Wellington-Dufferin-Guelph Public Health
COVID-19 Situational Update
Monday Feb 24, 2020, 8.30 a.m.

Note: A large and constantly changing volume of information on COVID-19 is available from official sources as well as via the media. The highlights below attempt to summarize the most current information relevant to risk assessment and communication at WDGPH. **New information in the body of this report is typed in *red italicized font.***

Highlights

- Several countries affected with community transmission in those countries is usual definition for a pandemic. Some think that WHO will declare a pandemic this week. At lease some experts consider COVID-19 to be 'Disease X'. WHO holding news conference at 9.30 a.m.
- As apparent decrease in daily new cases in China, sharp rise in cases in Singapore, South Korea (greatly increased case count over the weekend) and Italy (especially Lombardy region). Several areas in mass quarantine; South Korea has designated two cities 'special care zones' because of the increase in cases ; country on red alert. 52 illnesses linked to superspreader at church in SK ; more than 9,000 church members in self-quarantine.
- Iran : 47 confirmed cases and 12 deaths with unofficial reports of 50 deaths meaning many, many more undetected underlying cases in the community: a rapid increase in reported cases since the first 2 cases and deaths reported last Friday (Feb 21); most likely many more undetected.
- WHO say 'window of opportunity' for preventing further spread of the virus is now 'narrowing' (Section 3).
- Experts increasingly think that a pandemic is now likely. US CDC preparing for a pandemic; 34 cases in the US and more anticipated.
- Results of a study on 17 patients by Zhou et al. described in Section 4 suggest that "the viral nucleic acid shedding pattern of patients infected with SARS-CoV-2 resembles that of patients with influenza and appears different from that seen in patients infected with SARS-CoV." The authors state that their findings "are in concordance with reports that transmission may occur early in the course of infection and suggest that case detection and isolation may require strategies different from those required for the control of SARS-CoV."
- Several repatriated Diamond Princess passengers have tested positive (Section 1).
- A study recently published in Emerging Microbes and Infections suggests that some swab-negative patients may still be viraemic. This possibly explains the apparent poor performance of the tests currently being used for SARS-CoV-2 detection. The authors report that a serological test for antibodies developed in-house produced better results and suggest that this test be used as it appears to be more reliable (Sections 4 and 5).
- In China, recovered patients being quarantined for further 14 days after discharge, as some testing positive again after having apparently recovered (Section 1).
- Appeals in China for donations of blood from recovered patients to treat critical cases (Section 6).
- Letter from Chang et al to the Lancet states that 'aggressive measures (such as N95 masks, goggles, and protective gowns) [are warranted] to ensure the safety of health-care workers during this COVID-19 outbreak…"
- New cases in BC and Toronto, total in BC now 6. BC case had traveled from Iran and is first case in Canada not linked to China (Section 1).
- More than 500 inmates diagnosed with COVID-19 in 3 separate prisons in 3 provinces in China, causing another spike in case counts February 20 (Section 1).

SECTION 1: Case counts and Outbreak Progression

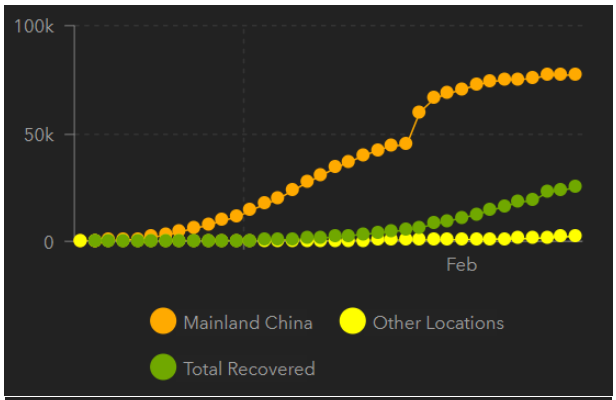
As of Monday February 24 (from BNO News):

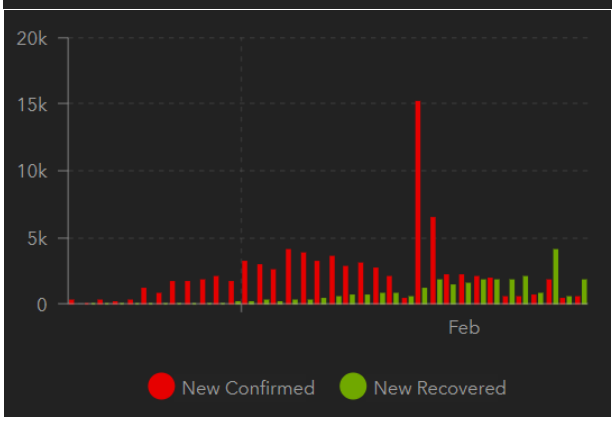
Region	Number of Reported Cases	Percentage of All Cases Worldwide	Number of Reported Deaths	Case Fatality (%)
Hubei province	64,482	81.6	2,495	3.9
China: Mainland (incl Hubei)	77,345	97.9	2,592	3.4
China: Mainland (excl Hubei)	12,863	16.3	97	0.8
Asia: Other (incl Hong Kong, Macau)	1,273	1.6	14	1.1
Other countries	399	0.5	18	4.5
TOTAL	**79,017**	**100.0**	**2,624**	**3.3**

[Other sources of timely counts: latest WHO daily situation report; European CDC; Johns Hopkin dashboard.]

The charts below (source Johns Hopkins dashboard) show the progression over time of cumulative and new case counts (respectively) reported from China and the rest of the world. *Note that the current day's case counts are updated in China on the evening of that day, Eastern time; therefore although counts in the table above reflect numbers reported as of the morning on the current day, the chart below may show partial case counts for the most recent day(s) displayed. In addition, because of some uncertainties about case definitions and testing challenges in China, any change in the slope of the chart should be interpreted with caution.*

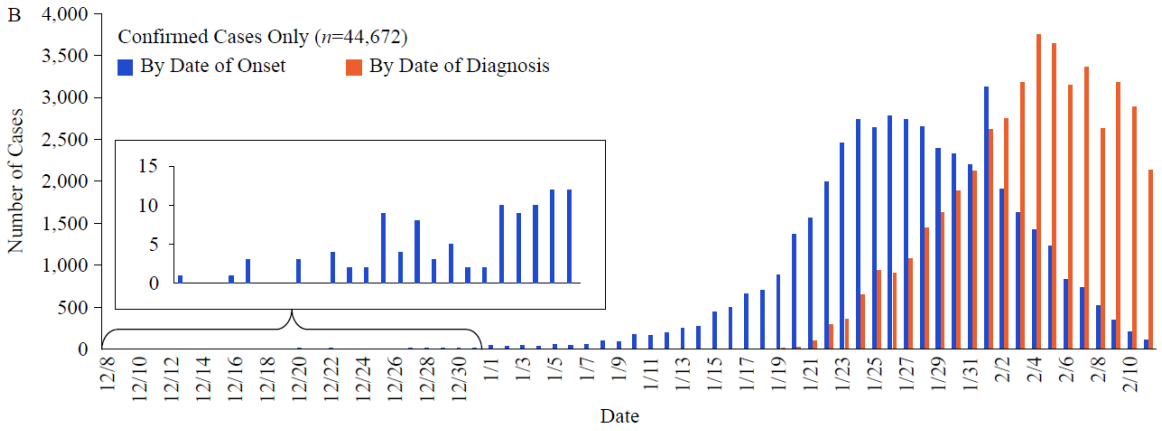
Note: *The sudden increase in case count in Hubei province seen on Feb 13 was due to the inclusion for the first time of cases diagnosed clinically and by CT scan (from Hubei only) in the reported case counts. Only a small percentage (about 10%) of the newly reported cases are reported to be lab-confirmed cases. The reported case fatality percentage after this change was lower than it had been when using the previous case definition; perhaps only the most severely ill are being tested in China for laboratory confirmation. On Feb 20, there was reportedly another change in the way cases were counted in China: cases diagnosed clinically in Hubei were once again excluded from case counts, leading to a marked decrease in new cases for that day.*





For a map of number of cases by country, see the WHO daily situation reports.

Below: Chart from study of over 70,000 patients recently released in Chinese CDC Weekly report:



- *Sudden large increases in the number of detected cases in South Korea, Italy and Iran over the weekend, with 12 deaths reported by Iran and unofficial reports of the death count being 50. With an estimated 2% confirmed case fatality ratio, even the 12 deaths officially reported in Iran imply that there were probably several hundreds of undetected/unreported cases two to three weeks ago, and many more now. This is supported by the recent detection of exported cases of COVID-19 from Iran in several countries including Canada and the UAE. The high death count from Iran and apparent under-reported case count has driven the mortality rate outside Asia from about 1% up to 4.5%; hopefully this artifact will soon be corrected with increased testing for the virus in Iran.*
- The number of confirmed infections is increasing in Japan, with spread of COVID-19 among taxi drivers following the infection of one driver by a group of tourists from China. *Case count also increasing in Singapore where several clusters are being investigated, including at least two associated with a churches.*
- *There are now more than 2,000 cases outside mainland China. February 19 saw highest daily new case count outside China to date.*
- *Last passenger has reportedly disembarked from the Diamond Princess. Total number of cases from the ship is currently 691. Third person in their 80s from the ship has died from pneumonia; test status unknown. Japan has apologized for allowing at least one positive case to disembark. Failed to properly test 23 passengers; trying now to track them down. At least 55 crew positive so far.*
- *Several repatriated cruise ship passengers have tested positive: US 18, Australia 7 and UK 4 passengers to date.*
- *Now 10 cases in Canada, including BC case arrived from Iran, which is first case in Canada not linked to China. Over the last weekend, UAE and Israel also reported cases imported from Iran.*
- First case of COVID-19 reported week of from the continent of Africa: visitor from China diagnosed in Egypt.
- First death reported from outside Asia: 80-yo man from Hubei who arrived in France in late January, became symptomatic and quarantined. Secondary lung infection was reportedly cause of death. Case reportedly turned away from two hospitals in France before finally being tested and isolated, as not thought to be at risk of having been infected by the virus.
- Anzhai et al. analyzed data on confirmed cases diagnosed outside China to estimate the impact of travel reduction the number of exported cases, the probability of a major epidemic, and the time delay to a major epidemic. They estimated that 226 exported cases (95% confidence interval: 86, 449) were prevented from 28 January to 7 February 2020 - a 70.4% reduction in incidence compared to the counterfactual scenario. With a median time delay to a major epidemic of only two days or less, the authors conclude that the decision to control travel volume through restrictions on freedom of movement should be balanced between the resulting estimated epidemiological impact and predicted economic fallout.

- *More than 500 inmates have been diagnosed with COVID-19 in 3 separate prisons in 3 provinces in China, causing spike in case counts February 20.*
- *Liu Q et al. (Feb 22) estimate that the COVID-19 epidemic curve for mainland China excluding Hubei will peak in early to mid-March at about 13,806 cases (95% CI: 11,926-15,845).*
- *Hubei is still seeing the majority (83.4%) of cases in mainland China. Hubei also still has a disproportionate number of deaths (now 96.3% of all mainland China) and a higher confirmed case fatality rate/percentage (cCFR): 3.9% vs 0.8% in the rest of mainland China and other Asian regions, in spite of a noticeable increase in the latter from 0.2% two weeks ago. A study published yesterday by Xu et al. (see Section 6) showed that cases seen in Zhejiang province were generally milder than those in Wuhan, and attribute this finding to the cases in Zhejiang being further down the chain of transmission of the virus than those in Wuhan.* The number of fatalities and cCFR outside of Hubei may continue to increase due to the lag in outbreak start dates in the rest of the mainland compared to Hubei; however, so far, the cCFR outside Hubei, although tripled from 0.2% to 0.6% in the last 2 weeks, remains far lower than that in Hubei. It is possible that there is a true difference between the cCFRs of Hubei and other regions within and outside mainland China because of a difference in the level of preparedness, case management and treatment in Hubei vs. elsewhere, delays in reporting mortalities and/or differences in the criteria for testing for the virus. Of their findings from data from 1,099 patients with COVID-19 from 31 mainland China provinces, Guan et al note that: "The fatality rate was lower (0.88%) when incorporating additional pilot data from Guangdong province (N=603) where effective prevention has been undertaken (unpublished data)… Early isolation, early diagnosis and early management might have collectively contributed to the marked reduction in mortality in Guangdong." However, over 1000 of the 1099 cases followed in the study were still in hospital at the time the manuscript was written, meaning that estimates of mortality in this cohort may be premature. For a good discussion on the challenges of calculating a true case fatality rate, see Battegay et al. In a study adjusting for the lag in deaths associated with COVID-19, Wilson et al. have estimated a CFR of 1.37% (95%CI: 0.57% to 3.22%) for COVID-19 cases in countries outside China where the healthcare systems are working relatively normally.
- A large study by the Chinese Centres for Disease Control (CCDC) of 44,672 confirmed cases in China as of Feb 11 reported that 80.9% of infections are classified as mild, 13.8% as severe and 4.7% as critical. Fatality rate increases with age, highest in those over 80 years old, and higher in males. It reports that, as seen by the numbers of cases and mortalities reported so far, the cCFR is higher in Hubei than the rest of the country (2.9% vs 0.4%). The work points toward the virus being highly transmissible, with 1716 confirmed infections and 5 deaths among health care workers as of Feb 11. The study also identifies which existing illnesses put patients at risk, with cardiovascular disease leading, followed by diabetes, chronic respiratory disease and hypertension (see Section6). The epidemic curve of cases by onset date is reported to have shown a decline from the 23-26 of January up until Feb 11. The peak number of cases diagnosed per day peaked approximately a week and a half later on February 4th (see chart directly above), reflecting the trends seen recently in reported case numbers from other sources. A much higher percentage of health workers were classified as critical compared to the study population in general (14.6% vs. 4.7%).
- Stories in the media describe an overburdened health care system in Wuhan, with late diagnosis and late or no treatment of cases in the earlier stages of the outbreak. This could possibly have contributed to the much higher fatality ratios seen in Hubei.
- In China, downward trend in daily number of new reported cases continues (see charts above). According to Mi Fang, head of the Chinese National Health Commission, the decrease is due to increased medical intervention, more medical resources directed toward Hubei and mild cases being detected and treated earlier. On Feb 19, for the first time, the number of cases recovered in China exceeded the number of newly confirmed cases.
- A study by Li et al. concludes that: "A majority of COVID-19 infections were undocumented prior to implementation of control measures on January 23, and these undocumented infections substantially contributed to virus transmission. These findings explain the rapid geographic spread of COVID-19 and indicate containment of this virus will be particularly challenging. Our findings also indicate that heightened awareness of the outbreak, increased use of personal protective measures, and travel restriction[s] have been associated with

reductions of the overall force of infection; however, it is unclear whether this reduction will be sufficient to stem the virus spread."

- NHC figures released Feb 13 indicate that 36,719 currently hospitalized, of which 73.8% were in mild condition, 21.7% serious and 4.6% critical.
- The head of the COVID-19 investigation team of China's National Health Commission has said that number of cases reported to have recovered in China appears very low because as a precautionary measure, patients being kept quarantined in hospitals long after symptoms have subsided.
- In a viewpoint article in JAMA, Swerdlow and Finelli discuss the necessity of being prepared for sustained transmission of SARS-CoV-2. The CDC has also mentioned the need to be prepared for community transmission of the virus in the US (Section 3). Boldog et al. have attempted assess the risk of the SARS-CoV-2 outbreak spreading to countries outside of China. They state that "This risk depends on three key parameters: the cumulative number of cases in areas of China which are not closed, the connectivity between China and the destination country, and the local transmission potential of the virus." As China is not likely to remain isolated indefinitely from other regions of the world, the main determining factor may be the number of cases on the mainland over the long term.
- Hermanowicz reports that several mathematical models run on data from consecutive periods of the outbreak produced consistent results on the timing of the peak, though with differing peak case numbers: "... all models show reaching a peak in mid-February...." The study showed a downward deviation from the exponential growth and a decreasing effective R from January 28.
- The head of the COVID-19 investigation team of China's National Health Commission has predicted that, based on 'mathematical modeling, recent events and government action', that the outbreak in China will peak in February and that he hopes that it will be over by April. This seems to be supported by a study posted February 18 by Zhang B et al., which concludes that a series of control measures in China have effectively prevented the spread of COVID-19, and the epidemic will end in early April. And Zhang L et al., in a study posted February 18, estimated an R_0 of 1.44 (interquartile range: 1.40-1.47). Based on these and other parameters estimated in the study, they predict that the number of infected individuals in Wuhan City may reach the peak around February 19 and that in March, the epidemic will gradually decline, ending around late March. The authors state that if the epidemic situation is not properly controlled, the peak number of infected may be further increased in magnitude, as well as delayed.

SECTION 2: China response:

- *China has begun emergency talks, describing the COVID-19 crisis as the worst crisis in their country for the past 70 years.*
- *Further 14 day quarantine to be instituted for recovered and discharged cases, since it has become known that several treated and discharged cases have been testing positive again.*
- Children of frontline medical workers to be given priority for places in good schools and universities and extra points in exams, as incentives to healthcare workers. Over 32,000 healthcare workers have been sent to Hubei to help.
- 10 new makeshift isolation centres being set up and Chinese government stepping up door-to-door checks and mandatory quarantine of cases.
- Beijing has ordered mandatory 14-day quarantine for all travelers returning to the city.
- In its latest measure to try to halt the spread, China said it would stagger the return of children to school. Several provinces have closed schools until the end of February (BBC News).
- Reports continue of aggressive measure to arrest to outbreak in China, with enforced quarantining of cases, residents being encouraged - sometimes by cash rewards - to report their own and others' illness, and arrests for breaking quarantine. However, there is uncertainty about how well this will work.
- Several Chinese officials have been removed from their positions over their handling of the outbreak. According to state media, there have been hundreds of sackings, investigations and warnings across Hubei and other provinces during the outbreak.

SECTION 3: Other countries' responses:

- *Iraq has banned arrivals from Iran amid fears about outbreak in Iran that became evident last weekend.*
- *US has issued a travel alert to South Korea. No restrictions.*
- *With the sharp rise of cases in several countries outside China over the weekend, the US CDC is now preparing for a pandemic, reviewing pandemic preparedness documents and adapting the for COVID-19 response.* Last week, With 15 cases detected in the US, the US Centers for Disease Control had said that they expect community spread in the country at some point and are reportedly preparing for the coronavirus to possibly "take a foothold in the US".
- *WHO says 'window of opportunity' for preventing further spread of the virus is now 'narrowing'.*
- *Ten towns in Lombardy region of Italy under lockdown: no trains stopping there, many public places closed and residents advised to stay home. Some panic buying has resulted.*
- *Iran to close schools and universities in the 2 worst affected cities.*
- The US has reportedly barred American passengers remaining on the Diamond Princess after the repatriation fights at the weekend from entering the country for 14 days after release from quarantine.
- Russia has barred all Chinese nationals from entering the country starting February 20, until further notice; only in-transit passage permitted. Non-Chinese nationals arriving from China will be allowed to enter.
- WHO has been concerned of spread of virus to Africa as weak resources. WHO sending kits to more labs on the continent. China is Africa's biggest trade partners with ~ 10,000 Chinese businesses and >1M Chinese living in African countries.
- Attempts are being made to trace passengers of the Westerdam after an 83-year-old American passenger tested positive for the virus after testing negative in Cambodia, traveling to Malaysia and then testing positive (presumptively and then confirmed). The woman and her husband (who tested negative) were reportedly the only two with symptoms among the 145 ship passengers who entered Malaysia, which has now barred other Westerdam passengers. There are still 236 passengers and 747 crew on the boat. Canadians required to report to local Public Health authorities and self-isolate at home upon return to Canada.
- In Japan, birthday celebrations for the new Emperor and the amateur part of the Tokyo marathon due to take place on March 1 have been canceled in an attempt to control the spread of SARS-CoV-2.
- Singapore has imposed mandatory 14 day self-isolation for people returning from China.
- Increasing concerns about impact of COVID-19 outbreak on economies of various countries (Section 3). E.g., effects of outbreak on Asian tourism projected to last until at least 2021.
- Vietnam has reportedly quarantined an entire town.
- Reports that cases of COVID-19 are appearing in Sinuiju, North Korea – on the border with China - due to illicit crossings of the border despite North Korea having closed the borders with China and Russia. Seoul-based website Daily NK reporting that 5 people have died in the city, with the earliest known death in late January, and that NK authorities attempting to cover up the deaths by quickly disposing of the bodies and withholding the information from the public. No reports of cases in North Korea from official sources such as the WHO.
- The UK has declared a "serious and imminent threat to public health," giving the government legal powers to forcibly quarantine people.

SECTION 4: Transmissibility of virus

- *In an article published in Emerging Microbes and Infections, Zhang W et al. detected SARS-CoV-2 in anal swabs and blood as well as in oral swabs, with more anal than oral swab positive in later stages of infection; of 15 patients who were found to be still carrying the virus after several days of medical treatment, 2 were positive by both oral swab and anal swab, but none of the blood positive cases were also swab-positive. The conclusion was that viral nucleotide may be found in anal swabs or blood even if not detectable in oral swabs, and although swabs may be negative, the patient might still be viremic. Because of its presence in anal swabs, the authors suggest that the virus can therefore be transmitted via the oral–fecal route as well as the more widely recognized*

routes of infection. The study also used a serology test and report that it improved the detection rate of cases and therefore should be considered used for diagnosis of cases.

- *Zhou et al. studied viral loads present in nasal and throat swabs from 17 patients with COVID-19. The authors found that, unlike what was observed for SARS-CoV, where transmission occurred mainly after days of illness with viral loads peaking approximately 10 days after symptom onset, "Higher viral loads [of SARS-CoV-2] … were detected soon after symptom onset, with higher viral loads detected in the nose than in the throat." The authors state: "Our analysis suggests that the viral nucleic acid shedding pattern of patients infected with SARS-CoV-2 resembles that of patients with influenza and appears different from that seen in patients infected with SARS-CoV. The viral load that was detected in the asymptomatic patient was similar to that in the symptomatic patients, which suggests the transmission potential of asymptomatic or minimally symptomatic patients. These findings are in concordance with reports that transmission may occur early in the course of infection and suggest that case detection and isolation may require strategies different from those required for the control of SARS-CoV."*
- *Hoehl et al. describe the repatriation of 126 mostly German nationals from Hubei to Frankfurt, Germany, with and symptom-screening at the airport on arrival. Diagnostic throat-swab testing was also offered, and 114 of the 115 passengers who had passed triage accepted. Of those 114, two passengers were found to be positive for the virus, including by culture which indicated an increased likelihood of infectivity. The authors point out that symptom screening had been ineffective in detecting those asymptomatic infections and shedding. In a letter to The Lancet, Pan et al. also describe asymptomatic infection in two members of a family of three with SARS-CoV-2; the third family member was symptomatic.*
- In a study posted February 19, Wang X et al. retrospectively collected infection data from a hospital of Wuhan University. They found that N95 respirators, disinfection and hand washing helped to reduce the risk of 2019-nCoV infection in medical staff: the medical staff in some departments of the hospital wore N95 respirator and disinfected and cleaned hands frequently, whereas those in other departments wore no medical masks and disinfected and cleaned hands only occasionally. In spite of higher exposure to COVID-19 cases, zero of 278 from the N95 group were infected by 2019-nCoV, while 10 out of 213 (77+136) from the no-mask group were confirmed infected. Similar results were observed at other hospitals. *Chang et al. in a letter the Lancet, emphasize the importance of personal protective equipment for healthcare workers in this outbreak: "aggressive measures (such as N95 masks, goggles, and protective gowns) [are warranted] to ensure the safety of health-care workers during this COVID-19 outbreak."*
- Linton et al., in a study posted February 18, found that the incubation period for COVID-9 falls within the range of 2-14 days with 95% confidence and has a mean of around 5 days. The mean time from illness onset to hospital admission (for treatment and/or isolation) was estimated at 3-4 days or 5-9 days, depending on the meth of estimation used. Based on the 95th percentile estimate of the incubation period, the authors recommend that the length of quarantine should be at least 14 days. However, Leung C estimated the distribution of incubation periods of patients infected in and outside Hubei province of China using clinical data collected from the individual cases reported by the media as they were not fully available on the official pages of the Chinese health authorities. That study found that the incubation period of patients with no travel history to Hubei was longer and more volatile than that of patients associated with Hubei. Leung recommends that the duration of quarantine should be extended to at least 3 weeks.
- Using recent estimated for COVID-19 transmission, Keeling et al. have investigated the likely efficacy of the current UK definition of a close contact (within 2 meters for 15 minutes or more) for contact tracing, and the distribution of secondary cases that may go untraced using that definition. They found that that fewer than 1 in 5 cases will generate any subsequent untraced cases, although the use of this definition for a contact results in a high logistical burden, with an average of 36.1 individuals (95th percentiles 0-182) traced per case. The authors state that "Changes to the definition of a close contact can reduce this burden, but with[an] increased risk of untraced cases; we estimate that any definition where close contact requires more than 4 hours of contact is likely to lead to uncontrolled spread."
- In a study using dates of illness onset for primary cases (infectors) and secondary cases (infectees) from published research articles and case investigation reports , Nishiura et al estimated a median serial interval (the

duration of time between the onset of symptoms in a primary case and the onset of symptoms in a secondary case infected by the primary case) for SARS-CoV-2 of 4.6 days and concluded that a substantial proportion of secondary transmission may occur prior to illness onset, providing further evidence of the asymptomatic and presymptomatic transmission suggested by several anecdotal accounts to date.

- Shen et al. evaluatedof the impact of lockdown on the 2019-nCov epidemic in Hubei province, China and concluded that it appears to have been effective in reducing about 60% of new infections and deaths, and that its effect also appears to be sustainable even after its removal. However, they acknowledge that the economic impact of the lockdown remains to be seen.
- Using an ecological modelling approach, Mizumoto et al have estimated an R_0 of 7.05 in Wuhan City early in the outbreak, with enhanced public health measures apparently decreasing that to about 3.24 since January 23rd.They estimate the total number of infections in Wuhan at nearly 1,000,000 (9.8% of the population), with a crude infection fatality ratio (IFR) and time–delay adjusted IFR is estimated to be 0.07% (95% CrI: 0.05%–0.09%) and 0.23% (95%CrI: 0.17–0.30% respectively - several orders of magnitude smaller than the crude cCFR at 4.06%
- An account in the New England Journal of Medicine of the infection of a Thai taxi driver who, like a taxi driver in Japan who recently tested positive used his vehicle to transport tourists from China, mentions that all household contacts as well as 10 other close contacts tested negative for the virus, although this Thai case was diagnosed relatively late in the course of his illness. Contrasting with reports of infections apparently having been contracted even by indirect contact or no known contact with a case, this report suggests that the capability of a case to transmit the infection can vary, for reasons that are currently unclear.
- Zhou et al located SARS-CoV-2 in the ocular fluid of 3 of 67 confirmed and suspected cases; the authors argue that ocular transmission is not supported by this data.
- For a list of published articles and commentaries relevant to transmissibility of SARS-CoV-2, please see Appendix 6. For other information on transmissibility, see Appendix 8.

SECTION 5: Testing and Screening Efficacy

- *In the article by Zhang W et al. described in Section 4, the authors report that none of the patients with viremia had positive swabs. Quote: "These patients would likely be considered as 2019-nCoV negative through routine surveillance, and thus pose a threat to other people. In contrast, we found viral antibodies in near all patients, indicating serology should be considered for 2019-nCoV epidemiology. A possible shift from oral positive during early infection to anal swab positive during late infection can be observed. This observation implied that we cannot discharge a patient purely based on oral swabs negative, who may still shed the virus by oral–fecal route. Above all, we strongly suggest using viral IgM and IgG serological test to confirm an infection, considering the unreliable results from oral swabs detection."*
- One of the most recent US cases detected was an evacuee being evaluated for COVID-19 in hospital. Tested positive after originally testing negative and being returned to the quarantine base, reportedly due to a mix-up at the lab. Additional cases in Singapore have also tested positive only after repeated negative tests. The U.S. Centers for Disease Control and Prevention (CDC) has said that some of the kits sent to U.S. states and at least 30 countries produced "inconclusive" results due to a flawed component. The CDC reportedly plans to send replacement materials improve the performance of the kits.
- Yang et al examined testing accuracy for different respiratory specimens for patients with mild and severe symptoms. Among 213 COVID-19 confirmed patients at varying days after symptom onset in Shenzhen, confirmation of infection via PCR on samples collected from the multiple sites revealed the following rates of samples testing positive:

	Throat		Nasal		Sputum		BALF	
	Severe	Mild	Severe	Mild	Severe	Mild	Severe	Mild
0-7 days	60%	61%	73%	72%	89%	82%	NA	NA
8-14 days	50%	30%	72%	54%	83%	74%	100%	0%
15+ days	37%	11%	50%	55%	61%	43%	78%	NA

Sputum and bronchoalveolar lavage samples seem to give the highest positive rates. Mild cases tended to test positive less frequently. Viral loads were highest among sputum and BALF samples. Overall, the authors suggest that negative PCR tests should not be enough to exclude patients as potential cases if they have relevant symptoms and exposure history.

- Repeat testing of initially negative cases appears to be the most reliable way of confirming or excluding SARS-CoV-2 infection. Study by Chan et al concludes that "repeat testing of upper respiratory tract samples or testing of lower respiratory tract samples [is] warranted in clinically suspected cases with an initially negative result in nasopharyngeal or throat swab."
- Gostic et al. estimate that under even optimal circumstances, traveler screening will miss at least half of cases because they are fundamentally undetectable due to lack of symptoms and lack of knowledge of exposure, and Quilty et al. predict that traveler screening will detect less than 40% of cases.
- Hellewell et al. produced multiple scenarios to examine the efficacy of contact tracing and isolation. For R_0 of 2.5 and 3.5 respectively, 70% and 90% of contacts had to be traced and isolated to control most outbreak scenarios. The proportion of contacts that must be isolated increases as R_0 and the delay between symptom onset and isolation increase.

SECTION 6: Symptoms, Severity and Clinical Management

- *Reports that plasma from recovered patients may help in the treatment of critically ill cases. More than 10 cases treated to date and results seem promising. Calls for blood donations from recovered patients. China's National Health Commission has listed plasma among treatment measures for critically ill patients in its latest treatment guideline.*
- In a study of over 70,000 cases published in the China CDC Weekly Report, case fatality ratios are reported by comorbidities: "While patients who reported no comorbid conditions had a case fatality rate of 0.9%, patients with comorbid conditions had much higher rates—10.5% for those with cardiovascular disease, 7.3% for diabetes, 6.3% for chronic respiratory disease, 6.0% for hypertension, and 5.6% for cancer." CFRs were also found to be much higher in patients over 70 (8.0% in those 70-79 years of age, and 14.8% for those over 80 and, as in previous studies, higher in males than females. Also, 14.6% of healthcare workers were classified as critical, vs. only 4.7% of the overall study population. The authors do not present any explanation for this; possibly the high viral load present in hospitals and clinics can help to explain to this result.
- In a study published on February 19, Xu et al describe the clinical findings in 62 patients diagnosed in Zhejiang province. Only 2 of the patients developed shortness of breath; the clinical profiles of cases were generally much milder than those of patients diagnosed in Wuhan. The authors apparently attribute this difference to the cases in Zhejiang province being from a later point in the chain of transmission than those at the epicenter: "We found that the clinical features of patients with symptoms for longer than 10 days in Zhejiang province were less severe than those of the primary infected patients from Wuhan. This phenomenon was also apparent during the transmission of MERS-CoV. The global case mortality of MERS-CoV was about 40%, whereas the mortality from second generation MERS-CoV was about 20%."
- Wang M et al., in a study posted February 18, report that "Clinical testing methods for 2019-nCoV require improvement. Importantly, 5.8% of 2019-nCoV infected and 18.4% of non-2019-nCoV-infected patients had [infections with other pathogens]. It is important to treat combined infections and perform rapid screening to avoid cross-contamination of patients. A test that quickly and simultaneously screens as many pathogens as possible is needed."
- Feng et al, in a study of 15 children diagnosed with SARS-CoV-2 infection, found that early chest CT images of children with 2019-nCoV infection are mostly small nodular ground glass opacities, and that the clinical symptoms are nonspecific. The authors conclude that dynamic reexamination of chest CT and nucleic acid are important.
- Wang et al, in a study of 34 children with the virus, concluded that the clinical manifestations of COVID-19 in children are non-specific and are milder than that in adults; 22 (65%) were classified as 'common' cases, 9 (26%) as mild cases and 3 (8.8%) were asymptomatic. No severe or critical cases were identified.

- In a large cohort study of 1099 confirmed cases from across China fever existed on admission to the hospital only among 43% of cases but developed in 88% of cases (Guan et al.). This large study adds significantly to our knowledge on symptoms and disease progression, but the authors are not clear how the cases were selected (the sample represents 14% of known Chinese cases on the date data were extracted), and care is ongoing for more than 90% of the cohort.
- The proportion of health care workers affected in this outbreak appears to be lower than those infected in the SARS and MERS outbreaks, based on analysis in that study.
- Evidence to date indicates that the clinical presentation of illness can vary widely between patients (see Appendix 4). In particular, fever alone is neither a specific nor a sensitive indicator of infection in the early days of infection.
- There is some evidence that antiviral drugs are effective in treating the illness. Holshue et al. describes that the patient improved rapidly when put on remdesivir, a drug in development. A Phase III clinical trial for remdesivir is underway in China. In earlier studies, the drug made by Gilead showed in vitro and in vivo activity against other coronaviruses such as SARS (severe acute respiratory syndrome) and MERS-CoV. The drug isn't licensed or approved, but Gilead has provided it for emergency use in a small number of COVID-19 patients, including at least one in the United States. Reports from Thailand suggest that large doses of lopinavir and ritonavir (both commonly used to treat HIV infection) in combination with oseltamivir (influenza) are also effective. Genetic analysis and molecular modeling (Richardson et al) identifies several compounds that may be effective, as does AI-based modeling (Beck et al). There are numerous articles claiming that a variety of antivirals are effective against SARS-CoV as well (e.g., Stockman et al., 2006). However, none of these reports rise to the evidence standard of well designed randomized clinical trials.
- For a summary of other studies and reports on this, please see Appendix 4.

Epidemiological Notes

- *The steps taken by the US CDC to prepare for a pandemic seem very appropriate in light of the rapid increase in cases in several countries outside China in the last few days. With travel restrictions still in place for mainland China, where most of the cases still are, there should at least be some lag time before an epidemic of COVID-19 begins in North America. However, as more and more countries outside mainland China see the start of outbreaks of the virus, it is unknown how long this lag time will be. To maximize the chance of mitigating the effects of an outbreak in Canada, preparation of public health and other health care systems within Canada should be considered a priority. In addition, public health authorities should consider beforehand the course of action that will be taken in the event of sudden increased local community transmission occurring, such as that recently seen in several countries.*
- *The results of the study by Zhou et al. described above could explain the extremely rapid and efficient community transmission of the virus seen in China to date and now being seen in some other countries. Unfortunately, this further decreases the likelihood of effective containment of the virus and avoidance of widespread transmission in many countries, if not globally.*
- In light of the rapidly rising number of infections in China, increasing numbers of clusters outside of mainland China and increasing evidence of apparent transmission of the virus without close contact with symptomatic cases, it is becoming increasingly unlikely that the spread of COVID-19 within the populations of other countries can be indefinitely contained; as the months go by and travel to and from China return to normal, the probability of increased and possibly sustained transmission in other countries will probably rise markedly. Planning for this eventuality should take place at some point. The long-term risk of within-country transmission in countries like Canada (though probably slow and mainly via close contacts) will be greater in the event of sustained 2019-nCoV transmission in China and other areas of Asia through 2020 and beyond. Fortunately, as for most infectious diseases with relatively high morbidity rates, current evidence to date indicates that the case fatality associated with 2019-nCoV is lower than that of SARS.

List of Scientific References and Additional Reading

Note: Because of the emerging and currently evolving nature of scientific information on 2019nCoV, many/most of the scientific reports listed here have not been peer-reviewed, or have been subjected only to an expedited peer-review process. Conclusions may change as further information becomes available, and should therefore not necessarily be accepted as established.

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Appendices

Appendix 1: Estimates of R_0

Study	Inclusive of data through	Basic Reproductive Number Estimate
Cao, Z. et al. (2020). Estimating the effective reproduction number of the 2019-nCoV in China.	Jan 25	R = 4.08
Cao, Z. et al. (2020). Incorporating human movement data to improve epidemiological estimates for COVID-19. doi: https://doi.org/10.1101/2020.02.07.20021071		R_0 prior to Wuhan quarantine on Jan 23 was 3.24
Imai, N. et al. (2020). Transmissibility of 2019n-CoV	Jan 23	R_e = 2.6
Jung et al. (2020). Real time estimation of the risk of death from novel coronavirus (2019-nCoV) infection: Inference using exported cases.	Jan 24	Two scenarios: 1) R_0 = 2.2 2) R_0 = 3.7
Hermanowicz S.W. (2020). Forecasting the Wuhan coronavirus (2019-nCoV) using a simple (simplistic) model	Jan 28	R_0 ~ 2.4 and decreasing. Don't take this paper seriously though…it was badly off in other estimates the day it was published.
Kucharski, A. et al. (2020). Analysis of early transmission dynamics of nCoV in Wuhan.		Initial R_0 of 1.5 to 4 Declining R_e after mid-January and travel restrictions
Kucharski, A et al. (2020). Early dynamics of transmission and control of 2019-nCoV: A mathematical modelling study.	Mid Dec through Mid Jan	R fluctuated between 1.6 and 2.9
Kucharski, A. et al. (2020). Analysis and projections of transmission dynamics of nCoV in Wuhan.		R_0 of 1.5 to 4.5 prior to Jan 23; Rt decreasing with time
Leung, G. & Wu, J. (2020). Real-time nowcast and forecast on the extent of the Wuhan CoV outbreak, domestic and international spread. Republished in updated form in the Lancet: Wu, J. et al. (2020). Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: A modeling study. *The Lancet*. https://doi.org/10.1016/S0140-6736(20)30260-9	Jan 25	R_0 = 2.13 initially; updated R_0 = 2.68
Li et al. (2020). Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *New England Journal of Medicine*. DOI: 10.1056/NEJMoa2001316	Jan 22	R_0 = 2.2
Liu, T. et al. (2020). Transmission dynamics of 2019 novel coronavirus (2019-nCoV).	Jan 22	R_0 = 2.9
Liu, T. et al. (2020-12 Feb). Transmission dynamics of Novel Coronavirus Pneumonia in China. BioRxiv preprint. https://doi.org/10.1101/2020.01.25.919787	Feb 7	R_0 in Wuhan = 4.4; R_0 elsewhere in China = 4.5; R_t is steadily decreasing
Majumder, M. & Mandl, K.D. (2020). Early transmissibility assessment of a novel coronavirus in Wuhan, China	Jan 24	R_0 = 2.2 to 3.1

Park, Sang Woo et al. (2020). Reconciling early-outbreak preliminary estimates of the basic reproductive number and its uncertainty: a new framework and applications to the novel coronavirus (2019-nCoV) outbreak		Pooled estimate of prior studies: Median R_0 = 3.1 (95% CI: 2.1-5.7) More recent paper says 2.9 (CI: 2.1 – 4.5)
Read, J. et al. (2020). Novel coronavirus 2019-nCoV: Early estimation of epidemiological parameters and epidemic predictions.	Jan 21	R_0 = 3.8 (Twitter update: revised to 2.5 with data through Jan 22) (Further update as of Jan 28 to 3.11)
Riou, J. & Althaus, C. L. (2020). Pattern of early human-to-human transmission of Wuhan 2019-nCoV Updated version published in Eurosurveillance: Riou, J. & Althaus, C.L. (2020). Pattern of rearly human-to-human transmission of Wuhan novel coronavirus (2019-nCoV), December 2019 to Jan 2020. *Eurosurveillance, 25*(4).	Jan 18	R_0 = median 2.2 (high density interval 1.4 – 3.8). Authors suggest high similarlity to SARS-CoV
Sanche, S et al. (2020). The novel coronavirus, 2019-nCoV, is highly contagious and more infectious than initially estimated. Medrxiv preprint.	End of January	Before control measures R_0 = 4.7 to 6.6 depending on the method and data used to calculate Post control measures R_e = 2.3 to 3.0
Shen, M. et al. (2020). Modeling the epidemic trend of the 2019 novel coronavirus outbreak in China.		Initial R_0 = 4.71 (Dec 12) Current R_e = 2.08 (Jan 22) R_e < 1 predicted within 2.5 months
Tuite, A.R. & Fisman, D. N. (2020). Reporting, epidemic growth, and reproduction numbers for the 2019 novel coronavirus (2019-nCoV) epidemic. *Annals of Internal Medicine*. DOI: 10.7326/M20-0358		Initial R_0 = 2.3; R_e ~ 1.5 around 3 Feb
Yang et al. (2020). Epidemiological and clinical features of the 2019 novel coronavirus outbreak in China.		Initial R_0 = 2.2 to 5.2 depending on modeling assumptions. Paper also examines Rt, suggests substantial decrease from peak
You, C et al. (2020—Feb 11). Estimation of the time-varying reproduction number of 2019-nCoV outbreak in China. Medrxiv preprint. https://doi.org/10.1101/2020.02.08.20021253		Initial R_0 = 2.3 to 3.7 for all of China, depending on method ~2 to ~6 for various specific cities Controlled R as of Feb 5: 1.7 to 2.3 for all of China
Zhang, C & Wang, M. (2020). Origin time and epidemic dynamics of the 2019 novel coronavirus.		R_e = 0.2 to 2.2 (varying by time)
Zhao S. et al. (2020). Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. Accepted for publication in International Journal of Infectious Diseases:	Jan 24	R_0 = 2.24 to 3.58

Zhao et al. (2020). Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. *International Journal of Infectious Diseases*. https://doi.org/10.1016/j.ijid.2020.01.050		
Zhao, Q. et al. (2020). Analysis of the epidemic growth of the early 2019-nCoV outbreak using internationally confirmed cases. doi: https://doi.org/10.1101/2020.02.06.20020941		R_0 = 5.7, based on analysis of international spread
Zhou T et al. (2020-12 Feb). Preliminary prediction of the basic reproduction number of the Wuhan coronavirus 2019-nCoV. *Joural of Evidence-Based Medicine.* https://doi.org/10.1111/jebm.12376		R_0 = 2.8 to 3.9, depending on source of data and parameters
Mizumoto et al Feb 13, 2020. Early epidemiological assessment of the transmission potential and virulence of 2019 Novel Coronavirus in Wuhan City: China, 2019-2020	Feb 13	R_0 = 7.05 (95%CrI: 6.11–8.18) In Wuhan City, China early in epidemic, and 3.24 (95%CrI: 3.16–3.32) after Jan 23 (following enhanced control measures).

Appendix 2: Timelines for Incubation and Disease Progression

New Additions	Study	Sample	Incubation Period Estimate
	Chan et al. (2020). A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *The Lancet*. https://doi.org/10.1016/S0140-6736(20)30154-9	Case study of 7 member extended family, 6 of whom tested positive	First symptoms developed within 4 to 6 days of earliest possible exposure One child case was asymptomatic but was shedding virus.
	Huang et al. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*. https://doi.org/10.1016/S0140-6736(20)30183-5	41 very early patients	While no info is provided on incubation per se (exposure is unclear, as half were on-going exposure to the wet market), on average 7 days passed before the start of symptoms and admission to hospital, 8 days to dyspnoae, 9 days to ARDS, 11 days to ICU admit
	Phan et al. (2020). Importation and Human-to-Human Transmission of a Novel Coronavirus in Vietnam. New England Journal of Medicine. DOI: 10.1056/NEJMc2001272	Case study: Family of three, two of whom tested positive	Son became symptomatic within 3 days of sharing room with father
	Liu et al. (2020). Transmission dynamics of 2019 novel coronavirus (2019-nCoV).	830 cases prior to Jan 23	Average incubation = 4.8 days
	Linton et al. (2020). Epidemiological characteristics of novel coronavirus infection: A statistical analysis of publicly available case data.		Median incubation: 4 to 5 days; 95% CI 2-9 days Median symptom onset to hospitalization: 3 days Median: symptom onset to death: 13.8 days
	Backer et al. (2020). The incubation period of 2019-nCoV infections among travellers from Wuhan, China Accepted in Eurosurvillance: Backer, J.A. et al. Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20–28 January 2020. *Eurosurveillance*, 25(5).	34 confirmed cases outside of Wuhan	Mean incubation: 5.8 days, ranging from 1.3 to 11.3 days
	Wang et al. (2020). Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. *Journal of Medical Virology*. DOI: 10.1002/jmv.25689	Summary of CNHC report on 17 deaths	Median days from first symptom until death: 14.0 (range 6-41)
	Li et al. (2020). Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *New England Journal of Medicine*. DOI: 10.1056/NEJMoa2001316	First 425 confirmed cases in Wuhan	Mean incubation period 5.2 days, ranging up to 12.5 days (95% of distribution)
	Rothe et al. (2020). Transmission of 2019-nCoV Infection from an Asymptomatic Contact in	5 cases in Germany	Of the four Germany patients with a known exposure history, all developed symptoms with 2-6 days of exposure

	Germany. New England Journal of Medicine. DOI: 10.1056/NEJMc2001468		BUT At least one case was able to infect others within 1-2 days of being exposed himself and several days before he developed symptoms
	Lauer et al. (2020). The incubation period of 2019-nCoV from publicly reported confirmed cases: estimation and application. doi: https://doi.org/10.1101/2020.02.02.20020016	101 confirmed cases in China	Median incubation period is estimated at 5.2 days; 97.5% of those who develop symptoms will do so within 10.5 days of infection. Conservatively estimated, 64 out of 10,000 cases will develop symptoms after 14 days of quarantine.
	Guan et al. (2020). Clinical characteristics of 2019 novel coronavirus infection in China. doi: https://doi.org/10.1101/2020.02.06.20020974	1099 confirmed cases from 31 Chinese provinces	Mean incubation period was 3.0 days (range 0 to 24)
	Sanche, S et al. (2020). The novel coronavirus, 2019-nCoV, is highly contagious and more infectious than initially estimated. Medrxiv preprint.	140 individual case reports	4.2 days from exposure to symptom onset (95% CI 3.5 to 5.1)
	Yang et al. (2020). Epidemiological and clinical features of the 2019 novel coronavirus outbreak in China.	125 patients with clearly defined exposure periods	4.8 days (IQR 3.0, 7.2)

Appendix 3: Comparative Case Definitions for Suspect Cases

Authority	Date Updated	Clinical Presentation		Travel/Exposure History
WHO	31 Jan	Severe acute respiratory infection (SARI), fever and cough, requiring admission to hospital, with no other etiological explanation for infection	AND	Travel to or live in China in the 14 days prior to symptom onset
		Person with any degree of acute respiratory tract illness (ARTI)	AND	Contact with a confirmed or probable nCoV case OR healthcare facility treating nCoV OR visit to live animal market in Wuhan
CDC	12 Feb	Fever **or** signs/symptoms of lower respiratory illness (e.g. cough or shortness of breath)	AND	Any person, including health care workers, who has had close contact with a laboratory-confirmed 2019-nCoV patient within 14 days of symptom onset
		Fever **and** signs/symptoms of a lower respiratory illness (e.g., cough or shortness of breath)	AND	A history of travel from **Hubei Province**, China within 14 days of symptom onset
		Fever **and** signs/symptoms of a lower respiratory illness (e.g., cough or shortness of breath) requiring hospitalization	AND	A history of travel from mainland **China** within 14 days of symptom onset
European CDPC	30 Jan	Any degree of ARTI (with at least one of cough, sore throat, SOB)	AND	Within 14 days of onset, Close contact with probable/confirmed case OR Travel history to areas with community transmission (includes all of mainlandChina) OR Visited health care facility where nCoV patients were being treated
Ireland	1 Feb	SARI requiring hospital admission (with evidence of pneumonia or ARDS) OR ARTI of any severity with at least one of cough, SOB, fever	AND	Matches EU CDPC
Australia	6 Feb	ARTI with or without fever OR Fever/hx of fever	AND	Travel to mainland China within 14 days OR Close contact within 14 days with confirmed case
United Kingdom	7 Feb	SARI requiring hospitalization (with evidence of pneumonia or ARDS) OR ARTI or any severity with one of SOB or cough OR fever	AND	Travel to or transit through China, Hong Kong, Japan, Macau, Malaysia, Republic of Korea, Singapore, Taiwan, or Thailand within 14 days OR Contact with confirmed case within 14 days
France	4 Feb	Acute LRTI with any severity AND with fever or perception of fever	AND	Travel to anywhere in mainland China within 14 days
		ARTI with any severity	AND	Within 14 days, close contact with a confirmed case OR having exposures similar to a confirmed case (i.e., travel to Hubei) OR working in a hospital with confirmed COVID-19 OR visited live animal market in Wuhan
Hong Kong	23 Jan	Fever OR ARTI OR SARI	AND	Within 14 days: Any travel history to Hubei OR Any travel history to a hospital in mainland China OR

				Close contact with a confirmed case while person was symptomatic
Germany	8 Feb	Respiratory symptoms of any severity	AND	Within 14 days: Stay in a "Risk area" (Hubei province plus Wenzhou, Hangzhou, Ningbo, Taizhou in Zhejiang province) or contact with a confirmed case
South Korea				Reportedly has done away with travel history requirement for testing; only based on clinical presentation

Appendix 4: Symptoms and Clinical Management

Study	Population	Symptoms											Notes
		Fever	*Cough*	*Fatigue / Myalgia*	*Rhinor-rhea or Sputum*	*Head-ache*	*Diarrhea*	*SOB*	*Haemo-ptysis*	*Chest Pain*	*Sore Throat*	*Nausea*	
Huang et al.	First 41 patients in Wuhan	98%	76%	44%	28%	8%	3%		5%				Is likely biased towards more severe cases
Chen et al.	99 cases in Wuhan admitted to ID hospital	83%	82%	11%	4%	8%	2%	31%		2%	5%		Is likely biased towards more severe cases
Chan et al.	6 cases in multigenerational family cluster in Shenzhen	5 / 6 (not in child; highest in oldest adults)	3 / 6 dry, 1 /6 product ive	3 / 6 (older adults only)	2 / 6 (middle aged adults only)		2 / 6 (middle aged adults only)			1 / 6	1 / 6		One confirmed pediatric case was asymptomatic
Holshue et al	1st American case (35yo man)	Yes	Yes	Yes	Yes		Yes	No		No		Yes	
Rothe et al.	4 German cases	Yes	Yes										
Chang et al.	13 young Chinese cases	12 /13 (1.5 days duratio n, low max)	46% (8 days duratio n)	23%	8%	23%	8%						Median age: 34; includes some pediatric patients. All recovered.
Wang et al.	138 consecutive patients in a single hospital in Wuhan	99%	60%	70%	27%	7%	10%	31%			18%	10%	34.1% of patients discharged, 4.3% died, 61.6% still in hospital
Guan et al.	1099 Chinese cases	44% at present ation	68%	38.1% / 14.8%	4.8% / 33.4%	13.6%	3.7%	18.6%	0.9%		13.9%	5.0%	Unclear how the sample was assembled (represents ~14% of existing Chinese cases at that time); 94% of cases still in hospital, 5% discharged, 1.4% dead
Li et al.	17 patients in Dazhou	67%	83%	42% / 17%			17%						Follow-up is ongoing

WHO report	Chinese data on 18,000 cases												Approximately 82% of cases shed the virus, with 15% of cases being severe and 3% critical. No information has been released on the testing criteria for these cases or whether any were asymptomatic.
Dorigatti et al.													Neil Ferguson's group has estimated (Dorigatti et al.) that the confirmed case fatality rate based on early data (26 deaths) from Hubei is 18% (95% CI 11%-81%) and based on data on the spread from outside of China will be between 1.2% and 5.6% depending on the estimation method. They recognize that the Hubei data is likely biased towards more severe cases and that international surveillance is catching more mildly or asymptomatic cases than is surveillance in China. Taking into account the data on the number of positive tests from evacuation flights, the estimated all case fatality rate is about 1%

Appendix 5: Estimates of COVID-19 Case Fatality

New Addition or Revision	Citation	Based on Data	Estimate
	Althaus, C.L. (2020, 4 Feb). Estimating case fatality ratio of 2019-nCoV from observed cases outside China. Unpublished Manuscript (University of Bern).	Cases outside of China through ~1 Feb, including a single death	CFR: 3.9% (95%CI: 0.2%-17.9%); while the single death makes this a very preliminary estimate, we include it so that readers can easily find updates to the authors' work
	Jung, Sung-mok et al. Real time estimation of the risk of death from novel coronavirus (2019-nCoV) infection: Inference using exported cases. Medrxiv preprint archive. https://doi.org/10.1101/2020.01.29.20019547		Scenario 1 (based on a growth rate starting Dec 8): 4.6% (95% CI: 3.1, 6.6) Scenario 2 (based on growth of exported cases): 7.7% (CI 4.9-11.3)
	Ferguson, N et al. Report 4: Severity of 2019-novel coronavirus (nCoV)		In Hubei: CFR = 18% (95% CI: 11%-81%) Outside of China: CFR = 1.2% to 5.6% depending on method ~1% (95%CI 0.5% to 4.0%) all case fatality rate
*	Yang et al. (2020). Epidemiological and clinical features of the 2019 novel coronavirus outbreak in China.		CFR estimates are adjusted for based on onset of disease and known outcomes (at the time, 58 confirmed cases were fatal): Based CFR for known outcomes: 1.44% CFR with patients with severe pneumonia: 5.88% Adjusted CFR for all confirmed cases 3.06% CFR for males: 4.45% CFR for females: 1.25% CFR for age >= 60: 5.30% CFR for age <= 60: 1.43% CFR for severe pneumonia: 6.23% CFR for long time until diagnosis: 3.07%

			CFR for <5 days to diag: 1.34%

Appendix 6: Studies on transmissibility of COVID-19

Study	Sample
Kang et al	have published a study that included analysis of exposures of 100 cases confirmed in Guangdong province during the month of January. They found that 84% of cases had traveled to Hubei. Average duration from onset of symptoms to diagnosis was 5.4 days. Of all of the cases, 84 (44.6%) were identified in 31 cluster infections, including family clusters. Genetic analysis of isolated virus from cases in the study indicated stability in the virus, with no mutations identified, in contrast to SARS early in that epidemic. The authors conclude that the strain is already established in humans, and was already well established in humans when it was first identified and human infections were considered to be spill-over infections from animals.
Lu et al.	in a letter to the Lancet published Feb 6, suggest that, as in the case of SARS, ocular transmission of SARS-CoV-2 may be a possibility. Quote: "On Jan 22, Guangfa Wang, a member of the national expert panel on pneumonia, reported that he was infected by [SARS-CoV-2] during the inspection in Wuhan. He wore an N95 mask but did not wear anything to protect his eyes. Several days before the onset of pneumonia, Wang complained of redness of the eyes. Unprotected exposure of the eyes to [SARS-CoV-2] in the Wuhan Fever Clinic might have allowed the virus to infect the body." Further, the authors state: "The fact that exposed mucous membranes and unprotected eyes increased the risk of SARS-CoV transmission suggests that exposure of unprotected eyes to SARS-CoV-2 could cause acute respiratory infection."
Favre et al.	In a letter to the Lancet published Feb 6, Favre et al express concern that SARS-CoV-2 infection may increase the risk of complications in pregnant women: "Members of the coronavirus family responsible for severe acute respiratory syndrome (SARS-CoV) and Middle East respiratory syndrome (MERS-CoV) are known to be responsible for severe complications during pregnancy." The authors recommend systematic screening of any suspected SARS-CoV-2 infection during pregnancy and follow-up for cases found to be positive during pregnancy.
Wang and Zhang	Comment in the Lancet: The basic and essential strategies that we should stick to remain the early detection, early diagnosis, early isolation, and early treatment of the disease. With the huge efforts from medical professionals to treat patients, substantial public health prevention measures, and accelerated research, we hope the downward turning points for both new cases of COVID-19 and the resulting fatal events might come soon.
Drosten et al.	Additional research on the German cases, confirmed by two laboratories, shows that the virus is reproducing in the nasopharynx and GI tract and is likely communicable even while cases have very mild symptoms resembling the common cold
Holshue et al.	Analysis of information collected on exposure of the first 425 cases in Wuhan for which medical intervention was needed indicated that, like the first case of COVID-19 confirmed in the USA and discussed by Holshue et al., over 70% of cases confirmed after January 1st reported no known contact with a symptomatic case. This may imply that the infection can be easily transmitted by casual or indirect contact with symptomatic cases and/or by close contact with asymptomatic cases. The apparent failure of cases imported by other countries from China to generate large numbers of secondary cases may imply the latter rather than the former.
	The Robert Koch Institute in Germany alleges that NEJM case study on the first German cases, which indicated that the Chinese national who brought the disease to Germany was asymptomatic, is incorrect. The authors did not contact the index case but relied on observations from her colleagues; when contacted by RKI, she indicated that she had experienced very mild symptoms while in Germany. That said, the article still claimed that the first German patient infected two of his contacts within a short period of time of becoming infected himself and several days before he reported symptoms. They also reported a continued high viral load after symptoms ceased. However, the overall credibility of this case study is undermined by the authors' failure to do necessary due diligence.

	Anecdotal evidence and case reports (such as those on the Vietnam case) published to date indicate that transmission occurs primarily by close contact, though no details are available on the exact duration and nature of contact necessary for effective transmission. On the other hand, reports emerging from Singapore indicate that at least two local people were infected by a Chinese tour group that visited their store, indicating that casual contact may be sufficient to transmit the virus, but these reports do not detail the duration of contact.
Holshue et al.	Reports suggest that the gastrointestinal tract may be a potential route of infection for SARS-CoV-2, which is not unexpected in view of the fact that gastrointestinal symptoms of infection can occur, and Holshue et al. isolated the virus from stool of a patient with GI symptoms.

Appendix 7: Models of Epidemic Progression

New or Revised	Citation	Epidemic Peak	Peak Cases
	Xiong H & Yan H. (2020-Feb 11). Simulating the infected population and spread trend of 2019-nCov under different policy by EIR model. Medxriv preprint. https://doi.org/10.1101/2020.02.10.20021519	Feb 16, 2020	49000
	Liu et al. (2020-Feb11). **Epidemic trends analysis and risk estimation of 2019-ncov outbreak. Medxriv preprint.** https://doi.org/10.1101/2020.02.09.20021444	Hubei: Feb 29, 2020 (95% CI Feb 25-March 8) Other mainland: March 8 to March 15. Epidemic ends 1.5-2 months after peak	63000 (95%CI 57000-70000)
*	Kucharski A et al. (2020-Feb 12) Analysis and projects of transmission dynamics of nCoV in Wuhan. https://cmmid.github.io/ncov/wuhan_early_dynamics/index.html	If Rt continues to vary in Wuhan according to current patterns, mid to late February 2020 In Wuhan	
	Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-NCOV outbreak originating in Wuhan, China: a modelling study. The Lancet January 31, 2020; DOI: https://doi.org/10.1016/S0140-6736(20)30260-9	Wuhan: April 2020	
	Ferguson, Neil. Video interview.	Wuhan: early March, later elsewhere in China	

Appendix 8: Transmissibility

- **Reproductive number:** Many of the new estimates for the basic reproductive number—the transmissibility of the virus in an immunologically naïve population with no attempts at infection control—of SARS-CoV-2 suggest it exceeds 4 (See Appendix 1). However, measurements of R over time suggest it is decreasing in Hubei and China, at least based on numbers of cases released by the Chinese government. For a reader-friendly discussion on the interpretation of R_0, see this article. For a discussion of the importance of propagating uncertainty estimates through R_0 calculations, see Sang Woo Park.
- With the emergence of COVID-19 on cruise ships, a reminder that the reproductive number of a virus is dependent on context and is generally higher in confined settings. A previous paper (Vynnycky et al.) reviewing the 1918 influenza pandemic estimates R of 1.2 to 3.0 in community settings (with substantial variation between cities) and 2.1 to 7.5 in confined settings such as ships and prisons (with substantial variation between contexts). The apparent high percentage of individuals positive for COVID-19 on the Diamond Princess cruise ship serves to illustrate this concept.
- **Asymptomatic transmission:** Of the 565 Japanese citizens evacuated from Wuhan screened for symptoms and tested using RT-PCR, 4 were positive symptomatic and 4 were positive asymptomatic. Hiroshi Nishiura and colleagues suggests that the asymptomatic ratio is therefore 50%. While Dr Nishiura is a respected modeler of infectious disease, the confidence interval on this estimate (95%CI 12.5%, 87.5%) is too wide to provide much insight, and the data was collected only 7 days after evacuees had left Wuhan, still well within the bounds of the incubation period. The paper does cite a study that influenza shows 56% to 80% asymptomatic infection.
- **Potential fecal transmission:** Hong Kong authorities partially evacuated a block of apartments as a precaution and placed residents in quarantine after a the country's 42nd case, a resident living 10 stories above the 10th case, was diagnosed with COVID-19 approximately 12 days after the region's 10th case, and 2 of her household contacts became symptomatic. Possibility of airborne transmission via faeces was considered, but initial investigations into the building's drainage system has reduced those concerns, and five symptomatic individuals have all tested negative. Authorities have described the evacuation as a precautionary measure. In the 2003 SARS epidemic, numerous cases resulted from a superspreading event via airborne faecal transmission in Amoy Gardens, a block of apartments in Hong Kong. In the study by Guan et al., 4 (6.5%) of 62 stool specimens from confirmed cases tested positive for the virus. Multiple studies (Appendix 4) suggest that 10% or fewer of patients experience diarrhea, but it is unclear if loose stool and the presence of SARS-CoV-2 in stool usually co-occur. An et al. say that confirmed COVID-19 cases may present only with digestive symptoms. Liang et al suggest that prevalence of diarrhea during COVID-19 is underestimated.
- **Viral persistence:** A review of multiple studies suggests that coronavirus (as a family of viruses, not necessarily SARS-CoV-2) persists on surfaces for up to 9 days but can be efficiently inactivated with ethanol, hydrogen peroxide, or bleach (Kampf et al). The WHO has reported that according to information they have received, the virus can stay on surfaces for 'short periods'.
- **Nosocomial infection**: A review of 138 consecutive cases in a single Wuhan hospital suggests that 41% of cases were hospital acquired, including 40 healthcare workers (Wang et al.); a review of 1099 cases across China say that only 2% were in healthcare workers (Guan et al.). According to a WHO epidemiologist, to the knowledge of the Organization, there has only been one reported incident of an outbreak in a hospital in China. The outbreak involved 15 health workers. The WHO has recently released a clinical case report form to help in the standardized data collection for hospitalized patients. Data collected using this form should provide better quality data for surveillance and assessment of the modes and risk of transmission of the virus.
- **Incubation period:** believed to be between 1 and 10 days; mean seems to be about 5 days with a long tail (Appendix 3). However, a review of 1,099 cases in China estimates a median incubation period of 3.0 days, with a range from 0 to 24 days and with no statistically significant difference for severe vs. non-severe cases (Guan et al.) - ten days longer than previously recognized. However, a maximum observation/isolation period of 14 days

seems justified by the data, with the caveat (modeled by Lauer et al.) that a small number of cases will exceed 14 days.

- **Other:** Promising findings from an investigation into the potential for intra-uterine transmission of SARS-CoV-2: 9 pregnant women infested with the virus were followed by Chen et al. through to the births of their babies; no virus was found in amniotic fluid, cord blood, and neonatal throat swab samples at birth, suggesting that no intrauterine fetal infections occurred as a result of COVID-19 infection during a late stage of pregnancy. Breastmilk samples were also negative. The authors state: "Our findings are in accordance with what was observed in SARS, which has a similar sequence to SARS-CoV-2.14 Previous studies have already shown no evidence of perinatal SARS infection among infants born to mothers who developed SARS infection during pregnancy." They acknowledge the limitation of a very small sample size. A comment has been published by Qiao in the Lancet on these findings.