

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

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

36

37 **KEYWORDS**

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

40

41

42 **1. INTRODUCTION**

43

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

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

50

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

59

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

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

74

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

$$80 \quad \text{Prob}(\text{outbreak}) = 1 - \left(\frac{1}{R}\right)^{I_0}, \quad (1)$$

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

93

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

111

112

2. METHODS

113

114 Epidemiological model

115

116 We performed our analyses using a stochastic branching process model that describes
117 virus transmission in the initial stages of a potential outbreak. In the model, following the
118 arrival of a case in the local population, new infections occur at rate $\beta(1 - \Lambda(t))$ and
119 infected individuals have a mean infectious period of $1/\mu$ days (Fig 1a). The function
120 $\Lambda(t)$ reflects the extent to which transmission has been reduced by vaccination, where a
121 value of $\Lambda(t) = 0$ corresponds to an entirely unvaccinated population.

122

123 To model an ongoing vaccination campaign, we set $\Lambda(t) = \eta_1 V_1(t - \alpha) + \eta_2 V_2(t - \alpha)$,
124 where $V_1(t)$ is the proportion of individuals in the population who have received a single
125 vaccine dose at time t and $V_2(t)$ is the proportion of individuals in the population who
126 have received two vaccine doses at time t (Fig 1b). The parameters η_1 and η_2 reflect
127 the effectiveness of the vaccine at preventing infection after one and two doses,
128 respectively, and the parameter α represents the delay between a vaccine dose being
129 administered and being effective in the recipient. In our main analyses, since we are
130 modelling relatively low prevalence settings, we do not consider immunity due to prior
131 infections, although we present a supplementary analysis in which we considered the
132 robustness of our results to this assumption.

133

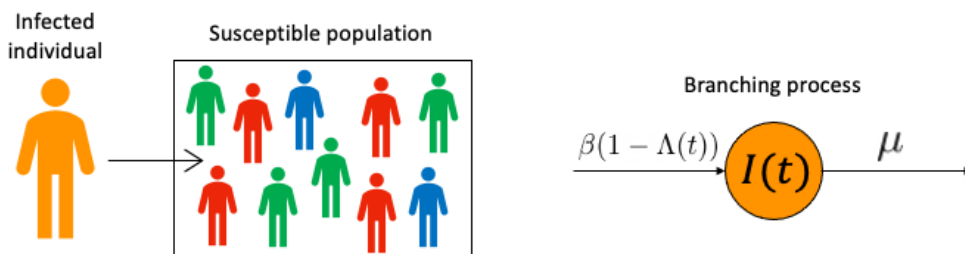
134 Under this model, the time-dependent reproduction number, accounting for any
135 vaccines that have been administered and are effective at time t , is given by

$$136 \quad R_V(t) = \frac{\beta(1 - \Lambda(t))}{\mu}. \quad (2)$$

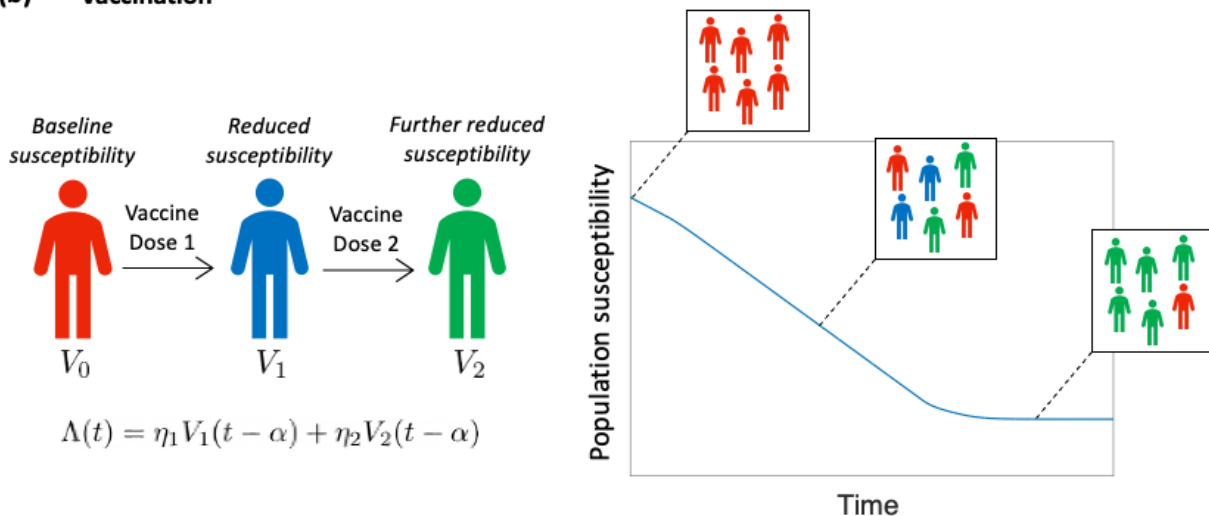
137

138 The value of $R_V(t)$ represents the expected number of secondary infections generated
 139 by a single infected individual in the population at time t , under the assumption that no
 140 further vaccinations take place in future. It is therefore representative of the
 141 “instantaneous” transmissibility at time t . Indeed, $R_V(t)$ is sometimes referred to as the
 142 instantaneous reproduction number [25–27]. In the absence of vaccination, so that $\Lambda(t) =$
 143 0, then $R_V(t)$ is equal to the basic reproduction number, R_0 .
 144

(a) Transmission model



(b) Vaccination



145
 146 Figure 1. The epidemiological model used in our analysis. (a) Following the introduction of an infected
 147 individual into the host population, local transmission may happen with infections occurring at rate $\beta(1 -$
 148 $\Lambda(t))$, where $\Lambda(t)$ reflects the vaccination coverage in the local population. Infected individuals have mean
 149 infectious period $1/\mu$ days. (b) The vaccination process is modelled by setting $\Lambda(t)$ according to the

150 proportion of individuals in the population who have been vaccinated with one (V_1) or two (V_2) doses. The
151 first vaccine dose is assumed to have effectiveness η_1 and the second vaccine dose has effectiveness η_2 .
152 Vaccine doses are effective α days after they are administered. This leads to declining population
153 susceptibility as a vaccine is rolled out across the population.

154

155

156 Vaccination data

157

158 In the model, $V_1(t)$ and $V_2(t)$ were set based on vaccination data from the location
159 under consideration (either the Isle of Man or Israel). Data describing the proportion of
160 the total population who had received one or two vaccine doses were available for the
161 periods up until 11th April 2021 (for the Isle of Man [28]) and 21st April 2021 (for Israel
162 [29]).

163

164 To explore how the risk of outbreaks is likely to change in future, we projected the
165 vaccine rollout forwards beyond these dates in the following way. We considered the
166 total population size of the location under consideration (denoted N), as well as the
167 numbers of individuals ($N_1(t)$ and $N_2(t)$) vaccinated with one or two doses, so that
168 $V_1(t) = N_1(t)/N$ and $V_2(t) = N_2(t)/N$. We assumed that a constant number of vaccine
169 doses are available each day in future (denoted D), and that there is a target period of τ
170 days between each vaccine dose. On any day in future, each available dose is assigned
171 to an individual who has been vaccinated with their first dose at least τ days ago, with
172 remaining doses then assigned to unvaccinated individuals. Resulting values of $N_1(t)$
173 and $N_2(t)$ were then converted to corresponding values of $V_1(t)$ and $V_2(t)$. To reflect the

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

180

181 Outbreak risk metrics

182

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

188

189 The first metric we considered is the *Instantaneous Outbreak Risk (IOR)*. This quantity
190 represents the expression shown in equation (1), with $R = R_V(t)$ and $I_0 = 1$. The IOR
191 reflects the risk of an outbreak occurring starting from a single infected individual at time
192 t , but under the assumption that the vaccine rollout does not continue after time t so
193 that pathogen transmissibility is unchanged. While the IOR straightforward to calculate,
194 it does not reflect changing population immunity due to vaccination over the initial phase
195 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

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

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

219 simulations to be run. The NOR, therefore, also represents the risk that a single infected
 220 individual introduced into the population at time t initiates an outbreak in which at least
 221 $M = 100$ individuals are ever infected simultaneously.

222

223 Table 1: Default parameter values used in our analyses.

Parameter	Description	Value	Source
β	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]
α	Delay between a vaccine dose being administered and being effective	14 days	[40]
η_1	Relative susceptibility of an individual vaccinated with a single effective dose (compared to an unvaccinated host)	0.4	[17]
η_2	Relative susceptibility of an individual vaccinated with two effective doses (compared to an unvaccinated host)	0.15	[17]
ν	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])
τ	Target period between vaccine doses (in future projections)	84 days (Isle of Man) and 21 days (Israel)	[43,44]

224

225

226

3. RESULTS

227

228 As described in the Methods, we first generated projections of the number of vaccinated

229 individuals in future for the Isle of Man (Fig 2a) and Israel (Fig 2d), based on past

230 vaccination data in those locations. To explore the impact of vaccination on virus

231 transmission, we calculated the time-dependent reproduction number ($R_V(t)$; equation

232 (2)) throughout the vaccination campaign. We considered two different scenarios. In the

233 first, we set the median value of R_0 (i.e., the reproduction number in the absence of

234 vaccination) equal to 3, as was the situation early in the COVID-19 pandemic (Fig 2b,e).

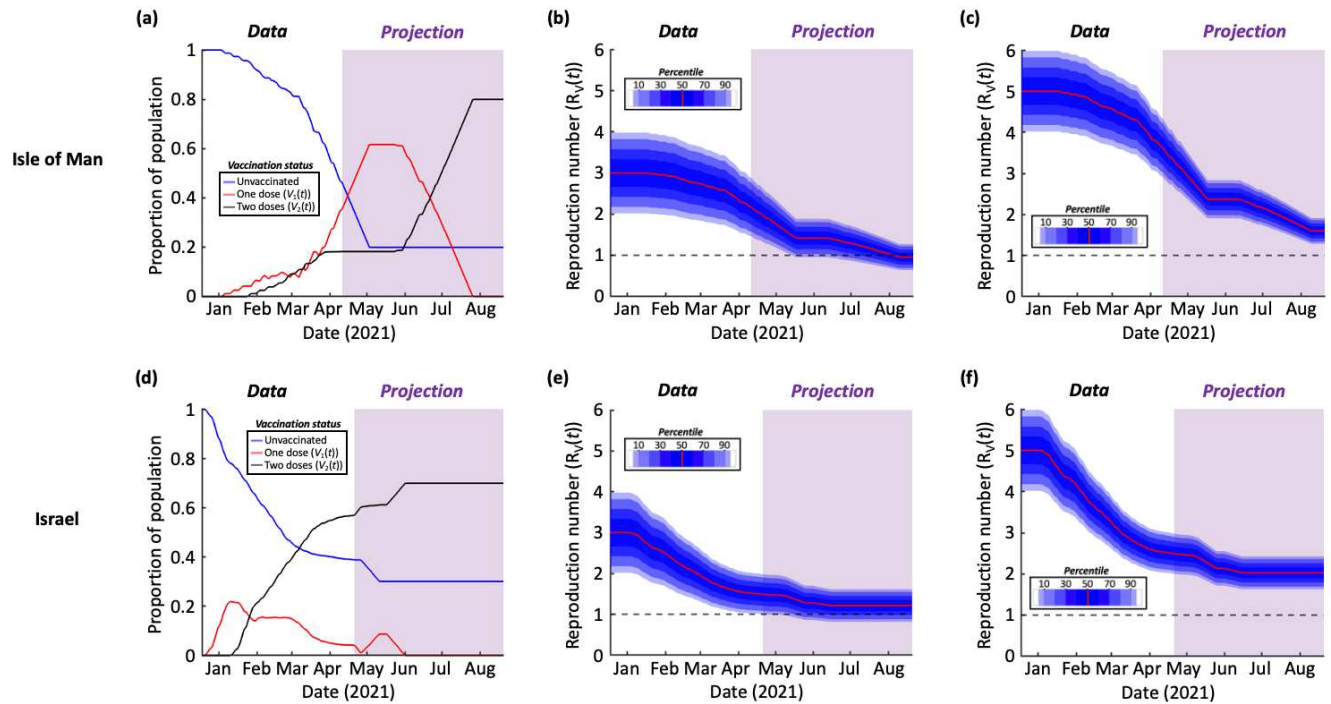
235 In the second scenario, we set the median value of R_0 equal to 5 (Fig 2c,f) to reflect the

236 fact that currently circulating SARS-CoV-2 variants are more transmissible than the

237 original virus [20]. This second scenario is therefore likely to be a more realistic

238 reflection of the current and future risk.

239



240

241 Figure 2. Effect of vaccination on population susceptibility. (a) The proportion of the population of the Isle
 242 of Man who are unvaccinated ($1 - V_1(t) - V_2(t)$), vaccinated with a single dose ($V_1(t)$) and vaccinated
 243 with two doses ($V_2(t)$). The period in which vaccination data were available is shown in white, and the
 244 period in which vaccination data were projected is shown in purple. (b) The time-dependent reproduction
 245 number ($R_V(t)$) corresponding to the vaccination data in panel a, starting from a median initial value of
 246 $R_V(0) = R_0 = 3$. To account for uncertainty in the value of R_0 , a normal distribution was assumed about
 247 the median value of R_0 with variance $\sigma^2 = 0.25$, which is reflective of the range of R_0 values estimated
 248 early in the COVID-19 pandemic [38]. (c) Analogous to panel b but starting from a median initial value of
 249 $R_V(0) = R_0 = 5$. (d)-(f) Analogous to panels a-c but using vaccination data for Israel. In all panels, $t = 0$
 250 days corresponds to 18th December 2020. Ticks on the x-axes refer to the starts of the months labelled.
 251 Parameter values are shown in Table 1.

252

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

256 entirely, so that $R_V(t)$ is not reduced by interventions other than vaccination. These
257 metrics then reflect the risk that a single case first entering into the population at the
258 date of introduction shown initiates an outbreak driven by sustained local transmission,
259 given that no NPIs are in place. For each metric, and each time during the vaccination
260 programme, we calculated the outbreak risk by integrating over the full distribution for
261 $R_V(t)$ shown in Fig 2. The resulting outbreak risk therefore represents a point estimate
262 of the risk accounting for uncertainty in pathogen transmissibility.

263

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

271

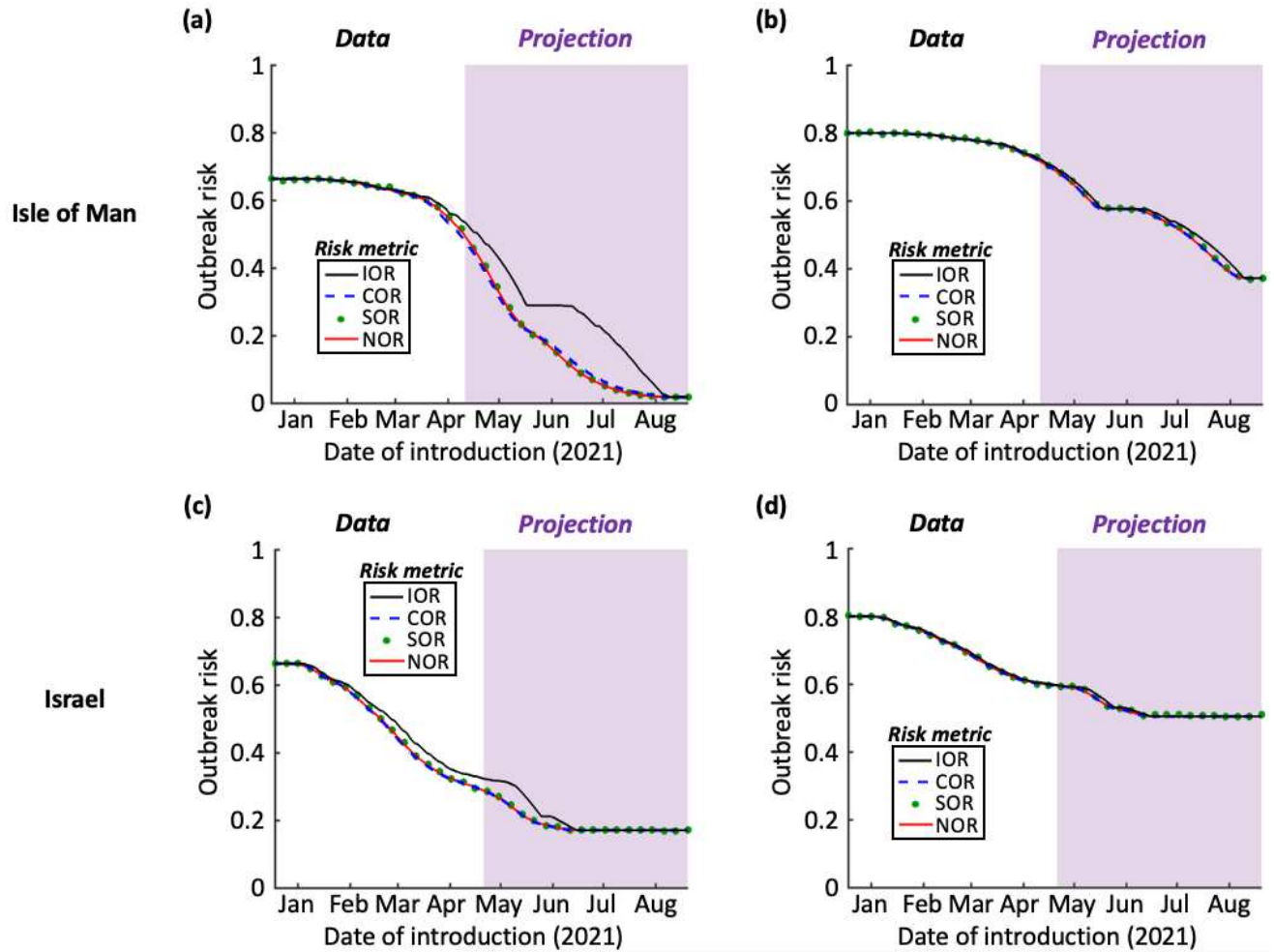
272 In contrast, we found close agreement between the COR, SOR and NOR. Due to the
273 high assumed vaccine uptake in the Isle of Man, the outbreak risk at the end of the
274 vaccination programme there was calculated to be lower than when the vaccine rollout
275 was completed in Israel (although we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

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

280

281 However, when the virus was assumed to be more transmissible (median $R_0 = 5$), as is
282 the case for newly emerged variants of concern such as B.1.1.7, the outbreak risk was
283 found to be substantial even following the projected end of the vaccination campaigns in
284 both the Isle of Man and Israel. For example, when the assumed vaccine uptake values
285 of $\nu = 0.8$ and $\nu = 0.7$ had been achieved in the Isle of Man and Israel, respectively, the
286 NOR took values of 0.373 (95% credible interval [0.223,0.477] calculating using the
287 95% credible interval for $R_V(t)$ at the end of the vaccination rollout) and 0.506
288 ([0.387,0.588]) in those locations.

289



290

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

300

301

4. DISCUSSION

302

303

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

314

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

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

328

329 One potential use of our modelling framework by policy-makers is to identify the dates
330 on which travel restrictions can be relaxed, based on a maximum acceptable outbreak
331 risk. As an example, if the maximum acceptable value of the NOR is 0.4, then our
332 analysis with $R_0 = 5$ suggests that travel restrictions can be lifted on the Isle of Man at
333 the end of July 2021 (Fig 3b; the first date on which the NOR falls below 0.4 is 29th July
334 2021). However, as described above, since the risk of local transmission following
335 introductions remains, it will be necessary to continue to monitor inbound passengers in
336 low prevalence settings to identify infected individuals, even once vaccine programmes
337 are complete.

338

339 Our modelling approach for assessing outbreak risks was motivated by studies in which
340 the potential for pathogen transmission varies periodically [30,34–36,45–48], due, for
341 example, to seasonal changes in weather conditions that affect transmission. In that
342 context, Carmona and Gandon [34] describe a “winter is coming effect”, in which the
343 risk of an outbreak is lower than current environmental conditions suggest if conditions
344 become less favourable for transmission in the near future. In the terminology used in
345 our manuscript, if current environmental conditions promote pathogen transmission,
346 then the IOR is expected to be high. This is because the IOR reflects the outbreak risk
347 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

371 (1st May 2021), there have been 1,154 confirmed cases in the Isle of Man and 838,000
372 confirmed cases in Israel. Since these case numbers correspond to a relatively small
373 proportion of the host population (representing 1.35% and 9.55% of the population in
374 the Isle of Man and Israel, respectively), we do not expect this assumption to affect our
375 key findings. Furthermore, immunity is likely to wane over time [51,52], reducing the
376 effect of previous exposures on the outbreak risk. To test the potential impact of
377 infection-induced immunity arising from cases occurring before May 2021, we also
378 conducted a supplementary analysis in which the value of R_0 is reduced by 1.35% in the
379 Isle of Man and 9.55% in Israel, and we found qualitatively similar results (Fig S2): even
380 in this “best case” scenario, there is still a risk of outbreaks due to imported cases once
381 the vaccination programmes are completed. Importantly, in other countries in which
382 higher numbers of cases have occurred, prior immunity may play a larger role in
383 reducing the risk of outbreaks compared to the low prevalence settings considered
384 here. Understanding the extent of this effect, based on the rate at which immunity
385 wanes, is an important target for further study.

386

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

394 for example the impact of population-structure on both vaccine efficacy [55] and
395 transmission [56,57], or the possibility that individuals' behaviour may be different
396 following the pandemic compared to beforehand, even when NPIs and travel restrictions
397 are removed. For precise quantitative outbreak risk predictions to be made, it may be
398 necessary to estimate R_0 in different locations. The value of R_0 might be expected to
399 differ between countries, and inference of pathogen transmissibility in low prevalence
400 settings where only limited case notification data are available is an important challenge
401 [58,59].

402

403 Despite its simplicity, our modelling approach has demonstrated the general principle
404 that, even following complete vaccination programmes in low prevalence settings, the
405 risk of outbreaks remains when NPIs are removed. Our intention is not to argue that
406 travel restrictions and other NPIs should not be relaxed once vaccination programmes
407 are sufficiently advanced, but rather that measures should be taken to ensure that any
408 clusters of cases are suppressed quickly if they arise. A local outbreak requires two
409 steps: first, the virus must be imported from elsewhere; second, local transmission must
410 occur. The first step emphasises the need for a global approach to minimising
411 transmission, since large case numbers at a potential source location translates into a
412 higher importation risk. The second step emphasises the need to ensure that, while
413 vaccination acts to reduce transmission substantially, continued surveillance of inbound
414 passengers for infection, combined with isolation and testing of contacts of detected
415 infected individuals, is important when travel restrictions and other NPIs are relaxed.
416 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.

427

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