Report 3: Transmissibility of 2019-nCoV

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Note: This is an extended version of an analysis previously shared with WHO, governments and academic networks between 22/1/20-24/1/20

Summary

Self-sustaining human-to-human transmission of the novel coronavirus (2019-nCov) is the only plausible explanation of the scale of the outbreak in Wuhan. We estimate that, on average, each case infected 2.6 (uncertainty range: 1.5-3.5) other people up to 18th January 2020, based on an analysis combining our past estimates of the size of the outbreak in Wuhan with computational modelling of potential epidemic trajectories. This implies that control measures need to block well over 60% of transmission to be effective in controlling the outbreak. It is likely, based on the experience of SARS and MERS-CoV, that the number of secondary cases caused by a case of 2019-nCoV is highly variable – with many cases causing no secondary infections, and a few causing many. Whether transmission is continuing at the same rate currently depends on the effectiveness of current control measures implemented in China and the extent to which the populations of affected areas have adopted risk-reducing behaviours. In the absence of antiviral drugs or vaccines, control relies upon the prompt detection and isolation of symptomatic cases. It is unclear at the current time whether this outbreak can be contained within China; uncertainties include the severity spectrum of the disease caused by this virus and whether cases with relatively mild symptoms are able to transmit the virus efficiently. Identification and testing of potential cases need to be as extensive as is permitted by healthcare and diagnostic testing capacity – including the identification, testing and isolation of suspected cases with only mild to moderate disease (e.g. influenza-like illness), when logistically feasible.

1. Introduction

A new human coronavirus, now termed 2019-nCoV, emerged during December 2019 in the Chinese city of Wuhan. As of 1900 GMT 24th January 2020, over 900 cases have been reported in China (with 26 deaths), and cases have been detected in at least 9 regions or countries outside mainland China. Initial phylogenetic analysis suggests that the new virus is similar to the SARS coronavirus when compared with other coronaviruses known to infect humans.

In our report published on January 22nd, we used an estimate of the frequency of international travel from Wuhan to estimate that 4000 cases (uncertainty range: 1000-9700) had occurred there with onset of symptoms up to 18th January [1].

Here we report estimates of the human-to-human transmissibility of 2019-nCoV. We generate a set of simulated epidemic trajectories using a mathematical model of 2019-nCoV transmission and examine the extent to which each trajectory is consistent with our prior estimates of outbreak size.

For our baseline estimates, we assume that two key characteristics of 2019-nCoV are similar to those observed for SARS: that there is high level of variability in the number of new infections generated by each infectious individual (negative binomial offspring distribution with k=0.16 [2]); and that the generation time (the average time between generations of infection) is the same as was estimated for SARS (mean of 8.4 days [3]). We also explore an alternative scenario which assumes that 2019-nCoV shows less case to case variation in infectiousness and has a shorter generation time. This scenario might

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be more realistic if a majority of 2019-nCoV cases have mild to moderate ('flu-like') symptoms and if both milder and severe cases are able to transmit infection onwards.

The estimates of transmissibility we derive depend upon the number of cases infected from the original animal source of this virus, which is currently unknown. Therefore, we explicitly consider a range of numbers of human cases caused by zoonotic exposure to the virus.

The transmissibility of a virus is measured by the reproduction number, R, which measures the average number of new infections generated by each infected person. When R is greater than 1, the outbreak is self-sustaining unless control measures are introduced to reduce R and slow or stop transmission. When R is less than 1, while some human-to-human transmission occurs, the number of new cases decreases over time and, eventually, the outbreak will stop. At the start of an outbreak, when the population is largely unaware of the new threat and everyone is susceptible, it is reasonable to assume that R is constant for a period of time. We call this initial transmissibility the basic reproduction number R_0.

Here, we describe different estimates of R_0 and assess the degree to which they are consistent with our estimates of the size of the outbreak in Wuhan: we measure the proportion of simulations that are statistically compatible with 4000 total cases by 18th January. Our best-case (most optimistic) estimate is the value of R_0 for which 5% of simulated trajectories match or exceed 4000 cases by 18th January. Our central estimate of R_0 gives 50% of simulated trajectories matching or exceeding 4000 cases. Our worst-case (most pessimistic) estimate is the value for which 95% of simulated trajectories match or exceed 4000 cases. Figure 1 illustrates our approach. As a sensitivity analysis, we also generate estimates assuming 1000 or 9700 cases by 18th January, the lower and upper bounds of the uncertainty range around our central estimate of 4000 cases by that date.

2. Results

Our analysis indicates that it is highly likely that the human-to-human transmissibility of 2019-nCoV is sufficient to support sustained human transmission (R_0>1) unless effective control measures are implemented.

We judge that the most likely estimate corresponds to the smallest level of zoonotic exposure explored here (40 cases), namely R_0=2.6 (Table 1 and Figure 1). Uncertainty caused by the intrinsically random nature of epidemics and the uncertainty in the level of zoonotic exposure gives a range of 1.5-3.5, assuming a total of 4000 cases by 18th January. Central estimates of R_0 for the (unlikely) scenario that the true outbreak size in Wuhan was at the lower end of the uncertainty range of our previous estimates (namely 1000 cases) vary from 1.7 to 2.6, depending on the level of zoonotic exposure. Estimates of R_0 assuming 9,700 cases by 18th January (our highest estimate from report 2) were higher, at R_0=3.1 (uncertainty: 1.9-4.2), for 40 cases caused by zoonotic exposure.

The only scenario which supports R_0<1 requires a low number (1000) of cases overall in Wuhan by 18th January and a very large number (200) of those cases being caused by zoonotic exposure (Table 1), and even then, R_0 is <1 only for our best case (most optimistic) estimate. Infection of 200 individuals with a novel virus with very limited genetic diversity would represent an unprecedently large point source zoonotic exposure event for the initial seeding of this epidemic. Current evidence of very limited genetic diversity in the published genetic sequences of the virus suggests a smaller seeding event (perhaps smaller than the 40 cases assumed in our lowest zoonotic seeding scenario) [4–6].

Our baseline analysis assumes SARS-like levels of case-to-case variability in the numbers of secondary cases generated by each case (i.e. it includes super-spreading type events), and a SARS-like generation time. We also examined sensitivity to these assumptions. Assuming a shorter generation time (mean of 6.8 days rather than 8.4 days) reduces our central estimate of R_0 to 2.1 (uncertainty range: 1.3-2.7), but does not change overall conclusions about the likelihood of self-sustaining human-to-human transmission. Increasing the generation time to 10.7 days results in a higher central estimate of R_0 of 3.1 (uncertainty range: 1.7-4.3) but again does not change basic conclusions.

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Table 1: Best-case, central and worst-case estimates of 2019-nCoV human-to-human R_0 compatible with either 4000 (top half of table) or 1000 (bottom half of table) total cases by 18/01/2020. Values of R_0 >1 represent self-sustaining human-to-human and are highlighted in red. Baseline estimates highlighted in bold.

Number of cases caused by zoonotic exposure	Assumed total number of cases by 18/01/2020	Best-case R_0	Central (median) R_0	Worst-case R_0
40	**4000**	**2.1**	**2.6**	**3.5**
80	4000	1.8	2.2	2.7
120	4000	1.7	2.0	2.4
160	4000	1.6	1.8	2.2
200	4000	1.5	1.7	2.0
40	1000	1.4	1.9	2.7
80	1000	1.2	1.5	2.0
120	1000	1.1	1.3	1.7
160	1000	1.0	1.2	1.5
200	1000	0.9	1.1	1.3

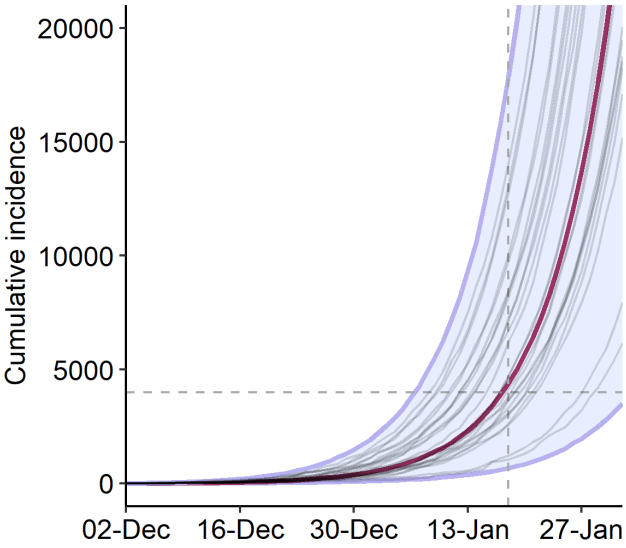

Figure 1: Illustration of estimation method for central estimate of R_0=2.6. Red curve represents median cumulative case numbers over time, calculated from 5000 simulated trajectories of the epidemic, assuming zoonotic exposure of 40 cases in December 2019 and the generation time and variability in infectiousness of SARS. The grey region indicates the 95 percentile range of trajectories – individual simulated epidemics (a random subset of which are shown as light grey curves) are highly variable, reflecting the random nature of disease transmission. Dotted lines indicate January 18th (vertical) and 4000 cumulative cases (horizontal).

Assuming a lower level of variability in infectiousness (at the minimum level statistically consistent with SARS data [1]) narrows the uncertainty range of R_0 but changes the central estimate only marginally: R_0=2.5 (uncertainty range 1.6-2.9), for a negative binomial offspring distribution with k=0.64. Assuming a lower level of variability in infectiousness (at the minimum level statistically consistent with SARS data [2]) narrows the uncertainty range of R_0 but changes the central estimate little: R_0=2.5 (uncertainty range 1.6-2.9), for a negative binomial offspring distribution with k=0.64.

If the current virus causes more cases with mild to moderate symptom severity than SARS, and these cases are infectious – a scenario consistent with some recently published data on a family cluster of cases [7], both the generation time and level of heterogeneity in infectiousness may be lower than for SARS. This scenario might be more realistic if a majority of 2019-nCoV cases have mild to moderate ('flu-like') symptoms and both milder and severe cases are able to transmit infection onwards. This results in both a lower central estimate of R_0 and a narrower uncertainty range: R_0 = 2.0 (uncertainty: 1.4-2.3) for a mean generation time of 6.7 days and k=0.64.

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3. Discussion

The unprecedented quarantining of multiple cities in Hubei province, China on 23rd January 2020 clearly marks a new stage of the public health response to this outbreak. Here, we explored a range of different scenarios for the extent of zoonotic (animal) exposure to estimate transmissibility of 2019-nCoV in Wuhan up to 18th January. We conclude that self-sustaining human-to-human transmission of the virus must have occurred, with a reproduction number estimate of 2.6 (uncertainty range: 1.5-3.5), to explain our previous central estimate of the scale of outbreak (namely 4000 cases by 18th January). Even assuming our lowest estimate of 1000 cases by 18th January, it is highly likely that sustained human-to-human transmission was occurring. Assuming that our upper bound estimate of 9700 cases occurred, R_0 estimates are correspondingly higher.

Whether transmission continues at the same rate now critically depends on the effectiveness of the intense control effort now underway in Wuhan and across China. We note the large body of evidence that suggests that the reproduction number for SARS changed considerably when populations became fully aware of the threat. If a similar change to contact patterns is occurring in this outbreak, rates of transmission are likely to be lower now than during the period for which these estimates were made, due to control measures and risk avoidance in the population. Whether the reduction in transmission is sufficient to reduce *R* to below 1 – and thus end the outbreak – remains to be seen. Reports point to mildly symptomatic but infectious cases of 2019-nCoV, which were not a feature of SARS. Prompt detection and isolation of such cases will be extremely challenging, given the larger number of other diseases (e.g. influenza) which can cause such non-specific respiratory symptoms. While more severe cases will always need to be prioritised, control may depend upon successful detection, testing and isolation of suspect cases with the broadest possible range of symptom severity.

Our results emphasise the need to track transmission rates over the next few weeks, especially in Wuhan. If a clear downwards trend is observed in the numbers of new cases, that would indicate that control measures and behavioural changes can substantially reduce the transmissibility of 2019-nCoV. Genetic data from Wuhan after the implementation of strong public health measures may also provide valuable insight into the patterns and rate of transmission.

Despite the recent decision of the WHO Emergency Committee to not declare this a Public Health Emergency of International Concern at this time, this epidemic represents a clear and ongoing global health threat. It is uncertain at the current time whether it is possible to contain the continuing epidemic within China. In addition to monitoring how the epidemic evolves, it is critical that the magnitude of the threat is better understood. Currently, we have only a limited understanding of the spectrum of severity of symptoms that infection with this virus causes, and no reliable estimates of the case fatality ratio – the proportion of cases who will die as a result of the disease. Characterising the severity spectrum, and how severity of symptoms relates to infectiousness, will be critical to evaluating the feasibility of control and the likely public health impact of this epidemic.

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