Individual quarantine versus active monitoring of contacts for the mitigation of COVID-19: a modelling study

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Summary

Background Voluntary individual quarantine and voluntary active monitoring of contacts are core disease control strategies for emerging infectious diseases such as COVID-19. Given the impact of quarantine on resources and individual liberty, it is vital to assess under what conditions individual quarantine can more effectively control COVID-19 than active monitoring. As an epidemic grows, it is also important to consider when these interventions are no longer feasible and broader mitigation measures must be implemented.

Methods To estimate the comparative efficacy of individual quarantine and active monitoring of contacts to control severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), we fit a stochastic branching model to reported parameters for the dynamics of the disease. Specifically, we fit a model to the incubation period distribution (mean 5·2 days) and to two estimates of the serial interval distribution: a shorter one with a mean serial interval of 4·8 days and a longer one with a mean of 7·5 days. To assess variable resource settings, we considered 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.

Findings Model fitting by sequential Monte Carlo resulted in a mean time of infectiousness onset before symptom onset of 0·77 days (95% CI −1·98 to 0·29) for the shorter serial interval, and for the longer serial interval it resulted in a mean time of infectiousness onset after symptom onset of 0·51 days (95% CI −0·77 to 1·50). Individual quarantine in high-feasibility settings, where at least 75% of infected contacts are individually quarantined, contains an outbreak of SARS-CoV-2 with a short serial interval (4·8 days) 84% of the time. However, in settings where the outbreak continues to grow (eg, low-feasibility settings), so too will the burden of the number of contacts traced for active monitoring or quarantine, particularly uninfected contacts (who never develop symptoms). When resources are prioritised for scalable interventions such as physical distancing, we show active monitoring or individual quarantine of high-risk contacts can contribute synergistically to mitigation efforts. Even under the shorter serial interval, if physical distancing reduces the reproductive number to 1·25, active monitoring of 50% of contacts can result in overall outbreak control (ie, effective reproductive number <1).

Interpretation Our model highlights the urgent need for more data on the serial interval and the extent of presymptomatic transmission to make data-driven policy decisions regarding the cost–benefit comparisons of individual quarantine versus active monitoring of contacts. To the extent that these interventions can be implemented, they can help mitigate the spread of SARS-CoV-2.

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Introduction

An outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China, first reported on Dec 31, 2019. It has since spread globally, with over 3·5 million confirmed cases of COVID-19 as of May 6, 2020. To reduce further spread of the disease, governments have implemented community measures to increase physical distancing for those at highest risk of infection.[1] In China, policies include unprecedented lockdowns to reduce contacts between individuals, travel restrictions, and door-to-door temperature checks with mandatory mass quarantine.[2]

Contact tracing, a core strategy to control disease, is used to identify individuals who may have been exposed to an infectious disease and to focus interventions on these individuals. If identified contacts are symptomatic when found, they are promptly isolated and treated in a health-care setting. More often, contacts are found healthy, and may not be infected. Depending on how much time has passed since exposure to the primary infected individual, those infected individuals may not yet be symptomatic—this period of time between infection and symptoms is an important epidemiological trait of an infectious disease called the incubation period. How to handle these symptom-free contacts is a recurring point of confusion and controversy, particularly for emerging infectious diseases. Two essential strategies are used: individual quarantine or active monitoring of

For **WHO COVID-19 guidance** see https://www.who.int/emergencies/diseases/novel-coronavirus-2019

For the **Johns Hopkins interactive COVID-19 dashboard** see https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6

Research in context

Evidence before this study

Two non-pharmaceutical interventions to prevent disease spread include voluntary individual quarantine and voluntary active monitoring. Previous research found that a disease's natural history, particularly the amount of transmission that occurs before symptom onset, greatly affects the ability to control outbreaks and the relative effectiveness of these two strategies. We searched PubMed and medRxiv for the terms "individual quarantine", "active monitoring", "contact tracing", "COVID19", and "nCoV" up to March 24, 2020, with no date or language restrictions. We identified several studies reporting estimates of epidemiological parameters of COVID-19, as well as others focused on measures to control the COVID-19 outbreak. However, few focused specifically on contact-based measures. A study on isolation for COVID-19 control found a potentially large effect of perfect isolation, although quarantine before symptom onset was outside the scope. However, estimates for the serial interval of COVID-19, which affects the amount of presymptomatic transmission, are varied.

Added value of this study

As severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to spread, better understanding of how to contain it becomes crucial. In this study, we used methods described in our previous work and disease-specific epidemiological parameters reported for COVID-19 to compare the ability of individual quarantine and active monitoring to reduce the effective reproductive number of COVID-19 to below the crucial threshold of 1. We provide an estimate of presymptomatic transmission specifically for COVID-19, a key parameter for understanding outbreak dynamics. We further develop a metric for the feasibility of scaling up active monitoring and individual quarantine and examine the synergistic effect of contact-tracing interventions with physical distancing, which can guide public health responses to this pandemic.

Implications of all the available evidence

Assuming a mean serial interval of 4·8 days, as reported in a previous study, the incremental benefit of individual quarantine over active monitoring was substantial as a result of the shorter time from infection to onward transmission and more presymptomatic transmission. However, using a mean serial interval of 7·5 days, as reported for the severe acute respiratory syndrome epidemic, individual quarantine and active monitoring are similarly effective at controlling onward transmission in a high-feasibility setting. The burden of placing uninfected contacts under individual quarantine can grow untenable due to a longer duration in quarantine before clearance (assumed 14 days) and a higher ratio of uninfected contacts traced per truly infected contact. In such settings, resources might be prioritised for broader physical distancing measures, and active monitoring or individual quarantine of high-risk contacts could contribute synergistically. The sensitivity of these results to the estimated serial interval highlights the urgent need for better data to guide policy decisions.

individuals. 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; this intervention requires private space, provision of essentials, and investment in enforcement. A less restrictive intervention, active monitoring, involves assessing the individual for symptoms at regular intervals such as twice-daily visits by health-care workers or phone-based self-monitoring,[3] and if symptoms are detected, the individual is promptly isolated.

The relation between symptoms of a disease and infectiousness to others is crucial to the success of containment strategies. Previous work has found that a disease's natural history, particularly the amount of transmission that occurs before symptom onset, greatly affects the ability to control outbreaks[4] and the relative effectiveness of individual quarantine versus active monitoring.[5] Short-course diseases such as influenza, and diseases with long periods of presymptomatic infectiousness such as hepatitis A, are affected more strongly by quarantine than by active monitoring. However, quarantine is of limited benefit over active monitoring for the coronaviruses causing Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS), where people usually show distinctive symptoms at or near the same time that they become infectious. Hellewell and colleagues[6] found a potentially large effect of perfect isolation on COVID-19, although quarantine before symptom onset was outside the scope. A mobile phone application for contact tracing could allow for instant contact tracing, decreasing the time to isolation of symptomatic contacts.[7] Our framework enables comparison of active monitoring with individual quarantine and considers parameters such as delays and imperfect isolation to account for known transmission of this respiratory virus after isolation in a health-care setting.[8]

One of the key uncertainties surrounding COVID-19 is the extent of asymptomatic and presymptomatic transmission. A study reporting asymptomatic transmission in Germany[9] was later found to be incorrect or misleading,[10] adding to the confusion. There has also been uncertainty about the serial interval—the time between symptom onset of infector–infectee pairs—which in turn reflects uncertainty about the extent of presymptomatic transmission. Early estimates by Nishiura and colleagues[11] (of 24 infector–infectee pairs) and Li and colleagues[12] (of six infector–infectee pairs) were derived from limited

	Serial interval scenario 1			Serial interval scenario 2		
	Median	Mean (95% CI)	Source	Median	Mean (95% CI)	Source
Basic reproductive number (R_0)	2·20	2·2 (1·46 to 3·31)	Riou and Althaus;[13] Li and colleagues[12]	2·20	2·2 (1·46 to 3·31)	Riou and Althaus;[13] Li and colleagues[12]
Serial interval (T_{LAT}), days	4·6	4·8 (1·02 to 9·81)	Nishiura and colleagues[11]	6·99	7·50 (2·39 to 15·48)	Li and colleagues[12]
Incubation period (T_{INC}), days	4·14	5·2 (1·11 to 15·53)	Li and colleagues[12]	4·14	5·2 (1·11 to 15·53)	Li and colleagues[12]
Dispersion (k)	..	0·54	Riou and Althaus[13]	..	0·54	Riou and Althaus[13]
Latent period offset (T_{LAT}–T_{INC}), days*	–0·71	–0·77 (–1·98 to 0·29)	Model fitting by sequential Monte Carlo method	0·59	0·51 (–0·77 to 1·50)	Model fitting by sequential Monte Carlo method
Duration of infectiousness (d_{INF}), days	1·8	2·4 (1·0 to 6·7)	Model fitting by sequential Monte Carlo method	4·4	4·8 (1·1 to 10·5)	Model fitting by sequential Monte Carlo method
Relative time of peak infectiousness (β_τ)†	0·38	0·43 (0 to 0·97)	Model fitting by sequential Monte Carlo method	0·37	0·38 (0 to 0·97)	Model fitting by sequential Monte Carlo method

Due to uncertainty in the serial interval, results are presented for two scenarios: scenario 1 assuming a shorter serial interval with mean 4·8 days,[11] and scenario 2 assuming a longer serial interval with mean 7·5 days.[12] COVID-19=coronavirus disease 2019. *Positive values indicate symptoms before infectiousness; negative values indicate infectiousness before symptoms. †Range 0–1, with 0 indicating linearly decreasing infectiousness, 0·5 indicating peak infectiousness at midpoint of duration of infectiousness, and 1 indicating linearly increasing infectiousness.

Table: **COVID-19 disease parameters**

data, and the estimates by Li and colleagues[12] reflected the distribution of the serial interval derived from SARS cases in 2003. Given the severe impact of quarantine on both resources and individual liberty, it is vital to assess under what conditions quarantine can effectively control COVID-19, and among these, under what conditions quarantine is substantially more effective than less restrictive approaches such as active monitoring, particularly given uncertainty in essential disease parameters. In this study, we used methods described in our previous work[5] and disease-specific epidemiological parameters reported for COVID-19[11,12] to compare the ability of individual quarantine and active monitoring to reduce the effective reproductive number (R_e) of COVID-19 to below the crucial threshold of 1. Although mass restrictions on movements within cities have been implemented during this outbreak and are sometimes referred to as quarantines, here we focus on the effectiveness of quarantine and active monitoring on an individual basis based on contact tracing.

Methods

Model structure

We built on a previously published approach for modelling active monitoring and individual quarantine to control emerging infectious diseases,[5] using published estimates of transmission dynamics for COVID-19 to account for essential questions and parameter uncertainties. Reflecting the uncertainty surrounding key parameters for COVID-19, we compared two sets of serial interval parameters: one from Nishiura and colleagues,[11] with a mean serial interval of 4·8 days, and another from Li and colleagues,[12] with a mean serial interval of 7·5 days (table).

Individuals in a stochastic branching model progress through a susceptible-exposed-infectious-recovered disease process focused on the early stages of epidemic growth. Upon infection, individuals progress through an incubation period (T_{INC}) before onset of symptoms and a latent period (T_{LAT}) before onset of infectiousness. During the duration of infectiousness (d_{INF}), the relative infectiousness follows a triangular distribution (β_τ) as a function of time (τ) since onset of infectiousness. The time offset between the latent and incubation periods (T_{LAT}–T_{INC}) indicates presymptomatic infectiousness if negative.

During each hour of infectiousness, an individual can generate new infections (basic reproductive number $[R_0]\times\beta_\tau$) following a negative binomial distribution with dispersion parameter (κ) with smaller values indicating more variability in infectiousness. Infectiousness while under individual quarantine (before symptom onset) is reduced by γ_q, and infectiousness while under isolation (after symptom onset) is reduced by γ_i, with values between 0 (indicating no reduction in infectiousness) and 1 (indicating no transmission during that hour). Upon isolation, the individual names a defined proportion of their contacts (P_{CT}), who are traced within a defined number of hours (D_{CT}) and placed under either active monitoring or quarantine. Those under active monitoring are checked with a defined frequency (D_{SM}), such as twice daily, and are promptly isolated if found to be symptomatic; however, before isolation there is no reduction in infectiousness.

Model parameterisation

Using published values of the incubation period (table), parameters for the duration of infectiousness, the time of peak infectiousness relative to the total duration of infectiousness, and the time offset between incubation and latent periods were fit using a sequential Monte Carlo algorithm, also known as particle filtering.[7] Particles with these three dimensions were resampled with an adaptive threshold to converge on a set of 2000 that yielded simulated serial intervals that most closely matched

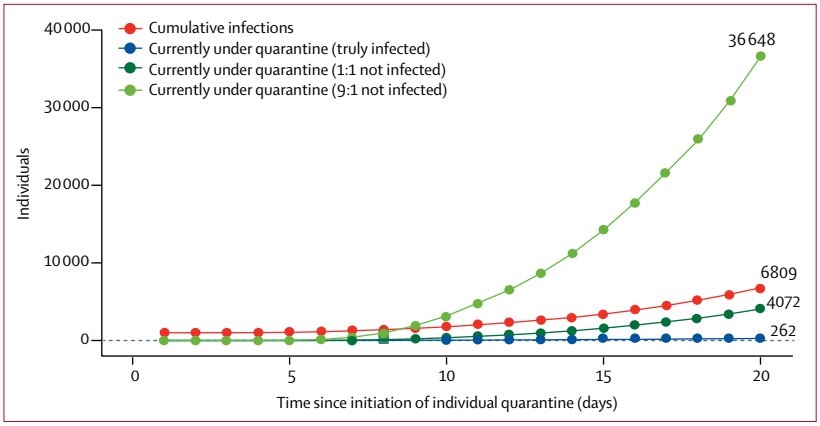

Figure 1: **Simulated daily growth of infections and individuals under quarantine**
When the ratio of uninfected to infected contacts under quarantine is 1:1, the prevalence of infection among traced contacts is 0·5, and when it is 9:1, the prevalence is 0·1. The model assumes individual quarantine of contacts begins at a cumulative case count of 1000, in a low-feasibility setting with a basic reproductive number of 2·2, and a mean serial interval of 4·8 days (table). As can be seen in figure 2, exponential growth occurs in low-feasibility settings regardless of the longer or shorter serial interval scenario. The shorter serial interval and low-feasibility setting is a combination that has the clearest and fastest exponential growth, and has been used as an example to illustrate the differences in growth rates for cases and uninfected contacts.

published values of the serial interval (table), as measured with the Kolmogorov-Smirnov test.

Feasibility settings

See Online for appendix

As described in previous work,[5] we defined two settings with respect to the feasibility of interventions (appendix p 3). A high-feasibility setting, presented as the main results, is defined as one where 90% of contacts are traced and put under either quarantine or active monitoring within an average of 0·5 days (range 0–1). Contacts under active monitoring are monitored every 0·5 days on average (range 0–1). A contact under individual quarantine has infectiousness reduced by 75% (γ_q=0·75) until symptoms emerge and prompt isolation. When symptoms emerge in a contact under quarantine or active monitoring, they are isolated in a setting that reduces infectiousness by 90% (γ_i=0·90), thereby greatly reducing but not eliminating infectiousness while isolated. Assuming perfect intervention performance is not possible, the high-feasibility parameters represent upper bounds of the expected ability to implement interventions based on contact tracing, and are reflected by multiple national contact investigation guidelines for COVID-19, including contact tracing within 24 h and twice-daily monitoring for symptoms.[1,14,15] A low-feasibility setting loosens these assumptions to account for imperfect recall of who may be exposed (P_{CT}=50%), delays in identifying or locating contacts (D_{CT}=2 days [range 0–4]), infrequent or untrained monitoring of symptoms (D_{SM}=2 days [range 0–4]), and imperfect quarantine (γ_q=0·25) and isolation (γ_i=0·5).

Model outputs

Unimpeded exponential epidemic growth driven by R_0 can be reduced by individual quarantine or active monitoring, as measured by R_e. We present estimates of R_e under individual quarantine (R_{IQ}) and active monitoring (R_{AM}) under high-feasibility and low-feasibility settings. The difference (R_{AM}–R_{IQ}) is the expected number of secondary cases prevented by quarantining one infected individual over actively monitoring that individual. If the prevalence of infection among traced contacts subject to quarantine or active monitoring is p, then the number of traced contacts who must be quarantined to prevent one secondary case relative to active monitoring is $1/(p\ [R_{AM}–R_{IQ}])$. We calculated this quantity from the model under varying assumptions about p, including an estimate for p of 0·0004 obtained during SARS control in Taiwan, where 24 of 55 632 quarantined contacts were found to be truly infected.[16] To capture synergy of community-based and contact-based interventions, we measured the incremental effect of individual quarantine or active monitoring over community-based interventions such as physical distancing, which we assume reduce R_0.

The number of days an individual is under quarantine or active monitoring is measured as the time difference between when an individual is identified via contact tracing and when symptoms prompt isolation. We assume individuals under active monitoring or quarantine who are uninfected are followed up for a duration of 14 days until clearance, consistent with previous interventions.[17]

We calculated the expected percentage of infections that result from presymptomatic infectiousness in the absence of interventions as the sum total of expected secondary cases caused by an individual before symptom onset ($R_{i,pre}$) divided by the total expected secondary infections for that individual (R_i) times 100. This percentage equals 0 when symptom onset precedes infectiousness and equals 100 when the entire duration of infectiousness concludes before symptom onset. Analyses were performed with R (version 3.6.2).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

We fit the model assuming short (mean 4·8 days; scenario 1) versus long (mean 7·5 days; scenario 2) serial interval estimates. Model fitting by sequential Monte Carlo for the shorter serial interval resulted in a mean duration of infectiousness of 2·4 days (95% CI 1·0 to 6·7), a mean time of peak relative infectiousness at 43% (95% CI 0 to 97) of the duration of infectiousness, and a mean time of infectiousness onset before symptom onset of 0·77 days (95% CI –1·98 to 0·29; table; appendix p 1). The longer serial interval in scenario 2 (mean 7·5 days) resulted in slower disease dynamics, with a mean duration of infectiousness of 4·8 days (95% CI 1·1

to 10·5), a mean time of peak relative infectiousness at 38% (95% CI 0 to 97) of the duration of infectiousness, and a mean time of infectiousness onset after symptom onset of 0·51 days (95% CI –0·77 to 1·50; table; appendix p 2). Therefore, given the same incubation period distribution (mean 5·2 days), a serial interval with a mean of 4·8 days is best fit by substantial presymptomatic infectiousness (mean 20·5% [95% CI 0–91·4]), while a longer serial interval with a mean of 7·5 days is best fit by limited presymptomatic infectiousness (mean 0·065% [95% CI 0–0·88]).

The burden of implementing interventions based on contact tracing grows quickly as a function of disease incidence and the fraction of traced contacts who are not infected. Figure 1 shows, in a low-feasibility setting where individual quarantine is unable to contain the exponential growth of cases, the number of uninfected contacts (who never develop symptoms and are cleared after 14 days) under quarantine grows more quickly than does the number of truly infected contacts. As the ratio of uninfected to infected contacts traced increases from 1:1 to 9:1, for example, the burden of uninfected contacts grows proportionally. Depending on the ratio of uninfected to infected contacts traced, individual quarantine may become infeasible as the epidemic grows, even if initially effective (eg, in Singapore),[18] and will need to be supplemented with scalable interventions such as physical distancing or deprioritised.

We found that the serial interval and extent of presymptomatic transmission are important determinants of the effectiveness of interventions. In a high-feasibility setting, the median effective reproductive number was 0·57 (95% CI 0·32–1·05) under individual quarantine and 1·55 (0·65–2·7) under active monitoring with the shorter serial interval (figure 2A). For the shorter serial interval in a high-feasibility setting, control (R_e <1) was achieved only by individual quarantine in 84% of simulations and by either intervention in 12% of simulations; in 4% of simulations neither active monitoring nor individual quarantine reduced R_e to below 1 (figure 2A). In a low-feasibility setting, R_{IQ} and R_{AM} remained above 1 for both serial interval scenarios, even when R_0 was 1·5. With the longer serial interval, the median effective reproductive number was 0·49 (95% CI 0·34–0·97) under individual quarantine and 0·54 (0·32–0·98) under active monitoring in a high-feasibility setting, and these numbers continue near the y=x equivalency line for low-feasibility settings as well (figure 2B). Therefore, the following figures focus on the larger differences observed for the shorter serial interval (scenario 1).

Under both serial interval scenarios, in a low-feasibility setting, R_e was rarely brought below 1 under either individual quarantine or active monitoring, although a median reduction in the reproductive number of 21·0% under individual quarantine and 13·6% under active monitoring for serial interval scenario 2 could still meaningfully slow the growth of an epidemic; for serial interval scenario 1, active monitoring resulted in only a 3% reduction in the

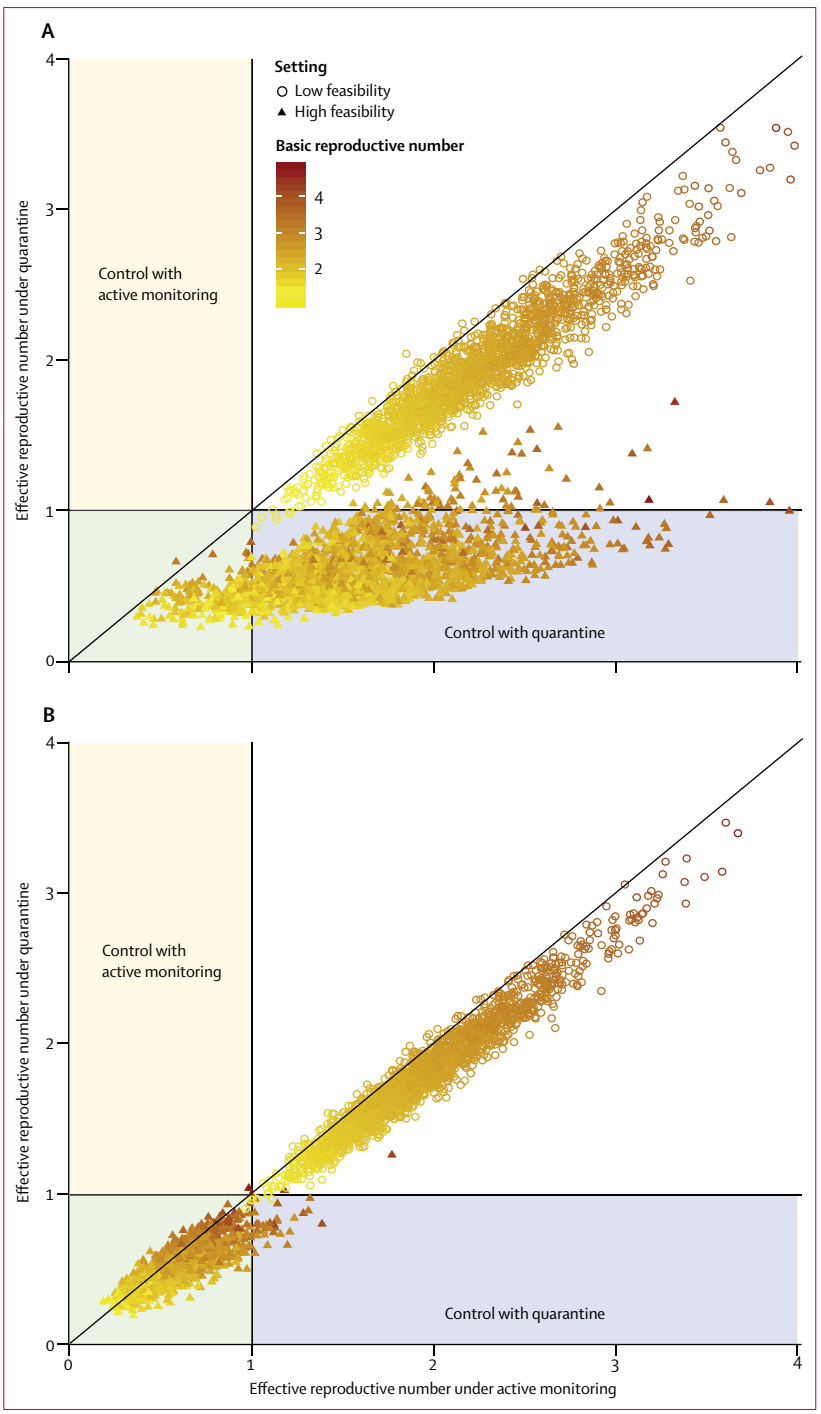

Figure 2: **Effective reproductive number under active monitoring and individual quarantine**
The effective reproductive number under active monitoring and individual quarantine increases with the basic reproductive number and in low-feasibility settings compared with high-feasibility settings in serial interval scenario 1 (A) with mean 4·8 days and scenario 2 (B) with mean 7·5 days. Equivalent control under individual quarantine and active monitoring would follow the y=x line.

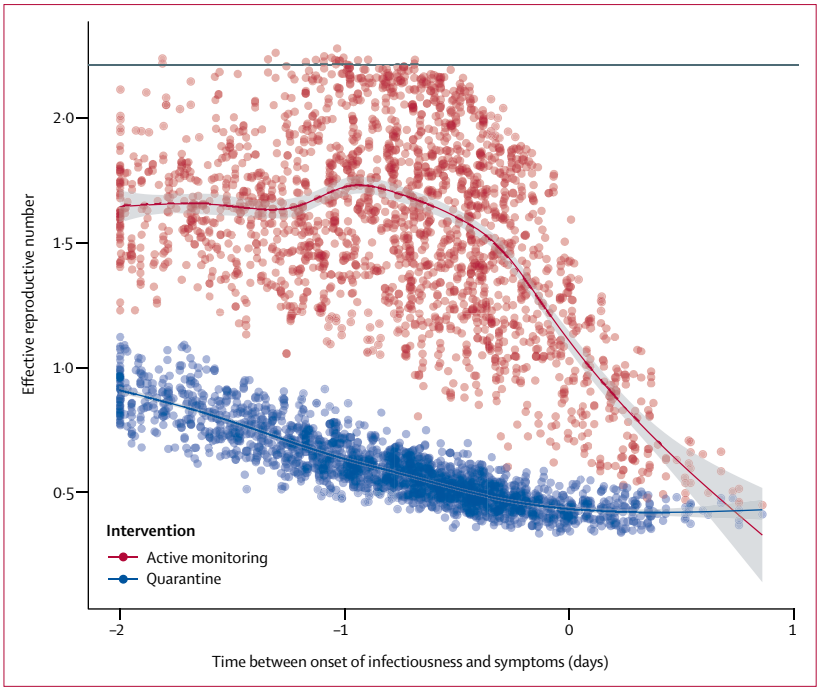

Figure 3: **Effect of presymptomatic infectiousness on effective reproductive number**
The grey borders around the Loess curves indicate 95% CIs. The dark grey line indicates the basic reproductive number. The effective reproductive number under active monitoring and individual quarantine decreases as the onset of infectiousness gets later with respect to the onset of symptoms in a high-feasibility setting, holding the basic reproductive number constant at 2·2. An offset of –2 days indicates infectiousness precedes symptoms by 2 days, an offset of 0 days indicates onset of both simultaneously, and an offset of 1 day indicates infectiousness onset occurs 1 day after symptom onset. The model assumes a mean serial interval of 4·8 days.

reproductive number, whereas individual quarantine resulted in a 17% reduction.

The effectiveness of active monitoring was particularly sensitive to an earlier onset of infectiousness relative to symptoms. When R_0=2·2, for example, R_{IQ} remained below 1 unless the onset of infectiousness preceded symptoms by more than 2 days, whereas R_{AM} had little tolerance for presymptomatic infectiousness (figure 3).

The fraction of contacts traced was another important determinant of the effectiveness of interventions. As the probability of tracing an infected contact decreases, more cases are able to transmit the infection without isolation and, therefore, there is a linear increase in the average R_{IQ} or R_{AM} across the population (figure 4). Even with other operational parameters reflecting a high-feasibility setting, at least 75% of contacts need to be traced and quarantined to reduce R_e below 1 in the population in the absence of other interventions (figure 4). For individuals who are traced and placed under active monitoring or individual quarantine, however, the effect of the interventions at reducing onward transmission by that person remains effective.

In a setting where COVID-19 cases continue to grow, resources may be prioritised for scalable community interventions such as physical distancing; however, close contacts such as family members of a patient may still undergo targeted interventions. In our modelling framework, physical distancing functions synergistically with quarantine or isolation by reducing the reproductive number of infected individuals in the community who are not in quarantine or isolation. If physical distancing reduces the reproductive number to 1·25 (eg, 50% of person-to-person contact is removed in a setting where R_0 is 2·5), active monitoring of 50% of contacts can result in overall outbreak control (ie, R_e<1; figure 5). Tracing 10%, 50%, or 90% of contacts in addition to physical distancing resulted in a median reduction in R_e of 3·2%, 15%, and 33%, respectively, for active monitoring, and 5·8%, 32%, and 66%, respectively, for individual quarantine.

Given the additional cost and burden of quarantine,[19] it might be important to consider the marginal benefits of individual quarantine over active monitoring. With a longer serial interval in a high-feasibility setting, the median additional number of secondary cases prevented by quarantining one infected individual over actively monitoring that individual is 0·043 (95% CI –0·16 to 0·11), which translates to a need to quarantine a median of 23 (95% CI 9·09–∞) truly infected contacts to avert one infection beyond active monitoring alone. This median value increases proportionally with the probability that a traced contact is not infected: 47 contacts need to be quarantined if 50% of contacts are infected; 468 contacts need to be quarantined if 5% of contacts are infected; and 53 907 contacts need to be quarantined if 0·04% of contacts are infected, as observed for SARS control in Taiwan.[16] For the shorter serial interval, the median additional number of secondary cases prevented by quarantining one infected individual over actively monitoring that individual is 0·93 (95% CI 0·23–1·93), corresponding to a need to quarantine a median of 1·1 (95% CI 0·52–4·22) infected contacts to prevent one secondary infection. However, if only 0·04% of traced contacts are infected, a median of 2495 individuals need to be quarantined to prevent one secondary infection relative to active monitoring.

Discussion

To the extent that interventions based on contact tracing can be implemented, they can help mitigate the spread of COVID-19. Our results suggest that individual quarantine could contain an outbreak of COVID-19 with a short serial interval (4·8 days), but only in settings with high intervention performance where at least 75% of infected contacts are individually quarantined. However, in settings where this performance is unrealistically high and the outbreak of COVID-19 continues to grow, so too will the burden of the number of contacts traced for active monitoring or quarantine. If the virus becomes widespread before any case-based control measures can be implemented and resources are prioritised for scalable interventions such as physical distancing,[20] we show active monitoring or individual quarantine of high-risk contacts can contribute synergistically with physical distancing.

Such synergy might be observed in the data released by WHO after its mission to China in February, 2020.[21] In Guangdong, WHO reported that the proportion of patients in fever clinics testing positive for SARS-CoV-2 declined from 0·47% on Jan 30, to 0·02% on Feb 16, during a period of intensive physical distancing interventions.[21] If we assume that these physical distancing interventions reduced transmission of nearly all infections that could cause attendance at a fever clinic, a lower total number of attendees might be expected, with proportionate declines in all causes of infectious fever that are affected by physical distancing. If we assume that most causes of fever are similarly affected by physical distancing, the declining proportion of SARS-CoV-2 cases among all fever cases might reflect the benefits of interventions aimed specifically at SARS-CoV-2, which is to say case-based interventions such as active monitoring, individual quarantine, and isolation.

In locations where the COVID-19 epidemic is at an early stage, the effectiveness of individual quarantine or active monitoring depends on aspects of the disease, especially the assumed serial interval and timing of presymptomatic transmission, and the setting, including the fraction of contacts traced. Briefly, a shorter serial interval, larger window of presymptomatic transmission, poor quality interventions, and a small fraction of contacts traced all reduce the ability of either intervention to decrease transmission.

The effectiveness of individual quarantine versus active monitoring, based on contact tracing, depends on the assumptions regarding the serial interval, the amount of transmission that occurs before symptom onset, and the feasibility setting. Under our fitted disease natural history parameters for serial interval scenario 1, with a short mean serial interval of 4·8 days and hence substantial presymptomatic infectiousness, individual quarantine was considerably more effective than active monitoring at reducing onward transmission by an infected contact. This relative benefit of individual quarantine compared with active monitoring could theoretically be offset, or reversed, by a correspondingly larger perverse incentive, should individuals report fewer contacts when under a policy of quarantine as compared with active monitoring. Both serial interval scenarios were fit using a mean incubation period of 5·2 days, which was derived from a previous study in 451 laboratory-confirmed cases from Wuhan;[12] other more recent estimates of the incubation period of COVID-19 include a mean of 6·4 days among 88 travellers[22] and a median of 4 days among 291 hospitalised patients and outpatients.[23] A shorter incubation period relative to the serial interval would be consistent with less presymptomatic transmission. By contrast, a study of cases in China and Singapore found longer average incubation periods (7·1 and 9·0 days) and shorter serial intervals (4·6 and 4·2),[24] which indicate an even higher proportion of presymptomatic transmission. In a scenario with these parameters, the relative benefit of individual quarantine over active monitoring would increase, whereas the total number of simulations where control is achieved under individual quarantine would decrease. The incubation period distribution, in addition to the serial interval distribution, is thus a key parameter to refine as additional information becomes available.

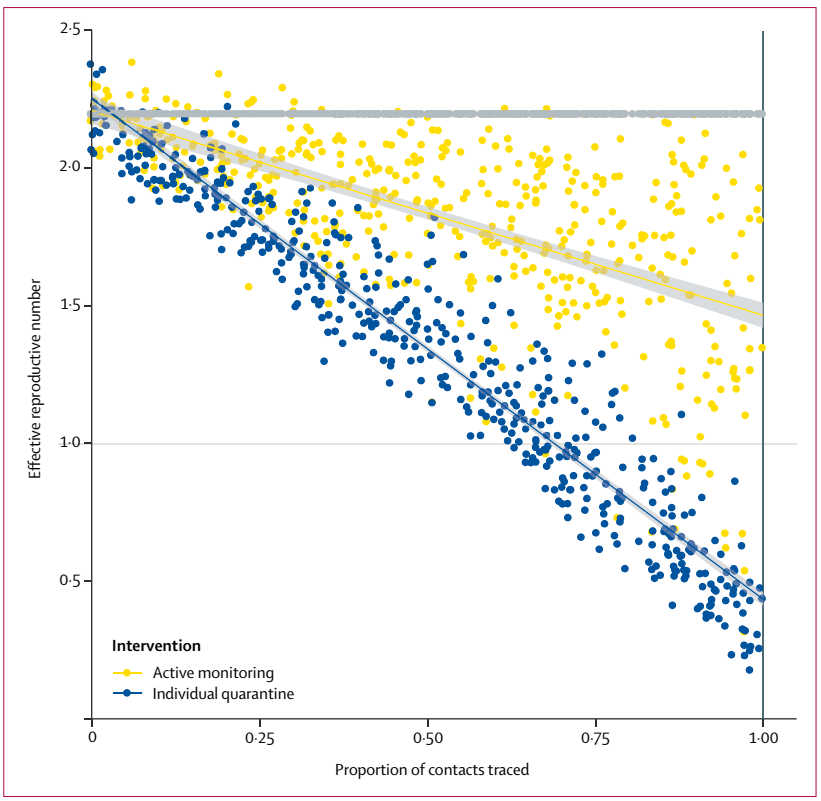

Figure 4: **Effect of proportion of contacts traced on effective reproductive number**
The grey borders around the linear regression indicate 95% CIs. The dark grey line indicates the basic reproductive number. The effective reproductive number under active monitoring and individual quarantine increases as the proportion of contacts traced decreases, assuming a mean serial interval of 4·8 days and a basic reproductive number of 2·2. Intervention parameters other than fraction of contacts traced are set to the high-feasibility setting.

Under our fitted disease natural history parameters for serial interval scenario 2, with a mean serial interval of 7·5 days and hence a low amount of presymptomatic transmission, we found that both active monitoring and individual quarantine effectively reduced the expected number of secondary cases per contact to below 1. The incremental benefit of individual quarantine over active monitoring was minimal in this scenario, requiring hundreds or thousands of suspected contacts to be quarantined to avert one infection beyond active monitoring alone. These results suggest that with a serial interval similar to that of SARS for COVID-19, there are few plausible conditions under which individual quarantine would offer a sufficient advantage over active monitoring to justify the substantial incremental resources required to implement individual quarantine and large incremental costs to those experiencing it. Furthermore, if the more restrictive policy of individual

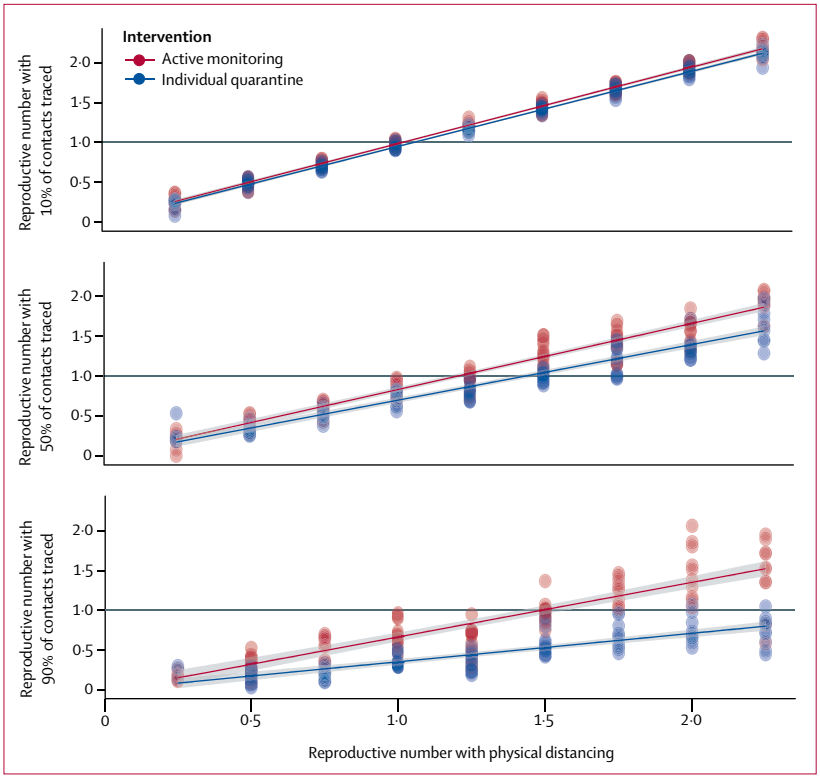

Figure 5: **Synergistic effect of physical distancing and interventions based on contact tracing**
The grey borders around the linear regression indicate 95% CIs. Active monitoring and individual quarantine of 10%, 50%, and 90% of contacts provide incremental benefit over physical distancing when the mean serial interval is 4·8 days and the basic reproductive number is 2·2. Intervention parameters other than the fraction of contacts traced are set to the high-feasibility setting.

quarantine instead of active monitoring leads to a decrease in the percentage of contacts traced, through hesitance to name contacts or avoidance of contact tracers, the small incremental benefit of individual quarantine over active monitoring in serial interval scenario 2 might be cancelled out or active monitoring might become more effective than individual quarantine.

If the epidemic continues to grow, the feasibility and social acceptability of quarantining individuals becomes a crucial consideration. In these circumstances, complementary interventions, such as physical distancing and pharmaceutical interventions, might be needed if efficient contact tracing and rapid isolation are not readily achievable, regardless of the extent of presymptomatic transmission. Furthermore, since contact tracing would be unable to identify contacts infected by individuals who never develop symptoms (ie, asymptomatic infectiousness rather than presymptomatic infectiousness), community interventions such as physical distancing are suited for mitigating transmission by asymptomatic infection, whereas interventions based on contact tracing can address those exposed to individuals known to have the disease. Even if only a small proportion of infected contacts are traced, the potential transmission chains from those contacts could be prevented. The extent to which it is worth investing in imperfect contact tracing will depend on the rate of epidemic growth, which affects feasibility, and the other mix of interventions being considered.

The findings of this study are limited by the reliability of input parameters, which are inherently uncertain during the early stages of disease emergence. The model-fitting procedure is tuned to accept a wide range of inputs consistent with published dynamics without over-fitting, thereby allowing for built-in uncertainty of input values. Additional limitations of the model include the focus on early epidemic growth in the absence of depletion of susceptible individuals, and the assumption of a consistent R_0 across scenarios with different serial intervals. By assuming that relative infectiousness follows a triangular distribution, we might underestimate the effect of contact-tracing interventions if relative infectiousness increases exponentially towards the end of disease instead, or overestimate their effect if relative infectiousness decreases exponentially after the earliest stages; however, our estimate of peak infectiousness at 38% of the duration of infectiousness suggests peak infectivity at neither end of the duration of infectiousness. By assuming the duration of infectiousness follows a uniform distribution, we might exclude long-duration shedders, which can lead to either an underestimation of the effect size if a larger fraction of an individual's infections happen long after isolation, or an overestimation of the effect size if the right tail is long enough such that individuals are released from interventions and are able to spark a second outbreak. Additionally, our choice to consider shifts of the latent period relative to the infectious period implicitly assumes a similar shape to the underlying distributions, albeit with different means. As the amount of presymptomatic transmission will depend not only on the average timing of the latent period relative to the incubation period, but also on the standard deviation of these distributions, more data on their true shapes are urgently needed.

The aim of this study was to compare individual quarantine with active monitoring targeted by contact tracing and not to simulate other approaches such as self-isolation or mass quarantine. In our model framework, self-isolation can be conceptualised as a scenario in which all contacts are traced and under active monitoring, since recognition of symptom onset is the event that triggers isolation. Mass quarantine is expected to result in prompt isolation upon symptom onset of any truly infected individuals, but the effect of this strategy on COVID-19 will depend heavily on whether presymptomatic exposure within the group is decreased or increased by the approach to confinement. That is, mass quarantine could reduce or increase the number of uninfected contacts who are exposed to presymptomatic infectiousness of those who go on to develop the disease. In serial interval scenario 1, where a mean of 20% of transmission is expected to occur before symptom onset, the positive effect of prompt isolation can be offset by an increase in presymptomatic transmission in a confined space. Mass quarantines

can also result in unintended consequences that can exacerbate transmission of SARS-CoV-2, such as avoidance of contact tracers and inaccurate recall, a reduction in health-care worker support and availability of supplies, and a rise in other infectious diseases more broadly.[24] The impact of travel restrictions on human mobility, a necessary first step in the causal chain to outbreak containment, is difficult to measure, but a strong reduction in movement, recorded by mobile phone call detail records, was documented in Sierra Leone during the national lockdowns implemented in response to the 2014–16 epidemic of Ebola virus disease.[25]

The conflicting conclusions from our two scenarios, driven largely by the differences in the extent of presymptomatic transmission, highlight the urgent need for more data to clarify key epidemiological parameters of COVID-19, particularly the serial interval and the extent of presymptomatic transmission, to inform response efforts. These highly influential parameters warrant further study to improve data-driven policy making.

Contributors

CMP analysed the data, CMP and RK wrote the first draft of the manuscript, and all authors participated in the writing, reviewing, and editing of the manuscript. All authors contributed to the study design.

Declaration of interests

We declare no competing interests.

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