

1 **2019-20 Wuhan coronavirus outbreak: Intense surveillance is vital for preventing**
2 **sustained transmission in new locations**

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12 **ABSTRACT**

13 The outbreak of pneumonia originating in Wuhan, China, has generated 830 confirmed
14 cases, including 26 deaths, as of 24 January 2020. The virus (2019-nCoV) has spread
15 elsewhere in China and to other countries, including South Korea, Thailand, Japan and
16 USA. Fortunately, there has not yet been evidence of sustained human-to-human
17 transmission outside of China. Here we assess the risk of sustained transmission
18 whenever the coronavirus arrives in other countries. Data describing the times from
19 symptom onset to hospitalisation for 47 patients infected in the current outbreak are used
20 to generate an estimate for the probability that an imported case is followed by sustained
21 human-to-human transmission. Under the assumptions that the imported case is
22 representative of the patients in China, and that the 2019-nCoV is similarly transmissible
23 to the SARS coronavirus, the probability that an imported case is followed by sustained
24 human-to-human transmission is 0.37. However, if the mean time from symptom onset to

25 hospitalisation can be halved by intense surveillance, then the probability that an imported
26 case leads to sustained transmission is only 0.005. This emphasises the importance of
27 current surveillance efforts in countries around the world, to ensure that the ongoing
28 outbreak will not become a large global epidemic.

29

30 **KEYWORDS**

31 2019-nCoV; mathematical modelling; infectious disease epidemiology; major epidemic;
32 forecasting; SARS

33

34

1. INTRODUCTION

35

36 The infectious agent driving the ongoing pneumonia outbreak (the 2019-nCoV) appears
37 to have transitioned from animals into humans at Huanan seafood wholesale market in
38 Wuhan, China [1–5]. Since then, cases have been recorded in other countries, and initial
39 estimates suggest a case fatality rate of around 14% [6]. Even countries without
40 confirmed cases are on high alert. For example, the United Kingdom has not yet seen a
41 confirmed case, but officials are reported to be attempting to trace as many as 2,000
42 visitors that have travelled to that country from Wuhan.

43

44 The most devastating infectious disease outbreaks are those that have a wide
45 geographical distribution, as opposed to being confined to a small region [7,8]. The
46 previously known virus that is most similar to the 2019-nCoV is the SARS coronavirus [9],
47 which generated cases in 37 countries in 2002-03 [9,10]. Since the 2019-nCoV is clearly

48 capable of being transmitted by infected hosts to countries around the world, an important
49 question for policy makers is whether or not these imported cases have the potential to
50 generate sustained human-to-human transmission in new locations.

51

52 Here, we present data describing the times from symptom onset to hospitalisation for 47
53 patients from the current outbreak, obtained from publicly available line lists [11]. We fit
54 an exponential distribution to these data, accounting for uncertainty due to the limited
55 numbers of patients from whom data were available. Assuming that this distribution
56 characterises the time spent by infected hosts generating new transmissions in the
57 community, it is then possible to infer the probability that a case arriving in a new location
58 is followed by an outbreak driven by sustained human-to-human transmission. We
59 estimate this probability under the assumption that the transmissibility of the 2019-nCoV
60 is similar to that of the SARS coronavirus, and then go on to consider the effect of
61 shortening the mean time from symptom onset to hospitalisation. This provides an
62 estimate of the risk that imported cases generate sustained outbreaks in new locations
63 under different surveillance levels.

64

65 **2. METHODS**

66

67 Time from symptom onset to hospitalisation

68

69 The distribution of times from symptom onset to hospitalisation was estimated using
70 patient data from the ongoing outbreak [11] (data are shown in Fig 1A). Since the precise

71 times of symptom onset and hospitalisation on the dates concerned were unknown, we
72 converted the times from symptom onset to hospitalisation to intervals describing possible
73 time periods. For example, for a case showing symptoms on 9 January 2020, and then
74 being hospitalised on 14 January 2020, the time between symptom onset and
75 hospitalisation lies between four and six days (see e.g. [12] for a similar calculation).

76
77 We then fitted the parameter (γ) of an exponential distribution to these interval-censored
78 data using Markov chain Monte Carlo (MCMC). A chain of length 100,000,000 in addition
79 to a burn-in of 100,000 was used. The chain was then sampled every 100 steps, giving
80 rise to a range of $n = 1,000,000$ equally possible distributions for the times from symptom
81 onset to hospitalisation, each characterised by a parameter estimate γ_i ($i = 1, 2, \dots, n$).

82

83 Estimating the probability of sustained transmission

84

85 The distributions of times from symptom onset to hospitalisation were used to estimate
86 the probability that an imported case will lead to sustained transmission, by assuming that
87 infections occur according to a branching process (e.g. [13–15]). In this branching
88 process, the effective reproduction number (accounting for control interventions, other
89 than intensified surveillance which we model explicitly) of the 2019-nCoV when the virus
90 arrives in a new location is denoted by $R = \beta/\gamma$, where the parameter β represents
91 pathogen transmissibility [16]. We assumed that the transmissibility of the virus is similar
92 to that of the SARS coronavirus, i.e. $\beta = R_{SARS} \gamma_{SARS}$, where $R_{SARS} = 3$ [17] and the mean
93 infection duration for SARS is $1/\gamma_{SARS} = 3.8$ days [18].

94

95 The probability of a major outbreak [15,16] can be estimated for each of the equally
96 possible distributions for the time from symptom onset to hospitalisation,

97
$$\text{Prob}(\text{Sustained transmission}|\gamma_i) = 1 - \frac{1}{(\beta/\gamma_i)}. \quad (1)$$

98 This can then be combined into a single estimate for the probability that an imported case
99 leads to sustained transmission, p , given by

100
$$p = \frac{1}{n} \sum_{i=1}^n \text{Prob}(\text{Sustained transmission}|\gamma_i). \quad (2)$$

101

102 To include intensified surveillance in these estimates, we simply replaced the mean time
103 from symptom onset to hospitalisation for each of the equally plausible distributions, $1/\gamma_i$,
104 by the modified expression $(1 - \rho)/\gamma_i$. In this approximation, the parameter ρ represents
105 the reduction in the mean infectious period due to intensified surveillance.

106

107 Multiple imported cases

108

109 The risk of sustained transmission given multiple imported cases was calculated by
110 considering the possibility that none of those cases led to sustained transmission.

111 Consequently,

112
$$\text{Prob}(\text{Sustained transmission}|m \text{ imported cases}) = 1 - (1 - p)^m. \quad (3)$$

113

114

3. RESULTS

115

116 As described in Methods, the distribution of times between symptom onset and
117 hospitalisation was estimated using Markov chain Monte Carlo (Fig 1B) from the patient
118 data in Fig 1A. This gave rise to a range of equally plausible distributions describing these
119 time periods (blue lines in Fig 1B). The average of these distributions is shown by the red
120 line in Fig 1B, however we used the full range of distributions in our calculations of the
121 probability of sustained transmission occurring from each imported case.

122

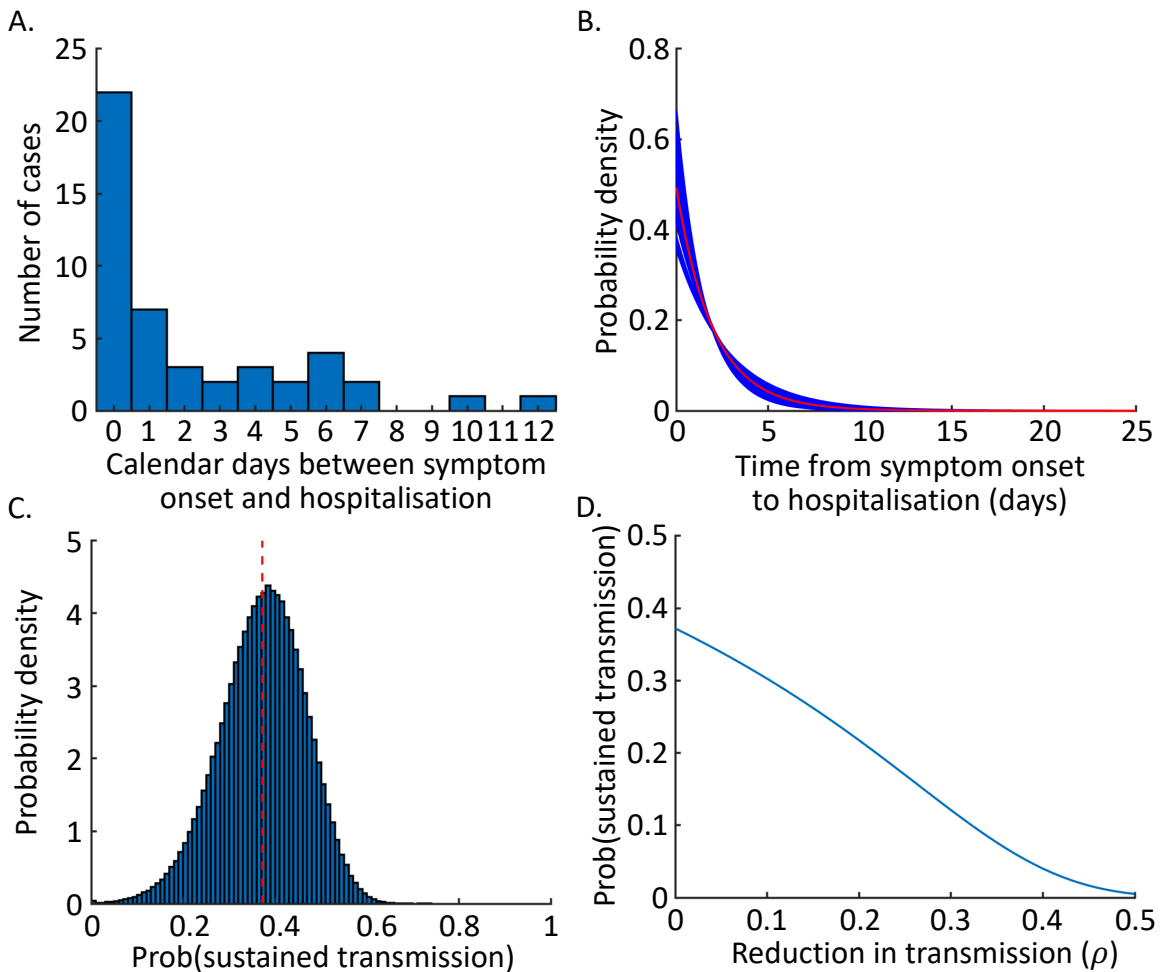
123 Each of the range of plausible distributions corresponded to an estimate for the probability
124 of a major epidemic (equation (1) and histogram in Fig 1C). However, the probability of
125 sustained transmission in fact takes a single value, which can be estimated by summing
126 over the range of distributions using equation (2). The resulting probability of sustained
127 transmission is 0.37 (red line in Fig 1C).

128

129 We then considered the reduction in the probability that an imported case leads to
130 sustained transmission if surveillance is more intense. Specifically, we assumed that
131 intensified surveillance led to a reduction in the mean period from symptom onset to
132 hospitalisation, governed by the parameter ρ (where $\rho = 0$ corresponds to no
133 intensification of surveillance, and $\rho = 1$ corresponds to an implausible scenario in which
134 symptomatic cases are hospitalised immediately). We found that, if surveillance is
135 intensified so that the mean time from symptom onset to hospitalisation is halved, the
136 probability that each imported case leads to sustained transmission is reduced to only
137 0.005 (Fig 1D).

138

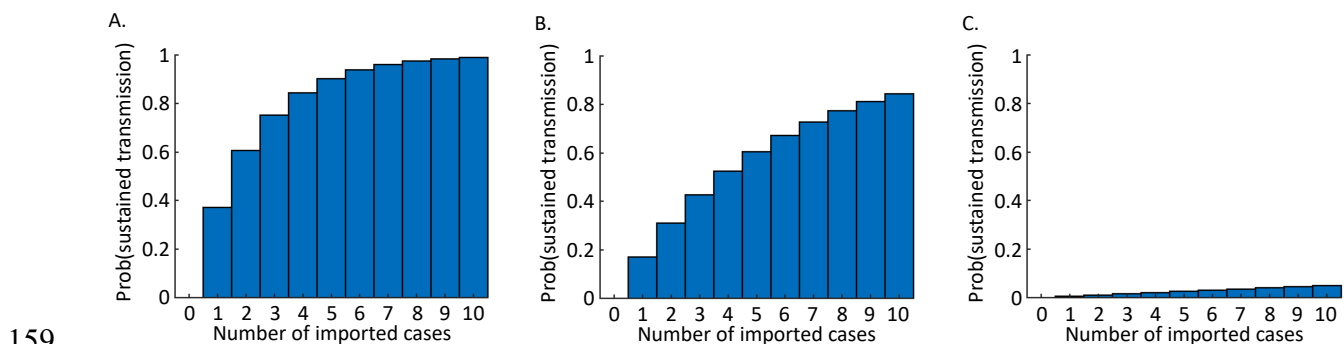
139 Finally, we considered the combined effect if multiple cases arrive in a new location. In
140 that scenario, intense surveillance has the potential to significantly reduce the risk of
141 sustained transmission compared to weak surveillance. For $\rho = 0.5$, the probability that
142 any of 10 imported cases generate a substantial outbreak is only 0.049 (Fig 2C). This
143 highlights the importance of rigorous surveillance, particularly in locations where infected
144 hosts are most likely to travel.
145



146

147 Figure 1. The probability of an outbreak driven by sustained human-to-human transmission arising
148 following the importation one infected individual. A. Data describing the number of days between
149 symptom onset and hospitalisation for 47 patients in the ongoing outbreak [11]. B. The estimated

150 distribution of times between symptom onset and hospitalisation, estimated by fitting to the data shown in
151 panel A. Blue lines show a range of equally possible distributions (see Methods; 50 distributions are
152 shown here, selected at random from the $n = 1,000,000$ distributions considered), and the red line shows
153 the average of the $n = 1,000,000$ distributions. C. The probability of sustained transmission for each
154 possible distribution of times from symptom onset to hospitalisation (equation (1); blue histogram) and the
155 probability of sustained transmission obtained by integrating over the possible distributions (equation (2);
156 red line). D. The probability that a single imported case leads to sustained transmission in a new location,
157 for different surveillance levels.
158



159
160 Figure 2. The probability of an outbreak driven by sustained human-to-human transmission arising from
161 multiple imported cases, under different surveillance levels. A. No intensification of surveillance ($\rho = 0$).
162 B. Medium level of surveillance intensification ($\rho = 0.25$). C. High level of surveillance intensification ($\rho =$
163 0.5). The results shown were calculated using equation (3).

166 4. DISCUSSION

167
168 There are concerns that the ongoing outbreak driven by 2019-nCoV could spread globally
169 [3,5,19,20] with sustained transmission in countries around the world. In the near future,
170 Chinese New Year presents a significant challenge, since this period often involves high
171 travel rates, potentially leading to importations of the virus to many new locations [3,9].

172

173 Here, we have estimated the potential for cases arriving in new locations to lead to
174 sustained transmission. According to the basic model that we have constructed, if
175 surveillance levels are similar to those in China at the beginning of the current outbreak,
176 and if this virus is similarly transmissible to the SARS coronavirus that spread globally in
177 2002-03, then the probability that each imported infected case generates an outbreak due
178 to sustained transmission is approximately 0.37 (Fig 1C). However, under a higher level
179 of surveillance, the risk of sustained outbreaks is substantially lower (Fig 1D). This result
180 is particularly striking when multiple cases travel to a new location, either simultaneously
181 or in sequence (Fig 2). In that scenario, intensified surveillance is particularly important.

182

183 Our study involves the simplest possible model that permits the risk of sustained
184 transmission to be estimated from the very limited data that have been collected in this
185 outbreak until now. As additional information becomes available, for example data
186 describing virus transmissibility, then it will be possible to estimate the risk of outbreaks
187 in new locations with more precision. We made the assumption that symptom appearance
188 coincides with the onset of infectiousness. One of the features of the SARS outbreak in
189 2002-03 that allowed it to eventually be brought under control was the low proportion of
190 onward transmissions occurring either prior to symptoms or from asymptomatic infectious
191 hosts [21]. It might be hoped that infections due to 2019-nCoV share this characteristic.

192

193 Since our results were obtained using patient data from early in the ongoing outbreak,
194 surveillance systems may not have been fully established when these data were

195 collected, and patients may not have been primed to respond quickly to early symptoms.
196 Our results might therefore be viewed as an upper bound on the risk posed by the 2019-
197 nCoV. As the outbreak continues, it might be expected that the time from symptom onset
198 to hospitalisation will decrease, leading to lower risks of sustained transmission, as has
199 been observed for outbreaks of other diseases (e.g. the ongoing outbreak of Ebola virus
200 disease in the Democratic Republic of the Congo).

201
202 Going forwards, it will be possible to include additional realism in the model. One example
203 might be to consider spatial variation in host population densities and surveillance levels,
204 leading to spatially inhomogeneous outbreak risks. It would also be possible to
205 differentiate between mild and severe cases in the model. On the one hand, a mild case
206 might be more likely to go unnoticed than a severe case, potentially leading to a higher
207 outbreak risk. On the other hand, mild infections may generate fewer secondary cases
208 than severe infections, thereby decreasing the outbreak risk. Complex interactions may
209 therefore affect the risk of sustained transmission in an unpredictable fashion.

210
211 Despite the necessary simplifications made in this study, our analyses are sufficient to
212 demonstrate the key principle that rigorous surveillance is important to minimise the risk
213 of the 2019-nCoV generating large outbreaks in countries worldwide. We therefore
214 support the ongoing work of the World Health Organization and policy makers from
215 around the world, who are working with researchers and public health experts to manage
216 this outbreak [2]. We also applaud efforts to make data publicly available [11]. Careful

217 analysis of the outbreak, and minimisation of transmission risk as much as possible, are
218 of clear public health importance.

219

220 **SUPPLEMENTARY MATERIAL**

221 Data S1. The number of calendar days between symptom onset and hospitalisation for
222 47 patients from the ongoing pneumonia outbreak in Wuhan, China.

223

224 **COMPETING INTERESTS**

225 There are no competing interests.

226

227 **FUNDING**

228 This research was funded by Christ Church, Oxford, via a Junior Research Fellowship.

229

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