International air travel-related control measures to contain the Covid-19 pandemic: A companion review to a Cochrane rapid review

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Abstract

Background: COVID-19 has proven to be challenging to manage for many reasons, including its high infection rate. One of the potential ways to limit its spread is by limiting international travel. The objective of this systematic review was to identify, critically appraise and summarise evidence on international air travel-related control measures for COVID-19.

Methods: This review is based on the Cochrane review: International travel-related control measures to contain the COVID-19 pandemic and followed the same methods. In brief, we searched for clinical and modelling studies in general health and COVID-19-specific bibliographic databases. The primary outcome categories were (i) cases avoided, (ii) a shift in epidemic development and, (iii) cases detected.

Results: From 6,202 citations identified by the search strategy, we included 22 new studies (modelling = 9, observational = 13) in addition to the 62 studies identified in the Cochrane review. Studies suggest that quarantine or microbial detection or a combination may avoid further cases. Similarly, these interventions may produce a positive shift in epidemic development and case detection may improve. Most studies were evaluated as having a moderate to critical risk of bias. The studies did not change the main conclusions of the Cochrane review nor the quality of the evidence (very low certainty); however, they added to the evidence base for most outcomes.

Conclusions: Weak evidence supports the use of international air travel-related control measures to limit the spread of COVID-19 via air travel. More real-world studies are required to support these conclusions.

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I. Background

In May 2020, the WHO Guideline Development Group (GDG) identified the effectiveness of quarantine, microbiological detection, and quarantine with microbiological detections as potential interventions to mitigate transmission of SARS-CoV-2, the coronavirus that leads to COVID-19, as a key public health intervention in need of immediate guidance. In response, two Cochrane Rapid Reviews [1,2] were published that summarized the evidence on the interventions till 13 November 2020. As the first review was early in the pandemic, researchers found no trials on this topic and instead used modelling and observational study designs that assessed the effectiveness of general international travel-related control measures during the COVID-19 pandemic on infectious disease transmission and screening-related outcomes. They reported that most studies compared travel-related control measures against a counterfactual scenario where the measure was not implemented [1]. Further, they noted that there was a common concern regarding the quality of modelling studies, particularly...
relating to potentially inappropriate assumptions about structure and input parameters and, an inadequate assessment of model uncertainty. For observational studies, the common concerns pertained to the selection of travellers, the reference tests, and the lack of clarity in reporting certain methodological aspects. They reported the effectiveness of travel restrictions aimed at reducing or stopping cross-border travel, quarantine, screening at borders, and the combination of quarantine and screening at borders to be of very low-certainty evidence.

Recently, the body of published and unpublished literature on COVID-19-related interventions grew exponentially. With this continuous growth in research, in June 2021, WHO commissioned an update to the Cochrane review in order to provide timely support for GDG activities.

The objective of this systematic review was to identify, critically-appraise and summarise evidence on international air travel-related measures to control the spread of SARS-CoV-2 transmission between countries and regions.

2. Methods

Since the goal of this rapid review was to update the Cochrane review, we aligned our methods to those in the published review by Burns et al., 2021 [1].

2.1. Criteria for considering studies for this review

We used the same criteria set out by Burns et al., 2021 [1]. We sought studies comprising:

Population: Human populations (without any age restriction) susceptible to SARS-CoV-2/COVID-19.

Intervention: Air travel-related control measures (specifically quarantine, microbiological detection or a combination thereof) affecting human travel across national borders.

Outcome(s): cases avoided due to the measure (e.g., number, proportion, rate of cases observed or predicted in the community with and without the intervention).

Shift in epidemic development due to the intervention (e.g., probability of epidemic, time to/delay in epidemic arrival or peak, size of epidemic peak, change in the effective reproduction number).

Cases detected due to the measure: we focused on outcomes we felt are most relevant for decision-makers in the current pandemic: the proportion of cases detected among the total number of cases (i.e., sensitivity, case detection rate) and the proportion of cases among those screening positive (i.e., the positive predictive value).

Types of studies: randomised trials, non-randomised trials, observational studies, and modelling studies on the effects of travel-related control measures affecting human travel during the COVID-19 pandemic.

2.2. Search methods for identification of studies

We adapted the search strategies from Burns et al., 2021 by excluding terms not-related to COVID-19 (such as MERS, H1N1, SARS01). Searches were conducted from the start of November 2020 until 6 June 2022. We did not add language restrictions to our search. We searched Scopus, PubMed (containing Medline citations), the Cochrane COVID-19 WHO COVID-19 Global Literature on Coronavirus disease, MedRXiv and BioRXiv. Due to limited access, we could not search Ovid MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions, Ovid Embase.

3. Data collection and analysis

3.1. Selection of studies

Each stage of the review was piloted. To ensure reporting accuracy, the team regularly met to discuss queries or difficulties arising during the review process. For study selection, two reviewers independently, and in duplicate, screened titles and abstracts in Rayyan [3]. Conflicting decisions were moved to full-text eligibility assessment. The same two reviewers independently, and in duplicate, screened full-text publications. Discrepancies were discussed among the review team until consensus was reached. The review team recorded the number of excluded citations and number and reasons for excluding full-text studies at the final selection stage.

3.2. Data extraction and risk of bias assessment

We designed, and piloted, data extraction and risk of bias forms using Microsoft Excel. We assessed risk of bias for observational studies using ROBINS-I [4]. There are no validated tools available to assess risk of bias of modelling studies; thus, we used the bespoke assessment tool described previously [1,5].

Data extraction, risk of bias of epidemiological studies and assessment of the quality of modelling studies was divided amongst the review team and cross-checked by at least one other reviewer for correctness and consistency. The two reviewers involved in these procedures discussed any discrepancies. It was essential that the author team reached consensus at every stage of this review. Thus, reviewers ensured that the highest methodological rigour was maintained.

3.3. Data synthesis

As we expected to find both observational studies and modelling studies, we separated the evidence based on study

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Furthermore, regardless of study design, it was expected that we would find extensive heterogeneity across all studies’ setting, population, intervention, and other contextual factors, as well as study methods. This meant that data would not be sufficiently similar to conduct meta-analyses. Therefore, we planned to descriptively synthesise the data, presenting the results as frequencies and in tables. We further stratified the evidence according to the interventions and outcomes. Further details on data synthesis are detailed in Burns et al., 2021 [1].

3.4. Assessment of heterogeneity and subgroup analyses

Similar to approach used by Burns et al., 2021 [1], we planned to ascertain and report the potential sources of heterogeneity that may influence intervention effectiveness.

3.5. Assessment of certainty of evidence

The certainty of evidence was rated as high, moderate, low or very low using the GRADE approach (Grading of Recommendation, Assessment, Development and Evaluation) [6]. We used the definitions described in Burns et al., 2021 to guide our reasons and decisions for rating observational studies and modelling studies [1]. Two reviewers independently assessed the evidence for the primary outcomes followed by discussion with another reviewer. Together they rated the certainty of evidence after consensus was reached. We descriptively synthesised the GRADE assessment in Summary of Findings (SoF) tables.

4. Results

4.1. Results of the search

The PRISMA flow diagram shown in Fig. 1 depicts the study selection process [7]. Of the screened 6,202 citations, and additional 16 studies, we included 22 studies that met the eligibility criteria: nine modelling studies [8–16] and 13 observational studies [17–29]. SoF tables depicting the evidence is provided in Tables 1–3. Characteristics of included studies are
TABLE 1. Quarantine (Summary of findings).

Interventions: implementing quarantine; implementing a highly stringent quarantine

Comparators: no measure; implementing an alternative measure; implementing a less stringent quarantine

| Outcome category: cases avoided due to the measure | Number of studies | Summary of findings | Certainty of evidence |
|--------------------------------------------------|-------------------|---------------------|-----------------------|
| Proportion of imported cases | 3 modelling studies [11,13,14] | All studies reported that quarantine (with or without symptoms) and with no testing is effective in reducing the risk of transmission. One study reported that 21-day quarantine had the highest efficiency at averting imported cases at 98.6% as compared with 14-day (91.8%) and 7-day (70.4%) periods; the remaining study demonstrated that quarantining passengers arriving from high-risk countries would result in a reduction in the proportion of imported cases ranging from 89% to 99%. The final study demonstrated the success of implementation of strict airport screening (no details available) and 14-day self-quarantine protocols in reducing the risk of importation of COVID-19 in arrivals from 3 international regions. No vaccination data included in the report. | Very low [B] |

| Outcome category: Shift in epidemic development | Number of studies | Summary of findings | Certainty of evidence |
|--------------------------------------------------|-------------------|---------------------|-----------------------|
| Time to diagnosis | 1 modelling study [15] | The study reported on the mean interval of diagnosis (in days) from arrival to laboratory confirmation. Results indicate both a maximal increase by 1.7 days, to a maximal decrease by 0.11 days. No vaccination data included in the report. | Very low [A] |

| Outcome category: cases detected due to the measure | Number of studies | Summary of findings | Certainty of evidence |
|--------------------------------------------------|-------------------|---------------------|-----------------------|
| Proportion of cases detected | 2 observational studies [20,21] | In the single study on quarantined commercial passengers with a PCR-negative result on arrival, 0.7% tested positive within 5–12 days of quarantine. In the second study on military, case positivity was 30.5%. | Very low [B] |
| Reduction in local transmission | 2 modelling studies [8,13] | These studies reported on isolation and quarantine. Chen demonstrated that implementing quarantine of all inbound travellers is the most efficient measure in preventing local transmission. Quarantine of symptomatic travellers only as compared with no quarantine results in a 5.1% and 23.3% reduction in local cases in China and Singapore, respectively. In the second study, immediate isolation following symptom onset prior to, or during, travel led to a 30–35% reduction in risk of transmission during travel. Quarantine (alone) implemented following exposure without symptom monitoring or testing, leads to a risk reduction from 64 to 95% (97 days) to 96–100% (14 days) | Very low [C] |
| Probability of releasing an infected individual into the community | 1 modelling study [15] | The study reported that the probability of an infectious person, with no scheduled testing, leaving quarantine period. The probability of releasing an infected individual into the community was 30.5% (21 days). No vaccination data included in the report. | Very low [D] |

*Downgraded –1 for indirectness, due to lack of reporting of external validation in some studies.
*Downgraded –1 for risk of bias due to quality concerns in some studies related to the appropriateness of the model’s structural elements, and the adequacy of assessment of the model’s uncertainty across some domains.
*Downgraded –1 for imprecision, due to only one contributing study.
*Downgraded –1 for imprecision, due to insufficient data reported to enable assessment of precision.
*Downgraded –1 for risk of bias due to quality concerns in the adequacy of assessment of the model’s uncertainty.
*Downgraded –1 for risk of bias due to quality concerns in one or more domains.
*Downgraded –1 for risk of bias due to quality concerns in one or more domains.
*Downgraded –1 for risk of bias, due to wide range of plausible effects.
*Downgraded –1 for indirectness, due to travellers not being representative of usual travellers.
*Downgraded –1 for risk of bias, due to uncertainty of temporal and geographical generalisability of data to all scenarios.

provided in Table S1. We excluded 56 studies with reasons for exclusion provided in Table S2. All studies were published in English.

4.2. Risk of bias and quality of included studies
We summarized the risk of bias for included observational studies and quality of the modelling studies in Table 4 and Table 5, respectively. Overall, the risk of bias is deemed to be critical and moderate across five and three studies, respectively.

4.3. Outcomes

1. Cases avoided due to the measure

4.3.1. Number or proportion of imported or exported cases
Together with three modelling studies identified in the search [11,13,14], a total of four studies [10,11,13,14] confirms that quarantine (with or without symptoms) and with no testing is effective in reducing the risk of transmission. Reduction in the proportion of imported cases ranged from 55% (7-days’ quarantine) to 99% (21 days’ quarantine). However, certainty of evidence was deemed as very low.

Two modelling studies on microbiological detection [11,15] was identified in the updated search. Assuming that exposure had occurred, pre-departure testing was predicted to improve the detection of cases by up to 84.4%, although results vary according to timing of the test.

Two modelling studies [10,11] demonstrated that a combination of quarantine and microbiological detection with a PCR test at day 7 significantly increases the proportion of cases averted as compared with quarantine alone, thus reducing the quarantine period.
One new modelling study [16] was identified in the updated search and reported that microbiological detection alone would delay an outbreak by 0.3 years. In combination with a 7-day quarantine or 21-day quarantine, the median time to outbreak respectively goes from to 0.6 years to virtual disappearance (very low-certainty evidence).

c. Risk of an outbreak

One new modelling study [16] reported that pre-flight testing together with mask usage, symptom reporting and contact tracing reduced the risk of an outbreak from 88% to 37% (very low-certainty evidence).

3. Cases detected due to the measure

This outcome is sub classified into (a) Proportion of cases detected, (b) Reduction in local transmission and (c) Probability of releasing an infected individual into the community.

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### TABLE 2. Microbiological Detection (Summary of findings).

| Outcome category: cases avoided due to the measure | Outcome | Number of studies | Summary of findings | Certainty of evidence |
|----------------------------------------------------|---------|-------------------|---------------------|-----------------------|
| Number or proportion imported | 2 modelling studies [1,15] | Assuming that exposure may have occurred at any time in the 7 days prior to departure, pre-departure testing can reduce risk of transmission during travel from 10% to 72%, with reduction in mean interval of diagnosis from arrival to diagnosis. The addition of entry testing to pre-departure testing improves the detection of cases imported from 57.2% (2-day pre-departure testing) to 84.8% (83.1% for rapid antigen pre-departure and on arrival). Results vary according to timing of pre-departure test. | Very lowα,c |

| Outcome category: Shift in epidemic development | Outcome | Number of studies | Summary of findings | Certainty of evidence |
|------------------------------------------------|---------|-------------------|---------------------|-----------------------|
| Median time to outbreak | 1 modelling study [16] | The study reported that pre-flight saliva testing (assuming a 62% sensitivity) will delay an outbreak by 0.3 years (95% range of simulations: 4 days to 1.7 years); mean number of flights to outbreak = 170. Increasing the number of testing days after arrival reduces the median waiting time to the next outbreak. For example, pre-flight testing plus PCR tests on days 1, 3 and 12 delayed an outbreak by 0.7y (19d–3.6y); mean number of flights to outbreak = 359 as compared with preflight testing and testing on day 1 only, 0.4y (6d–2.3y); 225 flights. The best result is observed with pre-flight testing plus PCR tests on days 1, 3 and 12 combined with mask usage until the last test, symptom reporting and contact tracing resulting in a delay of 1.5 years (20d–8.1 y); 802 flights | Very lowα,β |

| Outcome category: cases detected due to the measure | Proportion of cases detected | 10 observational studies [18,20,22–29] | Across the studies, the proportion of cases amongst all travellers detected ranged from 0.01% to 1.5% over the periods of the study. One of the studies reported success at utilising self-collection of samples conducted at 4 days post-arrival. | Very lowα,c |
|--------------------------------------------------|-----------------------------|------------------------------------------|-------------------------------------------------|-----------------------|
| Reduction in transmission | 1 modelling study [12] | Pre-departure testing can reduce risk of transmission during travel between 10 and 72% depending on time interval between testing and day of travel. Variation in results is dependent on time of specimen collection, (with greatest effectiveness if taken on day of travel), and degree of sensitivity of the test, (with higher sensitivity test giving a higher reduction in risk). A single test reduces the risk of transmission after travel from 29 to 33%, regardless if performed at one or two days post-arrival. | Very lowα,β |

αDowngraded –1 for indirectness, due to lack of reporting of external validation in some studies.
βDowngraded –1 for imprecision, due to insufficient data reported to enable assessment of precision.
γDowngraded –1 for risk of bias due to quality concerns in the adequacy of assessment of the model's uncertainty, and incomplete technical documentation.
δDowngraded –1 for imprecision, due to only one contributing study.
εDowngraded –1 for risk of bias due to quality concerns in one or more domains.
γDowngraded –1 for indirectness, due to variation in testing methods.

2. Shift in epidemic development

This outcome is sub classified into 3 categories, namely (a) Time to diagnosis, (b) Median time to outbreak and (c) Risk of an outbreak.

a. Time to diagnosis

One new modelling study [9] on quarantine alone and in combination with microbiological detection assesses time to diagnosis. The results suggest that these interventions would decrease the mean interval of diagnosis from arrival to laboratory-confirmation by up to 1.7 days. However, magnitude of effect may depend on testing sufficiency and lab capacity and policy implementation.

b. Median time to outbreak

One new modelling study [16] was identified in the updated search and reported that microbiological detection alone would delay an outbreak by 0.3 years. In combination with a 7-day quarantine or 21-day quarantine, the median time to outbreak respectively goes from to 0.6 years to virtual disappearance (very low-certainty evidence).

c. Risk of an outbreak

One new modelling study [16] reported that pre-flight testing together with mask usage, symptom reporting and contact tracing reduced the risk of an outbreak from 88% to 37% (very low-certainty evidence).

3. Cases detected due to the measure

This outcome is sub classified into (a) Proportion of cases detected, (b) Reduction in local transmission and (c) Probability of releasing an infected individual into the community.
### TABLE 3. Combination of Quarantine and Microbiological Detection (Summary of findings).

| Outcome category | Number of studies | Summary of findings | Certainty of evidence |
|------------------|-------------------|---------------------|-----------------------|
| **Outcome category: cases avoided due to the measure** | | | |
| Number or proportion | 2 modelling studies | One study demonstrated that a combination of quarantine with a day 7 PCR test/1 day delay in PCR. Very low results, gives a median reduction of 94% (UI 95%: 89%–98%) in infectious arriving-travellers being released into the community compared with no quarantine/no test scenario. For comparative outcomes with a no-testing scenario, a 14-day quarantine (median>99% with 95% UI = 98%–100%). A 5-day quarantine with a PCR-negative test results in a median reduction of 89% (UI, 83%–95%). Additionally, including pre-flight testing serves to reduce the duration of the quarantine period. The remaining study demonstrated that a PCR test on arrival increases the proportion of cases imported as compared with quarantine alone, especially for quarantined periods 7 days or less. The addition of a test upon exiting quarantine further increases the cases detected, especially at quarantine periods ≥ 5 days. Utilising a pre-departure test together with PCR on arrival and rapid antigen testing when exiting quarantine showed the best performance overall with detection of cases equal to 91.2% (3 days quarantine) to 99.3% (21 days quarantine). No vaccination data included in the report. | |
| **Outcome category: Shift in epidemic development** | | | |
| Time to Diagnosis | 1 modelling study [19] | The study reported on the mean interval of diagnosis (in days) from arrival to laboratory confirmation. Results indicate both a maximal increase by 0.92 days, to a maximal decrease by 0.79 days. No vaccination data included in the report. | Very low\(\text{a,b,c,d}\) |
| Risk of outbreak | 1 modelling study [16] | The study reported that pre-flight testing combined with 7-day quarantine has a risk of 67.8% of an annual outbreak; lengthening the quarantine period reduces the risk to 13.1% (14 days) to virtually zero risk with a 21-day quarantine period. No vaccination data included in the report. | Very low\(\text{a,b,c,e,f,g}\) |
| **Outcome category: cases detected due to the measure** | | | |
| Proportion of cases detected | 2 observational studies [17-19] | The two studies utilising a combination of testing and quarantine as interventions, reported COVID positivity on arrivals ranging from 0.87% to 1.2%. No vaccination data included in the report. | Very low\(\text{a}\) |
| Reduction in transmission | 1 modelling study [12] | On day 5–6: risk reduction = 97–100%. No vaccination data included in the report. | Very low\(\text{a}\) |
| Probability of releasing an infected individual into the community | 1 modelling study [15] | Quarantine with testing of all incoming travellers would result in a risk of imported cases being released into the community of 25% following a 7-day quarantine period. 1–7% of infected travellers will be released into the community depending on level of transmission with quarantine facilities. No vaccination data included in the report. | Very low\(\text{a}\) |

\(\text{a. Proportion of cases detected}\)

For this outcome, two observational studies on quarantine [20,21], were identified in the updated search, thus adding to the single earlier modelling study [30] which indicated an increasing positivity correlating with increased quarantine. Amongst participants released from quarantine following a negative test result on arrival, positive cases constituted in excess of 30% in observational studies (very low-certainty evidence). However, generalisability of these results may be impacted given that passengers in these studies were not stratified according to air vs travel, and the second study comprised military-related conditions.

Ten observational studies assessing the impact of microbiological detection alone on this outcome [18,20,22–29] reported detecting from 0.01% to 1.5% of cases amongst all travellers. One of the studies incorporated self-collection of samples conducted at 4 days post-arrival [18].

Two observational studies assessed the impact of a combining quarantine and microbiological detection on this outcome, reporting positivity rates of 0.2% and 0.6% following 10–14 days of quarantine amongst >25,000 PCR-negative arrivals to Bahrain [17]. The second study observed 26% positivity, with the majority detected within the first week [19].

\(\text{b. Reduction in local transmission}\)
Two modelling studies assessing the impact of isolation and quarantine on reducing local transmission [8,12] were identified by the updated search. Implementing quarantine for all inbound travellers is the most efficient measure in reducing local cases (by up to 23.3%). An even greater reduction (30–35%) was observed through immediate isolation following symptom onset prior to, or during, travel while quarantine implemented following exposure without symptom monitoring or testing, leads to a risk reduction from 64 to 95% at 7 days to 96–100% at 14 days.

A single study reported that pre-departure testing can reduce risk of transmission during travel by between 10 and 72% depending on time interval between testing and day of travel. Time of specimen collection, and degree of sensitivity of the test may introduce variability in the results.

Combination of interventions comprised a single study [12] showing that on day 5–6, risk reduction was equal to 97%–100%.

c. Probability of releasing an infected individual into the community

No new studies were identified in the updated search. The findings of the earlier review of three modelling studies [10,15,31] reported quarantine as having a positive effect on the probability of releasing an infected individual into the community. Steyn indicated that the probability of effect varies according to moderate and high transmission conditions [15].

Combination of interventions had a single study [15] indicating that quarantine with testing of all incoming travellers would result in a risk of imported cases being released into the community of 25% following a 7-day quarantine period.

5. Discussion

The positive effect of quarantine was previously shown to contain severe acute respiratory syndrome (SARS) [32]. Microbiological detection, a relatively novel approach to travel screening to avoid new cases and shifting the epidemic, had not been assessed prior to the onset of COVID-19. It is thus expected that, combining quarantine and microbiological detection presents a powerful intervention in pandemic scenarios [1]. This review found, for all outcomes evaluated, very low certainty of evidence on the effectiveness of quarantine, microbiological detection and, quarantine with microbiological detections as potential interventions to mitigate transmission of SARS-CoV-2. This work, a companion piece to a recent Cochrane Review [1], includes nine modelling studies and 13 observational studies as identified until 06 June 2022.
limitation to our findings is that none of the studies reported data or information on COVID-19 vaccines. Therefore limiting the true effectiveness of these interventions.

Prior to the global COVID-19 vaccine rollout, the interventions used in this particular field of research were rapidly growing. Many more studies of higher quality and better design were published since the earlier review, underscoring the importance of an updated search and review that combines our findings with those from Burns et al., 2021 to further strengthen the evidence base [1]. However, as in the earlier review, lack of information on the potential financial and human resources needed to employ the measures evaluated in the studies of this review, hampers the generalisability of the findings [1]. This information would indeed be necessary for low- and middle-income country regions with healthcare systems that are not well-resourced or resilient enough to take a further strain on resources, not to mention having been overburdened prior to the pandemic. Furthermore, none of the studies report the potential bio-psycho-social impact these interventions may have on the health of those receiving the intervention; for example, quarantine may negatively impact the mental well-being of travellers, not to mention those predisposed or with fragile mental health, including its effects on the financial impact on those unable to work and the potential economic bearing, as well as the societal disapproval of those with a positive diagnosis [1]. Lastly, each included study was conducted at different times of the pandemic and in different regions. This means that the pandemic waves differed between studies. In the same way, the COVID-19 variants likely differed depending on the region and the time of analysis.

5.1. Implications for practice, policy
Considering the findings reported in Burns et al., 2021 [1] and the findings from this companion review, it is implied, with very low certainty of the evidence, that these international air travel-related control measures positively impact mitigating the spread of COVID-19. These interventions’ actual effects may differ considerably from those reported in this review, be they in a more or less positive, or negative, direction. Generally, one may deduce that quarantine may reduce the spread of the virus. This control measure relies on strict compliance to policy implementation including the period of stay before discharge on the part of an individual, and border control staff. Furthermore, while screening may detect, at least, some COVID-19 cases, it remains questionable whether screening effectively detects enough cases to prevent regional outbreaks. Therefore, quarantine and screening combined is possibly the most effective travel-control measure of the three options investigated in this review. However, by providing a vaccine status, countries may choose to avoid these measures. Lastly, for this review, one needs to consider that changes in the travellers’ immunity as a result of vaccination or previous infection may impact the effectiveness of the measures conducted earlier in the pandemic compared with those conducted more recently.

TABLE 5. Summary of quality appraisal for modelling studies.

| Domain               | Questions                                                                 | Chen Z 2021 | Chen T 2021 | Dickens 2020 | Johansson 2021 | Lee 2021 | Pan 2021 | Steyn 2021 | Wilson 2021 | Clifford 2021 |
|----------------------|---------------------------------------------------------------------------|-------------|-------------|---------------|-----------------|-----------|-----------|------------|--------------|---------------|
| Model structure      | 1. Are the structural assumptions transparent and justified?              | Yes         | Yes         | Yes           | Yes             | Yes       | Yes       | Yes        | Yes          | No            |
|                      | 2. Are the structural assumptions reasonable given the overall objective,  | Yes         | Yes         | Yes           | Yes             | Yes       | Yes       | Yes        | Yes          | Yes           |
|                      |   perspective, and scope of the model?                                    |             |             |               |                 |           |           |            |              |               |
|                      | 3. Are the input parameters transparent and justified?                    | Yes         | Yes         | Yes           | Yes             | Yes       | Yes       | Yes        | Yes          | Yes           |
|                      | 4. Are the input parameters reasonable?                                   | Yes         | Yes         | Yes           | Yes             | Yes       | Yes       | Yes        | Yes          | Yes           |
| Validation (external)| 5. Has the external validation process been described?                    | No          | Yes         | No            | Yes             | Yes       | Yes       | Yes        | Yes          | No            |
|                      | 6. Has the model been shown to be externally valid?                       | No          | Yes         | No            | Yes             | Yes       | Yes       | Yes        | Yes          | No            |
| Validation (internal)| 7. Has the internal validation process been described?                    | No          | Yes         | No            | Yes             | Yes       | Yes       | Yes        | Yes          | No            |
|                      | 8. Has the model been shown to be internally valid?                       | Yes         | Yes         | Yes           | Yes             | Yes       | Yes       | Yes        | Yes          | Yes           |
| Uncertainty          | 9. Was there an adequate assessment of the effects of uncertainty?        | Yes         | Yes         | Yes           | Yes             | Yes       | Yes       | Yes        | Yes          | Yes           |
| Transparency         | 10. Was technical documentation, in sufficient detail to allow (potentially) for replication, made available openly or under agreements that protect intellectual property? | Yes         | Yes         | Yes           | Yes             | Yes       | Yes       | Yes        | Yes          | Yes           |
Although this review investigated three travel control measures, decision-makers need to note that mitigating cross-border COVID-19 transmission requires a multi-pronged approach in addition to those presented here. These include, but are not limited to, wearing face masks that are effective, acceptable and suitable, personal hygiene and physical distancing at the airport before, or after, flights and during air travel [1]. Moreover, policymakers need to consider that there is considerable variation in the implementation each of the interventions in this review. For example, quarantine may be implemented before, or after, travel, or at both stages. The length of quarantine may differ from 3 days up to 14 days. The manner in which passengers are quarantined may also vary: there are countless combinations where, in some cases, all passengers are quarantined together, or there is a division between those symptomatic to those asymptomatic and those that screened negative or positive alone may be placed in isolation or in groups. Similarly, we found different combinations of screening. The type of tests used, how tests are conducted e.g. nasal vs oral samples and who conducts tests may differ. In some cases, it may be done before, or after, travel. The time intervals before travel and after arrival may vary. Furthermore, policies may be adjusted according to changes in the epidemiology of the pandemic, i.e. changes in virus variants, such as those with greater infectiousness or greater severity or vice versa, including the prevalence at the time in a specific nation.

This review emphasizes the demand for updated high-quality research to facilitate the compilation of decision-makers’ policies. Collaboration between researchers and decision-makers in designing studies and developing questions to delay the spread of infection for the current pandemic, and those that may still arise, is essential. Naturally, observational studies are more likely to be conducted than modelling studies given that observational studies are considered to be methodologically superior in design. Since randomised controlled trials are costly, time-consuming and ethically questionable, depending on the exposure, meticulously conducting and reporting future observational studies will ensure that future systematic reviews can draw from the best available evidence that can then be used to advise on ever-changing and intricate decisions, especially given that availability of peer-reviewed risk of bias assessment tools for observational studies. Future primary research should consider the benefits and harms that these interventions may have on the bio-psycho-social aspects of passengers and the greater society, including the potential economic impacts. Our findings may be a useful proxy for future pandemics of this nature.

6. Conclusions

We identified 22 studies which consisted of modelling and observational studies in addition to the earlier Cochrane review’s 31 studies. These studies compared the effectiveness of air travel-related control measures (specifically quarantine, microbiological detection or a combination thereof) as a means to limit the spread of COVID-19. These additional studies do not alter the findings, nor the quality of the evidence (very low certainty) as found in the Cochrane Review. Due to the nature of GRADEing the certainty of the evidence for modelling and the observational studies, it is unlikely that more studies with these designs will change the quality of the evidence. Generally, the data, with very low certainty of evidence, indicate that these interventions are effective. However, there is a need for higher quality observational and experimental studies to support our findings.

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CRediT authorship contribution statement

Ammeer S-J Hohlfeld: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Writing – original draft, Project administration. Leila Abdullahi: Validation, Resources, Writing – review & editing. Ahmed M. Abou-Setta: Validation, Resources, Writing – review & editing. Mark E. Engel: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Writing – original draft, Project administration.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nmni.2022.101054.

References

[1] Burns J, Movsisyan A, Stratil JM, Biallas RL, Coenen M, Emmert-Fees KM, et al. International travel-related control measures to contain the COVID-19 pandemic: a rapid review. Cochrane Database Syst Rev 2021.

[2] Burns J, Movsisyan A, Stratil JM, Coenen M, Emmert-Fees KM, Geffert K, et al. Travel-related control measures to contain the
COVID-19 pandemic: a rapid review. Cochrane Database Syst Rev 2020.

[3] Ouzzani M, Hamzady H, Fedorowicz Z, Elmagarmid A, Rayyan—a web and mobile app for systematic reviews. Syst Rev 2016;5:1–10.

[4] Sterne JA, Hernan MA, Reeves BC, Savovic J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355:i4919.

[5] Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011;155:529–36.

[6] Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011;64:383–94.

[7] Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:e1000097.

[8] Chen T, Huang S, Li G, Zhang Y, Li Y, Zhu J, et al. An integrated framework for modelling quantitative effects of entry restrictions and travel quarantine on importation risk of COVID-19. J Biomed Inf 2021;180:103800.

[9] Chen Z, Yu M, Wang Y, L Z. The effect of the synchronized multi-dimensional policies on imported COVID-19 curtailment in China. PLoS One 2021;6:e0252224.

[10] Clifford S, Quilty BJCS, Flasche S, Kucharski AJ, Edmunds WJ, Russell TW, Liu Y, Chan YD, Pearson CAB, et al. Strategies to reduce the risk of SARS-CoV-2 importation from international travellers: modelling estimations for the United Kingdom. July 2020 Euro Surveill: bulletin European sur les maladies transmissibles = European communicable disease bulletin 2021;26.

[11] Dickens BL, Koo JR, Lim JT, Park M, Sun H, Sun Y, et al. Determining quarantine length and testing frequency for international border opening during the COVID-19 pandemic. J Trav Med 2021;28.

[12] Johannson MAWH, Paul P, Diaz PS, Chen T-H, Brown CM, Cetron MS, Alvarado-Ramy F. Reducing travel-related SARS-CoV-2 transmission with layered mitigation measures: symptom monitoring, quarantine, and testing (preprint). medRxiv 2020;2020.2020.20237412. 11.23.

[13] Lee H, Kim Y, Kim E, S L. Risk assessment of importation and local transmission of COVID-19 in South Korea: statistical modeling approach. JMR Publ Health Surveill 2021;7:e26784.

[14] Pan J, Tian J, Xiong H, Liu Z, Yao Y, Wang Y, et al. Risk assessment and evaluation of China’s policy to prevent COVID-19 cases imported by plane. PLoS Neglected Trop Dis 2020;14:e0008908.

[15] Steyn N, Plank MJ, James A, Binney RN, Hendy SC, Lustig A. Managing the risk of a COVID-19 outbreak from border arrivals. medRxiv 2020;2020.20154955. 07.15.

[16] Wilson NBM, Blakely T, Eichner M. Estimating the impact of control measures to prevent outbreaks of COVID-19 associated with air travel into a COVID-19-free country. Sci Rep 2021;11:10766.

[17] Abdulrahman AAM, AlAwadhi A, Al-Tawfiq JA, Rabaa AA, Atkin S, AlQahtani M. Quarantining arriving travelers in the era of COVID-19: balancing the risk and benefits a learning experience from Bahrain. Trop Dis Travel Med Vacin 2021;7:1.

[18] Cao-Lormeau VMTI, Teissier A, Richard V, Aubry M. Self-sampling kit delivered to travelers for COVID-19 testing 4 days after arrival in French Polynesia. July 2020-February 2021 Trav Med Infect Dis 2021;43:102098.

[19] Fotheringham P, Anderson T, Shaw M, Jewitt J, Storey H, Hutchings O, et al. Control of COVID-19 in Australia through quarantine: the role of special health accommodation (SHA) in New South Wales, Australia. BMC Publ Health 2021;21:225.

[20] Lunney M, Ronksley PE, Weaver RG, Barnieh L, Blue N, Avey MT, et al. COVID-19 infection among international travellers: a prospective analysis. BMJ Open 2021;11:e050667.

[21] O’Donnell MTKj, Mitchell CA, Gurney JM. Mitigating SARS-CoV-2 in the deployed environment. Mil Med 2021.

[22] Ohlsen EC, Porter KA, Mooring E, Cutchins C, Zink A, J M. Airport traveler testing program for SARS-CoV-2 - Alaska, June-November 2020. MMWR. Morb Mortal Weekly Rep 2021;70:583–8.

[23] Tande AJ, Bin Nickjer MJ, Ting HH, Del Rio C, Jali L, Brawner M, et al. SARS-CoV-2 testing before international airline travel. December 2020 to May 2021. Mayo Clin Proc 2021;96:2856–60.

[24] Zhang J, Qin F, Qin X, Li J, Tian S, Lou J, et al. Transmission of SARS-CoV-2 during air travel: a descriptive and modelling study. Ann Med 2021;53:1569–75.

[25] Williams GH, Llewelyn A, Brandao R, Chowdhary K, Hardisty K-M, Loddo M. SARS-CoV-2 testing and sequencing for international arrivals reveals significant cross border transmission of high risk variants into the United Kingdom. Eclinicalmedicine 2021;38:101021.

[26] Tsuibo M, Hachiya M, Ohtsu H, Akashi H, Miyoshi C, Umeda T. Epidemiology and risk of COVID-19 among travelers at airport and port quarantine stations across Japan: a nationwide descriptive analysis and an individually matched case-control study. Clin Infect Dis: an Official Publication of the Infectious Diseases Society of America 2021.

[27] Randremanana RV, Andriamandimby SF, Rakotondrampaja JM, Razanajatovo NH, Mangahasimbola RT, Randriambolamanantsoa TH, et al. The COVID-19 epidemic in Madagascar: clinical description and laboratory results of the first wave, march-september 2020. Influenza Other Respir Virus 2021;15:457–68.

[28] Molero-Salinas A, Rico-Luna C, Losada C, Buenestado-Serrano S, de la Cueva Garcia VM, Egido J, et al. High SARS-CoV-2 viral load in travelers arriving in Spain with a negative COVID-19 test prior to departure. J Trav Med 2022;29:taab180.

[29] Luo Z, Zhang Y, Zheng Y, Maclntyre CR, Liang Y, Wang Q, et al. Prevention of SARS-CoV-2 transmission from international arrivals: Xiaotangshan designated hospital, China. Bull World Health Organ 2021;99:137.

[30] Taylor R, McCarthy CA, Patel V, Moir R, Kelly L, Snary E. The risk of introducing SARS-CoV-2 to the UK via international travel in August 2021;99:260.

[31] Randremanana RV, Andriamandimby SF, Rakotondrampaja JM, Razanajatovo NH, Mangahasimbola RT, Randriambolamanantsoa TH, et al. The COVID-19 epidemic in Madagascar: clinical description and laboratory results of the first wave, march-september 2020. Influenza Other Respir Virus 2021;15:457–68.

[32] Lufton NA, Al-Arifi M, AlQahtani M. Quarantining arriving travelers in the era of COVID-19: balancing the risk and benefits a learning experience from Bahrain. Trop Dis Travel Med Vacin 2021;7:1.

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