Living Rapid Evidence Synthesis 13.2a: Effectiveness of isolation on the reduction of the transmission of respiratory infectious diseases (RIDs: i.e., COVID-19, H1N1, SARS, MERS)

Executive summary

Question

What is the effectiveness of isolation* on reducing the transmission of respiratory infectious diseases (RIDs) (i.e., coronavirus disease 2019 (COVID-19), influenza A virus subtype H1N1 (H1N1), severe acute respiratory syndrome (SARS), and middle eastern respiratory syndrome (MERS))?

*Isolation refers to the segregation of individuals who have tested positive for the diseases listed above or have symptoms related to the diseases listed above

Background

- Two key strategies to prevent the spread of RIDs are:
  1) for individuals who have been in contact with an individual who has tested positive to quarantine; and
  2) for individuals who are symptomatic and/or have tested positive for the disease to isolate (isolation).
- During the early phases of the COVID-19 pandemic, a duration of 14 days for these physical distancing measures was a common policy. Over time and across jurisdictions, there have been several variations in the duration and structure of isolation periods.
- It is unclear if and what effects different isolation durations or strategies have had on RID transmission rates.

Methods

- We retrieved candidate studies by searching: 1) EMBASE; 2) Medline; 3) PsycINFO; and 4) the National Institute of Health (NIH) iSearch COVID-19 portfolio.
- For this round a total of 2,526 studies were title and abstract screened, 772 were included for full-text appraisal. Of these, 5 modelling studies were included in this report. There were no empirical studies that could be included.

Key points

- There were 5 modelling studies which were identified, all of which focused on COVID-19.
- Three of the five included modelling studies indicated that *longer isolation periods were associated with lower secondary transmission*.
  - In a US-based simulation model of asymptomatic and mild cases, a protocol of a 10-day isolation with rapid antigen test on day 6 where if the person was negative they would end isolation, otherwise continue to day 10, was deemed to be the most effective at averting future infections (COVID-19; Maya & Khan) compared to other variations in length and testing protocols.
  - In a general simulation model of unvaccinated individuals, increasing the length of isolation up to 14 days consistently decreased the chances of secondary infections and outbreaks (Sararat et al). When vaccination was included in the model, there was still a

reduction in infections and outbreaks with longer isolation. However, this reached a low point at around 6 days of isolation.
    - In a simulation model of Korean adults, increasing the duration of isolation up to 7 days was associated with reductions in both the rates and absolute numbers of confirmed cases, severe cases, and deaths (Kim et al). This was relatively consistent even when the model considered a reduction in facemask wearing.
    - In contrast, one model found no differences between 0, 5, and 10 days of isolation on infections in internally displaced persons in Bangladesh (Aylett-Bullock et al) and a US-based school model found no effect of the time of isolation (up to 14-days) following the onset of fever on school-based attack rates (Burns & Gutfraind).

Considerations on the quality of the evidence

- The modelling studies included in this living rapid evidence synthesis had notable biases and limitations. The key biases across the studies were as follows: a lack of real-world data on case and testing data to validate model predictions (Aylett-Bullock et al., 2021); lack of applicability of the results to different populations; no consideration of inter-individual and demographic variability on symptom parameter information (Burns & Gutfraind, 2021); the impact of the bivalent vaccine (i.e., booster vaccine) was not considered (Kim et al., 2023); there were uncertainties on the viral kinetics of SARS-CoV-2 and sensitivity of antigen tests (Maya & Khan, 2023); the assumptions made on perfect adherence to isolation measures; and that SARS-CoV-2 infections would provide perfect immunity against reinfection (Sararat et al., 2022). Additional limitations of each study can be found in Table 1.3.

- It is important to note that isolation for RIDs is also informed by knowledge of the incubation period, the infectious period, viral load kinetics, the reproductive number and/or secondary attack rate, population susceptibility, adherence levels, and other complimentary public health measures in place. Studies focused on these variables and outcomes were not included in this synthesis.

Potential implications for health systems decision-making:

- It is clear from the evidence reported in the current review that there is a *significant dearth of empirical evidence (i.e., there are no identified empirical studies)* on the impact of different lengths of isolation on secondary RID transmission. Furthermore, the available modelling evidence, which was all focused on COVID-19, had notable biases, which makes interpretation problematic. That being said, there are some trends across the included studies which can provide some initial insights into the potential effects of isolation on transmission.
- Overall, the current evidence would suggest that isolation reduces transmission and that there is *an important benefit of longer durations of isolation on transmission and related outcomes*. However, there were some models in specific settings where this did not hold.
- Importantly, most of these studies were not conducted or accounted for scenarios where there is a relatively high level of vaccination across populations or, in the case of COVID-19, with a variant that is highly transmissible, i.e., Omicron.
- From a *public health preparedness perspective*, if isolation was deemed appropriate for a future pandemic outbreak, based on the limited available evidence, the isolation of infected individuals for longer

periods (i.e., informed by the infectious period) compared to shorter periods would likely be more effective at reducing overall transmission. However, if such a scenario should occur, then this would be an opportune time to capture much needed empirical evidence, with a low risk of bias, to provide important inputs for the continued development of RID isolation policies and guidance.

Suggested Tweet
The limited data means that there are no suggested tweets that we could propose.

Date of Literature Search: February 27, 2024

Suggested citation: Bacon SL, Wu N, Paquet L, Burdick J, Marques Vieira A, Joyal-Desmarais K, Léger C, Deslauriers F, and Sanuade C. COVID-19 Living Evidence Synthesis 13.2a: Effectiveness of isolation on the reduction of the transmission of respiratory infectious diseases (RIDs: i.e., COVID-19, H1N1, SARS, MERS). Montreal Behavioural Medicine Centre, CIUSSS-NIM, 7 May 2024.

Résumé

Question

Quelle est l'efficacité de l'isolation* pour réduire la transmission de maladies respiratoires infectieuses (c.-à-d. maladie à coronavirus (COVID-19), sous-type H1N1 de l'influenza A (H1N1), syndrome respiratoire aigu sévère (SARS) et syndrome respiratoire du Moyen-Orient (MERS))?

*Isolation réfère à la ségrégation des individus ayant testé positif à l'une des maladies citées ci-haut ou ayant des symptômes liés aux maladies citées ci-haut.

Contexte

- Deux stratégies clés pour prévenir la propagation des maladies respiratoires infectieuses sont:
  - 1) les personnes qui ont été en contact avec une personne qui a obtenu un résultat positif doivent se mettre en quarantaine ;
  - 2) les personnes qui sont symptomatiques ou qui ont obtenu un résultat positif à la maladie doivent s'isoler.
- Au cours des premières phases de la pandémie de COVID-19, une durée de 14 jours pour ces deux mesures était une politique courante. Au fil du temps et entre les administrations, il y a eu plusieurs variations dans la durée et la structure des périodes d'isolement.
- Il n'est pas clair si et quels effets différentes durées d'isolement ont eu sur les taux de transmission des maladies respiratoires infectieuses.

Méthode

- Nous avons collecté les études potentielles en cherchant : 1) EMBASE; 2) Medline; 3) PsycINFO; et 4) le portfolio iSearch sur la COVID-19 de l'institut National de la santé (NIH).
- Pour ce premier tour, 2 526 titres et résumés d'article ont été examinés, 772 de ces articles ont été inclus pour l'examen du texte intégral. Parmi ces derniers, 5 articles de modélisation et aucune étude empirique ont été inclus dans ce rapport.

Points clés

- Cinq études de modélisation ont été identifiées, toutes portant sur la COVID-19.
- Trois des cinq études de modélisation indiquaient que des *périodes d'isolement plus longues étaient associées à une transmission secondaire plus faible*.
  - Dans un modèle de simulation basé aux États-Unis sur les cas asymptomatiques et légers, un protocole d'isolement de 10 jours avec un test antigénique rapide au jour 6 lors duquel la personne mettait fin à l'isolement si elle était négative, sinon continuait jusqu'au jour 10, a été considéré comme le plus efficace pour éviter les infections futures (COVID-19; Maya & Khan) par rapport à d'autres variations de durée et de protocoles de test.
  - Dans un modèle de simulation général composé d'individus non vaccinés, l'augmentation de la durée de l'isolement jusqu'à 14 jours diminuait systématiquement les chances d'infections secondaires et d'épidémies (Sararat et al). Lorsque la vaccination était incluse dans le modèle, il y avait encore une réduction des infections et des épidémies avec un isolement plus long. Cependant, cela atteignait son point le plus bas autour de six jours d'isolement.

- Dans un modèle de simulation d'adultes coréens, l'augmentation de la durée de l'isolement jusqu'à sept jours était associée à des réductions à la fois des taux et des nombres absolus de cas confirmés, de cas graves et de décès (Kim et al). Cela demeurait relativement semblable lorsque le modèle prenait en considération une réduction du port de masque.
- Toutefois, un modèle n'a trouvé aucune différence entre 0, 5 et 10 jours d'isolement en ce qui concernait les infections chez les personnes déplacées à l'intérieur du Bangladesh (Aylett-Bullock et al) et un modèle scolaire basé aux États-Unis n'a trouvé aucun effet de la durée d'isolement (jusqu'à 14 jours) suivant le début de la fièvre sur les taux d'infection lors d'épidémies en milieu scolaire (Burns & Gutfraind)

Considérations sur la qualité des données

- Les études de modélisation incluses dans cette synthèse rapide des données vivantes présentaient des biais et des limites notables. Les principaux biais présents sont les suivants : l'absence de données réelles sur les cas et les tests pour valider les prédictions du modèle (Aylett-Bullock et al., 2021), le manque d'applicabilité des résultats à différentes populations et l'absence de prise en compte de la variabilité interindividuelle et démographique sur les informations relatives aux paramètres des symptômes (Burns & Gutfraind, 2021) l'impact du vaccin bivalent (c'est-à-dire le vaccin de rappel) n'a pas été pris en compte (Kim et al., 2023), il y avait des incertitudes sur la cinétique virale du SRAS-CoV-2 et la sensibilité des tests antigéniques (Maya & Khan, 2023) et des hypothèses ont été émises sur l'adhésion parfaite aux mesures d'isolement et sur le fait que les infections par le SRAS-CoV-2 fourniraient une immunité parfaite contre la réinfection (Sararat et al., 2022). Le tableau 1.3 présente d'autres limites pour chacune des études.
- Il est important de noter que l'isolement en raison des maladies respiratoires infectieuses est également informé par la connaissance de la période d'incubation, de la période infectieuse, de la cinétique de la charge virale, du taux de reproduction et/ou du taux d'attaque secondaire, de la susceptibilité de la population, des taux d'adhésion et des autres mesures complémentaires de santé publique en place. Les études axées sur ces variables et ces résultats n'ont pas été incluses dans la présente synthèse.

Implications potentielles pour la prise de décision des systèmes de santé :

- Il est clair d'après les preuves rapportées dans la revue actuelle qu'il existe une *pénurie significative de preuves empiriques (c'est-à-dire aucune étude empirique)* sur l'impact de différentes longueurs d'isolement sur la transmission secondaire des maladies infectieuses respiratoires. De plus, les preuves de modélisation disponibles, qui étaient toutes axées sur la COVID-19, présentaient des biais notables, ce qui rend l'interprétation problématique. Cela dit, certaines tendances à travers les études incluses peuvent fournir quelques aperçus initiaux des effets potentiels de différentes longueurs d'isolation sur la transmission.
- Dans l'ensemble, les preuves actuelles semblent suggérer que l'isolation diminue la transmission et que les *durées d'isolement plus longues sont avantageuses pour la transmission et les résultats associés*. Cependant, ce n'était pas le cas pour certains modèles dans des contextes spécifiques.
- Plus important encore, la plupart de ces études n'ont pas été menées ou n'ont pas pris en compte les scénarios où il y a un niveau relativement élevé de vaccination dans les populations, ou, dans le cas de la COVID-19, avec un variant hautement transmissible, c'est-à-dire Omicron.
- Dans une *perspective de planification en santé publique*, si l'isolation devait être jugée comme étant appropriée dans le cadre d'une autre pandémie, les données limités recueillies suggèrent qu'isoler

les individus infectés pour une durée plus longue (selon la période infectieuse) serait probablement plus efficace pour diminuer la transmission de la maladie qu'une isolation plus courte. Cependant, si un tel scénario devait se produire, il s'agirais du moment idéal pour collecter des données empiriques ayant un risque de biais faible. Cela serait utile au développement de politique et lignes directrices d'isolation en cas de maladies respiratoires infectieuses.

Suggestion de gazouillis

Les données limitées ne permettent pas de suggérer un gazouillis.

Methods

This living evidence synthesis (LES) was designed and executed by the Montreal Behavioural Medicine Centre, a collaborative Université du Québec à Montréal, Concordia University, and CIUSSS-NIM research centre, and in collaboration with a network of evidence-support units supported by a secretariat housed at the McMaster health forum.

This LES is also part of a suite of LESs of the best-available evidence about the effectiveness of PHSMs (public health and social measures, i.e., quarantine and isolation, masks, ventilation, physical distancing and reduction of contacts, hand hygiene and respiratory etiquette, cleaning, and disinfecting), as well as combinations of and adherence to these measures, in preventing transmission of respiratory infectious diseases. This is the 2nd version of this LES (LES 13), which has now been split into three separate reports about the effects of isolation (LES 13.2a), and quarantine (LES 13.2c) on secondary transmission, and the unintended consequences of isolation and quarantine (LES 13.2b). Beyond separating the reports, the LESs include enhancements in scope from the first version by expanding the target pathogen from COVID-19 isolation to include H1N1, SARS and MERS and the impact of different lengths of isolation across these viruses). The next update to this and other LESs in the series is to be determined, but the most up-to-date versions in the suite are available. The findings of previous round are available on the McMaster Health Forum.

General considerations for identifying, appraising, and synthesising evidence about PHSMs

- PHSMs are population-level interventions and typically evaluated in observational or modeling studies.
  - Many PHSMs are interventions implemented at a population level, rather than at the level of individuals or clusters of individuals such as in clinical interventions.
  - Since it is typically not feasible and/or ethical to randomly allocate entire populations to different interventions, the effects of PHSMs are commonly evaluated using observational study designs that evaluate PHSMs in real-word settings.
  - As a result, a lack of evidence from RCTs does not necessarily mean the available evidence in this series of LESs is weak.
- Instruments for appraising the risk of bias in observational studies have been developed; however, rigorously tested, and validated instruments are only available for clinical interventions.
  - Such instruments generally indicate that a study has less risk of bias when it was possible to directly assess outcomes and control for potential confounders for individual study participants.
  - Studies assessing PHSMs at the population level are not able to provide such assessments for all relevant individual-level variables that could affect outcomes, and therefore cannot be classified as low risk of bias.
- To date, there are no instruments for appraising the risk of bias in modeling studies; however, given that all modeling studies work on a series of key assumptions to infer effects, it is assumed that all these studies have a critical risk of bias.

Implications for synthesising evidence about PHSMs

- Decision-making with the best available evidence requires synthesising findings from studies conducted in real-world settings (e.g., with people affected by misinformation, different levels of adherence to an intervention, different definitions, and uses of the interventions, and in different stages of the epidemics and pandemic, such as before and after availability of COVID-19 vaccines). As such, there are a number of critical aspects that differ across studies that can't be fully accounted for in any synthesis, meaning that summary results need to be interpreted with some degree of caution.

Of note, RoB (and GRADE, which was not used for this report) were designed for clinical programs, services, and products, and there is an ongoing need to identify whether and how such assessments and the communication of such assessments, need to be adjusted for public-health programs, services, and measures and for health-system arrangements.

Study Selection: We retrieved candidate studies by searching: 1) EMBASE; 2) Medline; 3) PsycINFO; and 4) the National Institute of Health (NIH) iSearch COVID-19 portfolio. Searches were conducted for studies reported in English, published since January 1, 2009 for H1N1, January 1, 2003 for SARS, January 1, 2012 for MERS, and January 1, 2020 for COVID-19. Our detailed search strategy is included in **Appendix 8**.

Studies that report on empirical data as well as modelling studies were considered for inclusion in the main report, with case reports, case series, and press releases excluded. Empirical and modelling studies were screened and extracted. A full list of included empirical studies is provided in **Table 1.1-2, 2.1-2, 3.1-2, 4.1-2 and Appendix 1**. Studies excluded at the full-text stage of reviewing are provided in **Appendices 4, 5 and 6**. A full list of included modelling studies is provided in **Table 1.3, 2.3, 3.3, 4.3 and Appendix 2**.

The PRIMSA flow chart of included studies, including separate details for this round, can be found in **Appendix 3**.

Population of interest: All individuals who have COVID-19, H1N1, SARS or MERS related symptoms and/or have tested positive for one of these diseases.

Intervention: Isolating for any period of time (this can include discreet measures of isolation as well as continuous measures of isolation, includes studies using testing to modify the duration of isolation).

Comparison: Any other form of isolation, including individuals were confined for a different length of time or who used various testing strategies to variably alter isolation time. Intervention comparison could be across populations (different countries, those tested asymptomatically), settings (e.g., different location for isolation), or time periods (e.g., before/after a policy change, different time periods).

Primary outcomes:

- Transmission of any of the disease of interest, i.e., how many secondary infections came from those in the intervention and comparison arms/time periods.

- Measures of transmission could include: absolute number of infections; attack rates; estimated incidence; estimated infections averted; growth rate of cases or deaths; reproductive ratio (Ro or Rt); rates of hospitalisations; and intensive care unit (ICU) utilisation.

Data extraction: Data extraction was conducted by one team member and checked for accuracy and consistency by at least one other team member.

Critical appraisal: Risk of Bias (ROB) of individual studies was assessed using a version of the ROBINS-I which was validated for COVID-19. Revisions and subsequent iterations of this version of the ROBINS-I was decided by consensus within the synthesis team as needed. Additional ROB tools was added as needed to fit with other study designs. Our detailed approach to critical appraisal is provided in **Appendix 9**. Additional details about the approach to critical appraisal are provided here.

Comment on modelling studies: Modelling studies reflect works that use simulations to infer the effects of interventions, based on strict assumptions. As such, we advise caution when interpreting findings from these studies as their results are strongly impacted by these assumptions. This is primarily because the assumptions normally oversimplify scenarios and do not usually reflect the real-world status, e.g., 100% of the population being vaccinated, varying degrees of illness in individuals, etc.

Summaries: Data is reported by RID and then by the ROB of the studies identified (empirical studies without critical risk of bias, empirical studies with a critical risk of bias, and then modelling studies).

Results 1: Summary of studies about the effectiveness of isolation on the transmission of COVID-19

Table 1.1: Summary of empirical studies that were rated as ***not having a critical risk of bias***, reporting on effectiveness of isolation in preventing the transmission of COVID-19, presented in alphabetical order of 1st author

Reference	Date released	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome	RoB Rating
No studies					

Table 1.2: Summary of empirical studies rated as having a ***critical risk of bias***, reporting on effectiveness of isolation in preventing the transmission of COVID-19, presented in alphabetical order of 1st author

Reference	Date released	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome	RoB Rating
No studies					

Table 1.3: Summary of modelling studies reporting on effectiveness of isolation in preventing the transmission of COVID-19, presented in alphabetical order of 1st author

Reference	Date released	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome	Key Limitations
Aylett-Bullock et al., 2021	Paper submitted to Journal in March 2021.	Modeled after refugee and internally displaced person (IDP) settlements in Bangladesh.	**Model**: Agent-based model, based on the open-source framework "JUNE", which operates by simulating a "digital twin" of the environment where individuals interact. **Goal:** Examine the impact of isolation in refugee and internally displaced person settlements on COVID-19 transmissions. **Key Outcome**: Total number of infected cases.	Under a "best-case" scenario where: • All infected individuals isolate (100% compliance) • People isolate in isolation centres (not at home) • Time delay between testing and isolation is 2 days There is little difference between no isolation, 5 days of isolation, and 10 days of isolation. • No isolation: 433k total infections • 5-day isolation: 432k total infections • 10-day isolation: 432k total infections Most infections occurred within residences, before symptom onset, leading isolation (post-symptoms) in centres to be ineffective.	• Lack of case and testing availability which led to the absence of validation of model predictions with real world data. • They simulated the effects of the interventions as though they had been implemented since the onset of the simulated period. • Simplification made on the assumption that comorbidity prevalence in the settlement population is comparable to the country of origin. Future studies can provide data on the

			Accounts for: • Differences in geographical, social, and demographic factors. • Delays between testing, symptoms, and isolation. **Key Assumptions**: • People interact within shelters, even under isolation • 88 infected individuals seeded per modeled region at baseline • Moderate transmission rate: $R_0 \approx 2.0 - 3.0$ • In baseline model, symptomatic self-quarantine at home with a low compliance rate (30%) **VOCs**: Not considered. **Vaccination status**: Not considered **Terminology**: "Isolation" used to refer to symptomatic individuals who confine in isolation "Shelter" refers to a one or two room space housing an average of 7 person and often housing more than one family. Isolation centres may be used to isolate symptomatic cases.		comorbidities of specific populations in question. • Vaccination status and healthcare seeking behaviour in response to epidemic outbreaks were not considered.
Burns & Gutfraind, 2021	Published 30 March, 2021	Medium-sized US School (~ January to July), early in the pandemic.	**Model**: Susceptible, Exposed, Infectious, recovered (SEIR) model, which is a deterministic compartmental dynamical model. Each scenario examined was simulated 500 times. **Goal**: Evaluate effectiveness of home-based isolation (following	In general, the number of post-fever isolation days has little effect on COVID-19 outbreaks. Numbers reported are median effects (with interquartile ranges). No policy measures (i.e., no isolation). This is the baseline. • Attack rate = 10.0% (8.7-11.3) 1-day post-fever isolation: • Attack rate = 9.4% (8.3-10.6)	• The effect of the policy in the context of where it would be applied was not considered (i.e., the details of specific schools or institutions). • The findings from this study are limited to school-based contexts and when applied to other contexts such as workplaces,

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<td>fever) to reduce school-based transmission.

Key outcomes: Overall virus transmissibility, including attack rate (proportion (%) of population infected during outbreak.)

Accounts for: Schooling context, virus progression.

Key assumptions:
• School comprised of 6 grades; 70 students per grade

VOCs: Not considered.

Vaccination status: Examines effects of vaccination in some models, but not when modeling duration of isolation (for which model assumes no vaccination).

Terminology: Symptom-based “isolation” policy involves isolating individuals at the onset and for the duration of fever symptoms, normally followed by additional days of isolation.</td>
<td>2-day post-fever isolation:
• Attack rate = 9.2% (8.0-10.6)

14-day post-fever isolation:
• Attack rate = 8.5% (7.4-9.7)

.Note: In models, reducing the number of in-person school days per week had a much larger impact.</td>
<td>prisons or the broader community the results may differ.
• The symptom parameter information is based on average values for the population. Inter-individual and demographic variability were not considered.</td>
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<tr>
<td>Kim et al., 2023</td>
<td>Accepted: July 6, 2023

Published: July 21, 2023</td>
<td>An age diverse populatio n based in Korea</td>
<td>Model: Age-structured mathematical model to describe the COVID-19 dynamics in Korea across eight age groups (0–9 years; 10–19 years; 20–29 years; 30–39 years; 40–49 years; 50–59 years; 60–69 years; 70 years and older). Some of the populations were from hospital settings.

Goal: To examine the impact of easing COVID-19 control measures, such as the isolation time and mask-wearing requirements.</td>
<td>Higher transmission rates amplify the impact of vaccine effectiveness and exacerbate the consequences of early isolation release.

Rate of increase in the cumulative number from the specified date to 31/01/23 (compared to a 7-day isolation)
<table>
<tr><th>Isolation duration (days)</th><th>Confirmed cases</th><th>Severe cases</th><th>Death</th></tr>
<tr><td colspan="4">01/01/22</td></tr>
<tr><td>5</td><td>18.953</td><td>30.94</td><td>31.168</td></tr>
<tr><td>3</td><td>22.096</td><td>41.191</td><td>42.256</td></tr>
</table>
</td>
<td>• The reduction in the severity of reinfections was not considered.
• They did not consider the impact of the bivalent vaccine (i.e., booster vaccine that is highly effective against hospitalization and severe symptoms caused by the Omicron variants).</td>
</tr>
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Key outcomes: changes in confirmed cases, hospitalizations, and deaths over time.

Accounts for: The length of isolation, the rate of mask wearing, the screening rate, age, the effect of vaccination and the possibility of reinfections.

Key assumptions:

- Mean duration of case confirmation: 3 days
- Recovery of asymptomatic cases: 3.5 days
- Recovery or isolation period of mild cases: 7 days
- Patients who were released early (before 7 days) were still infectious, they affected the infection rate.
- Recovery rate of hospitalization varied according to age and if people were in the ICU but the value was assumed for each of these categories
- Period of stay in ICU: 7 days
- Mortality rate of ICU patients varied according to age and if people were vaccinated but the value was assumed for each of these categories
- Average duration of infectious antibodies: 180 days
- Second dose vaccine efficacy: 0.06
- Third dose vaccine efficacy: 0.39
- Fourth dose vaccine efficacy: 0.49
- Latent period: 5.2

0	27.836	61.436	64.212
17/04/22			
5	11.783	10.103	9.4061
3	15.852	16.792	16.157
0	23.372	29.912	29.387
21/06/22			
5	6.8044	3.7333	3.2896
3	10.855	10.035	9.8191
0	18.246	22.129	22.336
29/08/22			
5	4.1619	2.3935	1.9772
3	8.9826	9.1502	8.4419
0	17.935	22.29	21.049

Rate of increase in the cumulative number of cases 6 months from the specified date (compared to a 7-day isolation)

Isolation duration (days)	Confirmed cases	Severe cases	Death
01/01/22			
5	3.9979	10.97	9.1801
3	7.4031	22.023	20.271
0	13.944	46.547	45.673
17/04/22			

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<td>VOCs: Omicron variant

Vaccination status: Vaccination is accounted for in this model

Terminology:
Isolation: The current study erroneously refers to the confinement of individuals who tested positive as “quarantine”.</td>
<td>
<table>
<tr><td>5</td><td>6.2814</td><td>5.8873</td><td>5.2517</td></tr>
<tr><td>3</td><td>9.6573</td><td>11.325</td><td>10.489</td></tr>
<tr><td>0</td><td>16.359</td><td>22.564</td><td>21.228</td></tr>
<tr><td colspan="4">21/06/22</td></tr>
<tr><td>5</td><td>5.1155</td><td>2.7966</td><td>2.2936</td></tr>
<tr><td>3</td><td>9.6677</td><td>9.5834</td><td>9.1542</td></tr>
<tr><td>0</td><td>17.966</td><td>22.668</td><td>22.584</td></tr>
<tr><td colspan="4">29/08/22</td></tr>
<tr><td>5</td><td>5.1314</td><td>2.9351</td><td>2.4287</td></tr>
<tr><td>3</td><td>9.8331</td><td>9.6161</td><td>8.8357</td></tr>
<tr><td>0</td><td>18.493</td><td>22.548</td><td>21.299</td></tr>
</table>

The increase in the number of severe cases due to the shortening of the mandatory isolation period was substantially affected by the timing of the relaxation of isolation measures.

Shorter isolation periods led to increases in the numbers of confirmed cases, severe cases, and deaths.

The shorter the mandatory isolation period for confirmed cases, the relatively higher the numbers of severe cases and deaths.
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<td>Maya & Khan, 2023</td>
<td>Published online: May 11, 2023</td>
<td>Based on 100 individuals in the US who had COVID-19 and were on day 5 of isolation.</td>
<td>Model: Customized decision tree analysis

Goal: Evaluate six different protocols to determine when to end COVID-19 isolation. These varied the default duration of the isolation (5, 8, 10 days), and the rule for ending isolation early (symptom check or antigen/PCR test)).

Key outcomes:</td>
<td>Secondary infections under the 6 intervention conditions

Option 1: 5-day isolation, no possibility to end early:
• Secondary infections: 23.04

Option 2: 10-day isolation, with symptom check on day 5. If asymptomatic, end isolation, otherwise continue to day 10.
• Secondary infections: 17.83

Option 3: 10-day isolation, with rapid antigen test on day 5. If negative, end isolation, otherwise continue to day 10.
• Secondary infections: 5.68</td>
<td>• They had uncertainties in key inputs such as the viral kinetics of SARS-CoV-2 and sensitivity of antigen tests.
• They distributed the effective secondary reproduction number (i.e., accounts for infection prevention measures in place) over the 10 days proceeding confirmation of COVID-19 infection; however, some transmissions occur prior to</td>
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			• Secondary infections (per 100 persons) over a two-week period
			
			Accounts for: Health/infectivity factors, test sensitivity, intervention adherence.
			
			Key assumptions: For base model:
			• Only modeled asymptomatic & mild COVID-19 cases
			• Base sensitivity of tests:
			  ○ Symptom check: 23.8%
			  ○ Antigen test: 79.3%
			  ○ PCR test: 89.0%
			• 90% still infectious on day 5
			• 22% drop in infectiousness from day 5-6
			• Secondary reproduction number: 1.2
			• Intervention adherence: 100%
			• 100% testing access/coverage
			
			VOCs: Models used parameters according to Omicron variant when available; otherwise used data for Alpha or Delta.
			Vaccination status: Not considered
			
			Terminology: "Isolation" refers to confinement of persons with confirmed COVID-19.
				Option 4: 10-day isolation, with PCR test on day 5. If negative, end isolation, otherwise continue to day 10.
				• Secondary infections: 3.56
				
				Option 5: 10-day isolation, with rapid antigen test on day 6. If negative, end isolation, otherwise continue to day 10.
				• Secondary infections: 2.88
				
				Option 6: 8-day isolation, with rapid antigen test on day 5. If negative, end isolation, otherwise continue to day 8.
				• Secondary infections: 10.02
				
				Note. The most cost-effective de-isolation protocol was deemed option 5 (10-day isolation with an antigen test on day 6).
					COVID-19 confirmation and isolation. Consequently, they purposely overestimated the number of secondary infections in their model and underestimated cost-effectiveness ratios to account for the likely missed cases.
					• They did not consider the Omicron variant when assessing secondary infections and cost-effectiveness.

Sararat et al., 2022	Paper submitted to journal in February 2022 (accepted in	Not modeled after a specific populatio n.	**Model**: Individual-based compartmental model. A single infected individual ("index case") is introduced in a population.
			
			Goal: Assess the likelihood of secondary infections and the
				Baseline scenario: all individuals are unvaccinated. No additional non-pharmaceutical intervention is employed.
				• 14-day isolation. An infected case has:
				  ○ 3% chance of secondary infections
				  ○ <1% chance of successful outbreak
				• 10-day isolation. An infected case has:
				  ○ ~8% chance of secondary infections
					• They assumed that neither infection-acquired nor hybrid immunity existed in the initial population.
					• The model parameters used were based on the Delta variant and the BNT162b2 vaccine. Limiting the

	September 2022)		likelihood of an outbreak following isolation of an index case for a range of isolation periods and vaccination scenarios. **Key outcomes**: • ***Secondary transmission:*** probability a primary case makes *at least one* subsequent infection after isolation. • **Successful outbreak**: primary case leads to a sustained chain of transmission after isolation **Accounts for**: Transmission/infectivity factors, vaccination. **Key assumptions**: • Disease infectiousness peaks at 2.1 days before symptom onset • Incubation period lasts a mean of 5.8 days • Asymptomatic infectious individuals are less infectious than symptomatic ones. • Primary index cases isolated immediately after becoming infected. Subsequently infected individuals are isolated with a default delay of 6.8 days. • Basic reproduction number = 5.08 • Vaccine effectiveness (VE) against infections is 0.79 and against transmissions is 0.25 in most models. But ran some models setting VE against infections at either 0.50 or 0.90 and altering VE against transmissions between 0.00 to 0.40. • Symptomatic are isolated with a probability of 0.8,	○ ~6% chance of successful outbreak • 7-day isolation. An infected case has: ○ ~14% chance of secondary infections ○ ~6% chance of successful outbreak • No isolation. An infected case has: ○ ~28% chance of secondary infections ○ ~16% chance of successful outbreak **Best case vaccine scenario***: all* individuals are vaccinated: • The probability of secondary transmissions is >5% only at <6 days of isolation and remains <10% even at 0 days of isolation. • The probability of a successful outbreak is negligible (close to 0%) for all duration periods. **Second best scenario** whereby index case plus 75% of others are vaccinated: • At 8+ days of isolation: ○ ~ <3% chance of secondary infections ○ ~ <1% chance of successful outbreak • Otherwise: ○ For secondary infections, the chance is ~3% for a 7-day isolation, and rises linearly as isolation shortens, reaching ~15% at 0 days. ○ For successful outbreaks, the chance rises to ~1% at 7 days, and rises gradually with shorter intervals ▪ ~1.5% for 3- and 5-day isolation ▪ ~3% for no isolation **Equivalencies to Baseline.** 1. Conditions that are equivalent to a 14-day isolation in the baseline scenario for reducing *secondary transmissions*: • 10 days of isolation for a vaccinated index case when no one else is vaccinated. • ~8 days when index and 75% of others vaccinated, and ~6 days when 100% of people are vaccinated 2. Conditions that are equivalent to a 14-day isolation in the baseline scenario for reducing *successful outbreaks*: • 9.33 (95% CI: 8.68-9.98) days of isolation of a vaccinated index if 50% of others are vaccinated • 7.33 (95% CI: 6.68-7.98)) days of isolation of a vaccinated index if 75% of others are vaccinated **Vaccination Coverage**:	applicability to the most recent virus variant. • They assumed that SARS-CoV-2 infections would provide perfect immunity against reinfection. • They assumed perfect adherence to isolation measures.

			asymptomatic with a probability of 0.1
			
			VOCs: Mostly considered Delta, and to some extent Omicron (consideration only operationalized in terms of changes in VE)
			
			Vaccination status: Mostly considered primary series, but varied VE against transmissions from 0% to 40% to reflect low VE after waning vs. after a booster, and that VE could vary according to strain (e.g., be low against omicron).
			
			Terminology: "Isolation" focuses on confinement of primary cases (infected). Authors discuss quarantine of contacts, but quarantine is not modeled in the study.
				• Concludes that higher vaccine coverages decrease the chance of secondary transmission following the isolation of a (vaccinated) index case, especially when isolation duration is short.
				• For long isolation periods (e.g., 10+ days), vaccination coverage makes little difference.
				Vaccination Effectiveness (setting coverage at 75%)
				• VE against infections or against transmissions had little impact on the probability of secondary transmissions of different isolation durations (i.e., duration patterns similar to before, though generally higher at low VE)
				• However, against outbreaks VE mattered
				  ○ At very high VE against infections (VE = .90), the probability of outbreaks was low regardless of different isolation durations or VE against transmissions (always at 2% or lower)
				  ○ At a lower VE against infections (VE = 0.5), both duration and VE against transmissions mattered. At 7+ days of isolation, however, the probability of outbreaks was always ~2% or lower.
				
				**Note*: A tilde (~) indicates that this finding was extracted by visual analysis of a figure.	

Results 2: Summary of studies about the effectiveness of isolation on the transmission of HIN1

Table 2.1: Summary of empirical studies that were rated as ***not having a critical risk of bias***, reporting on effectiveness of isolation in preventing the transmission of H1N1, presented in alphabetical order of 1st author

Reference	Date released	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome	RoB Rating
No studies				●	

Table 2.2: Summary of empirical studies rated has having a ***critical risk of bias***, reporting on effectiveness of isolation in preventing the transmission of H1N1, presented in alphabetical order of 1st author

Reference	Date released	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome	RoB Rating
No studies				●	

Table 2.3: Summary of modelling studies reporting on effectiveness of isolation in preventing the transmission of H1N1, presented in alphabetical order of 1st author

Reference	Date released	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome
No studies				●

Results 3: Summary of studies about the effectiveness of isolation on the transmission of SARS

Table 3.1: Summary of empirical studies that were rated as ***not having a critical risk of bias***, reporting on effectiveness of isolation in preventing the transmission of SARS, presented in alphabetical order of 1st author

Reference	Date released	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome	RoB Rating
No studies				●	

Table 3.2: Summary of empirical studies rated has having a ***critical risk of bias***, reporting on effectiveness of isolation in preventing the transmission of SARS, presented in alphabetical order of 1st author

	Date released	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome	RoB Rating
No studies				•	

Table 3.3: Summary of modelling studies reporting on effectiveness of isolation in preventing the transmission of SARS, presented in alphabetical order of 1st author

Reference	Date released	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome
No studies				•

Results 4: Summary of studies about the effectiveness of isolation on the transmission of MERS

Table 4.1: Summary of empirical studies that were rated as ***not having a critical risk of bias***, reporting on effectiveness of isolation in preventing the transmission of MERS, presented in alphabetical order of 1st author

Reference	Date released	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome	RoB Rating
No studies				•	

Table 4.2: Summary of empirical studies rated has having a ***critical risk of bias***, reporting on effectiveness of isolation in preventing the transmission of MERS, presented in alphabetical order of 1st author

Reference	Date released	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome	RoB Rating
No studies				•	

Table 4.3: Summary of modelling studies reporting on effectiveness of isolation in preventing the transmission of MERS, presented in alphabetical order of 1st author

Reference	Date released	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome
No studies				•

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References

1. Aylett-Bullock J, Cuesta-Lazaro C, Quera-Bofarull A, Katta A, Hoffmann Pham K, Hoover B, et al. Operational response simulation tool for epidemics within refugee and IDP settlements: A scenario-based case study of the Cox's Bazar settlement. PLOS Computational Biology. 2021;17(10):e1009360. Available from: https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1009360
2. Burns AAC, Gutfraind A. Effectiveness of isolation policies in schools: evidence from a mathematical model of influenza and COVID-19. PeerJ. 2021 Mar 30;9:e11211. Available from: https://peerj.com/articles/11211/
3. Kim JE, Choi H, Lee M, Lee CH. The effect of shortening the quarantine period and lifting the indoor mask mandate on the spread of COVID-19: a mathematical modeling approach. Frontier public health. 2023;11(101616579):1166528. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10401846/
4. Maya S, Kahn JG. COVID-19 testing protocols to guide duration of isolation: a cost-effectiveness analysis. BMC Public Health. 2023;23:864. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10173903/
5. Sararat C, Wangkanai J, Wilasang C, Chantanasaro T, Modchang C. Individual-based modeling reveals that the COVID-19 isolation period can be shortened by community vaccination. Scientific Reports. 2022;12(1):17543. Available from: https://www.nature.com/articles/s41598-022-21645-y

Appendices