Report 2: Estimating the potential total number of novel Coronavirus cases in Wuhan City, China

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Background

On the 31st December 2019, the World Health Organization (WHO) China Country Office was informed of cases of pneumonia of unknown aetiology in Wuhan City, Hubei Province, China [1]. A novel Coronavirus (2019-nCoV) related to the Middle Eastern Respiratory Syndrome virus (MERS-CoV) and the Severe Acute Respiratory Syndrome virus (SARS-CoV) has since been implicated [2].

As of 4am 21st January (Beijing Time) 2020, 440 cases (including nine deaths) have been confirmed across 13 provinces in China, plus suspected cases in multiple other provinces [3]. As of 9:00 GMT 22nd January 7 confirmed cases in travellers from Wuhan with symptom onset on or before the 18th January were detected outside mainland China in Thailand (3 cases), Japan (1 case), South Korea (1 case), Taiwan (1 case) and the United States (1 case) [4–10]. Chinese authorities have also confirmed evidence of human-to-human transmission, as well as 15 cases in healthcare workers [11,12]. Of these cases, four travelled before exit screening in Wuhan International Airport was introduced on 15th January [13], three (South Korea, Taiwan, USA) on or after.

Using the number of cases detected outside mainland China with who had disease onset by 18th January, it is possible (see Report 1 [14]) to infer the number of clinically comparable cases within Wuhan City that may have occurred thus far. Here we update our estimates to account for the additional international exported cases (7 cases).

Summary

We estimate that a total of 4,000 cases of 2019-nCoV in Wuhan City (uncertainty range: 1,000 – 9,700) had onset of symptoms by 18th January 2020 (the last reported onset date of any case) [15].

Our estimates should not be interpreted as implying the outbreak has doubled in size in the period 12th January to 18th January – delays in confirming and reporting exported cases and incomplete information about dates of symptom onset together with the still very small numbers of exported cases mean we are unable to estimate the epidemic growth rate at the current time.

This estimate is based on the following assumptions:

- Wuhan International Airport has a catchment population of 19 million individuals [1].
- There is a mean 10-day delay between infection and detection, comprising a 5-6 day incubation period [16,17] and a 4-5 day delay from symptom onset to detection/hospitalisation of a case (the cases detected in Thailand and Japan were hospitalised 3 and 7 days after onset, respectively) [4,18].
- Total volume of international travel from Wuhan over the last two months has been 3,301 passengers per day. This estimate is derived from the 3,418 foreign passengers per day in the top 20 country destinations based on 2018 IATA data [19], and uses 2016 IATA data held by Imperial College London to correct for the travel

surge at Chinese New Year present in the latter data (which has not happened yet this year) and for travel to countries outside the top 20 destination list.

- Exit screening (which reportedly came into force on the 15th January [13]) had no impact on exported cases reported up to 16th January. *Exit screening may have reduced exports in recent days, in which case our baseline prediction may be an underestimate of the true number of cases in Wuhan*.
- We assume all cases in travellers flying to destinations outside mainland China are being detected at those destinations. This may well not be the case. *If cases are being missed in other countries, our baseline prediction will underestimate the true number of cases in Wuhan.*
- We now report uncertainty as the range spanned by the 95% confidence intervals of the first three scenarios in Table 1. Thus, our uncertainty range represents uncertainty in key assumptions as well as statistical assumptions.

Additional caveats

1. We assume that outbound trip durations are long enough that an infected Wuhan resident travelling internationally will develop symptoms and be detected overseas, rather than being detected after returning to Wuhan. We also do not account for the fact that international visitors to Wuhan (such as the case who was detected in Japan) might be expected to have a shorter duration of exposure and thus a lower infection risk than residents. *Accounting for either factor correctly requires additional data but would increase our estimate of the total number of cases.*
2. We estimate the potential number of symptomatic cases with disease severity of a level requiring hospitalisation (both the cases detected in Thailand and Japan were moderately severe). Our estimates do not include cases with mild or no symptoms.
3. The incubation period of 2019-nCov is not known and has been approximated with the estimates obtained for MERS-CoV and SARS [16,17].
4. We assume that international travel is independent of the risk of exposure to 2019n-CoV and of infection status. If zoonotic exposure were biased towards wealthier people, travel frequency may be correlated with exposure. Also, some travel might be causally linked to infection status (to seek healthcare overseas) or the infection status of contacts in Wuhan (this may apply to the case detected in Japan) [18]. *Accounting for either association would increase the probability of a case travelling and therefore reduce our estimates of the total number of cases.*
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Sensitivity analysis

We explore the sensitivity of estimates of total cases to our assumptions about: i) the catchment population size of Wuhan International Airport (restricting to the population of Wuhan City of 11 million individuals [20], rather than the population of the entire metropolitan area [1]), ii) the duration of the detection window (exploring a lower value of 8 days representing the uncertainty in the detection window or the potential effect of exit screening), and iiii) the number of exportations reported internationally (8 cases). Table 1 summarises the baseline assumptions and alternative scenarios explored.

Table 1: Estimated case numbers based on the baseline assumptions and alternative scenarios explored.

	Baseline[1]	**Smaller catchment[1]**	**Shorter detection window[1]**	**6 exported cases**	**8 exported cases**
Exported number of confirmed cases[2]	7	7	7	6	8
Daily international passengers travelling out of Wuhan International Airport[3]	3,301	3,301	3,301	3,301	3,301
Effective catchment population of Wuhan International Airport	19 million	11 million	19 million	19 million	19 million
Detection window (days)	10 days	10 days	8 days	10 days	10 days
Estimated total number of cases (95% CI)	4,000 (1,700 – 7,800)	2,300 (1,000 – 4,500)	5,000 (2,200 – 9,700)	3,400 (1,400 – 7,000)	4,600 (2,100 – 8,600)

[1]We now report uncertainty around our central estimate as the range spanned by the 95% confidence intervals of these three scenarios. [2]reported number of confirmed cases detected internationally. [3]calculated from the 3-month totals reported by [19] corrected for the travel surge during Chinese New Year (see Summary).

Conclusions

Our estimates of the size of the outbreak in Wuhan have more than doubled since our first report. This is a result of the number of cases detected outside mainland China having increased from 3 to 7. Our analysis does not allow the growth rate of the epidemic to be determined however. *Our estimates should not be interpreted as implying the outbreak has doubled in size in the period 12th January to 18th January* – delays in confirming and reporting exported cases and incomplete information about dates of symptom onset together with the still very small numbers of exported cases mean we are unable to estimate the epidemic growth rate at the current time.

It is likely that the outbreak of a novel coronavirus in Wuhan has caused substantially more cases of moderate or severe respiratory illness than have currently been detected and reported. However, recent rapid increases in officially reported confirmed case numbers in China suggest that case detection and reporting has been substantially enhanced in recent days. With further refinements to case definitions and testing and further expansion of surveillance (for instance, to primary care providers) it is to be hoped that the differences between our estimates and official case numbers will lessen further.

This analysis does not directly address transmission routes, but recent reports [11,21,22] and past experience with SARS and MERS-CoV outbreaks of similar scale suggests currently self-sustaining human-to-human transmission should not be ruled out. Given this evidence for human-to-human transmission, enhancing rapid case detection will be essential if the outbreak is to be controlled.

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Methods

Using internationally reported cases, it is possible to infer the magnitude of comparable cases within Wuhan City that may have occurred thus far.

The total number of cases requiring healthcare is given by:

$$Total\ number\ of\ cases = \frac{number\ of\ cases\ detected\ overseas}{probability\ any\ one\ case\ will\ be\ detected\ overseas}$$

where the probability any one case will be detected overseas (p) is given by:

$$p = \ daily\ probability\ of\ international\ travel\ \times mean\ time\ to\ detection\ of\ a\ case$$

The daily probability of travel is calculated by:

$$daily\ probability\ of\ international\ travel = \frac{daily\ outbound\ international\ travellers\ from\ Wuhan}{catchement\ population\ of\ Wuhan\ airport}$$

Finally, the mean time to detection can be approximated by:

$$mean\ time\ to\ detection = incubation\ period + mean\ time\ from\ onset\ of\ symptoms\ to\ detection$$

Confidence intervals can be calculated from the observation that the *number of cases detected overseas*, *X*, is binomially distributed as Bin(*p*,*N*), where *p* = *probability any one case will be detected* overseas, and *N* is the *total number of cases*. *N* is therefore a negative binomially distributed function of *X.* The results in Table 1 are maximum likelihood estimates obtained using this negative binomial likelihood function. We now report overall uncertainty as the range spanned by the 95% confidence intervals of the first three scenarios in Table 1.