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Evaluation of measures to reduce international spread of SARS

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SUMMARY

Mathematical models are used to quantify the effect of border control measures in reducing the international spread of SARS. Border screening is shown to play a relatively minor role in reducing disease spread. Assuming detection rates similar to those reported for arrival screening in Australia, screening can detect up to 10% (95% CI 3–23) of infected travellers, and reduce the probability of a large outbreak by up to 7% (95% CI 2–17). Rapid reductions in the time to diagnosis and effective facilities for the isolation of cases are essential to ensure that there will not be a large outbreak, and each week of delay in responding to imported infection approximately doubles the total number of cases. While the control response is being developed in a currently uninfected region, border screening can provide up to one week's additional time in which to improve methods for early isolation of cases.

INTRODUCTION

During the outbreak of severe acute respiratory syndrome (SARS), a number of control measures were put in place to try to prevent the disease spreading into uninfected countries [1]. Border screening was implemented in both infected and uninfected countries using health declaration cards and (in some cases) temperature scanners. Detection rates by these means were very low. Hong Kong screened around 36 million passengers, and detected two SARS cases [2]. In Canada, nearly 1 million outbound passengers, and over 3 million inbound passengers were screened, and no cases were detected [3]. Singapore screened 0·4 million people entering the country and did not detect any cases [4].

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Countries without local transmission of SARS also instituted border screening measures. During the peak of the global outbreak, there were 1·8 million arrivals into Australia. Of these, 734 were referred to an airport nurse on the basis of symptoms and travel history, and were assessed for clinical symptoms and fever [5]. Of the 29 people symptomatic on arrival into Australia that were subsequently investigated as either a suspected or possible SARS case, only four were detected by border screening [5]. Entry screening at the two international airports in Italy did not detect any of the 72 individuals (including four probable cases) that were subsequently admitted for clinical evaluation [6].

In addition to screening travellers, many countries also provided information to travellers about the symptoms of SARS, and gave advice on what to do if they should develop these symptoms. The benefit of this control measure was demonstrated on at least one occasion, when an infected passenger arriving in British Columbia followed the advice of the health

notice and thus avoided infecting any other individuals [3].

These border control measures were combined with a series of control measures in infected countries that reduced the numbers of infected individuals attempting to travel. The weekly average time from onset of symptoms to isolation of cases in Singapore dropped from around 9 days at the start of the outbreak to under 2 days in the later stages [7]. Analysis of the Hong Kong data showed that the mean time from onset of symptoms to admission to hospital dropped from 5 days to 3 days [8].

Preparation of health-care workers and facilities also reduced the probability that an infected individual arriving in the country would start an epidemic. Of the six cases imported into Singapore, only the first resulted in extensive secondary transmission, a fact that has been attributed to the 'relatively prompt identification and isolation of cases, together with a low potential for transmission' [4].

Once an outbreak has gathered momentum, a good measure of the effectiveness of control is the average reproduction number of infected individuals. The effect of control measures such as isolation of symptomatic cases, quarantine of household members or close contacts of cases, movement restrictions, and closing schools have been assessed in this way, using transmission models and SARS data from Hong Kong and Singapore [9–11]. However, relatively little has been done to quantify the contribution of border controls in containing outbreaks. Border controls aim to protect an uninfected locality against a major outbreak by reducing departures of infected individuals from the source region, seeking to detect them at borders, and reducing the chance that their arrival leads to a major outbreak. These interventions have most influence on the reproduction number of infected travellers, and so focus on disrupting transmission before an outbreak can gain momentum. If border controls fail to prevent an outbreak, control measures are then directed towards reducing the reproduction number of subsequent cases as rapidly as possible.

In this paper we seek to compare how control in the source region, border control, and prompt response in the uninfected region affect the probability and size of an outbreak. In particular we address the following questions:

- What proportion of infected travellers can be detected by border screening?
- What effect can rapid isolation of cases in infected regions have on the number of infected individuals departing the region?
- How much can providing information to travellers reduce the probability that an infected traveller will start an epidemic?
- What is the overall effect of border control on the probability of a major epidemic?
- How much can preparedness in achieving rapid isolation of cases in an uninfected country reduce the probability and size of a major epidemic?
- How does effort put into border screening compare to preparedness for an early response?

For the control of transmission we focus on early diagnosis and isolation. For border control we consider screening, a health declaration and providing travellers with an information card.

MATERIALS AND METHODS

Transmission model

The effect of border control measures on the spread of SARS was assessed using a mathematical model of disease transmission from an infected to an uninfected region that takes account of control measures in each region and at the border. The depletion of susceptible individuals was ignored, as all scenarios assumed that interventions were able to interrupt transmission before a substantial fraction of the community became infected. Each infected individual was assumed to have a similar potential to infect others. A glossary of fixed parameters, control parameters, and disease-risk indicators for the model is given in the Table, and mathematical details of the model are given in the Appendix.

We assumed that the disease had a basic reproduction number of 3 [9, 10], an incubation period of 3·8 days [8], and that onset of infectivity coincided with onset of symptoms. While minimal control measures were in place, infectious individuals were assumed to circulate in the community for 9 days, which is in line with the time from onset of symptoms to isolation of cases observed at the start of the epidemic in Singapore [7]. When control measures improved, individuals were isolated before the end of this 9-day period, and once isolated, they were unable to infect any further individuals.

The data on travel behaviour of infected individuals is very limited – while it seems likely that severely

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Table. *Glossary of fixed parameters, control parameters, and indicators of risk of disease transmission for the model*

Symbol	Description	Value or equation
p	Prevalence of infected individuals in the infected region	5×10^{-5}
R_0	Reproduction number (without control)	3
A	Days from infection until onset	3·8
G	Days from onset to isolation (without control)	9
s	Sensitivity of screening for symptomatic travelers	Varies with control
G_1	Days from onset to isolation in the infected region	Varies with control
G_2	Days from onset to isolation in (initially) uninfected region	Varies with control
G_3	Days from onset to isolation of an infected traveller	Varies with control
d	Proportion of individuals wishing to travel who are infected	See equation (A 1)
r	Proportion of travellers who are infected and are not detected by border screening	See equation (A 2)
m	Probability that an infected individual arriving in the uninfected region will cause a major epidemic	See equation (A 4)

ill individuals would not wish to travel, there is data to suggest that individuals away from home may delay seeking medical advice until returning home [12]. In the absence of detailed data on this issue, we have adopted the simplest assumption about behaviour, and assumed that infected individuals are equally likely to travel each day between infection and isolation. The prevalence of disease in the infected region was assumed to be 5/100 000, on the basis of data given in the Appendix. A fixed number of individuals were assumed to travel from the infected region to the uninfected region each day, and the probability that one (or more) of them is infected was calculated according to the disease prevalence and the control measures that were in place. Clearly travellers will not always have the same prevalence of disease as the host population. If many cases are nosocomial, we would expect a smaller prevalence amongst travellers; if outbreaks occur amongst tourists, we would expect a greater prevalence amongst travellers. In this paper, we focus largely on comparing the impact of interventions, as these comparisons are less sensitive to our estimate of disease prevalence in travellers, and we test the effect of changes in the disease prevalence on our results.

Assessing the impact of extra variation in the reproduction number

The effect of extra variation in the reproduction number was assessed using a mixture model outlined in the Appendix. Under this model, the basic reproduction number of an individual was R_A with probability ε, and R_B with probability $(1-\varepsilon)$, while the mean basic reproduction number remained equal to 3. To test the effect of extra variation, we set $\varepsilon = 0{\cdot}5$, and chose R_A and R_B so that the overall standard deviation in the reproduction number was 2·3. To test the effect of superspreaders, we considered two values of ε, namely 0·01 and 0·005, and set the reproduction number of non-superspreading individuals (R_A) to be 2·7 to agree with estimates for Hong Kong [10].

Control measures within regions

The effect of control measures in infected regions was measured using the mean time from onset of symptoms to isolation of infected cases in the region. For simplicity, we used the mean time to isolation of symptomatic individuals that could be achieved instantaneously as the indicator of the level of control in uninfected regions, and refer to this as the level of preparedness in the region. This represents the level of awareness of the symptoms of the disease and the availability of health-care facilities in the uninfected region. Additional interventions that reduce the rate of transmission, such as wearing masks, reducing mixing rates and quarantining members of affected households, were not taken into account.

Control measures at the border

Border control measures were applied between the infected and uninfected regions, ignoring any transmission during travel. Providing information to travellers was assumed to make them more aware of the symptoms of the disease, thereby reducing the time from onset of symptoms until isolation. Border

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screening detected some proportion of symptomatic individuals passing between the regions. The proportion of symptomatic travellers detected is referred to as the screening sensitivity. Evidence from the SARS outbreak suggests that the screening sensitivity was unlikely to be high. Only four of the 29 symptomatic arrivals into Australia that were subsequently investigated for SARS were detected at the border [5]. This would suggest a screening sensitivity of around 13·8% (95% CI 3·9–31·7). As the screening sensitivity may vary between regions, a variety of screening sensitivities were considered, with 13·8% used as a reference value.

Assessing the interventions

The effectiveness of control measures was assessed using indicators of the risk of disease transmission such as: the probability that an infected individual passes border screening, the probability of a major epidemic in the (initially) uninfected region, and the mean number of cases in this region. In this context, a 'major' epidemic was considered to be one that will not die out unless additional control measures are put in place, or the susceptible population has been significantly depleted.

Where possible, mathematical equations for the disease-risk indicators were derived from the model. Where these could not be derived analytically, simulations of the model were used. In particular, when calculating the mean size of an outbreak, it was assumed that control measures improved over time so that the time from onset of symptoms to isolation of cases decreased. This improvement in control was modelled using data from Singapore [7] where the time from onset to isolation dropped from 9 days to under 2 days over a 9-week period. Delays in implementing the control were modelled by assuming that the time from onset to isolation remained at 9 days for some number of days before the decline.

RESULTS

What proportion of infected travellers can be detected by border screening?

Figure 1 presents the proportion of all infected travellers that can be detected by border screening, the formula for which is given by equation (A 3) in the Appendix. One horizontal axis shows the time from onset of symptoms until isolation of infected individuals in the infected region. This variable ranges from 0, which corresponds to isolating infected individuals before they become infectious, to 9, the assumed time to isolation of SARS patients with minimal control. The other horizontal axis shows the screening sensitivity – that is, the proportion of symptomatic travellers that can be detected by screening. As we would expect, a greater proportion of infected travellers are detected by a highly sensitive screening technique. The figure also shows that a greater proportion of infected travellers are detected when control measures in the infected region are ineffective. As control measures in the infected region improve, a greater proportion of individuals will be incubating the disease during travel, and will not be detected by screening. In the extreme case where control measures in the infected region are able to isolate cases as they become infectious, border screening will not detect any additional cases. If control measures in the infected region are minimal, a perfect border screening test can detect 70% of infected travellers. Border screening with sensitivity calculated from Australian data would detect 10% (95% CI 3–23) of infected travellers when no control measures are in place in the infected region.

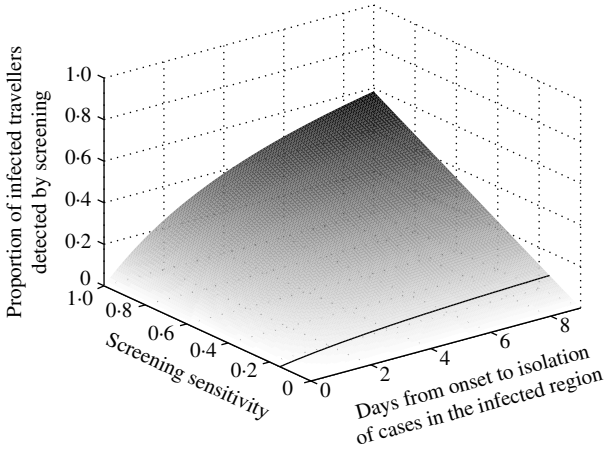

Fig. 1. The proportion of infected travellers that are detected by border screening. The sensitivity of the screening technique is the proportion of symptomatic travellers that are detected by screening. The sensitivity calculated for Australian border screening (solid line) with 95% confidence bounds (dotted lines) are also shown.

What effect does rapid isolation in the infected region have on the number of infected individuals departing the region?

The maximal reduction in the number of infected travellers departing the region occurs when all

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symptomatic cases are prevented from travelling, either by strict control in the infected region, or by highly sensitive screening. This reduces the number of infected individuals travelling by the fraction $A/(A+G)$. We have assumed that there will be five infected individuals per 100 000 travellers when minimal control is in place. If all symptomatic cases are prevented from travelling the number of infected travellers can be reduced to 1·5/100 000. In reality, control measures are unlikely to be perfect, in which case there is some benefit in combining controls, although there will always be around 1·5 infected individuals out of every 100 000 travellers that escape both screening and early diagnosis in the infected region because they are not yet displaying symptoms.

How much can providing information to passengers reduce the probability that they will start a major epidemic?

Figure 2 shows the probability that there will be a major epidemic in the (initially) uninfected region after 10 000 travellers have arrived from the infected region. Figure 2*a* assumes that border screening is not in place, Figure 2*b* assumes that border screening is in place, and that it has 13·8 % sensitivity, and Figure 2*c* assumes that border screening is in place and that it has 100 % sensitivity for symptomatic travellers. In each plot, the horizontal axis shows the time from onset of symptoms until isolation under control. Curve A gives the case where these control measures apply to individuals in the infected region only. In curve B, control measures in the infected region are combined with providing information on the disease to travellers so that they, too, will be isolated quickly. The effect of providing information to passengers is similar across all three plots. When the mean delay from onset of symptoms to isolation of cases is $\geqslant 4$ days, providing information to passengers can reduce the probability of a major epidemic by up to 30 %. If the delay from onset of symptoms to isolation is under 2 days, however, providing information to passengers reduces the probability of a major epidemic by >50 %.

How much can a rapid response to cases in an (initially) uninfected region reduce the probability of a major epidemic?

Curve C in Figure 2(*a–c*) shows the probability of a major epidemic if control measures are in place in the infected region, if information is provided to travellers, and if health facilities in the uninfected region are well prepared so that any local cases are diagnosed and isolated promptly. If all individuals in both regions can be isolated within 3 days of onset of symptoms, there is no chance of a major epidemic, regardless of whether screening is implemented.

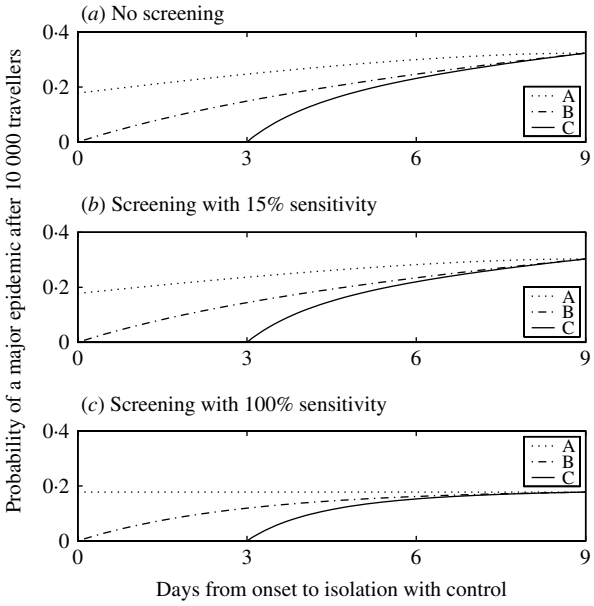

Fig. 2. The probability that there will be a major epidemic in the uninfected region after 10 000 travellers have arrived from the infected region. (*a*) The plot assumes that border screening is not in place; (*b*) the plot assumes that border screening is in place, and that it has 13·8 % sensitivity, and (*c*) the plot assumes that border screening is in place and that it has 100 % sensitivity for symptomatic travellers. Curve A gives the case where control measures are instituted in the infected region only. Curve B assumes that in addition to control measures in the infected region, information on the disease is supplied to travellers so that they too are isolated more quickly. Curve C combines control in the infected region and information to travellers with preparedness in the uninfected region, so that any new case in the (initially) uninfected region is also isolated quickly.

What is the overall effect of border screening on the probability of a major epidemic?

Comparing Figure 2(*a–c*), we can assess the impact of border control on the probability of a major epidemic. This impact is greatest when no other control measures are implemented, but if the screening sensitivity is equal to that calculated for Australia, border screening will reduce the probability of a major epidemic by up to 7 % (95 % CI 2–17).

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What is the effect of superspreaders or extra variation in the reproduction number on the probability of a major epidemic?

The first mixture model examined the effect of extra variation in the reproduction number that might arise from variability in the time to isolation of infected individuals. We found that this extra variation reduced the overall probability of a major epidemic by around 10% under most scenarios, and reduced it by no more than 20% in any scenario. The second model considered the effect of superspreaders by assuming that a small number (1 in 100, or 1 in 200) of individuals had a very high reproduction number. Under most scenarios, this alternative model displayed a slightly lower probability of a major epidemic. When there were no control measures in the uninfected region, the probability of a major epidemic was reduced by up to 10%, regardless of the level of screening. When strict preparedness measures were adopted in the uninfected region, the probability of a major epidemic was reduced by up to 50%. In this case, however, the overall probability of a major epidemic was small, so the addition of superspreaders to the model reduced the chance of a major epidemic from around 1% to around 0·5%. Overall, the effect of extra variation in the reproduction number on the probability of a major epidemic is minimal.

How much can preparedness in an infected region reduce the mean size of an outbreak?

Figure 3*a* shows the effect of improving control on the time from onset of symptoms to isolation of cases. The curve from week 0 onwards has been fitted to data from the SARS outbreak in Singapore [7]. Prior to week 0, the curve shows the time to isolation corresponding to minimal control. Each week before week 0 is thus 1 week's delay in implementing control measures. Figure 3*b* shows the effect of 1, 2, or 3 weeks' delay on the mean total number of cases, assuming that the outbreak is initiated by three primary cases (as occurred in Singapore [4]), and involves at least 10 cases in total. Each additional week of delay leads to approximately twice the number of total cases.

How does effort put into border screening compare to preparedness for an early response?

Figure 4 shows the percentage chance that there will be an outbreak of at least 100 cases at some time over a period of 30 days, assuming that there are 1000

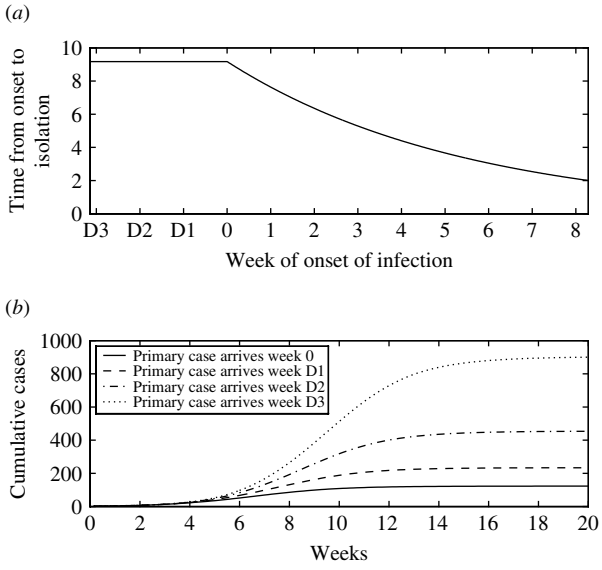

Fig. 3. (*a*) The plot shows the time from onset of symptoms to isolation of cases over time in the model. The curve from week 0 onwards has been fitted to data from the SARS outbreak in Singapore [7]. Each week before week 0 corresponds to 1 week's delay in implementing control measures. (*b*) The plot shows the effect of 1, 2, or 3 weeks' delay on the mean total number of cases, assuming that the outbreak is initiated by three primary cases, and involves at least 10 cases in total.

travellers from the infected region each day, and that the time from onset to isolation follows the curve in Figure 3*a*. The *x*-axis represents the start of the 30-day period, labelled as in Figure 3*a*, and the *y*-axis represents the screening sensitivity. Curves in this figure show the contours of equal probability: the curve marked '10' corresponds to conditions that will produce a 10% chance that there will be an outbreak of at least 100 cases during the 30-day period.

In order to ensure that the chance of 100 cases is $<10\%$ when there is no border screening, preparedness of health-care facilities must be 4 days ahead of that in Singapore. If border screening is in place and can detect all symptomatic cases, preparedness may be up to 3 days behind that of Singapore, while still ensuring that the chance of 100 cases is $<10\%$. In other words, perfect screening gains health-care workers an additional week to prepare if the goal is for a 10% chance of an epidemic of 100 cases.

If a more stringent assurance is required – for example that the chance of 100 cases is at most 1% – then the isolation plans must be considerably ahead of that in Singapore. If no screening is in place, the plan must be 17 days ahead of Singapore; if perfect screening is in place, it must be 13 days ahead of

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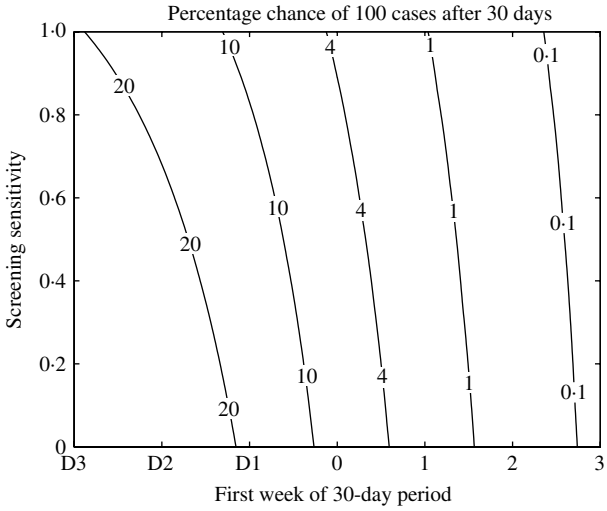

Fig. 4. The probability, expressed as a percentage, that there will be an outbreak of at least 100 cases in an uninfected region over a period of 30 days, assuming that there are 1000 travellers arriving from the infected region each day, and that the time from onset to isolation follows the curve in Figure 3*a*. The *x*-axis represents the first week of the 30-day period, labelled as in Figure 3*a*, and the *y*-axis represents the screening sensitivity. Curves in the figure show the contours of equal probability, so that the curve marked '10' corresponds to conditions that will produce a 10% probability of an outbreak of at least 100 cases during the 30-day period. The sensitivity calculated for Australian border screening (dashed line) with 95% confidence bounds (dotted lines) are also shown.

Singapore. When the goal is for a 1% chance of 100 cases, perfect screening allows health workers only 4 additional days. If the goal is for a 0·5% chance, perfect screening will provide only 3 additional days. In reality, screening is unlikely to be perfect. If the screening sensitivity is as low as 0·138, then introducing border screening corresponds to at most 1 additional day over no screening for each of a 0·5, 1 and 10% chance of 100 cases.

What is the effect of changes in the prevalence of disease?

We test the sensitivity of our results to the estimate of prevalence by comparing the results with prevalence of 5 cases/100 000 to those with a prevalence of 1 case/100 000 individuals. The results on the proportion of travellers detected by screening (Fig. 1), and the mean size of the outbreak (Fig. 3) are independent of the disease prevalence, and so are unchanged. The probability of a major epidemic after 10 000 travellers (Fig. 2) changes with the estimate of prevalence, but the relative effects of the various control measures remain very similar. For example, using our original estimate, we calculated that border controls can reduce the probability of a major epidemic by up to 7% (95% CI 2–17). With a prevalence of 1 case/100 000, border controls can reduce the probability of a major epidemic by up to 8% (95% CI 2–19). Similarly, although the percentage chance of 100 cases after 30 days (Fig. 4) will change with the estimate of prevalence, the shape of the contour lines on this graph is very little changed, so that the trade-off between screening and swift diagnosis of new cases remains very similar.

DISCUSSION

This paper shows that screening and distribution of information at borders play a relatively minor role in reducing the international spread of SARS when compared with control measures applied in the infected region and preparedness in the uninfected region. Border screening has most effect when other control measures are poorly implemented, however, if the screening sensitivity is as low as the estimated 13·8% for travellers arriving in Australia, it will detect up to 10% (95% CI 3–23) of infected travellers, and reduce the probability of a major outbreak by up to 7% (95% CI 2–17). Providing information to travellers is most effective when individuals can be isolated within 2 days of onset of symptoms. The only way to guarantee that there will not be a major outbreak is to put considerable effort into preparedness. It is essential that health-care workers and community members are aware of the symptoms of the disease, and that facilities are available to isolate suspected cases as quickly as possible. Any delay in implementing this strategy is costly – each week of delay approximately doubles the total number of cases.

While control measures in an uninfected region are being prepared, border screening can assist the control effort by delaying the time of arrival of the first infected individuals. However, with our assumed prevalence and number of arrivals from the infected locality, border screening is likely to postpone the entry of an infected person by a few days only. If the screening sensitivity is high, this measure can provide health-care workers with at most one additional week in which to prepare control measures. A change to either the prevalence or the number of daily arrivals alters the probability of a large outbreak, but does not greatly change this trade-off between border screening and preparedness. While border controls may often

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be seen as necessary for political reasons, it is unwise to allow any effort put into border screening to reduce the effort put into preparing health-care workers and facilities to isolate new cases quickly. Our results can inform such policy decisions by providing quantitative guidance on the relative effectiveness of control measures.

Although the model was created with SARS in mind, many of the results are relevant to a wider group of emerging and re-emerging infectious diseases. The benefits of screening techniques that rely on individuals displaying symptoms will always depend on the fraction of time from infection until the end of infectivity that an individual is symptomatic. For influenza, this fraction is around 2/3 [13], so that in the event of an influenza pandemic, a highly sensitive border screening technique could detect around 67% of travellers infected with influenza. If the sensitivity of such a screening test was as low as 13·8%, only 9% of individuals infected with influenza would be detected.

In this study, we did not distinguish between departure screening in infected regions and arrival screening in uninfected regions. If there is little chance of transmission during travel, there is unlikely to be much difference between these types of screening, unless the travel time is sufficiently long that many individuals become symptomatic while travelling. However, if transmission can take place during travel (and there is evidence that it did during the SARS outbreak [1, 14]), then departure screening has the important benefit that it helps to reduce the likelihood that this will occur. Nevertheless, if the detection rate of symptomatic patients achieved by Australian arrival screening is also typical of departure screening, there will be many opportunities for transmission during travel. Under these conditions, recording contact details of all travellers at the border may have significant benefits by allowing swift contact tracing in the event of an infected arrival. In future work we intend to quantify the risks of within-travel transmission, and the power of control measures to reduce these risks.

APPENDIX

Prevalence

We define the prevalence of the disease to be the proportion of the population that is infected and would not yet be isolated if minimal control measures were in place. Under these conditions, individuals incubate the disease for a period A, and then are able to infect other individuals in the community for a period G. SARS epidemic curves collated on the WHO website [15] give the number of cases with onset of symptoms on each day. Using these data, we calculate the prevalence on day t as:

$$P(t)=\frac{1}{N}\sum_{x=t-G+1}^{x=t+A} O(x),$$

where N is the size of the population and $O(x)$ is the number of cases with onset of symptoms on day x. Using data for Hong Kong, we found that the prevalence of disease ranged up to $\sim$12/100 000 during the course of the epidemic. For Singapore, the prevalence ranged up to $\sim$2/100 000. Throughout this paper we assume a prevalence of $p=0{\cdot}00005$ (5/100 000), which represents a fairly large outbreak of disease.

Number of infected individuals attempting to travel

The mean time from onset of symptoms to isolation of cases in the infected region is reduced from G to G_1 by control measures. Then d, the proportion of individuals attempting to travel who are infected, is given by

$$d=\frac{p(A+G_1)}{(A+G)}. \qquad \text{(A 1)}$$

Infected individuals not detected by border screening

If border screening is in place, a proportion of the infected travellers will be detected and isolated. We assume that individuals are not detected by border screening during their incubation period, and are detected with probability s, while symptomatic. If $u(t)$ is the probability that an individual infected at time 0 who travels at time t is not detected at the border, then

$$u(t)=\begin{cases}1 & 0\leqslant t\leqslant A\\ 1-s & A<t\leqslant A+G_1\\ 0 & A+G_1<t<A+G.\end{cases}$$

To calculate r, the proportion of travellers who are infected and undetected by border screening, we integrate over the possible travel times:

$$r=p\int_0^{A+G}\frac{u(t)\mathrm{d}t}{(A+G)}=p\frac{[A+(1-s)G_1]}{(A+G)}. \qquad \text{(A 2)}$$

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Finally, provided the number of travellers, T, is fairly large, and we expect r to be small, we can assume that the number of infected individuals passing border screening has a Poisson distribution with mean Tr. The probability of at least one individual passing border screening after T travellers is then $1-e^{Tr}$.

Fraction of infected travellers detected by screening

Of the infected individuals attempting to travel, some will be detected by border screening, while others will be missed – either because of poor sensitivity of the procedure, or because they are not yet displaying symptoms. The proportion of infected travellers detected by screening is

$$\frac{d-r}{d}=\frac{sG_1}{(A+G_1)}. \tag{A 3}$$

Probability of a major epidemic

We define a major epidemic as one that will not die out without additional control measures or without significant depletion of the number of susceptible individuals. The assumption of a constant infectious period and negligible depletion of susceptible individuals implies that the number of people infected by a case has a Poisson distribution, with mean R_0 when there is minimal control and mean G_2R_0/G when the time from onset of symptoms to isolation in the (initially) uninfected region is G_2. We set q to be the minimum positive solution to $r=\exp[G_2R_0(r-1)/G]$. For any local case in the (initially) uninfected region, the probability that they will cause a major epidemic is $1-q$. The probability, m, that an arriving infected traveller will cause a major epidemic is smaller, on average, than $1-q$ because some infected travellers will have a shorter infectious period remaining after arrival. The adjustment is given by

$$m=1-\frac{Aq^{G_3/G_2}}{[A+(1-s)G_1]}-\frac{G_2(1-s)q^{G_3/G_2}(1-q^{-G_1/G_2})}{[A+(1-s)G_1]\log q}. \tag{A 4}$$

The probability that there will be a major epidemic after T travellers have passed from the infected to the uninfected region is $1-e^{Trm}$.

Taking account of extra variation and superspreaders

We test the effect of extra variation in the reproduction number of individuals by considering an alternative model under which the basic reproduction number of an infected individual is Poisson with mean R_A with probability $(1-\varepsilon)$ and is Poisson with mean R_B with probability ε. Under this model, the formula form (see above) becomes

$$m=1-\frac{Aq_0}{A+(1-s)G_1}-\frac{G_2(1-s)}{A+(1-s)G_1}\times\left[\frac{(1-\varepsilon)q_A^{G_3/G_2}(1-q_A^{-G_1/G_2})}{\log q_A}+\frac{\varepsilon q_B^{G_3/G_2}(1-q_B^{-G_1/G_2})}{\log q_B}\right],$$

where

$$q_A=\exp[R_A(q-1)G_2/G],\quad q_B=\exp[R_B(q-1)G_2/G]$$

and

$$q_0=(1-\varepsilon)q_A^{G_3/G_2}+\varepsilon q_B^{G_3/G_2}.$$

To model superspreaders, we select these parameters so that the overall mean basic reproduction number is 3 (as before), and the reproduction number of non-superspreading individuals (R_A) is 2·7 to agree with estimates for Hong Kong [10]. We consider two scenarios: one in which superspreaders occur with probability 0·005 (1 in 200) and infect 150 individuals on average, and the second in which superspreaders occur with probability 0·01 (1 in 100), and infect 32·7 individuals on average.

To model extra variation in the reproduction number that might arise from variation in the time to isolation of cases, we consider a model in which $\varepsilon=0{\cdot}5$, $R_A=1{\cdot}5$ and $R_B=4{\cdot}5$, which ensures a mean basic reproduction number of 3, with a standard deviation of 2·3.

Mean number of cases

When an epidemic generated by an undetected infected traveller 'takes off' and additional control measures are not instituted, the total number of cases is high, and the epidemic will only die out when the numbers of susceptible individuals become sufficiently low. In practice, control measures are likely to be made increasingly stringent in the face of an uncontrolled epidemic, as in Singapore, where the mean time from onset of symptoms until isolation dropped from 9 days to under 2 days [7]. We used these data to estimate parameters in an exponential decay model, assuming that the time to isolation cannot be reduced below 1·5 days. Delays in introducing control measures were modelled as a period during which the time to isolation is maintained at 9 days (see Fig. 3*a*

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for a plot of this function). The mean cumulative cases generated by arriving infected individuals were calculated from repeated simulation of a stochastic model with basic reproduction number and incubation period as in the Table, and with the effective infectious period defined as the time to isolation.

Probability of at least 100 cases over a 30-day period

When preparedness in an uninfected region is improving, border screening may assist the control effort by delaying the arrival of the first case. Using the model of improving control outlined above, and assuming 1000 individuals arrive from the infected region each day, we calculated the probability that there will be an outbreak of 100 or more cases over a period of 30 days. This probability depends on the sensitivity of border screening, and on the delays in preparing control measures in the uninfected region.

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DECLARATION OF INTEREST

None.

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