# The risk of SARS-CoV-2 outbreaks in low prevalence settings following the removal of travel restrictions

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# The risk of SARS-CoV-2 outbreaks in low prevalence settings following the removal of travel restrictions


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## ABSTRACT

Countries around the world have introduced travel restrictions to reduce SARS-CoV-2 transmission. As vaccines are gradually rolled out, attention has turned to when travel restrictions and other non-pharmaceutical interventions (NPIs) can be relaxed. Here, using SARS-CoV-2 as a case study, we develop a mathematical branching process model to assess the risk that, following the removal of NPIs, cases introduced into new locations initiate a local outbreak. Our model accounts for changes in background population immunity due to vaccination. We consider two locations in which the vaccine rollout has progressed quickly – specifically, the Isle of Man (a British crown dependency in the Irish Sea) and the country of Israel. We show that the outbreak risk

is unlikely to be eliminated completely when travel restrictions and other NPIs are removed, even once the vaccine programmes in these locations are complete. Specifically, the risk that an imported case initiates an outbreak following the vaccine rollout and removal of NPIs is projected to be 0.373 (0.223,0.477) for the Isle of Man and 0.506 (0.387,0.588) for Israel. Key factors underlying these risks are the potential for transmission even following vaccination, incomplete vaccine uptake, and the recent emergence of SARS-CoV-2 variants with increased transmissibility. Combined, these factors suggest that when travel restrictions are relaxed, it will still be necessary to implement surveillance of incoming passengers to identify infected individuals quickly. This measure, as well as tracing and isolating contacts of detected infected passengers, should remain in place to suppress potential outbreaks until case numbers globally are reduced.

**KEYWORDS**

mathematical modelling; infectious disease epidemiology; outbreaks; non-pharmaceutical interventions; travel restrictions

## 1. INTRODUCTION

Combinations of non-pharmaceutical interventions (NPIs) have been introduced worldwide to counter the COVID-19 pandemic [1–3]. These measures include travel restrictions [4,5] and a range of other NPIs intended to reduce the numbers of contacts

between individuals [6]. The development and deployment of vaccines has also lowered transmission [7–10] and reduced the number of individuals experiencing clinical symptoms or severe disease once infected [11–13].

Effective NPIs have led to low levels of transmission in some locations. Australia and New Zealand have often been cited as examples of countries that have implemented NPIs effectively, with travel restrictions and quarantine of inbound travellers combined with short-term lockdowns and contact tracing to identify infected contacts whenever cases have been discovered [14–16]. At the time of writing (1st May 2021), Israel is the country that has vaccinated the largest proportion of its citizens, and the vaccination campaign there has been credited with reducing transmission [8], prompting some NPIs to be removed.

Despite the success of both NPIs and vaccines, the current overall picture is complicated. Vaccines do not prevent transmission entirely [7,17,18], and vaccine uptake is incomplete, particularly in some ethnic groups and in underserved communities [19]. Current tentative estimates suggest that first doses of the Pfizer and AstraZeneca SARS-CoV-2 vaccines are around 60% effective at preventing infection, with the second doses leading to 65-85% efficacy against infection [17]. Furthermore, the appearance of novel SARS-CoV-2 variants makes eliminating transmission more challenging. For example, the B.1.1.7 variant (VOC 202012/01) that first appeared in the United Kingdom in late 2020 has been found to be more transmissible than the SARS-CoV-2 virus that originally emerged in China [20]. Although public health

measures have had some successes, these concerns raise a key question: Can NPIs such as travel restrictions be removed without any risk in low prevalence settings where vaccines have been distributed widely, or might outbreaks occur initiated by SARS-CoV-2 reimportations from elsewhere?

Epidemiological models are often used to assess the risk of outbreaks in scenarios in which the potential for pathogen transmission is not changing. According to the mathematical theory of branching processes, the probability that cases introduced into a new host population generate an outbreak driven by sustained local transmission is given by

$$\text{Prob}(\text{outbreak}) = 1 - \left(\frac{1}{R}\right)^{I_0}, \qquad (1)$$

in which $R$ is the reproduction number of the pathogen and $I_0$ is the number of introduced infectious cases. This expression had been used to assess the risks of outbreaks of pathogen including the Ebola virus [21–23], before being applied early in the COVID-19 pandemic to assess outbreak risks outside China [24]. Equation (1) reflects the risk that introduced cases generate an outbreak, however it involves an assumption that pathogen transmissibility is fixed at its current level. In other words, the value of $R$ is implicitly assumed to remain constant over the initial phase of the potential outbreak. With a background of rapidly changing population immunity due to vaccination acting to reduce transmission, this assumption may not be accurate. To assess the risk of outbreaks if NPIs are removed during an ongoing vaccination campaign using branching process models, standard epidemiological modelling theory must be extended to account for temporally changing population immunity.

Here, we use branching processes to investigate whether or not an introduced case initiates an outbreak, accounting fully for temporal changes in population immunity due to an ongoing vaccination campaign. We use four metrics to assess the risk of an outbreak and consider two examples of vaccination campaigns from around the world, from the Isle of Man and the country of Israel. In both locations, vaccination is progressing quickly and prevalence is currently low. Given the relatively low numbers of cases in these locations during the pandemic, there is also likely to be a background of limited immunity from previous infections. We assess the risk of outbreaks in these places when travel restrictions and other NPIs are removed, considering scenarios in which NPIs are removed at different stages of the vaccination campaigns. Crucially, even when all vaccines have been deployed in those locations, we project that the combination of incomplete vaccine uptake, imperfect vaccination and variants of concern mean that the risk of outbreaks due to imported cases will not be eliminated completely when NPIs are removed. This highlights the need for careful monitoring of imported cases until global prevalence is reduced to low levels. Until vaccines are rolled out worldwide, there is still a risk of local transmission arising in low prevalence settings initiated by importations from elsewhere.

## 2. METHODS

Epidemiological model

We performed our analyses using a stochastic branching process model that describes virus transmission in the initial stages of a potential outbreak. In the model, following the arrival of a case in the local population, new infections occur at rate $\beta(1-\Lambda(t))$ and infected individuals have a mean infectious period of $1/\mu$ days (Fig 1a). The function $\Lambda(t)$ reflects the extent to which transmission has been reduced by vaccination, where a value of $\Lambda(t)=0$ corresponds to an entirely unvaccinated population.

To model an ongoing vaccination campaign, we set $\Lambda(t)=\eta_1 V_1(t-\alpha)+\eta_2 V_2(t-\alpha)$, where $V_1(t)$ is the proportion of individuals in the population who have received a single vaccine dose at time $t$ and $V_2(t)$ is the proportion of individuals in the population who have received two vaccine doses at time $t$ (Fig 1b). The parameters $\eta_1$ and $\eta_2$ reflect the effectiveness of the vaccine at preventing infection after one and two doses, respectively, and the parameter $\alpha$ represents the delay between a vaccine dose being administered and being effective in the recipient. In our main analyses, since we are modelling relatively low prevalence settings, we do not consider immunity due to prior infections, although we present a supplementary analysis in which we considered the robustness of our results to this assumption.

Under this model, the time-dependent reproduction number, accounting for any vaccines that have been administered and are effective at time $t$, is given by

$$R_V(t)=\frac{\beta(1-\Lambda(t))}{\mu}. \qquad (2)$$

The value of $R_V(t)$ represents the expected number of secondary infections generated by a single infected individual in the population at time $t$, under the assumption that no further vaccinations take place in future. It is therefore representative of the "instantaneous" transmissibility at time $t$. Indeed, $R_V(t)$ is sometimes referred to as the instantaneous reproduction number [25–27]. In the absence of vaccination, so that $\Lambda(t) = 0$, then $R_V(t)$ is equal to the basic reproduction number, $R_0$.

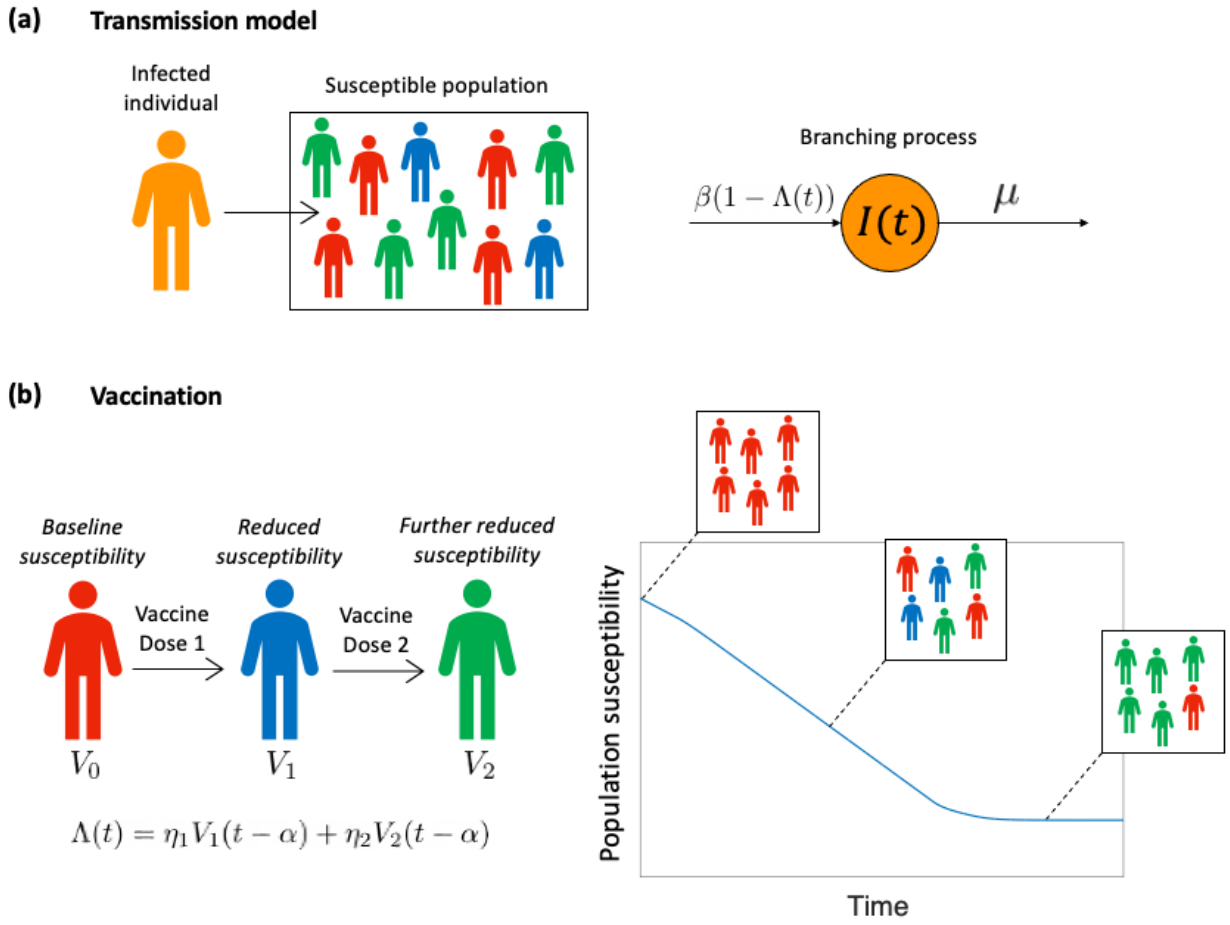


Figure 1. The epidemiological model used in our analysis. (a) Following the introduction of an infected individual into the host population, local transmission may happen with infections occurring at rate $\beta(1-\Lambda(t))$, where $\Lambda(t)$ reflects the vaccination coverage in the local population. Infected individuals have mean infectious period $1/\mu$ days. (b) The vaccination process is modelled by setting $\Lambda(t)$ according to the

proportion of individuals in the population who have been vaccinated with one ($V_1$) or two ($V_2$) doses. The first vaccine dose is assumed to have effectiveness $\eta_1$ and the second vaccine dose has effectiveness $\eta_2$. Vaccine doses are effective $\alpha$ days after they are administered. This leads to declining population susceptibility as a vaccine is rolled out across the population.

## Vaccination data

In the model, $V_1(t)$ and $V_2(t)$ were set based on vaccination data from the location under consideration (either the Isle of Man or Israel). Data describing the proportion of the total population who had received one or two vaccine doses were available for the periods up until 11th April 2021 (for the Isle of Man [28]) and 21st April 2021 (for Israel [29]).

To explore how the risk of outbreaks is likely to change in future, we projected the vaccine rollout forwards beyond these dates in the following way. We considered the total population size of the location under consideration (denoted $N$), as well as the numbers of individuals ($N_1(t)$ and $N_2(t)$) vaccinated with one or two doses, so that $V_1(t) = N_1(t)/N$ and $V_2(t) = N_2(t)/N$. We assumed that a constant number of vaccine doses are available each day in future (denoted $D$), and that there is a target period of $\tau$ days between each vaccine dose. On any day in future, each available dose is assigned to an individual who has been vaccinated with their first dose at least $\tau$ days ago, with remaining doses then assigned to unvaccinated individuals. Resulting values of $N_1(t)$ and $N_2(t)$ were then converted to corresponding values of $V_1(t)$ and $V_2(t)$. To reflect the

fact that vaccine uptake is imperfect, we assumed that a maximum proportion $\nu$ of the population can ever be vaccinated. Consequently, once the vaccination programme is complete, then $\Lambda(t) = \eta_2 \nu$. Since there is uncertainty in the vaccine uptake going forwards, we conducted supplementary analyses in which we considered a range of different values of $\nu$. Values of the model parameters used in the analyses in the main text for the Isle of Man and Israel are shown in Table 1.

Outbreak risk metrics

We used four different metrics to assess the risk that an infected individual, introduced into the population at time $t$, initiates an outbreak driven by sustained local transmission. The values of each of these metrics vary temporally. An overview of these metrics is provided here; additional details are available in the Supplementary Information.

The first metric we considered is the *Instantaneous Outbreak Risk (IOR)*. This quantity represents the expression shown in equation (1), with $R = R_V(t)$ and $I_0 = 1$. The IOR reflects the risk of an outbreak occurring starting from a single infected individual at time $t$, but under the assumption that the vaccine rollout does not continue after time $t$ so that pathogen transmissibility is unchanged. While the IOR straightforward to calculate, it does not reflect changing population immunity due to vaccination over the initial phase of the potential outbreak. This standard metric is often used to assess the risk of

196 outbreaks in scenarios where pathogen transmissibility does not vary temporally
197 [21,23,24,30–33].
198
199 The second metric is the *Case Outbreak Risk (COR)*. The COR is an extension of the
200 IOR, accounting for changes in population susceptibility due to vaccination over the
201 initial phase of the potential outbreak. The COR has previously been used to assess
202 outbreak risks using branching processes for models in which pathogen transmission
203 varies periodically [30,34–36]. Its calculation involves solving the differential equation

204 $$\frac{dq(t)}{dt} = \beta(1 - \Lambda(t))q(t)\big(1 - q(t)\big) + \mu(q(t) - 1). \qquad (3)$$

205 The COR at time $t$ is then given by $1 - q(t)$. Further details, including the derivation of
206 equation (3), are provided in the Supplementary Information.
207
208 The third metric we considered is the *Simulated Outbreak Risk (SOR)*. The SOR
209 involves repeated simulation of the branching process model, using the direct version of
210 the Gillespie stochastic simulation algorithm [37] adapted to account for temporally
211 varying pathogen transmissibility. Simulations were run starting with a single infected
212 individual introduced into the population at time $t$. The SOR then corresponds to the
213 proportion of simulations in which a local outbreak occurs; an outbreak is said to occur if
214 the total number of individuals infected simultaneously exceeds a pre-defined threshold
215 value, $M$. In our analyses, we set $M = 100$.
216
217 Finally, we consider the *Numerical Outbreak Risk (NOR)*. The NOR is analogous to the
218 SOR, but with the advantage that it does not require large numbers of model

simulations to be run. The NOR, therefore, also represents the risk that a single infected individual introduced into the population at time $t$ initiates an outbreak in which at least $M = 100$ individuals are ever infected simultaneously.

Table 1: Default parameter values used in our analyses.

| Parameter | Description | Value | Source |
|---|---|---|---|
| $\beta$ | Transmission rate parameter | Set so that $R_0 = \frac{\beta}{\mu}$ takes a prescribed value | Two scenarios were considered, with median $R_0$ values of 3 (sim. to original SARS-CoV-2 variant [38]) and 5 (sim. to novel variant B.1.1.7 [20]) |
| $1/\mu$ | Duration of infectiousness | 5 days | [39] |
| $\alpha$ | Delay between a vaccine dose being administered and being effective | 14 days | [40] |
| $\eta_1$ | Relative susceptibility of an individual vaccinated with a single effective dose (compared to an unvaccinated host) | 0.4 | [17] |
| $\eta_2$ | Relative susceptibility of an individual vaccinated with two effective doses (compared to an unvaccinated host) | 0.15 | [17] |
| $\nu$ | Vaccine uptake | 0.8 (Isle of Man) and 0.7 (Israel). Other values are considered in the Supplementary Information | [41] |
| $N$ | Total population size | 85,400 (Isle of Man) and 8,772,800 (Israel) | [42] |
| $D$ | Number of vaccine doses available each day (in future projections) | 1,000 (Isle of Man) and 56,000 (Israel) | Average number of doses administered each day in the previous 30 days (up to 11 April 2021 for Isle of Man [28] and 21 April 2021 for Israel [29]) |
| $\tau$ | Target period between vaccine doses (in future projections) | 84 days (Isle of Man) and 21 days (Israel) | [43,44] |

## 3. RESULTS

As described in the Methods, we first generated projections of the number of vaccinated individuals in future for the Isle of Man (Fig 2a) and Israel (Fig 2d), based on past vaccination data in those locations. To explore the impact of vaccination on virus transmission, we calculated the time-dependent reproduction number ($R_V(t)$; equation (2)) throughout the vaccination campaign. We considered two different scenarios. In the first, we set the median value of $R_0$ (i.e., the reproduction number in the absence of vaccination) equal to 3, as was the situation early in the COVID-19 pandemic (Fig 2b,e). In the second scenario, we set the median value of $R_0$ equal to 5 (Fig 2c,f) to reflect the fact that currently circulating SARS-CoV-2 variants are more transmissible than the original virus [20]. This second scenario is therefore likely to be a more realistic reflection of the current and future risk.

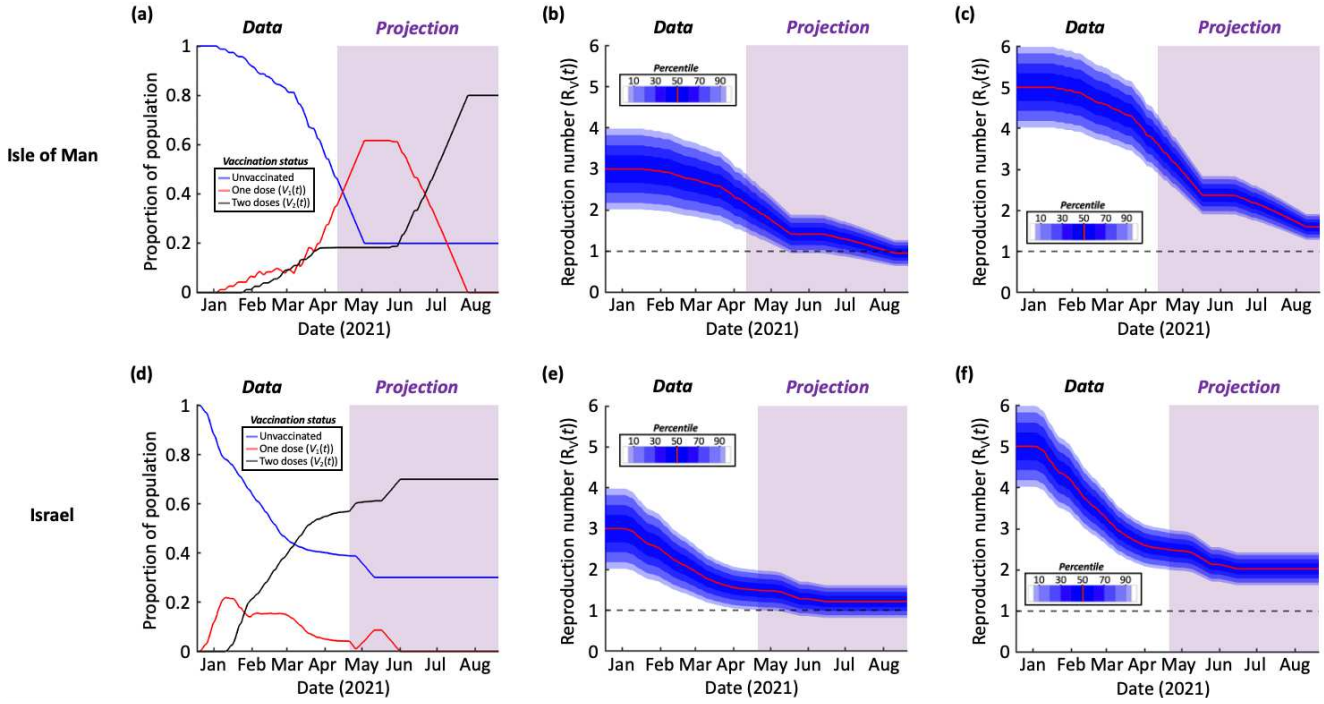


Figure 2. Effect of vaccination on population susceptibility. (a) The proportion of the population of the Isle of Man who are unvaccinated ($1 - V_1(t) - V_2(t)$), vaccinated with a single dose ($V_1(t)$) and vaccinated with two doses ($V_2(t)$). The period in which vaccination data were available is shown in white, and the period in which vaccination data were projected is shown in purple. (b) The time-dependent reproduction number ($R_V(t)$) corresponding to the vaccination data in panel a, starting from a median initial value of $R_V(0) = R_0 = 3$. To account for uncertainty in the value of $R_0$, a normal distribution was assumed about the median value of $R_0$ with variance $\sigma^2 = 0.25$, which is reflective of the range of $R_0$ values estimated early in the COVID-19 pandemic [38]. (c) Analogous to panel b but starting from a median initial value of $R_V(0) = R_0 = 5$. (d)-(f) Analogous to panels a-c but using vaccination data for Israel. In all panels, $t = 0$ days corresponds to 18th December 2020. Ticks on the x-axes refer to the starts of the months labelled. Parameter values are shown in Table 1.

We then calculated the values of the four different outbreak risk metrics throughout the period considered (18th December 2020 to 20th August 2021) based on these vaccination projections (Fig 3). This involves a scenario in which NPIs are removed

entirely, so that $R_V(t)$ is not reduced by interventions other than vaccination. These metrics then reflect the risk that a single case first entering into the population at the date of introduction shown initiates an outbreak driven by sustained local transmission, given that no NPIs are in place. For each metric, and each time during the vaccination programme, we calculated the outbreak risk by integrating over the full distribution for $R_V(t)$ shown in Fig 2. The resulting outbreak risk therefore represents a point estimate of the risk accounting for uncertainty in pathogen transmissibility.

The IOR represents the probability of sustained local transmission based only on the value of $R_V(t)$ at the precise instance that the virus is introduced into the population. When an introduction occurs while a vaccine is being deployed, there is a background of decreasing population susceptibility, and so $R_V(t)$ may in fact decrease over the initial stages of a potential outbreak. For that reason, it is unsurprising that the IOR sometimes overestimates the outbreak risk compared to the other risk metrics (see e.g. black lines in Fig 3a,c – and see Discussion).

In contrast, we found close agreement between the COR, SOR and NOR. Due to the high assumed vaccine uptake in the Isle of Man, the outbreak risk at the end of the vaccination programme there was calculated to be lower than when the vaccine rollout was completed in Israel (although we also considered supplementary analyses with different assumed vaccine uptake values – Fig S1). In the first scenario that we considered (median $R_0 = 3$), which is representative of the transmissibility of the original

SARS-CoV-2 virus, the outbreak risk was projected to be low following the vaccination programme in the Isle of Man.

However, when the virus was assumed to be more transmissible (median $R_0 = 5$), as is the case for newly emerged variants of concern such as B.1.1.7, the outbreak risk was found to be substantial even following the projected end of the vaccination campaigns in both the Isle of Man and Israel. For example, when the assumed vaccine uptake values of $\nu = 0.8$ and $\nu = 0.7$ had been achieved in the Isle of Man and Israel, respectively, the NOR took values of 0.373 (95% credible interval [0.223,0.477] calculating using the 95% credible interval for $R_V(t)$ at the end of the vaccination rollout) and 0.506 ([0.387,0.588]) in those locations.

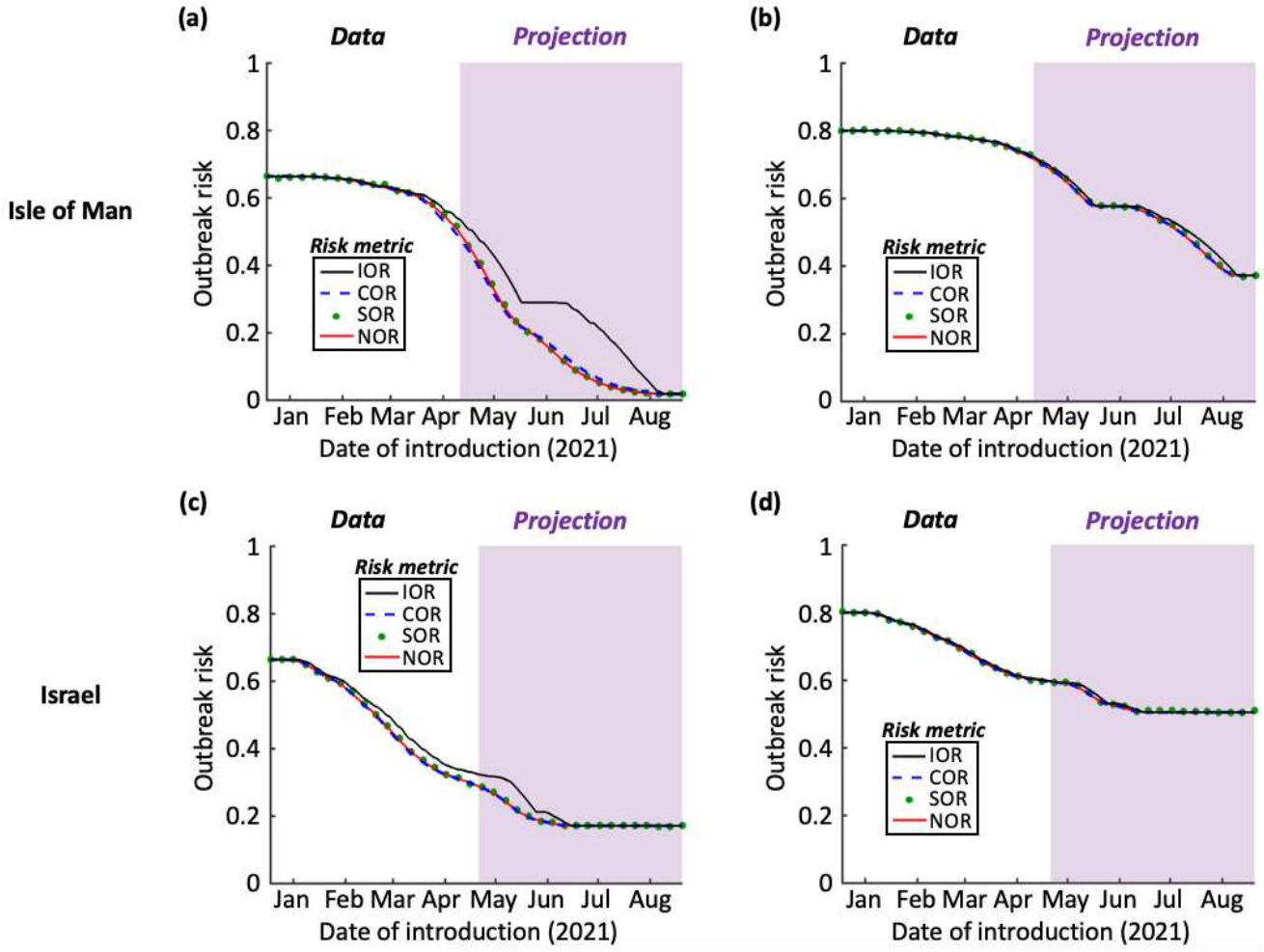


Figure 3. The risk that an infectious case introduced at each stage of the vaccination campaign initiates an outbreak, if travel restrictions and other NPIs are removed. (a) The outbreak risk assessed using the four metrics (IOR – black; COR – blue dashed; SOR – green dots; NOR – red), based on vaccination data from the Isle of Man and assuming $R_0 = 3$, as in Fig 2b. The period in which vaccination data were available is shown in white, and the period in which vaccination data were projected is shown in purple. (b) Analogous to panel b but with $R_0 = 5$ (see Fig 2c). (c) Analogous to panel a but using vaccination data for Israel (see Fig 2e). (d). Analogous to panel a but using vaccination data for Israel with $R_0 = 5$ (see Fig 2f). Ticks on the x-axes refer to the starts of the months labelled. Parameter values are shown in Table 1.

## 4. DISCUSSION

As vaccines are administered in countries around the world, attention has turned to the possibility that transmission will soon be reduced to the extent that travel restrictions and other NPIs can be relaxed. Here, we have investigated the impact of removing NPIs on the risk of outbreaks occurring in locations with low prevalence and a significant proportion of the population vaccinated. We used four metrics to quantify the risk that a case introduced at any stage in the vaccination rollout leads to an outbreak driven by local transmission, in a scenario in which NPIs are removed. We calculated temporal changes in the values of these metrics in the context of vaccination in the Isle of Man and in Israel, two locations with low prevalence and vaccination campaigns that have progressed quickly.

We found that vaccination is leading to a substantial drop in the potential for virus transmission in both the Isle of Man and Israel, as indicated by a decreasing value of the time-dependent reproduction number, $R_V(t)$ (Fig 2). However, even when the vaccine rollout is completed, a combination of vaccines not preventing transmission entirely, incomplete vaccine uptake and the emergence of novel SARS-CoV-2 variants suggests that the risk of outbreaks initiated by infected individuals arriving from elsewhere will not be eliminated when NPIs are removed (Fig 3). This conclusion remained true unless the vaccine uptake was very high (Fig S1). This suggests that, when NPIs such as travel restrictions are relaxed, it will still be advisable to be aware of the potential for local transmission. Ensuring that case numbers are reduced elsewhere

(i.e., in locations that imported cases might travel from) will reduce the risk of importations, and strategies should be considered to suppress local outbreaks quickly if importations occur.

One potential use of our modelling framework by policy-makers is to identify the dates on which travel restrictions can be relaxed, based on a maximum acceptable outbreak risk. As an example, if the maximum acceptable value of the NOR is 0.4, then our analysis with $R_0 = 5$ suggests that travel restrictions can be lifted on the Isle of Man at the end of July 2021 (Fig 3b; the first date on which the NOR falls below 0.4 is 29th July 2021). However, as described above, since the risk of local transmission following introductions remains, it will be necessary to continue to monitor inbound passengers in low prevalence settings to identify infected individuals, even once vaccine programmes are complete.

Our modelling approach for assessing outbreak risks was motivated by studies in which the potential for pathogen transmission varies periodically [30,34–36,45–48], due, for example, to seasonal changes in weather conditions that affect transmission. In that context, Carmona and Gandon [34] describe a “winter is coming effect”, in which the risk of an outbreak is lower than current environmental conditions suggest if conditions become less favourable for transmission in the near future. In the terminology used in our manuscript, if current environmental conditions promote pathogen transmission, then the IOR is expected to be high. This is because the IOR reflects the outbreak risk based on the conditions at the precise instance when the virus is introduced into the

348 population. However, if environmental conditions are expected to become less
349 favourable for transmission in the near future, then the values of the other risk metrics
350 are lower than the IOR, since those metrics account for changes in transmissibility over
351 the initial phase of the potential outbreak. Although in general we found a close
352 agreement between the four metrics that we considered, a background of decreasing
353 population susceptibility can lead to a similar effect in which the IOR is larger than the
354 COR, SOR or NOR (e.g. Fig 3a,c).
355
356 In this study, we used a simple branching process model to investigate the risk of
357 outbreaks when NPIs are removed during a vaccination programme. This involved
358 considering whether introduced cases are likely to lead to sustained local transmission
359 or instead fade out without causing an outbreak. We made the standard branching
360 process modelling assumption that population immunity is unaffected by infections in
361 the earliest stages of potential outbreaks [21–24,49,50]. In other words, infection-
362 acquired immunity following the arrival of the pathogen in the host population is not
363 considered. While this is reasonable when case numbers are low in the initial stages of
364 potential outbreaks, a more detailed model is needed to explore other quantities, such
365 as the eventual size of outbreaks. Following a vaccination programme, outbreaks are
366 likely to be smaller than those that occur before vaccines are widely administered.
367
368 Another simplification of our model is that we only accounted for changes in population
369 susceptibility due to the vaccine rollout. We did not account for prior immunity of some
370 members of the population due to previous exposures to the virus. At the time of writing

(1st May 2021), there have been 1,154 confirmed cases in the Isle of Man and 838,000 confirmed cases in Israel. Since these case numbers correspond to a relatively small proportion of the host population (representing 1.35% and 9.55% of the population in the Isle of Man and Israel, respectively), we do not expect this assumption to affect our key findings. Furthermore, immunity is likely to wane over time [51,52], reducing the effect of previous exposures on the outbreak risk. To test the potential impact of infection-induced immunity arising from cases occurring before May 2021, we also conducted a supplementary analysis in which the value of $R_0$ is reduced by 1.35% in the Isle of Man and 9.55% in Israel, and we found qualitatively similar results (Fig S2): even in this "best case" scenario, there is still a risk of outbreaks due to imported cases once the vaccination programmes are completed. Importantly, in other countries in which higher numbers of cases have occurred, prior immunity may play a larger role in reducing the risk of outbreaks compared to the low prevalence settings considered here. Understanding the extent of this effect, based on the rate at which immunity wanes, is an important target for further study.

In this research, we assumed that vaccines reduce transmission by lowering the probability that a vaccinated host becomes infected compared to an unvaccinated host. In reality, vaccination can reduce the probability of infection as assumed here [53], reduce the risk of onwards transmission following infection [7], reduce the risk of severe disease developing, or a combination of these effects [54]. In principle, it would be possible to develop a more complex model that accounts for each of these effects. It would also be possible to include other factors affecting transmission and vaccination,

for example the impact of population-structure on both vaccine efficacy [55] and transmission [56,57], or the possibility that individuals' behaviour may be different following the pandemic compared to beforehand, even when NPIs and travel restrictions are removed. For precise quantitative outbreak risk predictions to be made, it may be necessary to estimate $R_0$ in different locations. The value of $R_0$ might be expected to differ between countries, and inference of pathogen transmissibility in low prevalence settings where only limited case notification data are available is an important challenge [58,59].

Despite its simplicity, our modelling approach has demonstrated the general principle that, even following complete vaccination programmes in low prevalence settings, the risk of outbreaks remains when NPIs are removed. Our intention is not to argue that travel restrictions and other NPIs should not be relaxed once vaccination programmes are sufficiently advanced, but rather that measures should be taken to ensure that any clusters of cases are suppressed quickly if they arise. A local outbreak requires two steps: first, the virus must be imported from elsewhere; second, local transmission must occur. The first step emphasises the need for a global approach to minimising transmission, since large case numbers at a potential source location translates into a higher importation risk. The second step emphasises the need to ensure that, while vaccination acts to reduce transmission substantially, continued surveillance of inbound passengers for infection, combined with isolation and testing of contacts of detected infected individuals, is important when travel restrictions and other NPIs are relaxed. These measures are necessary, since only once the global prevalence of SARS-CoV-2

417 infections is reduced substantially can the risk of outbreaks in low prevalence settings
418 be eliminated.
419
420 **COMPETING INTERESTS**
421 We have no competing interests.
422
423 **AUTHORS' CONTRIBUTIONS**
424 Conceptualization: RS-P, RNT, LD; Methodology: RS-P, RNT; Investigation: RS-P;
425 Supervision: RNT, HMB; Writing – original draft: RNT, RS-P; Writing – review and editing:
426 All authors.
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