

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

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4     **AUTHORS**

5     R.N. Thompson<sup>1,2,\*</sup>

6     \*Correspondence to: [robin.thompson@chch.ox.ac.uk](mailto:robin.thompson@chch.ox.ac.uk)

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8     **AFFILIATIONS**

9     <sup>1</sup>Mathematical Institute, University of Oxford, Oxford, UK

10    <sup>2</sup>Christ Church, University of Oxford, Oxford, UK

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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 ( $\gamma$ ) 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  $\gamma_i$  ( $i = 1, 2, \dots, n$ ).

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  $\beta$  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  $\rho$  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

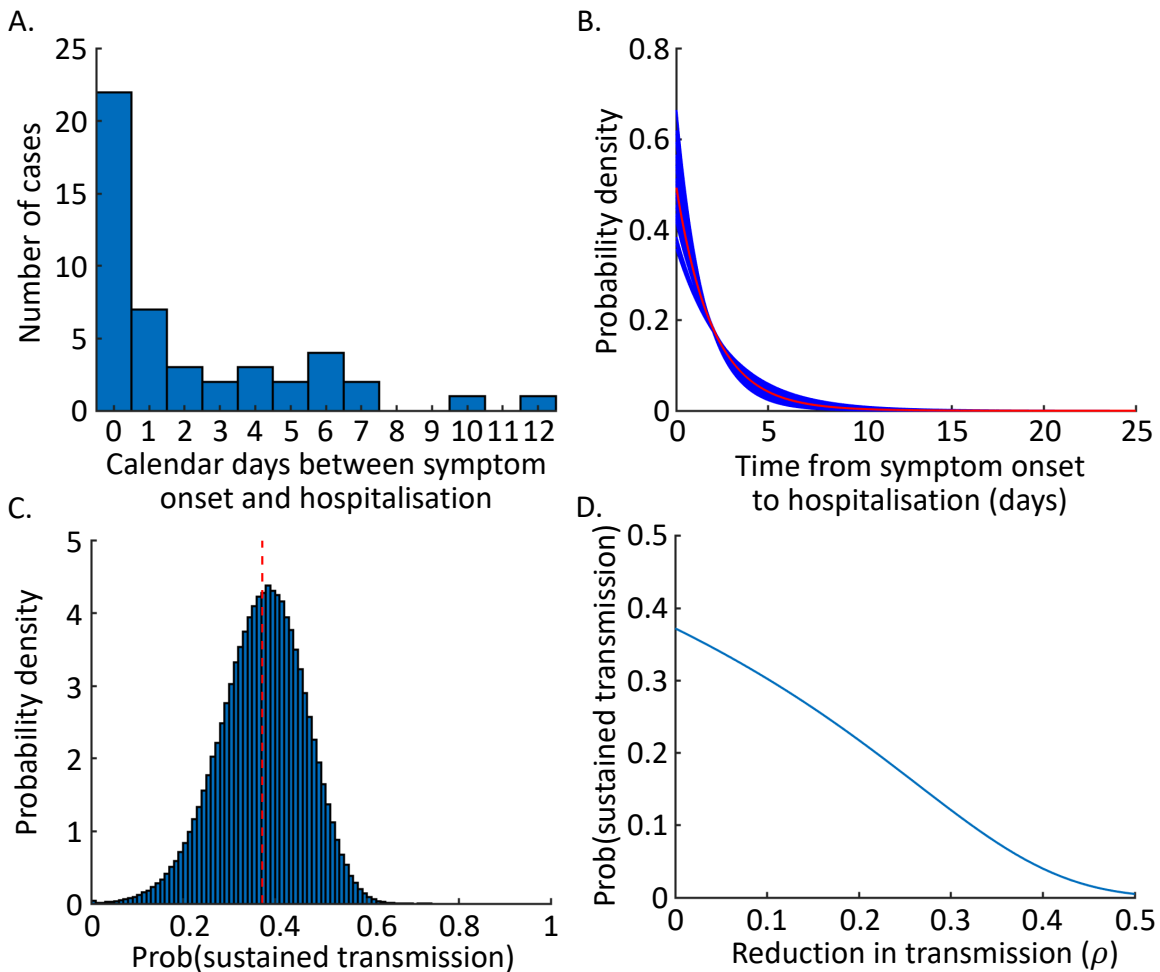
123 Each of the range of plausible distributions corresponded to an estimate for the probability  
124 of a major epidemic (equation (1) and histogram in Fig 1C). However, the probability of  
125 sustained transmission in fact takes a single value, which can be estimated by summing  
126 over the range 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  $\rho$  (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

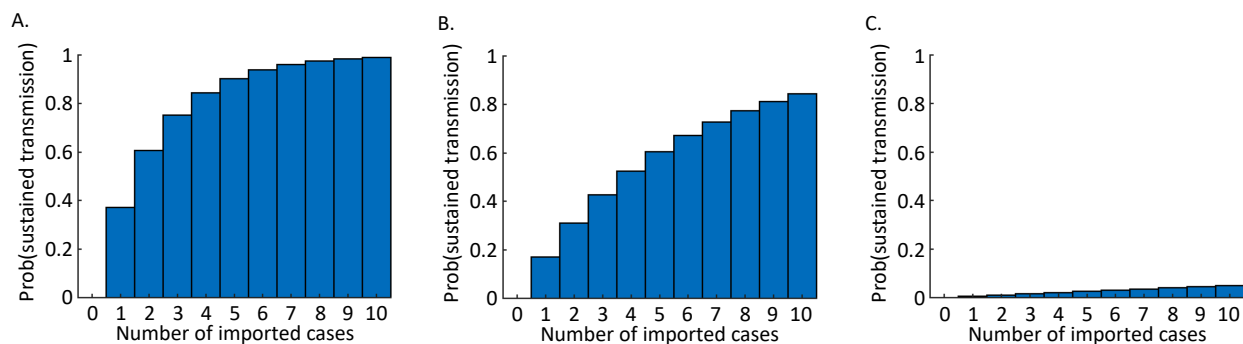
139 Finally, we considered the combined effect if multiple cases arrive in a new location. In  
140 that scenario, intense surveillance has the potential to significantly reduce the risk of  
141 sustained transmission compared to weak surveillance. For  $\rho = 0.5$ , the probability that  
142 any 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

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229

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