Testing and Quarantine Strategies for Travelers – An Evidence Based Analytic Model Using Bayes' Theorem

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Abstract

Background: Policies such as border closures and quarantines have been widely used to minimize the spread of SARS-CoV-2 during the COVID-19 pandemic. However, such policies curbed international trade, travel, and tourism, leading to economic loss.

Methods: We calculated the risks of individual travelers based on their expected transmission, defined as the expected number of subsequent infections resulting from an individual. It is calculated by multiplying the probability of travelers having COVID-19 after negative test(s), with the effective reproduction number (Rt) of the viral strain/variant. The expected transmission varies based on the incidence rate among unvaccinated or the breakthrough infection rates (BIRs) of the vaccinated; waning vaccine efficacy; transmissibility of the dominant variants; properties of various diagnostic tests used; and restriction policies in the arrival countries. For a traveler to be released, the expected transmission was benchmarked against that of an unvaccinated traveler quarantined for 14 days without testing, previously calculated to be 0.005.

Results: We found that all individuals with a negative preboarding test can be released with a negative post-arrival test, with both tests achieving sensitivity ≥ 90% and specificity ≥ 97%, which could be accomplished by rapid antigen tests. This is valid for an incidence rate up to 0.1 (prior to testing) and Rt up to 4 in the arrival country. In a sensitivity analysis scenario where the incidence rate is 0.4 and Rt is 16, a negative preboarding test and a negative post-arrival test, both with sensitivity ≥ 98% and specificity ≥ 97% (usually accomplished by a Polymerase Chain Reaction test or other Nucleic Acid Amplification tests) can ensure that a traveler has a lower expected transmission than an unvaccinated person who is quarantined for 14 days.

Conclusions: As vaccines become more available around the world, this study provides the scientific basis for setting policies of testing with or without quarantine for international travelers. In many cases, travelers with full vaccination (with or without booster) and a negative preboarding test can be released with a negative rapid antigen test upon arrival, which will allow the travelers to depart the airport within 30 minutes.

Background

Throughout the COVID-19 pandemic, policies such as border closure and quarantine have been widely used to control the viral spread across countries. Border closure curbs international trade, investments, travel, and tourism, leading to economic losses. Long quarantines after international travel incur financial burden on individuals, opportunity cost of time, and mental and emotional stress. High numbers of quarantined individuals also create strain on governments' tracking systems. As many countries reach high vaccination rates and have abundant supply of testing and masks, governments can formulate border control policies that provide similar protection without significantly interfering with international travel.

Science-based decision making is essential to ease restrictions without exposing people to risk of infection. Previously, Wells et al. reported that a 7-day quarantine with testing on exit is needed to achieve similar probability of post-quarantine transmission for unvaccinated individuals quarantining for 14 days.[1] Yet, there has not been a published model to provide guidance for policymakers on setting rules for travelers. Starting Summer 2021, many European countries required travelers to hold vaccine certificates to be exempt from testing or quarantining. However, the Omicron variant, which is highly transmissible and seemingly less virulent, is making many countries to reconsider their border control policies, with some continue to enforce the Zero-COVID policy (e.g., China), while others starting to shift their approach to live with the virus (e.g., Singapore and Spain).

With effective vaccines and various testing options available, we sought to formulate a testing and quarantine strategy for both fully vaccinated (with or without booster) travelers and unvaccinated travelers that is at least as safe as a 14-day quarantine for unvaccinated individuals, using available scientific evidence from the literature, and by applying different effective reproduction numbers (Rt) to model various variants and restrictive policies in the arrival country.

Methods

To formulate testing and quarantine policies for fully vaccinated travelers (defined as one dose for Janssen and two doses for other vaccines) and unvaccinated travelers, we drew a decision tree addressing current variants of concern (Table 1, 2, and 3) and performed a sensitivity analysis for our model (Fig. 1), where our outcome is the expected transmission (E_x). The expected transmission is defined as the expected number of subsequent infections resulting from an individual; it is calculated by multiplying the probability of travelers having COVID-19 after one or more negative tests, with Rt of the viral strain/variant. The Rt is dependent on the restriction policies in the arrival country; for Omicron, the most infectious variant, the reported Rt was 1.9 in South Korea where people are more compliant towards

protective measures (e.g., social distancing and masking),[2] and 3.7 in United Kingdom where people value freedom and normal life.[3] We benchmark the expected transmission of various vaccinated scenarios to the expected transmission threshold of an unvaccinated traveler quarantined for 14 days without testing, previously calculated to be 0.005.[1]

Definition

Vaccine efficacy for preventing infection, is one minus the quotient of breakthrough infection rate (BIR, defined as the percentage of COVID-19 cases among people who have been fully vaccinated) and the percentage of COVID-19 in an unvaccinated placebo group, multiplied by 100%. For example, the clinical trial of Pfizer vaccine reported vaccine efficacy of 94.6%, while the BIR is 0.000485.[4] In our study, we used BIR reported in the literature to calculate the probability of travelers having COVID-19 after a negative preboarding test, by applying Fagan's Nomogram with negative likelihood ratio (LR-, defined as the quotient of false negative and true negative, is dependent on the properties of the diagnostic test);[5] we assumed the risk of contracting COVID-19 on the flight is minimal if a preboarding test is used.[6]

Model

In Bayes' Theorem, the pretest probability typically is the prevalence of the disease. However, for COVID-19, incidence, the rate of new disease, may be more relevant for our calculations as people with mild to moderate disease usually are infectious no longer than 10 days after symptom onset.[7] The Fagan's Nomogram integrates pretest probability, likelihood ratios, and posttest probability to be calculated based on the sensitivity and specificity of the test.

(1) Expected transmission in travelers

$$= \text{Probability of having COVID-19} \times \text{Rt}$$

(In fully vaccinated travelers, probability of having COVID-19 is BIR; in unvaccinated travelers probability of having COVID-19 is the incidence rate of COVID-19 among the unvaccinated)

(2) Expected transmission in travelers with negative preboarding test E_1
= Preboarding posttest probability $P_1 \times \text{Rt}$

$$= \frac{\left(\frac{\text{BIR}}{1-\text{BIR}}\right) \times \text{LR-}}{\left[1 + \left(\frac{\text{BIR}}{1-\text{BIR}}\right) \times \text{LR-}\right]} \times \text{Rt}$$

(According to Fagan's Nomogram, LR- refers to the preboarding test type)[5]

In this case, if $E_1 \leq 0.005$, travelers can be released; if $E_1 > 0.005$, a post-arrival test is warranted.

(3) Expected transmission in travelers with negative preboarding and post-arrival tests E_2
= Post-arrival posttest probability $P_2 \times \text{Rt}$

$$= \frac{\left(\frac{\text{P1}}{1-\text{P1}}\right) \times \text{LR-}}{\left[1 + \left(\frac{\text{P1}}{1-\text{P1}}\right) \times \text{LR-}\right]} \times \text{Rt}$$

(According to Fagan's Nomogram, LR- refers to the post-arrival test type)[5]

In this case, if $E_2 \leq 0.005$, travelers can be released; if $E_2 > 0.005$, quarantine is warranted.

(4) Expected transmission in travelers with negative preboarding, post-arrival, and quarantine exit tests E_3
= Quarantine exit posttest probability × Rt

$$= \frac{\left(\frac{P2}{1-P2}\right) \times LR-}{\left[1+\left(\frac{P2}{1-P2}\right) \times LR-\right]} \times Rt$$

(According to Fagan's Nomogram, LR- refers to the quarantine exit test type)[5]

In this case, if $E_3 \leq 0.005$, travelers can be released; if $E_3 > 0.005$, an additional test is warranted.

Numbers

The BIRs in Table 1 and Table 2, are based on results from various clinical trials on symptomatic disease (0.000485 for Pfizer, 0.000778 for Moderna, 0.006081 for AstraZeneca, 0.005996 for Janssen, 0.002040 for Sinopharm, 0.001372 for Sinovac, 0.001425 for Novavax, and 0.002833 for Covaxin).[4,8–14] To account for asymptomatic infections, we assumed an equal number of asymptomatic infections (50%) and multiplied the BIR from clinical trials by two to get the adjusted BIR, given that the pooled percentage of asymptomatic infections among the confirmed population was reported to be 40.5% (95% CI, 33.5% – 47.5%).[15] The resulting adjusted BIRs range from 0.00097 to 0.01216. Further, we multiply the adjusted BIRs by ten, to account for current variants of concern and waning vaccine effectiveness. This gives the highest 20x BIR to be 0.1216. To provide a general policy for all vaccines, we chose 0.13 as the highest possible BIR for all World Health Organization (WHO) approved vaccines.

In Table 3, we assumed 0.5 to be the incidence rate of COVID-19 among the unvaccinated. According to Centers of Disease Control and Prevention (CDC), age-standardized case incidence rate ratio during December 2021 was 2.8 comparing unvaccinated people with fully vaccinated people without a booster shot.[16] As we modeled the general policy for vaccinated travelers with BIR (incidence rate among the 2-dose vaccinated) of 0.13, incidence rate of the unvaccinated would be approximately 0.364. To be more conservative and account for COVID-19 cases that did not get tested, we modeled Table 3 with incidence rate of 0.5 among the unvaccinated travelers. In addition, the modeled incidence rate is greater than the probability of getting infected among individuals who are close contacts of COVID-19 positive cases, which is reported to be 0.31.[17]

To account for different levels of restrictions across countries, we used Rt < 3 and Rt < 10 to model for policy options in countries with strict restrictions and loose restrictions, respectively (Table 1, 2, and 3).

In Fig. 1, we reported the sensitivity analysis of our model. We calculated the expected transmissions considering various incidence rates and Rt, with incidence rate up to 0.5 and Rt up to 32. The incidence rate for vaccinated people is the BIR.

We split diagnostic tests into three different categories: PCR, tests with sensitivity ≥ 98% and specificity ≥ 97%, usually achieved by Polymerase Chain Reaction (PCR) test or other Nucleic Acid Amplification (NAAT) tests; rapid test with higher sensitivity (RPD*), any test with sensitivity ≥ 90% and specificity ≥ 97%; and rapid test (RPD), any test with sensitivity ≥ 80% and specificity ≥ 97% based on recommendations from the WHO.[18]

Results

Model for Vaccinated and Unvaccinated Travelers

The decision tree in Table 1 describe testing and quarantine strategies for travelers fully vaccinated without booster, regardless of vaccine type (using 0.13 as the highest possible BIR for all WHO approved vaccines). To release fully vaccinated travelers with a negative preboarding test with sensitivity ≥ 90% and specificity ≥ 97% (RPD*) into an arrival country that has low vaccination rate and loose restriction policies (assumed Rt < 10), a post-arrival test with sensitivity ≥ 98% and specificity ≥ 97% (PCR) would be required to be valid for all WHO approved vaccines. However, if the preboarding test turns out to be unvalidated, these travelers should have a negative post-arrival test with sensitivity ≥ 98% and specificity ≥ 97% (PCR), quarantine for four days, and be released if the post-quarantine test with sensitivity ≥ 90% and specificity ≥ 97% (RPD*) is negative. The rationale of a four-day quarantine for individuals without valid

preboarding tests is that the current dominant Omicron variant has an incubation period of 72 hours; serial testing during this period should allow detection of the virus.[19]

Table 2 describes the strategy when individual vaccines are considered. In arrival countries with strict restriction policies (e.g., mask wearing, social distancing) in place (assumed Rt < 3), travelers vaccinated with Pfizer or Moderna can be released on arrival if they had a negative preboarding test with minimum sensitivity of 90% and specificity of 97% (RPD*); travelers vaccinated with Sinopharm, Sinovac, Novavax, or Covaxin would require an additional negative post-arrival test with sensitivity ≥ 80% and specificity ≥ 97% (RPD) to be released; travelers vaccinated with AstraZeneca or Janssen would require a more sensitive post-arrival test with sensitivity ≥ 90% and specificity ≥ 97% (RPD*) that is negative to be released.

In Table 3, we described the strategy for unvaccinated travelers. When unvaccinated travelers arrive in countries with strict restriction policy (R < 3), they can be released with a negative post-arrival test with sensitivity ≥ 98% and specificity ≥ 97% (PCR) if they had a negative preboarding PCR test. In situations where unvaccinated travelers presented with a preboarding test with sensitivity ≥ 80% and specificity ≥ 97% (RPD) at an arrival country with loose restriction policy (R < 10), they can be released after quarantining for four days with two negative tests: a post-arrival test with sensitivity ≥ 98% and specificity ≥ 97% (PCR) on quarantine day 1, and a quarantine exit test with sensitivity ≥ 80% and specificity ≥ 97% (RPD) on quarantine day 4.

Sensitivity Analysis of Our Model

Figure 1 shows the interventions needed for an individual to be released using the expected transmission threshold of 0.005, accounting for variants with different transmissibility (presented with Rt of 1, 2, 4, 8, 16, and 32) and possible incidence rates for vaccinated and unvaccinated individuals (0.01, 0.05, 0.1, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4, 0.45, and 0.5).

The color in each cell indicates the minimum intervention needed: direct release (white), post-arrival RPD test (lighter grey), post-arrival RPD* test (light grey), post-arrival PCR test (grey), post-arrival PCR test plus quarantine and RPD test before release (dark grey), post-arrival PCR test plus quarantine and RPD* test before release (darker grey), post-arrival PCR test plus quarantine and PCR test before release (darkest grey), and post-arrival PCR test plus quarantine and two tests with PCR and RPD before release (black).

For example, the Omicron variant has been reported to spread faster and infect more vaccinated people (higher Rt and BIR). If the incidence rate is assumed to be 1 in 20 (0.05), and Rt with restriction policies in place is estimated to be 4, travelers with a negative preboarding test with sensitivity ≥ 98% and specificity ≥ 97% (PCR) can be released directly (Fig. 1.1). If the preboarding test has sensitivity between 98% and 90%, and specificity above 97%, an additional negative post-arrival test with sensitivity ≥ 80% and specificity ≥ 97% (RPD) can ensure that the released traveler possess a lower risk of transmitting COVID-19 than an unvaccinated traveler quarantined for 14 days (Fig. 1.2).

From Fig. 1.1, we can conclude that even with a variant that has transmissibility of Rt = 8 and infected 1 in 5 people (incidence rate = 0.2), a traveler with a negative preboarding PCR test would only need a negative post-arrival RPD* test to be released. However, with the same variant dominating, travelers with an unvalidated preboarding test would need to take a post-arrival PCR test, quarantine for four days, and receive an RPD* test before release (Fig. 1.4).

Discussion

Our model shows that all individuals with a negative preboarding test can be released with a negative post-arrival test, with both tests achieving sensitivity ≥ 90% and specificity ≥ 97%, even when incidence rate reaches 0.1 and Rt is 4. The rapid tests can be implemented easily and quickly, which will allow the travelers to depart the airport within 30 minutes if tested negative.

In Table 1, 2, and 3, we assumed Rt < 3 in countries with strict restriction policies in place, with empirical evidence that Rt was 2.55 (2.26, 2.86) in South Africa in November 2021 when Omicron dominated.[20] For countries that prefer less restrictions, the tables provide Rt of 10 as the upper limit, when we believe governments will need to put some restrictions in place to flatten the curve. In addition, we modeled Table 1 and Table 2 with ten times the adjusted BIR of WHO approved vaccines (20 times the BIR from clinical trials) to account for waning effects of the vaccines and variants of concern. When Omicron dominated in the United States, the peak daily case rate in New York State was 254.5 per 100,000 in fully vaccinated people and 2023 per 100,000 in unvaccinated people.[21] Accordingly, the BIR is estimated to be 0.0025 in fully vaccinated people and the incidence rate is 0.0202 in unvaccinated people. Therefore, Table 1, 2, and 3 are still valid with Omicron being the dominant variant.

There are caveats to our study. First, we suggest that partially vaccinated individuals should be treated as unvaccinated individuals since the BIRs for partially vaccinated individuals differ greatly in the first three weeks after the first dose.[22] Second, governments can use Fig. 1 to extrapolate testing and quarantine strategies for the vaccines that we did not list in the tables. For example, the clinical trial BIR of Sputnik V is 0.001069 and the adjusted BIR accounting for asymptomatic infections is 0.002138.[23] Policymakers can refer to incidence rate, which is BIR for vaccinated people, of 0.05 in Fig. 1 as a conservative estimate when they are formulating policies for travelers vaccinated with Sputnik V (ten times adjusted BIR is 0.02138, accounting for waning vaccine efficacy). Third, travelers vaccinated with mixed vaccines can follow the general policy of fully vaccinated travelers or the policy for the least effective vaccine they received. For example, studies have shown a dose of AstraZeneca followed by an mRNA vaccine creates antibody responses higher than two doses of AstraZeneca;[24] as such, the AstraZeneca branch of our Table 2 may provide an overestimation for expected transmission and can be used in these travelers who have received these mix and match vaccines.

If we account for known waning immunity of the vaccines, the decision tree (Table 2) could still be valid for Pfizer, Moderna, Janssen, and AstraZeneca up to six months after the second dose. The BIR of people fully vaccinated with Pfizer after six months is 0.0035 in Israel,[25] less than ten times the adjusted BIR (0.0097) modeled for Pfizer in Table 2. Even though Moderna, Janssen, and AstraZeneca have not reported BIR six months after second dose, when compared to Pfizer, studies of these vaccines have shown slower decline rate of vaccine effectiveness five to six months after the second dose.[26] However, Sinovac, Sinopharm, Novavax, and Covaxin have not reported their rates of waning efficacy after six months. Once their efficacies are known, policies targeting these vaccines may need to be adjusted (Fig. 1).

Boosters are important in mitigating the waning effects of vaccines and can provide additional protection. For example, travelers vaccinated with three doses of Pfizer or AstraZeneca have vaccine efficacies above 93%, similar or better than the original clinical trials with Pfizer and AstraZeneca.[27] Also, booster vaccines can result in antibody levels higher than the original two doses, e.g., Moderna showed higher neutralization titers 28 days post booster compared to 28 days post second dose,[28] and the seroconversion rates of neutralizing antibodies towards COVID-19 variants were higher in people vaccinated with three doses of Sinovac compared to two doses.[29] Furthermore, early data on antibody levels suggest that boosters may further protect against Omicron.[29,30] With preliminary data suggesting that three doses of Pfizer produce an immune response against Omicron similar to that of two doses against earlier variants, governments may consider a three-shot requirement for travelers to qualify as fully vaccinated.

Our model is flexible and can be adapted to real-life situations. For example, when in doubt, governments can invalidate the preboarding test – not considering the information provided by the negative preboarding test at all – and refer to the “Unvalidated” rows in Table 1, 2, and 3.

Finally, the data from the randomized controlled clinical trials we based on may not be identical to the real-world data (Table 2). For example, Sinovac and Sinopharm reported lower BIR compared to AstraZeneca in published clinical trials; however, their effectiveness is less certain because they provided lower antibody responses compared to AstraZeneca and severe outbreaks were seen in countries mainly vaccinated with the two vaccines despite rollout success.[31] Real world BIRs are needed to provide additional evidence for decision making.

Conclusion

Our test and release strategy is evidence-based and applicable for different vaccination status, vaccine type, and testing options. This approach can be time and cost-saving. For those who are financially vulnerable (e.g., migrant workers, etc.), and those with time sensitive issues (e.g., business travelers, etc.), this policy could avoid the need to quarantine, unless it is necessary.

Abbreviations

Abbreviations	Full term or phrase
Rt	Effective reproduction number
BIR	Breakthrough infection rate
E	Expected transmission
LR-	Negative likelihood ratio
WHO	World Health Organization
CDC	Centers of Disease Control and Prevention
PCR	Polymerase chain reaction; also defined as any test with sensitivity ≥ 98% and specificity ≥ 97% in this article
NAAT	Nucleic acid amplification test
RPD*	Defined as any test with sensitivity ≥ 90% and specificity ≥ 97%
RPD	Defined as any test with sensitivity ≥ 80% and specificity ≥ 97%
mRNA	Messenger ribonucleic acid

Declarations

Ethics Approval And Consent To Participate This study does not involve human participants or animal participants; therefore, an ethic approval is not required. Consent For Publication This study does not contain data from any individual person; therefore, an ethic approval is not required. Availability of data and materials Not applicable. Data used in the model were found in the literature or reports. Competing Interest The authors declare no competing interests. Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. Authors' Contribution F.W.L. and C.J.W. developed the concept and approach of the paper. F.W.L. and J.W. acquired the data and performed analyses with contributions from C.J.W. All authors contributed to the interpretation of results and drafted the paper. All authors contributed to the revision of the paper and approved the final version of the paper. All authors agree to be accountable for all aspects of the work. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. Acknowledgements We thank Dr. Howard Bauchner for his valuable comments and guidance.

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Tables

Table 1. Testing and Quarantine Strategies for Fully Vaccinated Travelers (General)

Preboarding test type	E_1, if tested negative	Policy	Post-arrival test type	E_2, if tested negative	Policy	Quarantine exit test type	E_3, if tested negative	Policy
Rt < 3								
PCR	0.0092	Test	PCR	0.0002	Release			
			RPD*	0.0010	Release			
			RPD	0.0019	Release			
RPD*	0.0455	Test	PCR	0.0010	Release			
			RPD*	0.0048	Release			
			RPD	0.0095	Quarantine	RPD	0.0020	Release
RPD	0.0897	Test	PCR	0.0019	Release			
			RPD*	0.0095	Quarantine	RPD	0.0020	Release
			RPD	0.0189	Quarantine	RPD	0.0039	Release
Unvalidated	0.3900	Test	PCR	0.0092	Quarantine	RPD	0.0019	Release
			RPD*	0.0455	Quarantine	RPD*	0.0048	Release
			RPD	0.0897	Quarantine	PCR	0.0019	Release
Rt < 10								
PCR	0.0307	Test	PCR	0.0006	Release			
			RPD*	0.0032	Release			
			RPD	0.0063	Quarantine	RPD	0.0013	Release
RPD*	0.1517	Test	PCR	0.0032	Release			
			RPD*	0.0159	Quarantine	RPD	0.0033	Release
			RPD	0.0317	Quarantine	RPD*	0.0033	Release
RPD	0.2989	Test	PCR	0.0063	Quarantine	RPD	0.0013	Release
			RPD*	0.0317	Quarantine	RPD*	0.0033	Release
			RPD	0.0631	Quarantine	PCR	0.0013	Release
Unvalidated	1.3000	Test	PCR	0.0307	Quarantine	RPD*	0.0032	Release
			RPD*	0.1517	Quarantine	PCR	0.0032	Release
			RPD	0.2989	Quarantine	PCR	0.0063	Test with RPD

Abbreviations

- **PCR**: Any test that meets the minimum requirement of sensitivity ≥ 98% and specificity ≥ 97%, usually achieved by Polymerase Chain Reaction test or other Nucleic Acid Amplification tests
- **RPD***: Any test that meets the minimum requirement of sensitivity ≥ 90% and specificity ≥ 97%, can be achieved by many rapid antigen tests.
- **RPD**: Any test that meets the minimum requirement of sensitivity ≥ 80% and specificity ≥ 97% (WHO recommendation for COVID-19 diagnostic tests)

Assumptions (see main text for rationale)

- **Effective Reproduction number (Rt)**: The expected number of infections consequent to a single infected individual. We assume that countries with strict restrictive policies have Rt < 3, and countries with loose restrictive policies have Rt < 10.
- **Expected transmission (E_x)**: The expected number of subsequent infections resulting from an individual. The expected transmission equals to 0.005 in unvaccinated people who quarantined for 14 days. If the expected transmission is less than or equal to 0.005, the traveler can be released into the arrival country. However, if the expected transmission is greater than 0.005, he/she will need additional test(s) and/or quarantine in order to be released.
- The probability of contracting COVID-19 in fully vaccinated (with or without booster) individuals prior to testing is assumed to be 0.13 in the model. The highest breakthrough infection rate (BIR) among the WHO approved vaccines reported in the clinical trial is 0.01216. We multiplied the BIR by two to account for asymptomatic infections, and further multiplied by ten to account for current variant of concerns and waning vaccine effectiveness. This gives the highest 20x BIR to be 0.1216. Therefore, to provide a general policy for all vaccines, we chose 0.13 as the highest possible BIR for all WHO approved vaccines.

Caveats

- Travelers without a preboarding test can refer to the “Unvalidated” rows.

Table 2. Testing and Quarantine Strategies for Fully Vaccinated Travelers (Individual Vaccines)

Rt < 3					Rt < 10				
Vaccine type (Adjusted BIR x10)	Preboarding test	Policy if test negative	Post-arrival test	Policy if test negative	Vaccine type (Adjusted BIR x10)	Preboarding test	Policy if test negative	Post-arrival test	Policy if test negative
Pfizer	PCR	Release			**Pfizer**	PCR	Release		
(0.0097)	RPD*	Release			(0.0097)	RPD*	Test	PCR	Release
								RPD*	Release
								RPD	Release
	RPD	Test	PCR	Release		RPD	Test	PCR	Release
			RPD*	Release				RPD*	Release
			RPD	Release				RPD	Release
	Unvalidated	Test	PCR	Release		Unvalidated	Test	PCR	Release
			RPD*	Release				RPD*	Quarantine[a]
			RPD	Quarantine[a]				RPD	Quarantine[a]
Moderna	PCR	Release			**Moderna**	PCR	Release		
(0.0156)	RPD*	Release			(0.0156)	RPD*	Test	PCR	Release
								RPD*	Release
								RPD	Release
	RPD	Test	PCR	Release		RPD	Test	PCR	Release
			RPD*	Release				RPD*	Release
			RPD	Release				RPD	Quarantine[a]
	Unvalidated	Test	PCR	Release		Unvalidated	Test	PCR	Release
			RPD*	Release				RPD*	Quarantine[a]
			RPD	Quarantine[a]				RPD	Quarantine[b]
AstraZeneca	PCR	Test	PCR	Release	**AstraZeneca**	PCR	Test	PCR	Release
(0.1216)			RPD*	Release	(0.1216)			RPD*	Release
			RPD	Release				RPD	Quarantine[a]
	RPD*	Test	PCR	Release		RPD*	Test	PCR	Release
			RPD*	Release				RPD*	Quarantine[a]
			RPD	Quarantine[a]				RPD	Quarantine[b]
	RPD	Test	PCR	Release		RPD	Test	PCR	Quarantine[a]
			RPD*	Quarantine[a]				RPD*	Quarantine[b]
			RPD	Quarantine[a]				RPD	Quarantine[c]
	Unvalidated	Test	PCR	Quarantine[a]		Unvalidated	Test	PCR	Quarantine[b]
			RPD*	Quarantine[b]				RPD*	Quarantine[c]
			RPD	Quarantine[c]				RPD	Quarantine[d]

Rt < 3					Rt < 10				
Vaccine type (Adjusted BIR x10)	Preboarding test	Policy if test negative	Post-arrival test	Policy if test negative	Vaccine type (Adjusted BIR x10)	Preboarding test	Policy if test negative	Post-arrival test	Policy if test negative
Janssen	PCR	Test	PCR	Release	**Janssen**	PCR	Test	PCR	Release
(0.1199)			RPD*	Release	(0.1199)			RPD*	Release
Janssen	PCR	Test	RPD	Release	**Janssen**	PCR	Test	RPD	Quarantine[a]
(0.1199)	RPD*	Test	PCR	Release	(0.1199)	RPD*	Test	PCR	Release
			RPD*	Release				RPD*	Quarantine[a]
			RPD	Quarantine[a]				RPD	Quarantine[b]
	RPD	Test	PCR	Release		RPD	Test	PCR	Quarantine[a]
			RPD*	Quarantine[a]				RPD*	Quarantine[b]
			RPD	Quarantine[a]				RPD	Quarantine[c]
	Unvalidated	Test	PCR	Quarantine[a]		Unvalidated	Test	PCR	Quarantine[b]
			RPD*	Quarantine[b]				RPD*	Quarantine[c]
			RPD	Quarantine[c]				RPD	Quarantine[d]
Sinopharm	PCR	Release			**Sinopharm**	PCR	Test	PCR	Release
(0.0408)					(0.0408)			RPD*	Release
								RPD	Release
	RPD*	Test	PCR	Release		RPD*	Test	PCR	Release
			RPD*	Release				RPD*	Release
			RPD	Release				RPD	Quarantine[a]
	RPD	Test	PCR	Release		RPD	Test	PCR	Release
			RPD*	Release				RPD*	Quarantine[a]
			RPD	Quarantine[a]				RPD	Quarantine[a]
	Unvalidated	Test	PCR	Release		Unvalidated	Test	PCR	Quarantine[a]
			RPD*	Quarantine[a]				RPD*	Quarantine[b]
			RPD	Quarantine[b]				RPD	Quarantine[c]
Sinovac	PCR	Release			**Sinovac**	PCR	Test	PCR	Release
(0.0274)					(0.0274)			RPD*	Release
								RPD	Release
	RPD*	Test	PCR	Release		RPD*	Test	PCR	Release
			RPD*	Release				RPD*	Release
			RPD	Release				RPD	Quarantine[a]
	RPD	Test	PCR	Release		RPD	Test	PCR	Release

Rt < 3					Rt < 10				
Vaccine type (Adjusted BIR x10)	Preboarding test	Policy if test negative	Post-arrival test	Policy if test negative	Vaccine type (Adjusted BIR x10)	Preboarding test	Policy if test negative	Post-arrival test	Policy if test negative
			RPD*	Release				RPD*	Quarantine[a]
			RPD	Release				RPD	Quarantine[a]
	Unvalidated	Test	PCR	Release		Unvalidated	Test	PCR	Quarantine[a]
			RPD*	Quarantine[a]				RPD*	Quarantine[b]
			RPD	Quarantine[a]				RPD	Quarantine[c]
Novavax	PCR	Release			**Novavax**	PCR	Test	PCR	Release
(0.0285)					(0.0285)			RPD*	Release
Novavax					**Novavax**	PCR	Test	RPD	Release
(0.0285)	RPD*	Test	PCR	Release	(0.0285)	RPD*	Test	PCR	Release
			RPD*	Release				RPD*	Release
			RPD	Release				RPD	Quarantine[a]
	RPD	Test	PCR	Release		RPD	Test	PCR	Release
			RPD*	Release				RPD*	Quarantine[a]
			RPD	Release				RPD	Quarantine[a]
	Unvalidated	Test	PCR	Release		Unvalidated	Test	PCR	Quarantine[a]
			RPD*	Quarantine[a]				RPD*	Quarantine[b]
			RPD	Quarantine[a]				RPD	Quarantine[c]
Covaxin	PCR	Release			**Covaxin**	PCR	Test	PCR	Release
(0.0567)					(0.0567)			RPD*	Release
								RPD	Release
	RPD*	Test	PCR	Release		RPD*	Test	PCR	Release
			RPD*	Release				RPD*	Quarantine[a]
			RPD	Release				RPD	Quarantine[a]
	RPD	Test	PCR	Release		RPD	Test	PCR	Release
			RPD*	Release				RPD*	Quarantine[a]
			RPD	Quarantine[a]				RPD	Quarantine[b]
	Unvalidated	Test	PCR	Release		Unvalidated	Test	PCR	Quarantine[a]
			RPD*	Quarantine[a]				RPD*	Quarantine[c]
			RPD	Quarantine[b]				RPD	Quarantine[c]

[a] Quarantine for 4 days, release with negative exit RPD test

[b] Quarantine for 4 days, release with negative exit RPD* test

[c] Quarantine for 4 days, release with negative exit PCR test

[d] Quarantine for 4 days, requires negative exit PCR test on day 3, and an additional negative exit RPD test on day 4 to be released

Abbreviations

- **PCR**: Any test that meets the minimum requirement of sensitivity ≥ 98%, specificity ≥ 97%
- **RPD***: Any test that meets the minimum requirement of sensitivity ≥ 90%, specificity ≥ 97%
- **RPD**: Any test that meets the minimum requirement of sensitivity ≥ 80%, specificity ≥ 97%

Assumptions

- **Adjusted breakthrough infection rate (BIR)**: The probability of a fully vaccinated individual getting COVID-19. The adjusted BIRs are 2 times higher than the BIRs of the clinical trials, accounting for the assumed 50% asymptomatic breakthrough infection cases. We used 10 times the adjusted BIRs, to account for current variants of concern and waning vaccine effectiveness.
- **Effective Reproduction number (Rt)**: The expected number of infections consequent to a single infected individual. We assume that countries with strict restrictive policies have Rt < 3, and countries with loose restrictive policies have Rt < 10.
- The expected transmission (expected number of subsequent infections resulting from an individual) equals to 0.005 in unvaccinated people who quarantined for 14 days. If the expected transmission is less than or equal to 0.005, the traveler can be released into the arrival country. However, if the expected transmission is greater than 0.005, he/she will need additional test(s) and/or quarantine in order to be released.

Caveats

- Sinovac, Sinopharm, Novavax, and Covaxin have not reported their rates of waning efficacy after six months. Once their efficacies are known, policies targeting these vaccines may need to be adjusted (Figure 1).

Table 3. Testing and Quarantine Strategies for Unvaccinated Travelers

Preboarding test type	E_1, if tested negative	Policy	Post-arrival test type	E_2, if tested negative	Policy	Quarantine test type on day 3	E_3, if tested negative	Policy
Rt < 3								
PCR	0.0606	Test	PCR	0.0013	Release			
			RPD*	0.0064	Quarantine	PCR	0.0001	Release
						RPD*	0.0007	Release
						RPD	0.0013	Release
			RPD	0.0127	Quarantine	PCR	0.0003	Release
						RPD*	0.0013	Release
						RPD	0.0026	Release
RPD*	0.2804	Test	PCR	0.0064	Quarantine	PCR	0.0001	Release
						RPD*	0.0007	Release
						RPD	0.0013	Release
			RPD*	0.0315	Quarantine	PCR	0.0007	Release
						RPD*	0.0033	Release
						RPD	0.0066	Test[a]
			RPD	0.0624	Quarantine	PCR	0.0013	Release
						RPD*	0.0066	Test[a]
						RPD	0.0131	Test[a]
RPD	0.5128	Test	PCR	0.0127	Quarantine	PCR	0.0003	Release
						RPD*	0.0013	Release
						RPD	0.0026	Release
			RPD*	0.0624	Quarantine	PCR	0.0013	Release
						RPD*	0.0066	Test[a]
						RPD	0.0131	Test[a]
			RPD	0.1223	Quarantine	PCR	0.0026	Release
						RPD*	0.0131	Test[a]
						RPD	0.0261	Test[b]
Unvalidated	1.5000	Test	PCR	0.0606	Quarantine	PCR	0.0013	Release
						RPD*	0.0064	Test[a]
						RPD	0.0127	Test[a]
			RPD*	0.2804	Quarantine	PCR	0.0064	Test[a]
						RPD*	0.0315	Test[b]
						RPD	0.0624	Test[c]
			RPD	0.5128	Quarantine	PCR	0.0127	Test[a]
						RPD*	0.0624	Test[c]

						RPD	0.1223	Test[c]
Preboarding test type	E_1, if tested negative	Policy	Post-arrival test type	E_2, if tested negative	Policy	Quarantine test type on day 3	E_3, if tested negative	Policy
Rt < 10								
PCR	0.2020	Test	PCR	0.0042	Quarantine	PCR	0.0001	Release
						RPD*	0.0004	Release
						RPD	0.0009	Release
			RPD*	0.0212	Quarantine	PCR	0.0004	Release
						RPD*	0.0022	Release
						RPD	0.0044	Release
			RPD	0.0423	Quarantine	PCR	0.0009	Release
						RPD*	0.0044	Release
						RPD	0.0088	Test[a]
RPD*	0.9346	Test	PCR	0.0212	Quarantine	PCR	0.0004	Release
						RPD*	0.0022	Release
						RPD	0.0044	Release
			RPD*	0.1052	Quarantine	PCR	0.0022	Release
						RPD*	0.0109	Test[a]
						RPD	0.0219	Test[a]
			RPD	0.2081	Quarantine	PCR	0.0044	Release
						RPD*	0.0219	Test[a]
						RPD	0.0436	Test[b]
RPD	1.7094	Test	PCR	0.0423	Quarantine	PCR	0.0009	Release
						RPD*	0.0044	Release
						RPD	0.0088	Test[a]
			RPD*	0.2081	Quarantine	PCR	0.0044	Release
						RPD*	0.0219	Test[a]
						RPD	0.0436	Test[b]
			RPD	0.4078	Quarantine	PCR	0.0088	Test[a]
						RPD*	0.0436	Test[b]
						RPD	0.0869	Test[c]
Unvalidated	5.0000	Test	PCR	0.2020	Quarantine	PCR	0.0042	Release
						RPD*	0.0212	Test[b]
						RPD	0.0423	Test[b]
			RPD*	0.9346	Quarantine	PCR	0.0212	Test[b]
						RPD*	0.1052	Test[c]

				RPD	0.2081	Test[c]
	RPD	1.7094	Quarantine	PCR	0.0423	Test[b]
				RPD*	0.2081	Test[c]
				RPD	0.4078	Test[d]

[a] Release with an additional negative RPD test

[b] Release with an additional negative RPD* test

[c] Release with an additional negative PCR test

[d] Release with an additional negative test of sensitivity ≥ 99%, specificity ≥ 97%

Abbreviations

- **PCR**: Any test that meets the minimum requirement of sensitivity ≥ 98%, specificity ≥ 97%
- **RPD***: Any test that meets the minimum requirement of sensitivity ≥ 90%, specificity ≥ 97%
- **RPD**: Any test that meets the minimum requirement of sensitivity ≥ 80%, specificity ≥ 97%

Assumptions

- **Effective Reproduction number (Rt)**: The expected number of infections consequent to a single infected individual. We assume that countries with strict restrictive policies have Rt < 3, and countries with loose restrictive policies have Rt < 10.
- **Expected transmission (E_x)**: The expected number of subsequent infections resulting from an individual. The expected transmission equals to 0.005 in unvaccinated people who quarantined for 14 days. If E_x is less than or equal to 0.005, the traveler can be released into the arrival country. However, if E_x is greater than 0.005, he/she will need additional test(s) and/or quarantine in order to be released.
- The probability of contracting COVID-19 in unvaccinated individuals prior to testing is assumed to be 0.5 in the model.
    - The probability of contracting COVID-19 in fully vaccinated individuals prior to testing is assumed to be 0.13 (highest possible BIR for all WHO approved vaccines) in Table 1. According to CDC, age-standardized case incidence rate ratio during December 2021 (peak of Omicron wave) was 2.8 comparing unvaccinated people with fully vaccinated people without a booster shot. Therefore, incidence rate of the unvaccinated would be approximately 0.364.
    - To be more conservative and account for COVID-19 cases that did not get tested, we modeled Table 3 with incidence rate of 0.5 in the unvaccinated travelers.

Figures

Figure 1.1 Negative preboarding test with sensitivity ≥ 98%, specificity ≥ 97%

IR	Rt = 1	Rt = 2	Rt = 4	Rt = 8	Rt = 16	Rt = 32
0.01	0.0002	0.0004	0.0008	0.0017	0.0033	0.0014
0.05	0.0011	0.0022	0.0043	0.0018	0.0036	0.0036
0.10	0.0023	0.0046	0.0019	0.0038	0.0038	0.0015
0.15	0.0036	0.0015	0.0030	0.0030	0.0012	0.0024
0.20	0.0011	0.0021	0.0042	0.0042	0.0017	0.0034
0.25	0.0014	0.0028	0.0028	0.0011	0.0023	0.0045
0.30	0.0018	0.0036	0.0036	0.0015	0.0029	0.0012
0.35	0.0023	0.0046	0.0046	0.0018	0.0037	0.0015
0.40	0.0028	0.0028	0.0011	0.0023	0.0045	0.0019
0.45	0.0035	0.0035	0.0014	0.0028	0.0011	0.0023
0.50	0.0042	0.0042	0.0017	0.0034	0.0014	0.0028

Figure 1.2 Negative preboarding test with sensitivity ≥ 90%, specificity ≥ 97%

IR	Rt = 1	Rt = 2	Rt = 4	Rt = 8	Rt = 16	Rt = 32
0.01	0.0010	0.0021	0.0042	0.0017	0.0034	0.0034
0.05	0.0011	0.0022	0.0045	0.0045	0.0018	0.0036
0.10	0.0024	0.0047	0.0047	0.0019	0.0038	0.0016
0.15	0.0037	0.0037	0.0015	0.0030	0.0012	0.0025
0.20	0.0026	0.0011	0.0021	0.0042	0.0018	0.0035
0.25	0.0035	0.0014	0.0028	0.0012	0.0023	0.0047
0.30	0.0045	0.0018	0.0036	0.0015	0.0030	0.0030
0.35	0.0011	0.0023	0.0046	0.0019	0.0038	0.0038
0.40	0.0014	0.0028	0.0012	0.0023	0.0047	0.0047
0.45	0.0017	0.0035	0.0014	0.0029	0.0029	0.0011
0.50	0.0021	0.0042	0.0018	0.0035	0.0035	0.0014

Figure 1.3 Negative preboarding test with sensitivity ≥ 80%, specificity ≥ 97%

IR	Rt = 1	Rt = 2	Rt = 4	Rt = 8	Rt = 16	Rt = 32
0.01	0.0021	0.0042	0.0017	0.0034	0.0034	0.0014
0.05	0.0022	0.0045	0.0045	0.0018	0.0036	0.0015
0.10	0.0047	0.0047	0.0019	0.0038	0.0016	0.0031
0.15	0.0037	0.0015	0.0030	0.0012	0.0025	0.0049
0.20	0.0011	0.0021	0.0042	0.0018	0.0035	0.0035
0.25	0.0014	0.0028	0.0012	0.0023	0.0047	0.0047
0.30	0.0018	0.0036	0.0015	0.0030	0.0030	0.0012
0.35	0.0023	0.0046	0.0019	0.0038	0.0038	0.0015
0.40	0.0028	0.0012	0.0023	0.0047	0.0047	0.0019
0.45	0.0035	0.0014	0.0029	0.0029	0.0011	0.0023
0.50	0.0042	0.0018	0.0035	0.0035	0.0014	0.0028

Figure 1.4 Unvalidated preboarding test

IR	Rt = 1	Rt = 2	Rt = 4	Rt = 8	Rt = 16	Rt = 32
0.01	0.0021	0.0042	0.0042	0.0017	0.0033	0.0014
0.05	0.0011	0.0022	0.0043	0.0018	0.0036	0.0036
0.10	0.0023	0.0046	0.0019	0.0038	0.0038	0.0015
0.15	0.0036	0.0015	0.0030	0.0030	0.0012	0.0024
0.20	0.0011	0.0021	0.0042	0.0042	0.0017	0.0034
0.25	0.0014	0.0028	0.0028	0.0011	0.0023	0.0045
0.30	0.0018	0.0036	0.0036	0.0015	0.0029	0.0012
0.35	0.0023	0.0046	0.0046	0.0018	0.0037	0.0015
0.40	0.0028	0.0028	0.0011	0.0023	0.0045	0.0019
0.45	0.0035	0.0035	0.0014	0.0028	0.0011	0.0023
0.50	0.0042	0.0042	0.0017	0.0034	0.0014	0.0028

Color Key

White	Expected infection after a negative preboarding test
Lighter grey	Expected infection after negative arrival RPD
Light grey	Expected infection after negative arrival RPD*
Grey	Expected infection after negative arrival PCR
Dark grey	Expected infection after negative arrival PCR test, quarantine for 4 days, and exit RPD
Darker Grey	Expected infection after negative arrival PCR test, quarantine for 4 days, and exit RPD*
Darkest grey	Expected infection after negative arrival PCR test, quarantine for 4 days, and exit PCR
Black	Expected infection after negative arrival PCR test, quarantine for 4 days, and exit PCR plus RPD

Figure 1

Regardless of vaccine status, travelers' expected transmission with negative preboarding, with/without post-arrival, with/without post-quarantine tests (Figure legend)

Abbreviations

· Expected transmission: the expected number of subsequent infections resulting from an individual

· IR: Incidence rate; in fully vaccinated travelers, we use the breakthrough infection rate as the incidence rate

· Rt: Effective reproduction number, the expected number of infections consequent to a single infected individual

· **PCR**: Any test that meets the minimum requirement of sensitivity ≥ 98% and specificity ≥ 97%, usually achieved by Polymerase Chain Reaction test or other Nucleic Acid Amplification tests

· **RPD***: Any test that meets the minimum requirement of sensitivity ≥ 90% and specificity ≥ 97%, can be achieved by many rapid antigen tests

· **RPD**: Any test that meets the minimum requirement of sensitivity ≥ 80% and specificity ≥ 97% (WHO recommendation for COVID-19 diagnostic tests)