Evidence on transmissibility of SARS-CoV-2

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currently evolving nature of scientific information on 2019nCoV, many/most of the scientific reports listed here have not been peer-reviewed or have been subjected only to an expedited peer-review process.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.

Overview:

There is increasing evidence that SARS-Co-V is more contagious than both MERS and SARS, while having a lower confirmed case fatality rate/ratio (cCFR). Case-level evidence earlier in the outbreak (early to mid January) seemed to indicate that close and relatively prolonged contact between a symptomatic case and a susceptible individual was necessary for transmission of infection, and this pointed toward droplet transmission of the virus. However, as the outbreak unfolds in mainland China and elsewhere, results of aggregate analysis of cases as well as case reports in scientific journals and the media seem more and more to support that close and prolonged contact with symptomatic cases may not be necessary for transmission. Sources of information available to date (Wed Feb 19) that are relevant to the transmission of SARS-CoV-2 are summarized below:

Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) — China, 2020. CCDC Weekly / Vol. 2 / No. x

Sanche S. The Novel Coronavirus, 2019-nCoV, is Highly Contagious and More Infectious Than Initially Estimated. MedRXiv preprint. February 7, 2020. https://www.medrxiv.org/content/10.1101/2020.02.07.20021154v1. DOI 10.1101/2020.02.07.20021154

Shen M, Peng Z, Guo Y et al. Lockdown may partially halt the spread of 2019 novel coronavirus in Hubei province, China. MedRXiv preprint Posted Feb 13, 2020. doi: https://doi.org/10.1101/2020.02.11.20022236

The authors of this study (released in February 2020) on 72,314 patient records analyzed the spread of the virus through the regions of mainland China from early in December up to the end of the study period (February 11). They found that 14 counties had reported cases as of December 31, 2019, wheras by January 10,2020 (10 days later), 113 counties had cases. This increased to 1,310 counties by 21 days later (end of January) and, as of February 11, 1,386 counties were affected. Quote from the Discussion: *"A main finding of this characterization and exploratory analysis of the first 72,314 cases of COVID-19 found in China in the 40 days between first recognition of the outbreak of pneumonia with unknown etiology on December 31, 2019 to the end of the study period on February 11, 2020 is that this novel coronavirus is highly contagious. It has spread extremely rapidly from a single city to the entire country within only about 30 days. Moreover, it has achieved such far-reaching effects even in the face of extreme response measures including the complete shutdown and isolation of whole cities, cancellation of Chinese New Year celebrations, prohibition of attendance at school and work, massive mobilization of health and public health personnel as well as military medical units, and rapid construction of entire hospitals."* The same article describes the apparent effect of all of these measures on reducing the spread of the virus, stating that the peak of the current wave of the outbreak appears to have already

occurred; however, given the magnitude and rapidity of spread of the outbreak in the face of the extreme measures of control taken by the Chinese government, it is highly probable that in populations where such measures would not be feasible, the virus would spread far more rapidly through the population. The authors state that: *"…the downward trend in the overall epidemic curve suggests that perhaps isolation of whole cities, broadcast of critical information (e.g., promoting hand washing, mask wearing, and care seeking) with high frequency through multiple channels, and mobilization of a multi-sector rapid response teams is helping to curb the epidemic."* And later in the Discussion: "*In particular, this analysis chronicles the extremely rapid spread of the novel coronavirus despite extreme efforts to contain it."* They conclude: *"Huge numbers of people will soon be returning to work and school after the extended New Year holiday. We need to prepare for a possible rebound of the COVID-19 epidemic in the coming weeks and months."*

Shen et al. also evaluated 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. Based on mathematical modeling of the current outbreak, Sanche et al., in a paper titled "The Novel Coronavirus, 2019-nCoV, is Highly Contagious and More Infectious Than Initially Estimated", showed that quarantine and contact tracing of symptomatic individuals alone may not be effective and early, strong control measures may be needed to stop transmission of the virus. The authors state that: *"How contagious the 2019-nCoV is in other countries remains to be seen. If the value of R_0 is as high in other countries, our results suggest that active and strong population-wide social distancing efforts, such as closing down transportation system, schools, discouraging travel, etc., might be needed to reduce the overall contacts to contain the spread of the virus."*

Ease of transmission:

Chan et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. The Lancet February 15, 2020. DOI 10.1016/S0140-6736(20)30154-9

Danchin et al. A new transmission route for the propagation of the SARS-CoV-2 coronavirus. MedRXiv preprint. February 14, 2020. https://www.medrxiv.org/content/10.1101/2020.02.14.20022939v1

Holshue ML, DeBolt C, Lindquist S et al. First Case of 2019 Novel Coronavirus in the United States. New England Journal of Medicine. January 31, 2020; DOI: 10.1056/NEJMoa2001191

Kang M, Wu J, Ma W. Evidence and characteristics of human-to-human transmission of 2019-NCOV. MedRxiv preprint ; February 6, 2020 ; doi: https://doi.org/10.1101/2020.02.03.20019141

Kang et al. Evidence and characteristics of human-to-human transmission of SARS-CoV-2. MedRXiv preprint February 17, 2020. DOI 10.1101/2020.02.03.20019141. URL https://www.medrxiv.org/content/10.1101/2020.02.03.20019141v3

Li Q, Guan X, Wu P et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. New England Journal of Medicine January 29, 2020; DOI: 10.1056/NEJMoa2001316

Phan LT et al. Importation and Human-to-Human Transmission of a Novel Coronavirus in Vietnam. NEJM January 28, 2020. DOI: 10.1056/NEJMc2001272

Pongpirul WA, et al. Journey of a Thai Taxi Driver and Novel Coronavirus. NEJM February 12, 2020.DOI: 10.1056/NEJMc2001621

Wang X, Pan Z and Cheng Z. Association between 2019-nCoV transmission and N95 respirator use. MedRXiv preprint, Posted February 19, 2020. doi: https://www.medrxiv.org/content/10.1101/2020.02.18.20021881v1

Yu P et al. A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period. Journal of Infectious Diseases. February 18, 2020. ISSN1537-6613

Early in the outbreak on mainland China, most of the cases reported had apparently had some exposure to the wet market in Wuhan (Li et al.). As the outbreak unfolded in early January, however, human to human transmission, mainly to close contacts, became the most common exposure associated with infection. For example, Kang et al. published a study on February 6 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. There were several reports of family clusters (Chan et al.; Yu et al.), with little to no evidence of cases having contracted infections by distant or fleeting contact with known cases. There were anecdotal accounts of investigations of confirmed cases where follow-up of contacts revealed secondary infections only in close contacts and not in other more distant contacts. For example, in 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, Pongpirul et al. mentioned that all household contacts as well as 10 other close contacts had tested negative for the virus, although the Thai case had been diagnosed relatively late in the course of his illness. Similarly, details of Vietnam cases within a family, published in the same journal by Phan et al., described that the family had traveled to four cities across Vietnam using various forms of transportation, including planes, trains, and taxis. A total of 28 close contacts had been identified, and symptoms of an upper respiratory infection had not developed in any of them. Contrasting with more recent reports of infections apparently having been contracted even by indirect contact or no known contact with a case, this and other similar reports suggested that the virus was transmitted mainly by close contact. The fact that no secondary cases have been identified among contacts of imported cases confirmed in North America, other than some close or household contacts, seems consistent with transmission by close contact.

On the other hand, reports emerging toward the end of January and in February as human-to-human transmission began to occur in countries and regions outside mainland China suggested that close contact might not be required for transmission of SARS-CoV-2 (Kang et al., Feb 17). For example, reports 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. And on mainland China, analysis by Li et al. 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 described by Holshue et al., over 70% of cases confirmed after January 1st reported no known contact with a symptomatic case. This seemed to imply that the infection can be easily transmitted by casual or indirect contact (for example, via contamination of the environment; Danchin et al.) with symptomatic cases and/or by close contact with asymptomatic cases. Using mathematical modeling, Danchin et al. concluded that a secondary route of transmission (besides close direct contact with cases) might be responsible for the propagation of the epidemic: "Elaborating on the behavior of previous coronavirus outbreaks, we worked out the hypothesis that an alternative infection tropism (the gut tropism) linked to a secondary propagation route (through environment) is affecting the development of the present 2019-nCoV epidemic. *Our epidemic propagation model, when fit to existing data, indicated that, among all regions analysed (Wuhan city in the Hubei region in mainland China, Singapore, Shenzhen region), the propagation of the disease in the city of Wuhan underwent an original course. It appeared to be substantially facilitated by a secondary propagation route, thus substantiating the beneficial effect of an effective quarantine. The main message of our exploration is that relevant prevention measures that take into account both propagation routes should be implemented…"*

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.

Asymptomatic/Pre-symptomatic transmission:

Chang D, Xu H et al. Protecting health-care workers from subclinical coronavirus infection. The Lancet Published February 13, 2020. DOI:https://doi.org/10.1016/S2213-2600(20)30066-7

Drosten C et al. *Neuartiges* ***Coronavirus: Nachweis infektiöser Viren im Nasen-Rachen-Raum bei Personen mit schwachen Symptomen. February 5, 2020; Unpublished manuscript. Munich Clinic.***

Nishiura, H et al. Estimation of the asymptomatic ratio of novel coronavirus (2019-nCoV) infections among passengers on evacuation flights. Medrxiv preprint, 11 Feb 2020. https://doi.org/10.1101/2020.02.03.20020248

Nishiura H, Natalie M Linton NM and Akhmetzhanov AR. Serial interval of novel coronavirus (2019-nCoV) infections. MedRXiv preprint Feb 13, 2020 doi: https://doi.org/10.1101/2020.02.03.20019497

Zhou C. Evaluating new evidence in the early dynamics of the novel coronavirus COVID-19 outbreak in Wuhan, China with real time domestic traffic and potential asymptomatic transmissions MedRXiv preprint Feb 18, 2020 doi: https://www.medrxiv.org/content/10.1101/2020.02.15.20023440v1

Research by Drosten et al. on cases in Germany, confirmed by two laboratories, shows that the virus reproduces in the nasopharynx and GI tract and is likely communicable even while cases have very mild symptoms resembling the common cold.

Of the 565 Japanese citizens evacuated from Wuhan screened for symptoms and tested using RT-PCR, 7 were positive symptomatic and 5 were positive asymptomatic. Nishiura et al. therefore suggest that the asymptomatic ratio is 41.6%. However, the confidence interval on this estimate 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 which describes 56% to 80% of influenza infections as asymptomatic.

In another 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 pre-symptomatic transmission suggested by several anecdotal accounts to date, such as those described by Chang et al. in the Lancet. However, an article posted February 18 described a study by Zhou that evaluated empirical evidence for asymptomatic transmission. The author reports that that evidence was not demonstrated by the study, but also states that it is too early to conclusively rule out asymptomatic transmission. As mentioned, however, several anecdotal accounts support that pre-symptomatic transmission can occur; therefore at this point it would be safer to assume that this is the case.

Potential for fecal transmission:

An, P & Chen, H. Clinical features of 2019 novel coronavirus pneumonia presented gastrointestinal symptoms but without fever onset. The Lancet (preprint). https://ssrn.com/abstract=3532530

Guan W et al. Clinical characteristics of 2019 novel coronavirus infection in China. Medxriv preprint. 7 Feb 2020. doi: https://doi.org/10.1101/2020.02.06.20020974

Holshue ML, DeBolt C, Lindquist S et al. First Case of 2019 Novel Coronavirus in the United States. New England Journal of Medicine. January 31, 2020; DOI: 10.1056/NEJMoa2001191

Liang, W et al. Diarrhea may be underestimated: A missing link in 2019 novel coronavirus. Medrxiv preprint, 11 Feb 2020. https://doi.org/10.1101/2020.02.03.20020289

World Health Organization News Release 2003. Inadequate plumbing systems likely contributed to SARS transmission https://www.who.int/mediacentre/news/releases/2003/pr70/en/(Accessed February 21, 2020)

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.

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 (World Health Organization News Release 2003). In the study by Guan et al., 4 (6.5%) of 62 stool specimens from confirmed cases tested positive for the virus. Several studies 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.

Potential for ocular transmission:

Lu C, Liu X and Jia Z. 2019-nCoV transmission through the ocular surface must not be ignored. The Lancet. Published:February 06, 2020DOI: https://doi.org/10.1016/S0140-6736(20)30313-5

Zhou, Y. et al. Ophthalmologic evidence against the interpersonal transmission of 2019 novel coronavirus through conjunctiva. MedRxiv preprint. doi: https://doi.org/10.1101/2020.02.11.20021956

In a letter to the Lancet published Feb 6, Lu et al. 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." However, although Zhou et al located SARS-CoV-2 in the ocular fluid of 3 of 67 confirmed and suspected cases, those authors argue that ocular transmission is not supported by their findings.

Intrauterine transmission:

Chen H, Guo J, Wang C et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. The Lancet February 12, 2020. https://doi.org/10.1016/S0140-6736(20)30360-3

Qiao J. What are the risks of COVID-19 infection in pregnant women?T he Lancet. February 12, 2020. DOI:https://doi.org/10.1016/S0140-6736(20)30365-2

Nine 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: *"…because of the small number of cases analysed and the short duration of the study period, more follow-up studies should be*

done to further evaluate the safety and health of pregnant women and newborn babies who develop COVID-19 infection."

Viral persistence:

Kampf, G. et al. Persistence of coronaviruses on inanimate surfaces and its inactivation with biocidal agents. Journal of Hospital Infection, Feb 6, 2020. DOI: https://doi.org/10.1016/j.jhin.2020.01.022

A review of several 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'. Based on their review of the data, the researchers recommend doubling the typically used concentration of sodium hypochlorite solutions from 0.05 % to 0.1 % in hospitals with cases of COVID-19.

Nosocomial infection:

Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) — China, 2020. CCDC Weekly / Vol. 2 / No. x

Guan W et al. Clinical characteristics of 2019 novel coronavirus infection in China. Medxriv preprint. 7 Feb 2020. doi: https://doi.org/10.1101/2020.02.06.20020974

Wang D et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. Journal of the American Medical Association Feb 7, 2020. doi:10.1001/jama.2020.1585

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. However, in the study of over 70,000 cases of COVID-19 mentioned earlier, 3,019 were healthcare workers (including doctors, nurses and other hospital or clinic staff, of which 1,716 were lab-confirmed and 5 died. This study found that while only 4.6% of the general study population were classified as critically ill, 14.6% of the healthcare workers were classified as critical. No reasons for this were postulated; however, increased exposure to symptomatic cases with a higher viral load may explain this, at least in part.

Reproductive number:

Vynnycky, E et al. Estimates of the reproductive numbers of Spanish influenza using morbidity data. International Journal of Epidemiology, 36, 881-889. 2007.

Many of the earlier 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 suggested that it exceeded 4. 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; most current estimates of R_0 are between 1.5 and 2.5. For a reader-friendly discussion on the interpretation of R_0, see this article.

With the emergence of COVID-19 on cruise ships, it is worth remembering that the reproductive number of a virus is dependent on context and is generally higher in confined settings. A previous paper (Vynnycky et al.) reviewed the 1918 influenza pandemic estimates of R: 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 docked off the coast of Japan in February serves to illustrate this concept.

See Appendix 1 for a list of several studies that have estimated R for the virus.

References

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.

An, P & Chen, H. Clinical features of 2019 novel coronavirus pneumonia presented gastrointestinal symptoms but without fever onset. *The Lancet* (preprint). https://ssrn.com/abstract=3532530

Chan JF, Yuan S, Kok K. et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. The Lancet. January 24, 2020. DOI https://doi.org/10.1016/S0140-6736(20)30154

Chang D, Xu H et al. Protecting health-care workers from subclinical coronavirus infection. The Lancet Published February 13, 2020. DOI:https://doi.org/10.1016/S2213-2600(20)30066-7

Chen H, Guo J, Wang C et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. The Lancet (Published Feb 12, 2020). https://doi.org/10.1016/S0140-6736(20)30360-3

Danchin et al. A new transmission route for the propagation of the SARS-CoV-2 coronavirus. MedRXiv preprint. February 14, 2020. https://www.medrxiv.org/content/10.1101/2020.02.14.20022939v1

Drosten C et al. Neuartiges Coronavirus: Nachweis infektiöser Viren im Nasen-Rachen-Raum bei Personen mit schwachen Symptomen. February 5, 2020; Unpublished manuscript. Munich Clinic.

Guan W et al. Clinical characteristics of 2019 novel coronavirus infection in China. Medxriv preprint. 7 Feb 2020. doi: https://doi.org/10.1101/2020.02.06.20020974

Holshue ML, DeBolt C, Lindquist S et al. First Case of 2019 Novel Coronavirus in the United States. *New England Journal of Medicine*. January 31, 2020; DOI: 10.1056/NEJMoa2001191

Kampf, G. et al. Persistence of coronaviruses on inanimate surfaces and its inactivation with biocidal agents. *Journal of Hospital Infection,* Feb 6, 2020. DOI: https://doi.org/10.1016/j.jhin.2020.01.022

Kang M, Wu J, Ma W. Evidence and characteristics of human-to-human transmission of 2019-NCOV. MedRxiv preprint ; February 6, 2020 ; doi: https://doi.org/10.1101/2020.02.03.20019141

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Li Q, Guan X, Wu P et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. New England Journal of Medicine January 29, 2020; DOI: 10.1056/NEJMoa2001316

Liang, W et al. Diarrhea may be underestimated: A missing link in 2019 novel coronavirus. Medrxiv preprint, 11 Feb 2020. https://doi.org/10.1101/2020.02.03.20020289

Nishiura, H et al. Estimation of the asymptomatic ratio of novel coronavirus (2019-nCoV) infections among passengers on evacuation flights. Medrxiv preprint, 11 Feb 2020. https://doi.org/10.1101/2020.02.03.20020248

Nishiura H, Natalie M Linton NM and Akhmetzhanov AR. Serial interval of novel coronavirus (2019-nCoV) infections. MedRXiv preprint Feb 13, 2020 doi: https://doi.org/10.1101/2020.02.03.20019497

Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) — China, 2020. CCDC Weekly / Vol. 2 / No. x

Qiao J. What are the risks of COVID-19 infection in pregnant women?T he Lancet. February 12, 2020. DOI:https://doi.org/10.1016/S0140-6736(20)30365-2

Phan LT et al. Importation and Human-to-Human Transmission of a Novel Coronavirus in Vietnam. NEJM January 28, 2020. DOI: 10.1056/NEJMc2001272

Pongpirul WA, et al. Journey of a Thai Taxi Driver and Novel Coronavirus. NEJM February 12, 2020.DOI: 10.1056/NEJMc2001621

Sanche, S et al. The novel coronavirus, 2019-nCoV, is highly contagious and more infectious than initially estimated. Medrxiv preprint. 11 Feb 2020. https://doi.org/10.1101/2020.02.07.20021154

Shen M, Peng Z, Guo Y et al. Lockdown may partially halt the spread of 2019 novel coronavirus in Hubei province, China. MedRXiv preprint Posted Feb 13, 2020. doi: https://doi.org/10.1101/2020.02.11.20022236

Vynnycky, E et al. Estimates of the reproductive numbers of Spanish influenza using morbidity data. International Journal of Epidemiology, 36, 881-889. 2007.

Wang D et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. Journal of the American Medical Association Feb 7, 2020. doi:10.1001/jama.2020.1585

Wang X, Pan Z and Cheng Z. Association between 2019-nCoV transmission and N95 respirator use. MedRXiv preprint, Posted February 19, 2020. doi: https://www.medrxiv.org/content/10.1101/2020.02.18.20021881v1

World Health Organization News Release 2003. Inadequate plumbing systems likely contributed to SARS transmission https://www.who.int/mediacentre/news/releases/2003/pr70/en/ (Accessed February 21, 2020)

Yu P et al. A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period. Journal of Infectious Diseases. February 18, 2020. ISSN 1537-6613

Zhou, Y. et al. Ophthalmologic evidence against the interpersonal transmission of 2019 novel coronavirus through conjunctiva. MedRxiv preprint. doi: https://doi.org/10.1101/2020.02.11.20021956

Appendix 1: Studies estimating R0 for SARS-CoV-2. Note that this list includes only some of the studies that have estimated R for the virus; new studies are being published every week. However, most of the studies produce estimates within the range represented in this table.

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.	Jan 24	R_0 = 2.24 to 3.58

Accepted for publication in International Journal of Infectious Diseases: 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).