm6945a2.htm\)](https://www.cdc.gov/mmwr/volumes/69/wr/mm6945a2.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33180753?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33180753?tool=bestpractice.bmj.com)
123. McMichael TM, Clark S, Pogosjans S, et al. COVID-19 in a long-term care facility: King County, Washington, February 27 – March 9, 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Mar 27;69(12):339-42. [Full text \(https://www.cdc.gov/mmwr/volumes/69/wr/mm6912e1.htm?s_cid=mm6912e1_w\)](https://www.cdc.gov/mmwr/volumes/69/wr/mm6912e1.htm?s_cid=mm6912e1_w) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32214083?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32214083?tool=bestpractice.bmj.com)
124. Moriarty LF, Plucinski MM, Marston BJ, et al. Public health responses to COVID-19 outbreaks on cruise ships: worldwide, February-March 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Mar 27;69(12):347-52. [Full text \(https://www.cdc.gov/mmwr/volumes/69/wr/mm6912e3.htm?s_cid=mm6912e3_w\)](https://www.cdc.gov/mmwr/volumes/69/wr/mm6912e3.htm?s_cid=mm6912e3_w) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32214086?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32214086?tool=bestpractice.bmj.com)
125. Yang H, Thompson JR. Fighting covid-19 outbreaks in prisons. *BMJ.* 2020 Apr 2;369:m1362. [Full text \(https://www.bmj.com/content/369/bmj.m1362.long\)](https://www.bmj.com/content/369/bmj.m1362.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32241756?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32241756?tool=bestpractice.bmj.com)
126. Rogers JH, Link AC, McCulloch D, et al. Characteristics of COVID-19 in homeless shelters: a community-based surveillance study. *Ann Intern Med.* 2021 Jan;174(1):42-9. [Full text \(https://www.acpjournals.org/doi/10.7326/M20-3799\)](https://www.acpjournals.org/doi/10.7326/M20-3799) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32931328?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32931328?tool=bestpractice.bmj.com)
127. Centre for Evidence-Based Medicine; Durand-Moreau Q, Adisesh A, Mackenzie G, et al. What explains the high rate of SARS-CoV-2 transmission in meat and poultry facilities? 2020 [internet publication]. [Full text \(https://www.cebm.net/covid-19/what-explains-the-high-rate-of-sars-cov-2-transmission-in-meat-and-poultry-facilities\)](https://www.cebm.net/covid-19/what-explains-the-high-rate-of-sars-cov-2-transmission-in-meat-and-poultry-facilities)
128. Donahue M, Sreenivasan N, Stover D, et al. Notes from the field: characteristics of meat processing facility workers with confirmed SARS-CoV-2 infection – Nebraska, April-May 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Aug 7;69(31):1020-2. [Full text \(https://www.cdc.gov/mmwr/\)](https://www.cdc.gov/mmwr/)

- volumes/69/wr/mm6931a3.htm) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32759920?tool=bestpractice.bmj.com>)
129. Steinberg J, Kennedy ED, Basler C, et al. COVID-19 outbreak among employees at a meat processing facility: South Dakota, March–April 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Aug 7;69(31):1015–9. Full text (<https://www.cdc.gov/mmwr/volumes/69/wr/mm6931a2.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32759914?tool=bestpractice.bmj.com>)
 130. Erfani P, Uppal N, Lee CH, et al. COVID-19 testing and cases in immigration detention centers, April–August 2020. *JAMA.* 2021 Jan 12;325(2):182–4. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2772627>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33119038?tool=bestpractice.bmj.com>)
 131. Kennedy BS, Richeson RP, Houde AJ. Risk factors for SARS-CoV-2 in a statewide correctional system. *N Engl J Med.* 2020 Dec 17;383(25):2479–80. Full text (<https://www.nejm.org/doi/10.1056/NEJMc2029354>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33289970?tool=bestpractice.bmj.com>)
 132. Lopez AS, Hill M, Antezano J, et al. Transmission dynamics of COVID-19 outbreaks associated with child care facilities: Salt Lake City, Utah, April–July 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Sep 18;69(37):1319–23. Full text (<https://www.cdc.gov/mmwr/volumes/69/wr/mm6937e3.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32941418?tool=bestpractice.bmj.com>)
 133. Leeb RT, Price S, Sliwa S, et al. COVID-19 trends among school-aged children: United States, March 1–September 19, 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Oct 2;69(39):1410–5. Full text (<https://www.cdc.gov/mmwr/volumes/69/wr/mm6939e2.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33001869?tool=bestpractice.bmj.com>)
 134. Wilson E, Donovan CV, Campbell M, et al. Multiple COVID-19 clusters on a university campus: North Carolina, August 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Oct 2;69(39):1416–8. Full text (<https://www.cdc.gov/mmwr/volumes/69/wr/mm6939e3.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33001871?tool=bestpractice.bmj.com>)
 135. Xu W, Li X, Dozier M, et al. What is the evidence for transmission of COVID-19 by children in schools? A living systematic review. *J Glob Health.* 2020 Dec;10(2):021104. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7774027>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33437465?tool=bestpractice.bmj.com>)
 136. Stein RA. Super-spreaders in infectious diseases. *Int J Infect Dis.* 2011 Aug;15(8):e510–3. Full text ([https://www.ijidonline.com/article/S1201-9712\(11\)00024-5/fulltext](https://www.ijidonline.com/article/S1201-9712(11)00024-5/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/21737332?tool=bestpractice.bmj.com>)
 137. Xin H, Wong JY, Murphy C, et al. The incubation period distribution of coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *Clin Infect Dis.* 2021 Jun 12 [Epub ahead of print]. Full text (<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab501/6297425>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34117868?tool=bestpractice.bmj.com>)
 138. Liu Y, Gayle AA, Wilder-Smith A, et al. The reproductive number of COVID-19 is higher compared to SARS coronavirus. *J Travel Med.* 2020 Mar 13;27(2). Full text (<https://www.ncbi.nlm.nih.gov/>)

[pmc/articles/PMC7074654](https://pubmed.ncbi.nlm.nih.gov/32052846/)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32052846?tool=bestpractice.bmj.com>)

139. Xie Y, Wang Z, Liao H, et al. Epidemiologic, clinical, and laboratory findings of the COVID-19 in the current pandemic: systematic review and meta-analysis. *BMC Infect Dis*. 2020 Aug 31;20(1):640. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7457225>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32867706?tool=bestpractice.bmj.com>)
140. Billah MA, Miah MM, Khan MN. Reproductive number of coronavirus: a systematic review and meta-analysis based on global level evidence. *PLoS One*. 2020 Nov 11;15(11):e0242128. Full text (<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0242128>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33175914?tool=bestpractice.bmj.com>)
141. Ahammed T, Anjum A, Rahman MM, et al. Estimation of novel coronavirus (COVID-19) reproduction number and case fatality rate: a systematic review and meta-analysis. *Health Sci Rep*. 2021 Jun;4(2):e274. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8093857>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33977156?tool=bestpractice.bmj.com>)
142. Centers for Disease Control and Prevention. COVID-19 pandemic planning scenarios. 2021 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html>)
143. Inglesby TV. Public health measures and the reproduction number of SARS-CoV-2. *JAMA*. 2020 Jun 2;323(21):2186-7. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2765665>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32356869?tool=bestpractice.bmj.com>)
144. Hussein M, Toraih E, Elshazli R, et al. Meta-analysis on serial intervals and reproductive rates for SARS-CoV-2. *Ann Surg*. 2021 Mar 1;273(3):416-23. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33214421?tool=bestpractice.bmj.com>)
145. Tian T, Huo X. Secondary attack rates of COVID-19 in diverse contact settings, a meta-analysis. *J Infect Dev Ctries*. 2020 Dec 31;14(12):1361-7. Full text (<https://www.jidc.org/index.php/journal/article/view/13256>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33378276?tool=bestpractice.bmj.com>)
146. Thompson HA, Mousa A, Dighe A, et al. SARS-CoV-2 setting-specific transmission rates: a systematic review and meta-analysis. *Clin Infect Dis*. 2021 Feb 9 [Epub ahead of print]. Full text (<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab100/6131730>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33560412?tool=bestpractice.bmj.com>)
147. Madewell ZJ, Yang Y, Longini IM Jr, et al. Household transmission of SARS-CoV-2: a systematic review and meta-analysis. *JAMA Netw Open*. 2020 Dec 1;3(12):e2031756. Full text (<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2774102>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33315116?tool=bestpractice.bmj.com>)
148. Qiu X, Nergiz AI, Maraolo AE, et al. The role of asymptomatic and pre-symptomatic infection in SARS-CoV-2 transmission: a living systematic review. *Clin Microbiol Infect*. 2021 Apr;27(4):511-9. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7825872>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33484843?tool=bestpractice.bmj.com>)

149. Yung CF, Kam KQ, Chong CY, et al. Household transmission of severe acute respiratory syndrome coronavirus 2 from adults to children. *J Pediatr*. 2020 Oct;225:249-51. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7334921\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7334921) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32634405?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32634405?tool=bestpractice.bmj.com)
150. Macartney K, Quinn HE, Pillsbury AJ, et al. Transmission of SARS-CoV-2 in Australian educational settings: a prospective cohort study. *Lancet Child Adolesc Health*. 2020 Nov;4(11):807-16. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7398658\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7398658) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32758454?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32758454?tool=bestpractice.bmj.com)
151. Cevik M, Tate M, Lloyd O, et al. SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis. *Lancet Microbe*. 2021 Jan;2(1):e13-22. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7837230\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7837230) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33521734?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33521734?tool=bestpractice.bmj.com)
152. Marks M, Millat-Martinez P, Ouchi D, et al. Transmission of COVID-19 in 282 clusters in Catalonia, Spain: a cohort study. *Lancet Infect Dis*. 2021 May;21(5):629-36. [Full text \(https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30985-3/fulltext\)](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30985-3/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33545090?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33545090?tool=bestpractice.bmj.com)
153. Widders A, Broom A, Broom J. SARS-CoV-2: the viral shedding vs infectivity dilemma. *Infect Dis Health*. 2020 Aug;25(3):210-5. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7237903\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7237903) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32473952?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32473952?tool=bestpractice.bmj.com)
154. Xu K, Chen Y, Yuan J, et al. Factors associated with prolonged viral RNA shedding in patients with COVID-19. *Clin Infect Dis*. 2020 Jul 28;71(15):799-806. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7184421\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7184421) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32271376?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32271376?tool=bestpractice.bmj.com)
155. Aydiillo T, Gonzalez-Reiche AS, Aslam S, et al. Shedding of viable SARS-CoV-2 after immunosuppressive therapy for cancer. *N Engl J Med*. 2020 Dec 24;383(26):2586-8. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMc2031670\)](https://www.nejm.org/doi/full/10.1056/NEJMc2031670) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33259154?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33259154?tool=bestpractice.bmj.com)
156. Lancet Respiratory Medicine. COVID-19: pathophysiology of acute disease. 2021 [internet publication]. [Full text \(https://www.thelancet.com/series/COVID-19-pathophysiology\)](https://www.thelancet.com/series/COVID-19-pathophysiology)
157. Peiris S, Mesa H, Aysola A, et al. Pathological findings in organs and tissues of patients with COVID-19: a systematic review. *PLoS One*. 2021;16(4):e0250708. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8081217\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8081217) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33909679?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33909679?tool=bestpractice.bmj.com)
158. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. 2020 Apr 16;181(2):271-80. [Full text \(https://www.sciencedirect.com/science/article/pii/S0092867420302294\)](https://www.sciencedirect.com/science/article/pii/S0092867420302294) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32142651?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32142651?tool=bestpractice.bmj.com)
159. Chen Y, Guo Y, Pan Y, et al. Structure analysis of the receptor binding of 2019-nCoV. *Biochem Biophys Res Commun*. 2020 Feb 17;525(1):135-40. [Full text \(https://www.sciencedirect.com/\)](https://www.sciencedirect.com/)

science/article/pii/S0006291X20303399?via%3Dihub) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32081428?tool=bestpractice.bmj.com>)

160. Coutard B, Valle C, de Lamballerie X, et al. The spike glycoprotein of the new coronavirus 2019-nCoV contains a furin-like cleavage site absent in CoV of the same clade. *Antiviral Res.* 2020 Feb 10;176:104742. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32057769?tool=bestpractice.bmj.com>)
161. Piplani S, Singh PK, Winkler DA, et al. In silico comparison of SARS-CoV-2 spike protein-ACE2 binding affinities across species and implications for virus origin. *Sci Rep.* 2021 Jun 24;11(1):13063. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8225877>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34168168?tool=bestpractice.bmj.com>)
162. Lei Y, Zhang J, Schiavon CR, et al. SARS-CoV-2 spike protein impairs endothelial function via downregulation of ACE 2. *Circ Res.* 2021 Apr 30;128(9):1323-6. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8091897>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33784827?tool=bestpractice.bmj.com>)
163. Suzuki YJ, Gychka SG. SARS-CoV-2 spike protein elicits cell signaling in human host cells: implications for possible consequences of COVID-19 vaccines. *Vaccines (Basel).* 2021 Jan 11;9(1):36. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7827936>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33440640?tool=bestpractice.bmj.com>)
164. Ramanathan M, Ferguson ID, Miao W, et al. SARS-CoV-2 B.1.1.7 and B.1.351 spike variants bind human ACE2 with increased affinity. *bioRxiv.* 2021 Feb 22 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7924271>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33655251?tool=bestpractice.bmj.com>)
165. Osuchowski MF, Winkler MS, Skirecki T, et al. The COVID-19 puzzle: deciphering pathophysiology and phenotypes of a new disease entity. *Lancet Respir Med.* 2021 Jun;9(6):622-42. Full text ([https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00218-6/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00218-6/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33965003?tool=bestpractice.bmj.com>)
166. World Health Organization. Public health surveillance for COVID-19: interim guidance. 2020 [internet publication]. Full text (<https://www.who.int/publications/i/item/who-2019-nCoV-surveillanceguidance-2020.7>)
167. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): contact tracing. 2021 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/contact-tracing.html>)
168. Public Health England. Guidance for investigating and managing individuals with a possible or confirmed SARS-CoV-2 variant of concern. 2021 [internet publication]. Full text (<https://www.gov.uk/government/publications/sars-cov-2-voc-investigating-and-managing-individuals-with-a-possible-or-confirmed-case/guidance-for-investigating-and-managing-individuals-with-a-possible-or-confirmed-sars-cov-2-variant-of-concern>)
169. Pijls BG, Jolani S, Atherley A, et al. Demographic risk factors for COVID-19 infection, severity, ICU admission and death: a meta-analysis of 59 studies. *BMJ Open.* 2021 Jan 11;11(1):e044640. Full

- text (<https://bmjopen.bmj.com/content/11/1/e044640.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33431495?tool=bestpractice.bmj.com>)
170. Centers for Disease Control and Prevention. Risk for COVID-19 infection, hospitalization, and death by age group. 2021 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-age.html>)
 171. de Lusignan S, Dorward J, Correa A, et al. Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: a cross-sectional study. *Lancet Infect Dis*. 2020 Sep;20(9):1034-42. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7228715>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32422204?tool=bestpractice.bmj.com>)
 172. Bonanad C, García-Blas S, Tarazona-Santabalbina F, et al. The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. *J Am Med Dir Assoc*. 2020 Jul;21(7):915-8. Full text ([https://www.jamda.com/article/S1525-8610\(20\)30441-2/pdf](https://www.jamda.com/article/S1525-8610(20)30441-2/pdf)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32674819?tool=bestpractice.bmj.com>)
 173. Singhal S, Kumar P, Singh S, et al. Clinical features and outcomes of COVID-19 in older adults: a systematic review and meta-analysis. *BMC Geriatr*. 2021 May 19;21(1):321. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8133052>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34011269?tool=bestpractice.bmj.com>)
 174. Damayanthi HDWT, Prabani KIP. Nutritional determinants and COVID-19 outcomes of older patients with COVID-19: a systematic review. *Arch Gerontol Geriatr*. 2021 Mar 31;95:104411. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8010373>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33836322?tool=bestpractice.bmj.com>)
 175. Abate BB, Kassie AM, Kassaw MW, et al. Sex difference in coronavirus disease (COVID-19): a systematic review and meta-analysis. *BMJ Open*. 2020 Oct 6;10(10):e040129. Full text (<https://bmjopen.bmj.com/content/10/10/e040129>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33028563?tool=bestpractice.bmj.com>)
 176. Baldassarri M, Picchiotti N, Fava F, et al. Shorter androgen receptor polyQ alleles protect against life-threatening COVID-19 disease in European males. *EBioMedicine*. 2021 Feb 26;65:103246. Full text ([https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(21\)00039-6/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00039-6/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33647767?tool=bestpractice.bmj.com>)
 177. Sze S, Pan D, Nevill CR, et al. Ethnicity and clinical outcomes in COVID-19: a systematic review and meta-analysis. *EClinicalMedicine*. 2020 Dec;29:100630. Full text ([https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(20\)30374-6/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30374-6/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33200120?tool=bestpractice.bmj.com>)
 178. Mackey K, Ayers CK, Kondo KK, et al. Racial and ethnic disparities in COVID-19-related infections, hospitalizations, and deaths: a systematic review. *Ann Intern Med*. 2021 Mar;174(3):362-73. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7772883>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33253040?tool=bestpractice.bmj.com>)

179. Mathur R, Rentsch CT, Morton CE, et al. Ethnic differences in SARS-CoV-2 infection and COVID-19-related hospitalisation, intensive care unit admission, and death in 17 million adults in England: an observational cohort study using the OpenSAFELY platform. *Lancet*. 2021 May 8;397(10286):1711-24. [Full text \(https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00634-6/fulltext\)](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00634-6/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33939953?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33939953?tool=bestpractice.bmj.com)
180. Saatci D, Ranger TA, Garriga C, et al. Association between race and COVID-19 outcomes among 2.6 million children in England. *JAMA Pediatr*. 2021 Jun 21 [Epub ahead of print]. [Full text \(https://jamanetwork.com/journals/jamapediatrics/fullarticle/2780966\)](https://jamanetwork.com/journals/jamapediatrics/fullarticle/2780966) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34152371?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34152371?tool=bestpractice.bmj.com)
181. Romano SD, Blackstock AJ, Taylor EV, et al. Trends in racial and ethnic disparities in COVID-19 hospitalizations, by region: United States, March–December 2020. *MMWR Morb Mortal Wkly Rep*. 2021 Apr 16;70(15):560-5. [Full text \(https://www.cdc.gov/mmwr/volumes/70/wr/mm7015e2.htm\)](https://www.cdc.gov/mmwr/volumes/70/wr/mm7015e2.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33857068?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33857068?tool=bestpractice.bmj.com)
182. Centers for Disease Control and Prevention. Risk for COVID-19 infection, hospitalization, and death by race/ethnicity. 2021 [internet publication]. [Full text \(https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html\)](https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html)
183. Yehia BR, Winegar A, Fogel R, et al. Association of race with mortality among patients hospitalized with coronavirus disease 2019 (COVID-19) at 92 US hospitals. *JAMA Netw Open*. 2020 Aug 3;3(8):e2018039. [Full text \(https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2769387\)](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2769387) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32809033?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32809033?tool=bestpractice.bmj.com)
184. Kabarriti R, Brodin NP, Maron MI, et al. Association of race and ethnicity with comorbidities and survival among patients with COVID-19 at an urban medical center in New York. *JAMA Netw Open*. 2020 Sep 1;3(9):e2019795. [Full text \(https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770960\)](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770960) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32975574?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32975574?tool=bestpractice.bmj.com)
185. Rodriguez F, Solomon N, de Lemos JA, et al. Racial and ethnic differences in presentation and outcomes for patients hospitalized with COVID-19: findings from the American Heart Association's COVID-19 Cardiovascular Disease Registry. *Circulation*. 2020 Nov 17 [Epub ahead of print]. [Full text \(https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.052278\)](https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.052278) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33200953?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33200953?tool=bestpractice.bmj.com)
186. Raharja A, Tamara A, Kok LT. Association between ethnicity and severe COVID-19 disease: a systematic review and meta-analysis. *J Racial Ethn Health Disparities*. 2020 Nov 12 [Epub ahead of print]. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7659894\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7659894) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33180278?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33180278?tool=bestpractice.bmj.com)
187. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): people at increased risk. 2021 [internet publication]. [Full text \(https://www.cdc.gov/coronavirus/2019-ncov/specific-groups/people-at-higher-risk.html\)](https://www.cdc.gov/coronavirus/2019-ncov/specific-groups/people-at-higher-risk.html)
188. Burki T. England and Wales see 20 000 excess deaths in care homes. *Lancet*. 2020 May 23;395(10237):1602. [Full text \(https://www.thelancet.com/journals/lancet/article/\)](https://www.thelancet.com/journals/lancet/article/)

- PIIS0140-6736(20)31199-5/fulltext) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32446403?tool=bestpractice.bmj.com>)
189. Graham N, Junghans C, Downes R, et al. SARS-CoV-2 infection, clinical features and outcome of COVID-19 in United Kingdom nursing homes. *J Infect.* 2020 Sep;81(3):411-9. Full text ([https://www.journalofinfection.com/article/S0163-4453\(20\)30348-0/fulltext](https://www.journalofinfection.com/article/S0163-4453(20)30348-0/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32504743?tool=bestpractice.bmj.com>)
 190. Panagiotou OA, Kosar CM, White EM, et al. Risk factors associated with all-cause 30-day mortality in nursing home residents with COVID-19. *JAMA Intern Med.* 2021 Apr 1;181(4):439-48. Full text (<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2774729>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33394006?tool=bestpractice.bmj.com>)
 191. Liu H, Chen S, Liu M, et al. Comorbid chronic diseases are strongly correlated with disease severity among COVID-19 patients: a systematic review and meta-analysis. *Aging Dis.* 2020 May 9;11(3):668-78. Full text (<http://www.aginganddisease.org/article/2020/2152-5250/ad-11-3-668.shtml>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32489711?tool=bestpractice.bmj.com>)
 192. Centers for Disease Control and Prevention. Underlying medical conditions associated with high risk for severe COVID-19: information for healthcare providers. 2021 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html>)
 193. Kompaniyets L, Pennington AF, Goodman AB, et al. Underlying medical conditions and severe illness among 540,667 adults hospitalized with COVID-19, March 2020 – March 2021. *Prev Chronic Dis.* 2021 Jul 1;18:E66. Full text (https://www.cdc.gov/pcd/issues/2021/21_0123.htm) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34197283?tool=bestpractice.bmj.com>)
 194. Adams ML, Katz DL, Grandpre J. Updated estimates of chronic conditions affecting risk for complications from coronavirus disease, United States. *Emerg Infect Dis.* 2020 Jul 3;26(9). Full text (https://wwwnc.cdc.gov/eid/article/26/9/20-2117_article) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32620181?tool=bestpractice.bmj.com>)
 195. Adams SH, Park MJ, Schaub JP, et al. Medical vulnerability of young adults to severe COVID-19 illness: data from the National Health Interview Survey. *J Adolesc Health.* 2020 Jul 9;67(3):362-8. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7355323>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32674964?tool=bestpractice.bmj.com>)
 196. Ng WH, Tipih T, Makoah NA, et al. Comorbidities in SARS-CoV-2 patients: a systematic review and meta-analysis. *mBio.* 2021 Feb 9;12(1):e03647-20. Full text (<https://mbio.asm.org/content/12/1/e03647-20.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33563817?tool=bestpractice.bmj.com>)
 197. Popkin BM, Du S, Green WD, et al. Individuals with obesity and COVID-19: a global perspective on the epidemiology and biological relationships. *Obes Rev.* 2020 Nov;21(11):e13128. Full text (<https://onlinelibrary.wiley.com/doi/full/10.1111/obr.13128>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32845580?tool=bestpractice.bmj.com>)

198. World Obesity Federation. COVID-19 and obesity: the 2021 atlas. 2021 [internet publication]. [Full text \(https://www.worldobesityday.org/assets/downloads/COVID-19-and-Obesity-The-2021-Atlas.pdf\)](https://www.worldobesityday.org/assets/downloads/COVID-19-and-Obesity-The-2021-Atlas.pdf)
199. Du Y, Lv Y, Zha W, et al. Association of body mass index (BMI) with critical COVID-19 and in-hospital mortality: a dose-response meta-analysis. *Metabolism*. 2020 Sep 16;154:373. [Full text \(https://www.metabolismjournal.com/article/S0026-0495\(20\)30237-7/fulltext\)](https://www.metabolismjournal.com/article/S0026-0495(20)30237-7/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32949592?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32949592?tool=bestpractice.bmj.com)
200. Huang HK, Bukhari K, Peng CC, et al. The J-shaped relationship between body mass index and mortality in patients with COVID-19: a dose-response meta-analysis. *Diabetes Obes Metab*. 2021 Mar 25 [Epub ahead of print]. [Full text \(https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.14382\)](https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.14382) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33764660?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33764660?tool=bestpractice.bmj.com)
201. Gao M, Piernas C, Astbury NM, et al. Associations between body-mass index and COVID-19 severity in 6.9 million people in England: a prospective, community-based, cohort study. *Lancet Diabetes Endocrinol*. 2021 Jun;9(6):350-9. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8081400\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8081400) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33932335?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33932335?tool=bestpractice.bmj.com)
202. Kompaniyets L, Goodman AB, Belay B, et al. Body mass index and risk for COVID-19–related hospitalization, intensive care unit admission, invasive mechanical ventilation, and death: United States, March – December 2020. *MMWR Morb Mortal Wkly Rep*. 2021 Mar 12;70(10):355-61. [Full text \(https://www.cdc.gov/mmwr/volumes/70/wr/mm7010e4.htm\)](https://www.cdc.gov/mmwr/volumes/70/wr/mm7010e4.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33705371?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33705371?tool=bestpractice.bmj.com)
203. Chu Y, Yang J, Shi J, et al. Obesity is associated with increased severity of disease in COVID-19 pneumonia: a systematic review and meta-analysis. *Eur J Med Res*. 2020 Dec 2;25(1):64. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7708895\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7708895) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33267871?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33267871?tool=bestpractice.bmj.com)
204. Hendren NS, de Lemos JA, Ayers C, et al. Association of body mass index and age with morbidity and mortality in patients hospitalized with COVID-19: results from the American Heart Association COVID-19 Cardiovascular Disease Registry. *Circulation*. 2021 Jan 12;143(2):135-44. [Full text \(https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.051936\)](https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.051936) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33200947?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33200947?tool=bestpractice.bmj.com)
205. Hessami A, Shamshirian A, Heydari K, et al. Cardiovascular diseases burden in COVID-19: systematic review and meta-analysis. *Am J Emerg Med*. 2020 Oct 16 [Epub ahead of print]. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7561581\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7561581) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33268238?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33268238?tool=bestpractice.bmj.com)
206. Zuin M, Rigatelli G, Bilato C, et al. Pre-existing atrial fibrillation is associated with increased mortality in COVID-19 Patients. *J Interv Card Electrophysiol*. 2021 Apr 15 [Epub ahead of print]. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8046494\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8046494) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33855639?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33855639?tool=bestpractice.bmj.com)
207. Liang C, Zhang W, Li S, et al. Coronary heart disease and COVID-19: a meta-analysis. *Med Clin (Engl Ed)*. 2021 Jun 11;156(11):547-54. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8178966\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8178966) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34109276?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34109276?tool=bestpractice.bmj.com)

208. Bae S, Kim SR, Kim MN, et al. Impact of cardiovascular disease and risk factors on fatal outcomes in patients with COVID-19 according to age: a systematic review and meta-analysis. *Heart*. 2021 Mar;107(5):373-80. [Full text \(https://heart.bmj.com/content/early/2020/12/16/heartjnl-2020-317901.long\)](https://heart.bmj.com/content/early/2020/12/16/heartjnl-2020-317901.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33334865?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33334865?tool=bestpractice.bmj.com)
209. Pellicori P, Doolub G, Wong CM, et al. COVID-19 and its cardiovascular effects: a systematic review of prevalence studies. *Cochrane Database Syst Rev*. 2021 Mar 11;(3):CD013879. [Full text \(https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013879/full\)](https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013879/full) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33704775?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33704775?tool=bestpractice.bmj.com)
210. Hussain S, Baxi H, Chand Jamali M, et al. Burden of diabetes mellitus and its impact on COVID-19 patients: a meta-analysis of real-world evidence. *Diabetes Metab Syndr*. 2020 Aug 20;14(6):1595-602. [Full text \(https://www.sciencedirect.com/science/article/pii/S1871402120303179?via%3Dihub\)](https://www.sciencedirect.com/science/article/pii/S1871402120303179?via%3Dihub) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32862098?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32862098?tool=bestpractice.bmj.com)
211. Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia: a systematic review, meta-analysis, and meta-regression. *Diabetes Metab Syndr*. 2020 Apr 17;14(4):395-403. [Full text \(https://www.sciencedirect.com/science/article/pii/S1871402120300837?via%3Dihub\)](https://www.sciencedirect.com/science/article/pii/S1871402120300837?via%3Dihub) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32334395?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32334395?tool=bestpractice.bmj.com)
212. Barron E, Bakhai C, Kar P, et al. Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a whole-population study. *Lancet Diabetes Endocrinol*. 2020 Oct;8(10):813-22. [Full text \(https://www.thelancet.com/journals/landia/article/PIIS2213-8587\(20\)30272-2/fulltext\)](https://www.thelancet.com/journals/landia/article/PIIS2213-8587(20)30272-2/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32798472?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32798472?tool=bestpractice.bmj.com)
213. Dennis JM, Mateen BA, Sonabend R, et al. Type 2 diabetes and COVID-19-related mortality in the critical care setting: a national cohort study in England, March–July 2020. *Diabetes Care*. 2021 Jan;44(1):50-7. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7783930\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7783930) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33097559?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33097559?tool=bestpractice.bmj.com)
214. Chen Y, Yang D, Cheng B, et al. Clinical characteristics and outcomes of patients with diabetes and COVID-19 in association with glucose-lowering medication. *Diabetes Care*. 2020 Jul;43(7):1399-407. [Full text \(https://care.diabetesjournals.org/content/diacare/early/2020/05/13/dc20-0660.full.pdf\)](https://care.diabetesjournals.org/content/diacare/early/2020/05/13/dc20-0660.full.pdf) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32409498?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32409498?tool=bestpractice.bmj.com)
215. Holman N, Knighton P, Kar P, et al. Risk factors for COVID-19-related mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study. *Lancet Diabetes Endocrinol*. 2020 Oct;8(10):823-33. [Full text \(https://www.thelancet.com/journals/landia/article/PIIS2213-8587\(20\)30271-0/fulltext\)](https://www.thelancet.com/journals/landia/article/PIIS2213-8587(20)30271-0/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32798471?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32798471?tool=bestpractice.bmj.com)
216. Pal R, Banerjee M, Yadav U, et al. Clinical profile and outcomes in COVID-19 patients with diabetic ketoacidosis: a systematic review of literature. *Diabetes Metab Syndr*. 2020 Aug 18;14(6):1563-9. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7434433\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7434433) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32853901?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32853901?tool=bestpractice.bmj.com)

217. Papadopoulos VP, Koutroulos MV, Zikoudi DG, et al. Diabetes-related acute metabolic emergencies in COVID-19 patients: a systematic review and meta-analysis. *Diabetol Int*. 2021 Mar 23;1-15. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7985576\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7985576) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33777611?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33777611?tool=bestpractice.bmj.com)
218. Prattichizzo F, de Candia P, Nicolucci A, et al. Impact of pre-infection HbA1c levels on COVID-19 prognosis: systematic review and meta-analysis. *Diabetes Metab Res Rev*. 2021 May 20:e3476. [Full text \(https://onlinelibrary.wiley.com/doi/10.1002/dmrr.3476\)](https://onlinelibrary.wiley.com/doi/10.1002/dmrr.3476) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34018307?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34018307?tool=bestpractice.bmj.com)
219. Barrett CE, Park J, Kompaniyets L, et al. Intensive care unit admission, mechanical ventilation, and mortality among patients with type 1 diabetes hospitalized for COVID-19 in the U.S. *Diabetes Care*. 2021 Jun 22 [Epub ahead of print]. [Full text \(https://care.diabetesjournals.org/content/early/2021/06/21/dc21-0604\)](https://care.diabetesjournals.org/content/early/2021/06/21/dc21-0604) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34158365?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34158365?tool=bestpractice.bmj.com)
220. Li H, Tian S, Chen T, et al. Newly diagnosed diabetes is associated with a higher risk of mortality than known diabetes in hospitalized patients with COVID-19. *Diabetes Obes Metab*. 2020 Oct;22(10):1897-906. [Full text \(https://dom-pubs.onlinelibrary.wiley.com/doi/abs/10.1111/dom.14099\)](https://dom-pubs.onlinelibrary.wiley.com/doi/abs/10.1111/dom.14099) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32469464?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32469464?tool=bestpractice.bmj.com)
221. Lukito AA, Pranata R, Henrina J, et al. The effect of metformin consumption on mortality in hospitalized COVID-19 patients: a systematic review and meta-analysis. *Diabetes Metab Syndr*. 2020 Nov-Dec;14(6):2177-83. [Full text \(https://www.sciencedirect.com/science/article/pii/S1871402120304719?via%3Dihub\)](https://www.sciencedirect.com/science/article/pii/S1871402120304719?via%3Dihub) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33395778?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33395778?tool=bestpractice.bmj.com)
222. Yang Y, Cai Z, Zhang J. DPP-4 inhibitors may improve the mortality of coronavirus disease 2019: a meta-analysis. *PLoS One*. 2021;16(5):e0251916. [Full text \(https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0251916\)](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0251916) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34015003?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34015003?tool=bestpractice.bmj.com)
223. Kahkoska AR, Abrahamsen TJ, Alexander GC, et al. Association between glucagon-like peptide 1 receptor agonist and sodium-glucose cotransporter 2 inhibitor use and COVID-19 outcomes. *Diabetes Care*. 2021 Jun 16 [Epub ahead of print]. [Full text \(https://care.diabetesjournals.org/content/early/2021/06/14/dc21-0065.full-text.pdf\)](https://care.diabetesjournals.org/content/early/2021/06/14/dc21-0065.full-text.pdf) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34135013?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34135013?tool=bestpractice.bmj.com)
224. Apicella M, Campopiano MC, Mantuano M, et al. COVID-19 in people with diabetes: understanding the reasons for worse outcomes. *Lancet Diabetes Endocrinol*. 2020 Sep;8(9):782-92. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7367664\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7367664) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32687793?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32687793?tool=bestpractice.bmj.com)
225. Halpin DMG, Faner R, Sibila O, et al. Do chronic respiratory diseases or their treatment affect the risk of SARS-CoV-2 infection? *Lancet Respir Med*. 2020 May;8(5):436-8. [Full text \(https://www.thelancet.com/pdfs/journals/lanres/PIIS2213-2600\(20\)30167-3.pdf\)](https://www.thelancet.com/pdfs/journals/lanres/PIIS2213-2600(20)30167-3.pdf) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32251625?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32251625?tool=bestpractice.bmj.com)

226. Centre for Evidence-Based Medicine; Hartmann-Boyce J, Otunla A, Drake J, et al. Asthma and COVID-19: risks and management considerations. 2020 [internet publication]. [Full text \(https://www.cebm.net/covid-19/asthma-and-covid-19-risks-and-management-considerations\)](https://www.cebm.net/covid-19/asthma-and-covid-19-risks-and-management-considerations)
227. Gerayeli FV, Milne S, Cheung C, et al. COPD and the risk of poor outcomes in COVID-19: a systematic review and meta-analysis. *EClinicalMedicine*. 2021 Mar;33:100789. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7971471\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7971471) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33758801?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33758801?tool=bestpractice.bmj.com)
228. Bloom CI, Drake TM, Docherty AB, et al. Risk of adverse outcomes in patients with underlying respiratory conditions admitted to hospital with COVID-19: a national, multicentre prospective cohort study using the ISARIC WHO Clinical Characterisation Protocol UK. *Lancet Respir Med*. 2021 Mar 4 [Epub ahead of print]. [Full text \(https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00013-8/fulltext\)](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00013-8/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33676593?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33676593?tool=bestpractice.bmj.com)
229. World Health Organization. Asthma and COVID-19: scientific brief, 19 April 2021. 2021 [internet publication]. [Full text \(https://www.who.int/publications/i/item/who-2019-ncov-sci-brief-asthma-2021.1\)](https://www.who.int/publications/i/item/who-2019-ncov-sci-brief-asthma-2021.1)
230. Liu S, Cao Y, Du T, et al. Prevalence of comorbid asthma and related outcomes in COVID-19: a systematic review and meta-analysis. *J Allergy Clin Immunol Pract*. 2021 Feb;9(2):693-701. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7725230\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7725230) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33309934?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33309934?tool=bestpractice.bmj.com)
231. Sunjaya AP, Allida SM, Di Tanna GL, et al. Asthma and risk of infection, hospitalisation, ICU admission and mortality from COVID-19: systematic review and meta-analysis. *J Asthma*. 2021 Feb 8;:1-22. [Full text \(https://www.tandfonline.com/doi/full/10.1080/02770903.2021.1888116\)](https://www.tandfonline.com/doi/full/10.1080/02770903.2021.1888116) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33556287?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33556287?tool=bestpractice.bmj.com)
232. Soeroto AY, Purwiga A, Emmy H Pranggono EHP, et al. Asthma does not increase COVID-19 mortality and poor outcomes: a systematic review and meta-analysis. *Asian Pac J Allergy Immunol*. 2021 Apr 18 [Epub ahead of print]. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33865299?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33865299?tool=bestpractice.bmj.com)
233. Wu T, Yu P, Li Y, et al. Asthma does not influence the severity of COVID-19: a meta-analysis. *J Asthma*. 2021 Apr 16:1-11. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33863266?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33863266?tool=bestpractice.bmj.com)
234. Hariyanto TI, Kurniawan A. Obstructive sleep apnea (OSA) and outcomes from coronavirus disease 2019 (COVID-19) pneumonia: a systematic review and meta-analysis. *Sleep Med*. 2021 Apr 1;82:47-53. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8012298\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8012298) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33892451?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33892451?tool=bestpractice.bmj.com)
235. Strausz S, Kiiskinen T, Broberg M, et al. Sleep apnoea is a risk factor for severe COVID-19. *BMJ Open Respir Res*. 2021 Jan;8(1):e000845. [Full text \(https://bmjopenrespres.bmj.com/content/8/1/e000845.long\)](https://bmjopenrespres.bmj.com/content/8/1/e000845.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33436406?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33436406?tool=bestpractice.bmj.com)
236. Mathew HR, Choi MY, Parkins MD, et al. Systematic review: cystic fibrosis in the SARS-CoV-2/COVID-19 pandemic. *BMC Pulm Med*. 2021 May 20;21(1):173. [Full text \(https://www.ncbi.nlm.nih.gov/\)](https://www.ncbi.nlm.nih.gov/)

pmc/articles/PMC8135381) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34016096?tool=bestpractice.bmj.com>)

237. Wang Y, Feng R, Xu J, et al. An updated meta-analysis on the association between tuberculosis and COVID-19 severity and mortality. *J Med Virol*. 2021 Jun 1 [Epub ahead of print]. Full text (<https://onlinelibrary.wiley.com/doi/10.1002/jmv.27119>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34061374?tool=bestpractice.bmj.com>)
238. Castro-Rodriguez JA, Forno E. Asthma and COVID-19 in children: a systematic review and call for data. *Pediatr Pulmonol*. 2020 Sep;55(9):2412-8. Full text (<https://onlinelibrary.wiley.com/doi/abs/10.1002/ppul.24909>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32558360?tool=bestpractice.bmj.com>)
239. Lin YC, Lai TS, Lin SL, et al. Outcomes of coronavirus 2019 infection in patients with chronic kidney disease: a systematic review and meta-analysis. *Ther Adv Chronic Dis*. 2021;12:2040622321998860. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7985947>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33796245?tool=bestpractice.bmj.com>)
240. Nopsopon T, Kittrakulrat J, Takkavatakarn K, et al. Covid-19 in end-stage renal disease patients with renal replacement therapies: a systematic review and meta-analysis. *PLoS Negl Trop Dis*. 2021 Jun 15;15(6):e0009156. Full text (<https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0009156>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34129609?tool=bestpractice.bmj.com>)
241. Kunutsor SK, Laukkanen JA. Renal complications in COVID-19: a systematic review and meta-analysis. *Ann Med*. 2020 Jul 10;1-9. Full text (<https://www.tandfonline.com/doi/full/10.1080/07853890.2020.1790643>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32643418?tool=bestpractice.bmj.com>)
242. Gajbhiye RK, Sawant MS, Kuppusamy P, et al. Differential impact of COVID-19 in pregnant women from high-income countries and low- to middle-income countries: a systematic review and meta-analysis. *Int J Gynaecol Obstet*. 2021 Jun 23 [Epub ahead of print]. Full text (<https://obgyn.onlinelibrary.wiley.com/doi/10.1002/ijgo.13793>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34160059?tool=bestpractice.bmj.com>)
243. Zhang H, Ma S, Han T, et al. Association of smoking history with severe and critical outcome in COVID-19 patients: a systemic review and meta-analysis. *Eur J Integr Med*. 2021 Feb 18:101313. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7889467>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33619437?tool=bestpractice.bmj.com>)
244. Salah HM, Sharma T, Mehta J. Smoking doubles the mortality risk in COVID-19: a meta-analysis of recent reports and potential mechanisms. *Cureus*. 2020 Oct 7;12(10):e10837. Full text (<https://www.cureus.com/articles/39552-smoking-doubles-the-mortality-risk-in-covid-19-a-meta-analysis-of-recent-reports-and-potential-mechanisms>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33173643?tool=bestpractice.bmj.com>)
245. Cai G, Bossé Y, Xiao F, et al. Tobacco smoking increases the lung gene expression of ACE2, the receptor of SARS-CoV-2. *Am J Respir Crit Care Med*. 2020 Jun 15;201(12):1557-9. Full text

- (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7301735>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32329629?tool=bestpractice.bmj.com>)
246. World Health Organization. Smoking and COVID-19: scientific brief. 2020 [internet publication]. Full text (https://www.who.int/publications/i/item/WHO-2019-nCoV-Sci_Brief-Smoking-2020.2)
 247. Yu J Ouyang W, Chua ML, et al. SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China. *JAMA Oncol*. 2020 Mar 25;6(7):1108-10. Full text (<https://jamanetwork.com/journals/jamaoncology/fullarticle/2763673>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32211820?tool=bestpractice.bmj.com>)
 248. Venkatesulu BP, Chandrasekar VT, Girdhar P, et al. A systematic review and meta-analysis of cancer patients affected by a novel coronavirus. *JNCI Cancer Spectr*. 2021 Feb 24;5(2):pkaa102. Full text (<https://academic.oup.com/jncics/article/5/2/pkaa102/6149097>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33875976?tool=bestpractice.bmj.com>)
 249. Zarifkar P, Kamath A, Robinson C, et al. Clinical characteristics and outcomes in patients with COVID-19 and cancer: a systematic review and meta-analysis. *Clin Oncol (R Coll Radiol)*. 2021 Mar;33(3):e180-91. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7674130>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33261978?tool=bestpractice.bmj.com>)
 250. Kaur H, Thakur JS, Paika R, et al. Impact of underlying comorbidities on mortality in SARS-COV-2 infected cancer patients: a systematic review and meta-analysis. *Asian Pac J Cancer Prev*. 2021 May 1;22(5):1333-49. Full text (http://journal.waocp.org/article_89582_88818a41a7dc442aa8591bc9ae0c197a.pdf) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34048161?tool=bestpractice.bmj.com>)
 251. Boulad F, Kamboj M, Bouvier N, et al. COVID-19 in children with cancer in New York City. *JAMA Oncol*. 2020 Sep 1;6(9):1459-60. Full text (<https://jamanetwork.com/journals/jamaoncology/fullarticle/2766112>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32401276?tool=bestpractice.bmj.com>)
 252. Dorantes-Acosta E, Ávila-Montiel D, Klünder-Klünder M, et al. Survival and complications in pediatric patients with cancer and COVID-19: a meta-analysis. *Front Oncol*. 2020 Jan 21;10:608282. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7861039>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33552980?tool=bestpractice.bmj.com>)
 253. Xu J, Xiao W, Liang X, et al. The association of cerebrovascular disease with adverse outcomes in COVID-19 patients: a meta-analysis based on adjusted effect estimates. *J Stroke Cerebrovasc Dis*. 2020 Nov;29(11):105283. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7455117>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33066922?tool=bestpractice.bmj.com>)
 254. Patel U, Malik P, Shah D, et al. Pre-existing cerebrovascular disease and poor outcomes of COVID-19 hospitalized patients: a meta-analysis. *J Neurol*. 2021 Jan;268(1):240-7. Full text (<https://link.springer.com/article/10.1007%2Fs00415-020-10141-w>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32770412?tool=bestpractice.bmj.com>)
 255. Raja MA, Mendoza MA, Villavicencio A, et al. COVID-19 in solid organ transplant recipients: a systematic review and meta-analysis of current literature. *Transplant Rev (Orlando)*. 2020 Nov

- 14;35(1):100588. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7666542>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33246166?tool=bestpractice.bmj.com>)
256. Ao G, Wang Y, Qi X, et al. The association between severe or death COVID-19 and solid organ transplantation: a systematic review and meta-analysis. *Transplant Rev (Orlando)*. 2021 May 21;35(3):100628. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8137345>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34087553?tool=bestpractice.bmj.com>)
257. Clift AK, Coupland CAC, Keogh RH, et al. COVID-19 mortality risk in Down syndrome: results from a cohort study of 8 million adults. *Ann Intern Med*. 2021 Apr;174(4):572-6. Full text (<https://www.acpjournals.org/doi/10.7326/M20-4986>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33085509?tool=bestpractice.bmj.com>)
258. Williamson EJ, McDonald HI, Bhaskaran K, et al. Risks of covid-19 hospital admission and death for people with learning disability: population based cohort study using the OpenSAFELY platform. *BMJ*. 2021 Jul 14;374:n1592. Full text (<https://www.bmj.com/content/374/bmj.n1592>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34261639?tool=bestpractice.bmj.com>)
259. Clift AK, Saatci D, Coupland CAC, et al. Sickle cell disorders and severe COVID-19 outcomes: a cohort study. *Ann Intern Med*. 2021 July 20 [Epub ahead of print]. Full text (<https://www.acpjournals.org/doi/10.7326/M21-1375>)
260. Panepinto JA, Brandow A, Mucalo L, et al. Coronavirus disease among persons with sickle cell disease, United States, March 20 – May 21, 2020. *Emerg Infect Dis*. 2020 Jul 8;26(10). Full text (https://wwwnc.cdc.gov/eid/article/26/10/20-2792_article) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32639228?tool=bestpractice.bmj.com>)
261. Hussain FA, Njoku FU, Saraf SL, et al. COVID-19 infection in patients with sickle cell disease. *Br J Haematol*. 2020 Jun;189(5):851-2. Full text (<https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.16734>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32314798?tool=bestpractice.bmj.com>)
262. Nur E, Gaartman AE, van Tuijn CFJ, et al. Vaso-occlusive crisis and acute chest syndrome in sickle cell disease due to 2019 novel coronavirus disease (COVID-19). *Am J Hematol*. 2020 Jun;95(6):725-6. Full text (<https://onlinelibrary.wiley.com/doi/10.1002/ajh.25821>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32267016?tool=bestpractice.bmj.com>)
263. World Health Organization. Hypertension and COVID-19. 2021 [internet publication]. Full text (https://www.who.int/publications/i/item/WHO-2019-nCoV-Sci_Brief-Hypertension-2021.1)
264. Pranata R, Lim MA, Huang I, et al. Hypertension is associated with increased mortality and severity of disease in COVID-19 pneumonia: a systematic review, meta-analysis and meta-regression. *J Renin Angiotensin Aldosterone Syst*. 2020 Apr-Jun;21(2):1470320320926899. Full text (<https://journals.sagepub.com/doi/10.1177/1470320320926899>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32408793?tool=bestpractice.bmj.com>)
265. de Almeida-Pititto B, Dualib PM, Zajdenverg L, et al. Severity and mortality of COVID 19 in patients with diabetes, hypertension and cardiovascular disease: a meta-analysis. *Diabetol Metab Syndr*. 2020

- Aug 31;12:75. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456786>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32874207?tool=bestpractice.bmj.com>)
266. Du Y, Zhou N, Zha W, et al. Hypertension is a clinically important risk factor for critical illness and mortality in COVID-19: a meta-analysis. *Nutr Metab Cardiovasc Dis*. 2021 Mar 10;31(3):745-55. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7831720>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33549450?tool=bestpractice.bmj.com>)
267. Goldstein MR, Poland GA, Graeber CW. Are certain drugs associated with enhanced mortality in COVID-19? *QJM*. 2020 Jul 1;113(7):509-10. Full text (<https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaa103/5812790>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32219440?tool=bestpractice.bmj.com>)
268. Mackey K, King VJ, Gurley S, et al. Risks and impact of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers on SARS-CoV-2 infection in adults: a living systematic review. *Ann Intern Med*. 2020 Aug 4;173(3):195-203. Full text (<https://www.acpjournals.org/doi/10.7326/M20-1515>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32422062?tool=bestpractice.bmj.com>)
269. Mackey K, Kansagara D, Vela K. Update alert 7: risks and impact of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers on SARS-CoV-2 infection in adults. *Ann Intern Med*. 2021 Feb;174(2):W25-9. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7791405>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33395346?tool=bestpractice.bmj.com>)
270. Hariyanto TI, Putri C, Arisa J, et al. Dementia and outcomes from coronavirus disease 2019 (COVID-19) pneumonia: a systematic review and meta-analysis. *Arch Gerontol Geriatr*. 2020 Nov 19;93:104299. Full text (<https://www.sciencedirect.com/science/article/pii/S016749432030296X?via%3Dihub>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33285424?tool=bestpractice.bmj.com>)
271. Saragih ID, Saragih IS, Batubara SO, et al. Dementia as a mortality predictor among older adults with COVID-19: a systematic review and meta-analysis of observational study. *Geriatr Nurs*. 2021 Mar 14 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7955923>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33824009?tool=bestpractice.bmj.com>)
272. Office for National Statistics. Deaths involving COVID-19, England and Wales: deaths occurring in June 2020. 2020 [internet publication]. Full text (<https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsinvolvingcovid19englandandwales/deathsoccurringinjune2020>)
273. Wang Q, Davis PB, Gurney ME, et al. COVID-19 and dementia: analyses of risk, disparity, and outcomes from electronic health records in the US. *Alzheimers Dement*. 2021 Feb 9 [Epub ahead of print]. Full text (<https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.12296>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33559975?tool=bestpractice.bmj.com>)
274. Gianfrancesco M, Hyrich KL, Al-Adely S, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Ann Rheum Dis*. 2020 Jul;79(7):859-66. Full text (<https://ard.bmj.com/content/early/2020/05/29/annrheumdis-2020-217871>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32471903?tool=bestpractice.bmj.com>)

275. Nørgård BM, Nielsen J, Knudsen T, et al. Hospitalization for COVID-19 in patients treated with selected immunosuppressant and immunomodulating agents, compared to the general population: a Danish cohort study. *Br J Clin Pharmacol*. 2021 Apr;87(4):2111-20. [Full text \(https://bpspubs.onlinelibrary.wiley.com/doi/10.1111/bcp.14622\)](https://bpspubs.onlinelibrary.wiley.com/doi/10.1111/bcp.14622) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33098713?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33098713?tool=bestpractice.bmj.com)
276. Tassone D, Thompson A, Connell W, et al. Immunosuppression as a risk factor for COVID-19: a meta-analysis. *Intern Med J*. 2021 Feb;51(2):199-205. [Full text \(https://onlinelibrary.wiley.com/doi/10.1111/imj.15142\)](https://onlinelibrary.wiley.com/doi/10.1111/imj.15142) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33631862?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33631862?tool=bestpractice.bmj.com)
277. Bhaskaran K, Rentsch CT, MacKenna B, et al. HIV infection and COVID-19 death: a population-based cohort analysis of UK primary care data and linked national death registrations within the OpenSAFELY platform. *Lancet HIV*. 2021 Jan;8(1):e24-32. [Full text \(https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018\(20\)30305-2/fulltext\)](https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(20)30305-2/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33316211?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33316211?tool=bestpractice.bmj.com)
278. Tesoriero JM, Swain CE, Pierce JL, et al. COVID-19 outcomes among persons living with or without diagnosed HIV infection in New York State. *JAMA Netw Open*. 2021 Feb 1;4(2):e2037069. [Full text \(https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775827\)](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775827) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33533933?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33533933?tool=bestpractice.bmj.com)
279. Chanda D, Minchella PA, Kampamba D, et al. COVID-19 severity and COVID-19-associated deaths among hospitalized patients with HIV infection: Zambia, March-December 2020. *MMWR Morb Mortal Wkly Rep*. 2021 Jun 4;70(22):807-10. [Full text \(https://www.cdc.gov/mmwr/volumes/70/wr/mm7022a2.htm\)](https://www.cdc.gov/mmwr/volumes/70/wr/mm7022a2.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34081684?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34081684?tool=bestpractice.bmj.com)
280. Lee KW, Yap SF, Ngeow YF, et al. COVID-19 in people living with HIV: a systematic review and meta-analysis. *Int J Environ Res Public Health*. 2021 Mar 30;18(7):3554. [Full text \(https://www.mdpi.com/1660-4601/18/7/3554/html\)](https://www.mdpi.com/1660-4601/18/7/3554/html) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33808066?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33808066?tool=bestpractice.bmj.com)
281. Mellor MM, Bast AC, Jones NR, et al. Risk of adverse coronavirus disease 2019 outcomes for people living with HIV. *AIDS*. 2021 Mar 15;35(4):F1-10. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7924978\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7924978) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33587448?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33587448?tool=bestpractice.bmj.com)
282. Ssentongo P, Heilbrunn ES, Ssentongo AE, et al. Epidemiology and outcomes of COVID-19 in HIV-infected individuals: a systematic review and meta-analysis. *Sci Rep*. 2021 Mar 18;11(1):6283. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7973415\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7973415) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33737527?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33737527?tool=bestpractice.bmj.com)
283. Hariyanto TI, Rosalind J, Christian K, et al. Human immunodeficiency virus and mortality from coronavirus disease 2019: a systematic review and meta-analysis. *South Afr J HIV Med*. 2021 Apr 15;22(1):1220. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8063497\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8063497) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33936793?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33936793?tool=bestpractice.bmj.com)

284. World Health Organization. Clinical features and prognostic factors of COVID-19 in people living with HIV hospitalized with suspected or confirmed SARS-CoV-2 infection. 2021 [internet publication]. Full text (<https://www.who.int/publications/i/item/WHO-2019-nCoV-Clinical-HIV-2021.1>)
285. Baillargeon J, Polychronopoulou E, Kuo YF, et al. The impact of substance use disorder on COVID-19 outcomes. *Psychiatr Serv*. 2021 May 1;72(5):578-81. Full text (<https://ps.psychiatryonline.org/doi/10.1176/appi.ps.202000534>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33138712?tool=bestpractice.bmj.com>)
286. Allen B, El Shahawy O, Rogers ES, et al. Association of substance use disorders and drug overdose with adverse COVID-19 outcomes in New York City: January-October 2020. *J Public Health (Oxf)*. 2020 Dec 26 [Epub ahead of print]. Full text (<https://academic.oup.com/jpubhealth/advance-article/doi/10.1093/pubmed/fdaa241/6047762>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33367823?tool=bestpractice.bmj.com>)
287. Qeadan F, Tingey B, Bern R, et al. Opioid use disorder and health service utilization among COVID-19 patients in the US: a nationwide cohort from the Cerner Real-World Data. *EClinicalMedicine*. 2021 Jun 4:100938. Full text ([https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00218-2/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00218-2/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34109308?tool=bestpractice.bmj.com>)
288. Kompaniyets L, Agathis NT, Nelson JM, et al. Underlying medical conditions associated with severe COVID-19 illness among children. *JAMA Netw Open*. 2021 Jun 1;4(6):e2111182. Full text (<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780706>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34097050?tool=bestpractice.bmj.com>)
289. Kovalic AJ, Satapathy SK, Thuluvath PJ. Prevalence of chronic liver disease in patients with COVID-19 and their clinical outcomes: a systematic review and meta-analysis. *Hepatol Int*. 2020 Sep;14(5):612-20. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7386238>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32725453?tool=bestpractice.bmj.com>)
290. Iavarone M, D'Ambrosio R, Soria A, et al. High rates of 30-day mortality in patients with cirrhosis and COVID-19. *J Hepatol*. 2020 Nov;73(5):1063-71. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7280108>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32526252?tool=bestpractice.bmj.com>)
291. Pan L, Huang P, Xie X, et al. Metabolic associated fatty liver disease increases the severity of COVID-19: a meta-analysis. *Dig Liver Dis*. 2021 Feb;53(2):153-7. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7498251>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33011088?tool=bestpractice.bmj.com>)
292. Singh A, Hussain S, Antony B. Non-alcoholic fatty liver disease and clinical outcomes in patients with COVID-19: a comprehensive systematic review and meta-analysis. *Diabetes Metab Syndr*. 2021 Mar 31;15(3):813-22. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8011308>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33862417?tool=bestpractice.bmj.com>)
293. Targher G, Mantovani A, Byrne CD, et al. Risk of severe illness from COVID-19 in patients with metabolic dysfunction-associated fatty liver disease and increased fibrosis scores. *Gut*. 2020 Aug;69(8):1545-7. Full text (<https://gut.bmj.com/content/early/2020/05/15/gutjnl-2020-321611>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32414813?tool=bestpractice.bmj.com>)

294. Zhou YJ, Zheng KI, Wang XB, et al. Younger patients with MAFLD are at increased risk of severe COVID-19 illness: a multicenter preliminary analysis. *J Hepatol.* 2020 Sep;73(3):719-21. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7195041\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7195041) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32348790?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32348790?tool=bestpractice.bmj.com)
295. Liu N, Sun J, Wang X, et al. Low vitamin D status is associated with coronavirus disease 2019 outcomes: a systematic review and meta-analysis. *Int J Infect Dis.* 2021 Jan 2;104:58-64. [Full text \(https://www.ijidonline.com/article/S1201-9712\(20\)32600-X/fulltext\)](https://www.ijidonline.com/article/S1201-9712(20)32600-X/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33401034?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33401034?tool=bestpractice.bmj.com)
296. Yisak H, Ewunetei A, Kefale B, et al. Effects of vitamin D on COVID-19 infection and prognosis: a systematic review. *Risk Manag Healthc Policy.* 2021 Jan 7;14:31-8. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7800698\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7800698) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33447107?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33447107?tool=bestpractice.bmj.com)
297. Teshome A, Adane A, Girma B, et al. The impact of vitamin D level on COVID-19 infection: systematic review and meta-analysis. *Front Public Health.* 2021 Mar 5;9:624559. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7973108\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7973108) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33748066?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33748066?tool=bestpractice.bmj.com)
298. Pereira M, Dantas Damascena A, Galvão Azevedo LM, et al. Vitamin D deficiency aggravates COVID-19: systematic review and meta-analysis. *Crit Rev Food Sci Nutr.* 2020 Nov 4;1-9. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33146028?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33146028?tool=bestpractice.bmj.com)
299. Akbar MR, Wibowo A, Pranata R, et al. Low serum 25-hydroxyvitamin d (vitamin d) level is associated with susceptibility to COVID-19, severity, and mortality: a systematic review and meta-analysis. *Front Nutr.* 2021 Mar 29;8:660420. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8039288\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8039288) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33855042?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33855042?tool=bestpractice.bmj.com)
300. Wang Z, Joshi A, Leopold K, et al. Association of vitamin D deficiency with COVID-19 infection severity: systematic review and meta-analysis. *Clin Endocrinol (Oxf).* 2021 Jun 23 [Epub ahead of print]. [Full text \(https://onlinelibrary.wiley.com/doi/10.1111/cen.14540\)](https://onlinelibrary.wiley.com/doi/10.1111/cen.14540) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34160843?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34160843?tool=bestpractice.bmj.com)
301. Crafa A, Cannarella R, Condorelli RA, et al. Influence of 25-hydroxy-cholecalciferol levels on SARS-CoV-2 infection and COVID-19 severity: a systematic review and meta-analysis. *EClinicalMedicine.* 2021 Jul;37:100967. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8215557\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8215557) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34179737?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34179737?tool=bestpractice.bmj.com)
302. Bassatne A, Basbous M, Chakhtoura M, et al. The link between COVID-19 and vitamin D (VIVID): a systematic review and meta-analysis. *Metabolism.* 2021 Mar 24:154753. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7989070\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7989070) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33774074?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33774074?tool=bestpractice.bmj.com)
303. Grove A, Osokogu O, Al-Khudairy L, et al. Association between vitamin D supplementation or serum vitamin D level and susceptibility to SARS-CoV-2 infection or COVID-19 including clinical course, morbidity and mortality outcomes? A systematic review. *BMJ Open.* 2021 May 28;11(5):e043737.

- Full text (<https://bmjopen.bmj.com/content/11/5/e043737.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34049903?tool=bestpractice.bmj.com>)
304. Toubasi AA, AbuAnzeh RB, Khraisat BR, et al. A meta-analysis: Proton pump inhibitors current use and the risk of coronavirus infectious disease 2019 development and its related mortality. *Arch Med Res*. 2021 Mar 26 [Epub ahead of print]. Full text (<https://www.sciencedirect.com/science/article/pii/S0188440921000758?via%3Dihub>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33814207?tool=bestpractice.bmj.com>)
 305. Pranata R, Huang I, Lawrensia S, et al. Proton pump inhibitor on susceptibility to COVID-19 and its severity: a systematic review and meta-analysis. *Pharmacol Rep*. 2021 Apr 11 [Epub ahead of print]. Full text (<https://link.springer.com/article/10.1007%2Fs43440-021-00263-x>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33840053?tool=bestpractice.bmj.com>)
 306. Lee SW, Ha EK, Yeniova AÖ, et al. Severe clinical outcomes of COVID-19 associated with proton pump inhibitors: a nationwide cohort study with propensity score matching. *Gut*. 2021 Jan;70(1):76-84. Full text (<https://gut.bmj.com/content/early/2020/07/30/gutjnl-2020-322248.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32732368?tool=bestpractice.bmj.com>)
 307. Kow CS, Hasan SS. Use of proton pump inhibitors and risk of adverse clinical outcomes from COVID-19: a meta-analysis. *J Intern Med*. 2021 Jan;289(1):125-8. Full text (<https://onlinelibrary.wiley.com/doi/10.1111/joim.13183>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33078881?tool=bestpractice.bmj.com>)
 308. Yan C, Chen Y, Sun C, et al. Will proton pump inhibitors lead to a higher risk of COVID-19 infection and progression to severe disease? A meta-analysis. *Jpn J Infect Dis*. 2021 May 31 [Epub ahead of print]. Full text (https://www.jstage.jst.go.jp/article/yoken/advpub/0/advpub_JJID.2021.074/_pdf/-char/en) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34053958?tool=bestpractice.bmj.com>)
 309. Li GF, An XX, Yu Y, et al. Do proton pump inhibitors influence SARS-CoV-2 related outcomes? A meta-analysis. *Gut*. 2020 Nov 10 [Epub ahead of print]. Full text (<https://gut.bmj.com/content/gutjnl/early/2020/11/10/gutjnl-2020-323366.full.pdf>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33172925?tool=bestpractice.bmj.com>)
 310. Israelsen SB, Ernst MT, Lundh A, et al. Proton pump inhibitor use is not strongly associated with SARS-CoV-2 related outcomes: a nationwide study and meta-analysis. *Clin Gastroenterol Hepatol*. 2021 May 11 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8111907>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33989790?tool=bestpractice.bmj.com>)
 311. Akiyama S, Hamdeh S, Micic D, et al. Prevalence and clinical outcomes of COVID-19 in patients with autoimmune diseases: a systematic review and meta-analysis. *Ann Rheum Dis*. 2020 Oct 13 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7554412>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33051220?tool=bestpractice.bmj.com>)
 312. Saadoun D, Vieira M, Vautier M, et al. SARS-CoV-2 outbreak in immune-mediated inflammatory diseases: the Euro-COVIMID multicentre cross-sectional study. *Lancet Rheumatol*. 2021 Apr 28 [Epub ahead of print]. Full text (<https://www.thelancet.com/journals/lanrhe/article/>)

PIIS2665-9913(21)00112-0/fulltext) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33942031?tool=bestpractice.bmj.com>)

313. Saxena A, Guttmann A, Masson M, et al. Evaluation of SARS-CoV-2 IgG antibody reactivity in patients with systemic lupus erythematosus: analysis of a multi-racial and multi-ethnic cohort. *Lancet Rheumatol*. 2021 May 27 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8159192>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34075358?tool=bestpractice.bmj.com>)
314. D'Silva KM, Jorge A, Cohen A, et al. COVID-19 outcomes in patients with systemic autoimmune rheumatic diseases compared to the general population: a US multicenter, comparative cohort study. *Arthritis Rheumatol*. 2020 Dec 10 [Epub ahead of print]. Full text (<https://onlinelibrary.wiley.com/doi/10.1002/art.41619>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33305544?tool=bestpractice.bmj.com>)
315. Hsu TY, D'Silva KM, Patel NJ, et al. Laboratory trends, hyperinflammation, and clinical outcomes for patients with a systemic rheumatic disease admitted to hospital for COVID-19: a retrospective, comparative cohort study. *Lancet Rheumatol*. 2021 May 28 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8163294>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34095857?tool=bestpractice.bmj.com>)
316. Avouac J, Drumez E, Hachulla E, et al. COVID-19 outcomes in patients with inflammatory rheumatic and musculoskeletal diseases treated with rituximab: a cohort study. *Lancet Rheumatol*. 2021 Mar 25;3(6):e419-26. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7993930>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33786454?tool=bestpractice.bmj.com>)
317. Louapre C, Collongues N, Stankoff B, et al. Clinical characteristics and outcomes in patients with coronavirus disease 2019 and multiple sclerosis. *JAMA Neurol*. 2020 Sep 1;77(9):1079-88. Full text (<https://jamanetwork.com/journals/jamaneurology/fullarticle/2767776>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32589189?tool=bestpractice.bmj.com>)
318. Salter A, Fox RJ, Newsome SD, et al. Outcomes and risk factors associated with SARS-CoV-2 infection in a North American registry of patients with multiple sclerosis. *JAMA Neurol*. 2021 Mar 19 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jamaneurology/fullarticle/2777735>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33739362?tool=bestpractice.bmj.com>)
319. Barzegar M, Mirmosayyeb O, Gajarzadeh M, et al. COVID-19 among patients with multiple sclerosis: a systematic review. *Neurol Neuroimmunol Neuroinflamm*. 2021 Jul;8(4):e1001. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8142838>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34016734?tool=bestpractice.bmj.com>)
320. Singh S, Khan A, Chowdhry M, et al. Risk of severe coronavirus disease 2019 in patients with inflammatory bowel disease in the united states: a multicenter research network study. *Gastroenterology*. 2020 Oct;159(4):1575-8. Full text ([https://www.gastrojournal.org/article/S0016-5085\(20\)34755-7/fulltext](https://www.gastrojournal.org/article/S0016-5085(20)34755-7/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32522507?tool=bestpractice.bmj.com>)
321. Ungaro RC, Brenner EJ, Gearry RB, et al. Effect of IBD medications on COVID-19 outcomes: results from an international registry. *Gut*. 2021 Apr;70(4):725-32. Full text (<https://gut.bmj.com/content/>)

- early/2020/10/26/gutjnl-2020-322539.long) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33082265?tool=bestpractice.bmj.com>)
322. Singh AK, Jena A, Kumar-M P, et al. Risk and outcomes of coronavirus disease in patients with inflammatory bowel disease: a systematic review and meta-analysis. *United European Gastroenterol J*. 2021 Mar;9(2):159-76. Full text (<https://journals.sagepub.com/doi/10.1177/2050640620972602>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33210980?tool=bestpractice.bmj.com>)
323. Kennedy NA, Goodhand JR, Bewshea C, et al. Anti-SARS-CoV-2 antibody responses are attenuated in patients with IBD treated with infliximab. *Gut*. 2021 May;70(5):865-75. Full text (<https://gut.bmj.com/content/70/5/865>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33753421?tool=bestpractice.bmj.com>)
324. Putri C, Hariyanto TI, Hananto JE, et al. Parkinson's disease may worsen outcomes from coronavirus disease 2019 (COVID-19) pneumonia in hospitalized patients: a systematic review, meta-analysis, and meta-regression. *Parkinsonism Relat Disord*. 2021 Apr 24 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8065236>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33931304?tool=bestpractice.bmj.com>)
325. Chambergo-Michilot D, Barros-Sevillano S, Rivera-Torrejón O, et al. Factors associated with COVID-19 in people with Parkinson's disease: a systematic review and meta-analysis. *Eur J Neurol*. 2021 May 13 [Epub ahead of print]. Full text (<https://onlinelibrary.wiley.com/doi/10.1111/ene.14912>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33983673?tool=bestpractice.bmj.com>)
326. Sallis R, Young DR, Tartof SY, et al. Physical inactivity is associated with a higher risk for severe COVID-19 outcomes: a study in 48 440 adult patients. *Br J Sports Med*. 2021 Apr 13 [Epub ahead of print]. Full text (<https://bjsm.bmj.com/content/early/2021/04/07/bjsports-2021-104080.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33849909?tool=bestpractice.bmj.com>)
327. Hariyanto TI, Kurniawan A. Dyslipidemia is associated with severe coronavirus disease 2019 (COVID-19) infection. *Diabetes Metab Syndr*. 2020 Aug 1;14(5):1463-5. Full text (<https://www.sciencedirect.com/science/article/pii/S1871402120303027>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32771919?tool=bestpractice.bmj.com>)
328. Choi GJ, Kim HM, Kang H. The potential role of dyslipidemia in COVID-19 severity: an umbrella review of systematic reviews. *J Lipid Atheroscler*. 2020 Sep;9(3):435-48. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7521969>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33024735?tool=bestpractice.bmj.com>)
329. Zuin M, Rigatelli G, Bilato C, et al. Dyslipidaemia and mortality in COVID-19 patients: a meta-analysis. *QJM*. 2021 Apr 2 [Epub ahead of print]. Full text (<https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcab071/6209024>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33822215?tool=bestpractice.bmj.com>)
330. Atmosudigdo IS, Pranata R, Lim MA, et al. Dyslipidemia increases the risk of severe COVID-19: a systematic review, meta-analysis, and meta-regression. *J Clin Exp Hepatol*. 2021 Feb 8 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7868769>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33584063?tool=bestpractice.bmj.com>)

331. Yetmar ZA, Chesdachai S, Kashour T, et al. Prior statin use and risk of mortality and severe disease from coronavirus disease 2019: a systematic review and meta-analysis. *Open Forum Infect Dis.* 2021 Jul;8(7):ofab284. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8244756\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8244756) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34258316?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34258316?tool=bestpractice.bmj.com)
332. Doglietto F, Vezzoli M, Gheza F, et al. Factors associated with surgical mortality and complications among patients with and without coronavirus disease 2019 (COVID-19) in Italy. *JAMA Surg.* 2020 Jun 12;155(8):1-14. [Full text \(https://jamanetwork.com/journals/jamasurgery/fullarticle/2767370\)](https://jamanetwork.com/journals/jamasurgery/fullarticle/2767370) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32530453?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32530453?tool=bestpractice.bmj.com)
333. Lei S, Jiang F, Su W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. *EClinicalMedicine.* 2020 Apr 5:100331. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7128617\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7128617) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32292899?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32292899?tool=bestpractice.bmj.com)
334. COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. *Lancet.* 2020 Jul 4;396(10243):27-38. [Full text \(https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(20\)31182-X.pdf\)](https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)31182-X.pdf) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32479829?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32479829?tool=bestpractice.bmj.com)
335. Liu N, Zhang T, Ma L, et al. The impact of ABO blood group on COVID-19 infection risk and mortality: A systematic review and meta-analysis. *Blood Rev.* 2020 Dec 8:100785. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7834371\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7834371) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33309392?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33309392?tool=bestpractice.bmj.com)
336. Franchini M, Cruciani M, Mengoli C, et al. ABO blood group and COVID-19: an updated systematic literature review and meta-analysis. *Blood Transfus.* 2021 May 12 [Epub ahead of print]. [Full text \(http://www.bloodtransfusion.it/articolosing.aspx?id=001158\)](http://www.bloodtransfusion.it/articolosing.aspx?id=001158) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34059188?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34059188?tool=bestpractice.bmj.com)
337. Severe Covid-19 GWAS Group; Ellinghaus D, Degenhardt F, Bujanda L, et al. Genomewide association study of severe Covid-19 with respiratory failure. *N Engl J Med.* 2020 Oct 15;383(16):1522-34. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2020283\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2020283) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32558485?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32558485?tool=bestpractice.bmj.com)
338. Wu SC, Arthur CM, Wang J, et al. The SARS-CoV-2 receptor-binding domain preferentially recognizes blood group A. *Blood Adv.* 2021 Mar 9;5(5):1305-9. [Full text \(https://ashpublications.org/bloodadvances/article/5/5/1305/475250/The-SARS-CoV-2-receptor-binding-domain\)](https://ashpublications.org/bloodadvances/article/5/5/1305/475250/The-SARS-CoV-2-receptor-binding-domain) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33656534?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33656534?tool=bestpractice.bmj.com)
339. Yamamoto S, Saito M, Tamura A, et al. The human microbiome and COVID-19: a systematic review. *PLoS One.* 2021 Jun 23;16(6):e0253293. [Full text \(https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0253293\)](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0253293) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34161373?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34161373?tool=bestpractice.bmj.com)

340. Dhar D, Mohanty A. Gut microbiota and Covid-19- possible link and implications. *Virus Res.* 2020 May 13;285:198018. [Full text \(https://www.sciencedirect.com/science/article/pii/S0168170220304603?via%3Dihub\)](https://www.sciencedirect.com/science/article/pii/S0168170220304603?via%3Dihub) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32430279?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32430279?tool=bestpractice.bmj.com)
341. Zuo T, Zhang F, Lui GCY, et al. Alterations in gut microbiota of patients with COVID-19 during time of hospitalization. *Gastroenterology.* 2020 Sep;159(3):944-55. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7237927\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7237927) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32442562?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32442562?tool=bestpractice.bmj.com)
342. Gu S, Chen Y, Wu Z, et al. Alterations of the gut microbiota in patients with coronavirus disease 2019 or H1N1 influenza. *Clin Infect Dis.* 2020 Dec 17;71(10):2669-78. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7314193\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7314193) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32497191?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32497191?tool=bestpractice.bmj.com)
343. Yeoh YK, Zuo T, Lui GC, et al. Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19. *Gut.* 2021 Apr;70(4):698-706. [Full text \(https://gut.bmj.com/content/early/2021/01/04/gutjnl-2020-323020\)](https://gut.bmj.com/content/early/2021/01/04/gutjnl-2020-323020) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33431578?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33431578?tool=bestpractice.bmj.com)
344. Centre for Evidence-Based Medicine; Spencer EA, Brassey J, Jefferson T, et al. Environmental weather conditions and influence on transmission of SARS-CoV-2. 2020 [internet publication]. [Full text \(https://www.cebm.net/covid-19/environmental-weather-conditions-and-influence-on-transmission-of-sars-cov-2\)](https://www.cebm.net/covid-19/environmental-weather-conditions-and-influence-on-transmission-of-sars-cov-2)
345. Mecenas P, Bastos RTDRM, Vallinoto ACR, et al. Effects of temperature and humidity on the spread of COVID-19: a systematic review. *PLoS One.* 2020;15(9):e0238339. [Full text \(https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0238339\)](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0238339) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32946453?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32946453?tool=bestpractice.bmj.com)
346. Yao Y, Pan J, Liu Z, et al. No association of COVID-19 transmission with temperature or UV radiation in Chinese cities. *Eur Respir J.* 2020 May 7;55(5):2000517. [Full text \(https://erj.ersjournals.com/content/early/2020/04/01/13993003.00517-2020\)](https://erj.ersjournals.com/content/early/2020/04/01/13993003.00517-2020) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32269084?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32269084?tool=bestpractice.bmj.com)
347. Baker RE, Yang W, Vecchi GA, et al. Susceptible supply limits the role of climate in the early SARS-CoV-2 pandemic. *Science.* 2020 Jul 17;369(6501):315-9. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7243362\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7243362) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32423996?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32423996?tool=bestpractice.bmj.com)
348. Sehra ST, Saliccioli JD, Wiebe DJ, et al. Maximum daily temperature, precipitation, ultra-violet light and rates of transmission of SARS-Cov-2 in the United States. *Clin Infect Dis.* 2020 Dec 3;71(9):2482-7. [Full text \(https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa681/5849063\)](https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa681/5849063) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32472936?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32472936?tool=bestpractice.bmj.com)
349. Centre for Evidence-Based Medicine; Heneghan C, Jefferson T. Effect of latitude on COVID-19. 2020 [internet publication]. [Full text \(https://www.cebm.net/covid-19/effect-of-latitude-on-covid-19\)](https://www.cebm.net/covid-19/effect-of-latitude-on-covid-19)

350. Whittemore PB. COVID-19 fatalities, latitude, sunlight, and vitamin D. *Am J Infect Control*. 2020 Sep;48(9):1042-4. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7319635\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7319635) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32599103?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32599103?tool=bestpractice.bmj.com)
351. Centre for Evidence-Based Medicine; Hoang U, Jones NR. Is there an association between exposure to air pollution and severity of COVID-19 infection? 2020 [internet publication]. [Full text \(https://www.cebm.net/covid-19/is-there-an-association-between-exposure-to-air-pollution-and-severity-of-covid-19-infection\)](https://www.cebm.net/covid-19/is-there-an-association-between-exposure-to-air-pollution-and-severity-of-covid-19-infection)
352. Copat C, Cristaldi A, Fiore M, et al. The role of air pollution (PM and NO₂) in COVID-19 spread and lethality: a systematic review. *Environ Res*. 2020 Aug 24;191:110129. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7444490\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7444490) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32853663?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32853663?tool=bestpractice.bmj.com)
353. Frontera A, Cianfanelli L, Vlachos K, et al. Severe air pollution links to higher mortality in COVID-19 patients: the “double-hit” hypothesis. *J Infect*. 2020 Aug;81(2):255-9. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7240268\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7240268) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32447007?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32447007?tool=bestpractice.bmj.com)
354. Ogen Y. Assessing nitrogen dioxide (NO₂) levels as a contributing factor to coronavirus (COVID-19) fatality. *Sci Total Environ*. 2020 Apr 11;726:138605. [Full text \(https://www.sciencedirect.com/science/article/pii/S0048969720321215\)](https://www.sciencedirect.com/science/article/pii/S0048969720321215) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32302812?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32302812?tool=bestpractice.bmj.com)
355. Bowyer RCE, Varsavsky T, Thompson EJ, et al. Geo-social gradients in predicted COVID-19 prevalence in Great Britain: results from 1 960 242 users of the COVID-19 Symptoms Study app. *Thorax*. 2020 Dec 29 [Epub ahead of print]. [Full text \(https://thorax.bmj.com/content/76/7/723\)](https://thorax.bmj.com/content/76/7/723) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33376145?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33376145?tool=bestpractice.bmj.com)
356. World Health Organization. Interim recommendations for use of the Pfizer–BioNTech COVID-19 vaccine, BNT162b2, under emergency use listing. 2021 [internet publication]. [Full text \(https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BNT162b2-2021.1\)](https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BNT162b2-2021.1)
357. World Health Organization. Interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19: interim guidance. 2021 [internet publication]. [Full text \(https://www.who.int/publications/i/item/interim-recommendations-for-use-of-the-moderna-mrna-1273-vaccine-against-covid-19\)](https://www.who.int/publications/i/item/interim-recommendations-for-use-of-the-moderna-mrna-1273-vaccine-against-covid-19)
358. World Health Organization. Interim recommendations for use of the ChAdOx1-S [recombinant] vaccine against COVID-19 (AstraZeneca COVID-19 vaccine AZD1222, SII Covishield, SK Bioscience). 2021 [internet publication]. [Full text \(https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1\)](https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1)
359. World Health Organization. Interim recommendations for the use of the Janssen Ad26.COV2.S (COVID-19) vaccine. 2021 [internet publication]. [Full text \(https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE-recommendation-Ad26.COV2.S-2021.1\)](https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE-recommendation-Ad26.COV2.S-2021.1)

360. World Health Organization. Interim recommendations for use of the inactivated COVID-19 vaccine BIBP developed by China National Biotech Group (CNBG), Sinopharm, 7 May 2021. 2021 [internet publication]. [Full text \(https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BIBP-2021.1\)](https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BIBP-2021.1)
361. World Health Organization. Interim recommendations for use of the inactivated COVID-19 vaccine, CoronaVac, developed by Sinovac: interim guidance. 2021 [internet publication]. [Full text \(https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-Sinovac-Coronavac\)](https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-Sinovac-Coronavac)
362. Logunov DY, Dolzhikova IV, Zubkova OV, et al. Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia. *Lancet*. 2020 Sep 26;396(10255):887-97. [Full text \(https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00234-8/fulltext\)](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00234-8/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32896291?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32896291?tool=bestpractice.bmj.com)
363. Thiagarajan K. What do we know about India's Covaxin vaccine? *BMJ*. 2021 Apr 20;373:n997. [Full text \(https://www.bmj.com/content/373/bmj.n997\)](https://www.bmj.com/content/373/bmj.n997) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33879478?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33879478?tool=bestpractice.bmj.com)
364. Public Health England. Consent: the green book, chapter 2. 2021 [internet publication]. [Full text \(https://www.gov.uk/government/publications/consent-the-green-book-chapter-2\)](https://www.gov.uk/government/publications/consent-the-green-book-chapter-2)
365. Hacisuleyman E, Hale C, Saito Y, et al. Vaccine breakthrough infections with SARS-CoV-2 variants. *N Engl J Med*. 2021 Apr 21 [Epub ahead of print]. [Full text \(https://www.nejm.org/doi/10.1056/NEJMoa2105000\)](https://www.nejm.org/doi/10.1056/NEJMoa2105000) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33882219?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33882219?tool=bestpractice.bmj.com)
366. Teran RA, Walblay KA, Shane EL, et al. Postvaccination SARS-CoV-2 infections among skilled nursing facility residents and staff members: Chicago, Illinois, December 2020–March 2021. *MMWR Morb Mortal Wkly Rep*. 2021 Apr 30;70(17):632-8. [Full text \(https://www.cdc.gov/mmwr/volumes/70/wr/mm7017e1.htm\)](https://www.cdc.gov/mmwr/volumes/70/wr/mm7017e1.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33914721?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33914721?tool=bestpractice.bmj.com)
367. CDC COVID-19 Vaccine Breakthrough Case Investigations Team. COVID-19 vaccine breakthrough infections reported to CDC: United States, January 1–April 30, 2021. *MMWR Morb Mortal Wkly Rep*. 2021 May 28;70(21):792-3. [Full text \(https://www.cdc.gov/mmwr/volumes/70/wr/mm7021e3.htm\)](https://www.cdc.gov/mmwr/volumes/70/wr/mm7021e3.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34043615?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34043615?tool=bestpractice.bmj.com)
368. Centers for Disease Control and Prevention. COVID-19 vaccine breakthrough case investigation and reporting. 2021 [internet publication]. [Full text \(https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html\)](https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html)
369. Amit S, Beni SA, Biber A, et al. Post-vaccination COVID-19 among healthcare workers, Israel. *Emerg Infect Dis*. 2021 Feb 1;27(4). [Full text \(https://wwwnc.cdc.gov/eid/article/27/4/21-0016_article\)](https://wwwnc.cdc.gov/eid/article/27/4/21-0016_article) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33522478?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33522478?tool=bestpractice.bmj.com)
370. Barouch DH, Stephenson KE, Sadoff J, et al. Durable humoral and cellular immune responses 8 months after Ad26.COV2.S vaccination. *N Engl J Med*. 2021 Jul 14 [Epub ahead of print]. [Full text](#)

(<https://www.nejm.org/doi/full/10.1056/NEJMc2108829>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34260834?tool=bestpractice.bmj.com>)

371. Borobia AM, Carcas AJ, Pérez-Olmeda M, et al. Immunogenicity and reactogenicity of BNT162b2 booster in ChAdOx1-S-primed participants (CombiVacS): a multicentre, open-label, randomised, controlled, phase 2 trial. *Lancet*. 2021 Jun 25 [Epub ahead of print]. Full text ([https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)01420-3/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01420-3/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34181880?tool=bestpractice.bmj.com>)
372. Normark J, Vikström L, Gwon YD, et al. Heterologous ChAdOx1 nCoV-19 and mRNA-1273 vaccination. *N Engl J Med*. 2021 Jul 14 [Epub ahead of print]. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMc2110716>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34260850?tool=bestpractice.bmj.com>)
373. Shaw RH, Stuart A, Greenland M, et al. Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data. *Lancet*. 2021 May 12 [Epub ahead of print]. Full text ([https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)01115-6/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01115-6/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33991480?tool=bestpractice.bmj.com>)
374. Bourguignon A, Arnold DM, Warkentin TE, et al. Adjunct immune globulin for vaccine-induced thrombotic thrombocytopenia. *N Engl J Med*. 2021 Jun 9 [Epub ahead of print]. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMoa2107051>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34107198?tool=bestpractice.bmj.com>)
375. Scully M, Singh D, Lown R, et al. Pathologic antibodies to platelet factor 4 after ChAdOx1 nCoV-19 vaccination. *N Engl J Med*. 2021 Jun 10;384(23):2202-11. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMoa2105385>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33861525?tool=bestpractice.bmj.com>)
376. European Medicines Agency. AstraZeneca's COVID-19 vaccine: EMA finds possible link to very rare cases of unusual blood clots with low blood platelets. 2021 [internet publication]. Full text (<https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood>)
377. Medicines and Healthcare products Regulatory Agency. MHRA issues new advice, concluding a possible link between COVID-19 vaccine AstraZeneca and extremely rare, unlikely to occur blood clots. 2021 [internet publication]. Full text (<https://www.gov.uk/government/news/mhra-issues-new-advice-concluding-a-possible-link-between-covid-19-vaccine-astrazeneca-and-extremely-rare-unlikely-to-occur-blood-clots>)
378. World Health Organization. Interim statement of the COVID-19 subcommittee of the WHO global advisory committee on vaccine safety on AstraZeneca COVID-19 vaccine. 2021 [internet publication]. Full text (<https://www.who.int/news/item/07-04-2021-interim-statement-of-the-covid-19-subcommittee-of-the-who-global-advisory-committee-on-vaccine-safety>)
379. European Medicines Agency. AstraZeneca's COVID-19 vaccine: EMA to provide further context on risk of very rare blood clots with low blood platelets. 2021 [internet publication]. Full text (<https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-to-provide-further-context-on-risk-of-very-rare-blood-clots-with-low-blood-platelets>)

www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-provide-further-context-risk-very-rare-blood-clots-low-blood)

380. Muir KL, Kallam A, Koepsell SA, et al. Thrombotic thrombocytopenia after Ad26.COV2.S vaccination. *N Engl J Med*. 2021 Apr 14 [Epub ahead of print]. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMc2105869\)](https://www.nejm.org/doi/full/10.1056/NEJMc2105869) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33852795?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33852795?tool=bestpractice.bmj.com)
381. European Medicines Agency. COVID-19 vaccine Janssen: EMA finds possible link to very rare cases of unusual blood clots with low blood platelets. 2021 [internet publication]. [Full text \(https://www.ema.europa.eu/en/news/covid-19-vaccine-janssen-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood\)](https://www.ema.europa.eu/en/news/covid-19-vaccine-janssen-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood)
382. Sangli S, Virani A, Cheronis N, et al. Thrombosis with thrombocytopenia after the messenger RNA-1273 vaccine. *Ann Intern Med*. 2021 Jun 29 [Epub ahead of print]. [Full text \(https://www.acpjournals.org/doi/10.7326/L21-0244\)](https://www.acpjournals.org/doi/10.7326/L21-0244) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34181446?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34181446?tool=bestpractice.bmj.com)
383. Medicines and Healthcare products Regulatory Agency. Coronavirus vaccine: weekly summary of Yellow Card reporting. 2021 [internet publication]. [Full text \(https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting\)](https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting)
384. MacNeil JR, Su JR, Broder KR, et al. Updated recommendations from the Advisory Committee on Immunization Practices for use of the Janssen (Johnson & Johnson) COVID-19 vaccine after reports of thrombosis with thrombocytopenia syndrome among vaccine recipients: United States, April 2021. *MMWR Morb Mortal Wkly Rep*. 2021 Apr 30;70(17):651-6. [Full text \(https://www.cdc.gov/mmwr/volumes/70/wr/mm7017e4.htm\)](https://www.cdc.gov/mmwr/volumes/70/wr/mm7017e4.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33914723?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33914723?tool=bestpractice.bmj.com)
385. US Food and Drug Administration. FDA and CDC lift recommended pause on Johnson & Johnson (Janssen) COVID-19 vaccine use following thorough safety review. 2021 [internet publication]. [Full text \(https://www.fda.gov/news-events/press-announcements/fda-and-cdc-lift-recommended-pause-johnson-johnson-janssen-covid-19-vaccine-use-following-thorough\)](https://www.fda.gov/news-events/press-announcements/fda-and-cdc-lift-recommended-pause-johnson-johnson-janssen-covid-19-vaccine-use-following-thorough)
386. Shay DK, Gee J, Su JR, et al. Safety monitoring of the Janssen (Johnson & Johnson) COVID-19 vaccine: United States, March–April 2021. *MMWR Morb Mortal Wkly Rep*. 2021 May 7;70(18):680-4. [Full text \(https://www.cdc.gov/mmwr/volumes/70/wr/mm7018e2.htm\)](https://www.cdc.gov/mmwr/volumes/70/wr/mm7018e2.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33956784?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33956784?tool=bestpractice.bmj.com)
387. Norwegian Institute of Public Health. Norwegian Institute of Public Health's recommendation about AstraZeneca vaccine. 2021 [internet publication]. [Full text \(https://www.fhi.no/en/news/2021/astrazeneca-vaccine-removed-from-coronavirus-immunisation-programme-in-norw\)](https://www.fhi.no/en/news/2021/astrazeneca-vaccine-removed-from-coronavirus-immunisation-programme-in-norw)
388. Danish Health Authority. The Danish COVID-19 vaccine rollout continues without the COVID-19 vaccine from Johnson & Johnson. 2021 [internet publication]. [Full text \(https://www.sst.dk/en/English/news/2021/The-Danish-COVID-19-vaccine-rollout-continues-without-the-COVID-19-vaccine-from-Johnson-Johnson\)](https://www.sst.dk/en/English/news/2021/The-Danish-COVID-19-vaccine-rollout-continues-without-the-COVID-19-vaccine-from-Johnson-Johnson)

389. Public Health England. JCVI advises on COVID-19 vaccine for people aged under 40. 2021 [internet publication]. Full text (<https://www.gov.uk/government/news/jcvi-advises-on-covid-19-vaccine-for-people-aged-under-40>)
390. Department of Health and Social Care. JCVI statement on use of the AstraZeneca COVID-19 vaccine: 7 April 2021. 2021 [internet publication]. Full text (<https://www.gov.uk/government/publications/use-of-the-astrazeneca-covid-19-vaccine-jcvi-statement/jcvi-statement-on-use-of-the-astrazeneca-covid-19-vaccine-7-april-2021>)
391. Centers for Disease Control and Prevention. Interim clinical considerations for use of COVID-19 vaccines currently authorized in the United States. 2021 [internet publication]. Full text (<https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>)
392. Marshall M, Ferguson ID, Lewis P, et al. Symptomatic acute myocarditis in seven adolescents following Pfizer-BioNTech COVID-19 vaccination. *Pediatrics*. 2021 Jun 4 [Epub ahead of print]. Full text (<https://pediatrics.aappublications.org/content/early/2021/06/04/peds.2021-052478>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34088762?tool=bestpractice.bmj.com>)
393. Larson KF, Ammirati E, Adler ED, et al. Myocarditis after BNT162b2 and mRNA-1273 vaccination. *Circulation*. 2021 Jun 16 [Epub ahead of print]. Full text (<https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.121.055913>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34133884?tool=bestpractice.bmj.com>)
394. Kim HW, Jenista ER, Wendell DC, et al. Patients with acute myocarditis following mRNA COVID-19 vaccination. *JAMA Cardiol*. 2021 Jun 29 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jamacardiology/fullarticle/2781602>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34185046?tool=bestpractice.bmj.com>)
395. Bozkurt B, Kamat I, Hotez PJ. Myocarditis with COVID-19 mRNA vaccines. *Circulation*. 2021 Jul 20 [Epub ahead of print]. Full text (<https://www.ahajournals.org/doi/abs/10.1161/CIRCULATIONAHA.121.056135>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34281357?tool=bestpractice.bmj.com>)
396. US Food and Drug Administration. Coronavirus (COVID-19) update: June 25, 2021. 2021 [internet publication]. Full text (<https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-june-25-2021>)
397. European Medicines Agency. Comirnaty and Spikevax: possible link to very rare cases of myocarditis and pericarditis. 2021 [internet publication]. Full text (<https://www.ema.europa.eu/en/news/comirnaty-spikevax-possible-link-very-rare-cases-myocarditis-pericarditis>)
398. Medicines and Healthcare products Regulatory Agency. COVID-19 vaccines: updates for July 2021. 2021 [internet publication]. Full text (<https://www.gov.uk/drug-safety-update/covid-19-vaccines-updates-for-july-2021>)
399. Gargano JW, Wallace M, Hadler SC, et al. Use of mRNA COVID-19 vaccine after reports of myocarditis among vaccine recipients: update from the Advisory Committee on Immunization Practices: United States, June 2021. *MMWR Morb Mortal Wkly Rep*. 2021 Jul 9;70(27):977-82. Full

- text (https://www.cdc.gov/mmwr/volumes/70/wr/mm7027e2.htm?s_cid=mm7027e2_w) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34237049?tool=bestpractice.bmj.com>)
400. Montgomery J, Ryan M, Engler R, et al. Myocarditis following immunization with mRNA COVID-19 vaccines in members of the US military. *JAMA Cardiol.* 2021 Jun 29 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jamacardiology/fullarticle/2781601>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34185045?tool=bestpractice.bmj.com>)
401. Centers for Disease Control and Prevention. Clinical considerations: myocarditis and pericarditis after receipt of mRNA COVID-19 vaccines among adolescents and young adults. 2021 [internet publication]. Full text (<https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html>)
402. Castells MC, Phillips EJ. Maintaining safety with SARS-CoV-2 vaccines. *N Engl J Med.* 2021 Feb 18;384(7):643-9. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7787218>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33378605?tool=bestpractice.bmj.com>)
403. Shimabukuro TT, Cole M, Su JR. Reports of anaphylaxis after receipt of mRNA COVID-19 vaccines in the US: December 14, 2020 – January 18, 2021. *JAMA.* 2021 Mar 16;325(11):1101-2. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2776557>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33576785?tool=bestpractice.bmj.com>)
404. Greenhawt M, Abrams EM, Shaker M, et al. The risk of allergic reaction to SARS-CoV-2 vaccines and recommended evaluation and management: a systematic review, meta-analysis, GRADE assessment, and international consensus approach. *J Allergy Clin Immunol Pract.* 2021 Jun 18 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8248554>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34153517?tool=bestpractice.bmj.com>)
405. European Medicines Agency. Vaxzevria: EMA advises against use in people with history of capillary leak syndrome. 2021 [internet publication]. Full text (<https://www.ema.europa.eu/en/news/vaxzevria-ema-advises-against-use-people-history-capillary-leak-syndrome>)
406. European Medicines Agency. EMA advises against use of COVID-19 vaccine Janssen in people with history of capillary leak syndrome. 2021 [internet publication]. Full text (<https://www.ema.europa.eu/en/news/ema-advises-against-use-covid-19-vaccine-janssen-people-history-capillary-leak-syndrome>)
407. Matheny M, Maleque N, Channell N, et al. Severe exacerbations of systemic capillary leak syndrome after COVID-19 vaccination: a case series. *Ann Intern Med.* 2021 Jun 15 [Epub ahead of print]. Full text (<https://www.acpjournals.org/doi/10.7326/L21-0250>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34125573?tool=bestpractice.bmj.com>)
408. Beber A, Dellai F, Abdel Jaber M, et al. Systemic capillary leak syndrome triggered by SARS-CoV2 infection: case report and systematic review. *Scand J Rheumatol.* 2021 Jun 25:1-3. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34169783?tool=bestpractice.bmj.com>)
409. Ozonoff A, Nanishi E, Levy O. Bell's palsy and SARS-CoV-2 vaccines. *Lancet Infect Dis.* 2021 Apr;21(4):450-2. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7906673>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33639103?tool=bestpractice.bmj.com>)

410. Renoud L, Khouri C, Revol B, et al. Association of facial paralysis with mRNA COVID-19 vaccines: a disproportionality analysis using the World Health Organization pharmacovigilance database. *JAMA Intern Med.* 2021 Apr 27 [Epub ahead of print]. [Full text \(https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2779389\)](https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2779389) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33904857?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33904857?tool=bestpractice.bmj.com)
411. Shemer A, Pras E, Einan-Lifshitz A, et al. Association of COVID-19 vaccination and facial nerve palsy: a case-control study. *JAMA Otolaryngol Head Neck Surg.* 2021 Jun 24 [Epub ahead of print]. [Full text \(https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2781367\)](https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2781367) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34165512?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34165512?tool=bestpractice.bmj.com)
412. Cirillo N, Doan R. Bell's palsy and SARS-CoV-2 vaccines-an unfolding story. *Lancet Infect Dis.* 2021 Jun 7 [Epub ahead of print]. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8184125\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8184125) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34111409?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34111409?tool=bestpractice.bmj.com)
413. Adin ME, Isufi E, Kulon M, et al. Association of COVID-19 mRNA vaccine with ipsilateral axillary lymph node reactivity on imaging. *JAMA Oncol.* 2021 Jun 10 [Epub ahead of print]. [Full text \(https://jamanetwork.com/journals/jamaoncology/fullarticle/2780591\)](https://jamanetwork.com/journals/jamaoncology/fullarticle/2780591) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34110378?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34110378?tool=bestpractice.bmj.com)
414. Garreffa E, York J, Turnbull A, et al. Regional lymphadenopathy following COVID-19 vaccination: considerations for primary care management. *Br J Gen Pract.* 2021 Jun;71(707):284-5. [Full text \(https://bjgp.org/content/71/707/284\)](https://bjgp.org/content/71/707/284) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34045261?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34045261?tool=bestpractice.bmj.com)
415. Patel SU, Khurram R, Lakhani A, et al. Guillain-Barre syndrome following the first dose of the chimpanzee adenovirus-vectored COVID-19 vaccine, ChAdOx1. *BMJ Case Rep.* 2021 Apr 22;14(4):e242956. [Full text \(https://casereports.bmj.com/content/14/4/e242956\)](https://casereports.bmj.com/content/14/4/e242956) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33888484?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33888484?tool=bestpractice.bmj.com)
416. Márquez Loza AM, Holroyd KB, Johnson SA, et al. Guillain- Barré syndrome in the placebo and active arms of a COVID-19 vaccine clinical trial: temporal associations do not imply causality. *Neurology.* 2021 Apr 6 [Epub ahead of print]. [Full text \(https://n.neurology.org/content/96/22/1052\)](https://n.neurology.org/content/96/22/1052) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33824169?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33824169?tool=bestpractice.bmj.com)
417. European Medicines Agency. Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 5-8 July 2021. 2021 [internet publication]. [Full text \(https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-5-8-july-2021\)](https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-5-8-july-2021)
418. Wise J. Covid-19: AstraZeneca vaccine linked with small risk of ITP, real world data show. *BMJ.* 2021 Jun 10;373:n1489. [Full text \(https://www.bmj.com/content/373/bmj.n1489\)](https://www.bmj.com/content/373/bmj.n1489) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34112639?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34112639?tool=bestpractice.bmj.com)
419. European Medicines Agency. Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 3-6 May 2021. 2021 [internet publication]. [Full text \(https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-3-6-may-2021\)](https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-3-6-may-2021)
420. Blumenthal KG, Freeman EE, Saff RR, et al. Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. *N Engl J Med.* 2021 Apr 1;384(13):1273-7. [Full text \(https://](https://)

- www.ncbi.nlm.nih.gov/pmc/articles/PMC7944952) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33657292?tool=bestpractice.bmj.com>)
421. Johnston MS, Galan A, Watsky KL, et al. Delayed localized hypersensitivity reactions to the Moderna COVID-19 vaccine: a case series. *JAMA Dermatol.* 2021 May 12 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jamadermatology/fullarticle/2779643>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33978670?tool=bestpractice.bmj.com>)
 422. Hause AM, Gee J, Johnson T, et al. Anxiety-related adverse event clusters after Janssen COVID-19 vaccination: five U.S. mass vaccination sites, April 2021. *MMWR Morb Mortal Wkly Rep.* 2021 May 7;70(18):685-8. Full text (<https://www.cdc.gov/mmwr/volumes/70/wr/mm7018e3.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33956781?tool=bestpractice.bmj.com>)
 423. Shimabukuro TT, Kim SY, Myers TR, et al. Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons. *N Engl J Med.* 2021 Jun 17;384(24):2273-82. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMoa2104983>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33882218?tool=bestpractice.bmj.com>)
 424. Public Health England. JCVI issues new advice on COVID-19 vaccination for pregnant women. 2021 [internet publication]. Full text (<https://www.gov.uk/government/news/jcvi-issues-new-advice-on-covid-19-vaccination-for-pregnant-women>)
 425. Public Health England. The safety of COVID-19 vaccines when given in pregnancy. 2021 [internet publication]. Full text (<https://www.gov.uk/government/publications/safety-of-covid-19-vaccines-when-given-in-pregnancy/the-safety-of-covid-19-vaccines-when-given-in-pregnancy>)
 426. American College of Obstetricians and Gynecologists. COVID-19 vaccination considerations for obstetric–gynecologic care. 2021 [internet publication]. Full text (<https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/covid-19-vaccination-considerations-for-obstetric-gynecologic-care>)
 427. Perl SH, Uzan-Yulzari A, Klainer H, et al. SARS-CoV-2-specific antibodies in breast milk after COVID-19 vaccination of breastfeeding women. *JAMA.* 2021 May 18;325(19):2013-4. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2778766>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33843975?tool=bestpractice.bmj.com>)
 428. Golan Y, Prael M, Cassidy A, et al. Evaluation of messenger RNA from COVID-19 BTN162b2 and mRNA-1273 vaccines in human milk. *JAMA Pediatr.* 2021 Jul 6 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2781679>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34228115?tool=bestpractice.bmj.com>)
 429. Medicines and Healthcare products Regulatory Agency. The MHRA concludes positive safety profile for Pfizer/BioNTech vaccine in 12- to 15-year-olds. 2021 [internet publication]. Full text (<https://www.gov.uk/government/news/the-mhra-concludes-positive-safety-profile-for-pfizerbiontech-vaccine-in-12-to-15-year-olds>)
 430. US Food and Drug Administration. Coronavirus (COVID-19) update: FDA authorizes Pfizer-BioNTech COVID-19 vaccine for emergency use in adolescents in another important action in fight against pandemic. 2021 [internet publication]. Full text (<https://www.fda.gov/news-events/press->

[announcements/coronavirus-covid-19-update-fda-authorizes-pfizer-biontech-covid-19-vaccine-emergency-use\)](#)

431. Wallace M, Woodworth KR, Gargano JW, et al. The Advisory Committee on Immunization Practices' interim recommendation for use of Pfizer-BioNTech COVID-19 vaccine in adolescents aged 12-15 years: United States, May 2021. *MMWR Morb Mortal Wkly Rep*. 2021 May 21;70(20):749-52. [Full text \(https://www.cdc.gov/mmwr/volumes/70/wr/mm7020e1.htm\)](https://www.cdc.gov/mmwr/volumes/70/wr/mm7020e1.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34014913?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34014913?tool=bestpractice.bmj.com)
432. European Medicines Agency. First COVID-19 vaccine approved for children aged 12 to 15 in EU. 2021 [internet publication]. [Full text \(https://www.ema.europa.eu/en/news/first-covid-19-vaccine-approved-children-aged-12-15-eu\)](https://www.ema.europa.eu/en/news/first-covid-19-vaccine-approved-children-aged-12-15-eu)
433. Renck RW Jr, Klein NP, Kitchin N, et al. Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. *N Engl J Med*. 2021 May 27 [Epub ahead of print]. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2107456\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2107456) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34043894?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34043894?tool=bestpractice.bmj.com)
434. Joint Committee on Vaccination and Immunisation. JCVI issues advice on COVID-19 vaccination of children and young people. 2021 [internet publication]. [Full text \(https://www.gov.uk/government/news/jcvi-issues-advice-on-covid-19-vaccination-of-children-and-young-people\)](https://www.gov.uk/government/news/jcvi-issues-advice-on-covid-19-vaccination-of-children-and-young-people)
435. European Medicines Agency. EMA evaluating the use of COVID-19 vaccine Moderna in young people aged 12 to 17. 2021 [internet publication]. [Full text \(https://www.ema.europa.eu/en/news/ema-evaluating-use-covid-19-vaccine-moderna-young-people-aged-12-17\)](https://www.ema.europa.eu/en/news/ema-evaluating-use-covid-19-vaccine-moderna-young-people-aged-12-17)
436. Krammer F, Srivastava K, Alshammary H, et al. Antibody responses in seropositive persons after a single dose of SARS-CoV-2 mRNA vaccine. *N Engl J Med*. 2021 Apr 8;384(14):1372-4. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMc2101667\)](https://www.nejm.org/doi/full/10.1056/NEJMc2101667) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33691060?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33691060?tool=bestpractice.bmj.com)
437. Prendecki M, Clarke C, Brown J, et al. Effect of previous SARS-CoV-2 infection on humoral and T-cell responses to single-dose BNT162b2 vaccine. *Lancet*. 2021 Mar 27;397(10280):1178-81. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7993933\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7993933) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33640037?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33640037?tool=bestpractice.bmj.com)
438. Angyal A, Longet S, Moore S, et al; SSRN. T-cell and antibody responses to first BNT162b2 vaccine dose in previously SARS-CoV-2-infected and infection-naïve UK healthcare workers: a multicentre, prospective, observational cohort study. 2021 [internet publication]. [Full text \(https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3812375\)](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3812375)
439. Samanovic MI, Cornelius AR, Wilson JP, et al; medRxiv. Poor antigen-specific responses to the second BNT162b2 mRNA vaccine dose in SARS-CoV-2-experienced individuals. 2021 [internet publication]. [Full text \(https://www.medrxiv.org/content/10.1101/2021.02.07.21251311v1\)](https://www.medrxiv.org/content/10.1101/2021.02.07.21251311v1)
440. Shrestha NK, Burke PC, Nowacki AS, et al; medRxiv. Necessity of COVID-19 vaccination in previously infected individuals: a retrospective cohort study. 2021 [internet publication]. [Full text \(https://www.medrxiv.org/content/10.1101/2021.06.01.21258176v3\)](https://www.medrxiv.org/content/10.1101/2021.06.01.21258176v3)

441. Whitaker HJ, Tsang RSM, Byford R, et al. Pfizer-BioNTech and Oxford AstraZeneca COVID-19 vaccine effectiveness and immune response among individuals in clinical risk groups. 2021 [internet publication]. Full text (<https://khub.net/documents/135939561/430986542/RCGP+VE+riskgroups+paper.pdf/a6b54cd9-419d-9b63-e2bf-5dc796f5a91f>)
442. Frater J, Ewer KJ, Ogbe A, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 in HIV infection: a single-arm substudy of a phase 2/3 clinical trial. *Lancet HIV*. 2021 Jun 18 [Epub ahead of print]. Full text ([https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018\(21\)00103-X/fulltext](https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(21)00103-X/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34153264?tool=bestpractice.bmj.com>)
443. Obeid M, Fenwick C, Pantaleo G. Reactivation of IgA vasculitis after COVID-19 vaccination. *Lancet Rheumatol*. 2021 Jul 6 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8260100>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34250509?tool=bestpractice.bmj.com>)
444. Mahil SK, Bechman K, Raharja A, et al. The effect of methotrexate and targeted immunosuppression on humoral and cellular immune responses to the COVID-19 vaccine BNT162b2: a cohort study. *Lancet Rheumatol*. 2021 Jul 8 [Epub ahead of print]. Full text ([https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913\(21\)00212-5/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00212-5/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34258590?tool=bestpractice.bmj.com>)
445. King's College London. Delaying second vaccine dose leaves cancer patients vulnerable to virus. 2021 [internet publication]. Full text (<https://www.kcl.ac.uk/news/delaying-second-vaccine-dose-cancer-patients-vulnerable-virus>)
446. Boyarsky BJ, Werbel WA, Avery RK, et al. Immunogenicity of a single dose of SARS-CoV-2 messenger RNA vaccine in solid organ transplant recipients. *JAMA*. 2021 May 4;325(17):1784-6. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2777685>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33720292?tool=bestpractice.bmj.com>)
447. Bird S, Panopoulou A, Shea RL, et al. Response to first vaccination against SARS-CoV-2 in patients with multiple myeloma. *Lancet Haematol*. 2021 Apr 19;8(6):e389-92. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8055205>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33887255?tool=bestpractice.bmj.com>)
448. Herishanu Y, Avivi I, Aharon A, et al. Efficacy of the BNT162b2 mRNA COVID-19 vaccine in patients with chronic lymphocytic leukemia. *Blood*. 2021 Apr 16 [Epub ahead of print]. Full text (<https://ashpublications.org/blood/article/doi/10.1182/blood.2021011568/475742>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33861303?tool=bestpractice.bmj.com>)
449. Waissengrin B, Agbarya A, Safadi E, et al. Short-term safety of the BNT162b2 mRNA COVID-19 vaccine in patients with cancer treated with immune checkpoint inhibitors. *Lancet Oncol*. 2021 May;22(5):581-3. Full text ([https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045\(21\)00155-8/fulltext](https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(21)00155-8/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33812495?tool=bestpractice.bmj.com>)
450. Boyarsky BJ, Werbel WA, Avery RK, et al. Antibody response to 2-dose SARS-CoV-2 mRNA vaccine series in solid organ transplant recipients. *JAMA*. 2021 May 5 [Epub ahead of print]. Full text

(<https://jamanetwork.com/journals/jama/fullarticle/2779852>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33950155?tool=bestpractice.bmj.com>)

451. Shostak Y, Shafran N, Heching M, et al. Early humoral response among lung transplant recipients vaccinated with BNT162b2 vaccine. *Lancet Respir Med*. 2021 May 5 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8099313>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33964244?tool=bestpractice.bmj.com>)
452. Marion O, Del Bello A, Abravanel F, et al. Safety and immunogenicity of anti-SARS-CoV-2 messenger RNA vaccines in recipients of solid organ transplants. *Ann Intern Med*. 2021 May 25 [Epub ahead of print]. Full text (<https://www.acpjournals.org/doi/10.7326/M21-1341>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34029487?tool=bestpractice.bmj.com>)
453. Massarweh A, Eliakim-Raz N, Stemmer A, et al. Evaluation of seropositivity following BNT162b2 messenger RNA vaccination for SARS-CoV-2 in patients undergoing treatment for cancer. *JAMA Oncol*. 2021 May 28 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jamaoncology/fullarticle/2780584>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34047765?tool=bestpractice.bmj.com>)
454. Goshen-Lago T, Waldhorn I, Holland R, et al. Serologic status and toxic effects of the SARS-CoV-2 BNT162b2 vaccine in patients undergoing treatment for cancer. *JAMA Oncol*. 2021 Jul 8 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jamaoncology/fullarticle/2781608>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34236381?tool=bestpractice.bmj.com>)
455. Redjoul R, Le Bouter A, Beckerich F, et al. Antibody response after second BNT162b2 dose in allogeneic HSCT recipients. *Lancet*. 2021 Jul 13 [Epub ahead of print]. Full text ([https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)01594-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01594-4/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34270933?tool=bestpractice.bmj.com>)
456. Lim SH, Campbell N, Johnson M, et al. Antibody responses after SARS-CoV-2 vaccination in patients with lymphoma. *Lancet Haematol*. 2021 Jul 2 [Epub ahead of print]. Full text ([https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026\(21\)00199-X/fulltext](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(21)00199-X/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34224667?tool=bestpractice.bmj.com>)
457. Maneikis K, Šablauskas K, Ringelevičiūtė U, et al. Immunogenicity of the BNT162b2 COVID-19 mRNA vaccine and early clinical outcomes in patients with haematological malignancies in Lithuania: a national prospective cohort study. *Lancet Haematol*. 2021 Jul 2 [Epub ahead of print]. Full text ([https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026\(21\)00169-1/fulltext](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(21)00169-1/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34224668?tool=bestpractice.bmj.com>)
458. Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. *N Engl J Med*. 2021 Jun 23 [Epub ahead of print]. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMc2108861>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34161700?tool=bestpractice.bmj.com>)
459. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med*. 2020 Dec 31;383(27):2603-15. Full text (<https://www.nejm.org/doi/>

- full/10.1056/NEJMoa2034577) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33301246?tool=bestpractice.bmj.com>)
460. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med*. 2021 Feb 4;384(5):403-16. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7787219>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33378609?tool=bestpractice.bmj.com>)
 461. Medicines and Healthcare products Regulatory Agency. Information for healthcare professionals on COVID-19 vaccine AstraZeneca. 2021 [internet publication]. Full text (<https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-astrazeneca/information-for-healthcare-professionals-on-covid-19-vaccine-astrazeneca>)
 462. AstraZeneca. AZD1222 US phase III primary analysis confirms safety and efficacy. 2021 [internet publication]. Full text (<https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2021/azd1222-us-phase-iii-primary-analysis-confirms-safety-and-efficacy.html>)
 463. Sadoff J, Gray G, Vandebosch A, et al. Safety and efficacy of single-dose Ad26.COV2.S vaccine against Covid-19. *N Engl J Med*. 2021 Apr 21 [Epub ahead of print]. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMoa2101544>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33882225?tool=bestpractice.bmj.com>)
 464. Harder T, Koch J, Vygen-Bonnet S, et al. Efficacy and effectiveness of COVID-19 vaccines against SARS-CoV-2 infection: interim results of a living systematic review, 1 January to 14 May 2021. *Euro Surveill*. 2021 Jul;26(28). Full text (<https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.28.2100563>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34269175?tool=bestpractice.bmj.com>)
 465. Kow CS, Hasan SS. Real-world effectiveness of BNT162b2 mRNA vaccine: a meta-analysis of large observational studies. *Inflammopharmacology*. 2021 Jul 9 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8266992>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34241782?tool=bestpractice.bmj.com>)
 466. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. *BMJ*. 2021 May 13;373:n1088. Full text (<https://www.doi.org/10.1136/bmj.n1088>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33985964?tool=bestpractice.bmj.com>)
 467. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of BNT162b2 mRNA vaccine and ChAdOx1 adenovirus vector vaccine on mortality following COVID-19. 2021 [internet publication]. Full text (<https://khub.net/documents/135939561/430986542/Effectiveness+of+BNT162b2+mRNA+vaccine+and+ChAdOx1+adenovirus+vector+vaccine+on+mortality+following+COVID-19.pdf/9884d371-8cc8-913c-211c-c2d7ce4dd1c3>)
 468. Ismail SA, Garcia Vilaplana T, Elgohari S, et al. Effectiveness of BNT162b2 mRNA and ChAdOx1 adenovirus vector COVID-19 vaccines on risk of hospitalisation among older adults in England: an observational study using surveillance data. 2021 [internet publication]. Full text (<https://khub.net/documents/135939561/430986542/Effectiveness+of+BNT162b2+mRNA+and>

+ChAdOx1+adenovirus+vector+COVID-19+vaccines+on+risk+of+hospitalisation+among+older+adults+in+England.pdf/9e18c525-dde6-5ee4-1537-91427798686b)

469. Vasileiou E, Simpson CR, Shi T, et al. Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study. *Lancet*. 2021 May 1;397(10285):1646-57. [Full text \(https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00677-2/fulltext\)](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00677-2/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33901420?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33901420?tool=bestpractice.bmj.com)
470. Pritchard E, Matthews PC, Stoesser N, et al; medRxiv. Impact of vaccination on SARS-CoV-2 cases in the community: a population-based study using the UK's COVID-19 infection survey. 2021 [internet publication]. [Full text \(https://www.medrxiv.org/content/10.1101/2021.04.22.21255913v1\)](https://www.medrxiv.org/content/10.1101/2021.04.22.21255913v1)
471. Hall VJ, Foulkes S, Saei A, et al. COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study. *Lancet*. 2021 May 8;397(10286):1725-35. [Full text \(https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00790-X/fulltext\)](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00790-X/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33901423?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33901423?tool=bestpractice.bmj.com)
472. Harris RJ, Hall JA, Zaidi A, et al; Public Health England. Impact of vaccination on household transmission of SARS-COV-2 in England. 2021 [internet publication]. [Full text \(https://khub.net/documents/135939561/390853656/Impact+of+vaccination+on+household+transmission+of+SARS-COV-2+in+England.pdf/35bf4bb1-6ade-d3eb-a39e-9c9b25a8122a?t=1619601878136\)](https://khub.net/documents/135939561/390853656/Impact+of+vaccination+on+household+transmission+of+SARS-COV-2+in+England.pdf/35bf4bb1-6ade-d3eb-a39e-9c9b25a8122a?t=1619601878136)
473. Shrotri M, Krutikov M, Palmer T, et al. Vaccine effectiveness of the first dose of ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of long-term care facilities in England (VIVALDI): a prospective cohort study. *Lancet Infect Dis*. 2021 Jun 23 [Epub ahead of print]. [Full text \(https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00289-9/fulltext\)](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00289-9/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34174193?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34174193?tool=bestpractice.bmj.com)
474. Hyams C, Marlow R, Maseko Z, et al. Effectiveness of BNT162b2 and ChAdOx1 nCoV-19 COVID-19 vaccination at preventing hospitalisations in people aged at least 80 years: a test-negative, case-control study. *Lancet Infect Dis*. 2021 Jun 23 [Epub ahead of print]. [Full text \(https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00330-3/fulltext\)](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00330-3/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34174190?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34174190?tool=bestpractice.bmj.com)
475. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. *N Engl J Med*. 2021 Apr 15;384(15):1412-3. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2101765\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2101765) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33626250?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33626250?tool=bestpractice.bmj.com)
476. Haas EJ, Angulo FJ, McLaughlin JM, et al. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. *Lancet*. 2021 May 5;397(10287):1819-29. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8099315\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8099315) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33964222?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33964222?tool=bestpractice.bmj.com)
477. Rinott E, Youngster I, Lewis YE. Reduction in COVID-19 patients requiring mechanical ventilation following implementation of a national COVID-19 vaccination program: Israel, December 2020

- February 2021. MMWR Morb Mortal Wkly Rep. 2021 Mar 5;70(9):326-8. Full text (<https://www.cdc.gov/mmwr/volumes/70/wr/mm7009e3.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33661863?tool=bestpractice.bmj.com>)
478. Angel Y, Spitzer A, Henig O, et al. Association between vaccination with BNT162b2 and incidence of symptomatic and asymptomatic SARS-CoV-2 infections among health care workers. JAMA. 2021 May 6 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2779853>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33956048?tool=bestpractice.bmj.com>)
479. Benenson S, Oster Y, Cohen MJ, et al. BNT162b2 mRNA Covid-19 vaccine effectiveness among health care workers. N Engl J Med. 2021 May 6;384(18):1775-7. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMc2101951>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33755373?tool=bestpractice.bmj.com>)
480. Chodick G, Tene L, Patalon T, et al. Assessment of effectiveness of 1 dose of BNT162b2 vaccine for SARS-CoV-2 infection 13 to 24 days after immunization. JAMA Netw Open. 2021 Jun 1;4(6):e2115985. Full text (<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780700>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34097044?tool=bestpractice.bmj.com>)
481. Levi R, Wohl A. Concerns regarding the estimated efficiency of Pfizer's Covid-19 vaccine in two large-scale observational studies in Israel. 2021 [internet publication]. Full text (<https://www.bmj.com/content/372/bmj.n567/rr-0>)
482. Thompson MG, Burgess JL, Naleway AL, et al. Interim estimates of vaccine effectiveness of BNT162b2 and mRNA-1273 COVID-19 vaccines in preventing SARS-CoV-2 infection among health care personnel, first responders, and other essential and frontline workers: eight U.S. locations, December 2020 – March 2021. MMWR Morb Mortal Wkly Rep. 2021 Apr 2;70(13):495-500. Full text (<https://www.cdc.gov/mmwr/volumes/70/wr/mm7013e3.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33793460?tool=bestpractice.bmj.com>)
483. Tenforde MW, Olson SM, Self WH, et al. Effectiveness of Pfizer-BioNTech and Moderna vaccines against COVID-19 among hospitalized adults aged ≥65 years: United States, January–March 2021. MMWR Morb Mortal Wkly Rep. 2021 May 7;70(18):674-9. Full text (https://www.cdc.gov/mmwr/volumes/70/wr/mm7018e1.htm?s_cid=mm7018e1_w) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33956782?tool=bestpractice.bmj.com>)
484. Tang L, Hijano DR, Gaur AH, et al. Asymptomatic and symptomatic SARS-CoV-2 infections after BNT162b2 vaccination in a routinely screened workforce. JAMA. 2021 May 6 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2779854>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33956050?tool=bestpractice.bmj.com>)
485. Pilishvili T, Fleming-Dutra KE, Farrar JL, et al. Interim estimates of vaccine effectiveness of Pfizer-BioNTech and Moderna COVID-19 vaccines among health care personnel: 33 U.S. sites, January–March 2021. MMWR Morb Mortal Wkly Rep. 2021 May 21;70(20):753-8. Full text (<https://www.cdc.gov/mmwr/volumes/70/wr/mm7020e2.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34014909?tool=bestpractice.bmj.com>)
486. Christie A, Henley J, Mattocks L, et al. Decreases in COVID-19 cases, emergency department visits, hospital admissions, and deaths among older adults following the introduction of COVID-19 vaccine:

- United States, September 6, 2020–May 1, 2021. *MMWR Morb Mortal Wkly Rep*. 2021 Jun 8 [Epub ahead of print]. [Full text \(https://www.cdc.gov/mmwr/volumes/70/wr/mm7023e2.htm\)](https://www.cdc.gov/mmwr/volumes/70/wr/mm7023e2.htm)
487. Gohil SK, Olenslager K, Quan KA, et al. Asymptomatic and symptomatic COVID-19 infections among health care personnel before and after vaccination. *JAMA Netw Open*. 2021 Jul 1;4(7):e2115980. [Full text \(https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781727\)](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781727) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34236414?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34236414?tool=bestpractice.bmj.com)
488. Padron-Regalado E. Vaccines for SARS-CoV-2: lessons from other coronavirus strains. *Infect Dis Ther*. 2020 Apr 23;:1-20. [Full text \(https://link.springer.com/article/10.1007/s40121-020-00300-x\)](https://link.springer.com/article/10.1007/s40121-020-00300-x) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32328406?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32328406?tool=bestpractice.bmj.com)
489. Hotez PJ, Corry DB, Bottazzi ME. COVID-19 vaccine design: the Janus face of immune enhancement. *Nat Rev Immunol*. 2020 Jun;20(6):347-8. [Full text \(https://link.springer.com/article/10.1007/s40121-020-00300-x\)](https://link.springer.com/article/10.1007/s40121-020-00300-x) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32346094?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32346094?tool=bestpractice.bmj.com)
490. Xie X, Zou J, Fontes-Garfias CR, et al. Neutralization of N501Y mutant SARS-CoV-2 by BNT162b2 vaccine-elicited sera. *bioRxiv*. 2021 Jan 7 [Epub ahead of print]. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7805448\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7805448) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33442691?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33442691?tool=bestpractice.bmj.com)
491. Muik A, Wallisch AK, Sanger B, et al. Neutralization of SARS-CoV-2 lineage B.1.1.7 pseudovirus by BNT162b2 vaccine-elicited human sera. *Science*. 2021 Mar 12;371(6534):1152-3. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7971771\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7971771) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33514629?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33514629?tool=bestpractice.bmj.com)
492. Xie X, Liu Y, Liu J, et al. Neutralization of SARS-CoV-2 spike 69/70 deletion, E484K, and N501Y variants by BNT162b2 vaccine-elicited sera. *bioRxiv*. 2021 Jan 27 [Epub ahead of print]. [Full text \(https://www.biorxiv.org/content/10.1101/2021.01.27.427998v1\)](https://www.biorxiv.org/content/10.1101/2021.01.27.427998v1) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33532771?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33532771?tool=bestpractice.bmj.com)
493. Stamataatos L, Czartoski J, Wan YH, et al; medRxiv. Antibodies elicited by SARS-CoV-2 infection and boosted by vaccination neutralize an emerging variant and SARS-CoV-1. 2021 [internet publication]. [Full text \(https://www.medrxiv.org/content/10.1101/2021.02.05.21251182v1\)](https://www.medrxiv.org/content/10.1101/2021.02.05.21251182v1)
494. Liu Y, Liu J, Xia H, et al. Neutralizing activity of BNT162b2-elicited serum: preliminary report. *N Engl J Med*. 2021 Apr 15;384(15):1466-8. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMc2102017\)](https://www.nejm.org/doi/full/10.1056/NEJMc2102017) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33596352?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33596352?tool=bestpractice.bmj.com)
495. Abu-Raddad LJ, Chemaitelly H, Butt AA; National Study Group for COVID-19 Vaccination. Effectiveness of the BNT162b2 Covid-19 vaccine against the B.1.1.7 and B.1.351 variants. *N Engl J Med*. 2021 May 5 [Epub ahead of print]. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMc2104974\)](https://www.nejm.org/doi/full/10.1056/NEJMc2104974) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33951357?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33951357?tool=bestpractice.bmj.com)
496. Liu Y, Liu J, Xia H, et al. BNT162b2-elicited neutralization against new SARS-CoV-2 spike variants. *N Engl J Med*. 2021 May 12 [Epub ahead of print]. [Full text \(https://www.nejm.org/\)](https://www.nejm.org/)

- doi/full/10.1056/NEJMc2106083) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33979486?tool=bestpractice.bmj.com>)
497. Pfizer Inc. Pfizer and Biontech initiate a study as part of broad development plan to evaluate COVID-19 booster and new vaccine variants. 2021 [internet publication]. Full text (<https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-initiate-study-part-broad-development>)
498. Wu K, Werner AP, Moliva JI, et al. mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants. bioRxiv. 2021 Jan 25 [Epub ahead of print]. Full text (<https://www.biorxiv.org/content/10.1101/2021.01.25.427948v1>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33501442?tool=bestpractice.bmj.com>)
499. Wu K, Werner AP, Koch M, et al. Serum neutralizing activity elicited by mRNA-1273 vaccine: preliminary report. N Engl J Med. 2021 Apr 15;384(15):1468-70. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMc2102179>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33596346?tool=bestpractice.bmj.com>)
500. Edara VV, Pinsky BA, Suthar MS, et al. Infection and vaccine-induced neutralizing-antibody responses to the SARS-CoV-2 B.1.617 variants. N Engl J Med. 2021 Jul 7 [Epub ahead of print]. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMc2107799>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34233096?tool=bestpractice.bmj.com>)
501. Emary KRW, Golubchik T, Aley PK, et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): an exploratory analysis of a randomised controlled trial. Lancet. 2021 Apr 10;397(10282):1351-62. Full text ([https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00628-0/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00628-0/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33798499?tool=bestpractice.bmj.com>)
502. Moderna, Inc. Moderna announces first participants dosed in study evaluating COVID-19 booster vaccine candidates. 2021 [internet publication]. Full text (<https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-first-participants-dosed-study-evaluating>)
503. AstraZeneca. First COVID-19 variant vaccine AZD2816 phase II/III trial participants vaccinated. 2021 [internet publication]. Full text (<https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2021/first-covid-19-variant-vaccine-azd2816-phase-ii-iii-trial-participants-vaccinated.html>)
504. World Health Organization. Infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed: interim guidance. 2021 [internet publication]. Full text (<https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC-2021.1>)
505. Liu M, Cheng SZ, Xu KW, et al. Use of personal protective equipment against coronavirus disease 2019 by healthcare professionals in Wuhan, China: cross sectional study. BMJ. 2020 Jun 10;369:m2195. Full text (<https://www.bmj.com/content/369/bmj.m2195>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32522737?tool=bestpractice.bmj.com>)
506. Centre for Evidence-Based Medicine; Greenhalgh T, Chan XH, Khunti K, et al. What is the efficacy of standard face masks compared to respirator masks in preventing COVID-type respiratory illnesses in primary care staff? 2020 [internet publication]. Full text (<https://www.cebm.net/what-is-the-efficacy-of->

standard-face-masks-compared-to-respirator-masks-in-preventing-covid-type-respiratory-illnesses-in-primary-care-staff)

507. Razai MS, Doerholt K, Ladhani S, et al. Coronavirus disease 2019 (covid-19): a guide for UK GPs. *BMJ*. 2020 Mar 5;368:m800. [Full text \(https://www.bmj.com/content/368/bmj.m800.long\)](https://www.bmj.com/content/368/bmj.m800.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32144127?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32144127?tool=bestpractice.bmj.com)
508. World Health Organization. Coronavirus disease (COVID-19) advice for the public. 2021 [internet publication]. [Full text \(https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public\)](https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public)
509. Centers for Disease Control and Prevention. How to protect yourself and others. 2021 [internet publication]. [Full text \(https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html\)](https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html)
510. Centers for Disease Control and Prevention. Serious adverse health events associated with methanol-based hand sanitizers. 2020 [internet publication]. [Full text \(https://emergency.cdc.gov/han/2020/han00434.asp\)](https://emergency.cdc.gov/han/2020/han00434.asp)
511. Mahmood A, Eqan M, Pervez S, et al. COVID-19 and frequent use of hand sanitizers; human health and environmental hazards by exposure pathways. *Sci Total Environ*. 2020 Jun 27;742:140561. [Full text \(https://www.sciencedirect.com/science/article/pii/S0048969720340833?via%3Dihub\)](https://www.sciencedirect.com/science/article/pii/S0048969720340833?via%3Dihub) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32623176?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32623176?tool=bestpractice.bmj.com)
512. Martin GC, Le Roux G, Guindolet D, et al. Pediatric eye injuries by hydroalcoholic gel in the context of the coronavirus disease 2019 pandemic. *JAMA Ophthalmol*. 2021 Mar 1;139(3):348-51. [Full text \(https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2775155\)](https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2775155) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33475712?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33475712?tool=bestpractice.bmj.com)
513. US Food and Drug Administration. FDA warns that vapors from alcohol-based hand sanitizers can have side effects. 2021 [internet publication]. [Full text \(https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-vapors-alcohol-based-hand-sanitizers-can-have-side-effects\)](https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-vapors-alcohol-based-hand-sanitizers-can-have-side-effects)
514. Bundgaard H, Bundgaard JS, Raaschou-Pedersen DET, et al. Effectiveness of adding a mask recommendation to other public health measures to prevent SARS-CoV-2 infection in Danish mask wearers: a randomized controlled trial. *Ann Intern Med*. 2021 Mar;174(3):335-43. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7707213\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7707213) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33205991?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33205991?tool=bestpractice.bmj.com)
515. Nanda A, Hung I, Kwong A, et al. Efficacy of surgical masks or cloth masks in the prevention of viral transmission: systematic review, meta-analysis, and proposal for future trial. *J Evid Based Med*. 2021 May;14(2):97-111. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8014575\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8014575) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33565274?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33565274?tool=bestpractice.bmj.com)
516. Jefferson T, Del Mar CB, Dooley L, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. *Cochrane Database Syst Rev*. 2020 Nov 20;(11):CD006207. [Full text \(https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD006207.pub5/full\)](https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD006207.pub5/full) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33215698?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33215698?tool=bestpractice.bmj.com)

517. Chou R, Dana T, Jungbauer R, et al. Masks for prevention of respiratory virus infections, including SARS-CoV-2, in health care and community settings: a living rapid review. *Ann Intern Med*. 2020 Oct 6;173(7):542-55. [Full text \(https://www.acpjournals.org/doi/10.7326/M20-3213\)](https://www.acpjournals.org/doi/10.7326/M20-3213) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32579379?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32579379?tool=bestpractice.bmj.com)
518. Chou R, Dana T, Jungbauer R, et al. Update alert 6: masks for prevention of respiratory virus infections, including SARS-CoV-2, in health care and community settings. *Ann Intern Med*. 2021 Jul 13 [Epub ahead of print]. [Full text \(https://www.acpjournals.org/doi/10.7326/L21-0393\)](https://www.acpjournals.org/doi/10.7326/L21-0393) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34251900?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34251900?tool=bestpractice.bmj.com)
519. Sharma SK, Mishra M, Mudgal SK. Efficacy of cloth face mask in prevention of novel coronavirus infection transmission: a systematic review and meta-analysis. *J Educ Health Promot*. 2020 Jul 28;9:192. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7497125\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7497125) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33015206?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33015206?tool=bestpractice.bmj.com)
520. MacIntyre CR, Seale H, Dung TC, et al. A cluster randomised trial of cloth masks compared with medical masks in healthcare workers. *BMJ Open*. 2015 Apr 22;5(4):e006577. [Full text \(https://bmjopen.bmj.com/content/5/4/e006577\)](https://bmjopen.bmj.com/content/5/4/e006577) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/25903751?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/25903751?tool=bestpractice.bmj.com)
521. Lazzarino AI, Steptoe A, Hamer M, et al. Covid-19: important potential side effects of wearing face masks that we should bear in mind. *BMJ*. 2020 May 21;369:m2003. [Full text \(https://www.bmj.com/content/369/bmj.m2003\)](https://www.bmj.com/content/369/bmj.m2003) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32439689?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32439689?tool=bestpractice.bmj.com)
522. Bakhit M, Krzyzaniak N, Scott AM, et al. Downsides of face masks and possible mitigation strategies: a systematic review and meta-analysis. *BMJ Open*. 2021 Feb 22;11(2):e044364. [Full text \(https://bmjopen.bmj.com/content/11/2/e044364.long\)](https://bmjopen.bmj.com/content/11/2/e044364.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33619199?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33619199?tool=bestpractice.bmj.com)
523. Bendavid E, Oh C, Bhattacharya J, et al. Assessing mandatory stay-at-home and business closure effects on the spread of COVID-19. *Eur J Clin Invest*. 2021 Jan 5:e13484. [Full text \(https://onlinelibrary.wiley.com/doi/10.1111/eci.13484\)](https://onlinelibrary.wiley.com/doi/10.1111/eci.13484) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33400268?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33400268?tool=bestpractice.bmj.com)
524. Chu IY, Alam P, Larson H, et al. Social consequences of mass quarantine during epidemics: a systematic review with implications for the COVID-19 response. *J Travel Med*. 2020 Oct 13 [Epub ahead of print]. [Full text \(https://academic.oup.com/jtm/advance-article/doi/10.1093/jtm/taaa192/5922349\)](https://academic.oup.com/jtm/advance-article/doi/10.1093/jtm/taaa192/5922349) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33051660?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33051660?tool=bestpractice.bmj.com)
525. Public Health England. Guidance on shielding and protecting people who are clinically extremely vulnerable from COVID-19. 2021 [internet publication]. [Full text \(https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19\)](https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19)
526. Burns J, Movsisyan A, Stratil JM, et al. Travel-related control measures to contain the COVID-19 pandemic: a rapid review. *Cochrane Database Syst Rev*. 2020 Oct 5;(10):CD013717. [Full text](#)

- (<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013717/full>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33502002?tool=bestpractice.bmj.com>)
527. Viswanathan M, Kahwati L, Jahn B, et al. Universal screening for SARS-CoV-2 infection: a rapid review. *Cochrane Database Syst Rev*. 2020 Sep 15;(9):CD013718. Full text (<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013718/full>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33502003?tool=bestpractice.bmj.com>)
528. Dollard P, Griffin I, Berro A, et al. Risk assessment and management of COVID-19 among travelers arriving at designated U.S. airports, January 17-September 13, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Nov 13;69(45):1681-5. Full text (<https://www.cdc.gov/mmwr/volumes/69/wr/mm6945a4.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33180758?tool=bestpractice.bmj.com>)
529. Nussbaumer-Streit B, Mayr V, Dobrescu AI, et al. Quarantine alone or in combination with other public health measures to control COVID-19: a rapid review. *Cochrane Database Syst Rev*. 2020 Sep 15;(9):CD013574. Full text (<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013574.pub2/full>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33959956?tool=bestpractice.bmj.com>)
530. Mahase E. China coronavirus: what do we know so far? *BMJ*. 2020 Jan 24;368:m308. Full text (<https://www.bmj.com/content/368/bmj.m308/rr-2>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/31980434?tool=bestpractice.bmj.com>)
531. Brooks SK, Webster RK, Smith LE, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet*. 2020 Mar 14;395(10227):912-20. Full text ([https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30460-8/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30460-8/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32112714?tool=bestpractice.bmj.com>)
532. Ho FK, Celis-Morales CA, Gray SR, et al. Modifiable and non-modifiable risk factors for COVID-19, and comparison to risk factors for influenza and pneumonia: results from a UK Biobank prospective cohort study. *BMJ Open*. 2020 Nov 19;10(11):e040402. Full text (<https://bmjopen.bmj.com/content/10/11/e040402.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33444201?tool=bestpractice.bmj.com>)
533. National Institutes of Health. Coronavirus disease 2019 (COVID-19) treatment guidelines. 2021 [internet publication]. Full text (<https://covid19treatmentguidelines.nih.gov>)
534. Department of Health and Social Care. Everyone in the United Kingdom with symptoms now eligible for coronavirus tests. 2020 [internet publication]. Full text (<https://www.gov.uk/government/news/everyone-in-the-united-kingdom-with-symptoms-now-eligible-for-coronavirus-tests>)
535. Struyf T, Deeks JJ, Dinnes J, et al. Signs and symptoms to determine if a patient presenting in primary care or hospital outpatient settings has COVID-19 disease. *Cochrane Database Syst Rev*. 2021 Feb 23;(2):CD013665. Full text (<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013665.pub2/full>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33620086?tool=bestpractice.bmj.com>)

536. World Health Organization. Diagnostic testing for SARS-CoV-2: interim guidance. 2020 [internet publication]. Full text (<https://www.who.int/publications/i/item/diagnostic-testing-for-sars-cov-2>)
537. Irfan O, Muttalib F, Tang K, et al. Clinical characteristics, treatment and outcomes of paediatric COVID-19: a systematic review and meta-analysis. Arch Dis Child. 2021 Feb 16;106(5):440-8. Full text (<https://adc.bmj.com/content/106/5/440.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33593743?tool=bestpractice.bmj.com>)
538. World Health Organization. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19: scientific brief. 2020 [internet publication]. Full text (<https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19>)
539. British Society of Thoracic Imaging. Thoracic imaging in COVID-19 infection: guidance for the reporting radiologist - version 2. 2020 [internet publication]. Full text (https://www.bsti.org.uk/media/resources/files/BSTI_COVID-19_Radiology_Guidance_version_2_16.03.20.pdf)
540. Biobank. UK Biobank SARS-CoV-2 serology study. 2021 [internet publication]. Full text (https://www.ukbiobank.ac.uk/media/x0nd5sul/ukb_serologystudy_report_revised_6months_jan21.pdf)
541. Yang BY, Barnard LM, Emert JM, et al. Clinical characteristics of patients with coronavirus disease 2019 (COVID-19) receiving emergency medical services in King County, Washington. JAMA Netw Open. 2020 Jul 1;3(7):e2014549. Full text (<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2767993>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32639570?tool=bestpractice.bmj.com>)
542. Centers for Disease Control and Prevention. Ten clinical tips on COVID-19 for healthcare providers involved in patient care. 2020 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-tips-for-healthcare-providers.html>)
543. Sommer P, Lukovic E, Fagley E, et al. Initial clinical impressions of the critical care of COVID-19 patients in Seattle, New York City, and Chicago. Anesth Analg. 2020 Jul;131(1):55-60. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7172559>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32221172?tool=bestpractice.bmj.com>)
544. Goyal P, Choi JJ, Pinheiro LC, et al. Clinical characteristics of Covid-19 in New York City. N Engl J Med. 2020 Jun 11;382(24):2372-4. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMc2010419>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32302078?tool=bestpractice.bmj.com>)
545. Lechien JR, Chiesa-Estomba CM, Place S, et al. Clinical and epidemiological characteristics of 1,420 European patients with mild-to-moderate coronavirus disease 2019. J Intern Med. 2020 Sep;288(3):335-44. Full text (<https://onlinelibrary.wiley.com/doi/10.1111/joim.13089>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32352202?tool=bestpractice.bmj.com>)
546. ZOE COVID Symptom Study. What are the new top 5 COVID symptoms? 2021 [internet publication]. Full text (<https://covid.joinzoe.com/post/new-top-5-covid-symptoms>)
547. Matar R, Alrahmani L, Monzer N, et al. Clinical presentation and outcomes of pregnant women with coronavirus disease 2019: a systematic review and meta-analysis. Clin Infect Dis. 2021 Feb

- 1;72(3):521-33. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7337697>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32575114?tool=bestpractice.bmj.com>)
548. Lechien JR, Chetrit A, Chekkoury-Idrissi Y, et al. Parotitis-like symptoms associated with COVID-19, France, March-April 2020. *Emerg Infect Dis*. 2020 Jun 3;26(9). Full text (https://wwwnc.cdc.gov/eid/article/26/9/20-2059_article) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32491984?tool=bestpractice.bmj.com>)
549. Martín Carreras-Presas C, Amaro Sánchez J, López-Sánchez AF, et al. Oral vesiculobullous lesions associated with SARS-CoV-2 infection. *Oral Dis*. 2021 Apr;27 Suppl 3:710-2. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7267423>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32369674?tool=bestpractice.bmj.com>)
550. Marinho PM, Marcos AAA, Romano AC, et al. Retinal findings in patients with COVID-19. *Lancet*. 2020 May 23;395(10237):1610. Full text ([https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31014-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31014-X/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32405105?tool=bestpractice.bmj.com>)
551. Wambier CG, Vaño-Galván S, McCoy J, et al. Androgenetic alopecia present in the majority of hospitalized COVID-19 patients: the "Gabin sign". *J Am Acad Dermatol*. 2020 May 21;83(2):680-2. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7242206>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32446821?tool=bestpractice.bmj.com>)
552. Musuuza JS, Watson L, Parmasad V, et al. Prevalence and outcomes of co-infection and superinfection with SARS-CoV-2 and other pathogens: a systematic review and meta-analysis. *PLoS One*. 2021 May 6;16(5):e0251170. Full text (<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0251170>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33956882?tool=bestpractice.bmj.com>)
553. Moorthy A, Gaikwad R, Krishna S, et al. SARS-CoV-2, uncontrolled diabetes and corticosteroids: an unholy trinity in invasive fungal infections of the maxillofacial region? A retrospective, multicentric analysis. *J Maxillofac Oral Surg*. 2021 Mar 6;:1-8. Full text (<https://link.springer.com/article/10.1007/s12663-021-01532-1>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33716414?tool=bestpractice.bmj.com>)
554. Mahase E. Covid-19: Children less likely to report fever, persistent cough, or appetite loss, large UK study finds. *BMJ*. 2021 Feb 10;372:n408. Full text (<https://www.bmj.com/content/372/bmj.n408>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33568385?tool=bestpractice.bmj.com>)
555. Bolia R, Dhanesh Goel A, Badkur M, et al. Gastrointestinal manifestations of pediatric coronavirus disease and their relationship with a severe clinical course: a systematic review and meta-analysis. *J Trop Pediatr*. 2021 May 29 [Epub ahead of print]. Full text (<https://academic.oup.com/tropej/advance-article/doi/10.1093/tropej/fmab051/6288463>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34050766?tool=bestpractice.bmj.com>)
556. Lorenz N, Treptow A, Schmidt S, et al. Neonatal early-onset infection with SARS-CoV-2 in a newborn presenting with encephalitic symptoms. *Pediatr Infect Dis J*. 2020 Aug;39(8):e212. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32404789?tool=bestpractice.bmj.com>)

557. Chacón-Aguilar R, Osorio-Cámara JM, Sanjurjo-Jimenez I, et al. COVID-19: fever syndrome and neurological symptoms in a neonate. *An Pediatr (Engl Ed)*. 2020 Apr 27;92(6):373-4. [Full text \(https://www.sciencedirect.com/science/article/pii/S2341287920300661?via%3Dihub\)](https://www.sciencedirect.com/science/article/pii/S2341287920300661?via%3Dihub) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32341945?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32341945?tool=bestpractice.bmj.com)
558. Sinelli MT, Paterlini G, Citterio M, et al. Early neonatal SARS-CoV-2 infection manifesting with hypoxemia requiring respiratory support. *Pediatrics*. 2020 Jul;146(1):e20201121. [Full text \(https://pediatrics.aappublications.org/content/early/2020/04/30/peds.2020-1121.long\)](https://pediatrics.aappublications.org/content/early/2020/04/30/peds.2020-1121.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32366612?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32366612?tool=bestpractice.bmj.com)
559. Rubens JH, Akindele NP, Tschudy MM, et al. Acute covid-19 and multisystem inflammatory syndrome in children. *BMJ*. 2021 Mar 1;372:n385. [Full text \(https://www.bmj.com/content/372/bmj.n385\)](https://www.bmj.com/content/372/bmj.n385) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33648933?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33648933?tool=bestpractice.bmj.com)
560. Xia W, Shao J, Guo Y, et al. Clinical and CT features in pediatric patients with COVID-19 infection: different points from adults. *Pediatr Pulmonol*. 2020 May;55(5):1169-74. [Full text \(https://onlinelibrary.wiley.com/doi/full/10.1002/ppul.24718\)](https://onlinelibrary.wiley.com/doi/full/10.1002/ppul.24718) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32134205?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32134205?tool=bestpractice.bmj.com)
561. DeBiasi RL, Song X, Delaney M, et al. Severe COVID-19 in children and young adults in the Washington, DC metropolitan region. *J Pediatr*. 2020 Aug;223:199-203. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7217783\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7217783) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32405091?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32405091?tool=bestpractice.bmj.com)
562. Ikeuchi K, Saito M, Yamamoto S, et al. Relative bradycardia in patients with mild-to-moderate coronavirus disease, Japan. *Emerg Infect Dis*. 2020 Jul 1;26(10). [Full text \(https://wwwnc.cdc.gov/eid/article/26/10/20-2648_article\)](https://wwwnc.cdc.gov/eid/article/26/10/20-2648_article) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32610036?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32610036?tool=bestpractice.bmj.com)
563. Xie J, Tong Z, Guan X, et al. Critical care crisis and some recommendations during the COVID-19 epidemic in China. *Intensive Care Med*. 2020 May;46(5):837-40. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7080165\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7080165) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32123994?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32123994?tool=bestpractice.bmj.com)
564. National Institute for Health and Care Excellence. COVID-19 rapid guideline: managing COVID-19. 2021 [internet publication]. [Full text \(https://www.nice.org.uk/guidance/ng191\)](https://www.nice.org.uk/guidance/ng191)
565. Centers for Disease Control and Prevention. Interim clinical guidance for management of patients with confirmed coronavirus disease (COVID-19). 2021 [internet publication]. [Full text \(https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html\)](https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html)
566. US Food and Drug Administration. Pulse oximeter accuracy and limitations: FDA safety communication. 2021 [internet publication]. [Full text \(https://www.fda.gov/medical-devices/safety-communications/pulse-oximeter-accuracy-and-limitations-fda-safety-communication\)](https://www.fda.gov/medical-devices/safety-communications/pulse-oximeter-accuracy-and-limitations-fda-safety-communication)
567. Royal College of Physicians. NEWS2 and deterioration in COVID-19. 2020 [internet publication]. [Full text \(https://www.rcplondon.ac.uk/news/news2-and-deterioration-covid-19\)](https://www.rcplondon.ac.uk/news/news2-and-deterioration-covid-19)

568. Li LQ, Huang T, Wang YQ, et al. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. *J Med Virol*. 2020 Jun;92(6):577-83. [Full text \(https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.25757\)](https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.25757) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32162702?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32162702?tool=bestpractice.bmj.com)
569. Zhu J, Zhong Z, Ji P, et al. Clinicopathological characteristics of 8697 patients with COVID-19 in China: a meta-analysis. *Fam Med Community Health*. 2020 Apr;8(2). [Full text \(https://fmch.bmj.com/content/8/2/e000406\)](https://fmch.bmj.com/content/8/2/e000406) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32371463?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32371463?tool=bestpractice.bmj.com)
570. Zhang ZL, Hou YL, Li DT, et al. Laboratory findings of COVID-19: a systematic review and meta-analysis. *Scand J Clin Lab Invest*. 2020 May 23:1-7. [Full text \(https://www.tandfonline.com/doi/full/10.1080/00365513.2020.1768587\)](https://www.tandfonline.com/doi/full/10.1080/00365513.2020.1768587) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32449374?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32449374?tool=bestpractice.bmj.com)
571. Wu H, Zhu H, Yuan C, et al. Clinical and immune features of hospitalized pediatric patients with coronavirus disease 2019 (COVID-19) in Wuhan, China. *JAMA Netw Open*. 2020 Jun 1;3(6):e2010895. [Full text \(https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2766670\)](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2766670) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32492165?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32492165?tool=bestpractice.bmj.com)
572. Henry BM, Benoit SW, de Oliveira MHS, et al. Laboratory abnormalities in children with mild and severe coronavirus disease 2019 (COVID-19): a pooled analysis and review. *Clin Biochem*. 2020 Jul;81:1-8. [Full text \(https://www.sciencedirect.com/science/article/pii/S0009912020303313?via%3Dihub\)](https://www.sciencedirect.com/science/article/pii/S0009912020303313?via%3Dihub) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32473151?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32473151?tool=bestpractice.bmj.com)
573. Kronbichler A, Kresse D, Yoon S, et al. Asymptomatic patients as a source of COVID-19 infections: a systematic review and meta-analysis. *Int J Infect Dis*. 2020 Sep;98:180-6. [Full text \(https://www.ijidonline.com/article/S1201-9712\(20\)30487-2/fulltext\)](https://www.ijidonline.com/article/S1201-9712(20)30487-2/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32562846?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32562846?tool=bestpractice.bmj.com)
574. Thachil J, Tang N, Gando S, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. *J Thromb Haemost*. 2020 May;18(5):1023-6. [Full text \(https://onlinelibrary.wiley.com/doi/full/10.1111/jth.14810\)](https://onlinelibrary.wiley.com/doi/full/10.1111/jth.14810) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32338827?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32338827?tool=bestpractice.bmj.com)
575. Crozier A, Rajan S, Buchan I, et al. Put to the test: use of rapid testing technologies for covid-19. *BMJ*. 2021 Feb 3;372:n208. [Full text \(https://www.bmj.com/content/372/bmj.n208\)](https://www.bmj.com/content/372/bmj.n208) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33536228?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33536228?tool=bestpractice.bmj.com)
576. World Health Organization. WHO information notice for IVD users 2020/05. 2021 [internet publication]. [Full text \(https://www.who.int/news/item/20-01-2021-who-information-notice-for-ivd-users-2020-05\)](https://www.who.int/news/item/20-01-2021-who-information-notice-for-ivd-users-2020-05)
577. US Food and Drug Administration. SARS-CoV-2 viral mutations: impact on COVID-19 tests. 2021 [internet publication]. [Full text \(https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests\)](https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests)

578. World Health Organization. Recommendations for national SARS-CoV-2 testing strategies and diagnostic capacities: interim guidance. 2021 [internet publication]. [Full text \(https://www.who.int/publications/i/item/WHO-2019-nCoV-lab-testing-2021.1-eng\)](https://www.who.int/publications/i/item/WHO-2019-nCoV-lab-testing-2021.1-eng)
579. Public Health England. COVID-19: investigation and initial clinical management of possible cases. 2020 [internet publication]. [Full text \(https://www.gov.uk/government/publications/wuhan-novel-coronavirus-initial-investigation-of-possible-cases/investigation-and-initial-clinical-management-of-possible-cases-of-wuhan-novel-coronavirus-wncov-infection\)](https://www.gov.uk/government/publications/wuhan-novel-coronavirus-initial-investigation-of-possible-cases/investigation-and-initial-clinical-management-of-possible-cases-of-wuhan-novel-coronavirus-wncov-infection)
580. Centers for Disease Control and Prevention. Overview of testing for SARS-CoV-2 (COVID-19). 2021 [internet publication]. [Full text \(https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html\)](https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html)
581. American Academy of Pediatrics. COVID-19 testing guidance. 2021 [internet publication]. [Full text \(https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/covid-19-testing-guidance\)](https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/covid-19-testing-guidance)
582. Tsang NNY, So HC, Ng KY, et al. Diagnostic performance of different sampling approaches for SARS-CoV-2 RT-PCR testing: a systematic review and meta-analysis. *Lancet Infect Dis*. 2021 Apr 12 [Epub ahead of print]. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8041361\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8041361) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33857405?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33857405?tool=bestpractice.bmj.com)
583. Bastos ML, Perlman-Arrow S, Menzies D, et al. The sensitivity and costs of testing for SARS-CoV-2 infection with saliva versus nasopharyngeal swabs: a systematic review and meta-analysis. *Ann Intern Med*. 2021 Apr;174(4):501-10. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7822569\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7822569) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33428446?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33428446?tool=bestpractice.bmj.com)
584. Butler-Laporte G, Lawandi A, Schiller I, et al. Comparison of saliva and nasopharyngeal swab nucleic acid amplification testing for detection of SARS-CoV-2: a systematic review and meta-analysis. *JAMA Intern Med*. 2021 Mar 1;181(3):353-60. [Full text \(https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2775397\)](https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2775397) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33449069?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33449069?tool=bestpractice.bmj.com)
585. Cañete MG, Valenzuela IM, Garcés PC, et al. Saliva sample for the massive screening of SARS-CoV-2 infection: a systematic review. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2021 Feb 1 [Epub ahead of print]. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7849433\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7849433) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33637473?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33637473?tool=bestpractice.bmj.com)
586. Moreira VM, Mascarenhas P, Machado V, et al. Diagnosis of SARS-Cov-2 infection by RT-PCR using specimens other than naso- and oropharyngeal swabs: a systematic review and meta-analysis. *Diagnostics (Basel)*. 2021 Feb 21;11(2):363. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7926389\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7926389) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33670020?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33670020?tool=bestpractice.bmj.com)
587. Atieh MA, Guirguis M, Alsabeeha NHM, et al. The diagnostic accuracy of saliva testing for SARS-CoV-2: a systematic review and meta-analysis. *Oral Dis*. 2021 Jun 3 [Epub ahead of print]. [Full text \(https://onlinelibrary.wiley.com/doi/10.1111/odi.13934\)](https://onlinelibrary.wiley.com/doi/10.1111/odi.13934) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34080272?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34080272?tool=bestpractice.bmj.com)
588. Ibrahimi N, Delaunay-Moisan A, Hill C, et al. Screening for SARS-CoV-2 by RT-PCR: saliva or nasopharyngeal swab? Rapid review and meta-analysis. *PLoS One*. 2021 Jun

- 10;16(6):e0253007. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8191978>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34111196?tool=bestpractice.bmj.com>)
589. Centers for Disease Control and Prevention. Interim guidelines for collecting and handling of clinical specimens for COVID-19 testing. 2021 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html>)
590. Centers for Disease Control and Prevention. Nucleic acid amplification tests (NAATs). 2021 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/lab/naats.html>)
591. Infectious Diseases Society of America. Infectious Diseases Society of America guidelines on the diagnosis of COVID-19: molecular diagnostic testing. 2020 [internet publication]. Full text (<https://www.idsociety.org/practice-guideline/covid-19-guideline-diagnostics>)
592. Zhou Y, O'Leary TJ. Relative sensitivity of anterior nares and nasopharyngeal swabs for initial detection of SARS-CoV-2 in ambulatory patients: Rapid review and meta-analysis. PLoS One. 2021 Jul 20;16(7):e0254559. Full text (<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0254559>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34283845?tool=bestpractice.bmj.com>)
593. Gupta K, Bellino PM, Charness ME. Adverse effects of nasopharyngeal swabs: three-dimensional printed versus commercial swabs. Infect Control Hosp Epidemiol. 2020 Jun 11 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7308627>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32522313?tool=bestpractice.bmj.com>)
594. Koskinen A, Tolvi M, Jauhiainen M, et al. Complications of COVID-19 nasopharyngeal swab test. JAMA Otolaryngol Head Neck Surg. 2021 Apr 29 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2779393>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33914064?tool=bestpractice.bmj.com>)
595. Sullivan CB, Schwalje AT, Jensen M, et al. Cerebrospinal fluid leak after nasal swab testing for coronavirus disease 2019. JAMA Otolaryngol Head Neck Surg. 2020 Dec 1;146(12):1179-81. Full text (<https://jamanetwork.com/journals/jamaotolaryngology/article-abstract/2771362>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33022069?tool=bestpractice.bmj.com>)
596. Wu X, Cai Y, Huang X, et al. Co-infection with SARS-CoV-2 and influenza A virus in patient with pneumonia, China. Emerg Infect Dis. 2020 Mar 11;26(6). Full text (https://wwwnc.cdc.gov/eid/article/26/6/20-0299_article) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32160148?tool=bestpractice.bmj.com>)
597. Jarrom D, Elston L, Washington J, et al. Effectiveness of tests to detect the presence of SARS-CoV-2 virus, and antibodies to SARS-CoV-2, to inform COVID-19 diagnosis: a rapid systematic review. BMJ Evid Based Med. 2020 Oct 1 [Epub ahead of print]. Full text (<https://ebm.bmj.com/content/early/2020/09/30/bmjebm-2020-111511.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33004426?tool=bestpractice.bmj.com>)

598. Centre for Evidence-Based Medicine; Jefferson T, Heneghan C, Spencer EA, et al. Are you infectious if you have a positive PCR test result for COVID-19? 2020 [internet publication]. [Full text \(https://www.cebm.net/covid-19/infectious-positive-pcr-test-result-covid-19\)](https://www.cebm.net/covid-19/infectious-positive-pcr-test-result-covid-19)
599. Jefferson T, Spencer E, Brassey J, et al; medRxiv. Viral cultures for COVID-19 infectivity assessment: systematic review. 2020 [internet publication]. [Full text \(https://www.medrxiv.org/content/10.1101/2020.08.04.20167932v1\)](https://www.medrxiv.org/content/10.1101/2020.08.04.20167932v1)
600. Watson J, Whiting PF, Brush JE. Interpreting a covid-19 test result. *BMJ*. 2020 May 12;369:m1808. [Full text \(https://www.bmj.com/content/369/bmj.m1808\)](https://www.bmj.com/content/369/bmj.m1808) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32398230?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32398230?tool=bestpractice.bmj.com)
601. Jefferson T, Spencer EA, Brassey J, et al. Viral cultures for COVID-19 infectious potential assessment: a systematic review. *Clin Infect Dis*. 2020 Dec 3 [Epub ahead of print]. [Full text \(https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1764/6018217\)](https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1764/6018217) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33270107?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33270107?tool=bestpractice.bmj.com)
602. Bullard J, Dust K, Funk D, et al. Predicting infectious severe acute respiratory syndrome coronavirus 2 from diagnostic samples. *Clin Infect Dis*. 2020 Dec 17;71(10):2663-6. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7314198\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7314198) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32442256?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32442256?tool=bestpractice.bmj.com)
603. La Scola B, Le Bideau M, Andreani J, et al. Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards. *Eur J Clin Microbiol Infect Dis*. 2020 Jun;39(6):1059-61. [Full text \(https://link.springer.com/article/10.1007/s10096-020-03913-9\)](https://link.springer.com/article/10.1007/s10096-020-03913-9) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32342252?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32342252?tool=bestpractice.bmj.com)
604. Surkova E, Nikolayevskyy V, Drobniewski F. False-positive COVID-19 results: hidden problems and costs. *Lancet Respir Med*. 2020 Dec;8(12):1167-8. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7524437\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7524437) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33007240?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33007240?tool=bestpractice.bmj.com)
605. Floriano I, Silvino A, Bernardo WM, et al. Accuracy of the polymerase chain reaction (PCR) test in the diagnosis of acute respiratory syndrome due to coronavirus: a systematic review and meta-analysis. *Rev Assoc Med Bras (1992)*. 2020 Jul;66(7):880-8. [Full text \(https://www.scielo.br/scielo.php?pid=S0104-42302020000700880&script=sci_arttext&lng=en\)](https://www.scielo.br/scielo.php?pid=S0104-42302020000700880&script=sci_arttext&lng=en) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32844930?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32844930?tool=bestpractice.bmj.com)
606. Public Health Laboratory Network. PHLN statement on nucleic acid test false positive results for SARS-CoV-2. 2020 [internet publication]. [Full text \(https://www.health.gov.au/resources/publications/phln-statement-on-nucleic-acid-test-false-positive-results-for-sars-cov-2\)](https://www.health.gov.au/resources/publications/phln-statement-on-nucleic-acid-test-false-positive-results-for-sars-cov-2)
607. Australian Government Department of Health. COVID-19 testing in Australia: information for health professionals. 2020 [internet publication]. [Full text \(https://www.tga.gov.au/covid-19-testing-australia-information-health-professionals\)](https://www.tga.gov.au/covid-19-testing-australia-information-health-professionals)

608. US Food and Drug Administration. CDC 2019-novel coronavirus (2019-nCoV) real-time RT-PCR diagnostic panel. 2020 [internet publication]. [Full text \(https://www.fda.gov/media/134922/download\)](https://www.fda.gov/media/134922/download)
609. Government Office for Science; Scientific Advisory Group for Emergencies. Impact of false-positives and false-negatives in the UK's COVID-19 RT-PCR testing programme. 2020 [internet publication]. [Full text \(https://www.gov.uk/government/publications/gos-impact-of-false-positives-and-negatives-3-june-2020\)](https://www.gov.uk/government/publications/gos-impact-of-false-positives-and-negatives-3-june-2020)
610. Arevalo-Rodriguez I, Buitrago-Garcia D, Simancas-Racines D, et al. False-negative results of initial RT-PCR assays for COVID-19: a systematic review. PLoS One. 2020 Dec 10;15(12):e0242958. [Full text \(https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0242958\)](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0242958) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33301459?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33301459?tool=bestpractice.bmj.com)
611. Kucirka LM, Lauer SA, Laeyendecker O, et al. Variation in false-negative rate of reverse transcriptase polymerase chain reaction-based SARS-CoV-2 tests by time since exposure. Ann Intern Med. 2020 Aug 18;173(4):262-7. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7240870\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7240870) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32422057?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32422057?tool=bestpractice.bmj.com)
612. Watson J, Richter A, Deeks J. Testing for SARS-CoV-2 antibodies. BMJ. 2020 Sep 8;370:m3325. [Full text \(https://www.bmj.com/content/370/bmj.m3325\)](https://www.bmj.com/content/370/bmj.m3325) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32900692?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32900692?tool=bestpractice.bmj.com)
613. Centers for Disease Control and Prevention. Interim guidelines for COVID-19 antibody testing. 2021 [internet publication]. [Full text \(https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html\)](https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html)
614. Infectious Diseases Society of America. Infectious Diseases Society of America guidelines on the diagnosis of COVID-19: serologic testing. 2020 [internet publication]. [Full text \(https://www.idsociety.org/practice-guideline/covid-19-guideline-serology\)](https://www.idsociety.org/practice-guideline/covid-19-guideline-serology)
615. Long QX, Liu BZ, Deng HJ, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med. 2020 Jun;26(6):845-8. [Full text \(https://www.nature.com/articles/s41591-020-0897-1\)](https://www.nature.com/articles/s41591-020-0897-1) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32350462?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32350462?tool=bestpractice.bmj.com)
616. Qu J, Wu C, Li X, et al. Profile of immunoglobulin G and IgM antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Clin Infect Dis. 2020 Nov 19;71(16):2255-8. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7197626\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7197626) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32337590?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32337590?tool=bestpractice.bmj.com)
617. Deeks JJ, Dinnes J, Takwoingi Y, et al. Antibody tests for identification of current and past infection with SARS-CoV-2. Cochrane Database Syst Rev. 2020 Jun 25;(6):CD013652. [Full text \(https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013652/full\)](https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013652/full) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32584464?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32584464?tool=bestpractice.bmj.com)
618. World Health Organization. Advice on the use of point-of-care immunodiagnostic tests for COVID-19: scientific brief. 2020 [internet publication]. [Full text \(https://www.who.int/news-room/commentaries/detail/advice-on-the-use-of-point-of-care-immunodiagnostic-tests-for-covid-19\)](https://www.who.int/news-room/commentaries/detail/advice-on-the-use-of-point-of-care-immunodiagnostic-tests-for-covid-19)

619. Lisboa Bastos M, Tavaziva G, Abidi SK, et al. Diagnostic accuracy of serological tests for covid-19: systematic review and meta-analysis. *BMJ*. 2020 Jul 1;370:m2516. [Full text \(https://www.bmj.com/content/370/bmj.m2516\)](https://www.bmj.com/content/370/bmj.m2516) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32611558?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32611558?tool=bestpractice.bmj.com)
620. World Health Organization. Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays: interim guidance. 2020 [internet publication]. [Full text \(https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays\)](https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays)
621. Infectious Diseases Society of America. Infectious Diseases Society of America guidelines on the diagnosis of COVID-19: antigen testing. 2021 [internet publication]. [Full text \(https://www.idsociety.org/practice-guideline/covid-19-guideline-antigen-testing\)](https://www.idsociety.org/practice-guideline/covid-19-guideline-antigen-testing)
622. Centers for Disease Control and Prevention. Interim guidance for antigen testing for SARS-CoV-2. 2021 [internet publication]. [Full text \(https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html\)](https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html)
623. US Food and Drug Administration. Potential for false positive results with antigen tests for rapid detection of SARS-CoV-2: letter to clinical laboratory staff and health care providers. 2020 [internet publication]. [Full text \(https://www.fda.gov/medical-devices/letters-health-care-providers/potential-false-positive-results-antigen-tests-rapid-detection-sars-cov-2-letter-clinical-laboratory\)](https://www.fda.gov/medical-devices/letters-health-care-providers/potential-false-positive-results-antigen-tests-rapid-detection-sars-cov-2-letter-clinical-laboratory)
624. Dinnes J, Deeks JJ, Berhane S, et al. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. *Cochrane Database Syst Rev*. 2021 Mar 24;(3):CD013705. [Full text \(https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013705.pub2/full\)](https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013705.pub2/full) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33760236?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33760236?tool=bestpractice.bmj.com)
625. García-Fiñana M, Hughes DM, Cheyne CP, et al. Performance of the Innova SARS-CoV-2 antigen rapid lateral flow test in the Liverpool asymptomatic testing pilot: population based cohort study. *BMJ*. 2021 Jul 6;374:n1637. [Full text \(https://www.bmj.com/content/374/bmj.n1637\)](https://www.bmj.com/content/374/bmj.n1637) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34230058?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34230058?tool=bestpractice.bmj.com)
626. Wagenhäuser I, Knies K, Rauschenberger V, et al. Clinical performance evaluation of SARS-CoV-2 rapid antigen testing in point of care usage in comparison to RT-qPCR. *EBioMedicine*. 2021 Jun 26;69:103455. [Full text \(https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(21\)00248-6/fulltext\)](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00248-6/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34186490?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34186490?tool=bestpractice.bmj.com)
627. Poon LC, Yang H, Kapur A, et al. Global interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium from FIGO and allied partners: information for healthcare professionals. 2020 [internet publication]. [Full text \(https://obgyn.onlinelibrary.wiley.com/doi/10.1002/ijgo.13156\)](https://obgyn.onlinelibrary.wiley.com/doi/10.1002/ijgo.13156)
628. Song F, Shi N, Shan F, et al. Emerging coronavirus 2019-nCoV pneumonia. *Radiology*. 2020 Feb 6:200274. [Full text \(https://pubs.rsna.org/doi/10.1148/radiol.2020200274\)](https://pubs.rsna.org/doi/10.1148/radiol.2020200274) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32027573?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32027573?tool=bestpractice.bmj.com)
629. Islam N, Ebrahimzadeh S, Salameh JP, et al. Thoracic imaging tests for the diagnosis of COVID-19. *Cochrane Database Syst Rev*. 2021 Mar 16;(3):CD013639. [Full text \(https://www.cochranelibrary.com/\)](https://www.cochranelibrary.com/)

[cdsr/doi/10.1002/14651858.CD013639.pub4/full](https://doi.org/10.1002/14651858.CD013639.pub4/full) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33724443?tool=bestpractice.bmj.com>)

630. World Health Organization. Use of chest imaging in COVID-19: a rapid advice guide. 2020 [internet publication]. Full text (<https://www.who.int/publications/i/item/use-of-chest-imaging-in-covid-19>)
631. Centre for Evidence-Based Medicine; Park JY, Freer R, Stevens R, et al. The accuracy of chest CT in the diagnosis of COVID-19: an umbrella review. 2021 [internet publication]. Full text (<https://www.cebm.net/covid-19/the-accuracy-of-chest-ct-in-the-diagnosis-of-covid-19-an-umbrella-review>)
632. Tavare AN, Braddy A, Brill S, et al. Managing high clinical suspicion COVID-19 inpatients with negative RT-PCR: a pragmatic and limited role for thoracic CT. *Thorax*. 2020 Jul;75(7):537-8. Full text (<https://thorax.bmj.com/content/early/2020/04/21/thoraxjnl-2020-214916.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32317269?tool=bestpractice.bmj.com>)
633. American College of Radiology. ACR recommendations for the use of chest radiography and computed tomography (CT) for suspected COVID-19 infection. 2020 [internet publication]. Full text (<https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Recommendations-for-Chest-Radiography-and-CT-for-Suspected-COVID19-Infection>)
634. Li Z, Yi Y, Luo X, et al. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. *J Med Virol*. 2020 Sep;92(9):1518-24. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7228300>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32104917?tool=bestpractice.bmj.com>)
635. Yang W, Cao Q, Qin L, et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): a multi-center study in Wenzhou city, Zhejiang, China. *J Infect*. 2020 Apr;80(4):388-93. Full text ([https://www.journalofinfection.com/article/S0163-4453\(20\)30099-2/fulltext](https://www.journalofinfection.com/article/S0163-4453(20)30099-2/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32112884?tool=bestpractice.bmj.com>)
636. Long C, Xu H, Shen Q, et al. Diagnosis of the coronavirus disease (COVID-19): rRT-PCR or CT? *Eur J Radiol*. 2020 Mar 25;126:108961. Full text ([https://www.ejradiology.com/article/S0720-048X\(20\)30150-9/pdf](https://www.ejradiology.com/article/S0720-048X(20)30150-9/pdf)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32229322?tool=bestpractice.bmj.com>)
637. Chen C, Zhu C, Yan D, et al. The epidemiological and radiographical characteristics of asymptomatic infections with the novel coronavirus (COVID-19): a systematic review and meta-analysis. *Int J Infect Dis*. 2021 Mar;104:458-64. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7833455>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33444755?tool=bestpractice.bmj.com>)
638. Oshay RR, Chen MYC, Fields BKK, et al. COVID-19 in pregnancy: a systematic review of chest CT findings and associated clinical features in 427 patients. *Clin Imaging*. 2021 Jan 13;75:75-82. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7804384>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33508754?tool=bestpractice.bmj.com>)
639. Sun P, Qie S, Liu Z, et al. Clinical characteristics of hospitalized patients with SARS-CoV-2 infection: a single arm meta-analysis. *J Med Virol*. 2020 Jun;92(6):612-7. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7228300>)

- www.ncbi.nlm.nih.gov/pmc/articles/PMC7228255) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32108351?tool=bestpractice.bmj.com>)
640. Ojha V, Mani A, Pandey NN, et al. CT in coronavirus disease 2019 (COVID-19): a systematic review of chest CT findings in 4410 adult patients. *Eur Radiol*. 2020 Nov;30(11):6129-38. Full text (<https://link.springer.com/article/10.1007%2Fs00330-020-06975-7>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32474632?tool=bestpractice.bmj.com>)
641. Garg M, Gupta P, Maralakunte M, et al. Diagnostic accuracy of CT and radiographic findings for novel coronavirus 2019 pneumonia: systematic review and meta-analysis. *Clin Imaging*. 2020 Nov 11;72:75-82. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7657023>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33217674?tool=bestpractice.bmj.com>)
642. Hossein H, Ali KM, Hosseini M, et al. Value of chest computed tomography scan in diagnosis of COVID-19: a systematic review and meta-analysis. *Clin Transl Imaging*. 2020 Oct 12:1-13. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7549426>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33072656?tool=bestpractice.bmj.com>)
643. Zhao D, Yao F, Wang L, et al. A comparative study on the clinical features of COVID-19 pneumonia to other pneumonias. *Clin Infect Dis*. 2020 Jul 28;71(15):756-61. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7108162>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32161968?tool=bestpractice.bmj.com>)
644. Kumar J, Meena J, Yadav A, et al. Radiological findings of COVID-19 in children: a systematic review and meta-analysis. *J Trop Pediatr*. 2020 Jul 21 [Epub ahead of print]. Full text (<https://academic.oup.com/tropej/article/doi/10.1093/tropej/fmaa045/5874434>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32692815?tool=bestpractice.bmj.com>)
645. Ghodsi A, Bijari M, Alamdaran SA, et al. Chest computed tomography findings of COVID-19 in children younger than 1 year: a systematic review. *World J Pediatr*. 2021 May 7 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8104919>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33963512?tool=bestpractice.bmj.com>)
646. Park GS, Ku K, Baek SH, et al. Development of reverse transcription loop-mediated isothermal amplification assays targeting severe acute respiratory syndrome coronavirus 2. *J Mol Diagn*. 2020 Jun;22(6):729-35. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7144851>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32276051?tool=bestpractice.bmj.com>)
647. Baek YH, Um J, Antigua KJC, et al. Development of a reverse transcription-loop-mediated isothermal amplification as a rapid early-detection method for novel SARS-CoV-2. *Emerg Microbes Infect*. 2020 Apr 20:1-31. Full text (<https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1756698>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32306853?tool=bestpractice.bmj.com>)
648. Lu R, Wu X, Wan Z, et al. A novel reverse transcription loop-mediated isothermal amplification method for rapid detection of SARS-CoV-2. *Int J Mol Sci*. 2020 Apr 18;21(8). Full text (<https://www.mdpi.com/1422-0067/21/8/2826/htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32325642?tool=bestpractice.bmj.com>)

649. Subali AD, Wiyono L. Reverse Transcriptase Loop Mediated Isothermal Amplification (RT-LAMP) for COVID-19 diagnosis: a systematic review and meta-analysis. *Pathog Glob Health*. 2021 Jun 4;1-11. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8182821\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8182821) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34086539?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34086539?tool=bestpractice.bmj.com)
650. Mohamed MFH, Al-Shokri S, Yousaf Z, et al. Frequency of abnormalities detected by point-of-care lung ultrasound in symptomatic COVID-19 patients: systematic review and meta-analysis. *Am J Trop Med Hyg*. 2020 Aug;103(2):815-21. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7410428\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7410428) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32500849?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32500849?tool=bestpractice.bmj.com)
651. Moro F, Buonsenso D, Moruzzi MC, et al. How to perform lung ultrasound in pregnant women with suspected COVID-19 infection. *Ultrasound Obstet Gynecol*. 2020 May;55(5):593-8. [Full text \(https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1002/uog.22028\)](https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1002/uog.22028) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32207208?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32207208?tool=bestpractice.bmj.com)
652. Denina M, Scolfaro C, Silvestro E, et al. Lung ultrasound in children with COVID-19. *Pediatrics*. 2020 Jul;146(1):e20201157. [Full text \(https://pediatrics.aappublications.org/content/early/2020/04/17/peds.2020-1157\)](https://pediatrics.aappublications.org/content/early/2020/04/17/peds.2020-1157) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32317309?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32317309?tool=bestpractice.bmj.com)
653. Pillai K, Hewage S, Harky A. The role of the lung ultrasound in coronavirus disease 2019: a systematic review. *J Med Ultrasound*. 2020 Oct-Dec;28(4):207-12. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7869739\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7869739) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33659158?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33659158?tool=bestpractice.bmj.com)
654. Song G, Qiao W, Wang X, et al. Association of lung ultrasound score with mortality and severity of COVID-19: a meta-analysis and trial sequential analysis. *Int J Infect Dis*. 2021 Jun 16 [Epub ahead of print]. [Full text \(https://www.ijidonline.com/article/S1201-9712\(21\)00513-0/fulltext\)](https://www.ijidonline.com/article/S1201-9712(21)00513-0/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34146693?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34146693?tool=bestpractice.bmj.com)
655. Udeh R, Advani S, de Guadiana Romualdo LG, et al. Calprotectin, an emerging biomarker of interest in COVID-19: a systematic review and meta-analysis. *J Clin Med*. 2021 Feb 15;10(4):775. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7919496\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7919496) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33672040?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33672040?tool=bestpractice.bmj.com)
656. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020 Apr 30;382(18):1708-20. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2002032\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2002032) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32109013?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32109013?tool=bestpractice.bmj.com)
657. Islam MA, Kundu S, Alam SS, et al. Prevalence and characteristics of fever in adult and paediatric patients with coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis of 17515 patients. *PLoS One*. 2021;16(4):e0249788. [Full text \(https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0249788\)](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0249788) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33822812?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33822812?tool=bestpractice.bmj.com)
658. Lu X, Zhang L, Du H, et al. SARS-CoV-2 infection in children. *N Engl J Med*. 2020 Apr 23;382(17):1663-5. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMc2005073\)](https://www.nejm.org/doi/full/10.1056/NEJMc2005073) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32187458?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32187458?tool=bestpractice.bmj.com)

659. Song WJ, Hui CKM, Hull JH, et al. Confronting COVID-19-associated cough and the post-COVID syndrome: role of viral neurotropism, neuroinflammation, and neuroimmune responses. *Lancet Respir Med*. 2021 May;9(5):533-44. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8041436\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8041436) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33857435?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33857435?tool=bestpractice.bmj.com)
660. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020 Feb 7;323(11):1061-9. [Full text \(https://jamanetwork.com/journals/jama/fullarticle/2761044\)](https://jamanetwork.com/journals/jama/fullarticle/2761044) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32031570?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32031570?tool=bestpractice.bmj.com)
661. Grant MC, Geoghegan L, Arbyn M, et al. The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): a systematic review and meta-analysis of 148 studies from 9 countries. *PLoS One*. 2020 Jun 23;15(6):e0234765. [Full text \(https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0234765\)](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0234765) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32574165?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32574165?tool=bestpractice.bmj.com)
662. Agyeman AA, Chin KL, Landersdorfer CB, et al. Smell and taste dysfunction in patients with COVID-19: a systematic review and meta-analysis. *Mayo Clin Proc*. 2020 Aug;95(8):1621-31. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7275152\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7275152) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32753137?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32753137?tool=bestpractice.bmj.com)
663. Eliezer M, Hautefort C, Hamel AL, et al. Sudden and complete olfactory loss function as a possible symptom of COVID-19. *JAMA Otolaryngol Head Neck Surg*. 2020 Jul 1;146(7):674-5. [Full text \(https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2764417\)](https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2764417) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32267483?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32267483?tool=bestpractice.bmj.com)
664. Santos REA, da Silva MG, do Monte Silva MCB, et al. Onset and duration of symptoms of loss of smell/taste in patients with COVID-19: a systematic review. *Am J Otolaryngol*. 2021 Jan 6;42(2):102889. [Full text \(https://www.sciencedirect.com/science/article/pii/S0196070920305834?via%3Dihub\)](https://www.sciencedirect.com/science/article/pii/S0196070920305834?via%3Dihub) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33445036?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33445036?tool=bestpractice.bmj.com)
665. Renaud M, Thibault C, Le Normand F, et al. Clinical outcomes for patients with anosmia 1 year after COVID-19 diagnosis. *JAMA Netw Open*. 2021 Jun 1;4(6):e2115352. [Full text \(https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781319\)](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781319) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34165581?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34165581?tool=bestpractice.bmj.com)
666. Hariyanto TI, Rizki NA, Kurniawan A. Anosmia/hyposmia is a good predictor of coronavirus disease 2019 (COVID-19) infection: a meta-analysis. *Int Arch Otorhinolaryngol*. 2021 Jan;25(1):e170-4. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7857970\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7857970) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33552295?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33552295?tool=bestpractice.bmj.com)
667. Ferraro S, Tuccori M, Convertino I, et al. Olfactory and gustatory impairments in COVID-19 patients: role in early diagnosis and interferences by concomitant drugs. *Br J Clin Pharmacol*. 2021 May;87(5):2186-8. [Full text \(https://bpspubs.onlinelibrary.wiley.com/doi/full/10.1111/bcp.14634\)](https://bpspubs.onlinelibrary.wiley.com/doi/full/10.1111/bcp.14634) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33185930?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33185930?tool=bestpractice.bmj.com)
668. Parisi S, Borrelli R, Bianchi S, et al. Viral arthritis and COVID-19. *Lancet Rheumatol*. 2020 Nov;2(11):e655-7. [Full text \(https://www.thelancet.com/journals/lanrhe/article/\)](https://www.thelancet.com/journals/lanrhe/article/)

PIIS2665-9913(20)30348-9/fulltext) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33043303?tool=bestpractice.bmj.com>)

669. Tariq R, Saha S, Furqan F, et al. Prevalence and mortality of COVID-19 patients with gastrointestinal symptoms: a systematic review and meta-analysis. *Mayo Clin Proc.* 2020 Aug;95(8):1632-48. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7284248>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32753138?tool=bestpractice.bmj.com>)
670. Chen A, Agarwal A, Ravindran N, et al. Are gastrointestinal symptoms specific for coronavirus infection? A prospective case-control study from the United States. *Gastroenterology.* 2020 Sep;159(3):1161-3. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7229473>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32422209?tool=bestpractice.bmj.com>)
671. Aziz M, Haghbin H, Lee-Smith W, et al. Gastrointestinal predictors of severe COVID-19: systematic review and meta-analysis. *Ann Gastroenterol.* 2020 Nov-Dec;33(6):615-30. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7599357>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33162738?tool=bestpractice.bmj.com>)
672. Zeng W, Qi K, Ye M, et al. Gastrointestinal symptoms are associated with severity of coronavirus disease 2019: a systematic review and meta-analysis. *Eur J Gastroenterol Hepatol.* 2021 Jan 18 [Epub ahead of print]. Full text (https://journals.lww.com/eurojgh/Abstract/9000/Gastrointestinal_symptoms_are_associated_with.97315.aspx) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33470700?tool=bestpractice.bmj.com>)
673. Shehab M, Alrashed F, Shuaibi S, et al. Gastroenterological and hepatic manifestations of patients with COVID-19, prevalence, mortality by country, and intensive care admission rate: systematic review and meta-analysis. *BMJ Open Gastroenterol.* 2021 Mar;8(1):e000571. Full text (<https://bmjopengastro.bmj.com/content/8/1/e000571.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33664052?tool=bestpractice.bmj.com>)
674. Guotao L, Xingpeng Z, Zhihui D, et al. SARS-CoV-2 infection presenting with hematochezia. *Med Mal Infect.* 2020 May;50(3):293-6. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7141548>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32229159?tool=bestpractice.bmj.com>)
675. Mutiawati E, Syahrul S, Fahriani M, et al. Global prevalence and pathogenesis of headache in COVID-19: a systematic review and meta-analysis. *F1000Res.* 2020 Nov 12;9:1316. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8063523>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33953911?tool=bestpractice.bmj.com>)
676. Shao SC, Lai CC, Chen YH, et al. Prevalence, incidence and mortality of delirium in patients with COVID-19: A systematic review and meta-analysis. *Age Ageing.* 2021 May 12 [Epub ahead of print]. Full text (<https://academic.oup.com/ageing/advance-article/doi/10.1093/ageing/afab103/6274714>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33984129?tool=bestpractice.bmj.com>)
677. Pun BT, Badenes R, Heras La Calle G, et al. Prevalence and risk factors for delirium in critically ill patients with COVID-19 (COVID-D): a multicentre cohort study. *Lancet Respir Med.* 2021 Mar;9(3):239-50. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7832119>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33428871?tool=bestpractice.bmj.com>)

678. Cénat JM, Blais-Rochette C, Kokou-Kpolou CK, et al. Prevalence of symptoms of depression, anxiety, insomnia, posttraumatic stress disorder, and psychological distress among populations affected by the COVID-19 pandemic: a systematic review and meta-analysis. *Psychiatry Res.* 2020 Nov 26;295:113599. [Full text \(https://www.sciencedirect.com/science/article/pii/S0165178120332601?via%3DIihub\)](https://www.sciencedirect.com/science/article/pii/S0165178120332601?via%3DIihub) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33285346?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33285346?tool=bestpractice.bmj.com)
679. National Institute for Health Research. Brain and nerve complications are more common than expected in younger patients with severe COVID-19. 2020 [internet publication]. [Full text \(https://evidence.nihr.ac.uk/alert/brain-and-nerve-complications-are-more-common-than-expected-in-younger-patients-with-severe-covid-19\)](https://evidence.nihr.ac.uk/alert/brain-and-nerve-complications-are-more-common-than-expected-in-younger-patients-with-severe-covid-19)
680. Varatharaj A, Thomas N, Ellul MA, et al. Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study. *Lancet Psychiatry.* 2020 Oct;7(10):875-82. [Full text \(https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366\(20\)30287-X/fulltext\)](https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(20)30287-X/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32593341?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32593341?tool=bestpractice.bmj.com)
681. Nasiri N, Sharifi H, Bazrafshan A, et al. Ocular manifestations of COVID-19: a systematic review and meta-analysis. *J Ophthalmic Vis Res.* 2021 Jan-Mar;16(1):103-12. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7841281\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7841281) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33520133?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33520133?tool=bestpractice.bmj.com)
682. Inomata T, Kitazawa K, Kuno T, et al. Clinical and prodromal ocular symptoms in coronavirus disease: a systematic review and meta-analysis. *Invest Ophthalmol Vis Sci.* 2020 Aug 3;61(10):29. [Full text \(https://iovs.arvojournals.org/article.aspx?articleid=2770655\)](https://iovs.arvojournals.org/article.aspx?articleid=2770655) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32797198?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32797198?tool=bestpractice.bmj.com)
683. Ma N, Li P, Wang X, et al. Ocular manifestations and clinical characteristics of children with laboratory-confirmed COVID-19 in Wuhan, China. *JAMA Ophthalmol.* 2020 Oct 1;138(10):1079-86. [Full text \(https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2769877\)](https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2769877) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32845280?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32845280?tool=bestpractice.bmj.com)
684. Almufarrij I, Munro KJ. One year on: an updated systematic review of SARS-CoV-2, COVID-19 and audio-vestibular symptoms. *Int J Audiol.* 2021 Mar 22;1-11. [Full text \(https://www.tandfonline.com/doi/full/10.1080/14992027.2021.1896793\)](https://www.tandfonline.com/doi/full/10.1080/14992027.2021.1896793) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33750252?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33750252?tool=bestpractice.bmj.com)
685. Bandhala Rajan M, Kumar-M P, Bhardwaj A. The trend of cutaneous lesions during COVID-19 pandemic: lessons from a meta-analysis and systematic review. *Int J Dermatol.* 2020 Nov;59(11):1358-70. [Full text \(https://onlinelibrary.wiley.com/doi/10.1111/ijd.15154\)](https://onlinelibrary.wiley.com/doi/10.1111/ijd.15154) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32936462?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32936462?tool=bestpractice.bmj.com)
686. Kashetsky N, Mukovozov IM, Bergman J. Chilblain-like lesions (CLL) associated with COVID-19 ("COVID toes"): a systematic review. *J Cutan Med Surg.* 2021 Apr 13 [Epub ahead of print]. [Full text \(https://journals.sagepub.com/doi/10.1177/12034754211004575\)](https://journals.sagepub.com/doi/10.1177/12034754211004575) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33849305?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33849305?tool=bestpractice.bmj.com)

687. Bataille V, Visconti A, Rossi R, et al; medRxiv. Diagnostic value of skin manifestation of SARS-CoV-2 infection. 2020 [internet publication]. [Full text \(https://www.medrxiv.org/content/10.1101/2020.07.10.20150656v1\)](https://www.medrxiv.org/content/10.1101/2020.07.10.20150656v1)
688. Schwartzberg LN, Advani S, Clancy DC, et al. A systematic review of dermatologic manifestations among adult patients with COVID-19 diagnosis. *Skin Health Dis.* 2021 Jun;1(2):e20. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8250095\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8250095) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34235511?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34235511?tool=bestpractice.bmj.com)
689. Shah S, Akhade K, Ganguly S, et al. Cutaneous manifestations associated with COVID-19 in children: a systematic review. *J Family Med Prim Care.* 2021 Jan;10(1):93-101. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8132763\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8132763) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34017709?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34017709?tool=bestpractice.bmj.com)
690. Discepolo V, Catzola A, Pierri L, et al. Bilateral chilblain-like lesions of the toes characterized by microvascular remodeling in adolescents during the COVID-19 pandemic. *JAMA Netw Open.* 2021 Jun 1;4(6):e2111369. [Full text \(https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780866\)](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780866) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34110396?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34110396?tool=bestpractice.bmj.com)
691. Creta M, Sagnelli C, Celentano G, et al. SARS-CoV-2 infection affects the lower urinary tract and male genital system: a systematic review. *J Med Virol.* 2021 May;93(5):3133-42. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8013185\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8013185) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33595134?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33595134?tool=bestpractice.bmj.com)
692. Haghpanah A, Masjedi F, Salehipour M, et al. Is COVID-19 a risk factor for progression of benign prostatic hyperplasia and exacerbation of its related symptoms? A systematic review. *Prostate Cancer Prostatic Dis.* 2021 May 18 [Epub ahead of print]. [Full text \(https://www.nature.com/articles/s41391-021-00388-3\)](https://www.nature.com/articles/s41391-021-00388-3) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34007019?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34007019?tool=bestpractice.bmj.com)
693. Casey K, Iteen A, Nicolini R, et al. COVID-19 pneumonia with hemoptysis: acute segmental pulmonary emboli associated with novel coronavirus infection. *Am J Emerg Med.* 2020 Jul;38(7):1544. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7141630\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7141630) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32312574?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32312574?tool=bestpractice.bmj.com)
694. US Food and Drug Administration. Genetic variants of SARS-CoV-2 may lead to false negative results with molecular tests for detection of SARS-CoV-2: letter to clinical laboratory staff and health care providers. 2021 [internet publication]. [Full text \(https://www.fda.gov/medical-devices/letters-health-care-providers/genetic-variants-sars-cov-2-may-lead-false-negative-results-molecular-tests-detection-sars-cov-2?utm_medium=email&utm_source=govdelivery\)](https://www.fda.gov/medical-devices/letters-health-care-providers/genetic-variants-sars-cov-2-may-lead-false-negative-results-molecular-tests-detection-sars-cov-2?utm_medium=email&utm_source=govdelivery)
695. Danwang C, Endomba FT, Nneck JR, et al. A meta-analysis of potential biomarkers associated with severity of coronavirus disease 2019 (COVID-19). *Biomark Res.* 2020 Aug 31;8:37. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456766\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456766) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32879731?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32879731?tool=bestpractice.bmj.com)
696. Foy BH, Carlson JCT, Reinertsen E, et al. Association of red blood cell distribution width with mortality risk in hospitalized adults with SARS-CoV-2 infection. *JAMA Netw Open.* 2020 Sep 1;3(9):e2022058.

- Full text (<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770945>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32965501?tool=bestpractice.bmj.com>)
697. Huang W, Berube J, McNamara M, et al. Lymphocyte subset counts in COVID-19 patients: a meta-analysis. *Cytometry A*. 2020 Aug;97(8):772-6. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7323417>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32542842?tool=bestpractice.bmj.com>)
 698. Chen W, Li Z, Yang B, et al. Delayed-phase thrombocytopenia in patients of coronavirus disease 2019 (COVID-19). *Br J Haematol*. 2020 Jul;190(2):179-84. Full text (<https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.16885>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32453877?tool=bestpractice.bmj.com>)
 699. Chen D, Li X, Song Q, et al. Assessment of hypokalemia and clinical characteristics in patients with coronavirus disease 2019 in Wenzhou, China. *JAMA Netw Open*. 2020 Jun 1;3(6):e2011122. Full text (<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2767008>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32525548?tool=bestpractice.bmj.com>)
 700. Liu J, Han P, Wu J, et al. Prevalence and predictive value of hypocalcemia in severe COVID-19 patients. *J Infect Public Health*. 2020 Sep;13(9):1224-8. Full text (<https://www.sciencedirect.com/science/article/pii/S1876034120305323?via%3Dihub>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32622796?tool=bestpractice.bmj.com>)
 701. Martha JW, Wibowo A, Pranata R. Hypocalcemia is associated with severe COVID-19: a systematic review and meta-analysis. *Diabetes Metab Syndr*. 2021 Jan 18;15(1):337-42. Full text (<https://www.sciencedirect.com/science/article/pii/S1871402121000059?via%3Dihub>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33493853?tool=bestpractice.bmj.com>)
 702. Akbar MR, Pranata R, Wibowo A, et al. The prognostic value of hyponatremia for predicting poor outcome in patients with COVID-19: a systematic review and meta-analysis. *Front Med (Lausanne)*. 2021 Jun 14;8:666949. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8236602>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34195209?tool=bestpractice.bmj.com>)
 703. Lazarus G, Audrey J, Kharisma Wangsaputra V, et al. High admission blood glucose independently predicts poor prognosis in COVID-19 patients: a systematic review and dose-response meta-analysis. *Diabetes Res Clin Pract*. 2020 Dec 9:108561. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7725108>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33310127?tool=bestpractice.bmj.com>)
 704. Handayani DR, Juliastuti H, Nawangsih EN, et al. Prognostic value of fasting hyperglycemia in patients with COVID-19: diagnostic test accuracy meta-analysis. *Obes Med*. 2021 Apr 4:100333. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8019489>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33842733?tool=bestpractice.bmj.com>)
 705. Klonoff DC, Messler JC, Umpierrez GE, et al. Association between achieving inpatient glycemic control and clinical outcomes in hospitalized patients with COVID-19: a multicenter, retrospective hospital-based analysis. *Diabetes Care*. 2021 Feb;44(2):578-85. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7818335>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33323475?tool=bestpractice.bmj.com>)

706. Nugroho J, Wardhana A, Mulia EP, et al. Elevated fibrinogen and fibrin degradation product are associated with poor outcome in COVID-19 patients: a meta-analysis. *Clin Hemorheol Microcirc.* 2021;77(2):221-31. [Full text \(https://content.iospress.com/articles/clinical-hemorheology-and-microcirculation/ch200978\)](https://content.iospress.com/articles/clinical-hemorheology-and-microcirculation/ch200978) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33074221?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33074221?tool=bestpractice.bmj.com)
707. Shah S, Shah K, Patel SB, et al. Elevated D-dimer levels are associated with increased risk of mortality in COVID-19: a systematic review and meta-analysis. *Cardiol Rev.* 2020 Nov/Dec;28(6):295-302. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32665526?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32665526?tool=bestpractice.bmj.com)
708. Leonard-Lorant I, Delabranche X, Severac F, et al. Acute pulmonary embolism in COVID-19 patients on CT angiography and relationship to D-dimer levels. *Radiology.* 2020 Apr 23:201561. [Full text \(https://pubs.rsna.org/doi/10.1148/radiol.2020201561\)](https://pubs.rsna.org/doi/10.1148/radiol.2020201561) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32324102?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32324102?tool=bestpractice.bmj.com)
709. Mucha SR, Dugar S, McCrae K, et al. Coagulopathy in COVID-19. *Cleve Clin J Med.* 2020 Jul 31;87(8):461-8. [Full text \(https://www.ccjm.org/content/87/8/461.long\)](https://www.ccjm.org/content/87/8/461.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32409435?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32409435?tool=bestpractice.bmj.com)
710. Wungu CDK, Khaerunnisa S, Putri EAC, et al. Meta-analysis of cardiac markers for predictive factors on severity and mortality of COVID-19. *Int J Infect Dis.* 2021 Mar 9;105:551-9. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7942156\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7942156) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33711519?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33711519?tool=bestpractice.bmj.com)
711. Smilowitz NR, Kunichoff D, Garshick M, et al. C-reactive protein and clinical outcomes in patients with COVID-19. *Eur Heart J.* 2021 Jan 15 [Epub ahead of print]. [Full text \(https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaa1103/6100979\)](https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaa1103/6100979) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33448289?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33448289?tool=bestpractice.bmj.com)
712. Soraya GV, Ulhaq ZS. Interleukin-6 levels in children developing SARS-CoV-2 infection. *Pediatr Neonatol.* 2020 Jun;61(3):253-4. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7198182\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7198182) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32414693?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32414693?tool=bestpractice.bmj.com)
713. Cheng L, Li H, Li L, et al. Ferritin in the coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *J Clin Lab Anal.* 2020 Oct 19:e23618. [Full text \(https://onlinelibrary.wiley.com/doi/10.1002/jcla.23618\)](https://onlinelibrary.wiley.com/doi/10.1002/jcla.23618) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33078400?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33078400?tool=bestpractice.bmj.com)
714. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet.* 2020 Mar 28;395(10229):1033-4. [Full text \(https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30628-0/fulltext\)](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30628-0/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32192578?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32192578?tool=bestpractice.bmj.com)
715. Fu J, Huang PP, Zhang S, et al. The value of serum amyloid A for predicting the severity and recovery of COVID-19. *Exp Ther Med.* 2020 Oct;20(4):3571-7. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7444421\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7444421) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32855710?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32855710?tool=bestpractice.bmj.com)

716. Kim H, Hong H, Yoon SH. Diagnostic performance of CT and reverse transcriptase-polymerase chain reaction for coronavirus disease 2019: a meta-analysis. *Radiology*. 2020 Apr 17:201343. [Full text \(https://pubs.rsna.org/doi/10.1148/radiol.2020201343\)](https://pubs.rsna.org/doi/10.1148/radiol.2020201343) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32301646?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32301646?tool=bestpractice.bmj.com)
717. Lv M, Wang M, Yang N, et al. Chest computed tomography for the diagnosis of patients with coronavirus disease 2019 (COVID-19): a rapid review and meta-analysis. *Ann Transl Med*. 2020 May;8(10):622. [Full text \(http://atm.amegroups.com/article/view/43222/html\)](http://atm.amegroups.com/article/view/43222/html) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32566559?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32566559?tool=bestpractice.bmj.com)
718. Mair MDD, Hussain M, Siddiqui S, et al. A systematic review and meta-analysis comparing the diagnostic accuracy of initial RT-PCR and CT scan in suspected COVID-19 patients. *Br J Radiol*. 2020 Dec 22:20201039. [Full text \(https://www.birpublications.org/doi/10.1259/bjr.20201039\)](https://www.birpublications.org/doi/10.1259/bjr.20201039) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33353381?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33353381?tool=bestpractice.bmj.com)
719. Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. *Radiology*. 2020 Feb 26:200642. [Full text \(https://pubs.rsna.org/doi/10.1148/radiol.2020200642\)](https://pubs.rsna.org/doi/10.1148/radiol.2020200642) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32101510?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32101510?tool=bestpractice.bmj.com)
720. World Health Organization. Interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19: interim guidance. 2021 [internet publication]. [Full text \(https://www.who.int/publications/i/item/interim-recommendations-for-use-of-the-moderna-mrna-1273-vaccine-against-covid-19\)](https://www.who.int/publications/i/item/interim-recommendations-for-use-of-the-moderna-mrna-1273-vaccine-against-covid-19)
721. World Health Organization. Interim recommendations for use of the AZD1222 (ChAdOx1-S (recombinant)) vaccine against COVID-19 developed by Oxford University and AstraZeneca. 2021 [internet publication]. [Full text \(https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1\)](https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1)
722. US Food and Drug Administration. Stop using Innova Medical Group SARS-CoV-2 antigen rapid qualitative test: FDA safety communication. 2021 [internet publication]. [Full text \(https://www.fda.gov/medical-devices/safety-communications/stop-using-innova-medical-group-sars-cov-2-antigen-rapid-qualitative-test-fda-safety-communication\)](https://www.fda.gov/medical-devices/safety-communications/stop-using-innova-medical-group-sars-cov-2-antigen-rapid-qualitative-test-fda-safety-communication)
723. US Food and Drug Administration. Coronavirus (COVID-19) update: FDA authorizes antigen test as first over-the-counter fully at-home diagnostic test for COVID-19. 2020 [internet publication]. [Full text \(https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-antigen-test-first-over-counter-fully-home-diagnostic\)](https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-antigen-test-first-over-counter-fully-home-diagnostic)
724. Government of the United Kingdom. Order coronavirus (COVID-19) rapid lateral flow tests. 2021 [internet publication]. [Full text \(https://www.gov.uk/order-coronavirus-rapid-lateral-flow-tests\)](https://www.gov.uk/order-coronavirus-rapid-lateral-flow-tests)
725. US Food and Drug Administration. Coronavirus (COVID-19) update: FDA authorizes first COVID-19 test for self-testing at home. 2020 [internet publication]. [Full text \(https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-covid-19-test-self-testing-home\)](https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-covid-19-test-self-testing-home)

726. Centre for Evidence-Based Medicine; Heneghan C, Pluddemann A, Mahtani KR. Differentiating viral from bacterial pneumonia. 2020 [internet publication]. [Full text \(https://www.cebm.net/covid-19/differentiating-viral-from-bacterial-pneumonia\)](https://www.cebm.net/covid-19/differentiating-viral-from-bacterial-pneumonia)
727. Hani C, Trieu NH, Saab I, et al. COVID-19 pneumonia: a review of typical CT findings and differential diagnosis. *Diagn Interv Imaging*. 2020 May;101(5):263-8. [Full text \(https://www.sciencedirect.com/science/article/pii/S2211568420300917?via%3Dihub\)](https://www.sciencedirect.com/science/article/pii/S2211568420300917?via%3Dihub) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32291197?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32291197?tool=bestpractice.bmj.com)
728. Pormohammad A, Ghorbani S, Khatami A, et al. Comparison of influenza type A and B with COVID-19: a global systematic review and meta-analysis on clinical, laboratory and radiographic findings. *Rev Med Virol*. 2020 Oct 9:e2179. [Full text \(https://onlinelibrary.wiley.com/doi/10.1002/rmv.2179\)](https://onlinelibrary.wiley.com/doi/10.1002/rmv.2179) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33035373?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33035373?tool=bestpractice.bmj.com)
729. Solomon DA, Sherman AC, Kanjilal S. Influenza in the COVID-19 era. *JAMA*. 2020 Oct 6;324(13):1342-3. [Full text \(https://jamanetwork.com/journals/jama/fullarticle/2769676\)](https://jamanetwork.com/journals/jama/fullarticle/2769676) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32797145?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32797145?tool=bestpractice.bmj.com)
730. Song X, Delaney M, Shah RK, et al. Comparison of clinical features of COVID-19 vs seasonal influenza A and B in US children. *JAMA Netw Open*. 2020 Sep 1;3(9):e2020495. [Full text \(https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770250\)](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770250) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32897374?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32897374?tool=bestpractice.bmj.com)
731. Czubak J, Stolarczyk K, Orzeł A, et al. Comparison of the clinical differences between COVID-19, SARS, influenza, and the common cold: a systematic literature review. *Adv Clin Exp Med*. 2021 Jan;30(1):109-14. [Full text \(https://www.advances.umed.wroc.pl/pdf/2021/30/1/109.pdf\)](https://www.advances.umed.wroc.pl/pdf/2021/30/1/109.pdf) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33529514?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33529514?tool=bestpractice.bmj.com)
732. Beltrán-Corbellini Á, Chico-García JL, Martínez-Poles J, et al. Acute-onset smell and taste disorders in the context of COVID-19: a pilot multicenter PCR-based case-control study. *Eur J Neurol*. 2020 Sep;27(9):1738-41. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7264557\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7264557) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32320508?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32320508?tool=bestpractice.bmj.com)
733. National Institutes of Health. Coronavirus disease 2019 (COVID-19) treatment guidelines. 2021 [internet publication]. [Full text \(https://covid19treatmentguidelines.nih.gov\)](https://covid19treatmentguidelines.nih.gov)
734. Liu M, Zeng W, Wen Y, et al. COVID-19 pneumonia: CT findings of 122 patients and differentiation from influenza pneumonia. *Eur Radiol*. 2020 Oct;30(10):5463-9. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7216854\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7216854) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32399710?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32399710?tool=bestpractice.bmj.com)
735. Yin Z, Kang Z, Yang D, et al. A comparison of clinical and chest CT findings in patients with influenza A (H1N1) virus infection and coronavirus disease (COVID-19). *AJR Am J Roentgenol*. 2020 May 26;1-7. [Full text \(https://www.ajronline.org/doi/10.2214/AJR.20.23214\)](https://www.ajronline.org/doi/10.2214/AJR.20.23214) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32452731?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32452731?tool=bestpractice.bmj.com)
736. Luo Y, Yuan X, Xue Y, et al. Using the diagnostic model based on routine laboratory tests to distinguish patients infected with SARS-CoV-2 from those infected with influenza virus. *Int J Infect Dis*. 2020 May

- 1;95:436-40. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7194039>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32371192?tool=bestpractice.bmj.com>)
737. Zarei F, Reza J, Sefidbakht S, et al. Aspiration pneumonia or COVID-19 infection: a diagnostic challenge. *Acad Radiol*. 2020 Jul;27(7):1046. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7196404>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32381329?tool=bestpractice.bmj.com>)
738. National Institute for Health and Care Excellence. COVID-19 rapid guideline: delivery of systemic anticancer treatments. 2020 [internet publication]. Full text (<https://www.nice.org.uk/guidance/ng161>)
739. World Health Organization. Considerations for quarantine of contacts of COVID-19 cases: interim guidance. 2021 [internet publication]. Full text (<https://www.who.int/publications/i/item/WHO-2019-nCoV-IHR-Quarantine-2021.1>)
740. Public Health England. Guidance for contacts of people with confirmed coronavirus (COVID-19) infection who do not live with the person. 2020 [internet publication]. Full text (<https://www.gov.uk/government/publications/guidance-for-contacts-of-people-with-possible-or-confirmed-coronavirus-covid-19-infection-who-do-not-live-with-the-person/guidance-for-contacts-of-people-with-possible-or-confirmed-coronavirus-covid-19-infection-who-do-not-live-with-the-person>)
741. Department of Health and Social Care. Self-isolation to be eased for fully vaccinated adults in step 4. 2021 [internet publication]. Full text (<https://www.gov.uk/government/news/self-isolation-to-be-eased-for-fully-vaccinated-adults-in-step-4>)
742. Centers for Disease Control and Prevention. Options to reduce quarantine for contacts of persons with SARS-CoV-2 infection using symptom monitoring and diagnostic testing. 2020 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/more/scientific-brief-options-to-reduce-quarantine.html>)
743. World Health Organization. Updated WHO recommendations for international traffic in relation to COVID-19 outbreak. 2020 [internet publication]. Full text (https://www.who.int/ith/2019-nCoV_advice_for_international_traffic-rev/en)
744. Arima Y, Shimada T, Suzuki M, et al. Severe acute respiratory syndrome coronavirus 2 infection among returnees to Japan from Wuhan, China, 2020. *Emerg Infect Dis*. 2020 Apr 10;26(7). Full text (https://wwwnc.cdc.gov/eid/article/26/7/20-0994_article) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32275498?tool=bestpractice.bmj.com>)
745. Kwon KT, Ko JH, Shin H, et al. Drive-through screening center for COVID-19: a safe and efficient screening system against massive community outbreak. *J Korean Med Sci*. 2020 Mar 23;35(11):e123. Full text (<https://jkms.org/DOIx.php?id=10.3346/jkms.2020.35.e123>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32193904?tool=bestpractice.bmj.com>)
746. Medicines and Healthcare products Regulatory Agency. Don't rely on temperature screening products for detection of coronavirus (COVID-19), says MHRA. 2020 [internet publication]. Full text (<https://www.gov.uk/government/news/dont-rely-on-temperature-screening-products-for-detection-of-coronavirus-covid-19-says-mhra>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/insert id?tool=bestpractice.bmj.com>)

747. Aggarwal N, Garg M, Dwarakanathan V, et al. Diagnostic accuracy of non-contact infrared thermometers and thermal scanners: a systematic review and meta-analysis. *J Travel Med*. 2020 Oct 10 [Epub ahead of print]. [Full text \(https://academic.oup.com/jtm/advance-article/doi/10.1093/jtm/taaa193/5920642\)](https://academic.oup.com/jtm/advance-article/doi/10.1093/jtm/taaa193/5920642) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33043363?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33043363?tool=bestpractice.bmj.com)
748. Chen G, Xie J, Dai G, et al; medRxiv. Validity of wrist and forehead temperature in temperature screening in the general population during the outbreak of 2019 novel coronavirus: a prospective real-world study. 2020 [internet publication]. [Full text \(https://www.medrxiv.org/content/10.1101/2020.03.02.20030148v1\)](https://www.medrxiv.org/content/10.1101/2020.03.02.20030148v1)
749. Khan DS, Saultry MB, Adams DS, et al. Comparative accuracy testing of non-contact infrared thermometers and temporal artery thermometers in an adult hospital setting. *Am J Infect Control*. 2021 May;49(5):597-602. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7530626\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7530626) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33017627?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33017627?tool=bestpractice.bmj.com)
750. Centers for Disease Control and Prevention. Interim infection prevention and control recommendations for healthcare personnel during the coronavirus disease 2019 (COVID-19) pandemic. 2021 [internet publication]. [Full text \(https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html\)](https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html)
751. Infectious Diseases Society of America. COVID-19 real-time learning network. 2021 [internet publication]. [Full text \(https://www.idsociety.org/covid-19-real-time-learning-network\)](https://www.idsociety.org/covid-19-real-time-learning-network)
752. American Academy of Pediatrics. COVID-19 interim guidance. 2021 [internet publication]. [Full text \(https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance\)](https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance)
753. Infectious Diseases Society of America. Infectious Diseases Society of America guidelines on infection prevention in patients with suspected or known COVID-19. 2020 [internet publication]. [Full text \(https://www.idsociety.org/practice-guideline/covid-19-guideline-infection-prevention\)](https://www.idsociety.org/practice-guideline/covid-19-guideline-infection-prevention)
754. World Health Organization. Country & technical guidance - coronavirus disease (COVID-19). 2021 [internet publication]. [Full text \(https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance-publications\)](https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance-publications)
755. Public Health England. COVID-19: guidance for health professionals. 2021 [internet publication]. [Full text \(https://www.gov.uk/government/collections/wuhan-novel-coronavirus\)](https://www.gov.uk/government/collections/wuhan-novel-coronavirus)
756. Public Health England. COVID-19: investigation and management of suspected SARS-CoV-2 reinfections. 2021 [internet publication]. [Full text \(https://www.gov.uk/government/publications/covid-19-investigation-and-management-of-suspected-sars-cov-2-reinfections\)](https://www.gov.uk/government/publications/covid-19-investigation-and-management-of-suspected-sars-cov-2-reinfections)
757. European Centre for Disease Prevention and Control. COVID-19. 2021 [internet publication]. [Full text \(https://www.ecdc.europa.eu/en/novel-coronavirus-china\)](https://www.ecdc.europa.eu/en/novel-coronavirus-china)
758. Scottish Intercollegiate Guidelines Network. Assessment of COVID-19 in primary care. 2021 [internet publication]. [Full text \(https://www.sign.ac.uk/our-guidelines/assessment-of-covid-19-in-primary-care\)](https://www.sign.ac.uk/our-guidelines/assessment-of-covid-19-in-primary-care)

759. Scottish Intercollegiate Guidelines Network. COVID-19 position statement: presentations and management of COVID-19 in older people in acute care. 2021 [internet publication]. [Full text \(https://www.sign.ac.uk/media/1826/presentations-and-management-of-covid-19-in-older-people-v2-final.pdf\)](https://www.sign.ac.uk/media/1826/presentations-and-management-of-covid-19-in-older-people-v2-final.pdf)
760. Jin YH, Cai L, Cheng ZS, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res*. 2020 Feb 6;7(1):4. [Full text \(https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-020-0233-6\)](https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-020-0233-6) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32029004?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32029004?tool=bestpractice.bmj.com)
761. Li T. Diagnosis and clinical management of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection: an operational recommendation of Peking Union Medical College Hospital (V2.0). *Emerg Microbes Infect*. 2020 Mar;9(1):582-5. [Full text \(https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1735265\)](https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1735265) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32172669?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32172669?tool=bestpractice.bmj.com)
762. World Health Organization. Therapeutics and COVID-19: living guideline. 2021 [internet publication]. [Full text \(https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.2\)](https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.2)
763. Rochwerg B, Siemieniuk RA, Agoritsas T, et al. A living WHO guideline on drugs for covid-19. *BMJ*. 2020 Sep 4;370:m3379. [Full text \(https://www.bmj.com/content/370/bmj.m3379.long\)](https://www.bmj.com/content/370/bmj.m3379.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32887691?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32887691?tool=bestpractice.bmj.com)
764. Rochwerg B, Siemieniuk RA, Lamontagne R, et al. Update to living WHO guideline on drugs for covid-19. *BMJ*. 2021 Jul 6;374:n1703. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34230027?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34230027?tool=bestpractice.bmj.com)
765. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ*. 2020 May 22;369:m1966. [Full text \(https://www.bmj.com/content/369/bmj.m1966\)](https://www.bmj.com/content/369/bmj.m1966) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32444366?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32444366?tool=bestpractice.bmj.com)
766. CDC COVID-19 Response Team. Coronavirus disease 2019 in children: United States, February 12 - April 2, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Apr 10;69(14):422-6. [Full text \(https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e4.htm?s_cid=mm6914e4_w\)](https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e4.htm?s_cid=mm6914e4_w) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32271728?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32271728?tool=bestpractice.bmj.com)
767. Götzinger F, Santiago-García B, Noguera-Julián A, et al. COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study. *Lancet Child Adolesc Health*. 2020 Sep;4(9):653-61. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7316447\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7316447) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32593339?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32593339?tool=bestpractice.bmj.com)
768. Williams N, Radia T, Harman K, et al. COVID-19 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review of critically unwell children and the association with underlying comorbidities. *Eur J Pediatr*. 2021 Mar;180(3):689-97. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7483054\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7483054) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32914200?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32914200?tool=bestpractice.bmj.com)
769. Abate SM, Ahmed Ali S, Mantfardo B, et al. Rate of intensive care unit admission and outcomes among patients with coronavirus: a systematic review and meta-analysis. *PLoS*

One. 2020 Jul 10;15(7):e0235653. Full text (<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0235653>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32649661?tool=bestpractice.bmj.com>)

770. Armstrong RA, Kane AD, Kursumovic E, et al. Mortality in patients admitted to intensive care with COVID-19: an updated systematic review and meta-analysis of observational studies. *Anaesthesia*. 2021 Apr;76(4):537-48. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8013495>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33525063?tool=bestpractice.bmj.com>)
771. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in critically ill patients in the Seattle region: case series. *N Engl J Med*. 2020 May 21;382(21):2012-22. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7143164>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32227758?tool=bestpractice.bmj.com>)
772. Argenziano MG, Bruce SL, Slater CL, et al. Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: retrospective case series. *BMJ*. 2020 May 29;369:m1996. Full text (<https://www.bmj.com/content/369/bmj.m1996>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32471884?tool=bestpractice.bmj.com>)
773. Chang R, Elhusseiny KM, Yeh YC, et al. COVID-19 ICU and mechanical ventilation patient characteristics and outcomes: a systematic review and meta-analysis. *PLoS One*. 2021 Feb 11;16(2):e0246318. Full text (<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0246318>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33571301?tool=bestpractice.bmj.com>)
774. World Health Organization. Home care for patients with suspected or confirmed COVID-19 and management of their contacts: interim guidance. 2020 [internet publication]. Full text ([https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-\(ncov\)-infection-presenting-with-mild-symptoms-and-management-of-contacts](https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and-management-of-contacts))
775. Suter F, Consolaro E, Pedroni S, et al. A simple, home-therapy algorithm to prevent hospitalisation for COVID-19 patients: a retrospective observational matched-cohort study. *EClinicalMedicine*. 2021 Jun 9;100941. Full text ([https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00221-2/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00221-2/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34127959?tool=bestpractice.bmj.com>)
776. Centers for Disease Control and Prevention. Ending home isolation for persons with COVID-19 not in healthcare settings. 2021 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-in-home-patients.html>)
777. Public Health England. Guidance for stepdown of infection control precautions and discharging COVID-19 patients. 2020 [internet publication]. Full text (<https://www.gov.uk/government/publications/covid-19-guidance-for-stepdown-of-infection-control-precautions-within-hospitals-and-discharging-covid-19-patients-from-hospital-to-home-settings/guidance-for-stepdown-of-infection-control-precautions-and-discharging-covid-19-patients>)
778. European Medicines Agency. EMA gives advice on the use of non-steroidal anti-inflammatories for COVID-19. 2020 [internet publication]. Full text (<https://www.ema.europa.eu/en/news/ema-gives-advice-use-non-steroidal-anti-inflammatories-covid-19>)

779. US Food and Drug Administration. FDA advises patients on use of non-steroidal anti-inflammatory drugs (NSAIDs) for COVID-19. 2020 [internet publication]. [Full text \(https://www.fda.gov/drugs/drug-safety-and-availability/fda-advises-patients-use-non-steroidal-anti-inflammatory-drugs-nsaids-covid-19\)](https://www.fda.gov/drugs/drug-safety-and-availability/fda-advises-patients-use-non-steroidal-anti-inflammatory-drugs-nsaids-covid-19)
780. Little P. Non-steroidal anti-inflammatory drugs and covid-19. *BMJ*. 2020 Mar 27;368:m1185. [Full text \(https://www.bmj.com/content/368/bmj.m1185\)](https://www.bmj.com/content/368/bmj.m1185) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32220865?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32220865?tool=bestpractice.bmj.com)
781. Medicines and Healthcare products Regulatory Agency; Commission on Human Medicines. Commission on Human Medicines advice on ibuprofen and coronavirus (COVID-19). 2020 [internet publication]. [Full text \(https://www.gov.uk/government/news/commission-on-human-medicines-advice-on-ibuprofen-and-coronavirus-covid-19\)](https://www.gov.uk/government/news/commission-on-human-medicines-advice-on-ibuprofen-and-coronavirus-covid-19)
782. World Health Organization. The use of non-steroidal anti-inflammatory drugs (NSAIDs) in patients with COVID-19: scientific brief. 2020 [internet publication]. [Full text \(https://www.who.int/news-room/commentaries/detail/the-use-of-non-steroidal-anti-inflammatory-drugs-\(nsaids\)-in-patients-with-covid-19\)](https://www.who.int/news-room/commentaries/detail/the-use-of-non-steroidal-anti-inflammatory-drugs-(nsaids)-in-patients-with-covid-19)
783. National Institute for Health and Care Excellence. COVID-19 rapid evidence summary: acute use of non-steroidal anti-inflammatory drugs (NSAIDs) for people with or at risk of COVID-19. 2020 [internet publication]. [Full text \(https://www.nice.org.uk/advice/es23/chapter/Key-messages\)](https://www.nice.org.uk/advice/es23/chapter/Key-messages)
784. Wong AY, MacKenna B, Morton CE, et al. Use of non-steroidal anti-inflammatory drugs and risk of death from COVID-19: an OpenSAFELY cohort analysis based on two cohorts. *Ann Rheum Dis*. 2021 Jan 21 [Epub ahead of print]. [Full text \(https://ard.bmj.com/content/early/2021/01/20/annrheumdis-2020-219517.long\)](https://ard.bmj.com/content/early/2021/01/20/annrheumdis-2020-219517.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33478953?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33478953?tool=bestpractice.bmj.com)
785. Abuelgasim H, Albury C, Lee J. Effectiveness of honey for symptomatic relief in upper respiratory tract infections: a systematic review and meta-analysis. *BMJ Evid Based Med*. 2021 Apr;26(2):57-64. [Full text \(https://ebm.bmj.com/content/early/2020/07/28/bmjebm-2020-111336\)](https://ebm.bmj.com/content/early/2020/07/28/bmjebm-2020-111336) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32817011?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32817011?tool=bestpractice.bmj.com)
786. Whitcroft KL, Hummel T. Olfactory dysfunction in COVID-19: diagnosis and management. *JAMA*. 2020 Jun 23;323(24):2512-4. [Full text \(https://jamanetwork.com/journals/jama/fullarticle/2766523\)](https://jamanetwork.com/journals/jama/fullarticle/2766523) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32432682?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32432682?tool=bestpractice.bmj.com)
787. Centers for Disease Control and Prevention. Discontinuation of transmission-based precautions and disposition of patients with SARS-CoV-2 infection in healthcare settings. 2021 [internet publication]. [Full text \(https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html\)](https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html)
788. Pranata R, Henrina J, Lim MA, et al. Clinical frailty scale and mortality in COVID-19: a systematic review and dose-response meta-analysis. *Arch Gerontol Geriatr*. 2021 Mar-Apr;93:104324. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7832565\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7832565) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33352430?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33352430?tool=bestpractice.bmj.com)
789. Kastora S, Kounidas G, Perrott S, et al. Clinical frailty scale as a point of care prognostic indicator of mortality in COVID-19: a systematic review and meta-analysis. *EClinicalMedicine*. 2021

- Jun;36:100896. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8141355>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34036252?tool=bestpractice.bmj.com>)
790. Cosco TD, Best J, Davis D, et al. What is the relationship between validated frailty scores and mortality for adults with COVID-19 in acute hospital care? A systematic review. *Age Ageing*. 2021 May 5;50(3):608-16. Full text (<https://academic.oup.com/ageing/article/50/3/608/6097011>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33951151?tool=bestpractice.bmj.com>)
791. Centre for Evidence-Based Medicine; Allsop M, Ziegler L, Fu Y, et al. Is oxygen an effective treatment option to alleviate the symptoms of breathlessness for patients dying with COVID-19 and what are the potential harms? 2020 [internet publication]. Full text (<https://www.cebm.net/covid-19/is-oxygen-an-effective-treatment-option-to-alleviate-the-symptoms-of-breathlessness-for-patients-dying-with-covid-19-and-what-are-the-potential-harms>)
792. Alhazzani W, Evans L, Alshamsi F, et al. Surviving Sepsis Campaign guidelines on the management of adults with coronavirus disease 2019 (COVID-19) in the ICU: first update. *Crit Care Med*. 2021 Mar 1;49(3):e219-34. Full text (https://journals.lww.com/ccmjournal/Abstract/9000/Surviving_Sepsis_Campaign_Guidelines_on_the.95371.aspx) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33555780?tool=bestpractice.bmj.com>)
793. NHS England. Clinical guide for the optimal use of oxygen therapy during the coronavirus pandemic. 2020 [internet publication]. Full text (<https://www.nice.org.uk/Media/Default/About/COVID-19/Specialty-guides/specialty-guide-oxygen-therapy.pdf>)
794. Ponnappa Reddy M, Subramaniam A, Afroz A, et al. Prone positioning of nonintubated patients with coronavirus disease 2019: a systematic review and meta-analysis. *Crit Care Med*. 2021 Apr 30 [Epub ahead of print]. Full text (https://journals.lww.com/ccmjournal/Abstract/9000/Prone_Positioning_of_Nonintubated_Patients_With.95232.aspx) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33927120?tool=bestpractice.bmj.com>)
795. Chua EX, Zahir SMISM, Ng KT, et al. Effect of prone versus supine position in COVID-19 patients: a systematic review and meta-analysis. *J Clin Anesth*. 2021 Jun 22;74:110406. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8216875>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34182261?tool=bestpractice.bmj.com>)
796. Mojoli F, Mongodi S, Orlando A, et al. Our recommendations for acute management of COVID-19. *Crit Care*. 2020 May 8;24(1):207. Full text (<https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-02930-6>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32384909?tool=bestpractice.bmj.com>)
797. Centre for Evidence-Based Medicine; Jones L, Candy B, Roberts N, et al. How can healthcare workers adapt non-pharmacological treatment – whilst maintaining safety – when treating people with COVID-19 and delirium? 2020 [internet publication]. Full text (<https://www.cebm.net/covid-19/how-can-healthcare-workers-adapt-non-pharmacological-treatment-whilst-maintaining-safety-when-treating-people-with-covid-19-and-delirium>)
798. Public Health England. Mouth care for hospitalised patients with confirmed or suspected COVID-19. 2020 [internet publication]. Full text (<https://www.gov.uk/government/publications/covid-19-mouth->

care-for-patients-with-a-confirmed-or-suspected-case/mouth-care-for-hospitalised-patients-with-confirmed-or-suspected-covid-19)

799. Barnes GD, Burnett A, Allen A, et al. Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the Anticoagulation Forum. *J Thromb Thrombolysis*. 2020 Jul;50(1):72-81. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7241581\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7241581) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32440883?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32440883?tool=bestpractice.bmj.com)
800. Moores LK, Tritschler T, Brosnahan S, et al. Prevention, diagnosis, and treatment of VTE in patients with coronavirus disease 2019: CHEST guideline and expert panel report. *Chest*. 2020 Sep;158(3):1143-63. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7265858\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7265858) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32502594?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32502594?tool=bestpractice.bmj.com)
801. Pawlowski C, Venkatakrishnan AJ, Kirkup C, et al. Enoxaparin is associated with lower rates of mortality than unfractionated Heparin in hospitalized COVID-19 patients. *EClinicalMedicine*. 2021 Mar 9:100774. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7941023\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7941023) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33718845?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33718845?tool=bestpractice.bmj.com)
802. American Society Of Hematology. COVID-19 and VTE/anticoagulation: frequently asked questions. 2020 [internet publication]. [Full text \(https://www.hematology.org/covid-19/covid-19-and-vte-anticoagulation\)](https://www.hematology.org/covid-19/covid-19-and-vte-anticoagulation)
803. Lopes RD, de Barros E Silva PGM, Furtado RHM, et al. Therapeutic versus prophylactic anticoagulation for patients admitted to hospital with COVID-19 and elevated D-dimer concentration (ACTION): an open-label, multicentre, randomised, controlled trial. *Lancet*. 2021 Jun 4 [Epub ahead of print]. [Full text \(https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)01203-4/fulltext\)](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01203-4/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34097856?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34097856?tool=bestpractice.bmj.com)
804. Vaughn VM, Yost M, Abshire C, et al. Trends in venous thromboembolism anticoagulation in patients hospitalized with COVID-19. *JAMA Netw Open*. 2021 Jun 1;4(6):e2111788. [Full text \(https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780927\)](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780927) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34115129?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34115129?tool=bestpractice.bmj.com)
805. Flumignan RL, Tinôco JDS, Pascoal PI, et al. Prophylactic anticoagulants for people hospitalised with COVID-19. *Cochrane Database Syst Rev*. 2020 Oct 2;(10):CD013739. [Full text \(https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013739/full\)](https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013739/full) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33502773?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33502773?tool=bestpractice.bmj.com)
806. Moonla C, Sosothikul D, Chiasakul T, et al. Anticoagulation and in-hospital mortality from coronavirus disease 2019: a systematic review and meta-analysis. *Clin Appl Thromb Hemost*. 2021 Jan-Dec;27:10760296211008999. [Full text \(https://journals.sagepub.com/doi/10.1177/10760296211008999\)](https://journals.sagepub.com/doi/10.1177/10760296211008999) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33874753?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33874753?tool=bestpractice.bmj.com)
807. Langford BJ, So M, Raybardhan S, et al. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. *Clin Microbiol Infect*. 2021 Apr;27(4):520-31. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7785281\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7785281) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33418017?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33418017?tool=bestpractice.bmj.com)

808. WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group; Sterne JAC, Murthy S, Diaz JV, et al. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. JAMA. 2020 Oct 6;324(13):1330-41. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7489434\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7489434) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32876694?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32876694?tool=bestpractice.bmj.com)
809. RECOVERY Collaborative Group; Horby P, Lim WS, Emberson JR, et al. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med. 2021 Feb 25;384(8):693-704. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2021436\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2021436) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32678530?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32678530?tool=bestpractice.bmj.com)
810. Bhimraj A, Morgan RL, Hirsch Shumaker A, et al. Infectious Diseases Society of America guidelines on the treatment and management of patients with COVID-19. 2021 [internet publication]. [Full text \(https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management\)](https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management)
811. RECOVERY Collaborative Group. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. Lancet. 2021 May 1;397(10285):1637-45. [Full text \(https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00676-0/fulltext\)](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00676-0/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33933206?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33933206?tool=bestpractice.bmj.com)
812. REMAP-CAP Investigators; Gordon AC, Mouncey PR, Al-Beidh F, et al. Interleukin-6 receptor antagonists in critically ill patients with Covid-19. N Engl J Med. 2021 Apr 22;384(16):1491-502. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2100433\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2100433) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33631065?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33631065?tool=bestpractice.bmj.com)
813. US Food and Drug Administration. Coronavirus (COVID-19) update: FDA authorizes drug for treatment of COVID-19. 2021 [internet publication]. [Full text \(https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-drug-treatment-covid-19\)](https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-drug-treatment-covid-19)
814. Ghosn L, Chaimani A, Evrenoglou T, et al. Interleukin-6 blocking agents for treating COVID-19: a living systematic review. Cochrane Database Syst Rev. 2021 Mar 18;(3):CD013881. [Full text \(https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013881/full\)](https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013881/full) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33734435?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33734435?tool=bestpractice.bmj.com)
815. Siemieniuk RA, Bartoszko JJ, Ge L, et al. Drug treatments for covid-19: living systematic review and network meta-analysis. BMJ. 2020 Jul 30;370:m2980. [Full text \(https://www.bmj.com/content/370/bmj.m2980\)](https://www.bmj.com/content/370/bmj.m2980) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32732190?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32732190?tool=bestpractice.bmj.com)
816. Siemieniuk RA, Bartoszko JJ, Ge L, et al. Update to living systematic review on drug treatments for covid-19. BMJ. 2021 Mar 31;372:n858. [Full text \(https://www.bmj.com/content/372/bmj.n858.long\)](https://www.bmj.com/content/372/bmj.n858.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33789885?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33789885?tool=bestpractice.bmj.com)
817. WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group; Shankar-Hari M, Vale CL, Godolphin PJ, et al. Association between administration of IL-6 antagonists and mortality among patients hospitalized for COVID-19: a meta-analysis. JAMA. 2021 Jul 6 [Epub ahead of print]. [Full text \(https://jamanetwork.com/journals/jama/fullarticle/2781880\)](https://jamanetwork.com/journals/jama/fullarticle/2781880) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34228774?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34228774?tool=bestpractice.bmj.com)

818. Heath L, Carey M, Lowney AC, et al. Pharmacological strategies used to manage symptoms of patients dying of COVID-19: a rapid systematic review. *Palliat Med*. 2021 May 13 [Epub ahead of print]. [Full text \(https://journals.sagepub.com/doi/10.1177/02692163211013255\)](https://journals.sagepub.com/doi/10.1177/02692163211013255) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33983081?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33983081?tool=bestpractice.bmj.com)
819. Schünemann HJ, Khabsa J, Solo K, et al. Ventilation techniques and risk for transmission of coronavirus disease, including COVID-19. *Ann Intern Med*. 2020 Aug 4;173(3):204-16. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7281716\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7281716) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32442035?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32442035?tool=bestpractice.bmj.com)
820. Thomas R, Lotfi T, Morgano GP, et al. Update alert 2: ventilation techniques and risk for transmission of coronavirus disease, including COVID-19. *Ann Intern Med*. 2020 Dec 1;173(11):W152-3. [Full text \(https://www.acpjournals.org/doi/10.7326/L20-1211\)](https://www.acpjournals.org/doi/10.7326/L20-1211) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33045175?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33045175?tool=bestpractice.bmj.com)
821. Canelli R, Connor CW, Gonzalez M, et al. Barrier enclosure during endotracheal intubation. *N Engl J Med*. 2020 May 14;382(20):1957-8. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMc2007589\)](https://www.nejm.org/doi/full/10.1056/NEJMc2007589) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32243118?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32243118?tool=bestpractice.bmj.com)
822. Matava CT, Yu J, Denning S. Clear plastic drapes may be effective at limiting aerosolization and droplet spray during extubation: implications for COVID-19. *Can J Anaesth*. 2020 Jul;67(7):902-4. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7124129\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7124129) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32246431?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32246431?tool=bestpractice.bmj.com)
823. Lucchini A, Giani M, Isgrò S, et al. The "helmet bundle" in COVID-19 patients undergoing non invasive ventilation. *Intensive Crit Care Nurs*. 2020 Apr 2;102859. [Full text \(https://www.sciencedirect.com/science/article/pii/S0964339720300628?via%3Dihub\)](https://www.sciencedirect.com/science/article/pii/S0964339720300628?via%3Dihub) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32249028?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32249028?tool=bestpractice.bmj.com)
824. Adir Y, Segol O, Kompaniets D, et al. COVID-19: minimising risk to healthcare workers during aerosol producing respiratory therapy using an innovative constant flow canopy. *Eur Respir J*. 2020 May 21;55(5):2001017. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7173679\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7173679) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32312865?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32312865?tool=bestpractice.bmj.com)
825. McEnery T, Gough C, Costello RW. COVID-19: respiratory support outside the intensive care unit. *Lancet Respir Med*. 2020 Jun;8(6):538-9. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7146718\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7146718) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32278367?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32278367?tool=bestpractice.bmj.com)
826. NHS England. Guidance for the role and use of non-invasive respiratory support in adult patients with COVID19 (confirmed or suspected). 2020 [internet publication]. [Full text \(https://www.nice.org.uk/Media/Default/About/COVID-19/Specialty-guides/specialty-guide-NIV-respiratory-support-and-coronavirus.pdf\)](https://www.nice.org.uk/Media/Default/About/COVID-19/Specialty-guides/specialty-guide-NIV-respiratory-support-and-coronavirus.pdf)
827. Li J, Fink JB, Ehrmann S. High-flow nasal cannula for COVID-19 patients: low risk of bio-aerosol dispersion. *Eur Respir J*. 2020 May 14;55(5):2000892. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7163690\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7163690) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32299867?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32299867?tool=bestpractice.bmj.com)

828. Elsayed HH, Hassaballa AS, Ahmed TA, et al. Variation in outcome of invasive mechanical ventilation between different countries for patients with severe COVID-19: a systematic review and meta-analysis. PLoS One. 2021;16(6):e0252760. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8177443\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8177443) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34086779?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34086779?tool=bestpractice.bmj.com)
829. NHS England. Clinical guide for the management of critical care for adults with COVID-19 during the coronavirus pandemic. 2020 [internet publication]. [Full text \(https://www.nice.org.uk/Media/Default/About/COVID-19/Specialty-guides/Specialty-guide_Adult-critical-care.pdf\)](https://www.nice.org.uk/Media/Default/About/COVID-19/Specialty-guides/Specialty-guide_Adult-critical-care.pdf)
830. Gattinoni L, Coppola S, Cressoni M, et al. Covid-19 does not lead to a "typical" acute respiratory distress syndrome. Am J Respir Crit Care Med. 2020 May 15;201(10):1299-300. [Full text \(https://www.atsjournals.org/doi/pdf/10.1164/rccm.202003-0817LE\)](https://www.atsjournals.org/doi/pdf/10.1164/rccm.202003-0817LE) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32228035?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32228035?tool=bestpractice.bmj.com)
831. Gattinoni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or not? Crit Care. 2020 Apr 16;24(1):154. [Full text \(https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-02880-z\)](https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-02880-z) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32299472?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32299472?tool=bestpractice.bmj.com)
832. Gattinoni L, Chiumello D, Caironi P, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes? Intensive Care Med. 2020 Jun;46(6):1099-102. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7154064\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7154064) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32291463?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32291463?tool=bestpractice.bmj.com)
833. Marini JJ, Gattinoni L. Management of COVID-19 respiratory distress. JAMA. 2020 Jun 9;323(22):2329-30. [Full text \(https://jamanetwork.com/journals/jama/fullarticle/2765302\)](https://jamanetwork.com/journals/jama/fullarticle/2765302) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32329799?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32329799?tool=bestpractice.bmj.com)
834. Rello J, Storti E, Belliato M, et al. Clinical phenotypes of SARS-CoV-2: implications for clinicians and researchers. Eur Respir J. 2020 May 21;55(5):2001028. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7236837\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7236837) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32341111?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32341111?tool=bestpractice.bmj.com)
835. Tsolaki V, Siempos I, Magira E, et al. PEEP levels in COVID-19 pneumonia. Crit Care. 2020 Jun 6;24(1):303. [Full text \(https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-03049-4\)](https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-03049-4) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32505186?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32505186?tool=bestpractice.bmj.com)
836. Bos LD, Paulus F, Vlaar APJ, et al. Subphenotyping acute respiratory distress syndrome in patients with COVID-19: consequences for ventilator management. Ann Am Thorac Soc. 2020 Sep;17(9):1161-3. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7462326\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7462326) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32396457?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32396457?tool=bestpractice.bmj.com)
837. Jain A, Doyle DJ. Stages or phenotypes? A critical look at COVID-19 pathophysiology. Intensive Care Med. 2020 May 18;1-2. [Full text \(https://link.springer.com/article/10.1007%2Fs00134-020-06083-6\)](https://link.springer.com/article/10.1007%2Fs00134-020-06083-6) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32425310?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32425310?tool=bestpractice.bmj.com)
838. Rice TW, Janz DR. In defense of evidence-based medicine for the treatment of COVID-19 ARDS. Ann Am Thorac Soc. 2020 Jul;17(7):787-9. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7328187\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7328187) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32320268?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32320268?tool=bestpractice.bmj.com)

839. Dondorp AM, Hayat M, Aryal D, et al. Respiratory support in COVID-19 patients, with a focus on resource-limited settings. *Am J Trop Med Hyg.* 2020 Jun;102(6):1191-7. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7253105\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7253105) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32319424?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32319424?tool=bestpractice.bmj.com)
840. Carsetti A, Damia Paciarini A, Marini B, et al. Prolonged prone position ventilation for SARS-CoV-2 patients is feasible and effective. *Crit Care.* 2020 May 15;24(1):225. [Full text \(https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-02956-w\)](https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-02956-w) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32414420?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32414420?tool=bestpractice.bmj.com)
841. Ramanathan K, Antognini D, Combes A, et al. Planning and provision of ECMO services for severe ARDS during the COVID-19 pandemic and other outbreaks of emerging infectious diseases. *Lancet Respir Med.* 2020 May;8(5):518-26. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102637\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102637) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32203711?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32203711?tool=bestpractice.bmj.com)
842. NHS England. Clinical guide for extra corporeal membrane oxygenation (ECMO) for respiratory failure in adults during the coronavirus pandemic. 2020 [internet publication]. [Full text \(https://www.nice.org.uk/Media/Default/About/COVID-19/Specialty-guides/Speciality-Guide-Extra-Corporeal-Membrane-Oxygenation-ECMO-Adult.pdf\)](https://www.nice.org.uk/Media/Default/About/COVID-19/Specialty-guides/Speciality-Guide-Extra-Corporeal-Membrane-Oxygenation-ECMO-Adult.pdf)
843. Ramanathan K, Shekar K, Ling RR, et al. Extracorporeal membrane oxygenation for COVID-19: a systematic review and meta-analysis. *Crit Care.* 2021 Jun 14;25(1):211. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8201440\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8201440) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34127027?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34127027?tool=bestpractice.bmj.com)
844. Mustafa AK, Alexander PJ, Joshi DJ, et al. Extracorporeal membrane oxygenation for patients with COVID-19 in severe respiratory failure. *JAMA Surg.* 2020 Aug 11;155(10):990-2. [Full text \(https://jamanetwork.com/journals/jamasurgery/fullarticle/2769429\)](https://jamanetwork.com/journals/jamasurgery/fullarticle/2769429) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32780089?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32780089?tool=bestpractice.bmj.com)
845. Medicines and Healthcare products Regulatory Agency. Therapeutic anticoagulation (heparin) in the management of severe COVID-19 (SARS-CoV-2 positive) patients. 2020 [internet publication]. [Full text \(https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103129\)](https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103129)
846. INSPIRATION Investigators; Sadeghipour P, Talasaz AH, Rashidi F, et al. Effect of intermediate-dose vs standard-dose prophylactic anticoagulation on thrombotic events, extracorporeal membrane oxygenation treatment, or mortality among patients with COVID-19 admitted to the intensive care unit: the INSPIRATION randomized clinical trial. *JAMA.* 2021 Apr 27;325(16):1620-30. [Full text \(https://jamanetwork.com/journals/jama/fullarticle/2777829\)](https://jamanetwork.com/journals/jama/fullarticle/2777829) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33734299?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33734299?tool=bestpractice.bmj.com)
847. Sarfraz A, Sarfraz Z, Razzack AA, et al. Venous thromboembolism, corticosteroids and COVID-19: a systematic review and meta-analysis. *Clin Appl Thromb Hemost.* 2021 Jan-Dec;27:1076029621993573. [Full text \(https://journals.sagepub.com/doi/10.1177/1076029621993573\)](https://journals.sagepub.com/doi/10.1177/1076029621993573) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33571009?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33571009?tool=bestpractice.bmj.com)
848. Chen L, Jiang H, Zhao Y. Pregnancy with Covid-19: management considerations for care of severe and critically ill cases. *Am J Reprod Immunol.* 2020 Jul 4:e13299. [Full text \(https://](https://)

onlinelibrary.wiley.com/doi/10.1111/aji.13299) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32623810?tool=bestpractice.bmj.com>)

849. Campbell KH, Tornatore JM, Lawrence KE, et al. Prevalence of SARS-CoV-2 among patients admitted for childbirth in Southern Connecticut. *JAMA*. 2020 Jun 23;323(24):2520-2. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2766650>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32453390?tool=bestpractice.bmj.com>)
850. Fassett MJ, Lurvey LD, Yasumura L, et al. Universal SARS-Cov-2 screening in women admitted for delivery in a large managed care organization. *Am J Perinatol*. 2020 Sep;37(11):1110-4. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7516390>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32620022?tool=bestpractice.bmj.com>)
851. Bianco A, Buckley AB, Overbey J, et al. Testing of patients and support persons for coronavirus disease 2019 (COVID-19) infection before scheduled deliveries. *Obstet Gynecol*. 2020 Aug;136(2):283-7. Full text (https://journals.lww.com/greenjournal/Abstract/9000/Testing_of_Patients_and_Support_Persons_for.97342.aspx) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32433448?tool=bestpractice.bmj.com>)
852. Sutton D, Fuchs K, D'Alton M, et al. Universal screening for SARS-CoV-2 in women admitted for delivery. *N Engl J Med*. 2020 May 28;382(22):2163-4. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMc2009316>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32283004?tool=bestpractice.bmj.com>)
853. American College of Obstetricians and Gynecologists. Novel coronavirus 2019 (COVID-19). 2020 [internet publication]. Full text (<https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/03/novel-coronavirus-2019>)
854. Favre G, Pomar L, Qi X, et al. Guidelines for pregnant women with suspected SARS-CoV-2 infection. *Lancet Infect Dis*. 2020 Jun;20(6):652-3. Full text ([https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30157-2/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30157-2/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32142639?tool=bestpractice.bmj.com>)
855. Chen D, Yang H, Cao Y, et al. Expert consensus for managing pregnant women and neonates born to mothers with suspected or confirmed novel coronavirus (COVID-19) infection. *Int J Gynaecol Obstet*. 2020 May;149(2):130-6. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32196655?tool=bestpractice.bmj.com>)
856. Royal College of Obstetricians and Gynaecologists. Coronavirus (COVID-19) infection in pregnancy: information for healthcare professionals. 2021 [internet publication]. Full text (<https://www.rcog.org.uk/globalassets/documents/guidelines/2020-10-14-coronavirus-covid-19-infection-in-pregnancy-v12.pdf>)
857. American Academy of Pediatrics. Management of infants born to mothers with suspected or confirmed COVID-19. 2021 [internet publication]. Full text (<https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/faqs-management-of-infants-born-to-covid-19-mothers>)
858. Dumitriu D, Emeruwa UN, Hanft E, et al. Outcomes of neonates born to mothers with severe acute respiratory syndrome coronavirus 2 infection at a large medical center in New York

- City. JAMA Pediatr. 2021 Feb 1;175(2):157-67. Full text (<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2771636>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33044493?tool=bestpractice.bmj.com>)
859. World Health Organization. Breastfeeding and COVID-19: scientific brief. 2020 [internet publication]. Full text (<https://www.who.int/publications/i/item/10665332639>)
860. Ronchi A, Pietrasanta C, Zavattoni M, et al. Evaluation of rooming-in practice for neonates born to mothers with severe acute respiratory syndrome coronavirus 2 infection in Italy. JAMA Pediatr. 2021 Mar 1;175(3):260-6. Full text (<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2773311>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33284345?tool=bestpractice.bmj.com>)
861. Centers for Disease Control and Prevention. Evaluation and management considerations for neonates at risk for COVID-19. 2020 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/caring-for-newborns.html>)
862. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): care for breastfeeding women. 2020 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/care-for-breastfeeding-women.html>)
863. World Health Organization. Clinical management of COVID-19: interim guidance. 2020 [internet publication]. Full text (<https://www.who.int/publications-detail/clinical-management-of-covid-19>)
864. European Medicines Agency. Veklury. 2020 [internet publication]. Full text (<https://www.ema.europa.eu/en/medicines/human/EPAR/veklury>)
865. US Food and Drug Administration. FDA approves first treatment for COVID-19. 2020 [internet publication]. Full text (<https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-covid-19>)
866. WHO Solidarity Trial Consortium; Pan H, Peto R, Henao-Restrepo AM, et al. Repurposed antiviral drugs for Covid-19: interim WHO Solidarity trial results. N Engl J Med. 2021 Feb 11;384(6):497-511. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7727327>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33264556?tool=bestpractice.bmj.com>)
867. US Food and Drug Administration. Coronavirus (COVID-19) update: FDA authorizes monoclonal antibodies for treatment of COVID-19. 2021 [internet publication]. Full text (<https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-monoclonal-antibodies-treatment-covid-19-0>)
868. European Medicines Agency. EMA issues advice on use of REGN-COV2 antibody combination (casirivimab/imdevimab). 2021 [internet publication]. Full text (<https://www.ema.europa.eu/en/news/ema-issues-advice-use-regn-cov2-antibody-combination-casirivimab-imdevimab>)
869. RECOVERY Collaborative Group; Horby PW, Mafham M, Peto L, et al; medRxiv. Casirivimab and imdevimab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. 2021 [internet publication]. Full text (<https://www.medrxiv.org/content/10.1101/2021.06.15.21258542v1>)

870. Weinreich DM, Sivapalasingam S, Norton T, et al. REGN-COV2, a neutralizing antibody cocktail, in outpatients with Covid-19. *N Engl J Med*. 2021 Jan 21;384(3):238-51. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2035002\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2035002) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33332778?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33332778?tool=bestpractice.bmj.com)
871. Regeneron Pharmaceuticals, Inc. REGN-COV2 independent data monitoring committee recommends holding enrollment in hospitalized patients with high oxygen requirements and continuing enrollment in patients with low or no oxygen requirements. 2020 [internet publication]. [Full text \(https://investor.regeneron.com/news-releases/news-release-details/regn-cov2-independent-data-monitoring-committee-recommends\)](https://investor.regeneron.com/news-releases/news-release-details/regn-cov2-independent-data-monitoring-committee-recommends)
872. US Food and Drug Administration. Coronavirus (COVID-19) update: FDA authorizes additional monoclonal antibody for treatment of COVID-19. 2021 [internet publication]. [Full text \(https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-monoclonal-antibody-treatment-covid-19\)](https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-monoclonal-antibody-treatment-covid-19)
873. European Medicines Agency. EMA issues advice on use of sotrovimab (VIR-7831) for treating COVID-19. 2021 [internet publication]. [Full text \(https://www.ema.europa.eu/en/news/ema-issues-advice-use-sotrovimab-vir-7831-treating-covid-19\)](https://www.ema.europa.eu/en/news/ema-issues-advice-use-sotrovimab-vir-7831-treating-covid-19)
874. European Medicines Agency. EMA issues advice on use of antibody combination (bamlanivimab / etesevimab). 2021 [internet publication]. [Full text \(https://www.ema.europa.eu/en/news/ema-issues-advice-use-antibody-combination-bamlanivimab-etesevimab\)](https://www.ema.europa.eu/en/news/ema-issues-advice-use-antibody-combination-bamlanivimab-etesevimab)
875. Gottlieb RL, Nirula A, Chen P, et al. Effect of bamlanivimab as monotherapy or in combination with etesevimab on viral load in patients with mild to moderate COVID-19: a randomized clinical trial. *JAMA*. 2021 Feb 16;325(7):632-44. [Full text \(https://jamanetwork.com/journals/jama/fullarticle/2775647\)](https://jamanetwork.com/journals/jama/fullarticle/2775647) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33475701?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33475701?tool=bestpractice.bmj.com)
876. Cohen MS, Nirula A, Mulligan MJ, et al. Effect of bamlanivimab vs placebo on incidence of COVID-19 among residents and staff of skilled nursing and assisted living facilities: a randomized clinical trial. *JAMA*. 2021 Jun 3 [Epub ahead of print]. [Full text \(https://jamanetwork.com/journals/jama/fullarticle/2780870\)](https://jamanetwork.com/journals/jama/fullarticle/2780870) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34081073?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34081073?tool=bestpractice.bmj.com)
877. Dougan M, Nirula A, Azizad M, et al. Bamlanivimab plus etesevimab in mild or moderate Covid-19. *N Engl J Med*. 2021 Jul 14 [Epub ahead of print]. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2102685\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2102685) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34260849?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34260849?tool=bestpractice.bmj.com)
878. Jensen B, Luebke N, Feldt T, et al. Emergence of the E484K mutation in SARS-COV-2-infected immunocompromised patients treated with bamlanivimab in Germany. *Lancet Reg Health Eur*. 2021 Sep;8:100164. [Full text \(https://www.thelancet.com/journals/lanep/article/PIIS2666-7762\(21\)00141-1/fulltext\)](https://www.thelancet.com/journals/lanep/article/PIIS2666-7762(21)00141-1/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34278371?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34278371?tool=bestpractice.bmj.com)
879. US Food and Drug Administration. FDA in brief: FDA updates emergency use authorization for COVID-19 convalescent plasma to reflect new data. 2021 [internet publication]. [Full text \(https://www.fda.gov/news-events/press-announcements/fda-in-brief-fda-updates-emergency-use-authorization-covid-19-convalescent-plasma-reflect-new-data\)](https://www.fda.gov/news-events/press-announcements/fda-in-brief-fda-updates-emergency-use-authorization-covid-19-convalescent-plasma-reflect-new-data)

www.fda.gov/news-events/fda-brief/fda-brief-fda-updates-emergency-use-authorization-covid-19-convalescent-plasma-reflect-new-data)

880. Medicines and Healthcare products Regulatory Agency. Convalescent plasma in the management of hospitalised patients with COVID-19. 2021 [internet publication]. [Full text \(https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103152\)](https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103152)
881. The RECOVERY Collaborative Group; Horby PW, Estcourt L, Peto L, et al; medRxiv. Convalescent plasma in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. 2021 [internet publication]. [Full text \(https://www.medrxiv.org/content/10.1101/2021.03.09.21252736v1\)](https://www.medrxiv.org/content/10.1101/2021.03.09.21252736v1)
882. Joyner MJ, Senefeld JW, Klassen SA, et al; medRxiv. Effect of convalescent plasma on mortality among hospitalized patients with COVID-19: initial three-month experience. 2020 [internet publication]. [Full text \(https://www.medrxiv.org/content/10.1101/2020.08.12.20169359v1\)](https://www.medrxiv.org/content/10.1101/2020.08.12.20169359v1)
883. Janiaud P, Axfors C, Schmitt AM, et al. Association of convalescent plasma treatment with clinical outcomes in patients with COVID-19: a systematic review and meta-analysis. *JAMA*. 2021 Mar 23;325(12):1185-95. [Full text \(https://jamanetwork.com/journals/jama/fullarticle/2777060\)](https://jamanetwork.com/journals/jama/fullarticle/2777060) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33635310?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33635310?tool=bestpractice.bmj.com)
884. Gupta T, Kannan S, Kalra B, et al. Systematic review and meta-analysis of randomised controlled trials testing the safety and efficacy of convalescent plasma in the treatment of coronavirus disease 2019 (COVID-19): evidence-base for practise and implications for research. *Transfus Med*. 2021 Jun 29 [Epub ahead of print]. [Full text \(https://onlinelibrary.wiley.com/doi/10.1111/tme.12803\)](https://onlinelibrary.wiley.com/doi/10.1111/tme.12803) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34189780?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34189780?tool=bestpractice.bmj.com)
885. Klassen SA, Senefeld JW, Johnson PW, et al. The effect of convalescent plasma therapy on mortality among patients with COVID-19: systematic review and meta-analysis. *Mayo Clin Proc*. 2021 May;96(5):1262-75. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7888247\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7888247) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33958057?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33958057?tool=bestpractice.bmj.com)
886. Wardhani SO, Fajar JK, Wulandari L, et al. Association between convalescent plasma and the risk of mortality among patients with COVID-19: a meta-analysis. *F1000Res*. 2021 Feb 3;10:64. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8182694\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8182694) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34136130?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34136130?tool=bestpractice.bmj.com)
887. Piechotta V, Iannizzi C, Chai KL, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review. *Cochrane Database Syst Rev*. 2021 May 20;5(5):CD013600. [Full text \(https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013600.pub4/full\)](https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013600.pub4/full) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34013969?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34013969?tool=bestpractice.bmj.com)
888. RECOVERY Collaborative Group. Convalescent plasma in patients admitted to hospital with COVID-19 (RECOVERY): a randomised controlled, open-label, platform trial. *Lancet*. 2021 May 14 [Epub ahead of print]. [Full text \(https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00897-7/fulltext\)](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00897-7/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34000257?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34000257?tool=bestpractice.bmj.com)

889. Libster R, Pérez Marc G, Wappner D, et al. Early high-titer plasma therapy to prevent severe Covid-19 in older adults. *N Engl J Med*. 2021 Feb 18;384(7):610-18. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2033700\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2033700) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33406353?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33406353?tool=bestpractice.bmj.com)
890. National Institutes of Health. NIH halts trial of COVID-19 convalescent plasma in emergency department patients with mild symptoms. 2021 [internet publication]. [Full text \(https://www.nih.gov/news-events/news-releases/nih-halts-trial-covid-19-convalescent-plasma-emergency-department-patients-mild-symptoms\)](https://www.nih.gov/news-events/news-releases/nih-halts-trial-covid-19-convalescent-plasma-emergency-department-patients-mild-symptoms)
891. Thompson MA, Henderson JP, Shah PK, et al. Association of convalescent plasma therapy with survival in patients with hematologic cancers and COVID-19. *JAMA Oncol*. 2021 Jun 17 [Epub ahead of print]. [Full text \(https://jamanetwork.com/journals/jamaoncology/fullarticle/2780916\)](https://jamanetwork.com/journals/jamaoncology/fullarticle/2780916) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34137799?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34137799?tool=bestpractice.bmj.com)
892. US Food and Drug Administration. Coronavirus (COVID-19) update: FDA authorizes drug combination for treatment of COVID-19. 2020 [internet publication]. [Full text \(https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-drug-combination-treatment-covid-19\)](https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-drug-combination-treatment-covid-19)
893. European Medicines Agency. EMA starts evaluating use of Olumiant in hospitalised COVID-19 patients requiring supplemental oxygen. 2021 [internet publication]. [Full text \(https://www.ema.europa.eu/en/news/ema-starts-evaluating-use-olumiant-hospitalised-covid-19-patients-requiring-supplemental-oxygen\)](https://www.ema.europa.eu/en/news/ema-starts-evaluating-use-olumiant-hospitalised-covid-19-patients-requiring-supplemental-oxygen)
894. Kalil AC, Patterson TF, Mehta AK, et al. Baricitinib plus remdesivir for hospitalized adults with Covid-19. *N Engl J Med*. 2021 Mar 4;384(9):795-807. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2031994\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2031994) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33306283?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33306283?tool=bestpractice.bmj.com)
895. Wijaya I, Andhika R, Huang I, et al. The use of Janus Kinase inhibitors in hospitalized patients with COVID-19: systematic review and meta-analysis. *Clin Epidemiol Glob Health*. 2021 Jul-Sep;11:100755. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8088409\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8088409) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33969237?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33969237?tool=bestpractice.bmj.com)
896. Chen CX, Wang JJ, Li H, et al. JAK-inhibitors for coronavirus disease-2019 (COVID-19): a meta-analysis. *Leukemia*. 2021 May 14 [Epub ahead of print]. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8119232\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8119232) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33990684?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33990684?tool=bestpractice.bmj.com)
897. Caly L, Druce JD, Catton MG, et al. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. *Antiviral Res*. 2020 Jun;178:104787. [Full text \(https://www.sciencedirect.com/science/article/pii/S0166354220302011\)](https://www.sciencedirect.com/science/article/pii/S0166354220302011) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32251768?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32251768?tool=bestpractice.bmj.com)
898. European Medicines Agency. EMA advises against use of ivermectin for the prevention or treatment of COVID-19 outside randomised clinical trials. 2021 [internet publication]. [Full text \(https://www.ema.europa.eu/en/news/ema-advises-against-use-ivermectin-prevention-treatment-covid-19-outside-randomised-clinical-trials\)](https://www.ema.europa.eu/en/news/ema-advises-against-use-ivermectin-prevention-treatment-covid-19-outside-randomised-clinical-trials)

- www.ema.europa.eu/en/news/ema-advises-against-use-ivermectin-prevention-treatment-covid-19-outside-randomised-clinical-trials)
899. Indian Council of Medical Research. Technical documents and advisory. 2021 [internet publication]. Full text (<https://www.icmr.gov.in/ctechdocad.html>)
 900. Kory P, Meduri GU, Varon J, et al. Review of the emerging evidence demonstrating the efficacy of ivermectin in the prophylaxis and treatment of COVID-19. 2021;28(3):e299-318. Full text (https://journals.lww.com/americantherapeutics/Fulltext/2021/00000/Review_of_the_Emerging_Evidence_Demonstrating_the.4.aspx)
 901. Zein AFMZ, Sulistiyana CS, Raffaello WM, et al. Ivermectin and mortality in patients with COVID-19: a systematic review, meta-analysis, and meta-regression of randomized controlled trials. Diabetes Metab Syndr. 2021 Jun 27;15(4):102186. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8236126>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34237554?tool=bestpractice.bmj.com>)
 902. Bryant A, Lawrie TA, Dowswell T, et al. Ivermectin for prevention and treatment of COVID-19 infection: a systematic review, meta-analysis, and trial sequential analysis to inform clinical guidelines. Am J Ther. 2021 Jun 17 [Epub ahead of print]. Full text (https://journals.lww.com/americantherapeutics/Abstract/9000/Ivermectin_for_Prevention_and_Treatment_of.98040.aspx) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34145166?tool=bestpractice.bmj.com>)
 903. Kow CS, Merchant HA, Mustafa ZU, et al. The association between the use of ivermectin and mortality in patients with COVID-19: a meta-analysis. Pharmacol Rep. 2021 Mar 29 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8005369>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33779964?tool=bestpractice.bmj.com>)
 904. Padhy BM, Mohanty RR, Das S, et al. Therapeutic potential of ivermectin as add on treatment in COVID 19: a systematic review and meta-analysis. J Pharm Pharm Sci. 2020;23:462-9. Full text (<https://journals.library.ualberta.ca/jpps/index.php/JPPS/article/view/31457/21594>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33227231?tool=bestpractice.bmj.com>)
 905. Bartoszko JJ, Siemieniuk RAC, Kum E, et al. Prophylaxis against covid-19: living systematic review and network meta-analysis. BMJ. 2021 Apr 26;373:n949. Full text (<https://www.bmj.com/content/373/bmj.n949>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33903131?tool=bestpractice.bmj.com>)
 906. Mahmud R, Rahman MM, Alam I, et al. Ivermectin in combination with doxycycline for treating COVID-19 symptoms: a randomized trial. J Int Med Res. 2021 May;49(5):3000605211013550. Full text (<https://journals.sagepub.com/doi/10.1177/03000605211013550>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33983065?tool=bestpractice.bmj.com>)
 907. PRINCIPLE Trial Collaborative Group. Ivermectin to be investigated in adults aged 18+ as a possible treatment for COVID-19 in the PRINCIPLE trial. 2021 [internet publication]. Full text (<https://www.principletrial.org/news/ivermectin-to-be-investigated-as-a-possible-treatment-for-covid-19-in-oxford2019s-principle-trial>)
 908. European Medicines Agency. EMA starts evaluating the use of Kineret in adult COVID-19 patients at increased risk of severe respiratory failure. 2021 [internet publication]. Full text (<https://www.ema.europa.eu/en/news/ema-starts-evaluating-the-use-of-kineret-in-adult-covid-19-patients-at-increased-risk-of-severe-respiratory-failure>)

www.ema.europa.eu/en/news/ema-starts-evaluating-use-kineret-adult-covid-19-patients-increased-risk-severe-respiratory-failure)

909. National Institute for Health and Care Excellence. COVID 19 rapid evidence summary: anakinra for COVID-19 associated secondary haemophagocytic lymphohistiocytosis. 2020 [internet publication]. Full text (<https://www.nice.org.uk/advice/es26/chapter/Key-messages>)
910. Barkas F, Ntekouan SF, Kosmidou M, et al. Anakinra in hospitalized non-intubated patients with coronavirus disease 2019: a systematic review and meta-analysis. Rheumatology (Oxford). 2021 May 17 [Epub ahead of print]. Full text (<https://academic.oup.com/rheumatology/advance-article/doi/10.1093/rheumatology/keab447/6276997>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33999135?tool=bestpractice.bmj.com>)
911. Somagutta MKR, Lourdes Pormento MK, Hamid P, et al. The safety and efficacy of anakinra, an interleukin-1 antagonist in severe cases of COVID-19: a systematic review and meta-analysis. Infect Chemother. 2021 Jun;53(2):221-37. Full text (<https://www.icjournal.org/DOLx.php?id=10.3947/ic.2021.0016>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34216117?tool=bestpractice.bmj.com>)
912. European Medicines Agency. EMA issues advice on use of regdanvimab for treating COVID-19. 2021 [internet publication]. Full text (<https://www.ema.europa.eu/en/news/ema-issues-advice-use-regdanvimab-treating-covid-19>)
913. Celltrion Healthcare. Celltrion's COVID-19 treatment candidate receives Korean MFDS conditional marketing authorisation. 2021 [internet publication]. Full text (https://www.celltrionhealthcare.com/en-us/board/newsdetail?modify_key=442)
914. Celltrion Healthcare. Celltrion announces positive top-line results from global phase III trial of regdanvimab (CT-P59), an anti-COVID-19 monoclonal antibody treatment. 2021 [internet publication]. Full text (https://www.celltrionhealthcare.com/en-us/board/newsdetail?modify_key=498)
915. Celltrion Healthcare. Celltrion develops tailored neutralising antibody cocktail treatment with CT-P59 to tackle COVID-19 variant spread using its antibody development plat. 2021 [internet publication]. Full text (https://www.celltrionhealthcare.com/en-us/board/newsdetail?modify_key=446)
916. Xiang HR, Cheng X, Li Y, et al. Efficacy of IVIG (intravenous immunoglobulin) for corona virus disease 2019 (COVID-19): a meta-analysis. Int Immunopharmacol. 2021 Jul;96:107732. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8084608>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34162133?tool=bestpractice.bmj.com>)
917. ClinicalTrials.gov. Mesenchymal stem cell treatment for pneumonia patients infected with 2019 novel coronavirus. 2020 [internet publication]. Full text (<https://clinicaltrials.gov/ct2/show/NCT04252118>)
918. Mesoblast Limited. Mesoblast update on COVID-19 ARDS trial. 2020 [internet publication]. Full text (<http://investorsmedia.mesoblast.com/static-files/bc0ce366-1c50-46ce-a9d4-d06b7ce403e5>)
919. Monk PD, Marsden RJ, Tear VJ, et al. Safety and efficacy of inhaled nebulised interferon beta-1a (SNG001) for treatment of SARS-CoV-2 infection: a randomised, double-blind, placebo-controlled, phase 2 trial. Lancet Respir Med. 2021 Feb;9(2):196-206. Full text (<https://www.thelancet.com/>)

- journals/lanres/article/PIIS2213-2600(20)30511-7/fulltext) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33189161?tool=bestpractice.bmj.com>)
920. ClinicalTrials.gov. Interferon lambda for immediate antiviral therapy at diagnosis in COVID-19 (ILIAD). 2020 [internet publication]. Full text (<https://clinicaltrials.gov/ct2/show/NCT04354259>)
921. Eiger BioPharmaceuticals. Eiger BioPharmaceuticals announces positive results of investigator sponsored randomized controlled trial at University of Toronto with peginterferon lambda in outpatients with mild to moderate COVID-19. 2020 [internet publication]. Full text (<https://ir.eigerbio.com/news-releases/news-release-details/eiger-biopharmaceuticals-announces-positive-results-investigator>)
922. Grant WB, Lahore H, McDonnell SL, et al. Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. *Nutrients*. 2020 Apr 2;12(4). Full text (<https://www.mdpi.com/2072-6643/12/4/988/htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32252338?tool=bestpractice.bmj.com>)
923. McCartney DM, Byrne DG. Optimisation of vitamin D status for enhanced immuno-protection against Covid-19. *Ir Med J*. 2020 Apr 3;113(4):58. Full text (<http://imj.ie/optimisation-of-vitamin-d-status-for-enhanced-immuno-protection-against-covid-19>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32268051?tool=bestpractice.bmj.com>)
924. Jakovac H. COVID-19 and vitamin D: is there a link and an opportunity for intervention? *Am J Physiol Endocrinol Metab*. 2020 May 1;318(5):E589. Full text (<https://journals.physiology.org/doi/full/10.1152/ajpendo.00138.2020>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32297519?tool=bestpractice.bmj.com>)
925. Jolliffe DA, Camargo CA, Sluyter JD, et al. Vitamin D supplementation to prevent acute respiratory infections: systematic review and meta-analysis of aggregate data from randomised controlled trials. *medRxiv*. 2020 Nov 25 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7709175>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33269357?tool=bestpractice.bmj.com>)
926. National Institute for Health and Care Excellence. COVID-19 rapid guideline: vitamin D. Dec 2020 [internet publication]. Full text (<https://www.nice.org.uk/guidance/ng187>)
927. Stroehlein JK, Wallqvist J, Iannizzi C, et al. Vitamin D supplementation for the treatment of COVID-19: a living systematic review. *Cochrane Database Syst Rev*. 2021 May 24;(5):CD015043. Full text (<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD015043/full>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34029377?tool=bestpractice.bmj.com>)
928. Shah K, Saxena D, Mavalankar D. Vitamin D supplementation, COVID-19 & disease severity: a meta-analysis. *QJM*. 2021 Jan 24 [Epub ahead of print]. Full text (<https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcab009/6118232>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33486522?tool=bestpractice.bmj.com>)
929. Pal R, Banerjee M, Bhadada SK, et al. Vitamin D supplementation and clinical outcomes in COVID-19: a systematic review and meta-analysis. *J Endocrinol Invest*. 2021 Jun 24 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8223190>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34165766?tool=bestpractice.bmj.com>)

930. Castillo ME, Entrenas Costa LM, Vaquero Barrios JM, et al. Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: a pilot randomized clinical study. *J Steroid Biochem Mol Biol*. 2020 Aug 29;105751. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456194\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456194) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32871238?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32871238?tool=bestpractice.bmj.com)
931. Boretti A, Banik BK. Intravenous vitamin C for reduction of cytokines storm in acute respiratory distress syndrome. *PharmaNutrition*. 2020 Apr 21;100190. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7172861\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7172861) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32322486?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32322486?tool=bestpractice.bmj.com)
932. ClinicalTrials.gov. Vitamin C infusion for the treatment of severe 2019-nCoV infected pneumonia. 2020 [internet publication]. [Full text \(https://clinicaltrials.gov/ct2/show/NCT04264533\)](https://clinicaltrials.gov/ct2/show/NCT04264533)
933. Baladia E, Pizarro AB, Ortiz-Muñoz L, et al. Vitamin C for COVID-19: a living systematic review. *Medwave*. 2020 Jul 28;20(6):e7978. [Full text \(https://www.medwave.cl/link.cgi/English/Original/SystReviews/7978.act\)](https://www.medwave.cl/link.cgi/English/Original/SystReviews/7978.act) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32759894?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32759894?tool=bestpractice.bmj.com)
934. Zhang J, Rao X, Li Y; Research Square. Pilot trial of high-dose vitamin C in critically ill COVID-19 patients. 2020 [internet publication]. [Full text \(https://www.researchsquare.com/article/rs-52778/v2\)](https://www.researchsquare.com/article/rs-52778/v2)
935. Reyes AZ, Hu KA, Teperman J, et al. Anti-inflammatory therapy for COVID-19 infection: the case for colchicine. *Ann Rheum Dis*. 2020 Dec 8 [Epub ahead of print]. [Full text \(https://ard.bmj.com/content/early/2020/12/08/annrheumdis-2020-219174\)](https://ard.bmj.com/content/early/2020/12/08/annrheumdis-2020-219174) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33293273?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33293273?tool=bestpractice.bmj.com)
936. Medicines and Healthcare products Regulatory Agency. Colchicine in the management of COVID-19 (SARS-CoV 2) positive patients: trial use only. 2021 [internet publication]. [Full text \(https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103142\)](https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103142)
937. Hariyanto TI, Halim DA, Jodhinata C, et al. Colchicine treatment can improve outcomes of coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *Clin Exp Pharmacol Physiol*. 2021 Jun;48(6):823-30. [Full text \(https://onlinelibrary.wiley.com/doi/10.1111/1440-1681.13488\)](https://onlinelibrary.wiley.com/doi/10.1111/1440-1681.13488) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33719081?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33719081?tool=bestpractice.bmj.com)
938. Nawangsih EN, Kusmala YY, Rakhmat II, et al. Colchicine and mortality in patients with coronavirus disease 2019 (COVID-19) pneumonia: a systematic review, meta-analysis, and meta-regression. *Int Immunopharmacol*. 2021 Jul;96:107723. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8075849\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8075849) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34162130?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34162130?tool=bestpractice.bmj.com)
939. Tardif JC, Bouabdallaoui N, L'Allier PL, et al. Colchicine for community-treated patients with COVID-19 (COLCORONA): a phase 3, randomised, double-blinded, adaptive, placebo-controlled, multicentre trial. *Lancet Respir Med*. 2021 May 27 [Epub ahead of print]. [Full text \(https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00222-8/fulltext\)](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00222-8/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34051877?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34051877?tool=bestpractice.bmj.com)
940. Nuffield Department of Population Health. RECOVERY trial closes recruitment to colchicine treatment for patients hospitalised with COVID-19. 2021 [internet publication]. [Full text \(https://](https://)

www.recoverytrial.net/news/recovery-trial-closes-recruitment-to-colchicine-treatment-for-patients-hospitalised-with-covid-19

941. Centre for Evidence-Based Medicine; Ferner RE, Sofat R, Aronson JK. Drug vignettes: colchicine. 2021 [internet publication]. [Full text \(https://www.cebm.net/covid-19/colchicine\)](https://www.cebm.net/covid-19/colchicine)
942. Sukhatme VP, Reiersen AM, Vayttaden SJ, et al. Fluvoxamine: a review of its mechanism of action and its role in COVID-19. *Front Pharmacol*. 2021 Apr 20;12:652688. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8094534\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8094534) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33959018?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33959018?tool=bestpractice.bmj.com)
943. Lenze EJ, Mattar C, Zorumski CF, et al. Fluvoxamine vs placebo and clinical deterioration in outpatients with symptomatic COVID-19: a randomized clinical trial. *JAMA*. 2020 Dec 8;324(22):2292-300. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7662481\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7662481) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33180097?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33180097?tool=bestpractice.bmj.com)
944. Seftel D, Boulware DR. Prospective cohort of fluvoxamine for early treatment of coronavirus disease 19. *Open Forum Infect Dis*. 2021 Feb;8(2):ofab050. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7888564\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7888564) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33623808?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33623808?tool=bestpractice.bmj.com)
945. Blum VF, Cimerman S, Hunter JR, et al. Nitazoxanide superiority to placebo to treat moderate COVID-19: a pilot prove of concept randomized double-blind clinical trial. *EClinicalMedicine*. 2021 Jun 27;100981. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8235996\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8235996) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34222847?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34222847?tool=bestpractice.bmj.com)
946. Rocco PRM, Silva PL, Cruz FF, et al. Early use of nitazoxanide in mild COVID-19 disease: randomised, placebo-controlled trial. *Eur Respir J*. 2021 Jul 8;58(1):2003725. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7758778\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7758778) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33361100?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33361100?tool=bestpractice.bmj.com)
947. Temesgen Z, Burger CD, Baker J, et al. Lenzilumab efficacy and safety in newly hospitalized COVID-19 subjects: results from the live-air phase 3 randomized double-blind placebo-controlled trial. *medRxiv*. 2021 May 5 [Epub ahead of print]. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8109186\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8109186) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33972949?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33972949?tool=bestpractice.bmj.com)
948. Cremer PC, Abbate A, Hudock K, et al. Mavrilimumab in patients with severe COVID-19 pneumonia and systemic hyperinflammation (MASH-COVID): an investigator initiated, multicentre, double-blind, randomised, placebo-controlled trial. *Lancet Rheumatol*. 2021 Jun;3(6):e410-8. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7969143\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7969143) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33754144?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33754144?tool=bestpractice.bmj.com)
949. Ramakrishnan S, Nicolau DV Jr, Langford B, et al. Inhaled budesonide in the treatment of early COVID-19 (STOIC): a phase 2, open-label, randomised controlled trial. *Lancet Respir Med*. 2021 Apr 9 [Epub ahead of print]. [Full text \(https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00160-0/fulltext\)](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00160-0/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33844996?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33844996?tool=bestpractice.bmj.com)

950. Medicines and Healthcare products Regulatory Agency. COVID-19 therapeutic alert: inhaled budesonide for adults (50 years and over) with COVID-19. 2021 [internet publication]. [Full text \(https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103154\)](https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103154)
951. European Medicines Agency. Insufficient data on use of inhaled corticosteroids to treat COVID-19. 2021 [internet publication]. [Full text \(https://www.ema.europa.eu/en/news/insufficient-data-use-inhaled-corticosteroids-treat-covid-19\)](https://www.ema.europa.eu/en/news/insufficient-data-use-inhaled-corticosteroids-treat-covid-19)
952. PRINCIPLE Collaborative Group; Yu LM, Bafadhel M, Dorward J, et al; medRxiv. Inhaled budesonide for COVID-19 in people at higher risk of adverse outcomes in the community: interim analyses from the PRINCIPLE trial. 2021 [internet publication]. [Full text \(https://www.medrxiv.org/content/10.1101/2021.04.10.21254672v1\)](https://www.medrxiv.org/content/10.1101/2021.04.10.21254672v1)
953. Medicines and Healthcare products Regulatory Agency. COVID-19 therapeutic alert: antimicrobials (azithromycin and doxycycline) not beneficial in the management of COVID-19 (SARS-CoV-2) positive patients. 2021 [internet publication]. [Full text \(https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103137\)](https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103137)
954. Mangkuliguna G, Glenardi, Susanto N, et al. Efficacy and safety of azithromycin for the treatment of COVID-19: a systematic review and meta-analysis. *Tuberc Respir Dis (Seoul)*. 2021 May 20 [Epub ahead of print]. [Full text \(https://www.e-trd.org/journal/view.php?doi=10.4046/trd.2021.0075\)](https://www.e-trd.org/journal/view.php?doi=10.4046/trd.2021.0075) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34015868?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34015868?tool=bestpractice.bmj.com)
955. RECOVERY Collaborative Group. Azithromycin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet*. 2021 Feb 13;397(10274):605-12. [Full text \(https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00149-5/fulltext\)](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00149-5/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33545096?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33545096?tool=bestpractice.bmj.com)
956. University of Oxford. PRINCIPLE trial. 2020 [internet publication]. [Full text \(https://www.principletrial.org\)](https://www.principletrial.org)
957. Hinks TSC, Cureton L, Knight R, et al. Azithromycin versus standard care in patients with mild-to-moderate COVID-19 (ATOMIC2): an open-label, randomised trial. *Lancet Respir Med*. 2021 Jul 9 [Epub ahead of print]. [Full text \(https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00263-0/fulltext\)](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00263-0/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34252378?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34252378?tool=bestpractice.bmj.com)
958. PRINCIPLE Trial Collaborative Group. Azithromycin for community treatment of suspected COVID-19 in people at increased risk of an adverse clinical course in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial. *Lancet*. 2021 Mar 20;397(10279):1063-74. [Full text \(https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00461-X/fulltext\)](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00461-X/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33676597?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33676597?tool=bestpractice.bmj.com)
959. RECOVERY Collaborative Group. Lopinavir-ritonavir in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet*. 2020 Oct 5;396(10259):1345-52. [Full text \(https://www.thelancet.com/journals/lancet/article/\)](https://www.thelancet.com/journals/lancet/article/)

- PIIS0140-6736(20)32013-4/fulltext) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33031764?tool=bestpractice.bmj.com>)
960. Alhumaid S, Mutair AA, Alawi ZA, et al. Efficacy and safety of lopinavir/ritonavir for treatment of COVID-19: a systematic review and meta-analysis. *Trop Med Infect Dis*. 2020 Nov 28;5(4):E180. Full text (<https://www.mdpi.com/2414-6366/5/4/180/htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33260553?tool=bestpractice.bmj.com>)
961. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res*. 2020 Mar;30(3):269-71. Full text (<https://www.nature.com/articles/s41422-020-0282-0>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32020029?tool=bestpractice.bmj.com>)
962. Cortegiani A, Ingoglia G, Ippolito M, et al. A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. *J Crit Care*. 2020 Jun;57:279-83. Full text (<https://www.sciencedirect.com/science/article/pii/S0883944120303907>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32173110?tool=bestpractice.bmj.com>)
963. World Health Organization. WHO living guideline: drugs to prevent COVID-19 - interim guidance. 2021 [internet publication]. Full text (<https://www.who.int/publications/i/item/WHO-2019-nCoV-prophylaxes-2021-1>)
964. Lamontagne F, Agoritsas T, Siemieniuk R, et al. A living WHO guideline on drugs to prevent covid-19. *BMJ*. 2021 Mar 1;372:n526. Full text (<https://www.bmj.com/content/372/bmj.n526>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33649077?tool=bestpractice.bmj.com>)
965. Singh B, Ryan H, Kredo T, et al. Chloroquine or hydroxychloroquine for prevention and treatment of COVID-19. *Cochrane Database Syst Rev*. 2021 Feb 12;(2):CD013587. Full text (<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013587.pub2/full>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33624299?tool=bestpractice.bmj.com>)
966. Hernandez AV, Roman YM, Pasupuleti V, et al. Hydroxychloroquine or chloroquine for treatment or prophylaxis of COVID-19: a living systematic review. *Ann Intern Med*. 2020 Aug 18;173(4):287-96. Full text (<https://www.acpjournals.org/doi/10.7326/M20-2496>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32459529?tool=bestpractice.bmj.com>)
967. Hernandez AV, Roman YM, Pasupuleti V, et al. Update alert 3: hydroxychloroquine or chloroquine for the treatment or prophylaxis of COVID-19. *Ann Intern Med*. 2020 Dec 1;173(11):W156-7. Full text (<https://www.acpjournals.org/doi/10.7326/L20-1257>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33085507?tool=bestpractice.bmj.com>)
968. RECOVERY Collaborative Group; Horby P, Mafham M, Linsell L, et al. Effect of hydroxychloroquine in hospitalized patients with Covid-19. *N Engl J Med*. 2020 Nov 19;383(21):2030-40. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMoa2022926>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33031652?tool=bestpractice.bmj.com>)
969. Centers for Disease Control and Prevention. Healthcare workers: information on COVID-19. 2021 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-nCoV/hcp/index.html>)

970. Centers for Disease Control and Prevention. Interim U.S. guidance for risk assessment and work restrictions for healthcare personnel with potential exposure to SARS-CoV-2. 2021 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assessment-hcp.html>)
971. American Academy of Pediatrics. Caring for children and youth with special health care needs during the COVID-19 pandemic. 2021 [internet publication]. Full text (<https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/caring-for-children-and-youth-with-special-health-care-needs-during-the-covid-19-pandemic>)
972. Government of Canada. Coronavirus disease (COVID-19): outbreak update. 2021 [internet publication]. Full text (<https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection.html>)
973. Centers for Disease Control and Prevention. Interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 (COVID-19). 2020 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-home-care.html>)
974. Pan American Health Organization. COVID-19 guidance and the latest research in the Americas. 2021 [internet publication]. Full text (<https://covid19-evidence.paho.org>)
975. World Health Organization. Criteria for releasing COVID-19 patients from isolation: scientific brief. 2020 [internet publication]. Full text (<https://www.who.int/publications/i/item/criteria-for-releasing-covid-19-patients-from-isolation>)
976. Liu E, Smyth RL, Luo Z, et al. Rapid advice guidelines for management of children with COVID-19. *Ann Transl Med*. 2020 May;8(10):617. Full text (<http://atm.amegroups.com/article/view/43612/html>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32566554?tool=bestpractice.bmj.com>)
977. Poon LC, Yang H, Dumont S, et al. ISUOG interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium: information for healthcare professionals – an update. *Ultrasound Obstet Gynecol*. 2020 Jun;55(6):848-62. Full text (<https://obgyn.onlinelibrary.wiley.com/doi/epdf/10.1002/uog.22061>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32356590?tool=bestpractice.bmj.com>)
978. BMJ Publishing Group. BMJ's coronavirus (covid-19) hub. 2021 [internet publication]. Full text (<https://www.bmj.com/coronavirus>)
979. National Institute for Health and Care Excellence. Coronavirus (COVID-19). 2021 [internet publication]. Full text (<https://www.nice.org.uk/covid-19>)
980. NHS England. Coronavirus specialty guides. 2021 [internet publication]. Full text (<https://www.nice.org.uk/covid-19/specialty-guides>)
981. Public Health England. COVID-19: the green book, chapter 14a. 2021 [internet publication]. Full text (<https://www.gov.uk/government/publications/covid-19-the-green-book-chapter-14a>)
982. Royal College of General Practitioners; Association for Palliative Medicine. Community palliative, end of life and bereavement care in the COVID-19 pandemic. 2021 [internet publication]. Full text

- (https://elearning.rcgp.org.uk/pluginfile.php/149457/mod_page/content/55/COVID%20Community%20symptom%20control%20and%20end%20of%20life%20care%20for%20General%20Practice%20-%20Word%20FINAL%20v3.pdf?time=1589368447206)
983. Chalmers JD, Crichton ML, Goeminne PC, et al. Management of hospitalised adults with coronavirus disease 2019 (COVID-19): a European Respiratory Society living guideline. *Eur Respir J*. 2021 Apr 15;57(4):2100048. Full text (<https://erj.ersjournals.com/content/early/2021/03/07/13993003.00048-2021>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33692120?tool=bestpractice.bmj.com>)
 984. British Thoracic Society. COVID-19: information for the respiratory community. 2021 [internet publication]. Full text (<https://www.brit-thoracic.org.uk/about-us/covid-19-information-for-the-respiratory-community>)
 985. All India Institute Of Medical Sciences; Indian Council of Medical Research. Clinical guidance for management of adult COVID-19 patients. 2021 [internet publication]. Full text (<https://covid.aiims.edu/clinical-guidance-for-management-of-adult-covid-19-patients>)
 986. Ministry of Health Singapore. Updates on COVID-19 (coronavirus disease 2019) local situation. 2021 [internet publication]. Full text (<https://www.moh.gov.sg/covid-19>)
 987. Chinese Center for Disease Control and Prevention. Coronavirus disease. 2021 [internet publication]. Full text (http://www.chinacdc.cn/jkzt/crb/zl/szkb_11803)
 988. National Institute of Infectious Diseases Japan. New coronavirus infectious disease (COVID-19) related information page. 2021 [internet publication]. Full text (<https://www.niid.go.jp/niid/ja/diseases/ka/corona-virus/2019-ncov.html>)
 989. Japanese Association for Infectious Diseases. COVID-19 infection. 2021 [internet publication]. Full text (https://www.kansensho.or.jp/modules/topics/index.php?content_id=31)
 990. Department of Health Australia. Coronavirus disease 2019 (COVID-19). 2021 [internet publication]. Full text (<https://www1.health.gov.au/internet/main/publishing.nsf/Content/cdna-song-novel-coronavirus.htm>)
 991. National Institute for Health and Care Excellence. COVID-19 rapid guideline: managing the long-term effects of COVID-19. 2020 [internet publication]. Full text (<https://www.nice.org.uk/guidance/ng188>)
 992. Shang Y, Pan C, Yang X, et al. Management of critically ill patients with COVID-19 in ICU: statement from front-line intensive care experts in Wuhan, China. *Ann Intensive Care*. 2020 Jun 6;10(1):73. Full text (<https://annalsofintensivecare.springeropen.com/articles/10.1186/s13613-020-00689-1>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32506258?tool=bestpractice.bmj.com>)
 993. First Affiliated Hospital, Zhejiang University School of Medicine. Handbook of COVID-19 prevention and treatment. 2020 [internet publication]. Full text (<https://video-intl.alicdn.com/Handbook%20of%20COVID-19%20Prevention%20and%20Treatment.pdf>)
 994. National Health Commission of the People's Republic of China; National Administration of Traditional Chinese Medicine of the People's Republic of China. Diagnosis and

- treatment protocol for novel coronavirus pneumonia (trial version 7). *Chin Med J (Engl)*. 2020 May 5;133(9):1087-95. [Full text \(https://journals.lww.com/cmj/fulltext/2020/05050/diagnosis_and_treatment_protocol_for_novel.13.aspx\)](https://journals.lww.com/cmj/fulltext/2020/05050/diagnosis_and_treatment_protocol_for_novel.13.aspx) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32358325?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32358325?tool=bestpractice.bmj.com)
995. Ruan Q, Yang K, Wang W, et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med*. 2020 May;46(5):846-8. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7080116\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7080116) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32125452?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32125452?tool=bestpractice.bmj.com)
996. Hasan SS, Capstick T, Ahmed R, et al. Mortality in COVID-19 patients with acute respiratory distress syndrome and corticosteroids use: a systematic review and meta-analysis. *Expert Rev Respir Med*. 2020 Nov;14(11):1149-63. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7544968\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7544968) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32734777?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32734777?tool=bestpractice.bmj.com)
997. Dmytriw AA, Chibbar R, Chen PPY, et al. Outcomes of acute respiratory distress syndrome in COVID-19 patients compared to the general population: a systematic review and meta-analysis. *Expert Rev Respir Med*. 2021 Apr 21 [Epub ahead of print]. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33882768?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33882768?tool=bestpractice.bmj.com)
998. de la Calle C, Lalueza A, Mancheño-Losa M, et al. Impact of viral load at admission on the development of respiratory failure in hospitalized patients with SARS-CoV-2 infection. *Eur J Clin Microbiol Infect Dis*. 2021 Jan 7 [Epub ahead of print]. [Full text \(https://link.springer.com/article/10.1007/s10096-020-04150-w\)](https://link.springer.com/article/10.1007/s10096-020-04150-w) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33409832?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33409832?tool=bestpractice.bmj.com)
999. Elezkurtaj S, Greuel S, Ihlow J, et al. Causes of death and comorbidities in hospitalized patients with COVID-19. *Sci Rep*. 2021 Feb 19;11(1):4263. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7895917\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7895917) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33608563?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33608563?tool=bestpractice.bmj.com)
1000. Ioannidis JPA, Axfors C, Contopoulos-Ioannidis DG. Population-level COVID-19 mortality risk for non-elderly individuals overall and for non-elderly individuals without underlying diseases in pandemic epicenters. *Environ Res*. 2020 Sep;188:109890. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7327471\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7327471) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32846654?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32846654?tool=bestpractice.bmj.com)
1001. Smith C, Odd D, Harwood R, et al; medRxiv. Deaths in children and young people in England following SARS-CoV-2 infection during the first pandemic year: a national study using linked mandatory child death reporting data. 2021 [internet publication]. [Full text \(https://www.medrxiv.org/content/10.1101/2021.07.07.21259779v1\)](https://www.medrxiv.org/content/10.1101/2021.07.07.21259779v1)
1002. Docherty AB, Mulholland RH, Lone NI, et al. Changes in in-hospital mortality in the first wave of COVID-19: a multicentre prospective observational cohort study using the WHO Clinical Characterisation Protocol UK. *Lancet Respir Med*. 2021 May 14 [Epub ahead of print]. [Full text \(https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00175-2/fulltext\)](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00175-2/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34000238?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34000238?tool=bestpractice.bmj.com)
1003. Asch DA, Sheils NE, Islam MN, et al. Variation in US hospital mortality rates for patients admitted with COVID-19 during the first 6 months of the pandemic. *JAMA Intern Med*. 2021 Apr 1;181(4):471-8. [Full](#)

- text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7756246/>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33351068?tool=bestpractice.bmj.com>)
1004. Nguyen NT, Chinn J, Nahmias J, et al. Outcomes and mortality among adults hospitalized with COVID-19 at US medical centers. *JAMA Netw Open*. 2021 Mar 1;4(3):e210417. Full text (<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777028>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33666657?tool=bestpractice.bmj.com>)
1005. Finelli L, Gupta V, Petigara T, et al. Mortality among US patients hospitalized with SARS-CoV-2 infection in 2020. *JAMA Netw Open*. 2021 Apr 1;4(4):e216556. Full text (<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2778237>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33830226?tool=bestpractice.bmj.com>)
1006. Anesi GL, Jablonski J, Harhay MO, et al. Characteristics, outcomes, and trends of patients with COVID-19-related critical illness at a learning health system in the United States. *Ann Intern Med*. 2021 Jan 19 [Epub ahead of print]. Full text (<https://www.acpjournals.org/doi/10.7326/M20-5327>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33460330?tool=bestpractice.bmj.com>)
1007. Ioannidis JPA. Reconciling estimates of global spread and infection fatality rates of COVID-19: an overview of systematic evaluations. *Eur J Clin Invest*. 2021 Mar 26:e13554. Full text (<https://onlinelibrary.wiley.com/doi/10.1111/eci.13554>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33768536?tool=bestpractice.bmj.com>)
1008. Meyerowitz-Katz G, Merone L. A systematic review and meta-analysis of published research data on COVID-19 infection fatality rates. *Int J Infect Dis*. 2020 Dec;101:138-48. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7524446>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33007452?tool=bestpractice.bmj.com>)
1009. Rajgor DD, Lee MH, Archuleta S, et al. The many estimates of the COVID-19 case fatality rate. *Lancet Infect Dis*. 2020 Jul;20(7):776-7. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7270047>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32224313?tool=bestpractice.bmj.com>)
1010. Chen X, Chen Z, Azman AS, et al. Serological evidence of human infection with SARS-CoV-2: a systematic review and meta-analysis. *Lancet Glob Health*. 2021 May;9(5):e598-609. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8049592>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33705690?tool=bestpractice.bmj.com>)
1011. World Health Organization. Coronavirus disease (COVID-19) weekly epidemiological updates. 2021 [internet publication]. Full text (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>)
1012. Verity R, Okell LC, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis*. 2020 Jun;20(6):669-77. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7158570>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32240634?tool=bestpractice.bmj.com>)
1013. Sorbello M, El-Boghdadly K, Di Giacinto I, et al. The Italian COVID-19 outbreak: experiences and recommendations from clinical practice. *Anaesthesia*. 2020 Jun;75(6):724-32. Full text (<https://>

onlinelibrary.wiley.com/doi/full/10.1111/anae.15049) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32221973?tool=bestpractice.bmj.com>)

1014. Bixler D, Miller AD, Mattison CP, et al. SARS-CoV-2–associated deaths among persons aged <21 years: United States, February 12–July 31, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Sep 18;69(37):1324-9. Full text (<https://www.cdc.gov/mmwr/volumes/69/wr/mm6937e4.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32941417?tool=bestpractice.bmj.com>)
1015. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. *JAMA*. 2020 Apr 6;323(16):1574-81. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2764365>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32250385?tool=bestpractice.bmj.com>)
1016. Arentz M, Yim E, Klaff L, et al. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State. *JAMA*. 2020 Mar 19;323(16):1612-4. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2763485>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32191259?tool=bestpractice.bmj.com>)
1017. Centre for Evidence-Based Medicine; Oke J, Heneghan C. Global COVID-19 case fatality rates. 2020 [internet publication]. Full text (<https://www.cebm.net/global-covid-19-case-fatality-rates>)
1018. Mahase E. Covid-19: the problems with case counting. *BMJ*. 2020 Sep 3;370:m3374. Full text (<https://www.bmj.com/content/370/bmj.m3374>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32883657?tool=bestpractice.bmj.com>)
1019. Centre for Evidence-Based Medicine; Spencer E, Jefferson T, Brassey J, et al. When is Covid, Covid? 2020 [internet publication]. Full text (<https://www.cebm.net/covid-19/when-is-covid-covid>)
1020. Centre for Evidence-Based Medicine; Oke J, Heneghan C. Reconciling COVID-19 death data in the UK. 2020 [internet publication]. Full text (<https://www.cebm.net/covid-19/reconciling-covid-19-death-data-in-the-uk>)
1021. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA*. 2020 May 12;323(18):1775-6. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2763667>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32203977?tool=bestpractice.bmj.com>)
1022. Bilinski A, Emanuel EJ. COVID-19 and excess all-cause mortality in the US and 18 comparison countries. *JAMA*. 2020 Nov 24;324(20):2100-2. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2771841>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33044514?tool=bestpractice.bmj.com>)
1023. Izcovich A, Ragusa MA, Tortosa F, et al. Prognostic factors for severity and mortality in patients infected with COVID-19: a systematic review. *PLoS One*. 2020;15(11):e0241955. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7671522>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33201896?tool=bestpractice.bmj.com>)
1024. Booth A, Reed AB, Ponzo S, et al. Population risk factors for severe disease and mortality in COVID-19: a global systematic review and meta-analysis. *PLoS One*. 2021 Mar 4;16(3):e0247461.

Full text (<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0247461>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33661992?tool=bestpractice.bmj.com>)

1025. Zhang L, Hou J, Ma FZ, et al. The common risk factors for progression and mortality in COVID-19 patients: a meta-analysis. *Arch Virol*. 2021 Apr 2 [Epub ahead of print]. Full text (<https://link.springer.com/article/10.1007%2Fs00705-021-05012-2>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33797621?tool=bestpractice.bmj.com>)
1026. Dumitrascu F, Branje KE, Hladkiewicz ES, et al. Association of frailty with outcomes in individuals with COVID-19: a living review and meta-analysis. *J Am Geriatr Soc*. 2021 May 28 [Epub ahead of print]. Full text (<https://agsjournals.onlinelibrary.wiley.com/doi/epdf/10.1111/jgs.17299>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34048599?tool=bestpractice.bmj.com>)
1027. Bellou V, Tzoulaki I, van Smeden M, et al. Prognostic factors for adverse outcomes in patients with COVID-19: a field-wide systematic review and meta-analysis. *Eur Respir J*. 2021 Jun 25 [Epub ahead of print]. Full text (<https://erj.ersjournals.com/content/early/2021/06/10/13993003.02964-2020>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34172467?tool=bestpractice.bmj.com>)
1028. Santus P, Radovanovic D, Saderi L, et al. Severity of respiratory failure at admission and in-hospital mortality in patients with COVID-19: a prospective observational multicentre study. *BMJ Open*. 2020 Oct 10;10(10):e043651. Full text (<https://bmjopen.bmj.com/content/10/10/e043651>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33040020?tool=bestpractice.bmj.com>)
1029. Shi C, Wang L, Ye J, et al. Predictors of mortality in patients with coronavirus disease 2019: a systematic review and meta-analysis. *BMC Infect Dis*. 2021 Jul 8;21(1):663. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8264491>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34238232?tool=bestpractice.bmj.com>)
1030. Javanmardi F, Keshavarzi A, Akbari A, et al. Prevalence of underlying diseases in died cases of COVID-19: a systematic review and meta-analysis. *PLoS One*. 2020 Oct 23;15(10):e0241265. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7584167>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33095835?tool=bestpractice.bmj.com>)
1031. Ayoubkhani D, Khunti K, Nafilyan V, et al. Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study. *BMJ*. 2021 Mar 31;372:n693. Full text (<https://www.bmj.com/content/372/bmj.n693>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33789877?tool=bestpractice.bmj.com>)
1032. Lavery AM, Preston LE, Ko JY, et al. Characteristics of hospitalized COVID-19 patients discharged and experiencing same-hospital readmission: United States, March–August 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Nov 13;69(45):1695-9. Full text (<https://www.cdc.gov/mmwr/volumes/69/wr/mm6945e2.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33180754?tool=bestpractice.bmj.com>)
1033. Lund LC, Hallas J, Nielsen H, et al. Post-acute effects of SARS-CoV-2 infection in individuals not requiring hospital admission: a Danish population-based cohort study. *Lancet Infect Dis*. 2021 May 10 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8110209>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33984263?tool=bestpractice.bmj.com>)

1034. Mattiuzzi C, Henry BM, Sanchis-Gomar F, et al. SARS-CoV-2 recurrent RNA positivity after recovering from coronavirus disease 2019 (COVID-19): a meta-analysis. *Acta Biomed.* 2020 Sep 7;91(3):e2020014. [Full text \(https://www.mattioli1885journals.com/index.php/actabiomedica/article/view/10303\)](https://www.mattioli1885journals.com/index.php/actabiomedica/article/view/10303) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32921710?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32921710?tool=bestpractice.bmj.com)
1035. Azam M, Sulistiana R, Ratnawati M, et al. Recurrent SARS-CoV-2 RNA positivity after COVID-19: a systematic review and meta-analysis. *Sci Rep.* 2020 Nov 26;10(1):20692. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7691365\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7691365) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33244060?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33244060?tool=bestpractice.bmj.com)
1036. SeyedAlinaghi S, Oliaei S, Kianzad S, et al. Reinfection risk of novel coronavirus (COVID-19): a systematic review of current evidence. *World J Virol.* 2020 Dec 15;9(5):79-90. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7747024\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7747024) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33363000?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33363000?tool=bestpractice.bmj.com)
1037. Arafkas M, Khosrawipour T, Kocbach P, et al. Current meta-analysis does not support the possibility of COVID-19 reinfections. *J Med Virol.* 2021 Mar;93(3):1599-604. [Full text \(https://onlinelibrary.wiley.com/doi/10.1002/jmv.26496\)](https://onlinelibrary.wiley.com/doi/10.1002/jmv.26496) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32897549?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32897549?tool=bestpractice.bmj.com)
1038. Vibholm LK, Nielsen SS, Pahus MH, et al. SARS-CoV-2 persistence is associated with antigen-specific CD8 T-cell responses. *EBioMedicine.* 2021 Jan 30;64:103230. [Full text \(https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(21\)00023-2/fulltext\)](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00023-2/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33530000?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33530000?tool=bestpractice.bmj.com)
1039. Public Health England. New national surveillance of possible COVID-19 reinfection, published by PHE. 2021 [internet publication]. [Full text \(https://www.gov.uk/government/news/new-national-surveillance-of-possible-covid-19-reinfection-published-by-phe\)](https://www.gov.uk/government/news/new-national-surveillance-of-possible-covid-19-reinfection-published-by-phe)
1040. Wang J, Kaperak C, Sato T, et al. COVID-19 reinfection: a rapid systematic review of case reports and case series. *J Investig Med.* 2021 May 18 [Epub ahead of print]. [Full text \(https://jim.bmj.com/content/early/2021/05/18/jim-2021-001853.long\)](https://jim.bmj.com/content/early/2021/05/18/jim-2021-001853.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34006572?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34006572?tool=bestpractice.bmj.com)
1041. Zucman N, Uhel F, Descamps D, et al. Severe reinfection with South African SARS-CoV-2 variant 501Y.V2: a case report. *Clin Infect Dis.* 2021 Feb 10 [Epub ahead of print]. [Full text \(https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab129/6132402\)](https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab129/6132402) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33566076?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33566076?tool=bestpractice.bmj.com)
1042. Resende PC, Bezerra JF, de Vasconcelos RHT, et al. Spike E484K mutation in the first SARS-CoV-2 reinfection case confirmed in Brazil, 2020. 2021 [internet publication]. [Full text \(https://virological.org/t/spike-e484k-mutation-in-the-first-sars-cov-2-reinfection-case-confirmed-in-brazil-2020/584\)](https://virological.org/t/spike-e484k-mutation-in-the-first-sars-cov-2-reinfection-case-confirmed-in-brazil-2020/584)
1043. Naveca F, da Costa C, Nascimento V, et al. SARS-CoV-2 reinfection by the new variant of concern (VOC) P.1 in Amazonas, Brazil. 2021 [internet publication]. [Full text \(https://virological.org/t/sars-cov-2-reinfection-by-the-new-variant-of-concern-voc-p-1-in-amazonas-brazil/596\)](https://virological.org/t/sars-cov-2-reinfection-by-the-new-variant-of-concern-voc-p-1-in-amazonas-brazil/596)
1044. Nonaka CKV, Franco MM, Gräf T, et al. Genomic evidence of SARS-CoV-2 reinfection involving E484K spike mutation, Brazil. *Emerg Infect Dis.* 2021 Feb 19;27(5). [Full text \(https://wwwnc.cdc.gov/\)](https://wwwnc.cdc.gov/)

eid/article/27/5/21-0191_article) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33605869?tool=bestpractice.bmj.com>)

1045. Stephens DS, McElrath MJ. COVID-19 and the path to immunity. *JAMA*. 2020 Oct 6;324(13):1279-81. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2770758>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32915201?tool=bestpractice.bmj.com>)
1046. Qaseem A, Yost J, Etzeandía-Ikobaltzeta I, et al. What is the antibody response and role in conferring natural immunity after SARS-CoV-2 infection? Rapid, living practice points from the American College of Physicians (version 1). *Ann Intern Med*. 2021 Mar 16 [Epub ahead of print]. Full text (<https://www.acpjournals.org/doi/10.7326/M20-7569>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33721518?tool=bestpractice.bmj.com>)
1047. World Health Organization. COVID-19 natural immunity: scientific brief. 2021 [internet publication]. Full text (<https://www.who.int/publications/i/item/WHO-2019-nCoV-Sci-Brief-Immunity-passport-2021.1>)
1048. Savage HR, Santos VS, Edwards T, et al. Prevalence of neutralising antibodies against SARS-CoV-2 in acute infection and convalescence: a systematic review and meta-analysis. *PLoS Negl Trop Dis*. 2021 Jul 8;15(7):e0009551. Full text (<https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0009551>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34237072?tool=bestpractice.bmj.com>)
1049. Arkhipova-Jenkins I, Helfand M, Armstrong C, et al. Antibody response after SARS-CoV-2 infection and implications for immunity: a rapid living review. *Ann Intern Med*. 2021 Mar 16 [Epub ahead of print]. Full text (<https://www.acpjournals.org/doi/10.7326/M20-7547>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33721517?tool=bestpractice.bmj.com>)
1050. Flannery DD, Gouma S, Dhudasia MB, et al. Assessment of maternal and neonatal cord blood SARS-CoV-2 antibodies and placental transfer ratios. *JAMA Pediatr*. 2021 Jan 29 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2775945>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33512440?tool=bestpractice.bmj.com>)
1051. Foley MK, Searle SD, Toloue A, et al. Centenarians and extremely old people living with frailty can elicit durable SARS-CoV-2 spike specific IgG antibodies with virus neutralization functions following virus infection as determined by serological study. *EClinicalMedicine*. 2021 Jun 27:100975. Full text ([https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00255-8/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00255-8/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34222846?tool=bestpractice.bmj.com>)
1052. Long QX, Tang XJ, Shi QL, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nat Med*. 2020 Aug;26(8):1200-4. Full text (<https://www.nature.com/articles/s41591-020-0965-6>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32555424?tool=bestpractice.bmj.com>)
1053. Alfego D, Sullivan A, Poirier B, et al. A population-based analysis of the longevity of SARS-CoV-2 antibody seropositivity in the United States. *EClinicalMedicine*. 2021 May 24:100902. Full text ([https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00182-6/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00182-6/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34056568?tool=bestpractice.bmj.com>)

1054. Centre for Evidence-Based Medicine; Plüddemann A, Aronson JK. What is the role of T cells in COVID-19 infection? Why immunity is about more than antibodies. 2020 [internet publication]. [Full text \(https://www.cebm.net/covid-19/what-is-the-role-of-t-cells-in-covid-19-infection-why-immunity-is-about-more-than-antibodies\)](https://www.cebm.net/covid-19/what-is-the-role-of-t-cells-in-covid-19-infection-why-immunity-is-about-more-than-antibodies)
1055. Dan JM, Mateus J, Kato Y, et al. Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. *Science*. 2021 Jan 6 [Epub ahead of print]. [Full text \(https://science.sciencemag.org/content/early/2021/01/06/science.abf4063.long\)](https://science.sciencemag.org/content/early/2021/01/06/science.abf4063.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33408181?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33408181?tool=bestpractice.bmj.com)
1056. Shrotri M, van Schalkwyk MCI, Post N, et al. T cell response to SARS-CoV-2 infection in humans: a systematic review. *PLoS One*. 2021;16(1):e0245532. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7833159\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7833159) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33493185?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33493185?tool=bestpractice.bmj.com)
1057. Tarke A, Sidney J, Methot N, et al. Negligible impact of SARS-CoV-2 variants on CD4+ and CD8+ T cell reactivity in COVID-19 exposed donors and vaccinees. *bioRxiv*. 2021 Mar 1 [Epub ahead of print]. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7941626\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7941626) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33688655?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33688655?tool=bestpractice.bmj.com)
1058. Redd AD, Nardin A, Kared H, et al. CD8+ T cell responses in COVID-19 convalescent individuals target conserved epitopes from multiple prominent SARS-CoV-2 circulating variants. *medRxiv*. 2021 Feb 12 [Epub ahead of print]. [Full text \(https://www.medrxiv.org/content/10.1101/2021.02.11.21251585v1.full-text\)](https://www.medrxiv.org/content/10.1101/2021.02.11.21251585v1.full-text) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33594378?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33594378?tool=bestpractice.bmj.com)
1059. Gudbjartsson DF, Norddahl GL, Melsted P, et al. Humoral immune response to SARS-CoV-2 in Iceland. *N Engl J Med*. 2020 Oct 29;383(18):1724-34. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2026116\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2026116) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32871063?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32871063?tool=bestpractice.bmj.com)
1060. Chandrashekar A, Liu J, Martinot AJ, et al. SARS-CoV-2 infection protects against rechallenge in rhesus macaques. *Science*. 2020 Aug 14;369(6505):812-7. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7243369\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7243369) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32434946?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32434946?tool=bestpractice.bmj.com)
1061. Kirkcaldy RD, King BA, Brooks JT. COVID-19 and postinfection immunity: limited evidence, many remaining questions. *JAMA*. 2020 Jun 9;323(22):2245-6. [Full text \(https://jamanetwork.com/journals/jama/fullarticle/2766097\)](https://jamanetwork.com/journals/jama/fullarticle/2766097) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32391855?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32391855?tool=bestpractice.bmj.com)
1062. Ni L, Ye F, Cheng ML, et al. Detection of SARS-CoV-2-specific humoral and cellular immunity in COVID-19 convalescent individuals. *Immunity*. 2020 Jun 16;52(6):971-7. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7196424\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7196424) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32413330?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32413330?tool=bestpractice.bmj.com)
1063. Hall VJ, Foulkes S, Charlett A, et al. SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN). *Lancet*. 2021 Apr 17;397(10283):1459-69. [Full text \(https://www.ncbi.nlm.nih.gov/\)](https://www.ncbi.nlm.nih.gov/)

[pmc/articles/PMC8040523](https://pubmed.ncbi.nlm.nih.gov/33844963/)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33844963?tool=bestpractice.bmj.com>)

1064. Hansen CH, Michlmayr D, Gubbels SM, et al. Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study. *Lancet*. 2021 Mar 27;397(10280):1204-12. Full text ([https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00575-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00575-4/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33743221?tool=bestpractice.bmj.com>)
1065. Vitale J, Mumoli N, Clerici P, et al. Assessment of SARS-CoV-2 reinfection 1 year after primary infection in a population in Lombardy, Italy. *JAMA Intern Med*. 2021 May 28 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2780557>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34048531?tool=bestpractice.bmj.com>)
1066. Letizia AG, Ge Y, Vangeti S, et al. SARS-CoV-2 seropositivity and subsequent infection risk in healthy young adults: a prospective cohort study. *Lancet Respir Med*. 2021 Apr 15 [Epub ahead of print]. Full text ([https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00158-2/fulltext#%20](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00158-2/fulltext#%20)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33865504?tool=bestpractice.bmj.com>)
1067. Harvey RA, Rassen JA, Kabelac CA, et al. Association of SARS-CoV-2 seropositive antibody test with risk of future infection. *JAMA Intern Med*. 2021 May 1;181(5):672-9. Full text (<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2776810>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33625463?tool=bestpractice.bmj.com>)
1068. Lumley SF, O'Donnell D, Stoesser NE, et al. Antibody status and incidence of SARS-CoV-2 infection in health care workers. *N Engl J Med*. 2021 Feb 11;384(6):533-40. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMoa2034545>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33369366?tool=bestpractice.bmj.com>)
1069. Krutikov M, Palmer T, Tut G, et al. Incidence of SARS-CoV-2 infection according to baseline antibody status in staff and residents of 100 long-term care facilities (VIVALDI): a prospective cohort study. *Lancet Healthy Longev*. 2021 Jun;2(6):e362-70. Full text ([https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568\(21\)00093-3/fulltext](https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568(21)00093-3/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34104901?tool=bestpractice.bmj.com>)
1070. Doshi P. Covid-19: do many people have pre-existing immunity? *BMJ*. 2020 Sep 17;370:m3563. Full text (<https://www.bmj.com/content/370/bmj.m3563>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32943427?tool=bestpractice.bmj.com>)
1071. Ng KW, Faulkner N, Cornish GH, et al. Preexisting and de novo humoral immunity to SARS-CoV-2 in humans. *Science*. 2020 Dec 11;370(6522):1339-43. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7857411>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33159009?tool=bestpractice.bmj.com>)
1072. Tan BK, Mainbourg S, Friggeri A, et al. Arterial and venous thromboembolism in COVID-19: a study-level meta-analysis. *Thorax*. 2021 Feb 23 [Epub ahead of print]. Full text (<https://thorax.bmj.com/content/early/2021/02/22/thoraxjnl-2020-215383>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33622981?tool=bestpractice.bmj.com>)

1073. Mai V, Tan BK, Mainbourg S, et al. Venous thromboembolism in COVID-19 compared to non-COVID-19 cohorts: a systematic review with meta-analysis. *Vascul Pharmacol*. 2021 Jun 2;106882. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8169236\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8169236) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34087481?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34087481?tool=bestpractice.bmj.com)
1074. Miró Ò, Jiménez S, Mebazaa A, et al. Pulmonary embolism in patients with COVID-19: incidence, risk factors, clinical characteristics, and outcome. *Eur Heart J*. 2021 Jun 24 [Epub ahead of print]. [Full text \(https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehab314/6308640\)](https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehab314/6308640) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34164664?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34164664?tool=bestpractice.bmj.com)
1075. Wang C, Zhang H, Zhou M, et al. Prognosis of COVID-19 in patients with vein thrombosis: a systematic review and meta-analysis. *Eur Rev Med Pharmacol Sci*. 2020 Oct;24(19):10279-85. [Full text \(https://www.europeanreview.org/wp/wp-content/uploads/10279-10285.pdf\)](https://www.europeanreview.org/wp/wp-content/uploads/10279-10285.pdf) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33090439?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33090439?tool=bestpractice.bmj.com)
1076. Ranucci M, Ballotta A, Di Dedda U, et al. The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome. *J Thromb Haemost*. 2020 Jul;18(7):1747-51. [Full text \(https://onlinelibrary.wiley.com/doi/full/10.1111/jth.14854\)](https://onlinelibrary.wiley.com/doi/full/10.1111/jth.14854) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32302448?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32302448?tool=bestpractice.bmj.com)
1077. Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up. *J Am Coll Cardiol*. 2020 Jun 16;75(23):2950-73. [Full text \(https://www.sciencedirect.com/science/article/pii/S0735109720350087?via%3Dihub\)](https://www.sciencedirect.com/science/article/pii/S0735109720350087?via%3Dihub) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32311448?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32311448?tool=bestpractice.bmj.com)
1078. Bilaloglu S, Aphinyanaphongs Y, Jones S, et al. Thrombosis in hospitalized patients With COVID-19 in a New York City health system. *JAMA*. 2020 Aug 25;324(8):799-801. [Full text \(https://jamanetwork.com/journals/jama/fullarticle/2768715\)](https://jamanetwork.com/journals/jama/fullarticle/2768715) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32702090?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32702090?tool=bestpractice.bmj.com)
1079. Centre for Evidence-Based Medicine; Kernohan A, Calderon M. What are the risk factors and effectiveness of prophylaxis for venous thromboembolism in COVID-19 patients? 2020 [internet publication]. [Full text \(https://www.cebm.net/covid-19/20200\)](https://www.cebm.net/covid-19/20200)
1080. Levi M, Thachil J, Iba T, et al. Coagulation abnormalities and thrombosis in patients with COVID-19. *Lancet Haematol*. 2020 May 11;7(6):e438-40. [Full text \(https://www.thelancet.com/pdfs/journals/lanhae/PIIS2352-3026\(20\)30145-9.pdf\)](https://www.thelancet.com/pdfs/journals/lanhae/PIIS2352-3026(20)30145-9.pdf) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32407672?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32407672?tool=bestpractice.bmj.com)
1081. American Society of Hematology. ASH guidelines on use of anticoagulation in patients with COVID-19. 2020 [internet publication]. [Full text \(https://www.hematology.org/education/clinicians/guidelines-and-quality-care/clinical-practice-guidelines/venous-thromboembolism-guidelines/ash-guidelines-on-use-of-anticoagulation-in-patients-with-covid-19\)](https://www.hematology.org/education/clinicians/guidelines-and-quality-care/clinical-practice-guidelines/venous-thromboembolism-guidelines/ash-guidelines-on-use-of-anticoagulation-in-patients-with-covid-19)
1082. Demelo-Rodríguez P, Cervilla-Muñoz E, Ordieres-Ortega L, et al. Incidence of asymptomatic deep vein thrombosis in patients with COVID-19 pneumonia and elevated D-dimer levels. *Thromb Res*. 2020 May 13;192:23-6. [Full text \(https://www.thrombosisresearch.com/article/S0049-3848\(20\)30190-0/pdf\)](https://www.thrombosisresearch.com/article/S0049-3848(20)30190-0/pdf) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32405101?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32405101?tool=bestpractice.bmj.com)

1083. Wichmann D, Sperhake JP, Lütgehetmann M, et al. Autopsy findings and venous thromboembolism in patients with COVID-19: a prospective cohort study. *Ann Intern Med*. 2020 Aug 18;173(4):268-77. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7240772\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7240772) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32374815?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32374815?tool=bestpractice.bmj.com)
1084. Wang T, Chen R, Liu C, et al. Attention should be paid to venous thromboembolism prophylaxis in the management of COVID-19. *Lancet Haematol*. 2020 May;7(5):e362-3. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7158946\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7158946) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32278361?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32278361?tool=bestpractice.bmj.com)
1085. Taha M, Samavati L. Antiphospholipid antibodies in COVID-19: a meta-analysis and systematic review. *RMD Open*. 2021 May;7(2):e001580. [Full text \(https://rmdopen.bmj.com/content/7/2/e001580.long\)](https://rmdopen.bmj.com/content/7/2/e001580.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33958439?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33958439?tool=bestpractice.bmj.com)
1086. van Nieuwkoop C. COVID-19 associated pulmonary thrombosis. *Thromb Res*. 2020 Jul;191:151. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7252089\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7252089) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32386985?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32386985?tool=bestpractice.bmj.com)
1087. McGonagle D, O'Donnell JS, Sharif K, et al. Immune mechanisms of pulmonary intravascular coagulopathy in COVID-19 pneumonia. *Lancet Rheumatol*. 2020 Jul;2(7):e437-45. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7252093\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7252093) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32835247?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32835247?tool=bestpractice.bmj.com)
1088. Belen-Apak FB, Sarıalioğlu F. Pulmonary intravascular coagulation in COVID-19: possible pathogenesis and recommendations on anticoagulant/thrombolytic therapy. *J Thromb Thrombolysis*. 2020 Aug;50(2):278-80. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7200048\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7200048) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32372336?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32372336?tool=bestpractice.bmj.com)
1089. Perini P, Nabulsi B, Massoni CB, et al. Acute limb ischaemia in two young, non-atherosclerotic patients with COVID-19. *Lancet*. 2020 May 16;395(10236):1546. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7200129\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7200129) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32423583?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32423583?tool=bestpractice.bmj.com)
1090. Griffin DO, Jensen A, Khan M, et al. Arterial thromboembolic complications in COVID-19 in low-risk patients despite prophylaxis. *Br J Haematol*. 2020 Jul;190(1):e11-3. [Full text \(https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.16792\)](https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.16792) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32374029?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32374029?tool=bestpractice.bmj.com)
1091. Lodigiani C, Iapichino G, Carenzo L, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. *Thromb Res*. 2020 Apr 23;191:9-14. [Full text \(https://www.thrombosisresearch.com/article/S0049-3848\(20\)30140-7/pdf\)](https://www.thrombosisresearch.com/article/S0049-3848(20)30140-7/pdf) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32353746?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32353746?tool=bestpractice.bmj.com)
1092. Vulliamy P, Jacob S, Davenport RA. Acute aorto-iliac and mesenteric arterial thromboses as presenting features of COVID-19. *Br J Haematol*. 2020 Jun;189(6):1053-4. [Full text \(https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.16760\)](https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.16760) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32353183?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32353183?tool=bestpractice.bmj.com)

1093. Hemasian H, Ansari B. First case of Covid-19 presented with cerebral venous thrombosis: a rare and dreaded case. *Rev Neurol (Paris)*. 2020 Jun;176(6):521-3. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7211601\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7211601) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32414532?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32414532?tool=bestpractice.bmj.com)
1094. Buso G, Becchetti C, Berzigotti A. Acute splanchnic vein thrombosis in patients with COVID-19: a systematic review. *Dig Liver Dis*. 2021 May 26 [Epub ahead of print]. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8149197\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8149197) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34120860?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34120860?tool=bestpractice.bmj.com)
1095. Madjid M, Safavi-Naeini P, Solomon SD, et al. Potential effects of coronaviruses on the cardiovascular system: a review. *JAMA Cardiol*. 2020 Jul 1;5(7):831-40. [Full text \(https://jamanetwork.com/journals/jamacardiology/fullarticle/2763846\)](https://jamanetwork.com/journals/jamacardiology/fullarticle/2763846) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32219363?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32219363?tool=bestpractice.bmj.com)
1096. Liu PP, Blet A, Smyth D, et al. The science underlying COVID-19: implications for the cardiovascular system. *Circulation*. 2020 Jul 7;142(1):68-78. [Full text \(https://www.ahajournals.org/doi/pdf/10.1161/CIRCULATIONAHA.120.047549\)](https://www.ahajournals.org/doi/pdf/10.1161/CIRCULATIONAHA.120.047549) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32293910?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32293910?tool=bestpractice.bmj.com)
1097. Clerkin KJ, Fried JA, Raikhelkar J, et al. Coronavirus disease 2019 (COVID-19) and cardiovascular disease. *Circulation*. 2020 May 19;141(20):1648-55. [Full text \(https://www.ahajournals.org/doi/pdf/10.1161/CIRCULATIONAHA.120.046941\)](https://www.ahajournals.org/doi/pdf/10.1161/CIRCULATIONAHA.120.046941) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32200663?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32200663?tool=bestpractice.bmj.com)
1098. Hendren NS, Drazner MH, Bozkurt B, et al. Description and proposed management of the acute COVID-19 cardiovascular syndrome. *Circulation*. 2020 Jun 9;141(23):1903-14. [Full text \(https://www.ahajournals.org/doi/pdf/10.1161/CIRCULATIONAHA.120.047349\)](https://www.ahajournals.org/doi/pdf/10.1161/CIRCULATIONAHA.120.047349) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32297796?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32297796?tool=bestpractice.bmj.com)
1099. Sabatino J, De Rosa S, Di Salvo G, et al. Impact of cardiovascular risk profile on COVID-19 outcome: a meta-analysis. *PLoS One*. 2020 Aug 14;15(8):e0237131. [Full text \(https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0237131\)](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0237131) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32797054?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32797054?tool=bestpractice.bmj.com)
1100. Creel-Bulos C, Hockstein M, Amin N, et al. Acute cor pulmonale in critically ill patients with Covid-19. *N Engl J Med*. 2020 May 21;382(21):e70. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMc2010459\)](https://www.nejm.org/doi/full/10.1056/NEJMc2010459) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32374956?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32374956?tool=bestpractice.bmj.com)
1101. Zeng JH, Liu YX, Yuan J, et al. First case of COVID-19 complicated with fulminant myocarditis: a case report and insights. *Infection*. 2020 Apr 10;1-5. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7146072\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7146072) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32277408?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32277408?tool=bestpractice.bmj.com)
1102. Inciardi RM, Lupi L, Zaccone G, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020 Mar 27;5(7):1-6. [Full text \(https://jamanetwork.com/journals/jamacardiology/fullarticle/2763843\)](https://jamanetwork.com/journals/jamacardiology/fullarticle/2763843) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32219357?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32219357?tool=bestpractice.bmj.com)

1103. Hua A, O'Gallagher K, Sado D, et al. Life-threatening cardiac tamponade complicating myo-pericarditis in COVID-19. *Eur Heart J*. 2020 Jun 7;41(22):2130. [Full text \(https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaa253/5813280\)](https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaa253/5813280) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32227076?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32227076?tool=bestpractice.bmj.com)
1104. Singh S, Desai R, Gandhi Z, et al. Takotsubo syndrome in patients with COVID-19: a systematic review of published cases. *SN Compr Clin Med*. 2020 Oct 6:1-7. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7538054\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7538054) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33043251?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33043251?tool=bestpractice.bmj.com)
1105. Garcia-Zamora S, Lee S, Haseeb S, et al. Arrhythmias and electrocardiographic findings in coronavirus disease 2019: a systematic review and meta-analysis. *Pacing Clin Electrophysiol*. 2021 Apr 23 [Epub ahead of print]. [Full text \(https://onlinelibrary.wiley.com/doi/10.1111/pace.14247\)](https://onlinelibrary.wiley.com/doi/10.1111/pace.14247) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33890684?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33890684?tool=bestpractice.bmj.com)
1106. Rubin GA, Desai AD, Chai Z, et al. Cardiac corrected QT interval changes among patients treated for COVID-19 infection during the early phase of the pandemic. *JAMA Netw Open*. 2021 Apr 1;4(4):e216842. [Full text \(https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2779053\)](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2779053) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33890991?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33890991?tool=bestpractice.bmj.com)
1107. Li X, Pan X, Li Y, et al. Cardiac injury associated with severe disease or ICU admission and death in hospitalized patients with COVID-19: a meta-analysis and systematic review. *Crit Care*. 2020 Jul 28;24(1):468. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7386170\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7386170) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32723362?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32723362?tool=bestpractice.bmj.com)
1108. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol*. 2020 Mar 25;5(7):802-10. [Full text \(https://jamanetwork.com/journals/jamacardiology/fullarticle/2763524\)](https://jamanetwork.com/journals/jamacardiology/fullarticle/2763524) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32211816?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32211816?tool=bestpractice.bmj.com)
1109. He XW, Lai JS, Cheng J, et al. Impact of complicated myocardial injury on the clinical outcome of severe or critically ill COVID-19 patients [in Chinese]. *Zhonghua Xin Xue Guan Bing Za Zhi*. 2020 Mar 15;48(0):E011. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32171190?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32171190?tool=bestpractice.bmj.com)
1110. Santoso A, Pranata R, Wibowo A, et al. Cardiac injury is associated with mortality and critically ill pneumonia in COVID-19: a meta-analysis. *Am J Emerg Med*. 2020 Apr 19 [Epub ahead of print]. [Full text \(https://www.ajemjournal.com/article/S0735-6757\(20\)30280-1/pdf\)](https://www.ajemjournal.com/article/S0735-6757(20)30280-1/pdf) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32331955?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32331955?tool=bestpractice.bmj.com)
1111. Inciardi RM, Adamo M, Lupi L, et al. Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy. *Eur Heart J*. 2020 May 14;41(19):1821-9. [Full text \(https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaa388/5834516\)](https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaa388/5834516) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32383763?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32383763?tool=bestpractice.bmj.com)
1112. Siripanthong B, Nazarian S, Muser D, et al. Recognizing COVID-19-related myocarditis: the possible pathophysiology and proposed guideline for diagnosis and management. *Heart Rhythm*. 2020 Sep;17(9):1463-71. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7199677\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7199677) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32387246?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32387246?tool=bestpractice.bmj.com)

1113. Xiong TY, Redwood S, Prendergast B, et al. Coronaviruses and the cardiovascular system: acute and long-term implications. *Eur Heart J*. 2020 May 14;41(19):1798-800. [Full text \(https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaa231/5809453\)](https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaa231/5809453) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32186331?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32186331?tool=bestpractice.bmj.com)
1114. Puntmann VO, Carerj ML, Wieters I, et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020 Nov 1;5(11):1265-73. [Full text \(https://jamanetwork.com/journals/jamacardiology/fullarticle/2768916\)](https://jamanetwork.com/journals/jamacardiology/fullarticle/2768916) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32730619?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32730619?tool=bestpractice.bmj.com)
1115. Lin L, Wang X, Ren J, et al. Risk factors and prognosis for COVID-19-induced acute kidney injury: a meta-analysis. *BMJ Open*. 2020 Nov 10;10(11):e042573. [Full text \(https://bmjopen.bmj.com/content/10/11/e042573\)](https://bmjopen.bmj.com/content/10/11/e042573) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33172950?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33172950?tool=bestpractice.bmj.com)
1116. Chan KW, Yu KY, Lee PW, et al. Global REal Involvement of COReonavirus Disease 2019 (RECORD): a systematic review and meta-analysis of incidence, risk factors, and clinical outcomes. *Front Med (Lausanne)*. 2021 May 25;8:678200. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8185046\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8185046) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34113640?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34113640?tool=bestpractice.bmj.com)
1117. Raina R, Mahajan ZA, Vasistha P, et al. Incidence and outcomes of acute kidney injury in COVID-19: a systematic review. *Blood Purif*. 2021 Jun 15:1-14. [Full text \(https://www.karger.com/Article/FullText/514940\)](https://www.karger.com/Article/FullText/514940) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34130296?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34130296?tool=bestpractice.bmj.com)
1118. Lee SA, Park R, Yang JH, et al. Increased risk of acute kidney injury in coronavirus disease patients with renin-angiotensin-aldosterone-system blockade use: a systematic review and meta-analysis. *Sci Rep*. 2021 Jun 30;11(1):13588. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8245570\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8245570) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34193877?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34193877?tool=bestpractice.bmj.com)
1119. Stewart DJ, Hartley JC, Johnson M, et al. Renal dysfunction in hospitalised children with COVID-19. *Lancet Child Adolesc Health*. 2020 Jun 15;4(8):e28-9. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7295466\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7295466) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32553126?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32553126?tool=bestpractice.bmj.com)
1120. Farkash EA, Wilson AM, Jentzen JM. Ultrastructural evidence for direct renal infection with SARS-CoV-2. *J Am Soc Nephrol*. 2020 Aug;31(8):1683-7. [Full text \(https://jasn.asnjournals.org/content/31/8/1683.long\)](https://jasn.asnjournals.org/content/31/8/1683.long) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32371536?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32371536?tool=bestpractice.bmj.com)
1121. Nasr SH, Kopp JB. COVID-19-associated collapsing glomerulopathy: an emerging entity. *Kidney Int Rep*. 2020 May 4;5(6):759-61. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7196556\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7196556) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32368701?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32368701?tool=bestpractice.bmj.com)
1122. Gross O, Moerer O, Weber M, et al. COVID-19-associated nephritis: early warning for disease severity and complications? *Lancet*. 2020 May 16;395(10236):e87-8. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7202828\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7202828) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32423587?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32423587?tool=bestpractice.bmj.com)

1123. Li G, Yang Y, Gao D, et al. Is liver involvement overestimated in COVID-19 patients? A meta-analysis. *Int J Med Sci*. 2021;18(5):1285-96. [Full text \(https://www.medsci.org/v18p1285.htm\)](https://www.medsci.org/v18p1285.htm) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33526990?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33526990?tool=bestpractice.bmj.com)
1124. Bzeizi K, Abdulla M, Mohammed N, et al. Effect of COVID-19 on liver abnormalities: a systematic review and meta-analysis. *Sci Rep*. 2021 May 19;11(1):10599. [Full text \(https://www.nature.com/articles/s41598-021-89513-9\)](https://www.nature.com/articles/s41598-021-89513-9) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34012016?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34012016?tool=bestpractice.bmj.com)
1125. Alqahtani SA, Schattenberg JM. Liver injury in COVID-19: the current evidence. *United European Gastroenterol J*. 2020 Jun;8(5):509-19. [Full text \(https://journals.sagepub.com/doi/epub/10.1177/2050640620924157\)](https://journals.sagepub.com/doi/epub/10.1177/2050640620924157) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32450787?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32450787?tool=bestpractice.bmj.com)
1126. Wong GL, Wong VW, Thompson A, et al. Management of patients with liver derangement during the COVID-19 pandemic: an Asia-Pacific position statement. *Lancet Gastroenterol Hepatol*. 2020 Aug;5(8):776-87. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7308747\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7308747) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32585136?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32585136?tool=bestpractice.bmj.com)
1127. Favas TT, Dev P, Chaurasia RN, et al. Neurological manifestations of COVID-19: a systematic review and meta-analysis of proportions. *Neurol Sci*. 2020 Dec;41(12):3437-70. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7577367\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7577367) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33089477?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33089477?tool=bestpractice.bmj.com)
1128. Guerrero JI, Barragán LA, Martínez JD, et al. Central and peripheral nervous system involvement by COVID-19: a systematic review of the pathophysiology, clinical manifestations, neuropathology, neuroimaging, electrophysiology, and cerebrospinal fluid findings. *BMC Infect Dis*. 2021 Jun 2;21(1):515. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8170436\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8170436) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34078305?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34078305?tool=bestpractice.bmj.com)
1129. Taquet M, Geddes JR, Husain M, et al. 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. *Lancet Psychiatry*. 2021 May;8(5):416-27. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8023694\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8023694) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33836148?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33836148?tool=bestpractice.bmj.com)
1130. Restivo DA, Centonze D, Alesina A, et al. Myasthenia gravis associated with SARS-CoV-2 infection. *Ann Intern Med*. 2020 Dec 15;173(12):1027-8. [Full text \(https://www.acpjournals.org/doi/10.7326/L20-0845\)](https://www.acpjournals.org/doi/10.7326/L20-0845) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32776781?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32776781?tool=bestpractice.bmj.com)
1131. Scheiner NS, Smith AK, Wohlleber M, et al. COVID-19 and catatonia: a case series and systematic review of existing literature. *J Acad Consult Liaison Psychiatry*. 2021 Apr 20 [Epub ahead of print]. [Full text \(https://www.sciencedirect.com/science/article/pii/S266729602100077X?via%3Dihub\)](https://www.sciencedirect.com/science/article/pii/S266729602100077X?via%3Dihub) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33992595?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33992595?tool=bestpractice.bmj.com)
1132. Schulte EC, Hauer L, Kunz AB, et al. Systematic review of cases of acute myelitis in individuals with COVID-19. *Eur J Neurol*. 2021 Jun 1 [Epub ahead of print]. [Full text \(https://onlinelibrary.wiley.com/doi/10.1111/ene.14952\)](https://onlinelibrary.wiley.com/doi/10.1111/ene.14952) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34060708?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34060708?tool=bestpractice.bmj.com)

1133. Chua TH, Xu Z, King NKK. Neurological manifestations in COVID-19: a systematic review and meta-analysis. *Brain Inj.* 2020 Oct 19;1-20. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33074036?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33074036?tool=bestpractice.bmj.com)
1134. Lu Y, Zhao JJ, Ye MF, et al. The relationship between COVID-19's severity and ischemic stroke: a systematic review and meta-analysis. *Neurol Sci.* 2021 May 5 [Epub ahead of print]. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8098783\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8098783) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33954827?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33954827?tool=bestpractice.bmj.com)
1135. Yamakawa M, Kuno T, Mikami T, et al. Clinical characteristics of stroke with COVID-19: a systematic review and meta-analysis. *J Stroke Cerebrovasc Dis.* 2020 Aug 29;29(12):105288. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456266\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456266) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32992199?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32992199?tool=bestpractice.bmj.com)
1136. Nannoni S, de Groot R, Bell S, et al. Stroke in COVID-19: a systematic review and meta-analysis. *Int J Stroke.* 2021 Feb;16(2):137-49. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7859578\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7859578) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33103610?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33103610?tool=bestpractice.bmj.com)
1137. Valencia-Enciso N, Ortiz-Pereira M, Zafra-Sierra MP, et al. Time of stroke onset in coronavirus disease 2019 patients around the globe: a systematic review and analysis. *J Stroke Cerebrovasc Dis.* 2020 Sep 18;29(12):105325. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7500919\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7500919) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32992196?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32992196?tool=bestpractice.bmj.com)
1138. Tu TM, Seet CYH, Koh JS, et al. Acute ischemic stroke during the convalescent phase of asymptomatic COVID-2019 infection in men. *JAMA Netw Open.* 2021 Apr 1;4(4):e217498. [Full text \(https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2779040\)](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2779040) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33885771?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33885771?tool=bestpractice.bmj.com)
1139. Ntaios G, Michel P, Georgiopoulos G, et al. Characteristics and outcomes in patients with COVID-19 and acute ischemic stroke: the global COVID-19 stroke registry. *Stroke.* 2020 Sep;51(9):e254-8. [Full text \(https://www.ahajournals.org/doi/10.1161/STROKEAHA.120.031208\)](https://www.ahajournals.org/doi/10.1161/STROKEAHA.120.031208) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32787707?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32787707?tool=bestpractice.bmj.com)
1140. Qureshi AI, Abd-Allah F, Alsenani F, et al. Management of acute ischemic stroke in patients with COVID-19 infection: report of an international panel. *Int J Stroke.* 2020 Jul;15(5):540-54. [Full text \(https://journals.sagepub.com/doi/full/10.1177/1747493020923234\)](https://journals.sagepub.com/doi/full/10.1177/1747493020923234) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32362244?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32362244?tool=bestpractice.bmj.com)
1141. Palaiodimou L, Stefanou MI, Katsanos AH, et al. Prevalence, clinical characteristics and outcomes of Guillain-Barré syndrome spectrum associated with COVID-19: a systematic review and meta-analysis. *Eur J Neurol.* 2021 Apr 9 [Epub ahead of print]. [Full text \(https://onlinelibrary.wiley.com/doi/10.1111/ene.14860\)](https://onlinelibrary.wiley.com/doi/10.1111/ene.14860) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33837630?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33837630?tool=bestpractice.bmj.com)
1142. Abu-Rumeileh S, Abdelhak A, Foschi M, et al. Guillain-Barré syndrome spectrum associated with COVID-19: an up-to-date systematic review of 73 cases. *J Neurol.* 2021 Apr;268(4):1133-70. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7445716\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7445716) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32840686?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32840686?tool=bestpractice.bmj.com)

1143. Siow I, Lee KS, Zhang JJY, et al. Encephalitis as neurological complication of COVID-19: a systematic review and meta analysis of incidence, outcomes and predictors. *Eur J Neurol*. 2021 May 13 [Epub ahead of print]. Full text (<https://onlinelibrary.wiley.com/doi/10.1111/ene.14913>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33982853?tool=bestpractice.bmj.com>)
1144. Kubota T, Kuroda N. Exacerbation of neurological symptoms and COVID-19 severity in patients with preexisting neurological disorders and COVID-19: a systematic review. *Clin Neurol Neurosurg*. 2020 Nov 1;106349. Full text (<https://www.sciencedirect.com/science/article/pii/S0303846720306922?via%3Dihub>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33172719?tool=bestpractice.bmj.com>)
1145. Lu Y, Li X, Geng D, et al. Cerebral micro-structural changes in COVID-19 patients: an MRI-based 3-month follow-up study. *EClinicalMedicine*. 2020 Aug;25:100484. Full text ([https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(20\)30228-5/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30228-5/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32838240?tool=bestpractice.bmj.com>)
1146. LaRovere KL, Riggs BJ, Poussaint TY, et al. Neurologic involvement in children and adolescents hospitalized in the United States for COVID-19 or multisystem inflammatory syndrome. *JAMA Neurol*. 2021 May 1;78(5):536-47. Full text (<https://jamanetwork.com/journals/jamaneurology/fullarticle/2777392>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33666649?tool=bestpractice.bmj.com>)
1147. Centers for Disease Control and Prevention. Post-COVID conditions: information for healthcare providers. 2021 [internet publication]. Full text (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-conditions.html>)
1148. Wildwing T, Holt N. The neurological symptoms of COVID-19: a systematic overview of systematic reviews, comparison with other neurological conditions and implications for healthcare services. *Ther Adv Chronic Dis*. 2021 Jan 28;12:2040622320976979. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7970685>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33796241?tool=bestpractice.bmj.com>)
1149. Cabrera Martimbianco AL, Pacheco RL, Bagattini ÂM, et al. Frequency, signs and symptoms, and criteria adopted for long COVID: a systematic review. *Int J Clin Pract*. 2021 May 11 [Epub ahead of print]. Full text (<https://onlinelibrary.wiley.com/doi/10.1111/ijcp.14357>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33977626?tool=bestpractice.bmj.com>)
1150. Iqbal FM, Lam K, Sounderajah V, et al. Characteristics and predictors of acute and chronic post-COVID syndrome: a systematic review and meta-analysis. *EClinicalMedicine*. 2021 Jun;36:100899. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8141371>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34036253?tool=bestpractice.bmj.com>)
1151. Aminian A, Bena J, Pantalone KM, et al. Association of obesity with post-acute sequelae of COVID-19 (PASC). *Diabetes Obes Metab*. 2021 Jun 1 [Epub ahead of print]. Full text (<https://dom-pubs.onlinelibrary.wiley.com/doi/10.1111/dom.14454>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34060194?tool=bestpractice.bmj.com>)

1152. Whitaker M, Elliott J, Chadeau-Hyam M, et al; Imperial College London. Persistent symptoms following SARS-CoV-2 infection in a random community sample of 508,707 people. 2021 [internet publication]. Full text (https://spiral.imperial.ac.uk/bitstream/10044/1/89844/9/REACT_long_covid_paper_final.pdf)
1153. Fernández-de-Las-Peñas C, Palacios-Ceña D, Gómez-Mayordomo V, et al. Prevalence of post-COVID-19 symptoms in hospitalized and non-hospitalized COVID-19 survivors: a systematic review and meta-analysis. *Eur J Intern Med*. 2021 Jun 16 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8206636>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34167876?tool=bestpractice.bmj.com>)
1154. Wu X, Liu X, Zhou Y, et al. 3-month, 6-month, 9-month, and 12-month respiratory outcomes in patients following COVID-19-related hospitalisation: a prospective study. *Lancet Respir Med*. 2021 May 5 [Epub ahead of print]. Full text ([https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00174-0/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00174-0/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33964245?tool=bestpractice.bmj.com>)
1155. Havervall S, Rosell A, Phillipson M, et al. Symptoms and functional impairment assessed 8 months after mild COVID-19 among health care workers. *JAMA*. 2021 Apr 7 Full text (<https://jamanetwork.com/journals/jama/fullarticle/2778528>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33825846?tool=bestpractice.bmj.com>)
1156. Augustin M, Schommers P, Stecher M, et al. Post-COVID syndrome in non-hospitalised patients with COVID-19: a longitudinal prospective cohort study. *Lancet Reg Health Eur*. 2021 Jul;6:100122. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8129613>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34027514?tool=bestpractice.bmj.com>)
1157. Stavem K, Ghanima W, Olsen MK, et al. Persistent symptoms 1.5 to 6 months after COVID-19 in non-hospitalised subjects: a population-based cohort study. *Thorax*. 2020 Dec 3;76(4):405-7. Full text (<https://thorax.bmj.com/content/76/4/405.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33273028?tool=bestpractice.bmj.com>)
1158. Ludvigsson JF. Case report and systematic review suggest that children may experience similar long-term effects to adults after clinical COVID-19. *Acta Paediatr*. 2021 Mar;110(3):914-21. Full text (<https://onlinelibrary.wiley.com/doi/10.1111/apa.15673>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33205450?tool=bestpractice.bmj.com>)
1159. Radtke T, Ulyte A, Puhan MA, et al. Long-term symptoms after SARS-CoV-2 infection in children and adolescents. *JAMA*. 2021 Jul 15 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2782164>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34264266?tool=bestpractice.bmj.com>)
1160. Greenhalgh T, Knight M, A'Court C, et al. Management of post-acute covid-19 in primary care. *BMJ*. 2020 Aug 11;370:m3026. Full text (<https://www.bmj.com/content/370/bmj.m3026>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32784198?tool=bestpractice.bmj.com>)
1161. Weng J, Li Y, Li J, et al. Gastrointestinal sequelae 90 days after discharge for COVID-19. *Lancet Gastroenterol Hepatol*. 2021 May;6(5):344-6. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7943402>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33711290?tool=bestpractice.bmj.com>)

1162. Chopra V, Flanders SA, O'Malley M, et al. Sixty-day outcomes among patients hospitalized with COVID-19. *Ann Intern Med.* 2021 Apr;174(4):576-8. [Full text \(https://www.acpjournals.org/doi/10.7326/M20-5661\)](https://www.acpjournals.org/doi/10.7326/M20-5661) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33175566?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33175566?tool=bestpractice.bmj.com)
1163. So M, Kabata H, Fukunaga K, et al. Radiological and functional lung sequelae of COVID-19: a systematic review and meta-analysis. *BMC Pulm Med.* 2021 Mar 22;21(1):97. [Full text \(https://bmcpulmed.biomedcentral.com/articles/10.1186/s12890-021-01463-0\)](https://bmcpulmed.biomedcentral.com/articles/10.1186/s12890-021-01463-0) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33752639?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33752639?tool=bestpractice.bmj.com)
1164. Mandal S, Barnett J, Brill SE, et al. 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. *Thorax.* 2020 Nov 10 [Epub ahead of print]. [Full text \(https://thorax.bmj.com/content/early/2020/11/09/thoraxjnl-2020-215818\)](https://thorax.bmj.com/content/early/2020/11/09/thoraxjnl-2020-215818) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33172844?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33172844?tool=bestpractice.bmj.com)
1165. Hayek SS, Brenner SK, Azam TU, et al. In-hospital cardiac arrest in critically ill patients with covid-19: multicenter cohort study. *BMJ.* 2020 Sep 30;371:m3513. [Full text \(https://www.bmj.com/content/371/bmj.m3513\)](https://www.bmj.com/content/371/bmj.m3513) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32998872?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32998872?tool=bestpractice.bmj.com)
1166. Karakike E, Giamarellos-Bourboulis EJ, Kyprianou M, et al. Coronavirus disease 2019 as cause of viral sepsis: a systematic review and meta-analysis. *Crit Care Med.* 2021 Jul 12 [Epub ahead of print]. [Full text \(https://journals.lww.com/ccmjournal/Abstract/9000/Coronavirus_Disease_2019_as_Cause_of_Viral_Sepsis_.95156.aspx\)](https://journals.lww.com/ccmjournal/Abstract/9000/Coronavirus_Disease_2019_as_Cause_of_Viral_Sepsis_.95156.aspx) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34259663?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34259663?tool=bestpractice.bmj.com)
1167. Song JC, Wang G, Zhang W, et al. Chinese expert consensus on diagnosis and treatment of coagulation dysfunction in COVID-19. *Mil Med Res.* 2020 Apr 20;7(1):19. [Full text \(https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-020-00247-7\)](https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-020-00247-7) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32307014?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32307014?tool=bestpractice.bmj.com)
1168. Zhou X, Cheng Z, Luo L, et al. Incidence and impact of disseminated intravascular coagulation in COVID-19 a systematic review and meta-analysis. *Thromb Res.* 2021 Feb 17;201:23-9. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7886625\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7886625) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33631519?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33631519?tool=bestpractice.bmj.com)
1169. Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. *Blood.* 2020 Jun 4;135(23):2033-40. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7273827\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7273827) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32339221?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32339221?tool=bestpractice.bmj.com)
1170. Tang N, Bai H, Chen X, et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. *J Thromb Haemost.* 2020 May;18(5):1094-9. [Full text \(https://onlinelibrary.wiley.com/doi/abs/10.1111/jth.14817\)](https://onlinelibrary.wiley.com/doi/abs/10.1111/jth.14817) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32220112?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32220112?tool=bestpractice.bmj.com)
1171. Ippolito M, Misseri G, Catalisano G, et al. Ventilator-associated pneumonia in patients with COVID-19: a systematic review and meta-analysis. *Antibiotics (Basel).* 2021 May 7;10(5):545. [Full text](#)

(<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8150614>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34067186?tool=bestpractice.bmj.com>)

1172. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the 'cytokine storm' in COVID-19. *J Infect.* 2020 Jun;80(6):607-13. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7194613>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32283152?tool=bestpractice.bmj.com>)
1173. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ.* 2020 Mar 26;368:m1091. Full text (<https://www.bmj.com/content/368/bmj.m1091.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32217556?tool=bestpractice.bmj.com>)
1174. Wang Z, Yang B, Li Q, et al. Clinical features of 69 cases with coronavirus disease 2019 in Wuhan, China. *Clin Infect Dis.* 2020 Jul 28;71(15):769-77. Full text (<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa272/5807944>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32176772?tool=bestpractice.bmj.com>)
1175. Aziz M, Fatima R, Assaly R. Elevated interleukin-6 and severe COVID-19: a meta-analysis. *J Med Virol.* 2020 Nov;92(11):2283-5. Full text (<https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25948>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32343429?tool=bestpractice.bmj.com>)
1176. Pedersen SF, Ho YC. SARS-CoV-2: a storm is raging. *J Clin Invest.* 2020 May 1;130(5):2202-5. Full text (<https://www.jci.org/articles/view/137647/pdf>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32217834?tool=bestpractice.bmj.com>)
1177. Leisman DE, Ronner L, Pinotti R, et al. Cytokine elevation in severe and critical COVID-19: a rapid systematic review, meta-analysis, and comparison with other inflammatory syndromes. *Lancet Respir Med.* 2020 Dec;8(12):1233-44. Full text ([https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30404-5/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30404-5/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33075298?tool=bestpractice.bmj.com>)
1178. Pain CE, Felsenstein S, Cleary G, et al. Novel paediatric presentation of COVID-19 with ARDS and cytokine storm syndrome without respiratory symptoms. *Lancet Rheumatol.* 2020 May 15;2(7):e376-9. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7228732>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32427161?tool=bestpractice.bmj.com>)
1179. Abrams JY, Godfred-Cato SE, Oster ME, et al. Multisystem inflammatory syndrome in children associated with severe acute respiratory syndrome coronavirus 2: a systematic review. *J Pediatr.* 2020 Aug 5;226:45-54. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7403869>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32768466?tool=bestpractice.bmj.com>)
1180. Godfred-Cato S, Bryant B, Leung J, et al. COVID-19-associated multisystem inflammatory syndrome in children: United States, March–July 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Aug 14;69(32):1074-80. Full text (<https://www.cdc.gov/mmwr/volumes/69/wr/mm6932e2.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32790663?tool=bestpractice.bmj.com>)
1181. Jiang L, Tang K, Levin M, et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. *Lancet Infect Dis.* 2020 Nov;20(11):e276-88. Full text (<https://www.thelancet.com/>)

journals/laninf/article/PIIS1473-3099(20)30651-4/fulltext) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32818434?tool=bestpractice.bmj.com>)

1182. Belay ED, Abrams J, Oster ME, et al. Trends in geographic and temporal distribution of US children with multisystem inflammatory syndrome during the COVID-19 pandemic. *JAMA Pediatr.* 2021 Apr 6 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2778429>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33821923?tool=bestpractice.bmj.com>)
1183. Royal College of Paediatrics and Child Health. Guidance: paediatric multisystem inflammatory syndrome temporally associated with COVID-19. 2020 [internet publication]. Full text (<https://www.rcpch.ac.uk/resources/guidance-paediatric-multisystem-inflammatory-syndrome-temporally-associated-covid-19>)
1184. Centers for Disease Control and Prevention. Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19). 2020 [internet publication]. Full text (<https://emergency.cdc.gov/han/2020/han00432.asp>)
1185. Young TK, Shaw KS, Shah JK, et al. Mucocutaneous manifestations of multisystem inflammatory syndrome in children during the COVID-19 pandemic. *JAMA Dermatol.* 2021 Feb 1;157(2):207-12. Full text (<https://jamanetwork.com/journals/jamadermatology/fullarticle/2773994>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33295957?tool=bestpractice.bmj.com>)
1186. Zou H, Lu J, Liu J, et al. Characteristics of pediatric multi-system inflammatory syndrome (PMIS) associated with COVID-19: a meta-analysis and insights into pathogenesis. *Int J Infect Dis.* 2021 Jan;102:319-26. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7666570>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33202218?tool=bestpractice.bmj.com>)
1187. Yasuhara J, Watanabe K, Takagi H, et al. COVID-19 and multisystem inflammatory syndrome in children: a systematic review and meta-analysis. *Pediatr Pulmonol.* 2021 May;56(5):837-48. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8013394>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33428826?tool=bestpractice.bmj.com>)
1188. Davies P, Evans C, Kanthimathinathan HK, et al. Intensive care admissions of children with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in the UK: a multicentre observational study. *Lancet Child Adolesc Health.* 2020 Sep;4(9):669-77. Full text ([https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(20\)30215-7/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30215-7/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32653054?tool=bestpractice.bmj.com>)
1189. Centers for Disease Control and Prevention. Health department: reported cases of multisystem inflammatory syndrome in children (MIS-C) in the United States. 2021 [internet publication]. Full text (<https://www.cdc.gov/mis-c/cases/index.html>)
1190. Feldstein LR, Tenforde MW, Friedman KG, et al. Characteristics and outcomes of US children and adolescents with multisystem inflammatory syndrome in children (MIS-C) compared with severe acute COVID-19. *JAMA.* 2021 Mar 16;325(11):1074-87. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2777026>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33625505?tool=bestpractice.bmj.com>)

1191. Abrams JY, Oster ME, Godfred-Cato SE, et al. Factors linked to severe outcomes in multisystem inflammatory syndrome in children (MIS-C) in the USA: a retrospective surveillance study. *Lancet Child Adolesc Health*. 2021 May;5(5):323-31. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7943393\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7943393) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33711293?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33711293?tool=bestpractice.bmj.com)
1192. Valverde I, Singh Y, Sanchez-de-Toledo J, et al. Acute cardiovascular manifestations in 286 children with multisystem inflammatory syndrome associated with COVID-19 infection in Europe. *Circulation*. 2021 Jan 5;143(1):21-32. [Full text \(https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.050065\)](https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.050065) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33166189?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33166189?tool=bestpractice.bmj.com)
1193. Haghighi Aski B, Manafi Anari A, Abolhasan Choobdar F, et al. Cardiac abnormalities due to multisystem inflammatory syndrome temporally associated with Covid-19 among children: a systematic review and meta-analysis. *Int J Cardiol Heart Vasc*. 2021 Mar 22:100764. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7983575\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7983575) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33778151?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33778151?tool=bestpractice.bmj.com)
1194. Harwood R, Allin B, Jones CE, et al. A national consensus management pathway for paediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS): results of a national Delphi process. *Lancet Child Adolesc Health*. 2021 Feb;5(2):133-41. [Full text \(https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(20\)30304-7/fulltext\)](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30304-7/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32956615?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32956615?tool=bestpractice.bmj.com)
1195. Son MBF, Murray N, Friedman K, et al. Multisystem inflammatory syndrome in children: initial therapy and outcomes. *N Engl J Med*. 2021 Jun 16 [Epub ahead of print]. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2102605\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2102605) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34133855?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34133855?tool=bestpractice.bmj.com)
1196. McArdle AJ, Vito O, Patel H, et al. Treatment of multisystem inflammatory syndrome in children. *N Engl J Med*. 2021 Jun 16 [Epub ahead of print]. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMoa2102968\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2102968) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34133854?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34133854?tool=bestpractice.bmj.com)
1197. Henderson LA, Canna SW, Friedman KG, et al. American College of Rheumatology clinical guidance for multisystem inflammatory syndrome in children associated with SARS-CoV-2 and hyperinflammation in pediatric COVID-19: version 2. *Arthritis Rheumatol*. 2021 Apr;73(4):e13-29. [Full text \(https://onlinelibrary.wiley.com/doi/10.1002/art.41616\)](https://onlinelibrary.wiley.com/doi/10.1002/art.41616) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33277976?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33277976?tool=bestpractice.bmj.com)
1198. Penner J, Abdel-Mannan O, Grant K, et al. 6-month multidisciplinary follow-up and outcomes of patients with paediatric inflammatory multisystem syndrome (PIMS-TS) at a UK tertiary paediatric hospital: a retrospective cohort study. *Lancet Child Adolesc Health*. 2021 May 24 [Epub ahead of print]. [Full text \(https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(21\)00138-3/fulltext\)](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(21)00138-3/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34043958?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34043958?tool=bestpractice.bmj.com)
1199. Shulman ST. Pediatric coronavirus disease-2019-associated multisystem inflammatory syndrome. *J Pediatric Infect Dis Soc*. 2020 Jul 13;9(3):285-6. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7313948\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7313948) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32441751?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32441751?tool=bestpractice.bmj.com)

1200. Carter MJ, Fish M, Jennings A, et al. Peripheral immunophenotypes in children with multisystem inflammatory syndrome associated with SARS-CoV-2 infection. *Nat Med*. 2020 Nov;26(11):1701-7. Full text (<https://www.nature.com/articles/s41591-020-1054-6>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32812012?tool=bestpractice.bmj.com>)
1201. Kappanayil M, Balan S, Alawani S, et al. Multisystem inflammatory syndrome in a neonate, temporally associated with prenatal exposure to SARS-CoV-2: a case report. *Lancet Child Adolesc Health*. 2021 Apr;5(4):304-8. Full text ([https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(21\)00055-9/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(21)00055-9/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33675696?tool=bestpractice.bmj.com>)
1202. Divekar AA, Patamasucon P, Benjamin JS. Presumptive neonatal multisystem inflammatory syndrome in children associated with coronavirus disease 2019. *Am J Perinatol*. 2021 May;38(6):632-6. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33757142?tool=bestpractice.bmj.com>)
1203. Morris SB, Schwartz NG, Patel P, et al. Case series of multisystem inflammatory syndrome in adults associated with SARS-CoV-2 infection: United Kingdom and United States, March–August 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Oct 9;69(40):1450-6. Full text (<https://www.cdc.gov/mmwr/volumes/69/wr/mm6940e1.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33031361?tool=bestpractice.bmj.com>)
1204. Davogustto GE, Clark DE, Hardison E, et al. Characteristics associated with multisystem inflammatory syndrome among adults with SARS-CoV-2 infection. *JAMA Netw Open*. 2021 May 3;4(5):e2110323. Full text (<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2779957>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34009351?tool=bestpractice.bmj.com>)
1205. Schultz NH, Sørvoll IH, Michelsen AE, et al. Thrombosis and thrombocytopenia after ChAdOx1 nCoV-19 vaccination. *N Engl J Med*. 2021 Apr 9 [Epub ahead of print]. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMoa2104882>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33835768?tool=bestpractice.bmj.com>)
1206. Greinacher A, Thiele T, Warkentin TE, et al. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. *N Engl J Med*. 2021 Apr 9 [Epub ahead of print]. Full text (<https://www.nejm.org/doi/full/10.1056/NEJMoa2104840>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33835769?tool=bestpractice.bmj.com>)
1207. Pottegård A, Lund LC, Karlstad Ø, et al. Arterial events, venous thromboembolism, thrombocytopenia, and bleeding after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: population based cohort study. *BMJ*. 2021 May 5;373:n1114. Full text (<https://www.bmj.com/content/373/bmj.n1114>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33952445?tool=bestpractice.bmj.com>)
1208. British Society for Haematology. Guidance from the expert haematology panel (EHP) on Covid-19 vaccine-induced immune thrombocytopenia and thrombosis (VITT). 2021 [internet publication]. Full text (<https://b-s-h.org.uk/media/19590/guidance-version-17-on-mngmt-of-vitt-20210420.pdf>)
1209. American Society of Hematology. Thrombosis with thrombocytopenia syndrome (also termed vaccine-induced thrombotic thrombocytopenia). 2021 [internet publication]. Full text (<https://www.hematology.org/covid-19/vaccine-induced-immune-thrombotic-thrombocytopenia>)

1210. The Royal College of Emergency Medicine. Management of patients presenting to the emergency department/acute medicine with symptoms of Covid-19 vaccine induced thrombosis and thrombocytopenia (VITT). 2021 [internet publication]. [Full text \(https://www.rcem.ac.uk/docs/Policy/ED-AM%20%20Vaccine%20pathway%20concerns%20-%20RCP%20-%20SAM%20-%20RCEM.pdf\)](https://www.rcem.ac.uk/docs/Policy/ED-AM%20%20Vaccine%20pathway%20concerns%20-%20RCP%20-%20SAM%20-%20RCEM.pdf)
1211. American Heart Association/American Stroke Association Stroke Council Leadership. Diagnosis and management of cerebral venous sinus thrombosis with vaccine-induced immune thrombotic thrombocytopenia. *Stroke*. 2021 Apr 29 [Epub ahead of print]. [Full text \(https://www.ahajournals.org/doi/pdf/10.1161/STROKEAHA.121.035564\)](https://www.ahajournals.org/doi/pdf/10.1161/STROKEAHA.121.035564) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33914590?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33914590?tool=bestpractice.bmj.com)
1212. International Society on Thrombosis and Haemostasis. The ISTH releases interim guidance on vaccine-induced immune thrombotic thrombocytopenia (VITT). 2021 [internet publication]. [Full text \(https://www.isth.org/news/561406/The-ISTH-Releases-Interim-Guidance-on-Vaccine-Induced-Immune-Thrombotic-Thrombocytopenia-VITT-.htm\)](https://www.isth.org/news/561406/The-ISTH-Releases-Interim-Guidance-on-Vaccine-Induced-Immune-Thrombotic-Thrombocytopenia-VITT-.htm)
1213. Huntley BJF, Mulder IA, Di Mascio D, et al. Adverse pregnancy outcomes among individuals with and without severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): a systematic review and meta-analysis. *Obstet Gynecol*. 2021 Apr 1;137(4):585-96. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7984633\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7984633) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33706357?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33706357?tool=bestpractice.bmj.com)
1214. Stowe J, Smith H, Thurland K, et al. Stillbirths during the COVID-19 pandemic in England, April-June 2020. *JAMA*. 2021 Jan 5;325(1):86-7. [Full text \(https://jamanetwork.com/journals/jama/fullarticle/2774088\)](https://jamanetwork.com/journals/jama/fullarticle/2774088) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33284314?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33284314?tool=bestpractice.bmj.com)
1215. Dhir SK, Kumar J, Meena J, et al. Clinical features and outcome of SARS-CoV-2 infection in neonates: a systematic review. *J Trop Pediatr*. 2020 Aug 28 [Epub ahead of print]. [Full text \(https://academic.oup.com/tropej/advance-article/doi/10.1093/tropej/fmaa059/5898408\)](https://academic.oup.com/tropej/advance-article/doi/10.1093/tropej/fmaa059/5898408) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32856065?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32856065?tool=bestpractice.bmj.com)
1216. Koehler P, Cornely OA, Böttiger BW, et al. COVID-19 associated pulmonary aspergillosis. *Mycoses*. 2020 Jun;63(6):528-34. [Full text \(https://onlinelibrary.wiley.com/doi/abs/10.1111/myc.13096\)](https://onlinelibrary.wiley.com/doi/abs/10.1111/myc.13096) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32339350?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32339350?tool=bestpractice.bmj.com)
1217. Blaize M, Mayaux J, Nabet C, et al. Fatal invasive aspergillosis and coronavirus disease in an immunocompetent patient. *Emerg Infect Dis*. 2020 Apr 28;26(7). [Full text \(https://wwwnc.cdc.gov/eid/article/26/7/20-1603_article\)](https://wwwnc.cdc.gov/eid/article/26/7/20-1603_article) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32343223?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32343223?tool=bestpractice.bmj.com)
1218. van Arkel ALE, Rijpstra TA, Belderbos HNA, et al. COVID-19-associated pulmonary aspergillosis. *Am J Respir Crit Care Med*. 2020 Jul 1;202(1):132-5. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7328331\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7328331) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32396381?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32396381?tool=bestpractice.bmj.com)
1219. Mitaka H, Kuno T, Takagi H, et al. Incidence and mortality of COVID-19-associated pulmonary aspergillosis: a systematic review and meta-analysis. *Mycoses*. 2021 Apr 25 [Epub ahead

- of print]. Full text (<https://onlinelibrary.wiley.com/doi/10.1111/myc.13292>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33896063?tool=bestpractice.bmj.com>)
1220. Wang J, Yang Q, Zhang P, et al. Clinical characteristics of invasive pulmonary aspergillosis in patients with COVID-19 in Zhejiang, China: a retrospective case series. *Crit Care*. 2020 Jun 5;24(1):299. Full text (<https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-03046-7>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32503617?tool=bestpractice.bmj.com>)
1221. Verweij PE, Gangneux JP, Bassetti M, et al. Diagnosing COVID-19-associated pulmonary aspergillosis. *Lancet Microbe*. 2020 Jun;1(2):e53-5. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7211496>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32835328?tool=bestpractice.bmj.com>)
1222. Bakir Ekinci P, Kara E, Er AG, et al. Challenge in treating COVID-19 associate pulmonary aspergillosis: suprathreshold voriconazole levels. *Br J Clin Pharmacol*. 2021 Jun 26 [Epub ahead of print]. Full text (<https://bpspubs.onlinelibrary.wiley.com/doi/full/10.1111/bcp.14953>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34174111?tool=bestpractice.bmj.com>)
1223. Koehler P, Bassetti M, Chakrabarti A, et al. Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance. *Lancet Infect Dis*. 2020 Dec 14 [Epub ahead of print]. Full text ([https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30847-1/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30847-1/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33333012?tool=bestpractice.bmj.com>)
1224. John TM, Jacob CN, Kontoyiannis DP. When uncontrolled diabetes mellitus and severe COVID-19 converge: the perfect storm for mucormycosis. *J Fungi (Basel)*. 2021 Apr 15;7(4):298. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8071133>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33920755?tool=bestpractice.bmj.com>)
1225. Revannavar SM, P S S, Samaga L, et al. COVID-19 triggering mucormycosis in a susceptible patient: a new phenomenon in the developing world? *BMJ Case Rep*. 2021 Apr 27;14(4):e241663. Full text (<https://casereports.bmj.com/content/14/4/e241663.long>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33906877?tool=bestpractice.bmj.com>)
1226. Raut A, Huy NT. Rising incidence of mucormycosis in patients with COVID-19: another challenge for India amidst the second wave? *Lancet Respir Med*. 2021 Jun 3 [Epub ahead of print]. Full text ([https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00265-4/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00265-4/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34090607?tool=bestpractice.bmj.com>)
1227. Pal R, Singh B, Bhadada SK, et al. COVID-19-associated mucormycosis: an updated systematic review of literature. *Mycoses*. 2021 Jun 16 [Epub ahead of print]. Full text (<https://onlinelibrary.wiley.com/doi/10.1111/myc.13338>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34133798?tool=bestpractice.bmj.com>)
1228. Singh AK, Singh R, Joshi SR, et al. Mucormycosis in COVID-19: a systematic review of cases reported worldwide and in India. *Diabetes Metab Syndr*. 2021 May 21;15(4):102146. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8137376>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/34192610?tool=bestpractice.bmj.com>)

1229. Indian Council of Medical Research. Evidence based advisory in the time of COVID-19 (screening, diagnosis and management of mucormycosis). 2021 [internet publication]. Full text (https://www.icmr.gov.in/pdf/covid/techdoc/Mucormycosis_ADVISORY_FROM_ICMR_In_COVID19_time.pdf)
1230. Wang F, Wang H, Fan J, et al. Pancreatic injury patterns in patients with COVID-19 pneumonia. *Gastroenterology*. 2020 Apr 1;159(1):367-70. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7118654>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32247022?tool=bestpractice.bmj.com>)
1231. Bircakova B, Bruha R, Lambert L, et al. A bimodal pattern of the onset of COVID-19 related acute pancreatitis supports both the cytotoxic and immune-related pathogenesis: a systematic review. *Scand J Gastroenterol*. 2021 May 14 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8127174>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33989101?tool=bestpractice.bmj.com>)
1232. Gubatan J, Levitte S, Patel A, et al. Prevalence, risk factors and clinical outcomes of COVID-19 in patients with a history of pancreatitis in Northern California. *Gut*. 2021 Feb;70(2):440-1. Full text (<https://gut.bmj.com/content/70/2/440>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32493828?tool=bestpractice.bmj.com>)
1233. Lazarian G, Quinquenel A, Bellal M, et al. Autoimmune haemolytic anaemia associated with COVID-19 infection. *Br J Haematol*. 2020 Jul;190(1):29-31. Full text (<https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.16794>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32374906?tool=bestpractice.bmj.com>)
1234. Bhattacharjee S, Banerjee M. Immune thrombocytopenia secondary to COVID-19: a systematic review. *SN Compr Clin Med*. 2020 Sep 19:1-11. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7501509>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32984764?tool=bestpractice.bmj.com>)
1235. Aemaz Ur Rehman M, Farooq H, Ali MM, et al. The association of subacute thyroiditis with COVID-19: a systematic review. *SN Compr Clin Med*. 2021 Apr 29:1-13. Full text (<https://link.springer.com/article/10.1007/s42399-021-00912-5>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33942028?tool=bestpractice.bmj.com>)
1236. Giovanella L, Ruggeri RM, Ovčariček PP, et al. Prevalence of thyroid dysfunction in patients with COVID-19: a systematic review. *Clin Transl Imaging*. 2021 Mar 11:1-8. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7950424>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33728279?tool=bestpractice.bmj.com>)
1237. El Moheb M, Naar L, Christensen MA, et al. Gastrointestinal complications in critically ill patients with and without COVID-19. *JAMA*. 2020 Sep 24;324(18):1899-901. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2771160>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32970139?tool=bestpractice.bmj.com>)
1238. Keshavarz P, Rafiee F, Kavandi H, et al. Ischemic gastrointestinal complications of COVID-19: a systematic review on imaging presentation. *Clin Imaging*. 2020 Dec 8;73:86-95. Full text ([https://www.clinicalimaging.org/article/S0899-7071\(20\)30505-2/fulltext](https://www.clinicalimaging.org/article/S0899-7071(20)30505-2/fulltext)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33341452?tool=bestpractice.bmj.com>)

1239. Centre for Evidence-Based Medicine; Greenhalgh T, Treadwell J, Burrow R, et al. NEWS (or NEWS2) score when assessing possible COVID-19 patients in primary care? 2020 [internet publication].
Full text (<https://www.cebm.net/covid-19/should-we-use-the-news-or-news2-score-when-assessing-patients-with-possible-covid-19-in-primary-care>)
1240. Raschke RA, Agarwal S, Rangan P, et al. Discriminant accuracy of the SOFA score for determining the probable mortality of patients with COVID-19 pneumonia requiring mechanical ventilation. JAMA. 2021 Feb 17 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jama/fullarticle/2776737>)
Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33595630?tool=bestpractice.bmj.com>)
1241. George PM, Barratt SL, Condliffe R, et al. Respiratory follow-up of patients with COVID-19 pneumonia. Thorax. 2020 Nov;75(11):1009-16. Full text (<https://thorax.bmj.com/content/75/11/1009.long>)
Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32839287?tool=bestpractice.bmj.com>)
1242. Shah AS, Wong AW, Hague CJ, et al. A prospective study of 12-week respiratory outcomes in COVID-19-related hospitalisations. Thorax. 2020 Dec 3 [Epub ahead of print]. Full text (<https://thorax.bmj.com/content/early/2020/12/02/thoraxjnl-2020-216308>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33273023?tool=bestpractice.bmj.com>)
1243. Torres-Castro R, Vasconcello-Castillo L, Alsina-Restoy X, et al. Respiratory function in patients post-infection by COVID-19: a systematic review and meta-analysis. Pulmonology. 2020 Nov 25 [Epub ahead of print]. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7687368>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33262076?tool=bestpractice.bmj.com>)
1244. Fan G, Tu C, Zhou F, et al. Comparison of severity scores for COVID-19 patients with pneumonia: a retrospective study. Eur Respir J. 2020 Sep 10;56(3):2002113. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7366179>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32675205?tool=bestpractice.bmj.com>)
1245. Zou X, Li S, Fang M, et al. Acute physiology and chronic health evaluation II score as a predictor of hospital mortality in patients of coronavirus disease 2019. Crit Care Med. 2020 May 1;48(8):e657-65. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7217128>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32371611?tool=bestpractice.bmj.com>)
1246. Ji D, Zhang D, Xu J, et al. Prediction for progression risk in patients with COVID-19 pneumonia: the CALL score. Clin Infect Dis. 2020 Sep 12;71(6):1393-99. Full text (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7184473>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32271369?tool=bestpractice.bmj.com>)
1247. Liang W, Liang H, Ou L, et al. Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with COVID-19. JAMA Intern Med. 2020 Aug 1;180(8):1081-9. Full text (<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2766086>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/32396163?tool=bestpractice.bmj.com>)
1248. Moreno-Pérez Ó, Andrés M, León-Ramírez JM, et al. The COVID-GRAM tool for patients hospitalized with COVID-19 in Europe. JAMA Intern Med. 2021 Apr 5 [Epub ahead of print]. Full text (<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2778370>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/33818609?tool=bestpractice.bmj.com>)

1249. Fumagalli C, Rozzini R, Vannini M, et al. Clinical risk score to predict in-hospital mortality in COVID-19 patients: a retrospective cohort study. *BMJ Open*. 2020 Sep 25;10(9):e040729. [Full text \(https://bmjopen.bmj.com/content/10/9/e040729\)](https://bmjopen.bmj.com/content/10/9/e040729) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32978207?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32978207?tool=bestpractice.bmj.com)
1250. Berenguer J, Borobia AM, Ryan P, et al. Development and validation of a prediction model for 30-day mortality in hospitalised patients with COVID-19: the COVID-19 SEIMC score. *Thorax*. 2021 Feb 25 [Epub ahead of print]. [Full text \(https://thorax.bmj.com/content/early/2021/02/25/thoraxjnl-2020-216001\)](https://thorax.bmj.com/content/early/2021/02/25/thoraxjnl-2020-216001) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33632764?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33632764?tool=bestpractice.bmj.com)
1251. Clift AK, Coupland CAC, Keogh RH, et al. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. *BMJ*. 2020 Oct 20;371:m3731. [Full text \(https://www.bmj.com/content/371/bmj.m3731\)](https://www.bmj.com/content/371/bmj.m3731) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33082154?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33082154?tool=bestpractice.bmj.com)
1252. Nafilyan V, Humberstone B, Mehta N, et al. An external validation of the QCovid risk prediction algorithm for risk of mortality from COVID-19 in adults: a national validation cohort study in England. *Lancet Digit Health*. 2021 May 25 [Epub ahead of print]. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8148652\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8148652) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34049834?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34049834?tool=bestpractice.bmj.com)
1253. Department of Health and Social Care. New technology to help identify those at high risk from COVID-19. 2021 [internet publication]. [Full text \(https://www.gov.uk/government/news/new-technology-to-help-identify-those-at-high-risk-from-covid-19\)](https://www.gov.uk/government/news/new-technology-to-help-identify-those-at-high-risk-from-covid-19)
1254. Wongvibulsin S, Garibaldi BT, Antar AAR, et al. Development of severe COVID-19 adaptive risk predictor (SCARP), a calculator to predict severe disease or death in hospitalized patients with COVID-19. *Ann Intern Med*. 2021 Mar 2 [Epub ahead of print]. [Full text \(https://www.acpjournals.org/doi/10.7326/M20-6754\)](https://www.acpjournals.org/doi/10.7326/M20-6754) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33646849?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33646849?tool=bestpractice.bmj.com)
1255. Chua F, Vancheeswaran R, Draper A, et al. Early prognostication of COVID-19 to guide hospitalisation versus outpatient monitoring using a point-of-test risk prediction score. *Thorax*. 2021 Mar 10 [Epub ahead of print]. [Full text \(https://thorax.bmj.com/content/early/2021/03/09/thoraxjnl-2020-216425\)](https://thorax.bmj.com/content/early/2021/03/09/thoraxjnl-2020-216425) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33692174?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33692174?tool=bestpractice.bmj.com)
1256. Yadaw AS, Li YC, Bose S, et al. Clinical features of COVID-19 mortality: development and validation of a clinical prediction model. *Lancet Digit Health*. 2020 Oct;2(10):e516-25. [Full text \(https://www.thelancet.com/journals/landig/article/PIIS2589-7500\(20\)30217-X/fulltext\)](https://www.thelancet.com/journals/landig/article/PIIS2589-7500(20)30217-X/fulltext) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32984797?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32984797?tool=bestpractice.bmj.com)
1257. Knight SR, Ho A, Pius R, et al. Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO clinical characterisation protocol: development and validation of the 4C mortality score. *BMJ*. 2020 Sep 9;370:m3339. [Full text \(https://www.bmj.com/content/370/bmj.m3339\)](https://www.bmj.com/content/370/bmj.m3339) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32907855?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32907855?tool=bestpractice.bmj.com)

1258. Centers for Disease Control and Prevention. One health toolkit for health officials managing companion animals with SARS-CoV-2. 2021 [internet publication]. [Full text \(https://www.cdc.gov/coronavirus/2019-ncov/animals/toolkit.html\)](https://www.cdc.gov/coronavirus/2019-ncov/animals/toolkit.html)
1259. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): COVID-19 and animals. 2021 [internet publication]. [Full text \(https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/animals.html\)](https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/animals.html)
1260. Shi J, Wen Z, Zhong G, et al. Susceptibility of ferrets, cats, dogs, and other domesticated animals to SARS-coronavirus 2. *Science*. 2020 May 29;368(6494):1016-20. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7164390\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7164390) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32269068?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32269068?tool=bestpractice.bmj.com)
1261. IDEXX Laboratories. Leading veterinary diagnostic company sees no COVID-19 cases in pets. 2020 [internet publication]. [Full text \(https://www.idexx.com.au/en-au/about-idexx/no-covid-19-cases-pets\)](https://www.idexx.com.au/en-au/about-idexx/no-covid-19-cases-pets)
1262. Newman A, Smith D, Ghai RR, et al. First reported cases of SARS-CoV-2 infection in companion animals: New York, March-April 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Jun 12;69(23):710-3. [Full text \(https://www.cdc.gov/mmwr/volumes/69/wr/mm6923e3.htm?s_cid=mm6923e3_w\)](https://www.cdc.gov/mmwr/volumes/69/wr/mm6923e3.htm?s_cid=mm6923e3_w) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32525853?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32525853?tool=bestpractice.bmj.com)
1263. Halfmann PJ, Hatta M, Chiba S, et al. Transmission of SARS-CoV-2 in domestic cats. *N Engl J Med*. 2020 Aug 6;383(6):592-4. [Full text \(https://www.nejm.org/doi/full/10.1056/NEJMc2013400\)](https://www.nejm.org/doi/full/10.1056/NEJMc2013400) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32402157?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32402157?tool=bestpractice.bmj.com)
1264. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): if you have pets. 2021 [internet publication]. [Full text \(https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/pets.html\)](https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/pets.html)
1265. Salman D, Vishnubala D, Le Feuvre P, et al. Returning to physical activity after covid-19. *BMJ*. 2021 Jan 8;372:m4721. [Full text \(https://www.bmj.com/content/372/bmj.m4721\)](https://www.bmj.com/content/372/bmj.m4721) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33419740?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33419740?tool=bestpractice.bmj.com)
1266. Daniels CJ, Rajpal S, Greenshields JT, et al. Prevalence of clinical and subclinical myocarditis in competitive athletes with recent SARS-CoV-2 infection: results from the Big Ten COVID-19 Cardiac Registry. *JAMA Cardiol*. 2021 May 27 [Epub ahead of print]. [Full text \(https://jamanetwork.com/journals/jamacardiology/fullarticle/2780548\)](https://jamanetwork.com/journals/jamacardiology/fullarticle/2780548) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34042947?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34042947?tool=bestpractice.bmj.com)

Images

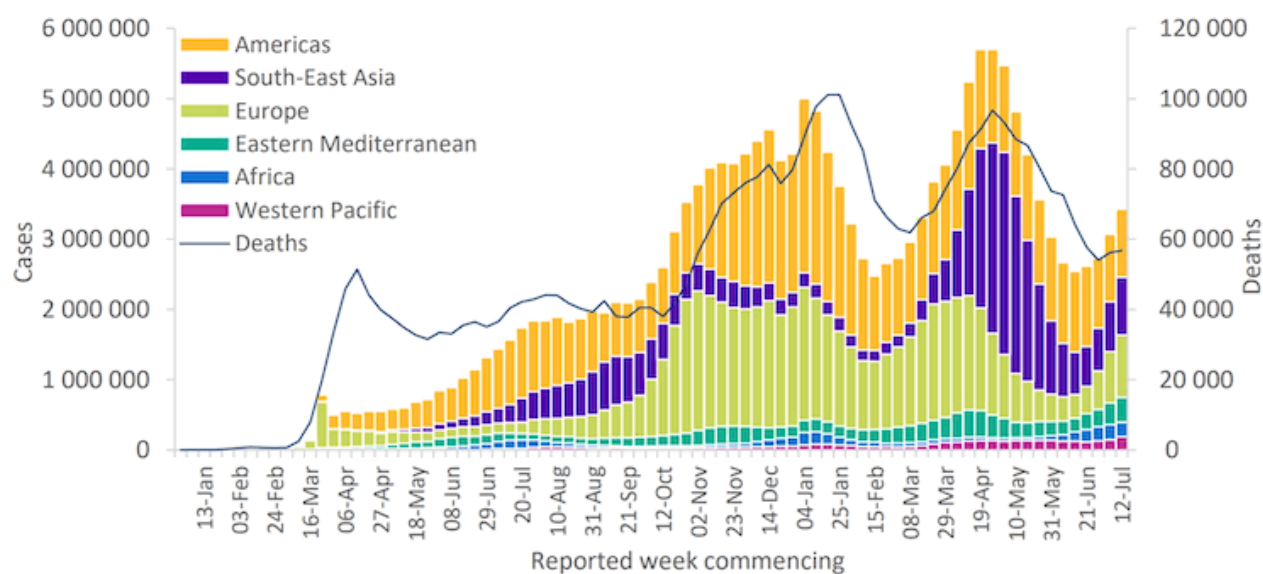


Figure 1: Number of COVID-19 cases reported weekly by WHO Region, and global deaths, as of 18 July 2021

World Health Organization

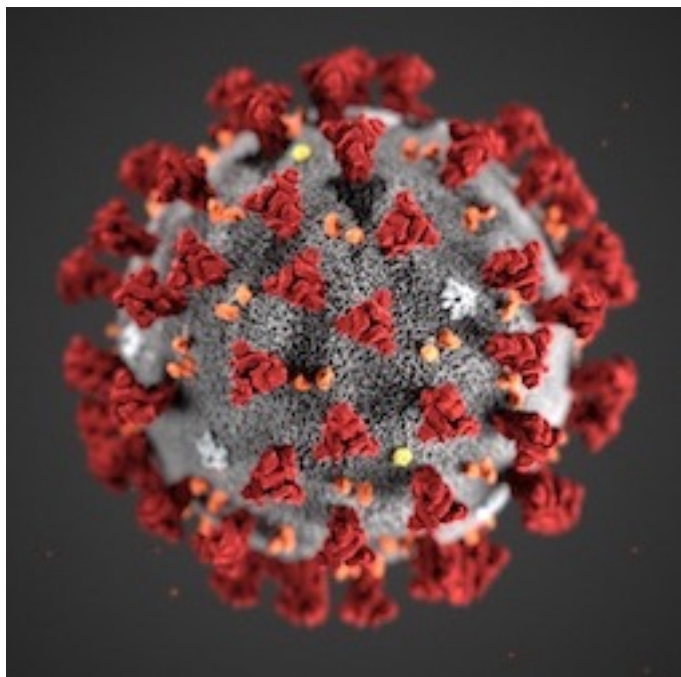


Figure 2: Illustration revealing ultrastructural morphology exhibited by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) when viewed with electron microscopically

Centers for Disease Control and Prevention

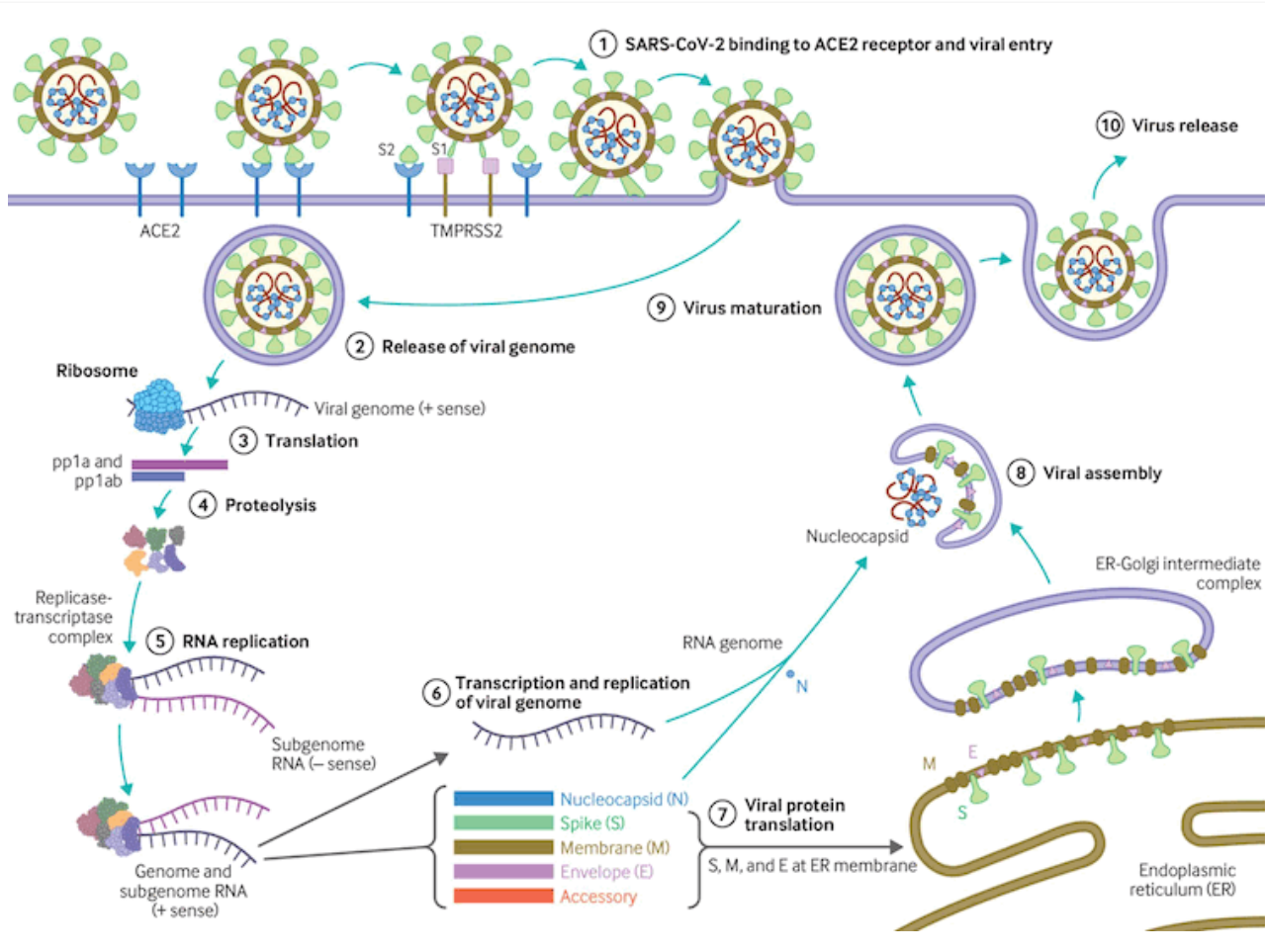


Figure 3: Virus replication cycle

BMJ. 2020;371:m3862

	0-4 years	5-17 years	18-29 years	30-39 years	40-49 years	50-64 years	65-74 years	75-84 years	85+ years
Hospitalization	<1 x	<1 x	Reference group	2x	2x	4x	6x	9x	15x
Death	<1 x	<1 x		4x	10x	35x	95x	230x	610x

Figure 4: Risk for hospitalization and death by age group (rate ratios compared with 18- to 29-year-olds)

Table based on data from the CDC

PFIZER/BIONTECH COVID-19 VACCINE*mRNA vaccine*

Efficacy*	95%	Age	≥12 years
Dose	0.3 mL (30 mcg) IM; second dose at least 3 weeks after		
Contraindications	Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine		
Precautions	History of anaphylaxis/allergic reactions Immunocompromised Pregnancy and breastfeeding History of myocarditis and pericarditis		
Adverse events	<p>Common injection-site reactions; fatigue; headache; myalgia; chills; arthralgia; fever</p> <p>Uncommon nausea; malaise; lymphadenopathy; anaphylaxis; hypersensitivity; myocarditis and pericarditis; diarrhea; vomiting; pain in extremity; acute peripheral facial paralysis; syncope</p>		
Interactions	Interactions with other vaccines/drugs have not been studied. The FDA recommends that COVID-19 vaccines and other vaccines may be administered without regard to timing.		

Figure 5: Information for the Pfizer/BioNTech COVID-19 vaccine is based on the US prescribing information. Consult your local drug formulary or guidelines for more detailed information. *Efficacy in preventing symptomatic infection in people ages 16 years and older according to clinical trials. Last updated: 8 July 2021

BMJ Best Practice editorial team; compiled using data from the US product information

MODERNA COVID-19 VACCINE <i>mRNA vaccine</i>			
Efficacy*	94.1%	Age	≥18 years
Dose	0.5 mL (100 mcg) IM; second dose at least 28 days after		
Contraindications	Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine		
Precautions	History of anaphylaxis/allergic reactions Immunocompromised Pregnancy and breastfeeding History of myocarditis and pericarditis		
Adverse events	Common injection-site reactions; fatigue; headache; myalgia; chills; arthralgia; nausea; vomiting; axillary swelling/tenderness; fever Uncommon lymphadenopathy; anaphylaxis; hypersensitivity; myocarditis and pericarditis; acute peripheral facial paralysis; face swelling (if dermatologic fillers present)		
Interactions	Interactions with other vaccines/drugs have not been studied. The FDA recommends that COVID-19 vaccines and other vaccines may be administered without regard to timing.		

Figure 6: Information for the Moderna COVID-19 vaccine is based on the US prescribing information. Consult your local drug formulary or guidelines for more detailed information. *Efficacy in preventing symptomatic infection in people ages 18 years and older according to clinical trials. Last updated: 8 July 2021

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JANSSEN COVID-19 VACCINE Viral vector vaccine			
Efficacy*	66.9%	Age	≥18 years
Dose	0.5 mL IM (5×10^{10} viral particles) as a single dose		
Contraindications	Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine		
Precautions	History of anaphylaxis/allergic reactions Immunocompromised Pregnancy and breastfeeding		
Adverse events	Common injection-site reactions; headache; fatigue; myalgia; nausea; fever Uncommon severe allergic reactions; anaphylaxis; urticaria; hypersensitivity; pain in extremity; generalized weakness; thrombosis with thrombocytopenia syndrome		
Interactions	Interactions with other vaccines/drugs have not been studied. The FDA recommends that COVID-19 vaccines and other vaccines may be administered without regard to timing.		

Figure 7: Information for the Janssen COVID-19 vaccine is based on the US prescribing information. Consult your local drug formulary or guidelines for more detailed information. *Efficacy in preventing symptomatic infection in people ages 18 years and older according to clinical trials. Last updated: 8 July 2021

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Early effectiveness of covid-19 vaccination

BNT162b2 mRNA and ChAdOx1-S adenovirus vector vaccines

Summary



One dose of either vaccine provides 60-70% protection against symptomatic covid-19 and about 80% protection against hospital admission

Study design



Test negative case-control

Included whole population of over 70s in England (approx. 7.5 million)

Population



153 441 individuals developed symptoms and were tested through community testing (8 Dec to 19 Feb 2021)

Outcomes

- BNT162b2 (Pfizer-BioNTech)
- ChAdOx1-S (Oxford-AstraZeneca)

Symptomatic covid-19 disease

Adjusted odds ratio for confirmed case by interval after vaccination dose 1, administered from 4 January 2021

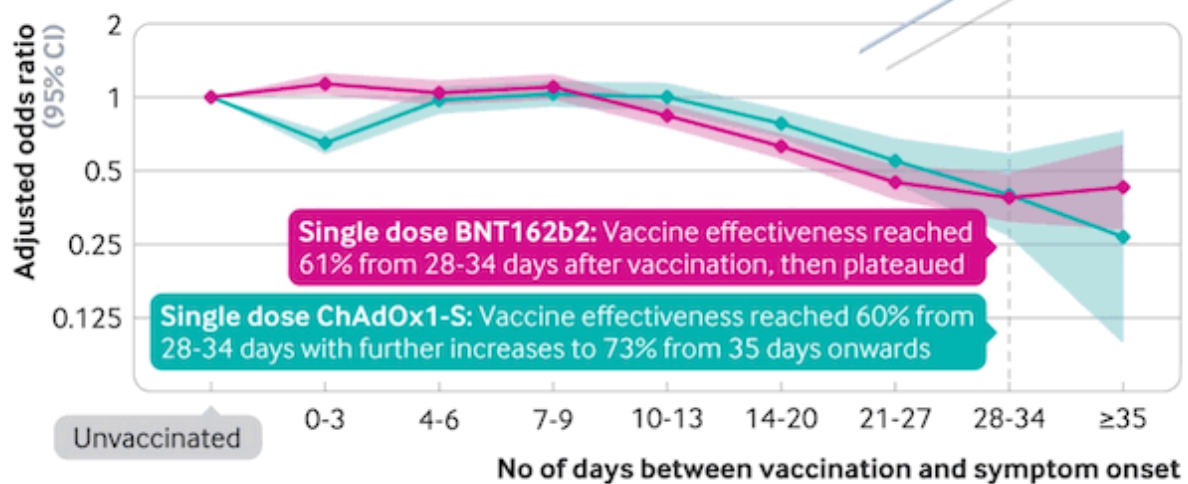


Figure 8: Early effectiveness of covid-19 vaccination

BMJ. 2021 May 13;373:n1088

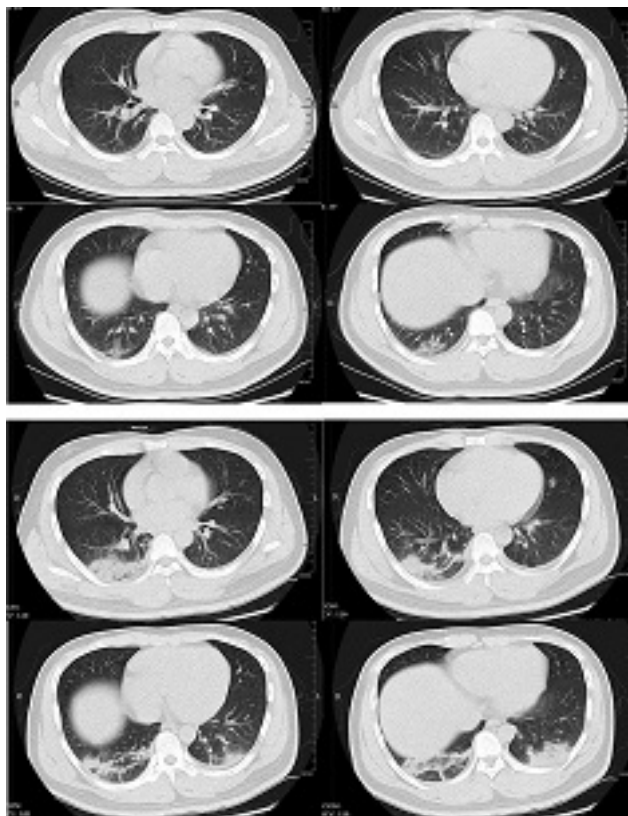


Figure 9: Transverse CT scans from a 32-year-old man, showing ground-glass opacity and consolidation of lower lobe of right lung near the pleura on day 1 after symptom onset (top panel), and bilateral ground-glass opacity and consolidation on day 7 after symptom onset

Xu XW et al. *BMJ*. 2020;368:m606

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Figure 1 – BMJ Best Practice Numeral Style

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Contact us

+ 44 (0) 207 111 1105

support@bmj.com

BMJ

BMA House

Tavistock Square

London

WC1H 9JR

UK

Contributors:

// Authors:

Nicholas J. Beeching, MA, BM BCh, FRCP, FRACP, FFTM RCPS (Glasg), FESCMID, DCH, DTM&H

Consultant and Emeritus Professor of Tropical and Infectious Diseases

Royal Liverpool University Hospital and Liverpool School of Tropical Medicine, Liverpool, UK

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Tom E. Fletcher, MBE, PhD, MBChB, MRCP, DTM&H

Senior Clinical Lecturer and Defence Consultant in Infectious Diseases

Royal Liverpool University Hospital and Liverpool School of Tropical Medicine, Liverpool, UK

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Robert Fowler, MDCM, MS (Epi), FRCP(C)

H. Barrie Fairley Professor of Critical Care

University Health Network and Interdepartmental Division of Critical Care Medicine, Director, Clinical Epidemiology and Health Care Research, Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Chief, Tory Trauma Program, Sunnybrook Hospital, Toronto, Canada

DISCLOSURES: RF declares that he has no competing interests.

// Peer Reviewers:

William A. Petri, Jr., MD, PhD

Professor

Division of Infectious Diseases and International Health, University of Virginia, Charlottesville, VA

DISCLOSURES: WAP declares that he has no competing interests.

Xin Zhang, MD, PhD

Attending Physician

The Fifth Medical Center of PLA General Hospital, Clinical Division and Research Center of Infectious Disease, Beijing, China

DISCLOSURES: XZ declares that he has no competing interests.

Ran Nir-Paz, MD

Associate Professor in Medicine

Contributors:

Department of Clinical Microbiology and Infectious Diseases, Hadassah Hebrew University Medical Center, Jerusalem, Israel

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