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Strategies at points of entry to reduce importation risk of COVID-19 cases and reopen travel

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Abstract

Background: With more countries exiting lockdown, public health safety requires screening measures at international travel entry points that can prevent the reintroduction or importation of the severe acute respiratory syndrome-related coronavirus-2. Here, we estimate the number of cases captured, quarantining days averted and secondary cases expected to occur with screening interventions.

Methods: To estimate active case exportation risk from 153 countries with recorded coronavirus disease-2019 cases and deaths, we created a simple data-driven framework to calculate the number of infectious and upcoming infectious individuals out of 100 000 000 potential travellers from each country, and assessed six importation risk reduction strategies; Strategy 1 (S1) has no screening on entry, S2 tests all travellers and isolates test-positives where those who test negative at 7 days are permitted entry, S3 the equivalent but for a 14 day period, S4 quarantines all travellers for 7 days where all are subsequently permitted entry, S5 the equivalent for 14 days and S6 the testing of all travellers and prevention of entry for those who test positive.

Results: The average reduction in case importation across countries relative to S1 is 90.2% for S2, 91.7% for S3, 55.4% for S4, 91.2% for S5 and 77.2% for S6. An average of 79.6% of infected travellers are infectious upon arrival. For the top 100 exporting countries, an 88.2% average reduction in secondary cases is expected through S2 with the 7-day isolation of test-positives, increasing to 92.1% for S3 for 14-day isolation. A substantially smaller reduction of 30.0% is expected for 7-day all traveller quarantining, increasing to 84.3% for 14-day all traveller quarantining.

Conclusions: The testing and isolation of test-positives should be implemented provided good testing practices are in place. If testing is not feasible, quarantining for a minimum of 14 days is recommended with strict adherence measures in place.

Key words: Lockdown, travel restrictions, border measures, SARS-CoV-2, quarantine, isolation, air passengers

Introduction

The coronavirus disease-2019 (COVID-19) pandemic has resulted in a global cessation of almost all cross-border travel where the public health implications and economic impact are unprecedented relative to other emerging infectious disease epidemics.[1–10] The lockdown in Wuhan, China, where severe acute respiratory syndrome–related coronavirus-2 (SARS-CoV-2) originated, had a major positive impact on reducing further spread within China and beyond[11,12] where a clear correlation was observed pre-lockdown between travel volume and subsequent seeding of epidemics elsewhere.[10] The accompanying travel restrictions during lockdown have contributed towards epidemic containment with estimations in early February of a 77% reduction in imported cases from mainland China to

other countries[13] an 81.3% reduction in case exportation on average.[14] In Australia, modelling showed that a full travel ban reduced cases by 86%, whilst the impact of a partial lifting of the ban was minimal,[15] demonstrating the need for strict compliance of no entry at borders. This however is unsustainable in the medium to long term as the SARS-CoV-2 outbreak continues to spread globally, making travel bans a delay strategy and not preventative, which has been previously observed by the World Health Organization who did not recommend their long-term use for global pandemics due to the severe economic impacts caused.[16,17] Pressure is thus increasing on countries to lift travel restrictions and implement alternative control measures at their borders, which includes screening.[18,19]

Many countries are additionally emerging from lockdowns, which have successfully suppressed outbreaks or reduced the epidemic size in multiple countries,[20] and to avoid further lockdowns from recurring or new outbreaks, the risk of case importation or exportation should be minimized. Case exportation risk has been previously explored which identified Thailand, Japan, South Korea and Singapore as high-risk countries for case importation from mainland China due to high traffic volumes in the early phase of the epidemic[21] but the global epidemic has and continues to rapidly evolve. Several studies have since shown that a 3–6% proportion of air passengers were SARS-CoV-2 positive during the height of the COVID-19 outbreaks in Europe[22,23] where the infectiousness[24] and high estimated asymptomatic rates[25,26] of SARS-CoV-2 have now left few countries or territories unaffected. Heterogeneity in the efficacy of ongoing control measures,[20] adherence and public perceptions of risk[27] and implementation times[28,29] have however caused remarkably different outbreaks and by extension exportation risks. Gaining understanding of importation risk therefore requires ongoing global and country-specific assessments to identify which countries are at high risk of case exportation.

Especially critical for high-risk countries, screening measures can be utilized to ensure infected travellers are no longer infectious when they enter the local population, thereby ensuring public safety whilst encouraging economic growth and protecting livelihoods. For countries with strained capacities in healthcare resources and limited incoming travel, such as those identified by Gilbert in the African continent,[30] screening measures can be highly beneficial, if successfully implemented, on the wider healthcare system by identifying imported cases and preventing ongoing community spread. Additionally, for countries with relatively suppressed epidemics from lockdown or post-lockdown strategies in place, identifying cases on entry saves the need for more immense contact tracing efforts which are both time-consuming and expensive, and reduces the risk of continued virus reintroduction.

Such implementation of present or future screening at entry points requires the exploration of different strategies with corresponding estimates of their relative success in capturing infections to be informative to policymakers. We therefore outline a method to quantify the risk of case exportation from 153 countries or territories per 100 000 travellers in 1000 simulations under six risk-mitigation strategies. In these strategies, we explore the use of isolation of test-positives and quarantining of all travellers for 7 and 14 days, and estimate the number of cases captured, quarantining days averted and secondary cases which occur from missed importations allowed entry.

Methods

To estimate the number of arrivals from 153 countries with recorded COVID-19 cases and deaths, we created a simple data-driven framework that calculates the number of infected people travelling based on the modelled time of infection and time difference to entry. As countries have different epidemic trajectories, they pose different risks of case exportation and are assessed separately. At arrival points, the effects of six strategies are explored in their efficacy to preventing the importation of cases.

Simulating the number of infected individuals

We simulate arrivals from a country of origin, C, calculating risks per 100 000 travellers in 1000 simulations to accommodate uncertain travel volumes. The conditional distribution of importation at different stages of infection is obtained from these 100 000 000 simulated travellers. Those who were infected but not yet recovered were extracted for further modelling. The amount of secondary transmission over their infected lifespan was then apportioned into transmission potential before arrival, during quarantine or isolation if any, and in the community. Quarantine and isolation measures were assumed to take place in a designated healthcare facility or centre where transmission risk is reduced to negligible levels, or at home with strict adherence where any family members present are also expected to follow the same measures.

We assumed travellers were administered a polymerase chain reaction (PCR) test upon arrival and estimated the likelihood of identifying each positive infection using a binomial distribution where the probability of detection was a function of their time from illness onset (symptom onset for those who are symptomatic and time of expected symptom onset for those who are asymptomatic) using data from Xiao *et al.*[31] (Fig. 1a). PCR sensitivity was assumed to be 85% for 2 days pre-illness onset, similar to sensitivity 2 days post-illness onset, and infections were undetectable at any earlier point during the incubation period. Asymptomatic individuals were assumed to follow the same detection profile as symptomatic individuals.

For a country of origin C and travel date$T$ assumed to be 23rd July 2020, we simulated the incidence of infection among 100 000 000 travellers that (i) occurred prior to T, (i) were not admitted to hospital, and (iii) did not become non-infectious prior to T. To obtain estimates of the daily number of infections in C, we utilized daily incidence and death data being published by the Center for Systems Science and Engineering at Johns Hopkins University[32] across 153 countries from 22nd January to 6th August 2020.

To estimate condition (1), we first simulated the time of infection (t_i^{IC}) for each individual i reported to have died at time t_i^{DC} in country C using estimates from Linton *et al.*[18] of the distribution of time of illness onset to death (ω_i for individual i) and incubation period (b_i) using the following relationship:

$$t_i^{IC} = t_i^{DC} - \omega_i - b_i,$$

where ω_i and b_i were given log-normal distributions with mean and standard deviation 20.2d and 11.6d for ω_i and 5.6d and 3.9d for b_i (Fig. 1b, c). All cases, regardless of symptom profile, were assumed to have the same illness onset and incubation

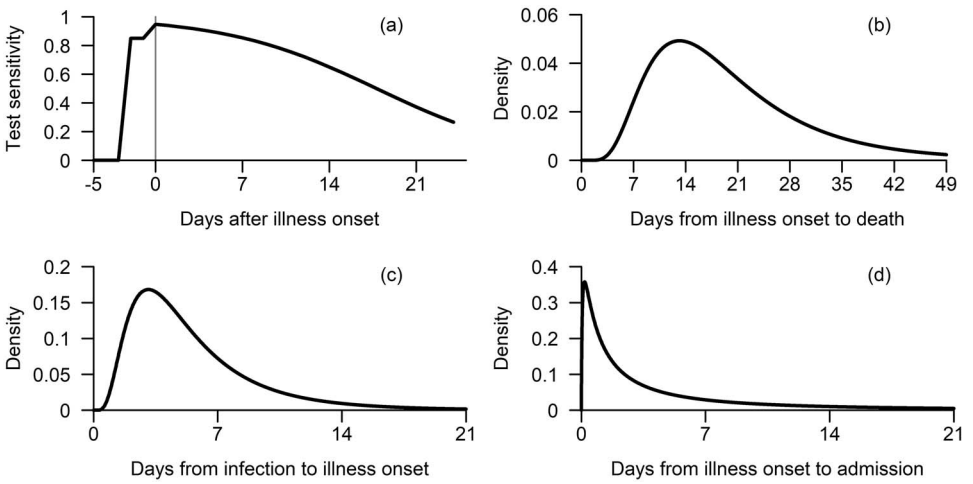

Figure 1. (a) The sensitivity of the PCR test over time. (b) The distributions used to estimate the number of infection days from illness onset to death and (c) from infection time to illness onset. (d) The distribution used for time to admission for cases that are hospitalised in the country of origin

period distributions where asymptomatic individuals did not show symptoms.

For condition (2), we used $\{t_i^{IC}\}$ to estimate the number of symptomatic and asymptomatic incident infections each day, assuming the case and infection fatality ratio (CFR and IFR) estimates derived by Russell *et al.*[33] at 1.2% and 0.6% to be similar to those in each country of origin. Hence, we approximated the total number of incident infections in country C in two categories, symptomatic (S_t^C) and asymptomatic (A_t^C), at time t as.

$$S_t^C \cong \frac{1}{CFR}\sum_i \mathbb{I}\left(t_i^{IC} = t\right),$$

and.

$$A_t^C \cong \left(\frac{1}{IFR} - \frac{1}{CFR}\right)\sum_i \mathbb{I}\left(t_i^{IC} = t.\right)$$

for $\mathbb{I}()$, the indicator function. A symptomatic patient may visit a healthcare facility, determined by the simulated date of i's hospital admission (t_i^{HC}), also based on estimates from Linton *et al.*[34] with a corresponding log-normal distribution (Fig. 1d). A random subset of the simulated symptomatic population was then removed each day based on the country's reported case count, leaving the remaining as mildly symptomatic and able to travel at T.

For condition (3), we compared the date of entry T to the date of clearance defined as the simulated reported date or first day of symptoms with an additional 10-day infectious period. Based on the control strategies, a proportion of infected people are expected to clear infection whilst under isolation or quarantining, or will be permitted entry whilst infectious or infected and not infectious yet.

Proposed Strategies

The six strategies are explored (Fig. 2) as follows:

(1) No screening—entry is allowed for all incoming travellers from the source country,
(2) Screening of all incoming travellers on arrival and 7-day isolation for test-positive travellers, with release into the community only with a negative test thereafter,
(3) Screening with 14-day isolation of test-positives followed by a negative test,
(4) No screening of travellers but a 7-day mandatory quarantine for all,
(5) No screening but 14 days of quarantine and
(6) Screening of all passengers and entry prohibited for those testing positive.

Strategy 1 serves as a baseline of no testing or quarantining where all individuals enter unconfirmed as to whether they are infected (Fig. 2). Strategy 2 assumes that testing occurs upon entry where individuals testing positive are isolated for 7 days and those who test negative are allowed entry. Those who test positive are only allowed entry once they are confirmed to be negative with a subsequent test on day 7. Strategy 3 is the equivalent of Strategy 2 but isolation occurs over 14 days for individuals testing positive who then receive a second test on day 14. For Strategy 4, all individuals are quarantined for 7 days, and for 14 days in Strategy 5. For Strategy 6, all travellers are tested and individuals testing positive are denied entry.

We summated the number of travellers at the point of entry or release from isolation or quarantine who were infectious or infected (and infectious later), depending on the strategy. We also calculated the number of quarantine days, defined as days spent at a quarantine facility or similar setting with minimal risk of infection to others) in all strategies, and measured the differences between Strategy 2 and 4, and Strategy 3 and 5, representing the time spent in a facility between isolation and quarantine methods for 7 and 14 days. The number of secondary cases was lastly calculated for each individual as the proportion of infectious days remaining out of the total 10 days of potentially active infection after the Strategy was implemented (release at day of entry, 7 days or 14 days) multiplied by 2, which is the assumed R_0.

Results

The 10 countries with the highest risk are presented where notable epidemics or surges in cases are being reported (Fig. 3; a

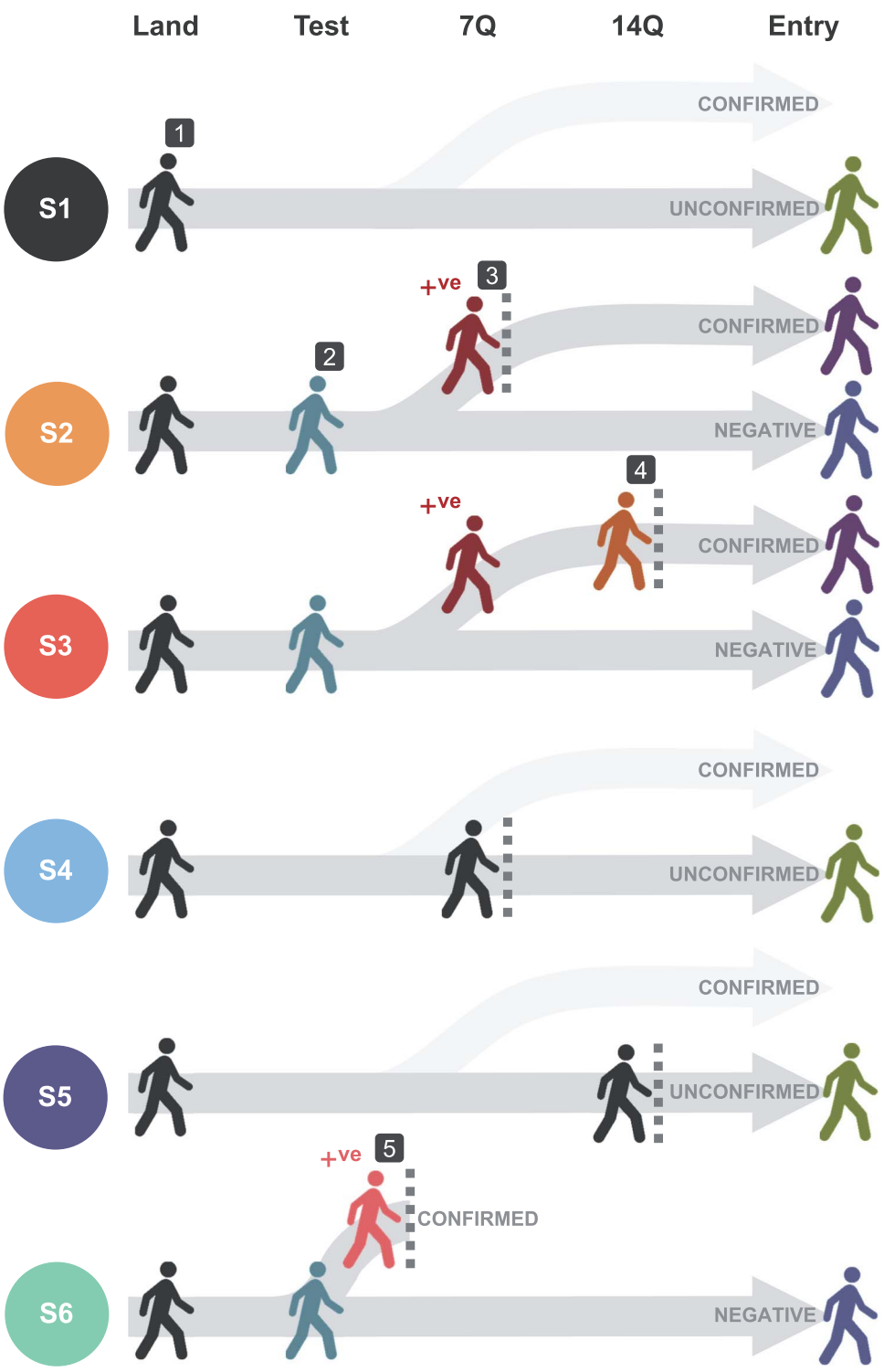

Figure 2. Depiction of scenarios (S1–S6) and outcomes, which are labelled and colour coded. Individuals who land or receive no testing measures in Strategy 1, 4 and 5 are displayed as (1) in dark grey. Individuals who land and are tested in Strategy 2, 3 and 6 are presented as (2) in blue and those who are tested positive and quarantined for at least 7 days are shown as (3) in red. For Strategy 3, individuals who are tested and remain quarantined until 14 days are represented as (4) in orange. For Strategy 6, individuals who are denied entry when tested upon landing are presented as (5) in pink. Dark grey routes represent active pathways on arrival and light grey signify inactive routes where no testing is conducted. A dotted line signifies the denial of entry up to that timepoint or complete denial of entry for Strategy 6. For Strategy 4 and 5, quarantine measures are in place at 7 days and 14 days, respectively, and for Strategy 2 and 3, isolation measures are in place for those who test positive. At the end time point, individuals who tested positive and have been cleared (purple), tested negative (dark blue) and are unconfirmed (green) are presented

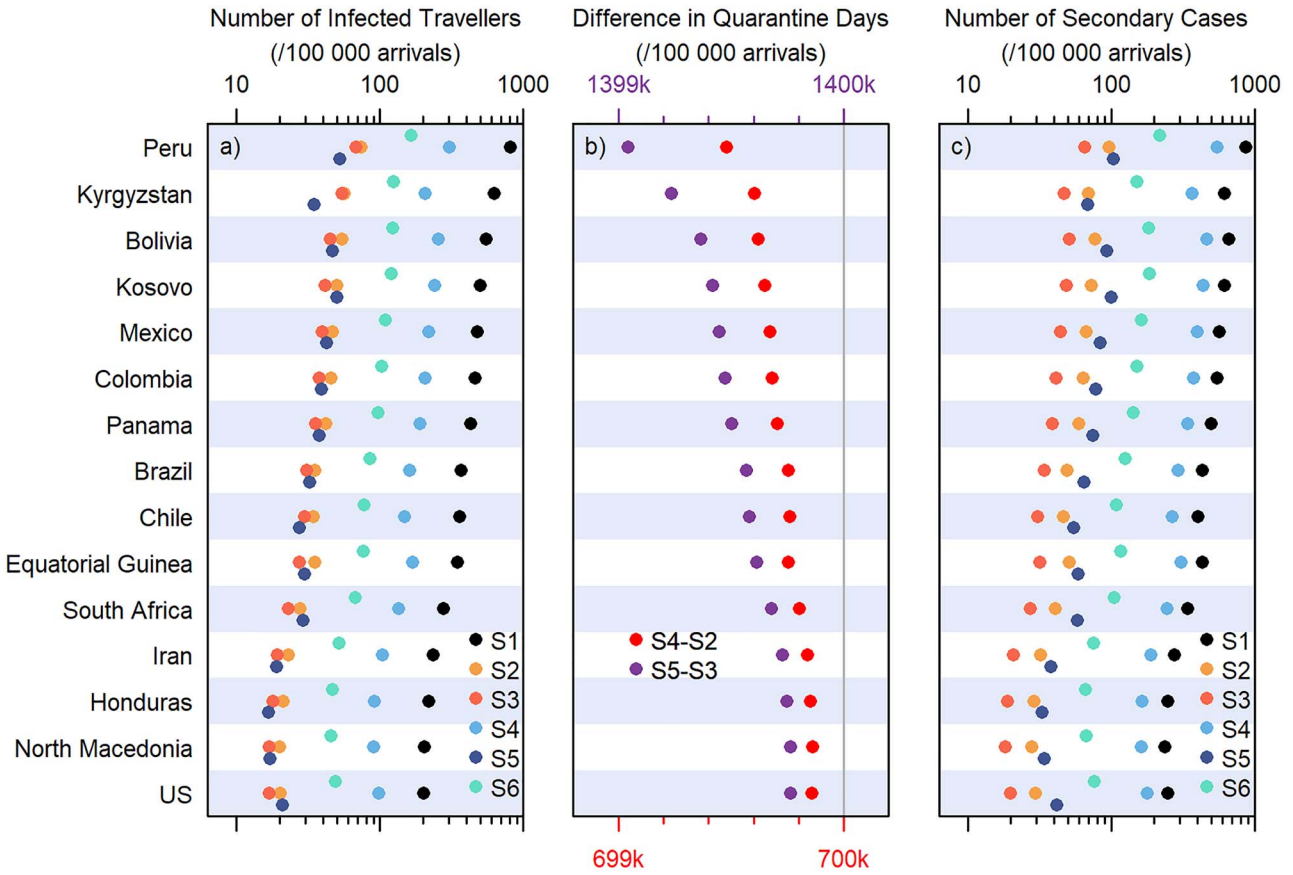

Figure 3. (a) The estimated number of infected travellers per 100 000 arrivals from countries of origin on a logarithmic scale, (b) the differences in quarantine days between Strategy 2 (7 day isolation) and Strategy 4 (7 day quarantine), and Strategy 3 (14 day isolation) and Strategy 5 (14 day quarantine) and (c) the number of secondary cases estimated to occur as individuals are permitted entry according to the travellers' infectious time remaining

complete list of all countries is available in Appendix 1 in Supplementary data available at *JTM* online). Relative to allowing all travellers in unchecked (Strategy 1; Fig. 3a), testing and isolating reduces case importation numbers by an average of 90.2% for 7 days (Strategy 2) and by 91.7% for 14 days of isolation for test-positives (Strategy 3). Declining to test and using quarantine instead reduces case importation by 55.4% for 7 days (Strategy 4) and by 91.2% for 14 days of quarantine (Strategy 5). Prohibiting test positives from entry with no quarantining reduces transmission by 77.2% (Strategy 6). The testing and isolation of positive individuals for 7 days substantially reduces importation risk, and the requirement of a negative test prior to release from isolation increases the effectiveness compared to quarantine of the same length without testing. At 14-day quarantining, the effects of testing and/or quarantining are comparable as the substantial majority of travellers are no longer infectious. The isolation of test-positive travellers rather than quarantining all 100 000 travellers for 14 days however notably reduces total quarantine days for Brazil's travellers by 1 399 564 days per 100 000, 1 399 897 days for the UK and 1 399 763 days for the USA (Fig. 3b and Appendix 1 in Supplementary data available at *JTM* online), which brings economic savings whilst minimizing importation risk.

An average of 79.6% of infected travellers are infectious on arrival (Fig. 4), with an estimated 30.5% having 1 to 3 days of infectious time remaining, 24.9% from 4 to 6 days, 24.2% from 7 to 10 days, and the remaining becoming infectious on arrival. If transmissibility is similar for travellers and the general public, then for an R_0 of 2 in July 2020, a no-screening or quarantine policy would lead to 250 secondary cases per 100 000 travellers from the USA, 433 from Brazil and 105 from the UK, but as few as two from Japan and five from Germany (Figure 3c and Appendix 1 in Supplementary data available at *JTM* online). For testing and 7-day isolation (Strategy 2) in the top 100 exporting countries, on average an 88.2% (86.9–89.4%) reduction in secondary cases in the destination country is expected; this would increase to 92.1% (91.5–92.8%) for 14-day quarantine. For 7-day quarantine without testing, a smaller reduction of 30.0% (24.1–40.5%) is expected. For 14-day quarantine without testing, an 84.3% (78.4–88.8%) reduction is estimated, which is lower in efficacy than with testing, as an average of 6.4% of travellers become infectious 14 days or more after arrival that may be captured through testing at Day 14 (Strategy 3).

Discussion

Our results support a policy of testing arriving passengers from countries with ongoing transmission, followed by isolation until an individual is identified as having cleared the infection and is no longer infectious. This strategy would reduce risk to a

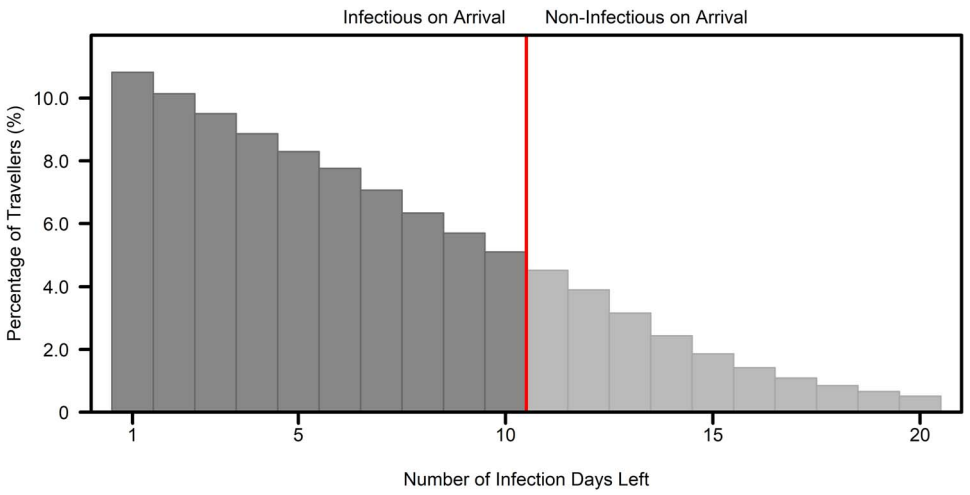

Figure 4. The number of infection days left shown as a proportion among travellers arriving. Those who are infectious on arrival are in dark grey, and those who are not infectious yet are in light grey

level that would permit necessary business and leisure travel to continue with test-trace-and-isolate programmes, thus detecting additional infections that were missed at the border.

Strategy 1, or no control, is not recommended as although travel restrictions may not act as a primary control measure, screening can prevent the entry of infectious and upcoming infectious travellers, which would otherwise require extensive contact tracing efforts and counteract ongoing control measures to maintain low levels of infection. Strategy 4 is also not recommended as it is relatively ineffective and implements the quarantining of all travellers, which is expected to heavily impact even resource rich countries. Strategy 6, although more effective, allows for the importation of individuals who are early in their infection and not yet detectable using PCR, which is assumed to be 3 days before illness onset in this analysis.

Strategy 2 tackles this issue by isolating test-positives until they present a negative result, only allowing the entry of potentially infected and infectious people through test failure, which is relatively low provided test practices are robust. Strategy 3 is more effective than Strategy 2 as test-positive individuals are kept in isolation until a minimum of 14 days where a greater proportion have cleared the infection and are no longer infectious. Where quarantining facility space is severely limited or long-term adherence is poor when individuals are quarantined at their home location, which may also expose their household members to infection, utilizing a minimal 7-day isolation period for test-positives remains a viable option. The usefulness of testing is shown for 7-day interventions with a 34.8% increase in caught infected travellers from Strategy 2 and 4 (90.2% vs 55.4%) where all traveller quarantining is substantially less effective. The extension of isolation days to a minimum of 14 days with and without testing has a difference of 0.5% (Strategy 3 and 5; 91.7% vs 91.2%), which is a relatively minor saving. In contrast, without testing, the extension of quarantining of all travellers from 7 days to 14 days without testing is critical, increasing the efficacy of the screening measure by 35.8% (Strategy 4 and 5; 55.4% vs 91.2%).

With ongoing concerns of false-negative rates in PCR testing,[35,36] strained test kit availability[37] and lack of trained manpower and laboratories,[38] the quarantining of all travellers for 14 days may be more feasible to implement over the conducting of rigorous and repeated testing of incoming travellers. The location for quarantine, whether it is home or institutional, will also likely impact the efficacy of the proposed screening strategies[39] and will depend on each country's ongoing control measures in place. For countries with good testing practices for travellers in place, the testing of travellers remains an effective strategy in reducing importation risk, and substantially negates the risk of community spread occurring from potential non-compliance of quarantining measures among travellers. Testing also substantially reduces the number of quarantining days among travellers by over 1 399 000 days for 14-day quarantining. Countries should thus assess whether testing or 14-day quarantining is viable and cost-effective, considering their own policies and access to testing or quarantining facilities. Where testing practices cannot maintain high case-finding rates as the sensitivity of the testing measures is reduced by a factor describing improper test handling, further country-specific analyses will be required to ascertain whether the quarantining of all travellers may be unavoidable (Appendix 2 in Supplementary data available at *JTM* online; Strategy 2 and 3 show a diminished reduction of 73.6% and 75.6% in an alternate scenario where the global PCR sensitivity profile is reduced by 75%).

Several challenges exist however in our estimations moving forward, requiring the ascertaining of PCR test sensitivity as a function of the whole infection period and asymptomatic status, considerations of country-specific test practices and examining of the actual proportions of travellers who are likely to travel between countries that remains a significant current unknown. Political concerns should also be accounted for where the limited entry of travellers in Strategy 6 who are returning to their home country after long periods of stay abroad may not be feasible and dependent on country-specific entry policies. The use of immunity passports[19,40] or similar certification could help mitigate such ethical issues and relieve resource use for testing and quarantining should the traveller be confirmed to have been previously positive, or a vaccine become available. Their use however requires a better understanding of the dynamics of waning immunity and test sensitivity over time. Lastly,

country-specific estimates will require continued updating where the same analysis at different time points (Appendix 3 in Supplementary data available at *JTM* online; equivalent of Fig. 3 carried out on 28 June 2020) will show countries moving ranks according to their ongoing reported case numbers and deaths, although the relative efficacies of the strategies explored are expected to remain largely the same.

Supplementary data

Supplementary data mentioned in the text are available to subscribers in *JTMEDI* online.

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Conflict of interest

None declared.

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