

Outbreak Report

Last updated February 21, 2020.

What's New

According to Chinese health authorities, more than 880 additional, confirmed cases (including 120 deaths) of COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been reported since February 20, 2020, throughout China, mainly in Hubei (> 630) and Shandong (> 200) provinces. Most recent deaths have occurred in Hubei Province, with 3 deaths in the cities of Chongqing and Shanghai and in Yunnan Province; 1,900 more patients have recovered and been discharged. More than 75,400 confirmed cases (including > 2,200 deaths)—reported through February 21 at 3:00 p.m. EST—have been officially reported since December 8, 2019. The confirmed case total in China and elsewhere for February 13-18 refers to laboratory-confirmed cases only, except for Hubei Province, where clinically confirmed cases are included in the confirmed case total. As of February 19, confirmed case numbers for Hubei Province no longer include clinically confirmed cases.

No additional, imported confirmed cases from China have been reported since February 16, just 3 in the past 7 days, and only 1 additional country has officially reported imported cases from China since February 2. Approximately 210 cases imported from China have been reported at international ports of entry since January 6 in 26 countries.

In contrast, more than 140 additional cases have been reported since February 20 in Canada, Iran (18 cases), Italy (16 cases), Japan, Lebanon, Singapore, South Korea (100 cases including 1 death), and Taiwan. Since January 14, more than 50 cases of severe disease and 12 deaths (at least 3 of these cases reported travel history to China) have been reported in cases exported from China or cases acquired outside of China. More than 85 of the South Korea cases were reported in the city of Daegu (2.5 million population) and surrounding Gyeongbuk Province; of the 204 total cases reported throughout the country, more than 150 cases are from Daegu (and surrounding areas), and a majority of these cases are associated with a single case in a super-spreading event linked to the Shincheonji Church of Jesus and the Cheongdo Daenam Hospital. Visitors and residents of Daegu have been urged to stay indoors, and all nonessential travel to Daegu is prohibited for active U.S. service members. Iran reported 13 of the additional cases (including 2 deaths); 2 exported cases from Iran were reported in Canada and Lebanon. More than 430 cases with transmission occurring outside of China (including locally acquired cases) have been reported since January 14 in 20 countries: Canada, Egypt, France, Germany, Hong Kong, Iran, Italy, Japan, Lebanon, Macau, Malaysia, Singapore, Spain (Canary Islands and Mallorca Island), South Korea, Taiwan, Thailand, United Arab Emirates, U.K., U.S., and Vietnam. Despite excellent public health infrastructure, Hong Kong, Japan, and Singapore have reported multiple known case clusters of COVID-19 with no established link to known transmission chains, which is worrisome for sustained transmission in those areas. In South Korea, Singapore, and Hong Kong, despite intensive efforts, locally acquired cases now outnumber imported cases 158 to 13 (South Korea), 56 to 13 (Hong Kong), and 55 to 23 (Singapore).

An additional 6 cases have been reported since February 20 among passengers who were aboard the Diamond Princess cruise ship; cases were among repatriated citizens in the U.S. (3 cases), Australia (2 cases), and Israel (1 case). Approximately 640 total cases (including 2 deaths and 27 in serious condition) have been reported; approximately 330 cases were asymptomatic at the time of diagnosis. The mandatory 14-day quarantine aboard the ship officially expired on February 19, and the disembarkation of approximately 1,800 passengers has begun for those who are asymptomatic and negative for SARS-CoV-2. Approximately 970 passengers have disembarked since February 19; Canada, Israel, and Taiwan repatriated some of their citizens beginning on February 20. Indonesia, Italy, the Philippines, and the U.K. plan to repatriate citizens aboard the ship beginning on February 21. Citizens will be required to be symptom free when boarding their respective flights and will uniformly be subject to quarantine upon arrival in country. Approximately 1,000 crew members will remain aboard to complete an additional 14-day quarantine, which is now expected to expire on March 6. Approximately 300 passengers remain aboard; 100 of these passengers have been identified as close contacts and will be removed and placed in a government-provided quarantine facility.

Italy is now instructing arrivals from affected areas in China in the past 14 days to self-quarantine.

In addition to U.S. CDC, only 3 U.S. states (California, Illinois, and Nebraska) can currently test for SARS-CoV-2; some of the testing kits previously sent to other states and at least 30 countries were flawed and produced inconclusive results. U.S. CDC has increased its testing capacity until the testing kits are replaced.

Overall Risk Assessment

Cases imported directly from China have almost ceased. Significant numbers of recent locally acquired cases in Iran, South Korea, Italy, and Japan together with repatriation of large numbers of individuals to many countries from the Diamond Princess are of immediate concern. Seven weeks since the first report of this outbreak, considerable uncertainties remain in assessing the risk of this event worsening or spreading due to a lack of robust epidemiological analyses, either in China or in other affected countries. In China, the constraint has been the limited reporting of mild and asymptomatic cases. The true spectrum of clinical disease—which involves ascertaining the proportions of infected persons who are asymptomatic; who are symptomatic but apparently (to others) asymptomatic; who have influenza-like illness, focal pneumonia, or severe respiratory compromise; and fatalities—remains the most important unknown. Despite this uncertainty, SARS-CoV-2 is clearly capable of efficient human-to-human transmission.

The reliability of case-number and fatality reporting by Chinese authorities is increasingly uncertain due to recent, unclear, back-and-forth changes (perhaps intentionally obfuscating) in case ascertainment and case definition. The above numbers mostly reflect a narrow case definition used during most of the outbreak in China, whereby pneumonia and viral replication were required to be counted as a case. Asymptomatic persons who test positive for SARS-CoV-2 have not been consistently counted as cases in China. Case definitions used by U.S. CDC and other public health authorities require only fever, respiratory symptoms, and viral replication; asymptomatic individuals who are discovered to have viral replication are also counted. Many models indicate that several hundred thousand infections may exist in China, and testing has yet to catch up to demand. Just prior to the cordoning off of Wuhan on January 23, over 5 million residents (many potentially infectious) left Wuhan, although most remained in Hubei Province and neighboring provinces. Those areas remain under quarantine. Other places in China may simply be early in the epidemiological curve, lagging behind Hubei by 1 to 2 months. Globally, the true number of infections, including those that are unreported and unrecognized due to mild (or lack of) symptoms, is much higher. Hidden cases may be present in many countries, which are only now receiving diagnostics.

More than 1,100 cases (ascertained using a broader case definition) have been imported into other countries or acquired in other countries (or on a ship) that have testing available for all symptomatic persons and increasingly for asymptomatic persons as well; more information on the typical clinical course should be available within the next 2 weeks if all countries outside of China are transparent and quickly share data. Indications so far are of milder disease in those cases, but at least 50 cases have required intensive care and 12 have died. Information on the Diamond Princess cohort is most likely to yield important information; so far, approximately 50% of persons discovered to be infected have been asymptomatic at the time of diagnosis.

Overall, due to uncertainty, justification is present for the most cautious approach of having arrivals from China stay at home or in a hotel for 14 days after their last possible exposure in China (which is already national policy in many countries). Detection of virus by PCR in the respiratory tract of an asymptomatic individual does not differentiate between 1) being able to infect others while asymptomatic; 2) remaining asymptomatic and never becoming capable of infecting others; and 3) becoming symptomatic and being capable of infecting others during clinical illness. Both viral detection and epidemiological evidence of transmission are required to prove cause and effect of human-to-human transmission by an asymptomatic person. Experts are increasingly convinced of the occurrence, although not the frequency, of asymptomatic human-to-human transmission. Rare outlier events often are magnified in importance if detected early in an outbreak. If a subset of super-spreading events occurs, index cases are likely to have been highly viremic and infectious in the asymptomatic stage. Such events appear to have already occurred in: Singapore at a business conference in a hotel; Munich, Germany at a business seminar; Hong Kong during a communal hot pot meal; South Korea in a church; and in several other clusters in Singapore. As of February 11, more than 1,700 confirmed cases (6 deaths) have occurred in health care workers (HCWs) since the outbreak began, of which 1,500 occurred in Hubei Province (mainly in Wuhan [73%]).

Fortunately, sequential sequencing of viral isolates over time, to date, indicates no significant new viral mutations; mutations often increase transmission or virulence. As of January 30, WHO considers the outbreak a Public Health Emergency of International Concern and assesses the risk of this event to be very high in China, high at the regional level, and high at the global level. The originally implicated animal market, now closed indefinitely, bears little relevance to the ongoing situation; human-to-human transmission in Wuhan appears to have been ongoing since mid-December. Whether the market was the focus of a single incidence of species jump from animals (possibly pangolins) to humans (indicated by sequencing data) or merely one of multiple amplification settings for initial cases is increasingly unclear. The degree of human-to-human spread outside of Hubei Province remains unclear. A reproductive number, R_0 , is estimated at 2–3 both by Chinese authorities and by multiple outside estimates. R_0 greater than 1 indicates that each case leads to more than 1 subsequent case, making control much more difficult.

The spectrum of disease manifestations has been assessed in a number of Chinese cohorts and also in a consolidated notifiable disease database from China CDC. A severe case rate of 20% has been consistent; older males with comorbidities have predominated, with a few cases aged ≤ 20 years. Case counts and morbidity incidence rates in these case series have only

predominantly considered the most severe cases and undercounted mild and asymptomatic cases; the broader definitions and broader testing in China will lead to much lower rates of severe outcomes.

Case fatality is impossible to ascertain at present. Lesser or greater clinical virulence compared to MERS-CoV or SARS-CoV remains speculative, and already published estimates have varied greatly. An accurate estimate of case fatality will not be possible and will require more data, such as blood tests to see how many people have antibodies, household studies to learn how often it infects family members, and further genetic sequencing to determine whether some strains are more dangerous than others. Based on available analyses, current IFR estimates by WHO range from 0.5% to 1%. However, as also stated by WHO, without population-based serologic studies, the proportion of the population that has been infected with SARS-CoV-2 is impossible to know. Significant rates of infection by minimally symptomatic people of a disease with low CFRs will cause more cases, and ultimately more deaths, than lower rates of transmission of a more virulent virus with higher CFRs that is restricted to symptomatic people. Closing borders never completely succeeds because all borders are somewhat porous. China may be focusing disproportionate resources on areas outside of Hubei to stem the onset of sustained transmission in important areas. However, border closings and aggressive screenings may slow the spread, allowing time for the development of drug treatments and vaccines.

Current Disease Situation

China

More than 75,400 confirmed cases (> 11,600 severe and critical cases and > 2,200 deaths)—reported through February 21 at 3:00 p.m. EST—have occurred since December 8, 2019, in the provinces of Hubei (> 62,600; mainly in Wuhan), Guangdong (> 1,300), Henan (> 1,200), Zhejiang (> 1,200), Hunan (> 1,000), Anhui (> 980), and Jiangxi (> 930); in the cities of Chongqing (> 560), Beijing (> 390), and Shanghai (> 330); and in 22 other provinces throughout the country. An additional 5,000 suspected cases have been reported since January 22. The confirmed case total in China and elsewhere for February 13-18 refers to laboratory-confirmed cases only, except for Hubei Province, where clinically confirmed cases are included in the confirmed case total. As of February 19, confirmed case numbers in Hubei Province no longer include clinically confirmed cases. Most cases are related to Wuhan, but multigenerational transmission is now occurring throughout the country. In the setting of a large outbreak (and with delays in testing still occurring), a high proportion of suspected cases will evolve into confirmed cases. More than 16,800 cases have been discharged. The number of confirmed COVID-19 cases reported by China has increased by more than 11,600 in the past 7 days. On February 13, a large spike in cases and deaths occurred in Hubei Province due to a temporarily expanded case definition, which included cases clinically diagnosed by a physician using lung imaging but not laboratory test results; this case definition only applied to cases in Hubei. These cases were added retrospectively and do not indicate a daily spike in cases. The new definition implies that (as suspected) many more cases infectious to others have been present since the beginning of this outbreak and indicates that downstream cases may also jump precipitously.

A study conducted by China CDC on the first 72,300 cases reported through February 11 showed that 44,600 of the cases were laboratory-confirmed; of these, 78% of cases were aged 30-69 years, 51% were male, and 75% were diagnosed in Hubei Province. Less than 10% of cases were under 30 years of age and less than 2% were under 20 years of age. The cases appear to have spread from 1 city to throughout the country in 30 days. According to this report, the outbreak peaked on February 1, 2020. Several international sources have questioned the availability and reliability of such clean and symmetric data on 45,000 persons within a week of closing the dataset. More than 1,700 of the confirmed cases occurred in health care workers (HCWs) in 422 medical facilities providing care to COVID-19 patients; to date, no published evidence suggests a super-spreader event has occurred in health facilities in China. The study is subject to the already widely known limitations of varying case definitions at different points in time and in different areas, limited testing capability as described above in the risk assessment, and missing variables of interest from some records.

Imported Cases from China

Approximately 210 imported cases of COVID-19 (confirmed after arrival) from China have been reported at international ports of entry since January 6 (through February 16 at 2:00 p.m. EST) in 26 countries. Of these cases, just 3 have been reported in the past 7 days. Only 1 additional country has officially reported imported cases from China since February 2.

An analysis of 1,200 cases identified outside of China showed that approximately 53% were acquired on cruise ships, 27% reported no recent travel outside their home country, 15% reported exposure history in China, 2% reported exposure history in countries outside of China, and 4% are still under investigation. The earliest symptom-onset date was December 31, 2019; none of the early cases had visited the implicated market.

The number of reported cases from Indonesia (0) and Cambodia (1) is notable because all models of air travel indicate that substantial numbers of cases should be present. Diagnostic capabilities in those countries are limited.

Japan (26 cases): Cases have been reported since January 6 (through February 16).

Thailand (23 cases): Cases have been reported since January 22 (through February 11).

Singapore (23 cases): Cases have been reported since January 24 (through February 17).

Malaysia (17 cases): Cases have been reported since January 27 (through February 16).

Australia (15 cases): Cases have been reported since January 27 (through February 6) in the states of New South Wales (Sydney; 4 cases), Victoria (Melbourne; 4 cases), South Australia (2 cases), and Queensland (5 cases).

South Korea (13 cases): Cases have been reported since January 24 (through February 9).

Hong Kong (13 cases; 1 death): Cases have been reported since January 19 (through February 7).

U.S. (13 cases): Cases have been reported since January 24 (through February 13) in 7 states: California (6 counties; 7 cases, including 2 cases in quarantined evacuees), Illinois (Chicago; 1 case), Arizona (Maricopa County; 1 case), Massachusetts (Boston; 1 case), Texas (San Antonio; 1 case in a quarantined evacuee), Washington (Seattle; 1 case) and Wisconsin (1 case).

Taiwan (12 cases): Cases have been reported since January 24 (through February 4).

Macau (9 cases): Cases have been reported since January 19 (through February 5).

Vietnam (8 cases): Cases have been reported since January 23 (through February 8) in Ho Chi Minh City and in Khanh Hoa, Thanh Hoa, and Vinh Phuc provinces.

Canada (7 cases): Cases have been reported since January 25 (through February 14) in the provinces of Ontario (Toronto; 3 cases) and British Columbia (Vancouver; 5 cases).

United Arab Emirates (6 cases): Cases have been reported since January 29 (through February 10); 4 of the cases were part of a family cluster.

France (5 cases; 1 death): Cases were reported on January 24 in the cities of Paris and Bordeaux and in Île-de-France Region.

India (3 cases): Cases have been reported since January 30 (through February 3) in Kerala State.

Italy (3 cases): Cases have been reported since January 31 (through February 7).

Philippines (3 cases; 1 death): Cases have been reported since January 30 (through February 5) in the city of Manila and in Bohol Province. One case (coinfected with *Streptococcus pneumoniae* and influenza B) died on February 2.

Germany (2 cases): Cases were reported on February 2.

Russia (2 cases): Cases were reported on January 31 in Western Siberia.

U.K. (2 cases): Cases have been reported since January 31 (through February 13).

Belgium (1 case): The case was reported on February 4.

Cambodia (1 case): The case was reported on January 23 in the city of Sihanoukville.

Finland (1 case): The case was reported on January 29 in Lapland Region.

Nepal (1 case): The case was reported on January 24 in Kathmandu.

Sri Lanka (1 case): The case was reported on January 27.

Sweden (1 case): The case was reported on January 31 in Jonkoping County.

The following countries have cases without a known epidemiological link (including travel to China, contact with a person from China, or contact with a confirmed case): Hong Kong (17 cases). The following countries have additional cases where transmission is under investigation: South Korea (29 cases), Singapore (8 cases), Thailand (7 cases), Japan (4 cases), Malaysia (2 cases), Canada (1 case), and United Arab Emirates (1 case).

Cases with Transmission Outside of China

More than 430 confirmed cases of COVID-19 (including locally acquired cases or cases acquired in a country outside of the reporting country and outside of China) with transmission occurring outside of China have been reported since January 14 (through February 21 at 2:00 p.m. EST) in 20 countries. Incubation periods in these cases may have been as short as 3 days.

South Korea (162 cases, 2 deaths): Cases have been reported since January 30 (through February 21); 158 locally acquired and 4 acquired in another country other than South Korea or China (2 cases were reported in South Korean nationals who attended the same conference in Singapore January 20-22). More than 150 cases have been reported in the city of Daegu and

surrounding areas, and a majority of these cases are associated with a single case in a super-spreading event linked to the Shincheonji Church of Jesus and the Cheongdo Daenam Hospital (now closed). Investigation continues for 29 additional cases without a known epidemiological link (including travel to China, contact with a person from China, or contact with a confirmed case).

Japan (62 cases; 1 death): Cases have been reported since January 16 (through February 21); 57 locally acquired and 5 acquired in another country other than Japan or China. One case died on February 13 and SARS-CoV-2 was confirmed post mortem; the case was a nontraveler contact of another case. Approximately 13 cases related to a Lunar New Year party aboard a Tokyo riverboat cruise have been reported since February 14 (through February 17). The event took place January 18 with approximately 70 attendees. These cases may indicate a super-spreading event. Investigations continue for 4 additional cases (including 1 HCW) without a known epidemiological link (including travel to China, contact with a person from China, or contact with a confirmed case). Also see Cases under International Conveyance (Cruise Ships) below.

Hong Kong (56 cases; 1 death): Cases have been reported since February 1 (through February 20); of these cases, 3 are close contacts of an imported case, 13 are close contacts of a local case, 17 are close contacts of a possibly local case, and 6 are possibly local cases. Investigation continues for 17 of these cases without a known epidemiological link (including travel to China, contact with a person from China, or contact with a confirmed case). Multigenerational transmission appears to have occurred for some of the locally acquired cases.

Singapore (55 cases): Locally acquired cases have been reported since February 4 (through February 21). Epidemiological investigations have identified 5 main (currently known) clusters: The Life Church and Missions Singapore (6 cases), Yong Thai Hang (Chinese health products store; 9 cases), Grace Assembly of God (22 cases), Seletar Aerospace Heights (5 cases), and a business meeting held January 20-22 at the Grand Hyatt Singapore (3 local cases). Additional cases related to this business meeting with 109 attendees, which may represent a super-spreading event, have been reported in France, Malaysia, South Korea, Spain (Mallorca Island), and the U.K. Investigation continues for 8 additional cases reported in Singapore without a known epidemiological link (including travel to China, contact with a person from China, or contact with a confirmed case). Multigenerational transmission appears to have occurred for some of the locally acquired cases.

Iran (18 cases; 4 deaths): Cases have been reported since February 19 (through February 21); the facts of these cases are still under investigation.

Italy (16 cases): Locally acquired cases were reported on February 21 in Lombardy and Veneto regions.

Germany (14 cases): Locally acquired cases have been reported since January 27 (through February 12). All cases are epidemiologically linked to a workplace-related exposure in Munich, Bavaria State (multigenerational transmission related to a single, imported case); 9 cases are workplace contacts (but only 2 were known to be close, direct contacts of the imported case), and 4 cases are household contacts.

Taiwan (14 cases; 1 death): Cases have been reported since January 28 (through February 21); 10 locally acquired, 3 with travel history through Hong Kong, and 1 with travel history through Macau. One case (diabetic and coinfecting with hepatitis B) died on February 15.

Vietnam (8 cases): Locally acquired cases have been reported since January 28 (through February 13).

U.K. (7 cases): Cases have been reported since February 6 (through February 11); 1 locally acquired and 6 acquired in another country other than the U.K. or China. One case occurred in a British national who attended a business meeting at the Grand Hyatt Singapore and went on to infect at least 11 people (including 6 British nationals staying in the same chalet at the French ski resort of Les Contamines-Montjoie near Mont Blanc [1 of whom traveled home to Mallorca, Spain] and 5 people in Brighton, U.K.; at least 2 cases in the U.K. have been reported in HCWs).

France (7 cases): Locally acquired cases have been reported since January 30 (through February 16). The first case (a doctor who had treated 2 imported cases) was reported in Île-de-France Region. Five additional cases were reported at the ski resort of Les Contamines-Montjoie near Mont Blanc in British nationals sharing a chalet; the index case for this cluster was a British national who attended a business meeting at the Grand Hyatt Singapore, which was the source of several other case clusters (Malaysia, Singapore, South Korea, and the U.K.).

Thailand (5 cases): Locally acquired cases have been reported since January 31 (through February 15).

Malaysia (3 cases): Cases have been reported since February 5 (through February 14); 2 locally acquired (including a close contact) and 1 acquired by a Malaysian national who attended a conference in Singapore January 20-22.

United Arab Emirates (2 cases): Locally acquired cases have been reported since February 8 (through February 17).

U.S. (2 cases): Locally acquired cases were reported on January 30 and February 3 in Chicago, Illinois and San Benito County, California, respectively. Currently, 50 persons are under investigation in 43 states (as of February 21).

Spain, Canary Islands and Mallorca Island (2 cases): One case was reported on January 31 on La Gomera Island; the case is part of a cluster of locally acquired cases in Germany. One case was reported on February 9 on Mallorca Island; the case reported recent travel to a French ski resort (likely the same resort implicated in a cluster outbreak).

Canada (1 case): One case was reported on February 21 in British Columbia Province; the case reported travel to Iran.

Egypt (1 case): The locally acquired case was reported on February 14; the case was a contact of a traveler from China.

Lebanon (1 case): One case was reported on February 21; the case reported travel to Iran.

Macau (1 case): The locally acquired case was reported on February 5.

The following countries have cases without a known epidemiological link (including travel to China, contact with a person from China, or contact with a confirmed case): Hong Kong (17 cases). The following countries have additional cases where transmission is under investigation: South Korea (29 cases), Singapore (8 cases), Thailand (7 cases), Japan (4 cases), Malaysia (2 cases), Canada (1 case), and United Arab Emirates (1 case).

Cases on an International Conveyance (Cruise Ships)

Approximately 640 cases (including 2 deaths and 27 in serious condition) in passengers and crew members (mainly hospitalized in Japan) were acquired aboard the Diamond Princess cruise ship, either at sea or while docked in Japan. Approximately 330 of the 640 cases were asymptomatic at the time of diagnosis. Approximately 17 cases have recovered. The mandatory 14-day quarantine aboard the ship officially expired on February 19, and the disembarkation of approximately 1,800 passengers has begun for those who are asymptomatic and negative for SARS-CoV-2. Approximately 970 passengers have disembarked since February 19. Indonesia, Italy, the Philippines, and the U.K. plan to repatriate citizens aboard the ship beginning on February 21. Citizens will be required to be symptom free when boarding their respective flights and will uniformly be subject to quarantine upon arrival in country. The following countries have repatriated citizens aboard the ship: Australia (170 citizens on February 19), Canada (129 citizens on February 20), Hong Kong, Israel (11 citizens on February 20), South Korea, Taiwan (20 citizens on February 21), and the U.S. (more than 320 citizens on February 17). Among these repatriated citizens, 21 cases have been reported: U.S. (18), Australia (2), and Israel (1). Approximately 1,000 crew members will remain aboard to complete an additional 14-day quarantine, which is now expected to expire on March 6. Approximately 300 passengers remain aboard; 100 of these passengers have been identified as close contacts and will be removed and placed in a government-provided quarantine facility. Japanese passengers have no restrictions once they receive clearance to disembark the ship.

Approximately 8 cases (Chinese nationals) were confirmed among passengers aboard the World Dream cruise ship January 19-24; contact tracing is underway among the 4,000 passengers who disembarked in southern China and Hong Kong. No cases were detected among the passengers and crew members (approximately 3,600) on the subsequent sailing in Hong Kong.

One case (a U.S. citizen) has been confirmed among passengers who were aboard the Westerdam cruise ship. More than 2,200 passengers and crew were aboard the ship, which sailed from Hong Kong on February 1. More than 1,200 passengers and crew disembarked in Cambodia on February 13, including the U.S. case who flew to Kuala Lumpur, Malaysia on February 15 and was subsequently confirmed to have COVID-19 while asymptomatic. Most of the other passengers have also left Cambodia. More than 1,500 passengers and crew members who remained in Cambodia have tested negative for SARS-CoV-2.

Entry/Exit Procedures

Screening

In a reversal of long-standing policy, WHO now recommends that all countries implement temperature screening at ports of entry for passengers arriving from COVID-19-affected countries. Screening should be accompanied by dissemination of risk-communication messages at ports of entry to later capture asymptomatic persons who are in the incubation phase.

Entry screening using questionnaires, fever screening, thermal scanning, or visual inspection at international ports of entry in almost all countries (including Australia, Canada, U.K., and U.S.) is now in place as stated above. In most cases, anyone with fever and respiratory symptoms who has been to China in the past 14 days will be detained and isolated or placed in self-isolation. Anyone without symptoms but with travel to China in the past 14 days may be placed in quarantine or self-quarantine depending on where in China exposures may have taken place.

Asymptomatic Arrivals

Additionally, many countries have begun instituting management procedures for asymptomatic travelers (including citizens) who have arrived within the past 14 days (unless otherwise noted) from Hubei Province, elsewhere in China, and other COVID-19-affected countries. These management procedures include self-observation (remain alert for symptoms), self-monitoring (take

temperature 2 times per day), social distancing (remaining out of congregate settings, avoiding public transportation, and maintaining a distance of 2 m [6 ft] from others), and quarantine (self or mandatory separation from others not exposed) for 14 days (unless otherwise noted). Information is provided for the following countries:

Australia: Arrivals from anywhere in China should self-quarantine.

Canada: Arrivals from Hubei Province should self-quarantine; those from elsewhere in China should self-observe.

China (Beijing): Arrivals from elsewhere in China should self-quarantine.

France: Arrivals from anywhere in China should self-monitor and observe social distancing.

Germany: Arrivals from Hubei Province and the cities of Hangzhou, Ningbo, Taizhou, and Wenzhou in Zhejiang Province should report to health officials to complete an individualized survey; those determined to be at high risk of infection should self-quarantine and self-monitor.

Hong Kong: Arrivals from China will be subject to mandatory quarantine in a government-designated location. Fourteen categories of persons are exempt from quarantine (including academic researchers, select government officials, flight and cruise-ship crew members, and cross-boundary drivers) but are required to self-monitor with public health supervision and wear masks during their stay in Hong Kong.

Israel: Arrivals from China, Hong Kong, Macau, Singapore, or Thailand (excluding those with only a connecting flight in these locations) should self-quarantine. Arrivals from these countries, as well as from Japan or South Korea, who develop a fever ($\geq 37.8^{\circ}\text{C}$ [100.4°F]), cough, trouble breathing, or any other respiratory symptoms should self-isolate and contact public health authorities.

Italy: Arrivals from affected areas in China should self-quarantine.

Japan: Arrivals from Hubei or Zhejiang provinces should report to a quarantine officer and follow the instructions provided; no protocol is in place for those from elsewhere in China.

New Zealand: Arrivals from anywhere in China should self-quarantine.

Philippines: Arrivals from anywhere in China, Hong Kong, or Macau will be subject to mandatory home quarantine.

Singapore: Arrivals from Hubei Province will be subject to mandatory quarantine in a government-designated location; those from elsewhere in China will be subject to mandatory home quarantine and should self-monitor.

South Africa: Arrivals from anywhere in China and COVID-19-affected countries should self-quarantine and self-monitor.

Taiwan: Arrivals from anywhere in China, Hong Kong, or Macau should self-quarantine.

U.K.: Arrivals from Hubei Province should self-quarantine. Arrivals from elsewhere in China, as well as from Hong Kong, Japan, Macau, Malaysia, Singapore, South Korea, Taiwan, or Thailand, who develop symptoms of cough or fever or shortness of breath within 14 days of arrival should self-isolate at that time and contact public health authorities.

U.S.: Arrivals from Hubei Province will be subject to mandatory quarantine or self-quarantine and active monitoring for 14 days; those from elsewhere in China should self-quarantine and self-monitor with public health supervision.

Travel Advisories

The following countries and/or organizations, among others, have published travel recommendations:

Country Issuing	Avoid Travel to Hubei Province	Avoid Travel to China	Avoid Nonessential Travel to China
Australia		X	
Canada	X		X
China	X		
France	X		X
Germany	X		X
India		X	

Country Issuing	Avoid Travel to Hubei Province	Avoid Travel to China	Avoid Nonessential Travel to China
Japan	X		X
New Zealand		X	
Singapore	X		X
Spain			X
U.K.	X		X
U.S. State Department		X	
U.S. CDC			X
WHO has no travel advisory.			

Travel Restrictions and Internal Disruptions

According to WHO, more than 70 countries have now implemented some form of travel restriction. Different types of travel restrictions are in effect:

Major International Airlines Still Serving China (mostly reduced frequency): Aeroflot, AirAsia, Air China, All Nippon Airways, Asiana Airlines, Cathay Pacific, China Eastern Airlines, China Southern Airlines, Emirates, Etihad Airways, Ethiopian Airlines, EVA Air, Hainan Airlines, Japan Airways, Korean Air, Malaysia Airlines, Pakistan International Airlines, SilkAir, Singapore Airlines, SriLankan Airlines, Thai Lion Air

No Flights from Wuhan: Wuhan Airport is closed to all scheduled international and domestic flights.

No Flights from China: Indonesia, Israel, Italy, Kazakhstan, Northern Mariana Islands, Palau (no flights from China, Hong Kong, or Macau), Russia (except for Aeroflot flights), Turkey, Vietnam

Land Borders with China Closed: Burma (Myanmar), Kyrgyzstan, Mongolia, North Korea, Russia (entire land border with China, except for the portion between Altai Republic and Nei Mongol Autonomous Region [Mongolia]); high speed rails, bus services, and ferry services are suspended, and all but 2 border crossings are closed in Hong Kong.

Table 2: Travel Restrictions (use browser search function to find country of interest)

Country	No Travelers from Hubei	No Travelers from China (Chinese Nationals)	No Travelers from China (Foreign Nationals)	No Travelers from Countries Other than China	Medical Certificate Required
Antigua and Barbuda		X	X		
Armenia, Azerbaijan		X (excluding those with predeparture visas)			
Australia		X (in past 14 days)	X (in past 14 days; excluding permanent residents)		
Bahamas, Somalia		X (in past 20 days)	X (in past 20 days)		
Bahrain		X (in past 14 days)	X (in past 14 days; excluding nationals of AE, KW, OM, QA, SA)		

Country	No Travelers from Hubei	No Travelers from China (Chinese Nationals)	No Travelers from China (Foreign Nationals)	No Travelers from Countries Other than China	Medical Certificate Required
Bangladesh		X		X (nationals of HK, MO, TW)	X (all travelers from CN, HK, MO, TW)
Belize, Cook Islands, Fiji, Grenada, Guam, Indonesia, Iraq, Jordan, Madagascar, Maldives, Saint Lucia, Saudi Arabia Suriname, Trinidad and Tobago, Tuvalu, U.S., Vietnam		X (in past 14 days)	X (in past 14 days)		
Brunei, Japan, Malaysia	X (also applies to Zhejiang and Jiangsu provinces, excluding nationals of BN, JP, MY)				
Burma (Myanmar)		X	X (if traveling on a Chinese airline)		
Czech Republic, El Salvador, Kazakhstan, Paraguay, Sri Lanka, Tajikistan		X			
Equatorial Guinea, Gabon, Mozambique, Northern Mariana Islands		X	X		
French Polynesia					X (nationals of CN, HK, IN, JP, KH, KR, LK, MO, MY, NP, PH, SG, TH, VN; certificate from ≤ 5 days prior to arrival)
Guatemala		X (in past 15 days)	X (in past 15 days)		
Hong Kong	X	X (if stay will be < 14 days)	X (if stay will be < 14 days)		
India		X (since January 15, excluding those with OCI card and flight crew)	X (since January 15, excluding those with OCI card and flight crew)		
Iran					X (nationals of CN, HK, MO)
Israel		X (in past 14 days)	X (in past 14 days)	X (travelers from CN, HK, MO, SG, TH in past 14 days, excluding IL nationals)	
Kiribati		X (in past 14 days)	X (in past 14 days)	X (all COVID-19-affected countries in past 14 days)	
Kosovo					X (Chinese nationals)

Country	No Travelers from Hubei	No Travelers from China (Chinese Nationals)	No Travelers from China (Foreign Nationals)	No Travelers from Countries Other than China	Medical Certificate Required
Kuwait		X (in past 14 days)	X (in past 14 days)	X (HK nationals and foreign nationals in HK in past 14 days)	
Macau					X (foreign nationals from Hubei Province in past 14 days)
Marshall Islands		X	X	X (travelers from HK or MO)	
Mauritius		X (in past 14 days)	X (in past 14 days)	X (nationals from CN, HK, MO, TW in past 14 days)	
Micronesia		X (since January 6)	X (since January 6)	X (travelers from COVID-19-affected countries in past 14 days)	X (travelers from a country not affected by COVID-19 for ≥ 14 days who were previously in a COVID-19-affected country)
Mongolia		X (since January 1)	X (since January 1)	X (nationals from CN, HK, MO, TW since January 1)	
Nauru		X (in past 14 days)	X (in past 14 days)	X (persons who have been in COVID-19-affected countries are banned from transiting)	
New Zealand		X (since February 2)	X (since February 2)		
Niue		X (in past 30 days)			X (foreign nationals from a country not affected by COVID-19 for ≥ 14 days who were previously in CN; certificate from ≤ 3 days prior to arrival)
North Korea	X (in past 14 days)				
Pakistan					X (all travelers)
Palau, Taiwan		X (in past 14 days)	X (in past 14 days)	X (travelers from HK or MO in past 14 days)	
Papua New Guinea	X	X (in past 14 days)	X (in past 14 days)	X (travelers from HK or MO in past 14 days)	
Philippines		X (in past 14 days)	X (in past 14 days)	X (travelers from HK or MO in past 14 days, excluding nationals of Philippines)	
Russia		X		X (nationals from HK, MO, TW)	
Samoa		X (in past 14 days)	X (in past 14 days)		X (nationals from AE, AU, CA, CN, DE, FR, HK, KR, MO, MY, TW, US [California], VN; nationals from > 14 days prior to arrival with 14-day self-quarantine in a country not affected by COVID-19)

Country	No Travelers from Hubei	No Travelers from China (Chinese Nationals)	No Travelers from China (Foreign Nationals)	No Travelers from Countries Other than China	Medical Certificate Required
Seychelles		X (in past 14 days)	X (in past 14 days)	X (nationals of HK and MO and travelers transiting through HK and MO, excluding SC nationals)	
Singapore	X	X	X		
Solomon Islands		X (in past 14 days)		X (persons who transited through FI, KI, NR, PG, VU if evidence that in past 14 days they have been in or transited through COVID-19-affected countries)	
South Korea	X (excluding residents and KR nationals)				
Thailand					X (all Chinese nationals)
Timor-Leste	X (in past 4 weeks)				X (all foreign nations in CN in past 4 weeks)
Tonga		X (in past 14 days)	X (in past 14 days)		X (all foreign nationals in CN > 14 days prior to arrival; certificate from ≤ 3 days prior to arrival)
Vanuatu		X (in past 14 days)	X (in past 14 days)	X (all travelers from CN, HK, MO, TW in past 14 days)	X (all travelers from CN, HK, MO, TW > 14 days prior to arrival)

Abbreviations: AE = United Arab Emirates, AU = Australia, BN= Brunei, CA = Canada, CN = China, DE = Germany, FJ = Fiji, FR = France, HK = Hong Kong, IL = Israel, IN = India, JP = Japan, KH= Cambodia, KI = Kiribati, KR = South Korea, KW = Kuwait, LK = Sri Lanka, MO = Macau, MY = Malaysia, NP = Nepal, NR = Nauru, OM = Oman, PG = Papua New Guinea, PH = Philippines, QA = Qatar, SA = Saudi Arabia, SC = Seychelles, SG = Singapore, TH = Thailand, TW = Taiwan, US = United States, VU = Vanuatu

Internal Disruptions in China: Restrictions exist on movement throughout the country, affecting approximately 500 million people, especially in Anhui, Jiangxi, and Liaoning provinces and in the cities of Beijing, Chongqing, and Shanghai. Most public transportation and interprovince shuttle buses have been suspended, and many intercity roads are closed. Much of the country has also closed bars, restaurants, shops, businesses, schools, and museums, as well as many major tourist attractions. Most large events and social gatherings have been canceled. Restaurants remain open for delivery services in Beijing and Guangzhou; supermarkets remain open, and some restaurants remain open for a limited number of patrons in Beijing. Masks are required to be worn while in public in Beijing and Guangzhou, and temperature screenings occur at entrances of public places (including hospitals). China has stopped all inbound and outbound tour groups but not individual travel. Following the extended Lunar New Year holiday, workers in China (excluding Hubei Province) are returning to workplaces in major cities; many workplaces remain closed, whereas others are allowing employees to work from home. A "cordon sanitaire" has quarantined 54 million people in Wuhan and surrounding areas, and some cities in Hubei Province have barred citizens from leaving their homes. Visitors from Hubei Province will be actively monitored for 14 days in Haikou, Hainan Province.

Internal Disruptions in Hong Kong: Schools will remain suspended until at least March 16, and civil servants may work from home until February 23. Hong Kong officials have recommended select businesses (including cinemas, karaoke rooms, education centers, and clubhouses) close for 14 days as of February 10, although many communal gyms and private clubs remain open. All large-scale events have been canceled. Persons are encouraged to maintain a suitable social distance (2 m [6 ft] from others) limit public outings, avoid crowded places, wear masks, and observe hand hygiene (frequent, thorough handwashing) and respiratory hygiene (cough and sneeze etiquette).

Internal Disruptions in Singapore: Singapore is currently under the Disease Outbreak Response System Condition (DORSCON) Orange, which introduces business continuity plans, daily health checks at the workplace, cancellations of or additional precautions for large-scale events, temperature screening at hospitals, suspended school activities, and limited visits to preschools and eldercare services. Singapore's Ministry of Health (MOH) has also requested all public hospital staff to limit their work to 1 hospital.

Repatriation Flights

Repatriated persons will be closely monitored for 14 days after arrival at the quarantine location and present little threat of onward transmission. Some countries are testing respiratory specimens from all repatriated persons for SARS-CoV-2, and asymptomatic carriers are being detected. Natural history and transmissibility studies in these persons may answer several pending questions.

Australia: On February 5, a flight evacuated 50 persons to Christmas Island on a New Zealand government-chartered flight. On February 3, a flight evacuated 241 persons to Christmas Island. To date, no cases among those evacuated have been reported. On February 8, an Australian government-chartered plane evacuated more than 200 persons to Manigurr-Ma Village in Howard Springs (Northern Territory). On February 19, a flight repatriated 170 citizens who were aboard the Diamond Princess cruise ship to Howard Springs, Northern Territory; 2 cases were reported after showing symptoms upon arrival and are now in isolation and under medical care. More than 40 citizens are still aboard the ship or are being treated in hospitals in Japan.

Canada: On February 10, a Canadian government-chartered plane evacuated 185 persons to Canadian Forces Base Trenton in Ontario. On February 7, a Canadian government-chartered plane evacuated 176 persons, and a U.S. government-chartered plane evacuated 39 persons to Canadian Forces Base Trenton. To date, no cases among those evacuated have been reported.

U.K.: A government-chartered plane is scheduled to repatriate 78 citizens aboard the Diamond Princess cruise ship on February 22, as long as they remain symptom free. On February 9, a U.K. government-chartered plane evacuated approximately 200 persons to Kents Hill Park in Milton Keynes. Twenty-five persons were evacuated February 2-4 on planes chartered by other countries. On January 31, a flight evacuated 83 persons to Arrowe Park Hospital in Wirral. To date, no cases among those evacuated have been reported.

U.S.: Eight government-chartered evacuation flights have occurred. To date, only 3 cases among the evacuees have been reported: 2 cases at Marine Corps Air Station Miramar in San Diego, California on February 11 and 12, and 1 case at Joint Base San Antonio-Lackland in Texas on February 13; the cases were all on different flights, and no epidemiologic links exist between them. The first flight evacuated 195 persons to March Air Reserve Base in Riverside County, California on January 29; this group was released from quarantine on February 11, with no cases reported. On February 5, two flights evacuated 178 persons to Travis Air Force Base in Fairfield, California and 172 persons to Marine Corps Air Station Miramar in San Diego, California; both groups were released from quarantine on February 18, with 1 case (still hospitalized) reported in San Diego. On February 7, three flights evacuated approximately 550 persons to Marine Corps Air Station Miramar in San Diego, California, Joint Base San Antonio-Lackland in San Antonio, Texas and Camp Ashland near Omaha, Nebraska. Two flights repatriated 328 U.S. citizens who were aboard the Diamond Princess cruise ship on February 17; 18 of the passengers have tested positive for SARS-CoV-2 but at least 15 were asymptomatic, and all are now in isolation and under medical care. All remaining evacuees will be quarantined for 14 days at Travis Air Force Base in California and Joint Base San Antonio-Lackland in Texas. More than 100 U.S. citizens are still aboard the ship or being treated in hospitals in Japan (> 40 cases); any passengers that disembark from the ship on February 19 or later are required to wait an additional 14 days before they are permitted to board flights to the U.S.

Transmission

The detailed epidemiology of possible causative animal exposures and zoonotic transmission at the outset of the outbreak remains unclear. Many (67%) of the cases in December 2019 and approximately 50% of cases in January 2020 were directly linked to South China Seafood City market in Jiangnan District, which sold seafood and other wildlife (including birds). Thirty-three environmental samples from the market tested positive for SARS-CoV-2, indicating that the market was an—or the—origin or amplification point of the large-scale outbreak. No samples taken directly from live animals have been reported as positive. The symptom-onset date of the first case identified in the outbreak was December 1, 2019; the case reported no exposure to the market; no epidemiological link has been detected between this case and later cases. An initial single jump of SARS-CoV-2 directly from bat to human, or from an intermediate animal host to a human, with subsequent initial human-to-human propagation within the seafood market, is increasingly likely.

Infected intermediate animal hosts, if they exist, may still be present, but the sale of live animals in markets in China has officially ceased. Preliminary data, not yet peer-reviewed and published, indicate pangolins may be a leading candidate. South China

Seafood City market, closed indefinitely since December 31, 2019, is irrelevant at the current phase of the epidemic. Sustained multigenerational human-to-human transmission is clear in Hubei; the degree of sustained community spread in other parts of China remains variable, with little specific data available. All evidence to date suggests that the main route of transmission is via respiratory droplets or close contact with an infected person. Aerosolized transmission, has been announced by some local health officials in China); however, no specific data or peer review are available. A reproductive number, R_0 , is estimated at 2–3 both by Chinese authorities and by multiple other international estimates. R_0 greater than 1 indicates that each case leads to more than 1 subsequent case, making control much more difficult. R_0 is not a constant number and changes with the ongoing circumstances and evolution of an outbreak. A pandemic is defined as an ongoing epidemic on 2 or more continents, and these criteria will be met if sustained transmission occurs outside of Asia. A pandemic can be global, but with levels of severity in individuals that range from mild (with low mortality) to severe.

In serial nose and throat swabs in a cohort of 17 symptomatic COVID-19 patients with exposure in Wuhan the highest viral loads were detected within 3 days after symptom onset, with higher viral loads detected in the nose than in the throat, especially in the early stage of illness. Viral loads peaked between 6-12 days after symptom onset and were highest in those most severely ill. Additionally, the viral load that was detected in 1 asymptomatic secondary case was similar to that in the symptomatic persons. These findings support possible transmission early in illness in a pattern similar to influenza. However, how the SARS-CoV viral load correlates with culturable or transmissible virus either in symptomatic or asymptomatic persons remains to be determined.

Several published cluster studies indicate at least asymptomatic shedding (but not necessarily transmission). After a repatriation flight to Japan, officials there screened and tested every passenger; 8 tested positive for SARS-CoV-2, but 4 of those were asymptomatic. On a German repatriation flight, 2 asymptomatic individuals tested positive, both by PCR and by viral culture. German virologists were able to culture SARS-CoV-2 from nasopharyngeal swabs from several minimally symptomatic cases in the Munich secondary cluster. Sequence data from several small clusters indicate identical virus in all subjects within the cluster. The frequency of asymptomatic transmission is unclear and, so far, appears to be an outlier or rare event, especially if super-spreaders with high viral loads early in the incubation phase exist. No case of COVID-19 has been attributed to transmission on an aircraft.

Based on modeling by a variety of groups, WHO has derived an estimated number of total infections, and proposes an infection fatality ratio (IFR) to clearly differentiate the ratio from a case-fatality rate (CFR), calculated using notifiable disease data. This IFR is meant to represent the fraction of all infections (both diagnosed and undiagnosed) that result in death. Based on these available analyses, current IFR estimates range from 0.3% to 1%. However, as also stated by WHO, without population-based serologic studies, the proportion of the population that has been infected with SARS-CoV-2 is impossible to know.

Limited experience indicates that no vertical transmission (from mother to fetus or newborn before, during, or immediately after delivery) of SARS-CoV-2 has been reported; SARS-CoV-2 was not detected in samples of amniotic fluid, and all infants tested negative. Limited data are available for vertical transmission for other coronaviruses (MERS-CoV and SARS-CoV).

Based on the limited data to date, SARS-CoV-2 has not been detected in the breast milk of infected women. Reports of breastfeeding women infected with SARS-CoV in 2002-03 were limited. The virus was not detected in breast milk, but SARS-CoV antibodies were detected in at least 1 sample.

More than 120,300 close contacts remain under surveillance in China (> 606,000 have been followed-up), and contact tracing is ongoing in affected provinces and municipalities. However, not all contacts are being ascertained or monitored adequately.

The survival rate of SARS-CoV-2 on surfaces or in the environment is unknown. In general, the survivability of zoonotic coronaviruses on surfaces is significant, generally 1 to 6 days (longest on plastic) depending on ambient conditions, including temperature, humidity, and the specific infected bodily fluid contaminating the surface. The risk of spread is very low from items shipped at ambient temperatures over several days. No evidence exists of SARS-CoV-2 transmission associated with imported goods; no associated cases have been reported to date. See Survival on Surfaces.

Disinfection processes that are effective for other zoonotic coronaviruses should be followed for now. Clean daily all "high-touch" surfaces, such as counters, tabletops, doorknobs, bathroom fixtures, toilets, phones, keyboards, tables, and bedside tables. Also, clean any surfaces that may have blood, bodily fluids, and/or secretions or excretions on them. After cleaning solid materials using a detergent, use a diluted bleach solution or a household disinfectant with a label that says "EPA-approved." To make a bleach solution, add 15 mL (1 tablespoon) of bleach to 1 L (1 quart) of water; for a larger supply, add 60 mL (2 oz) of bleach to 4 L (1 gallon) of water. For surfaces sensitive to bleach, at least 70% ethanol should be used. Alcohol-based hand disinfectants and common hospital personal disinfectants are all effective against SARS-CoV-2 but provide no ongoing protection between uses.

Clinical Manifestations

An incubation period of 2 to 7 days appears most common (5 days typical), with an upper range of 14 days. Most cases in China (using the Chinese case definition, which includes pneumonia) have reportedly exhibited symptoms of fever, respiratory compromise, and pneumonia, with focal ground glass-like infiltrates on chest x-ray or CT scan, which may progress to bilateral diffuse pneumonia. SARS-CoV and MERS-CoV induce excessive and aberrant ineffective host immune responses that are associated with severe lung pathology, leading to death. Some patients with COVID-19 have developed acute respiratory distress syndrome (ARDS), with characteristic pulmonary ground glass changes on imaging. A number of clinical reports are consistent with mild illness for up to 14 days, with late onset of severe respiratory compromise. A lymphocyte count of less than $1.5 \times 10^9/L$ was present in 82% of hospitalized patients in one cohort in China. Diarrhea may occur, but incidence has been highly variable in several cohorts. Based on a study conducted by China CDC on the first 44,600 confirmed cases, more than 80% had mild presentations, 14% were severe, and 5% were critical. The CFR among confirmed cases was 2.3% and was highest among persons aged ≥ 80 years and among people with comorbidities. The spectrum of early disease, overall disease, and case fatality in cases ascertained by non-Chinese criteria (requiring only respiratory symptoms) will become clearer once data on the evolution of the cases outside of China are available. Based on available information, only 12 cases with transmission outside of China have died (at least 3 of these cases reported travel history to China), and more than 50 cases have developed severe disease.

A non-peer-reviewed, ahead-of-print journal article from China describing a cohort of approximately 1,000 patients is notable for the finding that only 43% of patients ill enough for hospitalization had fever upon admission; 88% of patients had fever during their hospital stay. The proportion of afebrile patients in the setting of a radiologic abnormality is unclear.

No known drug treatment, vaccine, or therapeutic monoclonal exists for COVID-19. As of February 19, one hundred twenty-four studies have either commenced or are expected to do so shortly, with all but 3 taking place in China; 47 trials involve natural products. Favilavir, a Chinese antiviral, has been approved for use in China to treat COVID-19 cases. Chloroquine, remdesivir, and lopinavir/ritonavir have an inhibitory effect on SARS-CoV-2, and a clinical trial of remdesivir, chloroquine, and abidol has begun in China. Remdesivir is available from the U.S. CDC and has been used for 2 U.S. cases. Lopinavir/ritonavir (readily available as Kaletra in most countries) is being used empirically in China and elsewhere. Usual antiviral drugs are ineffective, including oseltamivir (Tamiflu) and acyclovir. Favipiravir, baloxavir, interferon-alpha, and ribavirin have weak activity but are being tried as part of drug combinations. Steroids should not be used. Hypoxemic respiratory-failure patients failing standard oxygen therapy (10-15 LPM through a non-rebreather mask) should not routinely be treated with high-flow nasal oxygen or noninvasive ventilation. Risk of treatment failure exists; if used, patients must be closely monitored for deterioration and the need for intubation.

Positive stool PCR for SARS-CoV-2 has been reported for the first time in an exported case and alluded to in China (data not available), but the implications are unknown. Stool-mediated transmission of SARS-CoV occurred but appeared not to be a significant driver of the 2003 outbreak.

Pregnant women are generally more susceptible to viral respiratory infections, including COVID-19. Adverse pregnancy outcomes (pregnancy loss, low birth weight, preterm birth) have occurred with influenza viruses and other related coronaviruses (MERS-CoV and SARS-CoV). No data are available regarding pregnancy loss in women with COVID-19, but preterm birth has been reported based on limited case reports. High fevers (from any cause) during the first trimester increase the risk of certain birth defects. No information is available on long-term health effects of SARS-CoV-2 infection in utero.

Virology

SARS-CoV-2 was initially isolated from 1 case; this information was published internationally by Chinese scientists on January 10. Electron microscopy of multiple specimens in labs inside and outside of China has demonstrated classic coronavirus particles. SARS-CoV-2 is the seventh member of the family of coronaviruses that infect humans. Novel coronaviruses from Wuhan, together with 2 bat-derived SARS-like strains, form a distinct clade in lineage B of the subgenus sarbecovirus. SARS-CoV-2 is a group 2b coronavirus (as are MERS-CoV and SARS-CoV), with a whole genome similarity of up to 80% to SARS-CoV but with a similarity between different gene segments ranging from 60% to 90%. SARS-CoV-2 exhibits a 96.5% similarity to the known bat coronavirus precursors in the same viral clade.

In the most sophisticated and authoritative analysis of the available data to date, 2 notable features of the SARS-CoV-2 genome have been identified: 1) the presence of a uniquely configured receptor binding domain (RBD) on the virus, which appears to be optimized for binding to the human ACE2 receptor and 2) a polybasic (furin) cleavage site on the protein spike extending from the virus surface. Several important observations have been made, although proof awaits. Pangolin CoV is identical to SARS-CoV-2 at all 6 key RBD residues, but no pangolin CoV (which does not carry the polybasic cleavage site insertion) has yet been identified that is sufficiently similar to SARS-CoV-2 across its entire genome to support direct human infection. A possibility exists that a progenitor to SARS-CoV-2 jumped from nonhuman animals to humans, with the genomic features described above

acquired through adaptation during subsequent human-to-human transmission. Once these adaptations were acquired (either together or in series), it would have enabled the outbreak to accelerate. If SARS-CoV-2 pre-adapted in an animal species (pangolin or other), then risk exists for future reemergence events in the continued presence of the intermediate animal host, even if the current epidemic is controlled. In contrast, if the described adaptive process occurred in humans, then even with repeated zoonotic transfers in the future, human transmission is unlikely to accelerate unless the same series of mutations occurs; this seems less likely.

The analysis also provides evidence that SARS-CoV-2 is neither a laboratory construct nor a purposefully manipulated virus. SARS-CoV-2 is not derived from any previously used or known virus backbone. Although SARS-CoV-2 is well suited to human infection, the unique RBD is not structured in such a way that someone with intent to manipulate would have predicted using current computational models and previously known coronavirus constructs. In terms of mutations introduced by repeated artificial laboratory passage of existing viruses, new polybasic cleavage sites have only been observed after prolonged passaging of low pathogenicity avian influenza virus (not coronaviruses) in cell culture or animals. Thus, although genomic evidence does not in any way support the idea that SARS-CoV-2 is a laboratory construct, proving or disproving any other theories of its origin is not completely possible at this time.

SARS-CoV-2 has been shown to use the same cell-entry receptor as SARS-CoV. Prediction of human-to-human transmissibility from sequence data is difficult because coronaviruses vary widely in their transmissibility; coronaviruses that are acquired from animals generally have some potential for human-to-human transmission. Evidence from subsequent whole genome sequences acquired over the past several weeks show little genetic variation, indicating that the virus jumped from an animal reservoir to humans within the past few months. Identical, recent mutations in epidemiologically unlinked cases support sustained human-to-human transmission.

Diagnosis

Sequence data available since early January have allowed national laboratories to rapidly develop PCR diagnostic kits, which are now available in most developed countries and most Asian countries. Twenty-four African countries have the reagents needed to conduct tests, but very few national laboratories in South America have them. PCR testing is centralized at national laboratories in most countries. An FDA Emergency Use Authorization for the U.S. CDC kit was granted on February 4 in the U.S. In addition to U.S. CDC, only 3 U.S. states (California, Illinois, and Nebraska) can currently test for SARS-CoV-2; some of the testing kits previously sent to other states and at least 30 countries were flawed and produced inconclusive results. U.S. CDC has increased its testing capacity until the testing kits are replaced. Some states (including Florida) are no longer reporting cases under investigation to U.S. CDC. The U.S. CDC assay protocol is publicly available, and results are obtained within approximately 4 hours. Viral loads appear to be highest in lower respiratory tract specimens (obtained by tracheal aspirate or bronchoalveolar lavage), but both these specimens and upper respiratory specimens from nasopharyngeal or oropharyngeal swabs should be sent for testing. Upper respiratory specimens alone are usually adequate for the U.S. CDC PCR. Serial PCR studies have not been performed on respiratory specimens from confirmed cases to determine onset or duration of viremia/infectiousness.

HKU1, NL63, 229E, and OC43 are human coronaviruses that are detected by some routine multiplex PCR panels used in routine clinical practice. These coronaviruses are associated with minor upper respiratory infections and viral pneumonia, but unlike SARS-CoV, MERS-CoV, and SARS-CoV-2, these agents are not associated with major outbreaks or severe respiratory distress syndrome.

SARS-CoV-2-specific blood antibody detection tests that would be especially useful for population-based studies to detect asymptomatic individuals are unavailable, even in research laboratories. Point-of-care rapid tests, presently unavailable, took months to develop during the 2014 Ebola outbreak, which involved a well-characterized virus. Refined rapid tests do not generally perform well in asymptomatic individuals with low pretest probability of infection (such as travelers); even with a specificity of $\geq 98\%$ in a low-risk population, more than 90% of positive tests will be false positives. Such tests work well on ill people in epidemic areas where the pretest probability is very high.

In the U.S., specimens from individuals with influenza-like symptoms who have tested negative for influenza will be tested for SARS-CoV-2 at 5 public health laboratories to provide an early warning of potential spread across the U.S. Guangzhou (China), Hong Kong, and Singapore are also implementing a similar strategy.

Criteria for Testing of Suspected Cases

U.S. CDC

Persons meeting the following criteria (clinical features and epidemiologic risk) for suspected cases of COVID-19 will be considered persons under investigation (PUI):

- Fever *or* signs/symptoms of lower respiratory illness (e.g., cough, shortness of breath) *plus* close contact with an ill, laboratory-confirmed COVID-19 case within 14 days of symptom onset
- Fever *and* signs/symptoms of lower respiratory illness (e.g., cough, shortness of breath) *plus* a history of travel from Hubei Province within 14 days of symptom onset
- Fever *and* signs/symptoms of lower respiratory illness (e.g., cough, shortness of breath) requiring hospitalization *plus* a history of travel from mainland China within 14 days of symptom onset

Fever may be subjective or confirmed. Close contact is defined as 1) being within 2 m (6 ft) of a confirmed COVID-19 case for a prolonged period of time and can occur while caring for, living with, or sharing a health care waiting area or room or 2) having direct contact with infectious secretions of a COVID-19 case. The precise definition of a prolonged period of time to be a close contact is left to a case-by-case assessment by public health authorities by the U.S. CDC; however, in the case of the contact being in the health care setting, the definition (out of caution) has been set to more than 1 to 2 minutes. In Hong Kong, the time limit for a close contact in the community setting has been set at more than 15 minutes of face-to-face exposure.

HCWs entering the room with a PUI should use standard precautions, contact precautions, airborne precautions, and eye protection (e.g., goggles or a face shield).

PUIs for COVID-19 should be asked to wear a surgical mask as soon as they are identified and be evaluated in a private room with the door closed, ideally in an airborne-infection isolation room if available.

Prevention

Travel to China

Travelers going to China should avoid animals (alive or dead), animal markets, products that come from animals (such as uncooked meat) and contact with ill-appearing persons. Quality of infection control at medical facilities in Wuhan is uncertain, and those with minor medical problems should avoid busy medical settings. Infection-control supplies have been depleted in medical facilities in the smaller cities in central China; the situation is critical in many areas, and resupply is uncertain. Current influenza vaccination is recommended to decrease the risk of simple influenza being mistaken for COVID-19 upon return.

In the Workplace

To help prevent workplace exposure to acute respiratory illnesses, including COVID-19, U.S. CDC recommends that, beginning immediately, employers actively encourage (through generous leave policies) employees with fever ($\geq 37.8^{\circ}\text{C}$ [100.4°F] using an oral thermometer), signs of fever, or symptoms of respiratory illness to remain at home, to observe hand hygiene (frequent, thorough handwashing) and social distancing if possible, and to avoid sharing of household items. Employees who become ill at work should be immediately isolated from other employees and sent home. Employee education on the aforementioned measures should be aggressive. Worksite hygiene measures and worksite disinfection should be active and continuous. Employees should not return to work until they are free of fever and other symptoms for at least 24 hours without the use of fever-reducing or other symptom-altering medications (e.g., cough suppressants). Generous leave policies should also be applied to employees that must stay home to care for a sick household member. Should an outbreak of COVID-19 occur in the U.S., large-scale absenteeism is possible. Contingency planning guidance is provided by U.S. CDC at <https://www.cdc.gov/coronavirus/2019-ncov/guidance-business-response.html>.

Employees, Students, Visitors, All Others Coming from China

Arrivals who develop fever or respiratory symptoms within 14 days of travel to China should self-isolate; observe respiratory hygiene (cough and sneeze etiquette), hand hygiene, and social distancing; wear a mask; and contact public health authorities (or telephone ahead before presenting to a hospital).

The extent of transmission from asymptomatic individuals infected with SARS-CoV-2 to others is unknown, but several apparent instances have been documented. Influenza viruses can be transmitted 1 to 2 days prior to symptom onset. SARS-CoV did not transmit until 4 days after symptom onset, which led to its eradication because all contacts with fever could be promptly identified and isolated. Management strategies for asymptomatic persons are based on the person's risk level, as shown in the table below.

Table 3: Management of Asymptomatic Persons with Potential SARS-CoV-2 Exposure

Risk Category	Movement Restrictions and Public Activities	Monitoring	Travel
High Hubei exposure ¹	Quarantined (voluntary or under public health orders) in a location determined by public health authorities (PHA). No public activities	Daily active monitoring (communication with PHA)	Controlled (travel must be coordinated with PHA)
Medium Other China exposure ² Certain aircraft exposure ³	Remain at home or in a comparable setting, if possible. Avoid congregate settings, limit public activities, and remain out of public places where close contact may occur.	Aircraft exposure: active monitoring (communication with PHA) Travel from China outside of Hubei Province: self-monitoring (take temperature 2 times per day and remain alert for symptoms) with PHA supervision	Postpone additional long-distance travel after reaching the final destination. Persons who do travel may not be able to return if they become symptomatic during travel.
Low Certain aircraft exposure ⁴	No restrictions	Self-observation (remain alert for symptoms)	No restrictions

1. Travel from Hubei Province in the past 14 days
2. Travel from mainland China outside of Hubei Province and not having a high-risk exposure
3. Seated on an aircraft within 2 m (6 ft; approximately 2 seats in each direction) of a symptomatic, laboratory-confirmed case of COVID-19; laboratory confirmation may not occur until after travel. Out of an abundance of caution, providers may presume the symptomatic case to be infected with SARS-CoV-2 and management of the exposed person implemented.
4. Seated on an aircraft not within 2 m of a symptomatic laboratory-confirmed case of COVID-19 infection and not otherwise having a medium- or high-risk exposure

In general, employers and schools in the U.S. and many Asian countries are excluding from the workplace or school all employees and students who returned from anywhere in China in the past 14 days. Asymptomatic persons arriving from Hubei Province, China (high-risk exposure) will be quarantined and subject to daily active monitoring (communication with public health authorities). Asymptomatic persons arriving from other locations in China (medium-risk exposure) should self-quarantine (remain at home or in a comparable setting) if possible and self-monitor (take temperature 2 times per day) and avoid congregate settings, limit public activities, and remain out of public places where close contact may occur. Several countries have specific national requirements for all returnees from China to self-quarantine for 14 days.

Asymptomatic persons with a low-risk exposure outside of China (same indoor environment with a symptomatic COVID-19 case but without close contact) should self-observe for 14 days after their last potential exposure, but they have no movement restrictions; however, an employer may choose to apply the aforementioned stricter recommendations to these individuals as well.

Based on advanced information and employee or visitor medical screening, additional preventive measures may be required (e.g., increased ventilation, larger meeting rooms with more personal space per participant, disinfection of work areas and lavatories, and provision of alcohol wipes). Data show that the public use of masks (including N-95 masks) by asymptomatic persons is not beneficial.

Household members of a PUI should observe hand hygiene and social distancing if possible and should avoid sharing household items. Such persons should self-monitor, and employers should consider the various options above, including exclusion from the workplace until 14 days after the last possible day of infectiousness for a PUI.

U.S. CDC, Singapore's MOH, and Hong Kong's Centre for Health Protection essentially state that household members of asymptomatic individuals in self-quarantine after arrival from China are not considered case contacts and may continue their daily activities (e.g., work or school) while continually monitoring their health and seeking medical attention if symptoms develop. However, businesses may conservatively opt to implement restrictions on a case-by-case basis.

Caregivers of a confirmed case or a PUI should take additional precautions to include the use of disposable gloves, gowns, and masks and the proper disposal of these items.

Key Unanswered Questions

- Spectrum of clinical disease: proportions of asymptomatic persons; persons who are symptomatic but apparently (to others) asymptomatic; those with influenza-like illness, focal pneumonia, or severe respiratory compromise; and fatalities
- Numerical risk for travelers going to areas with sustained transmission (i.e., destinations with cases occurring without known exposure to other cases)
- Implications of respiratory tract viral detection in asymptomatic individuals
- Onset and duration of infectivity with respect to symptoms
- Existence and frequency of super-spreading events
- Role of surfaces and inanimate objects in transmission
- Reproductive number: on average, how infectious is the typical case
- Differences in clinical manifestation in Chinese (smoking, pollution) versus other populations
- Likelihood of mutations within the genome with serial passage through humans
- Mechanism of species jump from bats to humans and whether animals still pose a threat
- Speed of vaccine development
- Utility of very traditional Chinese methods of social distancing and quarantine in the twenty-first century

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