



Summary of COVID-19 Published Literature

This document is a one-line summary of each of the published pieces of literature on COVID-19 from the following medical journals:

1. British Medical Journal
2. Journal of the American Medical Association
3. The Lancet
4. New England Journal of Medicine

How to use this document

- The one-line summaries are posted in reverse chronological order (newest at the top).
- New additions since the last update are noted in **red font**.
- If you want to access the full article, click on the hyperlinked citation.

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TRANSMISSION:

Asymptomatic Transmission:

- Suggests incubation period of 25 days in a young COVID-19 patient with history of non-Hodgkin lymphoma and chronic lymphocytic leukaemia; this is greater than the current estimate of 14 days ([Lancet, April 1, 2020](#))
- Confirmed case of **asymptomatic transmission** in Germany occurred during incubation period of index patient in whom illness was mild – this means asymptomatic persons are potential sources of infection ([NEJM, March 5, 2020](#)).
- Indicates possibility of **asymptomatic transmission** and suggested incubation period can be up to 24 days ([JAMA, February 28, 2020](#)).
- Percentage of **pre-symptomatic/asymptomatic transmission** remains undetermined; COVID-19 spreads via **respiratory route** and has high fatality rate ([NEJM, February 26, 2020](#)).
- Confirmed case of asymptomatic carrier with **incubation period of 19 days** (this is greater than previously suggested 1-14 days) who infected family of 5 in Anyang who had no contact with others from Wuhan ([JAMA, February 21, 2020](#)).
- Possibility of **asymptomatic transmission** found when similar viral load detected in asymptomatic and symptomatic patients ([NEJM, February 20, 2020](#)).

Community Transmission:

- Identifies the significance of mild infection and community transmission increasing the spread of disease; 5% rate of SARS-CoV-2 in the US among patients with mild influenza-like illness ([JAMA, March 31, 2020](#)).
- Identifies a possible case of community transmission in a public bath centre with high temperature and humidity; therefore, no signs of weakening in warm and humid conditions ([JAMA, March 30, 2020](#)).
- Confirms human-to-human transmission among close contacts (Wuhan, China; 425 cases) ([NEJM, March 26, 2020](#))
- Identifies possibility of transmission via **fecal route** (live virus detected in feces); transmission via respiratory and extrarrespiratory routes may help explain the rapid spread of disease ([JAMA, March 11, 2020](#))
- Confirmed case of **environment transmission** found significant contamination via respiratory droplets and viral fecal shedding – strict environmental and hand hygiene should be followed ([JAMA, March 4, 2020](#)).
- **Local transmission** was confirmed in Italy's Lombardy region ([Lancet, February 28, 2020](#)).
- **Human-to-human transmission** and asymptomatic infections are of concern during superspreader events, as transmission is mostly occurring among **close contacts** ([Lancet, February 27, 2020](#); [JAMA, February 24, 2020](#)).

OMA COVID-19 Research Summaries

Featuring articles from: BMJ, JAMA, Lancet and NEJM

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UPDATED: April 1, 2020

- Confirmed **human-to-human transmission** and found a case with an incubation period of 3 days or less; occurs primarily from symptomatic versus asymptomatic patients ([NEJM, February 27, 2020](#); [NEJM, February 20, 2020](#)).

Nosocomial Transmission:

- Risk of **nosocomial transmission** (transmission in health care facilities) can be minimized with regional facilities ([Lancet, February 27, 2020](#); [NEJM, February 20, 2020](#)).

Ocular Transmission:

- **This case series reports severe COVID-19 patients with ocular manifestations such as epiphora (excessive eye watering), conjunctival congestion, or chemosis; understanding ocular manifestations of COVID-19 can enhance the diagnosis and prevention of disease transmission** ([JAMA, March 31, 2020](#))
- **Identifies the epidemiologic importance of describing the ocular manifestations of COVID-19 patients; it confirms other reports that the virus can invade the conjunctiva, which might, in turn, serve as a source of its spread** ([JAMA, March 31, 2020](#))
- **Viral conjunctivitis** (pink eye) can be a possible presentation of COVID-19, suggesting transmission via ocular surface ([BMJ, March 2, 2020](#)).

Transmission Statistics:

- Calculated attack rates suggest **50%-60%** of China's population should eventually be infected; observed attack rate on *Diamond Princess* cruise ship remained slightly below 20% ([Lancet, March 3, 2020](#)).
- Basic reproduction rate (R_0) is **2.2**, so each infected person spreads infection to additional 2 persons; outbreak will continue to spread until R_0 falls below 1.0 ([NEJM, February 28, 2020](#); [Lancet, February 27, 2020](#)).
- Calculated a secondary attack rate of **35%** among close contacts, hence social interactions may increase transmission risk ([Lancet, February 27, 2020](#); [JAMA, February 24, 2020](#)).
- Retrospective case series study (62 patients, Zhejiang, China) - concludes median time from **exposure to onset of illness was 4 days** and their symptoms were mild compared to patients in Wuhan ([BMJ, February 19, 2020](#)).

Viral Shedding:

- Identifies occurrence of prolonged viral shedding of 2019-nCoV after recovery – this means there's a possibility patient can still be infectious ([NEJM, March 5, 2020](#))
- 15 COVID-19 patients in Singapore had mild respiratory tract infection and viral shedding from the nasopharynx (part of upper airway) of 7 days or longer– suggesting long infectious period ([JAMA, March 3, 2020](#)).
- High viral loads found in throat during early onset of disease and causes concern about increased infectivity during period of mild symptoms ([NEJM, February 28, 2020](#))

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UPDATED: April 1, 2020

- Case study of 4 infected health workers in China revealed that some recovered patients still may be **virus carriers** ([JAMA, February 27, 2020](#)).

PRESENTATION:

- **Pink eye**– potential clinical manifestation and useful for early diagnosis ([BMJ, March 2, 2020](#)).
- **CT abnormalities or fever**– not always seen on initial presentation, complicating diagnosis ([NEJM, February 28, 2020](#)).
- **High viral loads in oropharynx**– found in early onset of disease and causes concern about increased infectivity during period of **mild symptoms**; higher loads detected in nose than throat ([NEJM, February 28, 2020](#); [JAMA, February 20, 2020](#); [NEJM, February 20, 2020](#); [BMJ, February 19, 2020](#)).
- **Mild pneumonia and thrombocytopenia**– exhibited by the first imported case in Canada, and thrombocytopenia only seen in a few cases prior ([Lancet, February 13, 2020](#)).

DIAGNOSIS:

- Clinicians should obtain recent history of travel or exposure to sick contacts to ensure appropriate identification and prompt isolation of patients, so further transmission can be reduced ([NEJM, March 5, 2020](#)).
- Identifies need to expand diagnostic testing to encompass patients with unexplained ARDS, severe pneumonia, and mild symptoms consistent with COVID-19; also identifies need for serological assays for surveillance purposes and determining accurate case-fatality rate ([JAMA, March 3, 2020](#)).

TREATMENT:

- According to select preclinical studies, RAAS inhibitors may increase ACE2 expression, which is the functional receptor to sARS-CoV-2 – this raises safety concerns of RAAS inhibitor use in COVID-19 patients ;suggest RAAS inhibitors be continued in COVID-19 patients until more research is conducted on its effects ([NEJM, March 30, 2020](#)).
- Effectiveness of **convalescent plasma therapy** alone in critically ill COVID-19 patients needs to be further studied to understand its specific contribution to the clinical course/outcomes ([JAMA, March 27, 2020](#))
- An uncontrolled case series suggests **convalescent plasma** as possible treatment in critically ill COVID-19 patients; convalescent plasma containing neutralizing antibody + antiviral treatment resulted in clinical improvement (China, 5 cases) ([JAMA, March 27, 2020](#))
- Physicians and patients are recommended to continue treatment with their usual anti-hypertensive therapy as there is no clinical evidence to suggest that treatment with ACEIs or ARBs should be discontinued due to COVID-19 infection ([JAMA, March 24, 2020](#)).

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UPDATED: April 1, 2020

- WHO will be coordinating an international randomized, open-label trial of treatments for COVID-19 which will focus on: remdesivir, lopinavir-ritonavir, loptinavir-ritonavir + interferon β , and chloroquine ([BMJ, March 24, 2020](#))
- Randomized, controlled, open-label trial compared standard care alone vs **lopinavir-ritonavir + standard care** – addition of antiviral did not result in any improvement ([NEJM, March 18, 2020](#))
- **Corticosteroids** – cause immunosuppression, may exacerbate COVID-19 associated lung injury, and may be beneficial in hyperinflammation; evidence suggests all severe COVID-19 patients should be screened for hyperinflammation to identify need for immunosuppression and improve mortality ([Lancet, March 13, 2020](#))
- **Methylprednisolone** – suggests as treatment for COVID-19 patients w/ pneumonia; may be beneficial for those who developed ARDS on disease progression – *Retrospective cohort study, 201 patients, China* - ([JAMA, March 13, 2020](#))
- The occurrence of **spontaneous pneumomediastinum** in a COVID-19 patient can be a potential indicator of worsening disease, therefore should be monitored closely in patients ([Lancet, March 9, 2020](#))
- **Remdesivir** – used to treat first reported case in USA on day 7 and noticed improvement in patient's clinical condition on day 8 ([NEJM, March 5, 2020](#)).
- **Lopinavir-ritonavir**– used to treat 5 patients in Singapore; it reduced fever and supplemental oxygen requirement in 3 of 5 patients ([JAMA, March 3, 2020](#)).
- Treatment and vaccine development need to be accelerated ([NEJM, February 28, 2020](#)).
- Therapy consists of supportive care, and investigational approaches such as antiviral medication and variety of traditional Chinese medicine products are being explored ([NEJM, February 28, 2020](#)).
- Suggested **remdesivir** may be useful, **corticosteroids** not recommended, **lopinavir-ritonavir** didn't seem to be effective, and **favilavir** was recently approved for investigational therapy in China ([JAMA, February 28, 2020](#)).
- **Convalescent plasma** – possible that antibodies from convalescent plasma from recovered patients might suppress viremia without severe adverse events; therefore, suggested as possible treatment for COVID-19 ([Lancet, February 27, 2020](#))
- **Baricitinib + direct acting antivirals** - potential for this combination is suggested, as it could reduce viral infectivity, viral replication, and the aberrant host inflammatory response ([Lancet, February 27, 2020](#))

Randomized trials of **lopinavir-ritonavir** and **remdesivir** are underway in China ([JAMA, February 20, 2020](#)).

OUTCOMES:

- **Most serious complications of COVID-19 are sepsis and cardiovascular/ respiratory complications; no evidence exists on whether non-steroidal anti-inflammatory drugs (NSAIDs) increase these risks** ([BMJ, March 27, 2020](#))

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UPDATED: April 1, 2020

- COVID-19 is associated with a high inflammatory burden that can induce **vascular inflammation, myocarditis, and cardiac arrhythmias** ([JAMA, March 27, 2020](#))
- Study provides description of 3 clinical evolutions found in COVID-19 patients, which provides a better understanding of the disease prognosis ([Lancet, March 27, 2020](#))
- Limited information exists on unique risks of COVID-19 for those with underlying cardiovascular disease; data from 2 Chinese cohorts links myocardial injury and high mortality risk, but more research is required to confirm this link ([JAMA, March 27, 2020](#))
- Case report confirmed acute **myopericarditis** with **systolic dysfunction** in 53-year old COVID-19 patient with no history of cardiovascular disease; this suggests that COVID-19 can be associated with cardiac involvement, even without symptoms/ after resolution of the disease ([JAMA, March 27, 2020](#))
- Retrospective case series reports that regardless of cardiovascular disease history, acute cardiac injury and heart failure were common in deceased patients; and they often developed systemic inflammation and multi-organ dysfunction vs recovered patients ([BMJ, March 26, 2020](#))
- Study with 21 severe cases of older residents in a US nursing facility concludes a high rate of **ARDS** and a high risk of **death**, similar to published data from China, and also demonstrates poor short term outcomes among patients requiring mechanical ventilation ([JAMA, March 19, 2020](#))
- Study (*retrospective cohort study, 201 patients, China*) shows older age was associated with **ARDS and death** and it may be due to less robust immune system ([JAMA, March 13, 2020](#))
- Study reveals that higher CD3 and CD4 T-cell counts might protect patients from developing ARDS – further studies required to validate this ([JAMA, March 13, 2020](#))
- Patients requiring critical care have predominantly been older (median age ≈ 60years) and 40% of them had comorbid conditions, commonly diabetes and cardiac disease ([JAMA, March 11, 2020](#))
- **Septic shock** and **specific organ dysfunction** (i.e. acute kidney injury) occur in many COVID-19 patients – this is associated with increasing mortality ([JAMA, March 11, 2020](#))

SPECIAL POPULATIONS:

Pregnant women, fetuses, newborn infants

- **Newborn had elevated antibody (IgM) levels and abnormal cytokine test results 2 hours after birth; suggests infection via vertical transmission** ([JAMA, March 26, 2020](#); [JAMA, March 26, 2020](#))
- **Examined 6 cases of pregnant COVID-19 patients and found that newborns weren't infected, but virus-specific antibodies were detected in neonatal blood sera samples** ([JAMA, March 26, 2020](#))
- **No reliable evidence exists on vertical transmission of COVID-19; 36 hours after birth, three newborns found with COVID-19 – identifies need for further research to assess the risk and produce guidelines for delivery times/methods in COVID-19 patients** ([Lancet, March 24, 2020](#))

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UPDATED: April 1, 2020

- **Descriptive study of 7 pregnant COVID-19 patients concludes that very good maternal, fetal, and neonatal outcomes were achieved with intensive/active management; their clinical characteristics were similar to those of non-pregnant adults with COVID-19** ([Lancet, March 24, 2020](#))
- Perinatal exposure may be associated with substantial risk – limited cases with pregnant women makes disease course difficult to predict ([JAMA, March 11, 2020](#))
- No evidence so far of severe outcomes for mothers and infants with SARS-CoV-2 ([Lancet, March 3, 2020](#))
- Identifies perinatal transmission is unlikely so far ([JAMA, February 28, 2020](#)).

Children

- Children appeared to have a milder clinical course and asymptomatic infections were common ([NEJM, March 18, 2020](#))
- Symptomatic infections in children are rare and found very mild symptoms in 3 cases of young children in Singapore ([JAMA, February 20, 2020](#))

MORTALITY:

- **Current estimate of case fatality ratio in China is 1.38% - this is substantially higher than estimates from 2009 H1N1 influenza pandemic; also identifies estimates of the age-stratified case fatality ratio and infection fatality ratio that consider the different denominator populations in datasets** ([Lancet, March 30, 2020](#)).
- Overall case fatality rate in Italy (7.2%) is substantially higher than in China (2.3%), which may be explained by the high proportion of older COVID-19 patients in Italy ([JAMA, March 23, 2020](#))
- Case fatality rate in Italy is 7.2% ([JAMA, March 17, 2020](#))
- Mortality rate as of March 12 is approximately 3.7% ([Lancet, March 13, 2020](#))
- Mortality rate may be approximately 0.5% - 4% (among all infected patients), 5% - 15% (among hospitalized patients), and 22% - 62% (among critically ill patients) ([JAMA, March 11, 2020](#))
- Case fatality rate reported to be approximately 2% ([NEJM, February 28, 2020](#)).

REPORTS OF SPREAD:

- **Widespread community transmission now applies worldwide, particularly in urban areas** ([BMJ, March 31, 2020](#)).
- **February 2020 - Community transmission confirmed in Washington, USA** ([NEJM, March 30, 2020](#)).
- Local transmission confirmed in Italy's Lombardy region ([LANCET, February 28, 2020](#)).

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PUBLIC HEALTH PLANNING AND RESPONSE:

- Identifies the importance of improving mental health care for international Chinese students; suggests walk-in triage system, counselling training clinics, and more ([Lancet, April 1, 2020](#))
- Describes the difference between traditional vaccine development and vaccine development during a pandemic; and identifies the challenges of conducting clinical trials during a pandemic ([NEJM, March 30, 2020](#)).
- Ophthalmology patients in a Singapore hospital were triaged using 3 criteria to identify potential COVID-19 patients; appropriate PPE was provided to ophthalmologists when dealing with potential cases ([JAMA, March 31, 2020](#))
- Provides recommendations to protect health care workers involved in caring for COVID-19 patients to help preserve the health care workforce ([JAMA, March 31, 2020](#))
- Highlights some surgical considerations when planning for open tracheostomy in a COVID-19 patient; PPE is essential, location of surgery should be carefully considered, time of exposure to aerosolized secretions intraoperatively should be minimized, and postprocedural waste disposal and decontamination of equipment need careful consideration to minimize contamination of the environment ([JAMA, March 31, 2020](#))
- After Italy, Spain has been hit the hardest by COVID-19 and is overwhelming their health care system; more PPE is required to protect health care workers ([BMJ, March 31, 2020](#)).
- Identifies the importance of contact tracing and testing, especially to prevent/ control the spread during a second or third wave of the outbreak ([BMJ, March 30, 2020](#); [Lancet, April 1, 2020](#))
- Identifies the need for measures to mitigate COVID-19's impact on undocumented immigrants and public health at large; undocumented immigrants have limited access to primary care and the \$1 trillion relief package will not reach most of them ([NEJM, March 27, 2020](#))
- Long-term care facilities are at high risk for severe COVID-19 outcomes and require proactive steps to prevent/ control spread; and must implement appropriate infection prevention and control measures; case fatality rate for residents was 33.7% ([NEJM, March 27, 2020](#))
- Care homes require more PPE and staff testing to reduce the spread of COVID-19 ([BMJ, March 27, 2020](#))
- Suggests prioritizing treatment by triaging COVID-19 patients according to presence of underlying CVD and myocardial injury; case series reports a significant association between myocardial injury and fatal outcomes of COVID-19 ([JAMA, March 27, 2020](#))
- Suggests a new model to more accurately reflect what actually occurs with respiratory emissions so that more effective policies can be derived to limit the spread of a respiratory disease like COVID-19 ([JAMA, March 26, 2020](#))
- The Surviving Sepsis Campaign (SSC) COVID-19 guidelines represent evidence-informed care for patients with COVID-19; more robust evidence needs to be generated to improve these guidelines ([JAMA, March 26, 2020](#); [JAMA, March 26, 2020](#))

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- Identifies the need for more PPE and other key equipment in the US in order to care for patients and keep the health care workforce healthy as number of COVID-19 cases will continue to grow ([NEJM, March 25, 2020](#))
- Identifies need for UK specific dataset of COVID-19 patients in critical care as it will be beneficial to delivery of care ([BMJ, March 24, 2020](#)).
- Proposes a large-scale emergency program in the UK to train community health workers (CHWs) to support people in their homes ([Lancet, March 24, 2020](#)).
- Nursing homes in the US require policy attention to mitigate the potential consequences of COVID-19, as there is a lack of attention to the availability of testing and poor infection control ([JAMA, March 24, 2020](#)).
- Highlights the importance of discovering new therapies for COVID-19 and identifies need to prioritize RCTs that have an adaptive design during an outbreak so that multiple experimental therapies can be rapidly accepted/rejected throughout the trials ([JAMA, March 24, 2020](#)).
- This study highlights the need for transparency in reporting testing policies with clear reporting of the denominators used to calculate case-fatality rates and the age, sex, and clinical comorbid status of affected persons when comparing COVID-19 cases and mortality rates between different countries and regions ([JAMA, March 23, 2020](#)).
- Chinese health care workers have high risk of developing unfavourable mental health outcomes and may need psychological support or interventions ([JAMA, March 23, 2020](#))
- Created triage committees to help withdraw mechanical ventilation from patients to help mitigate the enormous emotional burden on caregivers ([NEJM, March 23, 2020](#))
- Highlights the need for governments and policy makers to help prevent the scarcity of medical resources and makes 6 recommendations in case scarcity does occur ([NEJM, March 23, 2020](#))
- Canada has been slow in sorting out safe and streamlined procedures for processing passengers arriving at international airports, and they are yet to yield a pan-Canadian digital system to track COVID-19 testing, infections, and treatment ([Lancet, March 21, 2020](#))
- Governments, institutions, and healthcare facilities should consider vulnerable communities when enacting policies ([BMJ, March 20, 2020](#))
- Important to consider the health and wellbeing of frontline healthcare workers in order to benefit entire population ([BMJ, March 20, 2020](#))
- General practitioners in England will be postponing their routine work to focus efforts on COVID-19 ([BMJ, March 20, 2020](#))
- UK is considering employing final year medical students in the COVID-19 response and may fast track their GMC provisional registration; GPs also moving to virtual care ([BMJ, March 20, 2020](#); [NEJM, March 20, 2020](#))
- Retired doctors in the UK are being re-registered automatically with the GMC to help with COVID-19 response if they want to ([BMJ, March 20, 2020](#))

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- Identifies the need for increased testing capacity of frontline healthcare workers to show who has had the infection and is immune and therefore able to safely return to work ([BMJ, March 19, 2020](#))
- UK government is pushing to increase capacity for COVID-19 testing to 25,000 people a day ([BMJ, March 19, 2020](#))
- Discusses how Medicaid should support health care workers and vulnerable populations in providing access to care, creatively expanding capacity of clinicians and health care centers, and promoting infection control – will help promote an effective response to this pandemic ([JAMA, March 19, 2020](#))
- Countries were unprepared to protect HCP - and thus, patients and the public - makes recommendations for future pandemic ([JAMA, March 19, 2020](#))
- EU needs to improve preparedness planning for all infectious disease outbreaks and increase funding for research and development ([BMJ, March 18, 2020](#))
- Identifies that there should be a careful balance between public health and individual rights, which requires adherence to 6 key principles, one of which is evidence-based interventions ([JAMA, March 18, 2020](#))
- Identifies the need for urgent action to ensure that capacities are in place to prevent and manage health emergencies - COVID-19 outbreak is another opportunity to review preparedness of all countries to better prepared for future health emergencies ([Lancet, March 18, 2020](#))
- Geographic and temporal clustering of outbreaks overwhelm health care systems – suggest hospital administrators to start preparing for worst case scenarios ([JAMA, March 17, 2020](#); [JAMA, March 12, 2020](#))
- Identifies the need to develop strategies to address increased social isolation and loneliness experienced as a result of social distancing ([JAMA, March 17, 2020](#))
- Suggests considering regional production of medical supplies for all continents to reduce risks of shortages of PPE at crucial times ([JAMA, March 16, 2020](#))
- Suggests self-service diagnosis for COVID-19 as a new clinical pathway to combat limited access to testing – benefits include wider availability with lower costs and mitigated risk of exposure to virus ([JAMA, March 16, 2020](#))
- Suggest health care systems need to work toward **collaborative emergency networks** in order to provide initial immediate surge response to provide ICU beds to every patient that needs it ([JAMA, March 13, 2020](#))
- Important to change strategy for slowing spread of outbreak from containment to mitigation approaches in the US – this could allow optimization of health care delivery ([JAMA, March 13, 2020](#))
- COVID-19 containment is difficult due to many unknowns: case fatality rate (CFR), potential for pre-symptomatic transmission, potential for significant asymptomatic cases, and duration of infectious period ([Lancet, March 6, 2020](#)).

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UPDATED: April 1, 2020

- Governments and global health institutions should consider sex and gender effects of the COVID-19 outbreak (more men vs women are dying) - likely due to sex-based immunological or gendered differences such as patterns and prevalence of smoking ([Lancet, March 6, 2020](#)).
- Clinicians should obtain recent history of travel or exposure to sick contacts to ensure appropriate identification and prompt isolation of patients, so further transmission can be reduced ([NEJM, March 5, 2020](#)).
- Identifies the need to increase production of protective equipment by 40% to meet demand ([BMJ, March 4, 2020](#)).
- Taiwan responded quickly to the outbreak while protecting interests of its citizens using big data analytics, new technology, and proactive testing ([JAMA, March 3, 2020](#)).
- Identifies need to expand diagnostic testing to encompass patients with unexplained ARDS, severe pneumonia, and mild symptoms consistent with COVID-19; also identifies need for serological assays for surveillance purposes and determining accurate case-fatality rate ([JAMA, March 3, 2020](#)).
- Using masks as a public health intervention may intercept transmission link ([Lancet, March 2, 2020](#)). ^[11]
- Full data sharing required for effective outbreak preparedness in decentralized countries ([BMJ, February 28, 2020](#)).
- Prevention of further transmission or future pandemics requires vaccine/antiviral distribution for people in greatest need versus selling to the highest bidder ([NEJM, February 28, 2020](#)).