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

Question

What is the effectiveness of quarantine* on reducing the transmission of respiratory infectious diseases (RID), including COVID-19, H1N1, severe acute respiratory syndrome (SARS), and middle eastern respiratory syndrome (MERS)?

* Quarantine refers to the segregation of individuals who have been in close contact (or suspected contact) with one or more-person(s) who has (have) tested positive for the respiratory infectious diseases (i.e., COVID-19, H1N1, SARS, and MERS) or has (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 quarantine periods.
- It is unclear if and what effects different quarantine 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, 17 studies were included in this report, including 5 empirical studies (2 of which had serious risk of bias and 3 of which had a critical risk of bias) and 12 modelling studies.

Key points

- Sixteen of the included studies focused on COVID-19, the other one focused on SARS

Overview of evidence and knowledge gap

It is important to note that RIDs related quarantine 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, sensitivity and specificity of tests, and other complimentary public health measures in place. Studies focused on these variables and outcomes were not included in this synthesis.

Data from the empirical studies without a critical risk of bias:

- Overall, two randomised controlled trials of similar interventions, serial antigen testing vs. quarantine found *inconsistent findings.* One in adults suggested that the serial antigen testing reduced infections, whereas the one in a school setting found no difference.
    - A non-critical risk of bias empirical non-inferiority randomised controlled trial of individuals in the UK who had been exposed to an individual with a positive COVID-19 test, found that 7 days of serial antigen test, with 24 hours of free movement following a negative test and isolation with a positive test, was non-inferior to 10-days of quarantine for secondary infections (COVID-19; Love et al). In addition, there was a suggestion that the serial antigen testing strategy may actually reduce secondary infections. However, the design of the study doesn't allow us to conclude this.
    - In a parallel cluster-randomised, controlled trial in schools in the UK, students and staff who had been exposed to an individual with a positive COVID-19 test were randomised to either 7 days of serial antigen testing, being able to attend class on days that they were negative and isolation when they were positive, or 10 days of quarantine. This study found no difference in attack rates between the 2 groups (COVID-19; Young et al)

Data from the empirical studies with a critical risk of bias:

- The two COVID-19 studies with a critical risk of bias found *no differences* between standard quarantine strategies (ranging from 7-14 days) and other potential quarantine protocols.
    - One study with a critical risk of bias replicated the interventions assessed above (Love et al study) using a cohort study design rather than an RCT. Though this study showed no statistically significant difference between the 2 groups, the average rates of secondary transmission were the same as in the RCT (the cohort study had greater variability which accounted for the lack of statistical significance).
    - In a US school setting, a modified quarantine protocol, where students who were in close contact with a COVID-19 case could attend school if a series of COVID-19 preventions measures were in place (e.g., mask mandate, physical distancing, etc.), had the same level of transmission rates as a standard 7-14 day at home quarantine (Dawson et al).
- There was 1 empirical study (with critical risk of bias) identified in the literature, focused on SARS.
    - This Canadian (Ontario) study found that in a very specific case of those who were in quarantine and tested positive, *quarantine led to a reduction in secondary cases of SARS*, compared to individuals who were not in quarantine. Furthermore, they were able to estimate that 7.5 exposed individuals needed to be placed in community quarantine to prevent one secondary cases.
    - This study (Bondy et al) had key biases due to a lack of statistical adjustment for important individual characteristics which might play notable roles in exposure and transmission (e.g., job role, age, sex, etc.).
    - It is also important to note that due to the population being studied (people who tested positive while they were in quarantine) it is hard to draw any conclusions about the potential role of traditional quarantine measures.

Data from the modelling studies:

- There was a general trend across the modelling studies to find that longer periods of quarantine were associated with reductions in transmissions, though this wasn't true for all studies. There was also support from several studies for early testing to reduce transmission, with *testing occurring around 5-7 days into quarantine* seeming to be the optimal window.

- Studies that support longer periods of quarantine:
    - In a general simulation model, that explored the differences in quarantine time, there were decreases in infections with longer lengths of quarantine (Zou et al).
- Studies that support longer quarantines, but provide information on optimal testing + quarantine strategies:
    - In a workforce model, with varied quarantine lengths of 1-14 days, the longer the length of quarantine the lower the subsequent/secondary transmission (Peng et al). The optimal testing + quarantine strategy was to test people on days 4, 5, and 6 and if all were negative to then allow release from quarantine.
    - In a general simulation model, that explored the differences in quarantine time and testing, there were decreases in secondary infections with longer lengths of quarantine, though this plateaued from day 6 to 8 before decreasing again from day 9 to 12 (Takeshita et al). Testing at both the start and after day 5 of quarantine further reduced infections.
    - In a general simulation model, increasing the length of quarantine up to 10 days consistently decreased the chances of secondary infections when compared to shorter lengths of quarantine (Ashcroft et al). The model also suggested that a testing strategy, such as testing on day 5 and releasing negative cases only on day 7, reduced transmission compared to 7 days of quarantine without testing. However, this relationship was dependent on the proportion of individuals in quarantine who were infected.
    - In a UK-based model, implementing any form of test-track-isolate (TTI) protocol reduced transmission compared to no TTI strategy, with no notable difference if a symptom-based or test-based strategy was used (He et al). Of note, the TTI strategy was only optimally effective (R <1.0) when conducted in parallel with other preventions measures notably either a lockdown or notable work and social restrictions.
- Studies that support testing + quarantine being better or equivalent to just quarantine:
    - In a workforce model that explored quarantine < 14 days with testing vs. 14 days of quarantine alone, quarantining with a test on day 6 provided the optimal strategy to minimise transmission (Wells et al).
    - In a general simulation model, 10 days of quarantine was compared to 7 days of serial antigen testing (DCT), with varying rates of adherence to quarantine. The model suggested that DCT was as effective as quarantine when adherence was around 60%, as adherence increased DCT was less effective, as adherence decreased DCT was more effective (Ferretti et al.). The model also identified that the DCT strategy significantly decreased the average number of days of quarantine irrespective of adherence to quarantine.
    - In an Australian model of unvaccinated Aboriginal individuals living in dense housing groups, the inclusion of entry and clearance testing and then isolating positive cases at

the start of quarantine reduced peak community infection prevalence by 10-30% in comparison to extended household-based contact tracing and quarantine (i.e., no entry testing) (Hui et al).
    - In a US-based university campus model, that explored the impacts of differences in vaccine effectiveness, testing, and quarantine, enhanced testing of reported contacts was equivalent to quarantining infections in the community (Motta et al). The effects of both testing and quarantine were enhanced as vaccine effectiveness reduced.
- Studies that support quarantine, with no differences between quarantine length:
    - In a US-based cost simulation model including testing costs, quarantine time, and deaths, there were minimal differences in deaths per 1000 index cases with varying lengths of quarantines, testing protocols, and using risk-based quarantine rules (Perrault et al). The optimal quarantine strategy included risk-based quarantine where a group of individuals with a common source of exposure were observed for symptoms when tracing began and if none of them develop symptoms, they were released from quarantine, including exit testing, with 4 additional days of quarantine if positive and active monitoring.
    - In a general simulation model, that explored the differences in quarantine time and testing, there were no differences in infections averted across different lengths of quarantine nor testing at the start or end of quarantine (Quilty et al).
- Study that found no differences in quarantine compared to active monitoring:
    - In a general simulation model, that explored the differences in quarantine vs. active monitoring of contacts in two scenarios (being able to trace 90% vs. 50% of contacts), there were no differences between the two interventions in their ability to reduce infections (Peak et al). In the scenario where 90% of contact can be traced, this resulted in a R below 1 for both interventions vs. the 50% contact tracing scenario where R was above 1.

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 non-biased empirical evidence* on the impact of quarantine on secondary RID transmission. Furthermore, evidence was predominately focused on COVID-19 (with 1 study on SARS), and consisted of studies that 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 RID quarantine.
- Overall, the current evidence from modelling studies on COVID-19 would suggest that there is an important *benefit of longer durations of COVID-19-related quarantine* on transmission and related outcomes (taking into consideration the COVID-19 incubation period).
- There was also support from several COVID-19-focused studies for early testing to reduce transmission, with *testing occurring around 5-7 days into quarantine* seeming to be the optimal window, especially in adult populations. However, the heterogeneity of study designs made comparison and synthesis of results very challenging.
- Importantly, most of these studies were not conducted during or account for scenarios where there is a relatively high level of COVID-19 vaccination across populations, with a variant that is

highly transmissible, i.e., Omicron, and a very low infection level within the population. As such, it is unclear how well this data translates to the current pandemic situation.

- From a *public health preparedness perspective*, should the severity and viral kinetics of any future outbreak of COVID-19 or emergence of an infectious disease threat warrant quarantine measures, a combination of quarantine and testing would likely be the most optimal strategy to reduce secondary infections. In addition, 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 quarantine 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 13.2c: Effectiveness of quarantine on the reduction of the transmission of respiratory infectious diseases (RIDs: i.e., COVID-19, H1N1, SARS, and MERS). Montreal Behavioural Medicine Centre, CIUSSS-NIM, 7 May 2024.

Résumé

Question
Quelle est l'efficacité de la quarantaine 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))?

* Quarantaine réfère à la ségrégation des individus ayant été en contact proche (ou suspecté) avec une ou plusieurs personnes 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 de quarantaine.
- Il n'est pas clair si et quels effets différentes durées de quarantaine 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, 17 articles ont été inclus dans ce rapport, incluant 5 études empiriques (2 ayant un risque de biais élevé et 3 ayant un risque de biais critique) et 12 études de modélisation.

Points clés
Seize des études inclues se focalisent sur la COVID-19 et une étude se focalise sur SARS

Résumé des données et des manques de connaissance
Il est important de noter que la quarantaine en lien avec les maladies respiratoires infectieuses est aussi informée par nos connaissances sur la période d'incubation, la période inflective, la cinétique de la charge virale, le taux de reproduction et/ou le taux d'attaque secondaire, la susceptibilité de la population, le taux d'adhérence, la sensibilité et spécificité des tests et les mesures de santé publique complémentaire mise en place. Les études se focalisant sur ces variables et résultats n'ont pas été inclues dans cette synthèse.

Données provenant des études empiriques n'ayant pas un risque de biais 'critique' :
- Deux études randomisées contrôlées utilisant des interventions similaires soit, une série de test à antigène en comparaison avec une quarantaine standard, ont trouvé des *résultats incohérents.* Celle

chez les adultes a déterminé qu'une série de test à antigène permettait de réduire le nombre d'infection, tandis que celle effectuée dans un contexte scolaire n'a vu aucune différence.

- Une étude randomisée contrôlée de non-infériorité chez des individus provenant du Royaume-Unis et ayant été exposé à un cas positif de la COVID-19 a déterminé qu'une série de test antigène de 7 jours, permettant de se déplacer librement pour 24 heures en cas de test négatif et obligeant l'isolation en cas de test positif, n'était pas inférieur à une quarantaine de 10 jours contre les infections secondaires (COVID-19; Love et al). De plus, il est suggéré qu'une stratégie de test à antigène en série pourrait permettre de réduire le taux d'infection secondaire. Par contre, le design de l'étude ne permet pas de faire de conclusion à ce sujet.
- En parallèle, une étude randomisée en bloc dans des écoles du Royaume-Unis, où les élèves et les membres du personnel ayant été exposés à un cas de COVID-19 devaient soit faire une série de test à antigène de 7 jours et pouvait participer aux cours en personne, soit faire 10 jours de quarantaine. Cette étude n'a vu aucune différence entre les deux groupes (COVID-19; Young et al).

Données provenant d'études empiriques ayant un risque de biais 'critique' :

- Les deux études sur la COVID-19 ayant un risque de biais critique n'ont vu *aucune différence* entre la quarantaine standard (de 7 à 14 jours) et les autres protocoles de quarantaine.
  - Une étude a reproduit l'intervention mentionné ci-haut; dans l'étude de Love et al., en utilisant une cohorte plutôt qu'une étude randomisée contrôlée. Malgré le fait qu'elle n'a pas démontré une différence statistiquement significative entre les deux groupes, le taux moyen de transmission secondaire était le même que dans l'étude randomisée contrôlée (la cohorte avait une plus grande variabilité, ce qui explique le manque de différence statistiquement significative) (Love et al).
  - Dans une étude se déroulant dans un contexte scolaire aux États-Unis, un protocole de quarantaine modifié où les élèves ayant été en contact avec un cas de COVID-19 pouvaient se présenter à l'école si une série de mesures de prévention de la COVID-19 étaient en place (p. ex., le port du masque, la distanciation physique, etc.), avait le même taux de transmission qu'une quarantaine standard de 7 à 14 jours à la maison (Dawson et al).
- Une seule étude empirique (avec un risque de biais critique) se focalisant sur SARS a été identifiée dans la littérature
  - Cette étude canadienne (Ontario) a déterminé que dans le cas très spécifique où des individus en quarantaine testait positif, la *quarantaine permet de réduire le nombre de cas secondaire de SARS*, en comparaison avec des individus qui n'étaient pas en quarantaine. De plus, ils ont estimé que 7,5 individus exposé à SARS doivent être placé en quarantaine pour réduire d'un le nombre de cas secondaire.
  - Cette étude (Bondy et al) comporte des risques de biais en raison du manque d'ajustement statistique pour des caractéristiques individuelles qui pourraient jouer un rôle dans l'exposition à la maladie et sa transmission (p. ex. emploi, âge, sexe, etc.).

Il est aussi important de noter qu'en raison de la population étudiée (individus ayant testé positif pendant qu'ils étaient en quarantaine) il est difficile de tirer une conclusion à propos du potentiel d'une quarantaine plus traditionnelle.

Données provenant d'études de modélisation:

- Il y avait une tendance disant que plus la quarantaine est longue, plus le risque de transmission est réduit. Cela n'était toutefois pas vrai pour toutes les études. Il y avait aussi plusieurs études supportant le fait de tester les individus tôt pendant la quarantaine pour diminuer le risque d'infection, disant que *tester entre les jours 5 à 7 de la quarantaine* semble être le moment idéal pour réduire au maximum les infections.

- Études supportant une quarantaine plus longue :
    - Dans une simulation plus générale explorant différentes durées de quarantaine, une diminution du risque d'infection en fonction d'une quarantaine plus longue a été démontré (Zou et al).
- Études supportant une quarantaine plus longue, mais procurant de l'information sur la stratégie de test/quarantaine optimale :
    - Dans un modèle de la main d'œuvre faisant varier la longueur de la quarantaine de 1 à 14 jours, il a été démontré que plus la quarantaine est longue, plus le risque de transmission secondaire est bas (Peng et al). Le modèle suggère aussi que la stratégie optimale de quarantaine/test serait de tester les individus aux jours 4, 5 et 6 de la quarantaine et de les libérer de la quarantaine à ce moment si les tests sont tous négatif.
    - Dans une simulation plus générale explorant les différences entre la quarantaine et les protocoles de test, une diminution du taux d'infection secondaire a été démontrée en corrélation avec une durée de quarantaine plus longue. Par contre, celle-ci semble stagner du jour 6 au jour 8 avant de diminuer de nouveau du jour 9 au jour 12 de quarantaine (Takeshita et al). Tester au début de la quarantaine et après le jour 5 permet de diminuer davantage le taux d'infection.
    - Toujours dans une simulation plus générale, augmenter la durée de la quarantaine jusqu'à 10 jours permet de diminuer le risque d'infection secondaire de manière régulière en comparaison avec une quarantaine plus courte (Ashcroft et al). Le modèle suggère aussi que de tester au jour 5 de la quarantaine et de libérer les cas négatifs seulement au jour 7 permet de réduire la transmission de la COVID en comparaison avec une quarantaine de 7 jours sans test. Par contre, il est bon de noter que cette relation est dépendante de la proportion d'individus infectés qui sont en quarantaine.
    - Dans un modèle basé sur la population du Royaume-Unis, le mise en place de n'importe quel protocole de type test, trouve et isole (TTI) permet de réduire la transmission en comparaison à ne pas utiliser ce protocole. Ce modèle n'a pas permis de voir de différence entre les protocoles basés sur les symptômes et ceux basés sur les tests (He et al). Il est bon de noter que ces protocoles de TTI sont plus efficaces ($R<1.0$) lorsqu'ils sont mis en œuvre en parallèle avec d'autres méthodes de préventions tel que le confinement ou des restrictions significatives dans les milieux de travail et social.
- Études supportant la combinaison de protocole de test et de quarantaine comme étant meilleure ou équivalente à la quarantaine seule :
    - Dans un modèle de la main d'œuvre, explorant une quarantaine de <14 jours avec des tests en comparaison avec une quarantaine de 14 jours, il semblerait que de tester au

jours 6 de la quarantaine soit le scénario optimal pour minimiser la transmission (Wells et al).
    - Dans un modèle de simulation général comparant une quarantaine de 10 jours à une quarantaine de 7 jours en combinaison avec une série de test à antigène (DCT) et variant le taux d'adhérence à la quarantaine. Le modèle suggère que la DCT était aussi efficace que la quarantaine standard si l'adhérence est autour de 60%, par contre, lorsque l'adhérence augmente, la DCT est moins efficace et lorsque l'adhérence diminue, la DCT est plus efficace (Ferretti et al.). Le modèle a aussi permis de déterminer que la DCT permet de diminuer de manière significative le nombre moyen de jour passé en quarantaine et ce, peu importe l'adhérence à la quarantaine.
    - Dans un modèle de simulation d'une population aborigène Australienne, non vacciné et vivant dans un milieu densément peuplé, l'utilisation de test à l'entrée et à la sortie ainsi que l'isolation d'individus positif au début de la quarantaine a permis de réduire la prévalence maximale d'infection communautaire de 10 à 30% en comparaison avec un suivi étendu des contacts basé sur les ménages (sans test d'entré) (Hui et al).
    - Dans une étude de simulation d'un campus universitaire Américain explorant l'impact de différentes efficacités du vaccin et protocoles de test et de quarantaine, une utilisation accrue des tests chez les contacts de cas de COVID-19 a été démontrée comme étant équivalente à la quarantaine en ce qui a trait aux taux d'infection dans la communauté (Motta et al). L'effet des tests et de la quarantaine était augmenté lorsque l'efficacité du vaccin était moindre.
- Études supportant la quarantaine n'ayant démontrées aucune différence en fonction de la longueur de la quarantaine :
    - Dans un modèle de simulation de coûts basé aux États-Unis et prenant en compte les coûts liés aux tests, au temps passé en quarantaine et à la mort, il y avait une différence minime dans le nombre de mort par 1000 cas index en fonction de différentes longueurs de quarantaine, protocoles de test et règles de quarantaine en fonction du risque (Perrault et al). La stratégie optimale était de combiner les règles de quarantaine en fonction du risque (où un groupe d'individu avec une source d'exposition commune été mis en observation pour voir s'ils développaient des symptômes, et si aucun d'eux ne développe de symptôme ils étaient libérés de quarantaine), la surveillance active ainsi qu'un test à la sortie de la quarantaine, si celui-ci est positif, 4 jours sont ajoutés à la quarantaine.
    - Dans un modèle de simulation plus général explorant les différences entre le temps passé en quarantaine et les protocoles de test, aucune différence n'a été démontrée quant au taux d'infection en fonction de la durée de la quarantaine ou de l'utilisation de test au début et à la fin de celle-ci (Quilty et al).
- Études n'ayant pas trouvé de différence entre la quarantaine et le monitoring actif
    - Dans un modèle de simulation plus général explorant la différence entre la quarantaine et la surveillance active des contacts dans deux scénarios (90% vs. 50% des contacts pouvant être surveillés), il n'y avait pas de différence entre les deux interventions quant à leur capacité de diminuer le nombre d'infection (Peak et al). Dans le scénario ou 90% des contacts peuvent être surveillés, la valeur R s'est retrouvée sous la valeur de 1 pour les deux interventions tandis que lorsque 50% des contacts peuvent être surveillés, la valeur R était supérieure à 1.

Implications potentielles pour la prise de décisions pour les systèmes de soins de santé

- Il est clair selon les données rapportées dans la présente revue de littérature qu'il y a *un manque de donnée empirique non biaisé* sur l'impact de la quarantaine sur la transmission secondaire des maladies respiratoires infectieuses. La plupart des données recueillies étaient au sujet de la COVID-19 (avec une étude sur SARS), et consistaient majoritairement d'études ayant un risque de biais notable, rendant l'interprétation des données difficile. Malgré cela, une certaine tendance à tout de même pu être observée parmi les études inclues, permettant d'avoir un aperçu des effets potentiels de la quarantaine pour les maladies respiratoires infectieuses.
- De manière générale, les données provenant d'études de modélisation de la COVID-19 suggèrent qu'être *en quarantaine en raison de la COVID-19 plus longtemps offre un bénéfice* significatif sur la transmission (en prenant en considération la période d'incubation de la COVID-19).
- Il y avait aussi plusieurs études se focalisant sur la COVID-19 supportant que de tester les individus tôt permet de réduire la transmission. *Tester au jour 5 ou 7 de la quarantaine* semble être le scénario optimal, surtout chez les adultes. En revanche, l'hétérogénéité du design des études rend la comparaison et la synthèse des résultats très difficile.
- Il est important de noter que la plupart de ces études n'ont pas été conduite pendant ou n'ont pas pris en compte des scénarios où il y avait une grande proportion de la population qui a été vacciné, ou où il y avait un variant très virulent (c.-à-d., Omicron) ou encore où il y avait un très faible taux d'infection dans la population. Ainsi, il n'est pas clair à quel point ces données peuvent se transmettre à la situation de pandémie actuelle.
- De la *perspective de la préparation en matière de santé public*, si la sévérité et la charge virale d'une épidémie future de COVID-19 ou d'une autre maladie infectieuse requérait des mesures de quarantaine, une combinaison de quarantaine et de test serait probablement la stratégie la plus optimale pour réduire les infections secondaires. Cependant, si un tel scénario devait se produire, cela serait une excellente opportunité de collecté des données empiriques ayant un risque de biais faible afin d'informer le développement de lignes directrices et politique de quarantaine en lien avec les maladies respiratoires infectieuses.

Suggestion de gazouillis

- Les données limitées ne nous 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 primary outcomes from COVID-19 transmission to include transmission or residual transmission post confinement for other prioritized respiratory infectious diseases (H1N1, SARS, MERS). 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. Modelling and empirical 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 been in close contact with someone who tested positive for or is suspected to have COVID-19, H1N1, SARS or MERS but haven't contracted the disease necessarily and are asked to quarantine.

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

Comparison: Any other form of quarantine, including individuals who were confined for a different length of time or who used various testing strategies to variably alter quarantine time. Intervention comparison could be across populations (different countries, those screened 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 were 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 quarantine 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 quarantine in preventing the transmission of COVID-19, presented in alphabetical order of 1st author

<table>
<tr><th>Reference</th><th>Date released</th><th>Setting and time covered</th><th>Study characteristics</th><th>Summary of key findings in relation to the outcome</th><th>RoB Rating</th></tr>
<tr>
<td>Love et al. 2022</td>
<td>Published:
October 10, 2022</td>
<td>England, United Kingdom

April 29 - August 9, 2021</td>
<td>Design: Two-arm, non-blinded, randomised, controlled, non-inferiority trial (non-inferiority margin of 1.9%) of up to 7 days of daily contact testing (DCT) vs. 10 days of quarantine. Simple randomisation without stratification, with allocation generated by the study team and concealed from individuals performing recruitment.

Sample: 54,923 adults (≥18 years) who were vaccinated or unvaccinated against SARS-CoV-2, identified as contacts of confirmed COVID-19 cases, and living in England.
Exclusions: symptomatic at recruitment; under travel-associated quarantine; participating in a workplace daily contact testing (DCT) programme; resident in a prison or social care institution; a contact of a case with a variant of concern between April 29 and June 7, 2021; did not provide an email or postage address; or if participant had duplicate registrations
• DCT: 26,123 (52.6%)
• Self-isolation: 23,500 (47.4%)

Intervention: Participants in the DCT group were asked to complete seven daily self-administered antigen tests, with release for 24 h based on a negative result, a PCR swab was requested for participants on receipt of a positive result or on the day of their last antigen test (if all previous tests were negative).

Comparison: Self-quarantine (a single self-taken PCR swab and self-quarantine for 10 days).</td>
<td>Intention to treat (ITT)
<table>
<tr><th></th><th>Self-quarantine group</th><th>DCT group</th><th>Total</th></tr>
<tr><td>Number of tertiary cases</td><td>393</td><td>325</td><td>718</td></tr>
<tr><td>Number of tertiary cases per participant</td><td>0.2</td><td>0.1</td><td>0.2</td></tr>
</table>
Most tertiary cases were from household contacts

Attack rates in secondary contacts (ITT)
<table>
<tr><th></th><th>Adjusted* attack rate (95% CI) n=10,252</th></tr>
<tr><td>DCT group</td><td>6.3% (5.6 to 7.0)</td></tr>
<tr><td>Self-isolation group</td><td>7.5% (6.7 to 8.3)</td></tr>
<tr><td>Difference: DCT vs self-isolation</td><td>–1.2% (–2.3 to –0.2)</td></tr>
</table>
As the upper limit of the confidence interval (i.e., -0.2%) is below the non-inferiority margin of 1.9%, it suggests that DCT is non-inferior to self-isolation

Attack rates in secondary contacts by vaccination status (ITT)</td>
<td>Serious</td>
</tr>
</table>

Key Outcomes:

- **Attack rate:** Proportion of secondary contacts of COVID-19 positive participants (who tested positive by PCR in the 2 days before and 14 days after recruitment) who became infected (tertiary cases). Attack rates were adjusted for household exposure, vaccination status, and ability to work from home.

Terminology: DCT=daily contact testing, the article uses the term 'self-isolation' to refer to individuals who were in contact with a case and were asked to quarantine

VOCs: Delta variant

Vaccination status: Immunisation data collected from the National Immunisation Management System (NIMS) using a combination of identifiers. Fully vaccinated and one-dose vaccinated individuals were defined as those vaccinated more than 14 days before recruitment. When NIMS vaccination status was unknown, self-reported vaccination status was used.

	Adjusted* attack rate (95% CI) n=10,252
DCT group: 0 or 1 vaccine dose	7.0% (6.0 to 8.0)
Self-isolation group: 0 or 1 vaccine dose	7.9% (6.8 to 9.0)
DCT group: 2 vaccine doses	5.4% (4.5 to 6.4)
Self-isolation group: 2 vaccine doses	7.0% (5.9 to 8.1)
Difference in attack rate (DCT vs self-isolation)	**0 or 1 vaccine dose:** –0.9% (–2.4 to 0.6) **2 vaccine doses:** –1.6% (–3.1 to –0.1)

*Adjusted for household exposure, vaccine status, and ability to work from home

Adjusted attack rates did not significantly differ between groups for secondary contacts who were unvaccinated, partially vaccinated, or fully vaccinated

Model testing for the group by vaccination status interaction was not statistically significant (adjusted model for group and vaccination status: p=0.46)

Model testing for the group by household exposure interaction was not statistically significant (adjusted model for group and household exposure: p=0.81).

<table>
<tr>
<td>Young et al. 2021</td>
<td>Published:
September 14, 2021</td>
<td>England, United Kingdom

March 18 - June 27, 2021</td>
<td>Design: Open-label, cluster-randomised, controlled trial in secondary schools and further education colleges. One arm where contacts were tested daily and one where they were asked to quarantine.

Sample: 214,552 students (aged 11+) and 12,229 staff members from 201 schools were included in either the intervention group or the control group.

Intervention: Contacts were offered the possibility to attend classes (and quarantine after class and on days they were not tested) if they tested daily for 7 days. Those with five negative tests over 7 or more days were released from quarantine.
They had to quarantine for 10 days if they did not consent to daily testing or if they had a household member who was isolating following a positive SARS-CoV-2 test.

Comparison: Individuals in close contact with a case less than 48h before symptom onset or positive test were required to quarantine for 10 days.

Key Outcomes:
• Estimated in-school COVID-19 transmission (from rates of symptomatic PCR confirmed infections recorded by NHS Test and Trace, after controlling for community case rates)
• Estimated rate of symptomatic and asymptomatic SARS-CoV-2 infections outside of first order contacts

Terminology: Contacts were asked to ‘self-isolate’.

VOCs: during a period of low to moderate community incidence, predominantly with the delta (B.1.617.2) variant.

Vaccination status: Not considered.</td>
<td>Intention to treat (ITT) multivariate analysis
The adjusted* incidence rate ratio (aIRR) shows no evidence of difference between study groups in symptomatic PCR-confirmed infection in school: 0.96 (95% CI 0.75-1.22), p=0.72
• Students: 0.94 (0.74-1.18), p=0.58
• Staff: 1.21 (0.81-1.81), p=0.35

There was no evidence that the effect of the intervention differed in staff and students

Rate (per 100,000 people per week) of symptomatic positive PCR test
<table>
<tr><th></th><th>Intervention (101 schools of 102)</th><th>Control (96 schools of 99)</th></tr>
<tr><td>Student</td><td>63.4 (n=683 cases)</td><td>61.7 (n=614 cases)</td></tr>
<tr><td>Staff</td><td>48.7 (n=57 cases)</td><td>38.1 (n=43 cases)</td></tr>
</table>
The intention-to-treat aIRR* shows no evidence of difference between study groups for any positive PCR result from routine community-based testing: 0.96 (95% CI 0.76-1.20), p=0.71
• Student: 0.94 (0.74-1.18), p=0.58
• Staff: 1.29 (0.91-1.83), p=0.15

There was no evidence that the effect of the intervention differed in staff and students.

Complier average causal effect (CACE)
The aIRR* shows no evidence of difference between study groups in symptomatic PCR-confirmed infection in school: 0.86 (95% CI 0.55-1.34), p=0.72
• Students: 0.85 (0.49-1.51)
• Staff: 1.33 (0.70-2.56)</td>
<td>Serious</td>
</tr>
</table>

				The aIRR* shows no evidence of difference between study groups for any positive PCR result from routine community-based testing: 0.88 (95% CI 0.57-1.41) • Student: 0.85 (0.52-1.43) • Staff: 1.46 (0.89-2.85) *Adjusted for the randomisation strata, participant type, and the community rate of SARS-CoV-2 infection in the previous week.	

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

<table>
<tr><th>Reference</th><th>Date released</th><th>Setting and time covered</th><th>Study characteristics</th><th>Summary of key findings in relation to the outcome</th><th>RoB Rating</th></tr>
<tr>
<td>Dawson et al 2022</td>
<td>Accepted:
15 September 2022

Published:
20 October 2022</td>
<td>Missouri (Greene and St. Louis County) – USA

January 25 - March 21, 2021.</td>
<td>Design: Prospective cohort study of quarantined individuals identified through school officials

Sample: 1,636 students or staff member who were in close contacts with a confirmed COVID-19 case (students or staff members who received a positive SARS-CoV-2 nucleic acid amplification test (NAAT) or antigen test)

Intervention: Modified quarantine (students were allowed to attend in person school during their quarantine if they were 18 or less, were exposed in the classroom, did not have direct physical contact for 15+ minutes in 24h and both the case and the close contact were wearing a mask during the exposure event).

Comparison: Standard quarantine (forfeit all in-person activities)
• Greene county: quarantine for 10 days with a possibility of quarantining for 7 days if they had a negative test between day 5 and day 7 and on day 7 post exposure.
• Quarantine for 14 days without any option to shorten the duration.

Key Outcomes: frequency of school-based SARS-CoV-2 transmission; relative risks of school-based transmission among schoolwide COVID-19 mitigation policies, incidence between schools implementing a modified quarantine and schools following standard quarantine.</td>
<td>Modified quarantine:
• Of 66 tested students, none infected another person in the school environment
• By extrapolation, a projected additional three cases (1% of 270) would be expected among the 270 student close contacts without test results for a total of six (2%) transmission events.

Standard quarantine
• A projected additional eight cases (1% of 835) would be expected among the 835 student close contacts without test results for a total of 14 (1%) transmission events

The difference between modified and standard quarantine was not statistically significant for the observed case (p=0.41) nor the projected cases (p=0.50)

Students in modified quarantine were not more likely to test positive or develop disease and pose a risk for onward school-based transmission than students in standard quarantine

<table>
<tr><th></th><th>In schools implementing modified quarantine (n=336)</th><th>In schools implementing standard quarantine (n=835)</th></tr>
<tr><td>Average crude incidence rate of school-based SARS-CoV-2 infections</td><td>1.94 per 100,000 per week</td><td>4.00 per 100,000 per week**</td></tr>
</table>
</td>
<td>Critical</td>
</tr>
</table>

<table>
<tr>
<td></td>
<td></td>
<td></td>
<td>Terminology: A close contact was defined as someone who was ≤6 feet away from a person with COVID-19 for ≥15 minutes in one 24-hour period.

VOCs: Not considered.
Vaccination status: Not considered (at that time, 70% of the US population 12–17 years had received at least one dose of a COVID-19 vaccine).</td>
<td>**p=0.2.

The adjusted hazard rates of school-based SARS-CoV-2 infections were not different between schools that implemented a modified quarantine policy vs standard quarantine policy (observed cases or total projected cases): HR = 1.00; 95% CI: 0.97–1.03)

The adjusted probability of school-based SARS-CoV-2 infections based on total projected cases reached a maximum of 0.83% (95% CI: 0.75–0.91%) by the end of the study.</td>
<td></td>
</tr>
<tr>
<td>Love et al. 2022</td>
<td>Accepted: May 31, 2022

Published: August 10 2022</td>
<td>England, United Kingdom

8 December 2020 - 12 January, 2021</td>
<td>Design: Prospective cohort study from the NHS Test and Trace records

Sample: 812 asymptomatic adult (>18 years) contacts exposed to a confirmed COVID-19 case within the preceding 48 h.

Intervention: Serial testing as an alternative to self-isolation using daily self-performed antigen test for the first 7 days post-exposure. Asymptomatic participants with a negative result were given 24 h of freedom from self-isolation between each test. A confirmatory PCR test was performed in case of a positive test or at the end of the testing period.

Comparison: Self-isolation for 10 days.

Key Outcomes:
• Attack rate: Proportion of secondary contacts of COVID-19 positive participants (who tested positive by PCR in the 2 days before and 14 days after recruitment) who became infected (tertiary cases).

Terminology: DCT=daily contact testing</td>
<td>Secondary attack rates (SAR) for contacts of confirmed cases of COVID-19 who tested positive for SARS-CoV-2 on study PCR swabs
<table>
<tr><th></th><th>SAR % (95% CI)</th></tr>
<tr><td>Study group (84 cases)</td><td>6.3 (2.4-11.1)</td></tr>
<tr><td>December (28 cases)</td><td>5.6 (1.9-15.1)</td></tr>
<tr><td>January (56 cases)</td><td>6.6 (3.2-13.0)</td></tr>
<tr><td>Comparison (18,070 cases)</td><td>7.6 (7.3-7.8)</td></tr>
<tr><td>December (10,581 cases)</td><td>7.8 (7.4-8.1)</td></tr>
<tr><td>January (7,489 cases)</td><td>7.3 (6.8-7.7)</td></tr>
</table>
There were no differences in the overall secondary attack rates for the study group compared with a comparator group.</td>
<td>Critical</td>
</tr>
</table>

			VOCs: The study was carried out when the alpha variant dominated in England. **Vaccination status:** Not considered.		

Table 1.3: Summary of modelling studies reporting on effectiveness of quarantine 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
Ashcroft et al., 2021	Paper received by journal on October 2, 2020, published on February 5 2021	No specific population	**Model:** Mathematical model based on the incubation time, infectivity, and generation time distributions **Goal:** To explore the effect of duration of quarantine on transmission from traced contacts of confirmed SARS-CoV-2 cases. **Key Outcomes:** Onward transmission, quarantine days **Accounts for:** contact tracing, testing, quarantine **Key Assumptions:** • Under the standard quarantine strategy, all potentially exposed individuals are quarantined for the same duration. • Test-release strategy uses testing during quarantine to release individuals with a negative test result earlier. • Individuals with a positive test result are isolated until they are no longer infectious. • Individuals released from quarantine have – in the post-quarantine phase – the same transmission probability as individuals who were not quarantined • Adherence to quarantine is 100%;	Shortening a contact's quarantine increases transmission risk, with the extent of risk depending on the duration reduction • Increasing quarantine duration beyond 10 days shows almost no additional benefit. • The standard quarantine protocol (here with a 3-day delay between exposure and the start of quarantine) can maximally prevent 90.8% [95% CI: 79.6%, 97.6%] of onward transmission from an infected traced contact, while release on day 10 prevents 90.1% [CI: 76.0%, 97.5%]. • Reducing the delay to quarantining individuals increases the fraction of total transmission that is preventable. Under the test-and-release quarantine protocol, the average time spent in quarantine is dependent on the fraction of infected individuals in quarantine. If the fraction of infected individuals in quarantine is 10%: • Testing on day 5 and releasing test-negative individuals on day 7 has a relative utility (the comparison of the ratio between the amount of overall transmission and the number of person-days spent in quarantine between two quarantine strategies) of 1.53 [CI: 1.45,1.62] compared to a standard 10-day quarantine. • Reducing the delay between test and result leads to a corresponding increase in utility: a rapid test (zero delay between test and result) on day 6 has a relative utility of 1.90 [CI: 1.83,1.98] for an almost equivalent efficacy than testing

			• The transmission prevented by quarantine for cases who develop symptoms is attributed to quarantine. **VOCs:** Not considered **Vaccination status:** Not considered **Terminology:** • "Quarantine" refers to individuals who are confined because they are a traced contact. • "Traced contacts" have a known (last) time of exposure to a confirmed case. • "Relative utility" is defined as the fraction of transmission prevented per day spent in quarantine. A higher utility means that compared to standard quarantine the alternative intervention reduced transmission.	on day 5 and releasing test-negative individuals on day 7 when compared to a standard 10-day quarantine. Shortening quarantine to increase adherence is of limited use • Shortening to 7 days (without testing) may be effective provided that adherence can increase by 30% (relative adherence 1.30 [CI: 1.08,1.55]). • However, under the test-and-release strategy the efficacy of the standard 10-day quarantine can be matched with release on day 5 or 6 if adherence is also increased by 30%.
Ferretti et al., 2021	Preprint article posted on August 8, 2021	No specific population	**Model**: Using an integrated model of COVID-19 transmission dynamics calibrated with the step-wise Bayesian parameter inference **Goal**: To evaluate the effectiveness of daily antigen testing. The comparison involved scenarios with varying factors such as contact tracing speed, test sensitivity, and adherence rates, with DCT consistently showing benefits over quarantine. **Key outcomes**: Transmission averted **Accounts for**: Individual viral load and transmission dynamics, vaccination, adherence to the measures **Key assumptions**: • Duration of quarantine: 10 days • Daily testing duration: 7 days • Time to contact identification: 3 days • That the onset of symptoms is driven by the peak of the viral load dynamics	The benefit of quarantine, in terms of reduced transmission, is greater for unvaccinated contacts than for vaccinated ones, but decreases more quickly as their adherence decreases as they are more likely to be infected, and thus to infect others. The effectiveness of DCT compared to quarantine also depends on how quickly contacts are traced, the rate of dropout from daily testing, the actual adherence to quarantine, etc. Varying the duration of the DCT period between 5 and 10 days, only has a marginal impact for vaccinated contacts and a more distinct improvement increasing the duration of DCT to 7-8 days for the unvaccinated contacts, but little improvement after that. Varying the duration of quarantine has a much greater impact on transmissions averted for both vaccinated and unvaccinated individuals. An uptake of 25% for DCT would be equivalent to 50% adherence to quarantine in terms of reduction of onward transmissions, while an uptake of 80% would be equivalent to 90% adherence to quarantine.

			• That the visible growth phases cannot typically last more than 15 days • That the visible clearance phases cannot typically last more than 30 days • Initial uptake of daily testing (i.e. probability to collect the tests and start using them): 50% • Probability of missing a test at random: 20% • Daily drop-out rate from testing regime: 5% • Effective reduction in contact rates during testing period, before a positive result or if no test is taken: 20% • Effective reduction in contact rates after a positive result: 80% **VOCs:** Not considered **Vaccination status**: Vaccination is considered in the model **Terminology**: "quarantine" refers to the confinement of traced contacts. "Daily contact testing (DCT)" refers to the daily testing of contacts, after each negative test they are released from quarantine for 24 hours (until the next test), if they test positive, they are then required to self-isolate.	An intermediate quarantine adherence rate of 75%, leading to an estimated 60% reduction in transmission during the quarantine period The authors found that DCT with 50% uptake is almost as effective in averting transmissions as quarantine with 75% adherence. This is true for both vaccinated and unvaccinated contacts.
He et al., 2021	Paper received August 20th, 2020, accepted March 2nd, 2021	Uses the BBC Pandemic data of 40 162 participants in the UK.	**Model:** Simulation-based model **Goal:** To quantify how the effectiveness and resource requirements of a test-trace-isolate (TTI) systems vary with respect to implementation and in conjunction with other non-pharmaceutical Interventions (NPIs). They consider 5 scenarios of other NPI of stringency levels ranging from: • Most stringent (S5): Models the lockdown scenario prior to May 9 • S4: Slightly relaxed work and social restrictions • Medium stringency (S3): Models a scenario with more social contacts, 50% of schools being open	**Contribution of various measures and parts of the TTI system to overall transmission rate:** With a low stringency level (S1-S2): • Index case isolation alongside quarantining of their household is responsible for the majority of prevented transmission Implemented on top of current UK government recommendations to self-isolate and quarantine households on COVID symptoms: • Test-based TTI strategies reduce R between 10-15% • Symptom-based TTI reduces between 15-20% • The most significant reduction in transmission of a TTI system is due to prompt self-isolation of a symptomatic case and the quarantining of their household

			and 45% of the working population working from home • S2: Strongly relaxed work and social restrictions • Least stringent (S1): Models no NPIs except for households being quarantined at home on presentation of symptoms They consider three core TTI strategies: 1) Symptom-based TTI: Start contact tracing and quarantine contacts as soon as a primary case reports COVID-like symptoms 2) Test-based TTI: Start contact tracing and quarantine contacts once a primary case is confirmed by a test to be COVID positive 3) Test-based TTI with contact testing: Start contact tracing and quarantine contacts once primary case is confirmed by a test to be COVID positive. Test the contacts of a confirmed COVID positive primary case. They also compare these three strategies with no TTI. For each strategy: • The primary case and members of their household are asked to isolate/quarantine at home when the primary case first presents symptoms • Contact tracing commences at either symptom presentation or test returning positive • All traced contacts are asked to quarantine for a total of 14 days • If traced contacts show symptoms, they are entered into the TTI system as primary cases themselves. • If contacts are tested and they test negative, they are released from quarantine **Key outcomes:** secondary attack rates (SAR; R) infection numbers, community transmission **Accounts for:** Test-trace-isolate (TTI) systems, isolating and quarantining recent research on the timeline of COVID infections, various logistical and temporal aspects of real-world implementations of TTI strategies. **Key Assumptions:**	For the TTI strategy to be effective both the **test and tracing delay** should be reduced: • Reducing the time from symptom onset to informing contacts to quarantine from 5 to 3 days improves effectiveness in reducing R by 60–70%. • In scenario S3 a 5-day delay has an effective R of 1.46 ± 0.04 while a 3-day delay has 1.37 ± 0.04. The scenario with no TTI lead to an effective R of 1.59 ± 0.04

			• A total of 20k new COVID infections each day, split between symptomatic and asymptomatic cases • For the infection timeline of each COVID positive primary case, they assume a latent period of 3 days, a mean duration of 2 days of presymptomatic infectious period before reporting symptoms, and a non-uniform infection profile over 10 days peaking on the day before the expected day of symptom presentation. • The total number of daily contacts for the primary case is broken down into (1) household, (2) work/school and (3) other. • Separate secondary attack rates (SAR) are given for household and non-household contacts • Base SAR of R= 3.87 in a no TTI scenario • Assume isolation and quarantines prevent all subsequent transmission • Assume a compliance level of 80% for both symptom reporting and requests to quarantine or isolate. • Assume that the time taken to obtain a test result is 2 days, and it takes 1 day following this for contacts to be manually traced **VOCs:** Not considered **Vaccination status:** Not considered **Terminology:** TTI systems identify infected individuals by testing them, identify their social contacts (trace), and isolate the infected individuals and quarantine their contacts to prevent onward transmission.	
Hui et al, 2021	Paper published on September 8, 2021.	Modeled non-pharmaceutical-based strategies in a remote Aboriginal community in Australia	**Model:** Individual-based model. Community sizes comprising 100, 500, 1000 or 3500 people are modeled **Goal:** To compare non-pharmaceutical-based strategies in a remote Aboriginal community, assessing the impact of alternative scenarios in an outbreak response, including: initial delays with testing, different definitions of case-contacts and consequent quarantine strategies.	**Impact of definition of contacts, and quarantine strategies** • The baseline model assumes no entry or clearance testing, the inclusion of extended household-based contact tracing and quarantine. This leads to a peak infection prevalence of approximately 40%, versus 50% for the history-based quarantine strategy. • The addition of entry testing of all contacts to quarantine reduces the peak infection prevalence for the extended household-based strategy to approximately 10% (versus 40%

			Key outcomes: • Prevalence (individuals infected with SARS-CoV-2) • COVID-19 outbreaks (cumulative infections, person-days in quarantine, number of tests conducted) **Accounts for:** Isolation, quarantine, testing **Key assumptions:** • A wholly susceptible, unvaccinated population • Each community member is infected with SARS-CoV2, and their status is monitored • Transmission of infection can occur upon contact between an infectious individual and a susceptible individual • Contacts can occur between household contacts and community contacts. • Individuals have family connections across multiple dwellings and each individual's total time "at home" is distributed between a main dwelling (core; 66% of the time), second dwelling (regular 23% of the time) and third dwelling (on/off; 9% of the time). • Assumes infectiousness starts 48h prior to symptom onset on average and stops with symptom resolution. • Incubation mean = 6.4 days ± 2.3 days • Disease lasted until the end of infectious period: 50% presenting proportion (self-present for testing), 50% non-presenting proportion • Exposed (latent) period mean = 4.5 days ± 0.9 days • Infectious period mean = 10 days ± 4 days • $R_0 = 5$ • Cases are assumed to be isolated immediately and effectively	for the history-based strategy) as it leads to additional rounds of contact tracing, isolation and quarantine. • The impact of clearance testing with various quarantine strategies on total infection numbers is greatest for the extended household-based contact tracing approach. • For extended household quarantine, the addition of clearance testing resulted in 66% being infected compared to 83% without clearance testing, fewer person-days in quarantine, but more tests, making it the most effective strategy.

			• Contacts of cases are quarantined alone and assumed to be completely separated from others • Isolation period lasts 10 days, a clearance test, if applied, is scheduled to occur on the 8th day of isolation. • Contacts of the case are also placed in quarantine for 14 days, with a clearance test, if applied, scheduled to occur on the 12th day of quarantine. • Both isolation and quarantine are ideal, and that an individual cannot transmit or be infected with SARS-CoV-2 while in isolation or quarantine. • 100% test sensitivity **VOCs:** Not considered **Vaccination status:** Unvaccinated population **Terminology:** • Entry testing = testing contacts at the start of quarantine • Clearance testing = testing prior to release from quarantine or isolation • Immediate household contacts = those who share the same dwelling at the time of tracing • Extended household contacts = those who share other dwellings that a case frequently inhabits • History-based contact tracing = contacts are those identified over the prior 2 days (close and casual)	
Motta et al. 2021	Published online on October 1, 2021	US On-campus population of 5,000 homogeneously mixing	**Model**: An agent-based model with SEIR disease dynamics. The off-campus population was modeled as a reservoir with a static prevalence of infection. **Goal**: investigate the effect of weekly surveillance testing (i.e., the testing the everyone on campus) and quarantine in an environment where 100% of	In simulations, surveillance testing showed marginal reduction in viral transmission at 90% vaccine effectiveness and could decrease infections by up to 93.6% at 50% to 75% effectiveness. A 10-day quarantine for exposures had modest infection reduction in comparison to surveillance only until vaccine effectiveness dropped to 50%, at which point quarantining contacts had a bigger effect on the reduction of infection.

<table>
<tr>
<td></td>
<td></td>
<td>agents (all vaccinated).

They also included an off-campus population used to model the “outside prevalence”</td>
<td>the student population is vaccinated, but where vaccine effectiveness may be reduced by variants or by waning immunity.

Key outcomes: Daily infection prevalence

Accounts for: daily interactions, the prevalence of the disease off campus, the vaccine effectiveness (VE), the number proportion of individuals initially infected and exposed

Key assumptions:
• Population: 5,000 vaccinated students
• Baseline interaction exposure probability (both on-campus and off-campus): 2.6%
• Days between surveillance tests: 7
• Number of tests pooled together for initial screening: 5
• False positive rate: 0.1%
• False negative rate: 1.0%
• Time to test results: 1 day
• Isolation and quarantine duration: 10 days
• Tracing effectiveness: 15%

VOCs: Not considered

Vaccination status: 100% of the on-campus individuals are vaccinated

Terminology: Quarantine is used to refer to the confinement of contacts and isolation is used to refer to the confinement of cases
Interaction multipliers were used to model scenarios where there was more or less interactions between individuals, a higher multiplier representing more interactions.
Outside prevalence represents the prevalence of the disease outside of the university campus.</td>
<td>Targeted testing of reported contacts was as effective as quarantine in limiting infections.

Model simulations estimated that quarantine does not substantially reduce infection numbers at 90% VE and only marginally reduces infections over the course of the semester at 75% VE. At most, quarantine was estimated to reduce infection totals by 16% to 17%, assuming a VE of 50% and an interaction multiplier of 20. In this scenario, testing every 2 days was a more effective strategy than quarantining reported contacts.

Cumulative infection prevalence, in % (IQR)

In a scenario where individual have few interactions (interaction multiplier of 1)
<table>
<tr><th>VE</th><th colspan="3">Mitigation strategies</th></tr>
<tr><th></th><th>None</th><th>Surveillance and quarantine</th><th>Surveillance and testing contacts</th></tr>
<tr><td colspan="4">Outside prevalence of 0.1%</td></tr>
<tr><td>90%</td><td>0.2 (0.1)</td><td>0.2 (0.1)</td><td>0.2 (0.1)</td></tr>
<tr><td>75%</td><td>0.3 (0.1)</td><td>0.3 (0.1)</td><td>0.3 (0.1)</td></tr>
<tr><td>50%</td><td>0.4 (0.1)</td><td>0.3 (0.1)</td><td>0.3 (0.1)</td></tr>
<tr><td colspan="4">Outside prevalence of 1.0%</td></tr>
<tr><td>90%</td><td>0.4 (0.1)</td><td>0.5 (0.1)</td><td>0.4 (0.1)</td></tr>
<tr><td>75%</td><td>0.8 (0.2)</td><td>0.8 (0.2)</td><td>0.8 (0.2)</td></tr>
<tr><td>50%</td><td>1.6 (0.2)</td><td>1.5 (0.2)</td><td>1.5 (0.3)</td></tr>
</table>
In a scenario where individual have moderate interactions (interaction multiplier of 10)
<table>
<tr><th>VE</th><th colspan="3">Mitigation strategies</th></tr>
<tr><th></th><th>None</th><th>Surveillance and quarantine</th><th>Surveillance and testing contacts</th></tr>
<tr><td colspan="4">Outside prevalence of 0.1</td></tr>
<tr><td>90%</td><td>0.6 (0.2)</td><td>0.5 (0.1)</td><td>0.5 (0.2)</td></tr>
<tr><td>75%</td><td>2.8 (1.1)</td><td>1.1 (0.3)</td><td>1.1 (0.2)</td></tr>
<tr><td>50%</td><td>55.8 (6.0)</td><td>3.0 (0.8)</td><td>2.7 (0.6)</td></tr>
<tr><td colspan="4">Outside prevalence of 1.0</td></tr>
<tr><td>90%</td><td>3.6 (0.5)</td><td>2.9 (0.3)</td><td>2.9 (0.3)</td></tr>
</table>
</td>
</tr>
</table>

<table>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>
<table>
<tr><td>75%</td><td>18.5 (2.0)</td><td>8.1 (0.7)</td><td>8.0 (0.7)</td></tr>
<tr><td>50%</td><td>75.0 (1.4)</td><td>21.2 (1.5)</td><td>20.2 (1.1)</td></tr>
</table>
In a scenario where individual have more interactions (interaction multiplier of 20)
<table>
<tr><th>VE</th><th colspan="3">Mitigation strategies</th></tr>
<tr><th></th><th>None</th><th>Surveillance and quarantine</th><th>Surveillance and testing contacts</th></tr>
<tr><td colspan="4">Outside prevalence of 0.1</td></tr>
<tr><td>90%</td><td>1.6 (0.5)</td><td>0.9 (0.2)</td><td>0.8 (0.2)</td></tr>
<tr><td>75%</td><td>55.8 (6.1)</td><td>3.0 (0.8)</td><td>2.7 (0.6)</td></tr>
<tr><td>50%</td><td>96.6 (0.4)</td><td>26.5 (5.7)</td><td>20.1 (5.1)</td></tr>
<tr><td colspan="4">Outside prevalence of 1.0</td></tr>
<tr><td>90%</td><td>11.2 (1.3)</td><td>6.1 (0.6)</td><td>6.2 (0.5)</td></tr>
<tr><td>75%</td><td>74.9 (1.4)</td><td>21.1 (1.5)</td><td>20.1 (1.3)</td></tr>
<tr><td>50%</td><td>97.4 (0.3)</td><td>61.7 (2.2)</td><td>57.6 (2.1)</td></tr>
</table>
</td>
</tr>
<tr>
<td>Peak et al. 2020</td>
<td>Published Online May 20, 2020</td>
<td>Not specified</td>
<td>Model: Stochastic branching model

Goal: To estimate the comparative efficacy of individual quarantine and active monitoring of contacts for 14 days to control severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Key Outcomes: Growth of infections expected number of secondary cases prevented by quarantining.

Accounts for:
• Imperfect recall of who may be exposed (Proportion of contact traced: 50%),
• Delays in identifying or locating contacts (2 days [range 0–4]),
• infrequent or untrained monitoring of symptoms (on average every 2 days but the model accounted for it ranging from every 0 to 4 days])
• Imperfect quarantine (0.25) and isolation (0.5), where 0 indicates no reduction in transmission</td>
<td>With a longer serial interval, the median effective reproductive number under individual quarantine was 0.49 (95% CI 0.34–0.97), while under active monitoring in a high-feasibility setting, it was 0.54 (0.32–0.98).

In low-feasibility settings, regardless of the serial interval, neither individual quarantine nor active monitoring often brought R_e below 1. However, there was a median reduction in the reproductive number of 21.0% under individual quarantine and 13.6% under active monitoring, indicating a somewhat higher reduction under individual quarantine.

In a high-feasibility setting with a longer serial interval, the median additional number of secondary cases prevented by quarantining one infected individual over actively monitoring them is 0.043 (95% CI –0.16 to 0.11). This suggests that approximately 23 (95% CI 9.09–∞) truly infected contacts would need to be quarantined to avert one infection beyond active monitoring alone. For the shorter serial interval, quarantining one infected individual over actively monitoring them prevents a median of 0.93 (95% CI 0.23–1.93) additional secondary cases. This corresponds to needing to quarantine a median of 1.1 (95% CI 0.52–4.22) infected contacts to prevent one secondary</td>
</tr>
</table>

			rates and 1 indicates no transmission rates during that hour.
			•
			
			Key Assumptions:
			• 2 scenarios with different serial interval duration (time between symptom onset of infectior-infectee pairs)
			  ○ Short: mean serial interval of 4.8 days (scenario 1) versus
			  ○ Long: mean serial interval of 7.5 days
			• Two feasibility settings: a high-feasibility setting with 90% of contacts traced, a half-day average delay in tracing and symptom recognition, and 90% effective isolation; and a low-feasibility setting with 50% of contacts traced, a 2-day average delay, and 50% effective isolation.
			• The model assumes individual quarantine of contacts begins at a cumulative case count of 1,000, in a low-feasibility setting with a basic reproductive number of 2.2, and a mean serial interval of 4.8 days.
			• Individuals under active monitoring or quarantine who are uninfected are followed up for a duration of 14 days until clearance, consistent with previous interventions.
			
			VOCs: Not considered.
			
			Vaccination status: Not considered.
			
			Terminology: Individual quarantine involves the separation from others of an individual who is believed to be exposed to the disease but not currently showing symptoms of it.
				infection. However, if only 0.04% of traced contacts are infected, a median of 2,495 individuals need to be quarantined to prevent one secondary infection relative to active monitoring.

Peng et al. 2021	Paper received by journal on February 25 2021	Simulates an environment composed of a workforce,	**Model**: Stochastic individual-based forward-time simulation COVID-19 outbreak simulator.	**Impact of testing use:** Assumes use of RT-PCR tests with sensitivity of 95% and a 1-day turnaround time to get results. • PQRT reduced from 0.12% for a 14-day quarantine without testing to…

		in which a whole group is confined at once.	**Goal**: Evaluate the performance of a quarantine strategy with the following characteristics: • All individuals enter quarantine while asymptomatic • Those who test positive or show symptoms during quarantine are isolated until recovery (i.e., they are removed from the model). • Quarantine duration varied between 1-14 days • Testing with different sensitivities was either not done or done at the *end* of the quarantine. Multiple tests could also be administered. Quarantine was evaluated under a condition of: • *Simultaneous exposure*: Individuals were infected simultaneously (e.g., due to a common exposure/event) **Key outcomes**: • **Post-quarantine transmission risk** (**PQTR**): whether a quarantine individual causes any (i.e., one or more) infections post quarantine. **Accounts for**: Viral load course, behaviours (e.g., mask use or social distancing) **Key assumptions**: • Model ONLY simulates people who are infected (ignores uninfected people who are put into quarantine) • Isolated individuals can never infect again or be re-infected (i.e., removed from model) • Reproduction number = 2.10 among symptomatic and 0.42 among asymptomatic • Average incubation time was 5.5 days • Infectivity period is higher before symptoms • On average, 25% of persons are asymptomatic **VOCs**: Not considered.	○ 0.006% when tested at end of a 14-day quarantine ○ 0.09% when tested at end of a 9-day quarantine Longer quarantines are needed to compensate for lower sensitivity tests. Testing at day 1 had no benefit, but this is purely an artifact of the model assuming individuals had no detectable viral load at the start of the simulation. **Impact of Testing frequency for different types of tests.** Increasing the number of tests during quarantine led shorter quarantines to outperform a test-free 14-day quarantine, mostly by reducing false-negatives through repeated testing. Claims that an optimal way to most quickly release people from quarantine would be a 95% sensitivity test on days 4,5,6, requiring people to test negative on all three tests before releasing them on day 6. The next best option would follow a similar procedure with a 7-day quarantine with tests on days 4, 5 (or 6) and 7. Overall, quarantine duration (higher duration), testing frequency (more tests), and testing sensitivity (higher sensitivity) all contribute to reductions in PQTR. The article provides tables (Tables 3 and 4) that designate optimal combinations of these factors.

			Vaccination status: Not considered **Terminology**: Uses the term "quarantine" when modeling the containment of *infected* individuals following a common exposure at a stage when they are still asymptomatic (there is no quarantining of non-infected individuals). The paper models "isolation" in a manner that removes all symptomatic (or positive testing) individuals from the model.	
Perrault et al., 2020	Paper posted online in November 2020	US-based population is simulated	**Model**: Agent-based branching process model **Goal**: Evaluate a risk-based quarantine (RBQ) procedure based on contact tracing, where individuals who have experienced contact with a case are put in quarantine within a cluster and: • Monitored on day 1, and if no one within the cluster shows symptoms, the entire cluster is then released Compared to approaches that use RT-PCR tests to reduce quarantine duration. The default quarantine duration without early release is 14 days. **Key outcomes**: • **Reproduction number (R_{eff})** among close contacts • **Mean reduction in R_{eff}** compared to a policy without contact tracing/quarantine **Accounts for**: Test sensitivity/delays, people's age, transmission heterogeneity, dropout from quarantine **Key assumptions**: • "Contacts" with infected are of >15 min to initiate quarantine • The top 20% of index cases report 50% of the close contacts and 80% of infections • 18.8% attack rate among household close contacts; otherwise, 6% attack rate	**Results according to 9 conditions:** **1. No contact tracing/quarantine** • R_{eff}: 1.36 • Reduction in R_{eff}: Reference **2. Quarantine only** (of all close contacts for 14 days) • R_{eff}: 0.926 • Reduction in R_{eff} vs no contact tracing/quarantine: 31.8% **3. 1-day RBQ** procedure (no testing) • R_{eff}: 1.00 • Reduction in R_{eff} vs no contact tracing/quarantine: 26.1% **4. RBQ + exit testing**. RBQ, but clusters need negative RT-PCR tests to be released. • R_{eff}: 0.967 • Reduction in R_{eff} vs no contact tracing/quarantine: 28.8% **5. RBQ + 4 extra days for small clusters**: If clusters have 8 or less people, the RBQ period before considering release lasts an extra 4 days. • R_{eff}: 0.968 • Reduction in R_{eff} vs no contact tracing/quarantine: 28.7% **6. RBQ + active monitoring**. RBQ, but non-quarantined contacts are monitored and complete symptom screening each day. • R_{eff}: 0.967 • Reduction in R_{eff} vs no contact tracing/quarantine: 28.8%

<table>
<tr>
<td></td>
<td></td>
<td></td>
<td>

Model calibration results in R_0 of 1.88
Mean incubation time = 1.57 days
By default, quarantines last 14 days from last exposure, and isolation of index cases lasts 10 days from symptom onset
Contact tracers paid $20 per hour
Results of tests take 1 day to be available

VOCs: Not considered

Vaccination status: Not considered

Terminology: Uses “quarantine” to refer to individuals in confinement initiated due to contact with an infected individual who develops symptoms.
</td>
<td>
7. RBQ + exit testing + 4 extra days + active monitoring. A combination of the 4 variants of RBQ above

R_{eff}: 0.926
Reduction in R_{eff} vs no contact tracing/quarantine: 31.8%

8. Single-test release. Once traced, people are tested. Released if test negative; otherwise, 14-day quarantine

R_{eff}: 1.17
Reduction in R_{eff} vs no contact tracing/quarantine: 13.8%

9. Double-test release. Similar to single test, but after results of a test are available, another is taken. People are released after they show 2 negative tests or quarantine ends.

R_{eff}: 1.1
Reduction in R_{eff} vs no contact tracing/quarantine: 19.1%

Sensitivity analyses show the performance of the conditions with quarantine can each vary importantly based on the time it takes from test administration to results.

Overall, RBQ performs only slightly worse than quarantine for everyone, but reduces the average days in quarantine substantially. Procedures only based on testing are more expensive and perform less well to reduce transmissions.
</td>
</tr>
<tr>
<td>Quilty et al., 2021</td>
<td>Published online on January 20, 2021</td>
<td>No specific population</td>
<td>
Model: Stochastic individual-based model

Goal: To evaluate the effect of different quarantine and testing strategies on reducing onward transmission from traced secondary infections

Key outcomes: Transmission averted

Accounts for: Cases infectivity, testing, quarantine duration, probability of detection, adherence to quarantine and isolation

Key assumptions:
</td>
<td>
Self-isolation on symptom onset alone can prevent 35% (95% UI 10–59) of onward transmission potential

Contact tracing and quarantine of contacts
<table>
<tr><th></th><th>Transmission averted (%)</th><th>RR* (95%CI)</th></tr>
<tr><td>7 days</td><td>43 (16-68)</td><td>0.92 (0.68-1.00)</td></tr>
<tr><td>10 days</td><td>46 (18-77)</td><td>1.00 (0.85-1.07)</td></tr>
<tr><td>14 days*</td><td>48 (18-79)</td><td>Reference</td></tr>
</table>
</td>
</tr>
</table>

			• Median (IQR) incubation period: 5.1 (3.9-6.7), 95%CI: 2.3-11.5 days
			• Mean (SD) infectious period:
			  ○ Symptomatic: 7.56 (1.54) days
			  ○ Asymptomatic: 4.32 (1.09) days
			• Median (IQR) proportion of infections that are asymptomatic: 0.31 (0.28-0.33), 95%CI: 0.24-0.38
			• For PCR testing, the probability of detection is 100% for Ct values below 35 and 0% for values above 35
			• For LFA testing, the probability of detection is approximately 95% for Ct values below 27, 65% for Ct values between 27 and 30, 30% for Ct values between 30 and 35, and 0% for values above 35.
			
			VOCs: Not considered
			
			Vaccination status: Not considered
			
			Terminology: Uses the term "quarantine" to refer to individuals who were in contact with a case and were then confined. Individuals were put in "self-isolation" at symptom onset, however, "self-isolation" is also used to refer to the confinement of contacts.
				<table><tr><td>Lateral flow antigen (LFA) on first day of quarantine**</td><td>46 (19-71)</td><td>0.95 (0.55-1.46)</td></tr><tr><td>PCR on first day of quarantine**</td><td>52 (24-81)</td><td>1.05 (0.67-1.75)</td></tr></table>
				*The comparison scenario = a 14-day quarantine period with no testing, 3 days from testing of the index case to tracing, 50% adherence to quarantine, and 67% adherence to self-isolation.
				**Individuals who tested negative were immediately released from quarantine
				
				The amount of transmission potential averted can be increased if testing (LFA or PCR) is done on the final day of quarantine.
				
				As the quarantine period increases in length, the relative contribution of a test is lessened, as the majority of the infectious period has been spent in quarantine.
				
				<table><tr><td></td><td>Transmission averted (%)</td><td>RR (95%CI)</td></tr><tr><td>14 days quarantine (No testing)</td><td>48 (18-79)</td><td>Reference</td></tr><tr><td>14 days (LFA or PCR)</td><td>48 (18-82)</td><td>1.00 (1.00-1.07)</td></tr><tr><td colspan="3">With a LFA at the end</td></tr><tr><td>7 days</td><td>49 (20-78)</td><td>1.00 (0.82-1.28)</td></tr><tr><td>10 days</td><td>48 (18-80)</td><td>1.00 (0.87-1.15)</td></tr><tr><td colspan="3">With a PCR at the end</td></tr></table>

				<table><tr><td>**7 days**</td><td>50 (23-80)</td><td>1.02 (0.88-1.41)</td></tr><tr><td>**10 days**</td><td>48 (18-80)</td><td>1.00 (0.97-1.18)</td></tr></table> Quarantine with release after a negative PCR test 7 days after exposure might avert a similar proportion (50%, 95% UI 23–80) to that of the 14-day quarantine period. Quarantine with a negative LFA test 7 days after exposure or daily LFA testing without quarantine for 5 days after tracing could also prevent around 49-50% of transmission if all tests are negative. If traced contacts are required to take a daily LFA test for n days after tracing instead of having to quarantine, 5 days of testing might avert 50% (95%CI 24–79; RR 1.04, 95% CI 0.69–1.79) of transmission, with additional days of testing averting a similar amount

Takeshita et al., 2023	**Accepted**: June 28, 2023
	
	Published: July 12, 2023
		No specific population (but more applicable to smaller populations)	**Model:** Discrete time Susceptible - Exposed - Infectious - Recovered (SEIR) model, in which individuals transition through five sequential statuses: susceptible (S); exposed (E); pre-symptomatic (P); infected (I) (divided in symptomatic and asymptomatic); and recovered. Each scenario was simulated 100 times.
			
			Goal: To investigate the effect of requiring a negative test certification after quarantining on the infection risk as well as the possibility of reducing the duration of quarantine by combining the two most common tests.
			To assess how negative antigen test results, without quarantine, contribute to reducing the infection risk in a population that is likely to be infected (such as contacts).
			
			Key outcomes: Infection and non-infection probability based on different durations of quarantine
				For both contacts of confirmed cases and contacts of symptomatic cases, the infection probability decreased sharply from day 0 to day 5 of quarantine and then, remained roughly the same from day 6 to day 8, and decreased from day 9 to day 12. Implying that a five-day quarantine period would still allow to decrease the risk of infections.
				
				Risk of infection for a secondary contact (by change in quarantine length)
				• 14 to 5 days: increase of 0.17% for contacts of confirmed cases and of 0.14% for contacts of symptomatic cases when 25% of the population is in close contact with a case.
				• 7 to 5 days: roughly an increase of 0.01% for both types of contacts.
				• For a 5-day quarantine if x% of the population is in the close contact of a confirmed case, compared to a 14-day quarantine:
				  ○ 25% : 0.17% risk increase
				  ○ 30%: 0.21% increase
				  ○ 50%: 0.35% increase
				  ○ 60%: 0.35% increase

			Accounts for: The existence of two types of tests and their combination (sensitivity and specificity)
			
			Key assumptions:
			• Makes the assumption of a homogenous population
			• Sensitivity of an antigen test: 0.7, they however note that this can vary with the variant, without accounting for it.
			• After an individual is exposed to the coronavirus, they are in:
			  ○ Status E for 3 days,
			  ○ Status P for 2 days,
			  ○ Status Is or Ia for 7 days
			  ○ Remain in Status R (no possibility of re-infection)
			
			VOCs: Not considered
			
			Vaccination status: Not considered
			
			Terminology: Quarantine of individuals who were in contact with a case, however, they use the term "isolation" to refer those individuals.
				○ 90%: 0.65% increase
				• For a 5-day quarantine if x% of the population is a contact of a symptomatic case, compared to a 14-day quarantine:
				  ○ 25% : 0.14% increase
				  ○ 30%: 0.17% increase
				  ○ 50%: 0.28% increase
				  ○ 60%: 0.34% increase
				  ○ 90%: 0.52% increase
				
				As the infection probability on day 5 is less than 20% of that on day 0, the five-day quarantine period and double test would result in an 80% risk reduction, relative to the risk of infection on day 0 .
				
				If one wants to achieve 90% and 100% risk reduction, the quarantine period after an initial negative PCR test should be 10 and 12 days, respectively. 80% of the risk can be reduced within the first 5 days, but an additional 5 days are required to reduce another 10%, and a further 7 days are needed to reduce an additional 20%.

Wells et al., 2021	Paper submitted to journal on October 12, 2020	No specific population, but applies & validates model using an offshore work context (e.g., offshore oil facility)	**Model:** Unspecified type of mathematical model. **Goal:** Compare shorter quarantine durations (<14 days) paired with testing to longer quarantine periods (e.g., 14-days) without testing. Evaluation is limited to individuals who are infected, but who have not manifested symptoms by the end of the quarantine. **Key outcomes**: • **Post-Quarantine Transmission (PQT)**: causing one or more infections after exiting the quarantine period.	**Quarantine based on contact tracing (without a strict known time of exposure):** When testing on exit, a shorter duration quarantine maintained high effectiveness relative to longer quarantines without testing • E.g., With exit testing, a quarantine of 5+ days had a PQT of <5%, whereas quarantines without testing needed to be >11 days in duration to reach PQT <5%) • A 7-day quarantine with testing on exit (or a 6-day quarantine with testing both on entry and exit) both had equivalent or lower PQTs relative to a 14-day quarantine without testing (PQTs < 2.5%) • Overall, testing on entry had little benefits to reducing the required length of quarantine.

			Accounts for: Infectivity profiles, sensitivity of RT-PCR testing. **Key assumptions**: • R_0 = 2.5 at baseline • Assumed perfect isolation of symptomatic cases, reducing R_0 to 1.6. • Incubation period = 8.29 days • 30.8% of infections never become symptomatic • Tracing of contacts initiated by onset of symptoms in the index case. • Symptomatic and asymptomatic cases are equally infectious **VOCs**: Not considered **Vaccination status**: Not considered **Terminology**: Discusses quarantine as "quarantine initiated by contact tracing". Also uses "quarantine" to discuss other forms of confinement (e.g., initiated due to travel).	When quarantines are 6 days or less, the optimal time to give an exit test was the final day of quarantine. At quarantine durations of 7-14 days, this leveled off, such that the optimal time to give a test was always on day 6.

Zou et al., 2023	**Accepted:** March 22, 2023
	
	Published: July, 2023
		No specific population	**Model:** Deterministic compartmental model to simulate COVID-19 transmission, contact tracing, and quarantine.
			
			Goal: They aim to explore how compliance dynamics can influence optimal quarantine strategies to minimize transmission. They therefore investigate the entry into quarantine via contact tracing, the duration of quarantine (5, 10 or 14 days) and the compliance to the duration of quarantine.
			
			Key outcomes: Overall COVID-19 attack rate
			
			Accounts for: Compliance to the duration of quarantine, contact tracing, the duration of the quarantine.
				Risk difference between various duration of quarantine when:
				• Shortening quarantine has no effect on compliance:
				  ○ Marginal risk difference between 10-day and 14-day
				  ○ Risk of infection associated with a 5-day quarantine was consistently higher when compared to a 10-day or 14-day quarantine
				  ○ As quarantine compliance decreases, there is a more rapid increase in the secondary attack rate in the 14-day and 10-day quarantine relative to the 5-day quarantine. However, the absolute levels of attack rate in the 5-day quarantine are still consistently higher than in the longer duration quarantines.
				• Initial period of perfect compliance followed by increasing noncompliance
				  ○ Compliance during the final 2 days of quarantine doesn't significantly impact attack rates.

			Key assumptions:
			• R_0 = 2.5
			• Assumes it takes only a day
			  ○ To isolate a symptomatic individual outside of quarantine
			  ○ To quarantine a contact
			• Probability of infection per contact: 10%
			• Incubation period = 6 days
			• 30% of infections are asymptomatic
			• Infectious period: 10 days
			  ○ Asymptomatic period: 8 days
			  ○ Presymptomatic period: 2 days
			• Quarantined and isolated individuals are not considered to be infectious
			• Individuals are isolated for 10 days
			• Tracing of contacts initiated by onset of symptoms in the index case.
			• Delay between the beginning of isolation and symptom outset among individuals who have left the quarantine: 5 days
			• Symptomatic and asymptomatic cases are equally infectious
			
			VOCs: The model was also run in a delta specific scenario
			
			Vaccination status: A version of this model accounted for individuals who were fully vaccinated
			
			Terminology: Discusses quarantine as "quarantine initiated by contact tracing" and uses "isolation" to refer to confined cased of COVID-19
				○ High compliance during the initial days of quarantine are crucial for transmission control.

Results 2: Summary of studies about the effectiveness of quarantine on the transmission of H1N1

Table 2.1: Summary of empirical studies that were rated as *not having a critical risk of bias,* reporting on effectiveness of quarantine 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 that were rated as *having a critical risk of bias,* reporting on effectiveness of quarantine 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 quarantine 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 quarantine 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 quarantine 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 that were rated as *having a critical risk of bias,* reporting on effectiveness of quarantine 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

Bondy et al. 2009	**Accepted:** 24 December 2009 **Published:** 24 December 2009	Ontario (Canada) Data from 2003	**Design:** Retrospectively observational study **Sample:** 332 index cases with a final disposition of suspect or probable SARS of whom 204 had at least one community contact uniquely associated with them in Public Health records. Individuals who were confirmed to not have SARS were excluded. **Intervention:** Index cases who were in quarantine at the time of symptom onset. **Comparison:** Individuals who were not in quarantine at symptom onset. **Key Outcomes:** For all community contacts, outcome status as a secondary SARS case was defined. • Secondary case count ratio (SSCR): the ratio of secondary cases (per index case) in the isolation condition relative to the non-isolation condition. • Difference in average secondary cases per index case between the two groups (secondary case count difference, SCCD), and the inverse of the SCCD, the number needed to quarantine (misused the term quarantine here) (NNQ). **Terminology:** Community contacts were classified by closest level of exposure to the index case (e.g., level 1 being closest at ≥30 minutes within a distance of one metre). **Vaccination status:** Not considered (Comments on limitations are provided: "statistical challenges" section)Canonical	Canonical Poisson and negative binomial regression with log link functions using all 332 index cases as the unit of analysis • SCCR estimate of 0.316, indicating that there was less than one third of the number of secondary cases for quarantined versus non-quarantined index cases. This was significant with the Poisson regression (p=0.026) but not the negative binomial (p=0.057) nor the bootstrapped model (p=0.573) Generalized linear model with Poisson regression model (Poisson error term and identity link function). • The average difference in secondary SARS cases in moving from non-quarantine to quarantine status was estimated at 0.133 secondary cases per index case. The SCCD estimate was significant for both the Poisson regression (p=0.001) and the negative binomial (p=0.002) but not the bootstrapped model (p=1.00). • The NNQ suggests that 7.51 SARS index cases be placed in quarantine to reduce the number of secondary cases by one. This was also significant for the Poisson regression (p=0.001) and the negative binomial (p=0.002) but not the bootstrapped model (p=1.00). This suggests that quarantine can be an effective preventive measure, although these estimates lack statistical precision. When adjusting for total and close contacts the number of close contacts was significantly associated with the number of secondary cases (p=0.005). This remained statistically significant even in the bootstrapped model (p=0.009). When including the 140 false positives (index cases that were then confirmed to not have	Critical

				SARS), the NNQ estimate dropped from 7.51 to 5.74, giving the appearance of a still greater benefit (data not shown; again, statistically significant under the large sample assumption, and not when using bootstrap methods).	

Table 3.3: Summary of modelling studies reporting on effectiveness of quarantine 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 quarantine 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 quarantine 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 that were rated as *having a critical risk of bias,* reporting on effectiveness of quarantine 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 quarantine 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				•

Land Acknowledgements
The Montreal Behavioural Medicine Centre, Concordia University, UQAM, and the CIUSSS-NIM are located on unceded Indigenous lands. The Kanien'kehá:ka Nation is recognized as the custodians of the lands and waters on which these institutions stand today. Tiohtiá:ke commonly known as Montreal is historically known as a gathering place for many First Nations. Today, it is home to a diverse population of Indigenous and other peoples. We respect the continued connections with the past, present, and future in our ongoing relationships with Indigenous and other peoples within the Montreal community.

McMaster University is located on the traditional territories of the Mississauga and Haudenosaunee nations, and within the lands protected by the "Dish With One Spoon" wampum, an agreement to peaceably share and care for the resources around the Great Lakes.

We are grateful to have the opportunity to work on these lands.

Funding: This LES was commissioned and funded by the Office of the Chief Science Officer, Public Health Agency of Canada.

The members of the Montreal Behavioural Medicine Centre are supported by a variety of career and scholarship awards. Dr. Bacon is supported by the CIHR-SPOR initiative through the Mentoring Chair program (SMC-151518) and by the Fonds de recherche du Québec: Santé (FRQS) through the Chaire de recherche double en Intelligence Artificielle / Santé Numérique ET sciences de la vie program (309811). Ms. Burdick and Ms. Léger are supported by CIHR-CGS-M (Canada graduate scholarship, master's award) and FRQS Master's Scholarship. Ms. Sanuade is supported by the CIHR-SPOR Mentoring Chair program (SMC-151518). Dr. Wu and Dr Joyal-Desmarais were also supported by this scholarship previously. Dr. Wu is currently supported by a FRQS Postdoctoral scholarship and Ms. Vieira and Ms. Deslauriers are supported by a FRQS PhD scholarships, respectively.

The opinions, results, and conclusions are those of the team that prepared the evidence synthesis, and independent of the Government of Canada, the Public Health Agency of Canada, CIHR, or FRQS. No endorsement by the Government of Canada, the Public Health Agency of Canada, CIHR, or FRQS is intended or should be inferred.

References

1. Ashcroft P, Lehtinen S, Angst DC, Low N, Bonhoeffer S. Quantifying the impact of quarantine duration on covid-19 transmission. eLife. 2021;10:1–33. Available from: https://elifesciences.org/articles/63704
2. Bondy SJ, Russell ML, Laflèche JM, Rea E. Quantifying the impact of community quarantine on SARS transmission in Ontario: estimation of secondary case count difference and number needed to quarantine. BMC Public Health. 2009 Dec;9(1):1–10.
3. Dawson P, Worrell MC, Malone S, Fritz SA, McLaughlin HP, Montgomery BK, et al. Modifications to student quarantine policies in K–12 schools implementing multiple COVID-19 prevention strategies restores in-person education without increasing SARS-CoV-2 transmission risk, January-March 2021. PLoS ONE. 2022. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0266292
4. Ferretti L, Wymant C, Nurtay A, Zhao L, Hinch R, Bonsall D, et al. Modelling the effectiveness and social costs of daily lateral flow antigen tests versus quarantine in preventing onward transmission of COVID-19 from traced contacts [Internet]. medRxiv; 2021 [cited 2024 Mar 26]. p. 2021.08.06.21261725. Available from: https://www.medrxiv.org/content/10.1101/2021.08.06.21261725v1
5. He B, Zaidi S, Elesedy B, Hutchinson M, Paleyes A, Harling G, et al. Effectiveness and resource requirements of test, trace and isolate strategies for COVID in the UK. Royal Society Open Science. 2021;8(3):201491. Available from: https://royalsocietypublishing.org/doi/10.1098/rsos.201491
6. Hui BB, Brown D, Chisholm RH, Geard N, McVernon J, Regan DG. Modelling testing and response strategies for COVID-19 outbreaks in remote Australian Aboriginal communities. BMC Infectious Diseases [Internet]. 2021;21. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8424150/
7. Love NK, Ready DR, Turner C, Verlander NQ, French CE, Martin AF, et al. Daily use of lateral flow devices by contacts of confirmed COVID-19 cases to enable exemption from isolation compared with standard self-isolation to reduce onward transmission of SARS-CoV-2 in England: a randomised, controlled, non-inferiority trial. The Lancet Respiratory Medicine. 2022;10:1074–85. Available from: https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00267-3/fulltext#:~:text=This%20study%2C%20which%20provided%20evidence,adverse%20effects%20of%20self%2Disolation.
8. Love NK, Ready DR, Turner C, Yardley L, Rubin GJ, Hopkins S, et al. The acceptability of testing contacts of confirmed COVID-19 cases using serial, self-administered lateral flow devices as an alternative to self-isolation. Journal of Medical Microbiology [Internet]. 2022;71. Available from: https://www.microbiologyresearch.org/content/journal/jmm/10.1099/jmm.0.001567
9. Motta F.C., McGoff K.A., Deckard A., Wolfe C.R., Bonsignori M., Moody M.A., et al. Assessment of Simulated Surveillance Testing and Quarantine in a SARS-CoV-2-Vaccinated Population of Students on a University Campus. JAMA Health Forum. 2021;2(10):e213035. Available from: https://jamanetwork.com/journals/jama-health-forum/fullarticle/2784740
10. Peak CM, Kahn R, Grad YH, Childs LM, Li R, Lipsitch M, et al. Individual quarantine versus active monitoring of contacts for the mitigation of COVID-19: a modelling study. The Lancet Infectious Diseases. 2020 Sep 1;20(9):1025–33. Available from: https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30361-3/fulltext
11. Peng B, Zhou W, Pettit RW, Yu P, Matos PG, Greninger AL, et al. Reducing COVID-19 quarantine with SARS-CoV-2 testing: A simulation study. BMJ Open [Internet]. 2021 [cited 7AD Jan 1];11. Available from: https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed22&AN=635499990
12. Perrault A, Charpignon M, Gruber J, Tambe M, Majumder M. Designing Efficient Contact Tracing Through Risk-Based Quarantining [Internet]. National Bureau of Economic Research; 2020 [cited 2024 Mar 26]. (Working Paper Series). Available from: https://www.nber.org/papers/w28135

13. Quilty BJ, Clifford S, Flasche S, Kucharski AJ, Group CCW, John Edmunds W. Quarantine and testing strategies in contact tracing for SARS-CoV-2: a modelling study. Lancet [Internet]. 2020; Available from: https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(20)30308-X/fulltext
14. Takeshita JI, Murakami M, Kamo M, Naito W, Yasutaka T, Imoto S. Quantifying the Effect of Isolation and Negative Certification on Covid-19 Transmission. Scientific Reports [Internet]. 2023;13. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10338484/
15. Wells CR, Townsend JP, Pandey A, Moghadas SM, Krieger G, Singer B, et al. Optimal COVID-19 quarantine and testing strategies. Nature Communications [Internet]. 2021;12. Available from: https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emexb&AN=2010128717
16. Young BC, Eyre DW, Kendrick S, White C, Smith S, Beveridge G, et al. Daily testing for contacts of individuals with SARS-CoV-2 infection and attendance and SARS-CoV-2 transmission in English secondary schools and colleges: an open-label, cluster-randomised trial. The Lancet. 2021 Oct 2;398(10307):1217–29. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01908-5/fulltext?s%3Fs?s%3Fs
17. Zou K, Hayashi M, Simon S, Eisenberg JNS. Trade-off Between Quarantine Length and Compliance to Optimize COVID-19 Control. Epidemiology. 2023;34(4):589–600. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10231873/

Appendices