SARS-CoV-2 screening: effectiveness and risk of increasing transmission

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Testing asymptomatic people for SARS-CoV-2 aims to reduce COVID-19 transmission. Screening programmes’ effectiveness depends upon testing strategy, sample handling logistics, test sensitivity and individual behaviour, in addition to dynamics of viral transmission. The interaction between these factors is not fully characterized. We investigated the interaction between these factors to determine how to optimize reduction of transmission. We estimate that under idealistic assumptions 70% of transmission may be averted, but under realistic assumptions only 7% may be averted. We show that programmes that overwhelm laboratory capacity or reduce isolation of those with minor symptoms have increased transmission compared with those that do not: programmes need to be designed to avoid these issues, or they will be ineffective or even counter-productive. Our model allows optimal selection of whom to test, quantifies the balance between accuracy and timeliness, and quantifies potential impacts of behavioural interventions. We anticipate our model can be used to understand optimal screening strategies for other infectious diseases with substantially different dynamics.

1. Background

Repeatedly screening asymptomatic individuals for SARS-CoV-2, with the aim of isolating infected people and thereby reducing transmission, has been undertaken in hospitals [1], institutions [2,3], professional sports leagues [4] and the White House. It has been undertaken at town and city level [5,6], with the aim of expansion to national level [7]. This reduction in transmission aims not only to save lives but also to permit continuance of activities that would otherwise be halted as part of disease control efforts.

The success of such screening in reducing infections does not rely only upon screening frequency, test sensitivity and viral shedding profiles. It encompasses every element of the screening process, from those affecting whether people with infection undergo screening, through the speed with which screening can inform people they are infectious, to the actions people take on learning they are infectious. Understanding the contributions from and interactions between these elements is key to designing an effective screening programme. Crucially, it is key for avoiding a programme that loses effectiveness or even increases infection rates by allowing the wrong circumstances to come together.

We have derived an expression for the proportion of infections averted by a screening programme. Our expression accounts for real-world engagement with screening and the time taken to process samples. We show that in realistic situations, screening (with isolation following a positive screen) alone results in only a modest reduction in infections. When the presence of screening results in a relaxation of precautions taken by those with minor symptoms, we show that...
this combination can result in an overall increase in infections compared with no screening. We demonstrate that the success of screening depends upon a rapid turnaround of tests. As a result, we show that a screening programme running comfortably under capacity is more successful than one that pushes capacity and generates backlogs. Our derived expression can be used to compare the effectiveness of proposed testing strategies in complex scenarios where there are different infection rates and different test availabilities—such situations might occur in a small screening programme, for example in a hospital with ward-to-ward variation in infection, or in a large programme, for example in a national programme with city-to-city variation in infection and in laboratory locations.

2. Results

We began by considering two different screening scenarios. The first scenario is an ideal (maximum impact) scenario. In this scenario, screening is performed daily with a high-sensitivity test. Test turnaround is rapid. All those eligible for screening present on every occasion, and all those with positive screens immediately isolate. The second scenario is a realistic scenario for mass population screening. In this scenario, screening is performed weekly with a high-sensitivity test. Samples for testing must be transported by courier from the sampling site to the testing laboratory. Test turnaround follows the distribution of real turnaround times sampled from a large laboratory operating within capacity. There is attrition reducing those eligible who present for screening and those who isolate following positive screens, similar to the attrition observed in other screening programmes. The difference between the two scenarios is marked. In the ideal scenario, we estimate screening alone can eliminate 70% of onward transmissions (95% confidence interval 66–74%). In the realistic scenario, the proportion of transmissions eliminated reduces to 7% (95% confidence interval 5–11%).

We next considered what happens if the presence of screening reassures those with minor symptoms, so that instead of isolating they continue with their daily lives. We divided our infected population into three categories: those who never display any symptoms of infection and always continue with their daily lives, those who display typical symptoms and isolate as soon as these symptoms manifest, and those who display minor symptoms and variably reduce their contact with others when such symptoms manifest. If, instead of isolating, those with minor symptoms behave as usual, the total number of transmissions increases, and because on average an infected person remains infectious for longer (having not isolated), the proportion of transmissions eliminated by screening increases. However, because screening does not identify all the additional individuals in the population with minor symptoms but behaving as usual, the net result is a relative increase in the number of transmissions. If the behaviour change is seen in a sufficiently high proportion of those with minor symptoms, the net result of the screening programme can be an absolute increase in transmissions compared with no screening programme, even though the programme appears to be more successful (figure 1).

Following this, we considered the impact of testing turnaround times on the ability of screening to reduce viral transmission. In general, one would expect a greater number of screening tests to be able to detect a greater number of infections, and therefore to yield a greater reduction in transmissions. However, when the number of tests requested exceeds a laboratory’s capacity, a backlog develops with consequent increase in turnaround time. This effect was seen in English laboratories at the end of April 2020, when a policy of testing large numbers of asymptomatic people in residential facilities was implemented. We modelled the effect of exceeding laboratory capacity using turnaround time data from April to June 2020 in our regional clinical microbiology and public health laboratory in Cambridge, England (figure 2). Our output shows that reliably keeping laboratory demand slightly below capacity results in a greater reduction in transmissions than when capacity is exceeded. We then proceeded to consider the general effect of laboratory turnaround time on the ability of screening to reduce viral transmission. Our
output shows that the extent of transmission reduction depends strongly upon turnaround time.

A full consideration of screening effectiveness takes into account individual engagement with screening. We considered this in our model, via the proportion of those offered screening who ever take it up, the proportion of those who attend each screening event, and the proportion who isolate when asked. The first and last of these have a linear effect on testing effectiveness (electronic supplementary material, figure S1). For a weekly screening interval, the second is also approximately linear, reflecting that this screening interval only gives one opportunity to prevent most transmission. With more frequent screening intervals, the impact on transmissions of increased per-screen uptake becomes nonlinear, with diminishing returns as the uptake is higher (figure 3).

Because our model takes infectivity and testing distributions as input, limited only by the tractability of the resultant numerical integration, it can be used to predict the impact of different testing strategies in complex scenarios where rates of infection, access to testing or uptake vary within a population (figure 4). This allows us to, for example, consider the impact of a programme using rapid near-patient tests daily, where such tests have lower sensitivity than laboratory-based nucleic acid amplification testing [9]. Assuming total and per-test uptake remains the same (increased frequency balanced by increased convenience), our model predicts a reduction in transmissions from such a programme between 25% for self-administered tests and 32% for laboratory-staff-administered tests (95% confidence intervals 22–28% and 29–35%, respectively), compared with the 7% reduction (95% confidence interval 5–11%) from a centralized mass testing programme.

Our model is sufficiently robust to changes in modelling assumptions regarding viral transmission dynamics to make predictions that can be used in practice (electronic supplementary material, table S1).

### 3. Discussion

Ultimate control of the COVID-19 pandemic is unlikely prior to deployment of effective vaccines. Screening and isolation acts as a bridge to this goal, saving lives and permitting some resumption of economic and social activity. It must, however, be recognized that unintended behavioural responses to screening may not only remove the opportunity to resume desired activity, but indeed may make disease transmission worse than if no screening had occurred.

Pursuing centralized testing strategies may rapidly increase testing capacity. However, the critical impact of turnaround time on testing effectiveness means that such strategies must have highly streamlined logistics chains to retain effectiveness. If rapid centralized turnaround of tests is not possible, then less accurate, localized testing may be more effective. As with the historical introduction of screening programmes, in SARS-CoV-2 testing it is crucial we move from simply counting numbers of tests, to more sophisticated measures of their effectiveness.

Engagement with screening substantially impacts success and must not be taken for granted [10]. A holistic approach considering the social, economic and political impacts, acknowledging the incidence of false-positive results and balancing their impact, and combined with good communication, is therefore a key part of a successful programme.
Testing strategies that employ confirmatory testing to reduce false-positive rates need clear protocols for communicating with those awaiting confirmatory testing, to retain the benefit of earlier isolation.

Our results can only be as accurate as the estimates on which our model is based (for example, of test sensitivity and of duration of asymptomatic viral shedding). We note that the exact values of these estimates depend upon underlying data that may depend upon population characteristics and are sometimes sparse, but would anticipate our numerical results to covary with such estimates in a way that allows comparison between different scenarios. The heterogeneity of the underlying estimates makes the provision of meaningful confidence intervals for derived results difficult. It is important to understand that the main value of our results comes from the insight yielded into which strategic decisions to take when optimizing a screening programme, rather than providing a before/after recipe of the effect of introducing screening de novo. However, where inaccurate underlying estimates limit the accuracy of our predictions, our model highlights what additional information is required. (Our model is also limited by numerical accuracy in the calculations, but the underlying estimates represent a greater uncertainty.) In any case, our model demonstrates the impact of the different modifiable factors in a screening programme, enabling policymakers to prioritize those that give most benefit. The code we have provided (electronic supplementary material, code S1) can be updated with revised estimates as more data become available.

Our study does not account for the potential impact on transmission rate of isolating contacts of those who screen positive. When screening itself does not identify all those infected but not isolating, its impact can be potentiated by isolating contacts or by targeting contacts for additional screening as a higher risk group (similar to the scenario in figure 4b). The impact of contact isolation on transmission is highest at an intermediate screening impact, where screening de novo. However, where inaccurate underlying estimates limit the accuracy of our predictions, our model highlights what additional information is required. (Our model is also limited by numerical accuracy in the calculations, but the underlying estimates represent a greater uncertainty.) In any case, our model demonstrates the impact of the different modifiable factors in a screening programme, enabling policymakers to prioritize those that give most benefit. The code we have provided (electronic supplementary material, code S1) can be updated with revised estimates as more data become available.

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4. Methods

Our model considers the total infectivity of a population over a period of time, and the proportion of this infectivity that is averted by screening and isolating infectious people. The only major assumption underlying the model is that those being offered screening are representative of the overall population in terms of potential infectiousness and behaviour: if this assumption cannot be met, but the population can be broken down into subpopulations where the assumption can be met, then the model can still be used. In particular, we note that the model can be used when the population is not static (individuals entering and leaving the population), but in small populations where there is substantial temporal clustering of both cases of infection and screening events, the actual proportion of transmissions averted may deviate substantially from the estimate.

Infectivity is deemed to end naturally at the end of asymptomatic viral shedding, or when an individual develops symptoms and isolates from others. We construct the model by starting with a simplified screening scenario. We then add more realistic components stepwise until we have reached the final model. Ultimately, the model takes as input distributions of virus shedding duration, infectivity, intervals between tests, testing turnaround times, detection probabilities, and population engagement with screening.

We begin by considering the scenario represented in electronic supplementary material, figure S2. Asymptomatic/ presymptomatic shedding lasts for a duration $m \in M$. It begins during a screening interval of duration $j \in J$ (in principle, successive screening interval durations can be drawn from different distributions $J_0, J_1, \ldots$). The shedding begins $k \in K$ time prior to the end of the interval. There is a delay $d \in D$ from the screening event prior to isolating an infectious individual, reflecting the turnaround time of the test.
different shedding durations can have different total infectivities. The shedding period and total duration of shedding: groups with the same shedding profile of an individual. The most obvious way in which \( g \) can be interpreted as a composite reflecting the average shedding profile of an individual. The most obvious way in which \( g \) can be seen to be a composite is that if the same shedding period can represent both asymptomatic and presymptomatic shedding, then \( g \) represents a composite of the two normalized by their respective probabilities.

Next, we reflect that screening does not pick up all infectious individuals by introducing a probability of detection \( p_d(t, \theta) \). This probability is allowed to depend on the total duration of shedding (i.e. the total duration of shedding \( \tau \) is used to parameterize how easy it is to detect viral shedding at a given time \( t \)). It represents a composite of the probability that an individual presents for screening, the sensitivity of the screening test, and the probability that the individual isolates following a positive test. For nucleic acid amplification testing for SARS-CoV-2, both \( g(t, \theta) \) and \( p_d(t, \theta) \) are related to viral shedding, and hence they are related to each other. However, shedding of non-viable RNA later in the course of infection means that \( p_d(t, \theta) \) tapers more slowly than \( g(t, \theta) \) over time.

We now proceed to derive a generalized expression for the relative infectivity in the presence of a given screening regimen. First, we derive an expression for \( f_M(x) \), the density function for the amount of time before the first screen that shedding starts.
We assume a constant hazard for the commencement of shedding over time. This assumption is valid as long as screening maintains an equilibrium of infections (there is not a large growth or contraction in infection prevalence between successive screens), and as long as the time of onset of infectiousness can be assumed independent between individuals (true in all but very small populations). Note, however, that the screening interval length \( j \) can vary. This means that the time before the first screen that shedding starts, \( K \), is not simply distributed uniformly across the sampled screening interval \( j \), but needs to be conditioned upon the probability that shedding begins in a particular interval. For \( f \) the distribution of the screening interval length in which the shedding begins, we have

\[
 f_J(x) = \frac{x f_J(y)}{E(\bar{J})}.
\]

and by integrating both sides with respect to \( x \) we can derive the constant of proportionality and conclude that

\[
 f_J(x) = \frac{x f_J(y)}{E(\bar{J})}.
\]

It then follows that

\[
 f_J(x) = \int_0^\infty \frac{x f_J(y)}{y} f(x \in (0, y)) \, dy
 = \int_0^\infty \frac{x f_J(y)}{E(\bar{J})} f_J(x \in (0, y)) \, dy
 = \frac{1 - F_J(x)}{E(\bar{J})}.
\]

Now that we have a density function for the time from the start of shedding to the next screen, we can write down a density function for the time from the start of shedding to the time an individual with a positive screen result can be isolated. This is simply the convolution

\[
 f_{1 \rightarrow \infty}(x) = \int_0^\infty f_J(y) f_J(x - y) \, dy
 = \int_0^\infty \left( 1 - F_J(x - y) \right) f_J(x - y) \, dy.
\]

This convolution is independent of the total shedding duration. However, its sampled value can exceed the total shedding duration, that is, shedding can have ended before it is possible to act on a screening result.

We can now write down our first, simplified expression for averted infectivity. In this simplified case, a screen always identifies an infectious individual, and that individual then perfectly isolates. Conditioned upon a total shedding time \( \tau \), the normalized infectivity averted is

\[
 \int_0^\tau f_{1 \rightarrow \infty}(\tau) \int_{\min(\tau, \tau)} g(x, \tau) \, dx \, d\tau,
\]

where the min reflects the possibility of shedding having ended prior to the screen.

Using \( g(x, \tau) = 0 \) for \( x > \tau \) we can expand the components of the integral to give a normalized infectivity averted for shedding time \( \tau \) of

\[
 A_1(\tau) = \int_0^\infty \int_{\min(\tau, \tau)} \left( 1 - F_J(y) \right) f_J(t - y) g(x, \tau) \, dx \, dy \, dt.
\]

The total normalized infectivity averted from one infectivity-abolishing screen is therefore

\[
 A_1 = \int_0^\infty A_1(\tau) f_M(\tau) \, d\tau
 = \int_0^\infty \int_0^\infty \int_{\min(\tau, \tau)} \left( 1 - F_J(y) \right) f_J(t - y) g(x, \tau) \, dx \, dy \, d\tau.
\]

Next, we consider the situation where the probability that a screen abolishes infectivity need not be 1. In this case, conditioned upon an overall probability \( p_M \) of ever detecting infection in an individual given arbitrarily many tests over arbitrarily short testing intervals, a successful screen at time \( y \) occurs with probability \( p_M(\tau, \tau) \) and unsuccessful screens happen at time \( a_{(1,1)} = a_{(1,2)} = a_{(2,1)} = a_{(2,2)} \ldots \), \( \ldots \) with \( \tau \) with probabilities \( 1 - p_M(a_{(1,1)}, \tau), 1 - p_M(a_{(1,2)}, \tau), 1 - p_M(a_{(2,2)}, \tau), \ldots \) (In our earlier notation, \( p_M(\tau, \tau) = p_M(\tau, \tau) \)). Note that the length of shedding in the interval before the first screen is still described by the random variable \( K \), but in subsequent intervals shedding occurs across the entire interval unless it finishes altogether, so is described by \( f_J(\iota) \iota \geq 2 \). Electronic supplementary material, figure S3, gives a schematic of this set-up to illustrate the notation used. Testing turnaround time is only applicable after the last, successful, screen. (If turnaround time is highly variable, it is in principle possible to have two positive screens with the result of the second available before the first. In practice, most laboratory testing is first in, first out, so we neglect this possibility.)

For any given number of screens prior to successful detection, we can express the infectivity averted by taking a convolution of the distributions of testing times as an extension to the expression for \( f_{1 \rightarrow \infty}(x) \). This yields a general expression for the distribution of the time of beginning of shedding (with total shedding length \( \tau \)) to isolation of an individual with a positive test result:

\[
 f_1(\tau | \tau) = p_M \int_0^\infty p(y, \tau) f_J(y) f_J(\tau - y) \, dy
 + p_M \int_0^\infty p(y, \tau) f_J(y) f_J(\tau - y) \, dy
 + p_M \int_0^\infty p(y, \tau) f_J(y) f_J(\tau - y) \, dy
 + \cdots
 + p_M \int_0^\infty p(y, \tau) f_J(y) f_J(\tau - y) \, dy
 + \cdots
\]

The total infectivity averted from screening is therefore

\[
 A_1 = \int_0^\infty \int_0^\infty \int_{\min(\tau, \tau)} \left( 1 - F_J(y) \right) f_J(t - y) g(x, \tau) \, dx \, dy \, d\tau
 = p_M \sum_{n=1} A_n,
\]

where

\[
 A_1 = \int_0^\infty \int_0^\infty \int_{\min(\tau, \tau)} \left( 1 - F_J(y) \right) f_J(t - y) g(x, \tau) \, dx \, dy \, d\tau,
 A_2 = \int_0^\infty \int_0^\infty \int_{\min(\tau, \tau)} \left( 1 - F_J(y) \right) f_J(t - y) g(x, \tau) \, dx \, dy \, d\tau,
 A_n = \int_0^\infty \int_0^\infty \int_{\min(\tau, \tau)} \left( 1 - F_J(y) \right) f_J(t - y) g(x, \tau) \, dx \, dy \, d\tau.
\]

These integrals are high-dimensional, but we have successfully implemented code to calculate them in Mathematica [13], using its numerical integration algorithms. (We use the global adaptive numerical integration method unless otherwise stated, but have
implemented other methods in the code for cross-checking.) The finite limits on many of the integrals, plus the ability to truncate the infinite integral when the probability of shedding is low, mean that the first few terms in the sum are computationally tractable in full.

When successive screens are close together, so that multiple terms in the sum become relevant, performing the full multi-dimensional integrals becomes computationally intractable. However, when the time between one screening opportunity and the following opportunity is very similar for all individuals eligible for screening, the above convolutions can be approximated computationally. The approximate simplification is the approximation $t_i(t) = \delta(t - t_i)$ for $i \geq 2$, where $\delta$ is the Dirac delta and $t_i$ are fixed intervals between successive screens (which may differ from each other). This allows reduction of all the $A_i$ to four-dimensional integrals: $A_1$ is unchanged, and we have

$$A_2 = \sum_{i=1}^{\infty} \int_{t_{i-1}}^{t_i} \int_{t_{i-1}}^{t_i} \int_{t_{i-1}}^{t_i} \int_{t_{i-1}}^{t_i} f_0(t) p(y, \tau)(1 - p(y - \tau, \tau)) \left(1 - F(t_i - \tau, \tau) \right) f_0(t - \tau) g(x, \tau) \, dx \, dy \, dt \, d\tau$$

and

$$A_{n+1} = \sum_{i=1}^{\infty} \int_{t_{i-1}}^{t_i} \int_{t_{i-1}}^{t_i} \int_{t_{i-1}}^{t_i} \int_{t_{i-1}}^{t_i} \left(1 - p(y - \tau, \tau)\right) \left(1 - F(t_i - \tau, \tau) \right) f_0(t - \tau) g(x, \tau) \, dx \, dy \, dt \, d\tau.$$  

where $t_i(t)$ is defined analogously to $a_i(t)$. In a programme undertaking many screens at short intervals, this approximation is likely to prove more accurate than early truncation of a series containing the full, multiple-integral, terms. We note that the approximation is better as $p(t, \tau)$ is more smooth, although the variability in the time to initial sampling means that even when $p(t, \tau)$ is rapidly varying, the approximation is still good as long as the intervals between successive screens are similar.

4.1. Model parameters

To evaluate the effects of different screening scenarios, we set parameters of the model according to estimates for SARS-CoV-2 or the parameters we wished to evaluate. These are described in detail in the electronic supplementary material.

Data accessibility. The datasets supporting this article have been uploaded as part of the supplementary material, and include machine-readable versions of data from Zhao et al. [14]; Xia et al. [13]; Lauer et al. [16]; Hu et al. [17]; Arons et al. [18]; Rivett et al. [11]; Ferretti et al. [19]; Zhao et al. [8]; PHE Porton Down & University of Oxford SARS-CoV-2 LFD test development and validation cell [9].

Competing interests. I declare I have no competing interests.

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References

1. Rivett L et al. 2020 Screening of healthcare workers for SARS-CoV-2 highlights the role of asymptomatic carriage in COVID-19 transmission. elife 9, e58728. (doi:10.7554/eLife.58728)

2. Dora AI, Winnett A, Jatt LP, Davar K, Watanabe M, Sohn L, Kern HS, Graber CJ, Goetz MB. 2020 Universal and serial laboratory testing for SARS-CoV-2 at a long-term care skilled nursing facility for veterans—Los Angeles, California, 2020. MMWR Morb. Mortal. Wkly Rep. 69, 651–655. (doi:10.15585/mmwr.mm6921e1)

3. Njuguna H et al. 2020 Serial laboratory testing for SARS-CoV-2 infection among incarcerated and detained persons in a correctional and detention facility—Louisiana, April–May 2020. MMWR Morb. Mortal. Wkly Rep. 69, 836–840. (doi:10.15585/mmwr.mm6926e2)

4. Küssler SM et al. 2020 Viral dynamics of SARS-CoV-2 infection and the predictive value of repeat testing. medRxiv. (doi:10.1101/2020.10.21.20117042)

5. Lavezzi E et al. 2020 Suppression of a SARS-CoV-2 outbreak in the Italian municipality of Vo’. Nature 584, 425–429. (doi:10.1038/s41586-020-2488-1)

6. Iacobucci G. 2020 Covid-19: mass population testing is rolled out in Liverpool. BMJ 371, m4268. (doi:10.1136/bmj.m4268)

7. Iacobucci G, Coombes R. 2020 Covid-19: government plans to spend £100bn on expanding testing to 10 million a day. BMJ 370, m3520. (doi:10.1136/bmj.m3520)

8. Zhao J et al. 2020 Antibody responses to SARS-CoV-2 in patients with novel coronavirus disease 2019. Clin. Infect. Dis. 71, 2027–2034. (doi:10.1093/cid/ciaa144)

9. PHE Porton Down & University of Oxford SARS-CoV-2 LFD test development and validation cell. Preliminary report from the Joint PHE Porton Down & University of Oxford SARS-CoV-2 test development and validation cell: rapid evaluation of Lateral Flow Viral Antigen detection devices (LFDs) for mass community testing; https://www.ox.ac.uk/sites/files/oxford/media_wysiwyg/UK%20evaluation_PHE%20Porton%20Down%20&%20University%2020%20Lateral%20Flow%20Viral%20Antigen%20Detection%20device.pdf.

10. Smith LE, Potts HWW, Amiöt R, Fear NT, Richie S, Rubin GJ. 2021 Adherence to the test, trace and isolate system in the UK: results from 37 nationally representative surveys. BMJ 372, n608. (doi:10.1136/bmj.n608)

11. Skittell JP, Wilton M, Smiewska AA, Parmar S, Fortune MD, Sparker D, Curran MD, Zhang H, Jalal H. 2021 Specificity and positive predictive value of SARS-CoV-2 nucleic acid amplification testing in a low-prevalence setting. Clin. Microbiol. Infect. 27, 469.e9–469.e15. (doi:10.1016/j.cmi.2020.01.003)

12. Skittell JP, Fortune MD, Jalal H, Zhang H, Enoch DA, Brown NM, Swift A. 2021 Diagnostic tool or screening programme? Asymptomatic testing for SARS-CoV-2 needs clear goals and protocols. Lancet Reg. Health Eur. 1, 100002. (doi:10.1016/j.lanepe.2020.100002)

13. Wolfram Research, Inc. 2020 Mathematica, Version 12.1.

14. Zhao Q, Ju N, Bacallado S, Shah RD. 2021 BETS: the dangers of selection bias in early analyses of the coronavirus disease (COVID-19) pandemic. Ann. Appl. Stat. 15, 363–390. (doi:10.1214/20-AOAS1401)

15. Xia W et al. 2020 Transmission of coronavirus disease 2019 during the incubation period may lead to a quarantine loophole. medRxiv. (doi:10.1101/2020.03.06.20031955)

16. Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, Azman AS, Reich NG, Lessler J. 2020 The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. Ann. Intern. Med. 172, 577–582. (doi:10.7326/M20-0504)

17. Hu Z et al. 2020 Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Sci. China Life Sci. 63, 706–711. (doi:10.1007/s11427-020-1661-4)

18. Arons MM et al. 2020 Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. New Engl. J. Med. 382, 2081–2090. (doi:10.1056/NEJMoa2008457)

19. Ferretti L, Wyman C, Kendall M, Zhao L, Nurtay A, Aber-Dörner L, Parker M, Bonsall D, Fraser C. 2020 Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing. Science 368, eabb6936. (doi:10.1126/science.abb6936)