Emerging Evidence on COVID-19

Evidence Brief of COVID-19 quarantine length reduction strategies and effectiveness, Update 1

Introduction

What is the effectiveness of shortened quarantine with and without testing for SARS-CoV-2?

This evidence brief identifies and summarizes published and pre-published data on alternative quarantine strategies (e.g. combinations of RT-PCR testing and quarantine) to explore the potential trade offs compared to the 14-day quarantine currently used. Studies up to December 3, 2020 are included.

Quarantine was one of several public health interventions adopted early in the COVID-19 pandemic by many jurisdictions. Quarantine period in this brief refers to the length of time that must elapse before a person potentially exposed to SARS-CoV-2 can be considered incapable of developing or transmitting COVID-19. The practice may be applied for incoming travellers to a region, suspected cases and/or known contacts of an index case. While many studies have explored the effectiveness of quarantine in reducing COVID-19 transmission, here we focus on the effectiveness of reduced quarantine length with and without testing. Countries have been managing the COVID-19 pandemic for roughly 10 months, and are now looking for effective interventions to reduce transmission while also limiting the negative impact of quarantine on the individual, society and the economy.

It is estimated that the current incubation period for SARS-CoV-2, the time from exposure to symptom onset averages five days (with a range of 1-14 days). It is also estimated that the infectious period may start 1-2 days before symptom onset and continue in mild cases for approximately 8-10 days (1). Exposed contacts may have knowledge of when they were most likely exposed to a known COVID-19 case, if identified by contact tracing. Travellers entering a country may be at any point in their infection from recently exposed to late in an infection at arrival. Quarantine strategies for case contacts and travellers will likely differ in their approach, but the goal is similar, to prevent transmission of SARS-CoV-2 from infected individuals.

An active SARS-CoV-2 infection is most commonly established by RT-PCR testing of a nasopharyngeal or other respiratory mucous membrane swab. The sensitivity of the RT-PCR test depends on many factors including virus load in the sample. Early in an infection the virus load may be very low and there is a high likelihood of a false negative result, which decreases as virus load increases; an example from a meta-analysis indicates false negative results are ~100% on days 1-3, 67% on day 4, 38% on day 5 (symptom onset) and 20% on day 8 post exposure (2, 3). Models included in this review consider a distribution for the sensitivity of the RT-PCR from exposure through infectious period with sensitivity increasing rapidly two days before infection to over 80% and remains high for eight or more days after symptom onset (4). Usually as infection progresses the viral load will increase, studies show variability in peak viral load timing from just before to up

to five days after symptom onset and gradually decreasing as the infection is cleared. Rapid antigen detection tests (RADT) have also started to emerge as a diagnostic tool for COVID-19 (5). RADT tests are cheaper, quicker and easier to perform than the RT-PCR, but likely suffer from lower sensitivity (5). The field performance of RADTs are less certain than RT-PCR, thus models that explored the use of RADTs as a testing option frequently cited a dearth of data on RADT performance (5). Within this review, the test modelled is mainly RT-PCR with the exception of the most recent models which look at scenarios with RT-PCR separately from RADTs.

Key Points

- Since the first version of this evidence brief, one pre-published model was updated, and one rapid review and thirteen models have been released, eleven of which are prepublications that have not completed a peer review process. The rapid review confirms that there was very little research prior to June 26 on the efficacy of quarantine for SARS-CoV-2 as well as SARS-CoV-1 and MERS. The publications in Table 1 and 2 have been issued since the review was conducted and include eight studies that focus on effective quarantine period strategies in the community for contacts of cases and fourteen studies focus on quarantine strategies for travellers to reduce the risk of importation of SARS-CoV-2.
- Two epidemiological studies in Table 1 and 2 and the rapid review in Table 3 describe observed data about the effectiveness of the 14-day quarantine period for both case contacts and travellers. These studies indicate that the 14-day quarantine was effective and the addition of an RT-PCR improved the effectiveness of the quarantine strategy.
- Quantitative models (n=17) concur the 14-day quarantine strategy is effective and explore several alternative scenarios for quarantine and test strategies in the community (Table 1) and for travellers (Table 2).
    - Shorter quarantines (seven or more days) with at least one test completed near the end of the quarantine were fairly equivalent to 14 days with no test (Table 1 & 2). Scenarios where quarantine was less than seven days were consistently less effective compared to longer quarantine.
    - Without the addition of a test, effectiveness increased over time from seven days (50-60% median range) to ten days (68-84%) compared to fourteen days.
    - Testing travellers on arrival and not quarantining those with a negative result was significantly less effective (~40%) than quarantine strategies of one week or longer with various testing strategies.
    - Testing close to the end of the quarantine period was the most effective time point in most scenarios, because individuals initially in the incubation period have a longer time for virus load to increase and thus be detected. This was particularly true to all quarantine scenarios less

than seven days. For quarantines seven days and longer, a test at seven days was just as effective as a test performed later.

- Testing multiple times during the quarantine period resulted in minimal reduction in the risk of releasing an infectious person into the community compared to testing one time close to the end of quarantine.

- Evidence from quantitative models suggests that testing and quarantine strategies for community contacts and travellers are similar when considering testing at quarantine lengths greater than one week. For strategies less than one week, test and quarantine strategies are less effective in the community because case contacts may be early in their incubation period and test results would have a high false negative rate. This is less of an issue for travellers that may be at any point in their infection, but there is still a risk of releasing travellers early in their incubation period.
- For both community contacts and travellers, the models captured have started to look at quarantine strategies that use RT-PCR or RADTs. The RADT sensitivity is predicted in most of the models to lag behind the RT-PCR, which translated to optimal test and quarantine model results suggesting that doing an RT-PCR on day five of quarantine or the RADT on day six was equivalent. However, depending on the turn around time for the RT-PCR test (reported to be 24 to 96 hours), the RADT would shorten the quarantine period because results would be obtained on day six assuming there is minimal wait for RADT results.
- Adherence to quarantine was also discussed and modelled in several studies. All studies concluded that adherence is higher with shorter quarantines and the impact of quarantine in real life is likely much lower than reflected in the models due to a lack of compliance.

Overview of the Evidence

The review identified and summarized twenty published and pre-published studies. The limited research focused on quarantine to reduce transmission among case contacts in the community and by traveller introduction of COVID-19.
Seventeen quantitative models and risk assessments were included. These do not identify actual outcomes of strategies that have been tested, but rather present a range of plausible outcomes within theoretical scenarios being studied. Their results are useful to compare different options as part of a decision-making process, however the results should be interpreted with caution as the models will vary on their assumptions, input values based on the epidemic period and region specific parameters used.

Two epidemiological investigations, related to contact tracing or quarantine and surveillance of passengers arriving at the airport were identified. These observational studies have a moderate to high risk of bias due to selection, reporting and follow-up biases.

A single rapid review was conducted, it is considered of moderate quality by AMSTAR because only on person assessed and extracted data from each study. Within this review six additional epidemiological investigations and one model were identified for SARS-CoV-2 with similar biases as noted above.

Important knowledge gaps were identified. The knowledge base on quarantine scenarios is largely supported by models, thus there is a lack of empirical evidence on the impact quarantine has on the epidemic, particularly in a local context. Additional information on adherence to quarantine could help with future decision making on this issue. It was also noted that little performance data exists for new diagnostic tools such as RADTs, thus testing and quarantine scenarios for RADTs may change as data becomes available.

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QUARANTINE EFFECTIVENESS: CASE CONTACTS

Table 1 presents nine studies that examined quarantine within the community. An epidemiological account of the epidemic in Macao is presented that implemented a 14-day quarantine with a test on day 13 which successfully prevented known onward transmission (6). Seven modelling studies and one risk assessment explored the role of quarantine in controlling the epidemic. One model looked at how contact tracing (or delays in contract tracing) and adherence affect the effectiveness of different quarantine strategies ranging from no quarantine with symptom based isolation to 7, 10 or 14 day quarantines with or without one to two RT-PCR tests and concluded a 7-day quarantine with a test was equivalent to a 14-day quarantine (7). Quarantine and test strategies from quantitative models suggests that testing and quarantine strategies for community contacts and travellers is similar when considering testing quarantine lengths greater than one week. However, strategies less than one week, test and quarantine strategies are less effective in the community because case contacts may be early in their incubation period.

Other important considerations, particularly in the most recent studies, were type of test and adherence to quarantine. Models have started to look at quarantine strategies that use RT-PCR or a RADTs and strategy optimization findings were test dependent. Adherence to quarantine was examined and results suggest that adherence is higher with shorter quarantines and the impact of quarantine is likely much lower than reflected in the models due to a lack of compliance.

Table 1: Epidemiologic and modelling studies on quarantine of suspected symptomatic and/or potentially exposed individuals in the community. (n=9)

STUDY	METHOD	KEY OUTCOMES
Epidemiological studies		
Lio (2020) (6) Case investigations Macao Jan-Apr 2020	This paper describes successful quarantine (14 days) of individuals who developed symptoms of COVID-19 or were identified as possibly exposed through contact tracing in Macao, a special administration region of China January 22 through April 8, 2020. A 14-day quarantine with an RT-PCR test on day 13 to confirm negative status was implemented in Macao.	Based on surveillance data no, infectious cases were released from quarantine, two people tested positive on the day 13 RT-PCR test. The total number of people quarantined was not reported.
Modelling studies		
Quilty (2020) (7) *preprint updated* Modelling study UK* 2020*	An agent-based model was developed to simulate different quarantine scenarios for identified contacts of a confirmed index case of COVID-19. The model accounts for the time of identification and contact tracing (average is 4 days) as well as the risk of releasing an infected person from quarantine.	This study explored quarantine scenarios from 3-15 days (in graphs) and effectiveness of quarantine based on adherence. Key outcomes for prevention of onward transmission: • Self isolation based on symptoms (no quarantine) prevents 39% (95%UI; 34 – 45%) onward transmission. • 14-day quarantine prevents 70% (95%UI: 39 – 90%) onward transmission. • A negative RT-PCR upon being traced as a contact (~4 days post exposure) prevents 62% (95%UI: 40 - 84%) onward transmission. • A negative RT-PCR 7 days post exposure prevents 68% (95%UI: 40 - 88%) onward transmission. 10 days 69% (95%UI: 41-90%) and 14 days 70% (95%UI: 40-91%).

		• The 7-day quarantine with 1 test was equivalent to the 14-day quarantine with no test. • Testing upon contact tracing and at the end of quarantine had minimal gains in preventing transmission. • A delay of notifying a contact of exposure of 4 days is estimated to result in transmission potential of 26% (95%UI: 7 - 56%) and halving that to 2 days would decrease the transmission potential to 14% (95%UI: 5 - 42%).
Lewis (2020) (8) *preprint* Risk Assessment USA* 2020*	Using the 14-day quarantine as the benchmark for acceptable risk of a COVID-19 case being released from quarantine (estimated to be 0.5%), the authors use this benchmark to quantitatively explore other quarantine strategies. In this risk assessment the outcome is presented as the likelihood of being infectious given a person was symptom-free in quarantine for *x* days.	• A non-symptomatic person with a negative COVID-19 test at day 7-8 would have a lower risk of being infectious (0.4%) than someone completing a 14-day quarantine. This relationship was robust regardless of someone's initial exposure risk. Type of test received was not explored. • Shorter quarantine would improve compliance, decrease economic burden and may better identify asymptomatic infected individuals.
Peng (2020) (9) *preprint* Modelling study USA* 2020*	Simulations (individual-based forward-time simulation method) of quarantine strategies were used to explore the efficacy of strategies that include one or more tests administered during quarantine. The statistical models developed estimate the transmissibility and viral loads of SARS-CoV-2 infections, and the sensitivities of available SARS-CoV-2 testing methods.	Optimal alternative strategies to the 14-day strategy with no test included: RT-PCR • 10-day quarantine with 1 test 1-2 days before the end of quarantine (90% sensitivity RT-PCR) • 8-day quarantine with 2 tests (day 6-7 and day 8). (both RT-PCRs) • 6-day quarantine with 3 tests (days 4, 5, 6), (95% sensitivity RT-PCR) Antigen • 9-day quarantine with 2 tests (days 7 & 8)

	Tests: They model RT-PCR with 95% and 90% sensitivity and an antigen test with a 1 hour turnaround time.	• 11-day quarantine with 2 tests (days 9 & 10) • Note: Additional strategies presented in Table 2 of the paper
Van der Toorn (2020) (5) *preprint* Modelling study Germany 2020*	This paper describes a model (stochastic transit compartment model) and software interface developed to calculate the reduction in the transmissibility of COVID-19 through quarantine or isolation policies with or without testing strategies. The user chooses between three different modi (i) isolation of infected individuals *(not relevant to this review)*, (ii) management of potentially infected contacts and (iii) quarantine of incoming travelers *(see Table 2).* The user customizes the strategy. The model accounts for infection time, temporal changes in test sensitivity (Antigen test assumed to be 85% sensitivity of RT-PCR due to lack of data), incubation and infectious periods and time to symptom onset.	Outcome is a fold risk reduction (ie: x times less risk). Data is provided for each day of quarantine and test type, however only the strategies that were equivalent to a 14-day quarantine and those associated with a 10-day quarantine are reported below. Contact management with symptom screening: • 14-day quarantine 12.22 (7.88 – 22.13) • 8-day quarantine + RT-PCR test 14.48 (13.39 – 15.80) • 10-day quarantine + RDT test 14.51 (11.89-19.92) • 10-day quarantine with RT-PCR test day 5= 23.20 (19.02-31.50) • 10-day quarantine = 4.65 (3.80 – 6.46) The 14-day quarantine was equal to an 8-day with PCR test or 10 day with an antigen test. Benefits to testing include identification of asymptomatic cases and reduction of uncertainty of the quarantine strategy.
Ashcroft (2020) (10) *preprint* Modelling study Switzerland* Oct 2020*	A mathematical model was developed to explore the impact of quarantine strategies to reduce transmission of COVID-19 based on the empirical data of incubation period, infectivity and generation time. Quarantine strategies explored are for close contacts of a confirmed case that has been traced and	Results are largely presented in graphs: • Optimal duration of quarantine is 6 to 8 days, depending on the delay from exposure to quarantine (estimated to be 0-4 days). • Requiring a negative test result before release on day *n* improves transmission prevention, compared to standard release after *n* days. • Efficacy of test-and-release increases with the time from starting quarantine to testing.

	placed in quarantine for *n* days after their exposure to the case (Traveller quarantine strategies, see Table 2). Scenarios investigated: i) Test-and-release. ii) Release upon negative test with reinforced hygiene.	• Rapid testing reduces quarantine by one day, with equivalent efficacy to RT-PCR testing. For example: Day 6 rapid test (efficacy 80.5%) is equivalent to day 5 RT-PCR test with result obtained day 7 (efficacy 82.4%). • Adherence to quarantine has a large impact on efficacy.
Eilersen (2020) (11) Modelling study Denmark* Oct 2020*	Contact tracing and quarantine strategies within the community are explored to facilitate planning the lifting of a lockdown. To do this, an agent-based SEIR model was developed to simulate a society divided into families, workplace and social groups, with noted connections.	The model shows that quarantine periods longer than 5 days have limited effect on the peak infected fraction throughout the epidemic (figure 3d).
Pak (2020) (12) Modelling study Korea* Sept 2020*	Authors evaluate reasons for variability in incubation period and how that may affect quarantine periods. The authors develop a model for incubation period based on epidemiological data (n=312 cases) reported in the literature. They examined the influence of patient demographics on incubation period of documented cases.	Patients > 42 years of age had, on average, longer incubation periods than patients ≤ 42 years old. Analysis indicates that age-specific quarantine may allow for reduced quarantine duration for those less than 42 years old, without increasing the risk of releasing an infected individual from quarantine. Outcome: risk of infection to others before symptom onset: • 14-day quarantine ≤ 42 years, 8.4% > 42 years. 17.1% • 21-day quarantine ≤ 42 years, 2.2% > 42 years. 5.8% Outcome: quarantine duration required for 90% of cases to manifest symptoms before release: • ≤ 42 years, 13.1 days

		• > 42 years, 17.4 days
Wells (2020) (13) *preprint* Modelling study USA* 2020*	A mathematical model was developed to explore various quarantine scenarios: 1) Quarantine for travel, initiated at random times across the infectious course (see Table 2); 2) Quarantine prompted by contact-tracing and therefore initiated early in the infectious course; Quarantine when the time of exposure is known.	The outcome is the epidemiological equivalence to the standard 14 day quarantine to reduce the probability of post-quarantine transmission (PQT): Scenario (1 &) 2 • Testing on initiation of and exit from quarantine could reduce quarantine time by 50% • Testing at initiation only could reduce quarantine time by one day. • 7 day quarantine with testing on exit from quarantine and 6 day quarantine with testing on initiation and exit was equal to 14 day quarantine • testing during quarantine consistently outperformed testing upon tracing • optimal timing for test was one day prior to end of quarantine for periods < 7 days and on day 7 for longer periods of quarantine Scenario 3 • If testing one day post exposure, an additional test on day 6 was optimal. If entering quarantine >6 days after exposure, testing on day of entry was optimal.

*The location or timing of the study was estimated from the author affiliations and publication date respectively. UI= 95% Uncertainty Interval for super spreading events,

QUARANTINE EFFECTIVENESS: TRAVELLERS

Table 2 presents two epidemiological and twelve models related to quarantine strategies for travellers. The epidemiological studies report on the results of the quarantine program for incoming travellers which was 14 days and incorporated RT-PCR testing. In these studies there were no known infective cases released from quarantine in the reported studies.

Twelve modelling studies explore traveller quarantine lengths from zero through 14 days, with various testing strategies. Compared to a 14-day quarantine period, testing around day 5-7 and being released upon a negative test was shown to be equivalent in six models that examined this scenario. Similarly testing earlier than seven days with quarantine shorter than seven days was generally less protective than 14-day quarantine. Testing as close to the end of quarantine as possible in the less than seven day scenarios was most effective. Testing and releasing negative passengers with no quarantine was not effective.

Having multiple tests within a quarantine period resulted in marginal gains to the predicted efficacy of the quarantine scenario. In scenarios with no testing, a seven day quarantine was shown to be between 50-60% effective. A ten day quarantine was better than seven, but not as effective as fourteen.

Other important considerations, particularly in the most recent studies, were type of test and adherence to quarantine. Models have started to look at quarantine strategies that use RT-PCR or a RADTs and strategy optimization was test dependent. Adherence to quarantine was examined and results suggest that adherence is higher with shorter quarantines and the impact of quarantine is likely much lower than reflected in the models due to a lack of compliance.

TABLE 2: Epidemiologic and modelling studies of quarantine length and testing strategies for travellers (n=14)

STUDY	METHOD	KEY OUTCOMES
Epidemiologic studies		
Laiger (2020) (14) Case investigations France 2020	Repatriated travellers from Wuhan, China (n=337). A 14-day quarantine was observed with RT-PCR testing on arrival and day 5.	0/328 repatriated travellers were positive or developed COVID-19. The other 9 travellers: 1 traveller refused to be tested and 8 were only tested on arrival and had a negative result.
Lio (2020) (6) Case investigations Macao Jan-Apr 2020	This paper describes successful quarantine (14 days) of travellers (n=4347) arriving to Macao, a special administration region of China, January 22 through April 8, 2020. A 14-day quarantine with an RT-PCR test on day 13 to confirm negative status was implemented in Macao.	43/4347 travellers were identified to be infected and successfully isolated. Based on surveillance data no infectious cases were released from quarantine.
Modelling studies		

Clifford (2020) (15) *preprint* Modelling study UK* 2020*	A simulation model (generalized additive model with binomial likelihood and P-spline) of air travellers arriving to the UK from the EU or USA was developed to explore four levels of quarantine stringency: 1) Low - no mandatory quarantine, with and without arrival testing; 2) Moderate - mandatory 3, 5 or 7 day quarantine, with and without a test at end of quarantine; 3) High - mandatory quarantine until two negative tests (taken day 0-2 and 2-6 days after first), or 14 days after a positive test; 4) Maximum - mandatory 14-day quarantine with and without a single test at the end of quarantine. The outcome of the model was the number of infectious individuals who enter the country while infectious in each scenario. That result is converted into the proportion of cases prevented from entering the community due to the quarantine scenarios.	1) All scenarios are compared to no quarantine which in mid-July was predicted to be approximately 23 cases from the USA per week and 12 from the EU per week into the UK. Outcome= the proportion of cases prevented from entering the community due to the quarantine scenarios 2) 7 days, no test = 80% 6 days, test day 5 = 88% 8 days, test day 7= 94% 3) Results not extractable 4) 14 days, no test = 99% 15 days, test day 14= 99% (95%UI 97 – 100%) • There was limited utility of pre-departure testing when testing after arrival was in place. • Testing more than one time had limited benefit. Although the uncertainty interval is not presented in the paper, the figures presented in this paper show that quarantines as short as 8 days with testing on day 7 were almost equivalent to the results of a 14 day quarantine.
Dickens (2020) (4) Modelling study Singapore* 2020*	Six scenarios are simulated for preventing importation of COVID-19 cases into a country using a data-driven framework with information from 153 affected countries. Strategies explored include an arrival test and quarantine positive travellers or prohibit entry vs. quarantine only for 7 or 14 days.	Outcome= the reduction in imported cases. Quarantine scenario: • 7 days – no test = 55.4% • 14 days- no test = 91.2% • 0 days- arrival test and positives denied entry = 77.2%

	This model does not account for varying RT-PCR sensitivity through infection.	• 7 days if positive test on arrival and day 7 test = 90.2% • 14 days if positive test on arrival and test on day 14 = 91.7% 14-day quarantine of all passengers is most effective, but also the highest negative impact to travellers.
Steyn (2020) (3) *preprint* Modelling study New Zealand 2020*	A continuous time branching process model for COVID-19 transmission that includes a time-dependent probability of a false-negative test is used to simulate New Zealand's quarantine facility and each simulation is seeded with a case infected up to 14 days prior to arrival. New Zealand has a 14-day quarantine for all international arrivals that includes a minimum of two tests. The model explores 14-day quarantine without testing, 5-day quarantine with test on day 3 and pre-departure and post-arrival testing as different strategies.	Outcome: the percentage of infected travellers prevented from entering the community assuming no transmission in the quarantine facility. • 14 days, tests on day 3 & 12 = 99.9% • 14 days, no tests = 96% • 14 days, chance of early release on day 7 due to a negative test on day 3 or 8 = 99.9% • 5 days, test on arrival and day 3 = 75% • 0 days, negative test pre-departure and on arrival, positives denied entry = 50% If transmission within the quarantine facility should occur, the effectiveness of quarantine goes down and the importance of multiple tests during quarantine increases to both prevent transmission in the facility and to identify newly infected individuals.
Wells (2020) (13) *preprint* Modelling study USA* 2020*	A mathematical model was developed to explore various quarantine scenarios: 1) Quarantine for travel, initiated at random times across the infectious course; 2) Quarantine prompted by contact-tracing and therefore initiated early in the infectious course (*see Table 1)*,	The outcome is the epidemiological equivalence to the standard 14-day quarantine to reduce the probability of post-quarantine transmission (PQT): Scenario 1 & 2 • Testing on arrival and exit from quarantine could reduce quarantine time by 50%. • Testing on arrival only could reduce quarantine time by one day.

	3) Quarantine when the time of exposure is known (*see Table 1)*.	• 7-day quarantine with testing on exit from quarantine and 6-day quarantine with testing on arrival and exit was equal to 14-day quarantine. • Testing during quarantine consistently outperformed testing on arrival. • Optimal timing for test was one day prior to end of quarantine for periods < 7 days and on day 7 for longer periods of quarantine. Example of oil rig workers: • This was applied to an oil rig screening program with both arrival and exit from quarantine testing. 47/4040 employees were positive by this strategy, 16 would have been missed by entry only testing and could have lead to 9 different outbreaks. No infected worker went unidentified.
Russell (2020) (16) *preprint* Modelling study USA* 2020*	A mathematical model was developed to evaluate quarantine and testing strategies. Web application is accessible. Quarantine length examined in days: 0, 2, 5, 7, 14. Testing scenarios: no test, on arrival, 24 hours before the end of quarantine or both. Outcome is days at risk of community transmission assuming 1/10000 travellers are infected and a transmission risk of 0.5 per person-day at risk of transmission.	• Testing during quarantine consistently outperformed testing on arrival (if quarantine compliance is high). • Testing benefits diminished the longer the quarantine period; median reduction of 0.30, 0.10, and 0.004 days at risk for 2, 7, and 14-day quarantine, respectively. • The benefit of quarantine was highly sensitive to compliance where 40% compliance resulted in 1.7-2.1 days at risk, 100% compliance reduced this to 0.00-0.05 days at risk.
Johansson (2020) (17) *preprint*	A mathematical model was developed to analyze the expected effectiveness of symptom monitoring, testing, and quarantine strategies under different	Outcome: reduction in risk of transmission: • Testing on the day of departure could reduce the transmission risk while

Modelling study USA* 2020*	estimates of the infectious period, test-positivity relative to time of infection, and test sensitivity to reduce the risk of transmission from infected travelers during and after travel.	travelling by 37-61%, but 3 days before was a 5-9% reduction. • Testing and no quarantine 0-77% depending on the day of infectious period the test was performed. • Pre and post arrival test 40-66%. • Testing at arrival and 3-4 days later = 45-70%. • Isolation based on symptom monitoring = 36-52%. • 14-day quarantine = 97-100%. • 10-day quarantine = 84-100%. • 7-day quarantine = 65-95% • 7-day quarantine with a test on day 3-4 = 95-99%.
Taylor (2020) (18) *preprint* Modelling study UK Aug 2020	This study estimated that 895 (95%CI 834-958) infectious travellers were arriving in the UK in a single week in August 2020, 87% were on the UK quarantine list, and no quarantine is required for travellers from destinations not on the list. The quarantine is a 14 day self isolation (assumed to be ~80% effective due to compliance), alternative strategies were explored. They considered symptom screening at airports, self isolation for 7, 10 or 14 days and the addition of RT-PCR tests (a 48h turnaround is assumed on test results). A model was created to estimate different quarantine scenarios, but the methods section of the manuscript has been omitted from the prepublication documents, so it cannot be assessed.	• 14-day self isolation is estimated to be 78% effective (95%CI 74.4-81.6). • Thermal scanners detect 1/128 infectious travellers. • Arrival test is 39.6% effective (95%CI 35.2-43.7) – detects 2/5 infectious travellers. • 6-day quarantine with test at 4 days after arrival is 64.3% effective (95%CI 60.0-68.3). • 6-day quarantine with test at arrival and 4 days is 68.9% effective (95%CI: 64.9-73.0). • 7-day quarantine 51.3% effective (95%CI 47.2 – 55.7). • 10-day quarantine 68.8% effective (95%CI 65.1-72.9). • 9-day quarantine with test on day 7 is 74.3% effective (95%CI: 70.0-78.0).

		• 9-day quarantine with test at arrival and on day 7 is 75.9% effective (95%CI: 72.3-79.6). Strategies with testing on day 7 to clear a traveller were almost as effective as the 14-day quarantine.

Van der Toorn (2020) (5) *preprint*
 	
Modelling study
 	
Germany
 	
2020*
	This paper describes a model (stochastic transit compartment model) and software interface developed to calculate the reduction in the transmissibility through quarantine or isolation policies with or without testing strategies.
	
	The user chooses between three different modi
	
	(i) isolation of infected individuals *(not relevant to this review);*
	
	(ii) management of potentially infected contacts *(see Table 1);* and
	(iii) quarantine of incoming travelers.
	
	The user customizes the strategy.
	
	The model accounts for infection time, temporal changes in test sensitivity (Antigen test assumed to be 85% sensitivity of RT-PCR due to lack of data), incubation and infectious periods and time to symptom onset.
		Outcome is a fold risk reduction. (ie: x times less risk)
		
		Travellers with symptom screening:
		
		• Symptom screening and testing at arrival
		  ○ RT-PCR = 4.69 (4.19 – 4.83)
		  ○ rapid test (RDT 87% sensitivity) = 3.59 (3.22-3.69)
		• 14-day quarantine = 43.09 (21.82-94.40)
		• 10-day quarantine = 15.66 (9.77- 27.44)
		• 8-day quarantine + RT-PCR test = 47.56 (33.27-73.34)
		• 10-day quarantine + RDT test = 49.92 (30.54 – 85.67)
		• 10-day quarantine with RT-PCR test day 5 = 78.27 (48.87 – 136.94)
		
		Data is provided for each day of quarantine by test type. The 14-day quarantine was equal to an 8-day with PCR test or 10 day with an antigen test.

Ashcroft (2020) (10) *preprint* Predictive Model Switzerland* Oct 2020*	A mathematical model was developed to explore the impact of quarantine strategies to reduce transmission of COVID-19 based on the empirical data of incubation period, infectivity and generation time. Quarantine strategies explored are for travellers that has been placed in	Results are largely presented in graphs. Outcome: fraction of local transmission prevented: • Quarantine of 10 days upon arrival prevents nearly 100% of local transmission. • Testing on arrival is a poor strategy for limiting transmission: testing upon return

	quarantine for *x* days after their arrival. *(Case contacts, see Table 1).* Scenarios investigated: I. Test-and-release. II. Release upon negative test with reinforced hygiene.	at day zero only prevents 54.1% of local transmission, but testing on day five and releasing on day seven prevents 98.5% of local transmission. • Rapid testing reduces quarantine by one day, with minimal loss to efficacy compared to RT-PCR testing.
Arino (2020) (19) *preprint* Modelling study Canada* Dec 2020*	A stochastic model was developed to simulate a small population, homogeneously mixing, and the potential transmission chains that result after a case importation. Efficacy of quarantine is compared to duration of post-arrival quarantine, including how strictly quarantine is observed. Scenarios of 7, 10 and 14-day quarantines are analyzed.	Probability of preventing local transmission from an imported case increased with duration of quarantine and detection of cases from testing. • The efficacy for 7, 10, and 14-day quarantines are shown graphically (figure 7). • If 10% of cases are undetected, 14-day quarantine efficacy is 90%. • Increasing undetected cases to 90%, 14-day quarantine efficacy is 70%.
Matsinos (2020) (20) *preprint* Modelling study USA* Oct 2020*	A Monte-Carlo model is applied to the effect of quarantine length for travellers returning from high-risk COVID-19 regions. Model distributions: -Travel duration: beta(1-21 days, avg 12) -Infection timing : random -Infection probability: i) constant during travel ii) increasing with time, linear iii) increasing with time, logarithmic The model was run nine times, each simulating one million traveller scenarios.	Outcome: Probability of new infections resulting from infectious travellers being released from quarantine: • 8-day quarantine= 5% • 12-day quarantine= 1% • 16-day quarantine= 0.1% The model results do not support a reduction of quarantine from the current 10-14 day requirement of European countries.
Wilson (2020) (21) *preprint* Modelling study	A stochastic SEIR model was developed to explore the impact of various control measures upon likelihood that an infectious traveller would cause an outbreak when coming from a low	Outcome: average time between outbreaks due to travel into a COVID-19 free country: • No intervention = 1.7 years.

New Zealand* Jun 2020*	prevalence area (Australia) to a COVID-19 free area (New Zealand). Quarantine standard of 14 days and reduced 7 days were modelled as well as utilizing a test-and-release policy.	• 14-day quarantine = 34.5 years or more for all scenarios considered. • 7-day quarantine = 5.8 years. • PCR testing on days 3 & 12, release if both negative = 29.6 years

*The location or timing of the study was estimated from the author affiliations and publication date respectively. UK= United Kingdom, USA= United States of America, EU= European Union. UI = uncertainty interval, 95%CI= confidence interval

QUARANTINE EFFECTIVENESS SYNTHESIS RESEARCH

A single rapid review was identified that covered travel-related control measures. Quarantine was a component of this review and included research from SARS-CoV-1, MERS and SARS-CoV-2 up to June 26, 2020. Based on this rapid review there was very little relevant research up to June on quarantine strategies for travellers at the time of the search.

Table 3: Synthesis research related to quarantine length and testing

STUDY	METHOD	KEY OUTCOMES
Burns (2020) (22) Rapid Review Germany* 2020	Rapid review conducted by Cochrane (AMSTAR =moderate quality due to single reviewer) includes 36 studies on travel-related control measures to contain a pandemic. Search up to June 26, 2020 and included relevant studies on SARS-CoV-2 as direct evidence and SARS-CoV-1 and MERS as indirect evidence. The review includes 17 modelling studies, 7 observational screening studies and one observational ecological study on COVID-19, four modelling and six observational studies on SARS, and one modelling study on SARS and MERS, covering a variety of settings and epidemic stages.	For quarantine outcomes: • 1 COVID-19 study was included and concluded that 14-day quarantines reduced the risk of transmission from imported cases and the effectiveness of the quarantine depended on compliance (very low certainty of evidence) (Table 7). • 4 studies on SARS-1 or MERS were reported, however these looked at the impact of quarantine as a public health intervention and did not explore different quarantine strategies (Table 7). • Six COVID-19 observational studies are described particularly for repatriation flights where travellers were quarantined for 14 days and both symptom and

	None appear to have looked at different quarantine strategies, but some speak to the impact and effectiveness of the 14-day quarantine with symptom based screening or testing.	testing during quarantine was conducted. The results generally indicate that the 14 days alone or based on symptoms is not as sensitive as the use of an RT-PCR test during quarantine (no inference about shortening quarantine can be drawn from these studies) (Table 6). Other outcomes covered, but not summarized here: entry/exit symptom screening, border closures, and border restrictions.

*The location or timing of the study was estimated from the author affiliations and publication date respectively.

Methods:

A daily scan of the literature (published and pre-published) related to COVID-19 is conducted by the Emerging Science Group, PHAC; and has been ongoing since the beginning of the outbreak. The literature is retrieved from Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced, the WHO COVID literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. A search to retrieve relevant literature for this evidence summary was conducted in the Refworks database. Targeted keyword searching is conducted within these databases to identify relevant citations on COVID-19 and SARS-CoV-2. The search algorithms used isolation AND length, quarantine AND length, quarantine AND testing AND (reduce OR travel). 414 citations were screened for relevance and data was extracted from relevant articles into the review. This review contains research related to quarantine, and testing as a means to reduce quarantine duration, published up to December 3, 2020.

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