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 (SARSCoV) 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).

背景介绍

2019 年 12 月 31 日，世界卫生组织驻华代表处获悉了中国湖北省武汉市病因不明的肺炎病例[1]。病例被认为与相似于中东呼吸综合征病毒（MERS-

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CoV）和重症急性呼吸综合征病毒（SARS-CoV）的新型冠状病毒（2019-nCoV）相关 [2]。

截至 2020 年 1 月 21 日（北京时间）凌晨 4 点，中国有 13 个省份已确诊 440 例病例（包括 9 例死亡），其他多个省份也出现了疑似病例[3]。截至 1 月 22 日早九点（格林威治时间），中国大陆以外的国家和地区也出现了 7 例确诊病例，皆为武汉旅客，他们都在 1 月 18 日甚至更早之前就出现了相应症状，其中泰国 3 例，日本 1 例，韩国 1 例，台湾 1 例和美国 1 例[4-10]。中国有关机构已经证实了该新型病毒能在人与人之间传播，医护人员中也确诊了 15 例被感染的病例[11,12]。在国际案例中，四名旅客于 1 月 15 日武汉国际机场实行出境检查之前离境的，其余三名旅客（分别赴韩国，台湾，美国）则在此之后离境[13]。

根据截至 1 月 18 日在中国大陆以外发现的疾病发病病例数，我们有可能（见报告 1 [14]）推断武汉市内迄今为止可能发生的临床病例中具有可比性的数字。我们在此更新了估算值，以覆盖国际上的 7 个案例。

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.

摘要

截止至 2020 年 1 月 18 日（任一病例的末次报告发作的日期），我们估计武汉市共有 4,000 例 2019-nCoV 病例（不确定性范围：1,000 – 9,700）[15]。

我们的估计值不应被理解为疾病爆发在 1 月 12 日至 1 月 18 日期间扩大了一倍 -- 确认和收到境外病例报告的延时，症状发作日期的信息不完整以及境外病例数目仍然很少等种种因素，意味着我们目前无法估算疫情的增长率。

该估计值基于以下假设：

- 武汉国际机场的服务范围人口为 1900 万[1]。
- 从感染到确诊之间平均有 10 天的延迟，包括 5-6 天的潜伏期[16,17]，以及从症状发作至确诊/住院之间的 4-5 天的延迟（在泰国和日本被发现的病患入院治疗时间分别在自症状出现后 3 天和 7 天住院[4,18]）。
- 在过去的两个月中，从武汉出发的国际旅客总量为每天 3,301 人次。这一估计是基于 2018 年 IATA 数据[19]中排名前 20 的国家/地区目的地旅行量为每日 3,418 名外国旅客，并使用伦敦帝国理工学院持有的 2016 年 IATA 数据来修正中国春节期间的旅行激增数据（今年尚未发

生）以及前往前 20 名旅行目的地名单以外的国家/地区的旅行数量对这一数据的影响。

- 出境检查（据报道于 1 月 15 日生效[13]）对截至 1 月 16 日报告的境外病例数没有影响。*最近几日的出境检验可能减少了出境人数，在此情况下，我们的基准预测可能会低于武汉市的实际病例数。*
- 我们假设飞往中国大陆以外目的地的所有病例都已在这些目的地确诊，但实际情况可能并非如此。*如果在其他国家/地区遗漏了病例，我们的基准预测将低于武汉的真实病例数。*

目前我们报告的不确定性为涵盖了表 1 中前三种情况的 95%置信区间的范围。因此，我们的不确定性范围代表了关键假设和统计假设中的不确定性。

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 2019nCoV 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.*

其他注意事项

1. 我们假定出境旅行的持续时间足够长，使得一名被感染的武汉出国旅行的居民会出现症状并在海外被发现，而不是返回武汉后被发现。我们也未将以下这种情况纳入考虑，即抵达武汉的国际旅客（例如在日本发现的病例）的预期暴露时间更短，从而感染风险低于本地居民。*正确解释以上所提到的两个因素需要更多的额外数据，但都会增加对病例总数的估计。*
2. 我们估计的对象为潜在的疾病症状严重程度为需要住院的病例（在泰国和日本发现的病例均为中度严重），不包括轻度或无症状的病例。
3. 未知的 2019-nCov 潜伏期可根据 MERS-CoV 和 SARS 的潜伏期估计得出[16,17]。
4. 我们假设 2019nCoV 的暴露风险及感染风险与国际旅行相互独立，即无关。如果人畜共患病暴露偏向于更富裕人群，则旅行频率可能与暴露风险相关。并且，有些旅行活动可能与感染状况（如：寻求海外医疗保健）或武汉接触者的感染状况（这可能适用于在日本发现的案件）[18]存在因果关系。*考虑到这两种关联都会增加病患旅行的可能性，因而降低我们对病例总数的估计。*

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 iii) the number of exportations reported internationally (8 cases). Table 1 summarises the baseline assumptions and alternative scenarios explored.

敏感性分析

我们探索了总病例估计值对以下假设的敏感性：i) 武汉国际机场服务人口规模（假设将武汉市人口数量限制在 1100 万人[20]，而非整个大都市的人口 [1]），ii）检测窗口的持续时间（探索 8 天的较低值代表了检测窗口中

的不确定性或出境检验的潜在影响），iii）国际报告上的输出数量（8例）。 表 1 总结了基线假设和探索的其他情况。

表 1 基于基线假设和探索的其他情况的估计病例数量

	基线[2]	较少服务人口 [1]	较短检测窗口 [1]	六例输出病例	八例输出病例
输出确诊病例数[3]	7	7	7	6	8
每日从武汉国际机场出发的国际旅客数量[4]	3,301	3,301	3,301	3,301	3,301
武汉国际机场有效服务人口数量	1900 万	1100 万	1900 万	1900 万	1900 万
检测窗口（天）	10 天	10 天	8 天	10 天	10 天
估计病例总数（95%置信区间）	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)

[2]目前我们报告的是围绕中心估计的不确定性，范围涵盖了这三种情况的 95%置信区间。
[3]报告的国际确诊病例的数量。
[4]根据[19]报告的 3 个月总数并矫正了中国春节期间的旅行高峰计算得出（见总结）。

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.

结论

自我们的第一份报告以来，我们对武汉市暴发规模的估计已增加了一倍以上。这是由于在中国大陆以外发现的病例数已从 3 增至 7。但是我们的分析无法确定流行增长率。*我们的估计值不应被理解为疾病爆发在 1 月 12 日至 1 月 18 日期间扩大了一倍 -- 确认和收到境外病例报告的延时，症状发作日期的信息不完整以及境外病例数目仍然很少等因素，意味着我们目前无法估算疫情的增长率。*

武汉市新型冠状病毒的爆发导致中度或重度呼吸道疾病的病例可能多于目前已发现和报道的病例。但是，最近的中国官方报告的确诊病例数迅速增加表明，在最近几日中，对病例的确诊和报告已大量增多。通过对病例定义和检测的进一步完善以及对监视的进一步扩展（例如，扩展到初级医疗提供者），我们的估计值与官方病例数之间的差异有望进一步减小。

该分析并没有直接涉及传播途径，但是近日的报道[11,21,22]和以往类似规模的 SARS 和 MERS-CoV 爆发的经验表明，目前不应该排除人与人之间自我维持的传播。鉴于存在人与人之间传播的证据，如果要控制疫情暴发，需要加强迅速检测病例的能力。

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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:

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

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.

备注：计算方法

利用国际报告的病例，可以推断出武汉市内可能出现的相当病例的规模。

需要就医的病例总数可由下式计算得出：

$$总病例数 = \frac{海外检测病例数量}{任一病例在海外被检测出的概率}$$

其中任一病例在海外被检测出的概率(p)可由下式计算得出：

$$p = \textit{每日国际旅行的概率} \times \textit{平均检测出一例病例的概率}$$

每日旅行概率由下式计算得出：

$$\textit{每日国际旅行概率} = \frac{\textit{武汉每日出境的国际旅客数量}}{\textit{武汉机场服务人口数}}$$

最后，每例病例被检测出的平均时间可由下式得到近似值：

$$\textit{平均检出时间} = \textit{潜伏期} + \textit{从症状发作至检测的平均时间}$$

根据海外检测出的病例数 X 服从二项分布 Bin(p,N)的观察结果可计算出置信区间，其中 p = 海外检测出任一病例的概率，N 为总病例数。因此 N 为 X 的服从负二项分布的函数。表 1 的结果是从该负二项分布似然函数中得到的最大似然估计（MLE）。目前我们报告的整体不确定性为涵盖了表 1 中前三种情况的 95%置信区间的范围。