



**Health
Information
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An tÚdarás Um Fhaisnéis
agus Cáilíocht Sláinte

Evidence summary for the incubation period of COVID-19, or time to first positive test, in individuals exposed to SARS-CoV-2

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About the Health Information and Quality Authority

The Health Information and Quality Authority (HIQA) is an independent statutory authority established to promote safety and quality in the provision of health and social care services for the benefit of the health and welfare of the public.

HIQA's mandate to date extends across a wide range of public, private and voluntary sector services. Reporting to the Minister for Health and engaging with the Minister for Children and Youth Affairs, HIQA has responsibility for the following:

- **Setting standards for health and social care services** — Developing person-centred standards and guidance, based on evidence and international best practice, for health and social care services in Ireland.
- **Regulating social care services** — The Chief Inspector within HIQA is responsible for registering and inspecting residential services for older people and people with a disability, and children's special care units.
- **Regulating health services** — Regulating medical exposure to ionising radiation.
- **Monitoring services** — Monitoring the safety and quality of health services and children's social services, and investigating as necessary serious concerns about the health and welfare of people who use these services.
- **Health technology assessment** — Evaluating the clinical and cost-effectiveness of health programmes, policies, medicines, medical equipment, diagnostic and surgical techniques, health promotion and protection activities, and providing advice to enable the best use of resources and the best outcomes for people who use our health service.
- **Health information** — Advising on the efficient and secure collection and sharing of health information, setting standards, evaluating information resources and publishing information on the delivery and performance of Ireland's health and social care services.
- **National Care Experience Programme** — Carrying out national service-user experience surveys across a range of health services, in conjunction with the Department of Health and the HSE.

List of abbreviations used in this report

CDC	Centers for Disease Control and Prevention
CI	confidence interval
COVID-19	Coronavirus disease 2019
EAG	expert advisory group
ECDC	European Centre for Disease Prevention and Control
HIQA	Health Information and Quality Authority
HPSC	Health Protection Surveillance Centre
HSE	Health Service Executive
HTA	health technology assessment
NPHE	National Public Health Emergency Team
RQ	research question
RT-PCR	reverse transcription polymerase chain reaction
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SCOPI	Study to investigate COVID-19 Infection in People Living in Ireland
WHO	World Health Organization

Evidence summary for the incubation period of COVID-19, or time to first positive test, in individuals exposed to SARS-CoV-2

Key points

- Public health interventions aim to minimise the burden of COVID-19 by reducing the spread of SARS-CoV-2. Important interventions that may be associated with specific durations of time include 'self-isolation' and 'restriction of movements' (or 'quarantine').
- 'Restriction of movements' is defined as separating and restricting the movements of people who were exposed or potentially exposed to COVID-19. This is performed as a precautionary measure to prevent transmission should exposed individuals later become diagnosed.
- 'Restriction of movements' is distinct from isolation (or self-isolation) which is defined as separating those with symptoms of, or diagnosed with COVID-19, from people who are not infected.
- Individuals may be infectious before, or soon after they show symptoms of COVID-19. This disease is also associated with a large proportion of asymptomatic individuals who will never develop symptoms, but may transmit the disease. Therefore, the implementation of an adequate period of restricted movements for those exposed, or potentially exposed to SARS-CoV-2 is essential to reducing transmission.
- The incubation period of a disease, defined as the time from exposure to symptom onset, can help to inform the necessary duration of restricted movements. Given the high proportion of asymptomatic individuals, it is also important to identify when the virus is detectable in those who have no symptoms. This evidence summary aimed to estimate both of these aspects to inform the necessary duration of restricted movements.
- This evidence summary looked at 98 studies; with 96 containing data relevant to the incubation period, and three with data on time to first positive test in asymptomatic individuals based on serial testing.
- In terms of incubation period, it is important to try to estimate the cumulative proportion of people who are likely to show symptoms by each day from exposure. This form of data was provided in 14 of the 98 studies and were

used to inform the main analysis where the distribution of the data was quantified.

- The results of this analysis indicate that the median incubation period of COVID-19 is between five and six days. On average, approximately 95% of individuals who experience symptoms will do so by day 14, indicating that approximately 1 in 20 develop symptoms after this time. Approximately 82% to 87% of individuals will develop symptoms by day 10, indicating that approximately one in six develop symptoms at a later date. Some individuals may take 21 days or more to exhibit symptoms; however, there is considerable uncertainty associated with the tail of the distribution.
- Additional analyses were conducted including all studies with sufficient data relevant to estimating the incubation period of COVID-19 (n=88); results were similar, with no significant difference noted by data type, adding confidence to the results overall.
- Studies involving the serial testing of asymptomatic populations were limited to three low quality studies of small sample size. A narrative synthesis of results highlighted that these individuals may typically be detected by day 10 since exposure, but this duration may be substantially longer in some individuals.
- Insufficient data were available to conduct subgroup analyses by exposure type or setting. Limited low quality data suggested that the incubation period may be longer for children and older adults (aged ≥ 60 years) than those presented for the general populations; however, the confidence in these findings is low.
- The majority of evidence comes from studies of low quality design, and there were important limitations associated with the studies and the quantitative analysis undertaken within this evidence summary.
- This analysis aimed to estimate the incubation period of COVID-19, and the time to detect the virus in asymptomatic populations, with the goal of informing the required duration of restriction of movements. The results indicate that the widely recommended 14-day period is likely to capture approximately 95% of individuals who will become symptomatic. Information regarding the time since exposure to when infected asymptomatic populations can be detected is limited.

Evidence summary for the incubation period of COVID-19, or time to first positive test, in individuals exposed to SARS-CoV-2

The Health Information and Quality Authority (HIQA) has developed a series of 'Evidence Summaries' to inform advice that is provided to key stakeholders, including the National Public Health Emergency Team (NPHE) in their response to COVID-19. These summaries are based on specific research questions (RQs). This evidence summary was developed to address the following research question:

"What is the incubation period of COVID-19, or time to first positive test, in individuals exposed to SARS-CoV-2?"

Background

The transmissibility and impact of the SARS-CoV-2 virus is reflected in the continued growth of COVID-19 cases and associated mortality worldwide, with many countries that had previously suppressed the virus to low levels experiencing a considerable resurgence of infections.⁽¹⁾ In the absence of effective treatment options or a vaccine for an infectious disease such as COVID-19, two non-pharmaceutical public health interventions are paramount to reducing transmission:⁽²⁾

1. isolation of infected cases, and
2. tracing and restricting the movements of their contacts.

Although intertwined in the collective public health strategy employed in the COVID-19 pandemic, these concepts are distinct. Isolation (or self-isolation) is defined as the separation of those diagnosed with, or suspected of having, COVID-19 from people who are not infected. 'Restriction of movements' (or self-quarantine, or quarantine) is defined as the separation, and restriction of movements, of people who were exposed, or potentially exposed, to SARS-CoV-2, as a precautionary measure because they may have the disease.^(3, 4)

A number of factors have resulted in a larger emphasis being placed on the importance of the restricted movements element of the COVID-19 response than has been seen with previous disease outbreaks.⁽⁵⁾ Firstly, there is evidence of substantial viral shedding from the upper respiratory tract in patients with COVID-19, facilitating a high risk of transmission.^(5, 6) Secondly, the time period between a person being infected and becoming infectious is considered to be relatively short and variable in its path.^(5, 7, 8) During the SARS outbreak in 2003, this time period was interrupted with the onset of symptoms which typically identified a person as a case prior to their infectious period beginning, meaning the use of symptom-based surveillance

was largely effective in identifying cases.^(2, 5, 6) However, evidence for the SARS-CoV-2 virus indicates that it is likely a person can be infectious prior to symptom onset, with further evidence suggesting a peak viral load around the time of symptom onset, or just thereafter.⁽⁷⁻⁹⁾ Lastly, the potentially large proportion of asymptomatic cases adds further complexity to the COVID-19 pandemic.⁽⁶⁾

Estimates of the prevalence of asymptomatic infection vary, with one living systematic review and meta-analysis highlighting 20% (95% CI 17 to 25) of all infections as asymptomatic; while further noting considerable heterogeneity among studies with some estimates being significantly higher.⁽¹⁰⁾ Irish data from the seroprevalence-based 'Study to Investigate COVID-19 Infection in People Living in Ireland (SCOPI)' highlights that 27% of participants with antibodies to SARS-CoV-2 did not report any symptoms, as described in the COVID-19 case definition.⁽¹¹⁾ While estimating the amount of pre-symptomatic and asymptomatic transmission is difficult to establish and uncertainty still remains, it has been acknowledged that these factors exist and could play a considerable role in the COVID-19 pandemic.^(6-8, 12) These populations' contribution to the spread of the SARS-CoV-2 virus further emphasises caution in an overreliance on symptom-based surveillance and the need for robust measures of restricted movements for those exposed, or potentially exposed, to an individual with COVID-19.^(5, 6)

The requirement for restriction of movements is based on the potential risk that someone has been exposed to COVID-19. The implementation of restricted movements for an individual may be due to close-contact with a known or suspected case, or due to travel from a location with a particular level of disease. In terms of close-contacts, Ireland currently recommends a 14-day restriction of movements for all close-contacts of a confirmed case, or symptomatic probable case, from last point of exposure.⁽³⁾ This stance is largely reflected in the guidance released by a number of organisations and health authorities including the World Health Organization (WHO),⁽¹³⁾ the European Centre for Disease Prevention and Control (ECDC),⁽¹⁴⁾ the Centers for Disease Control and Prevention (CDC),⁽¹⁵⁾ New Zealand Ministry of Health,⁽¹⁶⁾ and the UK National Health Service.⁽¹⁷⁾ The ECDC has provided updated a proposal (published 24 September 2020) noting that a negative PCR test on day 10 can cease the quarantine period for an individual. Some countries, such as Austria,⁽¹⁸⁾ Norway,⁽¹⁹⁾ and the Netherlands,⁽²⁰⁾ have implemented a shorter 10-day period. In terms of restriction of movements guidance relating to travel exposure, Ireland has implemented a 'green list' highlighting areas with low levels of viral transmission meaning that individuals entering Ireland from these areas do not need to quarantine. However, individuals entering Ireland from countries not on the list must restrict their movements for 14 days.⁽²¹⁾ At the time of writing, similar zonal and quarantine precautions have been implemented across a number of countries

with the duration of restricted movement ranging from seven to 14 days,^(16, 19, 22-26) and some implementing additional testing measures. Of note, the European Commission has put forward a common approach to travel for consideration and adoption by member states which emphasises the use of a colour-coded system comprising quarantining *or* testing measures on arrival dependent on the level of disease in the country from which the traveller has originated.⁽²⁷⁾

Ensuring an appropriate duration of restricted movements for those exposed to an infectious disease is crucial given the associated personal and societal implications.^(5, 28) Durations which are too long will have implications for the quality of life of the individual, and contribute to absenteeism or availability for work, with implications for the economy. Durations that are too short risk those who are infectious re-entering the community.⁽⁵⁾ Given the scale of the COVID-19 pandemic and the reliance on adherence by individuals who are not sick, it is essential that the importance and evidence-based nature of the restricted movement period is communicated.⁽²⁸⁾

The incubation period, defined as the time period between exposure to a pathogen and the onset of symptoms of disease, is an important epidemiological marker that can be used to guide the necessary duration of restriction of movements.⁽²⁹⁾ The incubation period varies widely between infectious diseases, but also within infectious diseases for individual cases due to the influence of potential variables such as host immune response and dose of infective agent received.⁽²⁹⁾ As incubation periods are variable between individuals, it is insufficient to consider measures of their central tendency in isolation (for example, mean or median), as these do not provide information regarding the variation in the population. This consideration of variation is crucial to understanding the incubation period in terms of key percentiles; estimating the likely number of days since exposure at which the upper bound of the population will experience the onset of symptoms (for example, the 95th and 99th percentiles are the times by which 95% and 99%, respectively, of individuals will have developed symptoms). As such, to adequately inform restricted movement periods, it is important to establish both the average incubation period of an infectious disease and the likely variation across a population as a whole;⁽²⁹⁾ this variation can be expressed statistically as a distribution. Furthermore, given the high prevalence of asymptomatic cases of COVID-19, an accurate estimation of the likely earliest time from exposure to detectable SARS-CoV-2, as identified through serial testing, would be equally useful in informing the necessary duration, and potential testing strategies, for this complex and novel disease.

The aim of this evidence summary is to estimate the incubation period of COVID-19, or time to first positive test in asymptomatic individuals, for those exposed to the

SARS-CoV-2 virus in order to inform the necessary duration of restriction of movements.

Methods

The processes as outlined in HIQA's protocol (available [here](#)) were followed.

A detailed overview of the statistical analysis undertaken for this evidence summary is provided in the associated protocol. In brief, incubation periods are not fixed; they vary within the population and across studies. The variation of estimates can be expressed as a statistical distribution. Parametric distributions are commonly chosen to model the incubation period for a population based on a sample of observed data. Parametric methods assume that sample data comes from a population whose data can be modelled using a probability distribution that has a fixed set of parameters. Three common parametric distributions that are considered appropriate for representing the variation in incubation periods include log-normal, Weibull, or gamma. As such, it was anticipated that these parameters (the values that describe the statistical distribution) would be reported in the literature alongside the visual display of the distribution and the summary of the central tendency (for example, the median value). An important feature of the incubation period data is that extreme high values (termed 'right-skew') are possible. This right-skew of the data is particularly important to the public health question of potentially recommending a change to the duration of restricted movements based on the incubation period. When estimating the time by which the vast majority of persons will develop symptoms, it is important to have a quantifiable estimate such as the 95th, 97.5th, 99th percentile.

In order to capture variation, this current research question aimed to estimate the incubation period based on pooling results of the available literature. In this case, pooling primarily involves meta-analysis of the parameters of the statistical distributions used to characterise the observed incubation period distribution in individual studies. Where reported in the included studies these parameters of incubation period distributions were extracted for each distribution type: log-normal, Weibull, and gamma. It was assumed that the distribution parameters were themselves normally distributed. A random-effects model was used with a restricted maximum-likelihood estimator for heterogeneity in the meta-analysis.

The pooled distribution parameters were used to generate curves of the cumulative proportion of cases that are symptomatic by days since exposure. The confidence intervals and prediction intervals were also computed. The analysis considered both the number of days to achieve a certain level of coverage of cases (for example, 95th percentile) and the cumulative percentage cases that have become symptomatic a

given number of days after exposure (for example, 14 days). As the evidence synthesis team did not have access to the raw data used by the majority of studies, an assumption of which distribution constitutes as the best fit is not appropriate; therefore all three are presented for interpretation.

Studies that did not report fitted distribution parameters were not used in the main analysis, but were used to determine whether those used in the main analysis may be biased or in some way systematically different from the remaining studies.

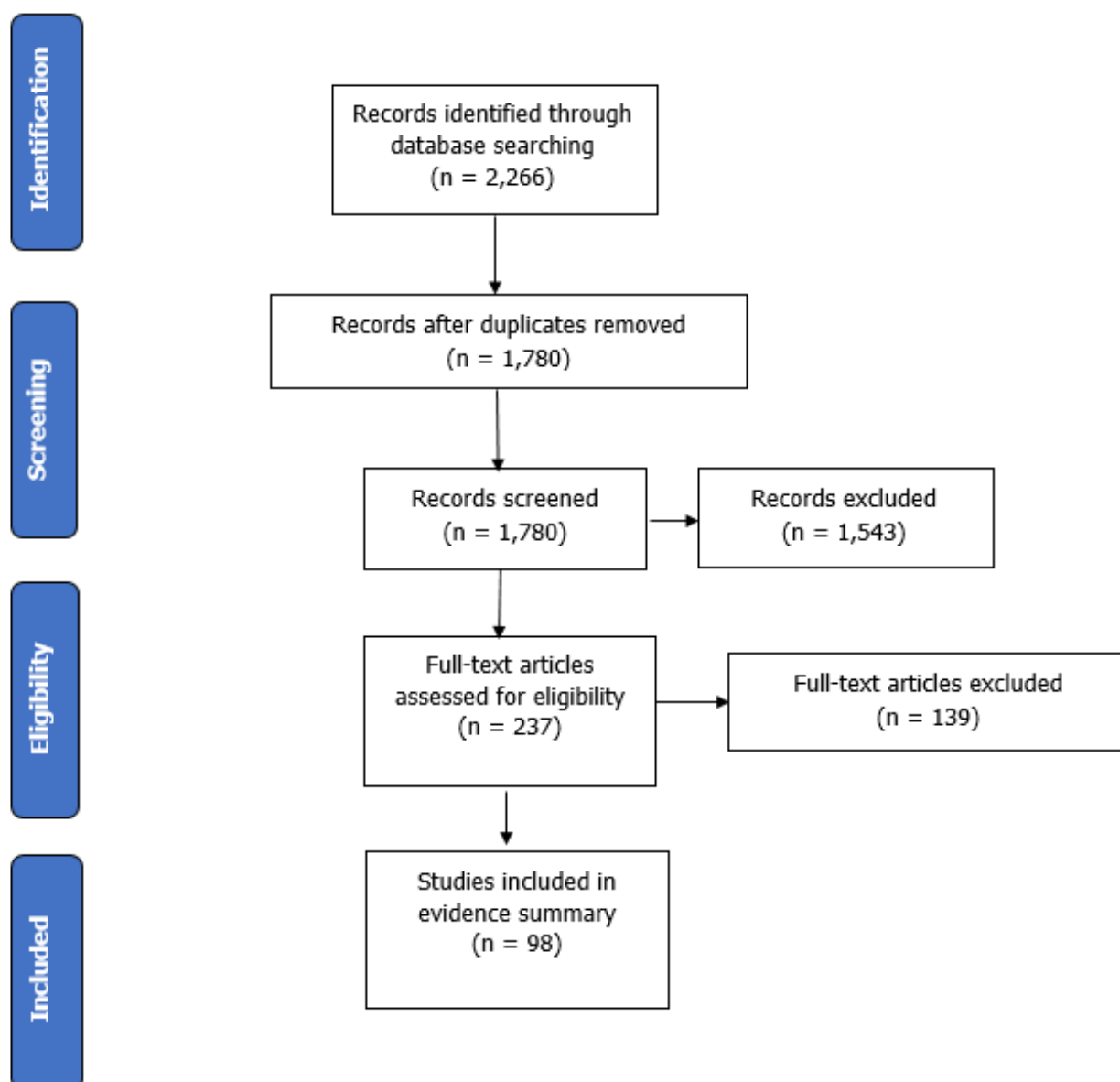
Results

Below is a summary of all relevant evidence for the incubation period, or time to first positive test, in COVID-19 cases identified from 1 January 2020 until 1 September 2020.

Search results

As shown in the PRISMA flow diagram in Figure 1, the collective search up until 1 September 2020 resulted in 2,266 citations; following removal of duplicates 1,780 citations were screened for relevance, with 237 full-texts assessed for eligibility and 139 subsequently excluded. Accordingly, 98 studies were identified for inclusion in this evidence summary.⁽³⁰⁻¹²⁷⁾

Figure 1. PRISMA flow diagram



Characteristics of included studies

The 98 included studies were all observational in nature; 16 were considered to be prospective in design,^(31, 37, 42, 60, 68, 75, 77, 80, 83, 98, 103, 104, 106, 112-114) while the remaining studies were retrospective. The majority of studies included participant data from China exclusively (n=74);^(30, 34-36, 40, 41, 44-57, 61, 62, 64, 67-73, 76-79, 81, 83-86, 88-92, 96-101, 104-127) five were from South Korea;^(43, 58, 60, 66, 102) two each were from Brunei,^(48, 103) Saudi Arabia,^(31, 32) the UK,^(59, 75) and Vietnam;^(38, 65) one each from Germany,⁽³⁷⁾ India,⁽⁸⁰⁾ Iran,⁽³³⁾ Singapore,⁽⁸⁷⁾ Taiwan,⁽⁷⁴⁾ Thailand,⁽⁸²⁾ Argentina,⁽⁹⁵⁾ Japan,⁽⁹⁴⁾ and Hong Kong;⁽⁶³⁾ while one study included data from China and Singapore,⁽⁹³⁾ and one included data from China and Taiwan.⁽⁴²⁾ The vast majority of studies noted an end date of data collection in the first quarter of 2020;^(30-51, 53, 55-57, 59, 60, 62-73, 75-81, 83-94, 96-101, 104-123, 125-127) eight studies included April and or May in their data.^(38, 52, 54, 74, 82, 95, 102, 103) Most contained data from government or health authority sources (n=40),^(32, 34, 36, 37, 39, 44, 45, 50-52, 55, 60, 61, 63, 64, 66, 69, 72, 74-76, 78, 80, 81, 85-87, 89, 91, 93, 94, 100, 101, 103, 105, 107, 108, 113, 115, 127) or hospital settings (n=34).^(30, 33, 40, 41, 49, 53, 57, 59, 65, 70, 71, 73, 82, 84, 90, 92, 96, 97, 99, 102, 106, 109-111, 114, 116, 117, 119-123, 125, 126)

The median number of participants across all studies was 70, ranging from eight to 2,907. The majority of studies included adult or mixed populations; five studies included children exclusively or reported on a subgroup of children,^(50, 53, 61, 113, 119) while five reported a subgroup of older adults (aged ≥ 60 years).^(32, 44, 55, 61, 113) In terms of exposure type, the majority of studies included a mixture of exposure types or general close-contacts; eight studies included participants, or subgroups of participants, with imported or travel related exposure;^(34, 47, 61, 85, 91, 111, 115, 127) four related to household or familial exposure,^(67, 75, 104, 106) and three to healthcare-related exposure.^(59, 98, 99) Given the insufficient data to explore such subgroups in the main analysis, for studies that reported a total estimation and data by subgroup, the former was used in the main analysis.

Of the 98 included studies, 95 contained outcomes relevant to the incubation period of COVID-19,^(30-57, 59-76, 78-123, 125-127) while two studies provided outcomes relating to time to first positive test in asymptomatic populations,^(58, 124) and one provided information on both outcomes.⁽⁷⁷⁾ Summaries of the included studies based on relevant outcomes are provided in Appendix 1 and Appendix 2.

Estimation of the incubation period of COVID-19

Of the 96 studies with data relevant to the incubation period of COVID-19, prior to undertaking quantitative analysis four studies were excluded; three due to insufficient data and one as it reported implausible data.^(35, 77, 87, 114) A further four studies,^(70, 100, 117, 119) and subgroups from three studies,^(45, 111, 115) were excluded

following preliminary analysis as the discrepancy between the observed data and the distribution fit to it was deemed too large for appropriate inclusion. The median number of participants across the six studies that were excluded from all analyses was 30 (range: 12 to 483). Accordingly, 88 studies containing data relevant to the incubation period of COVID-19 were included in at least one of the analyses within this review. The included studies presented a variety of estimates of the incubation period including: fitted distributions (n=14),^(36, 42-44, 46, 52, 55, 64, 69, 85, 89, 93, 108, 118) mean and percentiles (n=5),^(68, 71, 76, 88, 96) mean and variance (n=20),^(30, 40, 49, 51, 53, 54, 60, 65, 72, 74, 75, 79, 80, 92, 95, 102, 106, 122, 126, 127) median and interquartile range (n=3),^(32, 39, 103) median and percentiles (n=44 including 53 datasets),^(31, 33, 34, 37, 38, 41, 45, 47, 48, 50, 56, 57, 59, 61-63, 67, 73, 78, 81-84, 86, 90, 91, 94, 97, 98, 101, 104, 105, 107, 109-113, 115, 116, 120, 121, 123, 125) and median and variance (n=2).^(66, 99)

As previously highlighted, incubation periods are variable between individuals, and therefore isolated measures of their means and medians do not provide information regarding the variation in the population. The use of fitted statistical distributions provides an estimation of the incubation period along with information regarding the cumulative proportion of the population that would be expected to exhibit symptoms of COVID-19 by number of days since exposure. As such, a main analysis was undertaken with results first analysed as pooled estimates of the parameters of each distribution type (log-normal, Weibull, and or gamma) from a subset of 14 studies which provided sufficient information for this quantitative synthesis.^(36, 42-44, 46, 52, 55, 64, 69, 85, 89, 93, 108, 118) Parameter values for each distribution type were then estimated for the wider set of included studies to determine whether the 14 studies reporting distributions were reflective of the wider available, albeit less detailed, evidence base. The results are outlined in these stages below.

Main analysis: pooled estimates of distribution parameters and incubation period from subset of eligible studies (n=14)

Details of three types of fitted distributions, including sufficient detail regarding estimated parameters and associated precision, were reported by 14 studies,^(36, 42-44, 46, 52, 55, 64, 69, 85, 89, 93, 108, 118) with one study providing two datasets:⁽⁹³⁾ log-normal (n = 10), Weibull (n = 9), and gamma (n = 9). As the evaluation team of this review did not have access to the raw data used by the majority of studies, an assumption of which distribution constitutes as the best fit is not appropriate, therefore all three are presented for interpretation. The resulting forest plots, and measures of heterogeneity are provided in Appendix 3.

Pooling parameter data from the 10 studies,^(36, 43, 44, 46, 52, 55, 64, 89, 93, 118) including one which provided two separate datasets,⁽⁹³⁾ reporting fitted log-normal distributions resulted in a distribution with a mean incubation period of 6.0 days, with a median

of 5.0 days, as shown in Table 1. This was based on pooled parameter estimates of a mean μ of 1.62 (95% CI: 1.45 to 1.77) and mean σ of 0.60 (95% CI: 0.51 to 0.70). As shown in Table 1, the nine studies that reported fitted Weibull distributions,^(43, 44, 46, 52, 85, 89, 93, 108, 118) including one with two separate subgroups,⁽⁹³⁾ resulted in a mean incubation period of 6.4 days, and a median of 6.0 days based on pooled parameter estimates of a mean $shape$ value of 1.88 (95% CI: 1.71 to 2.06) and a mean $scale$ of 7.25 (95% CI: 5.99 to 8.51). Of the fitted gamma distributions reported by nine studies,^(42-44, 46, 52, 69, 89, 93, 118) including one with two separate subgroups,⁽⁹³⁾ the pooled parameter estimates resulted in a mean incubation period of 6.7 days, with a median of 6.0 days, from mean $shape$ value of 3.11 (95% CI: 2.50 to 3.73) and mean $rate$ value of 0.47 (95% CI: 0.39 to 0.55). The density plot for the three distribution types is provided in Figure 2.

Table 1. Summary of findings for distribution-based studies (n=14)

	Log-normal		Weibull		Gamma	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
Mean (days)	6.0	(5.1 to 7.1)	6.4	(5.3 to 7.5)	6.7	(5.1 to 8.7)
Median (days)	5.0	(4.3 to 5.9)	6.0	(4.9 to 7.0)	6.0	(4.4 to 7.9)
95 th percentile (days)	13.6	(10.8 to 16.9)	13.0	(10.7 to 15.4)	13.9	(11.0 to 17.5)
97.5 th percentile (days)	16.5	(12.8 to 20.9)	14.5	(11.9 to 17.3)	15.9	(12.7 to 19.9)
99 th percentile (days)	20.6	(15.5 to 26.8)	16.4	(13.4 to 19.5)	18.5	(14.9 to 22.9)
Percent symptomatic at day 7 (%)	71	(61 to 80)	61	(50 to 74)	61	(42 to 78)
Percent symptomatic at day 10 (%)	87	(80 to 93)	84	(74 to 93)	82	(67 to 93)
Percent symptomatic at day 14 (%)	95	(91 to 98)	96	(92 to 99)	95	(87 to 99)

Figure 2. Density plot of fitted distributions

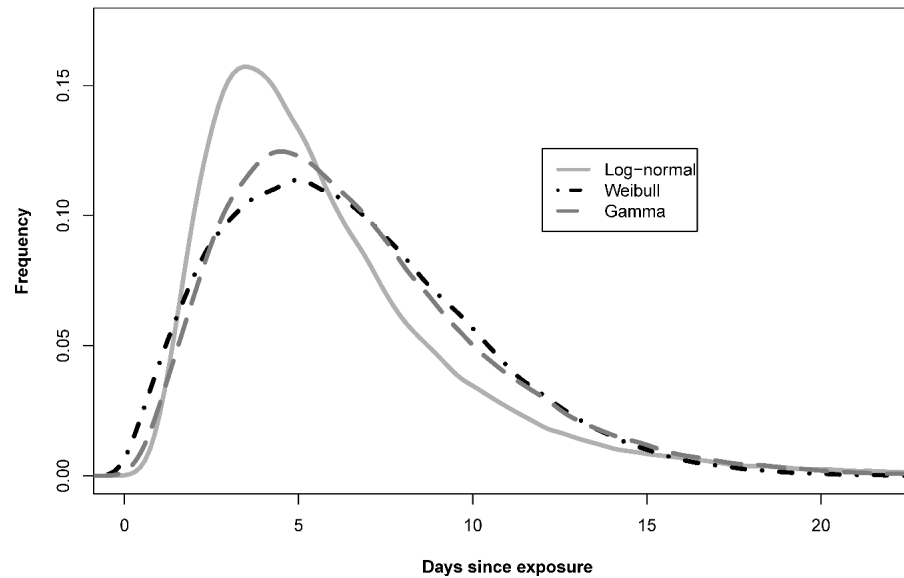


Table 2, and the corresponding cumulative density function plots in Figure 3, outline the estimated cumulative of proportion of individuals expected to be symptomatic by day since exposure based on the three distributions. Taking the current 14-day period, it is estimated that on average between 95% and 96% of individuals will display symptoms by day 14 depending on the distribution used (log-normal 95%, 95% CI 91% to 98%; Weibull 96%, 95% CI 92% to 99%; gamma 95%, 95% CI 87% to 99%). At a duration of 10 days, as implemented by a number of European countries, it is estimated that 82% to 87% of individuals will display symptoms within this time frame, with notably higher degrees of uncertainty (log-normal 87%, 95% CI 80% to 93%; Weibull 84%, 95% CI 74% to 93%; gamma 82%, 95% CI 67% to 93%). At seven days, an estimated 61% to 71% of individuals will display symptoms (log-normal 0.71, 95% CI 61% to 80%; Weibull 61%, 95% CI 50% to 74%; gamma 61%, 95% CI 42% to 78%).

Considering the distribution results in terms of percentiles, as shown in Table 1 the 95th percentile (the time point at which 19 out of 20 are likely to be symptomatic) of the incubation period is between 13 and 14 days (log-normal 13.6; Weibull 13.0; Gamma 13.9). The 99th percentile ranges from 16 days to 21 days (log-normal 20.6; Weibull 16.4; Gamma 18.5). Notably, these percentiles are all associated with a considerable level of associated uncertainty.

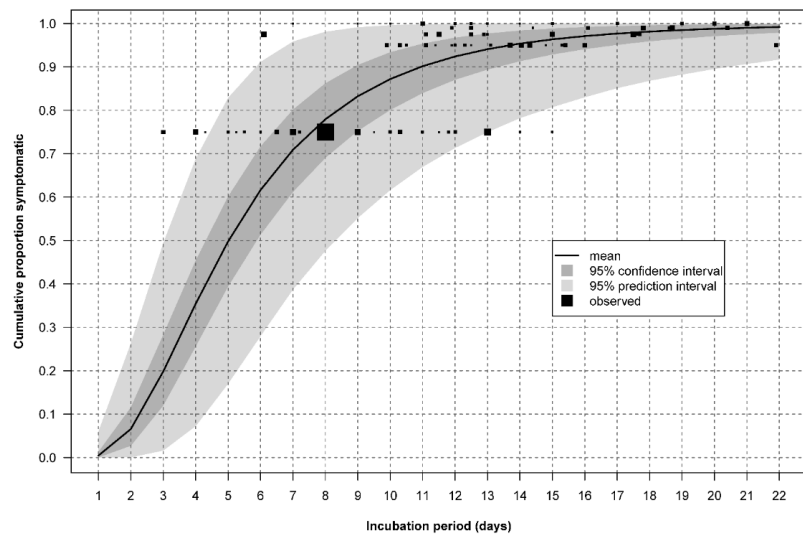
For rigour, a sensitivity analysis was conducted considering the distribution parameters as independent versus correlated variables. As shown in Appendix 3, the results were not significantly different between these methods, and hence the above estimates can be interpreted as the main analysis.

Table 2. Cumulative proportion of individuals becoming symptomatic by days since exposure

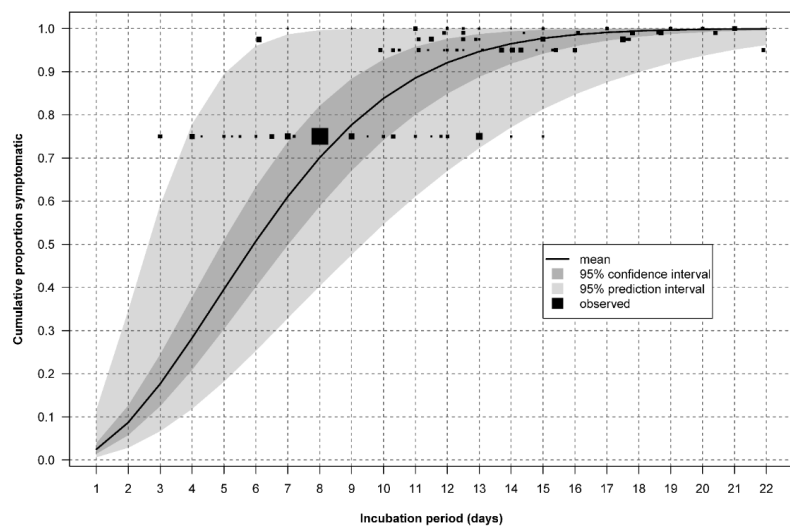
Days since exposure	Log-normal		Weibull		Gamma	
	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)
1	0.00	(0.00 to 0.01)	0.02	(0.01 to 0.04)	0.01	(0.00 to 0.03)
2	0.07	(0.03 to 0.12)	0.09	(0.06 to 0.13)	0.06	(0.02 to 0.14)
3	0.20	(0.12 to 0.28)	0.18	(0.12 to 0.24)	0.16	(0.06 to 0.29)
4	0.35	(0.26 to 0.45)	0.28	(0.21 to 0.38)	0.27	(0.13 to 0.44)
5	0.50	(0.39 to 0.60)	0.40	(0.30 to 0.51)	0.39	(0.22 to 0.58)
6	0.62	(0.51 to 0.72)	0.51	(0.40 to 0.63)	0.51	(0.32 to 0.69)
7	0.71	(0.61 to 0.80)	0.61	(0.50 to 0.74)	0.61	(0.42 to 0.78)
8	0.78	(0.69 to 0.86)	0.70	(0.59 to 0.82)	0.70	(0.51 to 0.84)
9	0.83	(0.75 to 0.90)	0.78	(0.67 to 0.88)	0.77	(0.60 to 0.89)
10	0.87	(0.80 to 0.93)	0.84	(0.74 to 0.93)	0.82	(0.67 to 0.93)
11	0.90	(0.84 to 0.95)	0.89	(0.80 to 0.96)	0.87	(0.74 to 0.95)
12	0.92	(0.87 to 0.97)	0.92	(0.85 to 0.98)	0.90	(0.79 to 0.97)
13	0.94	(0.89 to 0.98)	0.95	(0.89 to 0.99)	0.93	(0.84 to 0.98)
14	0.95	(0.91 to 0.98)	0.96	(0.92 to 0.99)	0.95	(0.87 to 0.99)
15	0.96	(0.93 to 0.99)	0.98	(0.94 to 1.00)	0.96	(0.90 to 0.99)
16	0.97	(0.94 to 0.99)	0.99	(0.96 to 1.00)	0.97	(0.93 to 0.99)
17	0.98	(0.95 to 0.99)	0.99	(0.97 to 1.00)	0.98	(0.94 to 1.00)
18	0.98	(0.96 to 1.00)	0.99	(0.98 to 1.00)	0.99	(0.96 to 1.00)
19	0.98	(0.97 to 1.00)	1.00	(0.99 to 1.00)	0.99	(0.97 to 1.00)
20	0.99	(0.97 to 1.00)	1.00	(0.99 to 1.00)	0.99	(0.98 to 1.00)
21	0.99	(0.98 to 1.00)	1.00	(0.99 to 1.00)	0.99	(0.98 to 1.00)
22	0.99	(0.98 to 1.00)	1.00	(1.00 to 1.00)	1.00	(0.99 to 1.00)

Figure 3. Cumulative density plots by distribution type

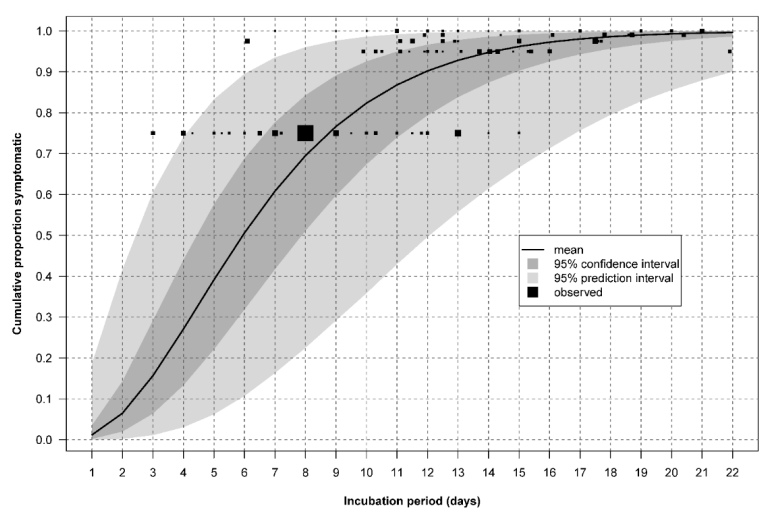
Log-normal distribution



Weibull distribution



Gamma distribution



Secondary analysis: pooled estimation of incubation period across all included studies (n=88)

Distribution parameter values were estimated from the data presented across the remaining 74 included studies, as per the methods outlined in the protocol for this review.^(30-34, 37-41, 45, 47-51, 53, 54, 56, 57, 59-63, 65-68, 71-76, 78-84, 86, 88, 90-92, 94-105, 107-113, 115, 116, 120-123, 125-127) Cumulatively, these estimates resulted in 83 datasets being eligible for a log-normal distribution, 88 datasets for a Weibull distribution and 81 datasets for a Gamma distribution. The resulting estimates of the incubation period are presented in Tables 3 to 5 below, alongside the 95th, 97.5th and 99th percentiles. As shown, the results remain similar and relatively consistent for the log-normal and Weibull distributions, with no significant differences noted between the data types used to estimate the results (distributions, quantiles, others). There are some differences observed for the gamma distributions, although those estimates are subject to wider uncertainty. Based on a meta-regression with data type as a covariate, there was no statistically significant difference in parameter estimates by data type for any of the three statistical distributions. Accordingly, these analyses add confidence to the estimates provided by the subset of distribution-based studies within the main analysis.

Table 3. Log-normal distribution estimates for all included study types

	Study method of reporting incubation time data					
	Distribution (n=15)		Quantiles (n=44)		Other (n=25)	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
Mean (days)	6.5	(5.5 to 7.6)	6.5	(5.9 to 7.1)	6.5	(5.6 to 7.6)
Median (days)	5.5	(4.7 to 6.3)	5.4	(4.9 to 5.8)	5.5	(4.8 to 6.4)
95 th percentile (days)	14.3	(11.6 to 17.4)	14.7	(13.0 to 16.6)	14.3	(11.7 to 17.3)
97.5 th percentile (days)	17.2	(13.7 to 21.4)	17.8	(15.6 to 20.4)	17.1	(13.8 to 21.1)
99 th percentile (days)	21.4	(16.6 to 27.1)	22.3	(19.2 to 25.8)	21.2	(16.6 to 26.6)

Table 4. Weibull distribution estimates for all included study types

	Study method of reporting incubation time data					
	Distribution (n=15)		Quantiles (n=49)		Other (n=25)	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
Mean (days)	6.5	(5.6 to 7.3)	6.2	(5.7 to 6.6)	6.5	(5.6 to 7.4)
Median (days)	6.0	(5.2 to 6.8)	5.7	(5.3 to 6.1)	5.9	(5.1 to 6.7)
95 th percentile (days)	13.3	(11.5 to 15.1)	12.4	(11.2 to 13.7)	13.7	(11.6 to 16.1)
97.5 th percentile (days)	14.9	(12.9 to 17.0)	13.8	(12.4 to 15.4)	15.5	(12.9 to 18.4)
99 th percentile (days)	16.8	(14.5 to 19.3)	15.6	(13.9 to 17.6)	17.6	(14.5 to 21.2)

Table 5. Gamma distribution estimates for all included study types

	Study method of reporting incubation time data					
	Distribution (n=15)		Quantiles (n=42)		Other (n=25)	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
Mean (days)	7.3	(5.2 to 9.8)	6.0	(4.7 to 7.4)	6.3	(4.2 to 9.2)
Median (days)	6.6	(4.6 to 9.0)	5.3	(4.1 to 6.7)	5.6	(3.6 to 8.3)
95 th percentile (days)	14.8	(11.1 to 19.2)	12.5	(10.2 to 15.3)	13.2	(9.4 to 18.8)
97.5 th percentile (days)	16.8	(12.8 to 21.7)	14.3	(11.8 to 17.5)	15.2	(10.9 to 21.4)
99 th percentile (days)	19.4	(14.9 to 25.0)	16.7	(13.8 to 20.3)	17.6	(12.8 to 24.8)

Incubation period of COVID-19 in children and older adults

Insufficient data were presented to enable subgroup analysis based on exposure type or setting; while limited data were presented for age-related analysis. Five studies included in this review reported data relevant to the incubation period of COVID-19 for children exclusively or a reported subgroup of children,^(50, 53, 61, 113, 119) while five studies reported a subset of older adults (aged ≥ 60 years).^(32, 44, 55, 61, 113)

With regards to children, the five studies were very limited in terms of sample size and were associated with large levels of uncertainty. However, the limited evidence suggests that the incubation period of COVID-19 may be longer for this population than the estimates provided for the general population above. Four studies reported a median and interquartile range: Guo et al.⁽⁵⁰⁾ reported a median of nine days (IQR 6 to 13, n=85); Zhang et al.⁽¹¹⁹⁾ reported a median of 10.5 (IQR 7.8 to 25.25, n=34); Yang et al. estimated a median of eight days (IQR 7.0 to 8.5, n=3); and Kong et al.⁽⁶¹⁾ estimated a median of 13.5 days (IQR 10.0 to 15.5, n=4). Hua et al.⁽⁵³⁾ reported a mean incubation period of 9.1 days (SD=3.7) for a sample of 43 children.

Similarly, the data presented by five studies for subgroups of older adults were limited and uncertain; however, this limited evidence again suggests a possibly longer incubation than those provided for the overall population. The relevant studies all reported the median incubation period; Kong et al.⁽⁶¹⁾ reported 11.2 days (90% CI 9.0 to 13.5, n=22), Yang et al.⁽¹¹³⁾ reported nine days (IQR 6 to 11, n=25), Jiang et al.⁽⁵⁵⁾ noted 10.9 days (95% CI 8.9 to 12.6, n=22), and Dai et al.⁽⁴⁴⁾ reported 7.7 days (95% CI 6.9 to 8.4, n=30). Alsofayan et al.⁽³²⁾ did not provide a sample size for a subgroup of older adults analysed in their study of 309 cases, but reported a median of 10.9 days (IQR 16.3, percentiles not provided).

It should be noted that the results presented by these included studies largely reflected measures of the central tendency, rather than the distribution, of the incubation period. A quantitative analysis was conducted on studies which provided sufficient data, as shown in Appendix 4, which further suggests the possibility of longer incubation periods in these populations. However, again given the limited sample size and heterogeneity in the presented studies, confidence in these estimates is low.

Time to first positive test in asymptomatic individuals

Three studies were identified which employed a degree of serial testing following an exposure event for the detection of SARS-CoV-2 in asymptomatic populations, and provided an estimate of days to first positive test in these individuals.^(58, 77, 124) A summary of the included studies is provided in Appendix 2.

Zhou et al.⁽¹²⁴⁾ reported data from repeated viral nucleic acid testing of 26 asymptomatic patients who were placed in isolation following close-contact exposure with confirmed COVID-19 cases in China. The authors reported an average of eight days from exposure to the detection of SARS-CoV-2 RNA, with a range of five to 22 days. The individual who had detectable SARS-CoV-2 RNA on day 22 had four previous samples with undetectable SARS-CoV-2 RNA. Of note, nine of the individuals within this study subsequently developed symptoms inferring that these cases were diagnosed in their pre-symptomatic phase rather than truly being asymptomatic (that is, never symptomatic) as the authors suggest. Data was not presented for these groups separately.

Luo et al.⁽⁷⁷⁾ reported the characteristics of 129 confirmed cases of COVID-19 identified through a prospective study of close-contacts, including a quarantine period with RT-PCR testing every two days, in China. Of the 129 cases identified, eight were asymptomatic infections with all diagnosed within 10 days of being placed in quarantine (of reported data: median 1.5 days, range 0-10). Of note, the authors highlighted a median delay of two days from last contact exposure to the beginning of quarantine in those who tested positive.

Jung et al.⁽⁵⁸⁾ reported the characteristics of cases identified during a 14-day mandatory self-quarantine introduced in South Korea for those who were identified as close-contacts of confirmed cases, or were returning from travel abroad. Individuals were tested between days 12 and 14, with an active surveillance following release from quarantine. Of 19,296 individuals quarantined, 56 cases (0.29%) had SARS-CoV-2 RNA detected. Two individuals who had undetected SARS-CoV-2 RNA, and were classified as being asymptomatic on release from mandatory quarantine, subsequently tested positive on day 16 and day 20, respectively, with the former also developing symptoms.

Methodological quality of included studies

Methodological quality of the included studies was assessed using an abridged version of the *de novo* quality appraisal tool for case series developed to inform HIQA evidence summaries for COVID-19.⁽¹²⁸⁾ The abridged tool considered four key domains: adequate reporting of inclusion criteria and avoidance of inappropriate exclusion, use of appropriate statistical methods with adequate description, definition of the incubation period, and peer-review status. A summary graph and full description of the quality appraisal for each included study is provided in Appendix 5. In general, the methodological quality of the included studies was considered to be low, with concerns raised across all domains.

The criteria for including or excluding participants from the studies were not well described with 42 of the studies not providing any information related to this domain,^(30, 34, 36, 40, 42, 44, 46, 50, 51, 54, 56, 57, 64, 66, 68, 69, 71, 78-81, 84, 86, 87, 89, 91-93, 95, 97, 99-102, 105, 108, 111, 113, 117, 120, 123, 124) and six presenting exclusion criteria deemed to be inappropriate in the context of this research question;^(60, 61, 75, 106, 109, 122) the remaining 50 studies were deemed to satisfy these criteria. Additionally, the majority (n=62) of the included studies were noted to be retrospective in nature, where patients do not appear to have been selected or sampled systematically.

In terms of the appropriateness and adequate reporting of statistical methods employed, 64 studies were noted to satisfy these criteria; 20 studies did not report the statistical methods used,^(34, 54, 58, 60, 62, 65, 68, 69, 76, 81, 83, 88, 89, 94, 95, 98, 100, 106, 113, 124) while 14 studies were identified as using potentially inappropriate methods.^(35, 45, 57, 59, 61, 71, 79, 80, 86, 87, 99, 107, 115, 127)

With regards to the definition of incubation period, for the 96 studies reporting this outcome, 71 studies provided a description,^(32-40, 42-44, 46, 48-53, 55, 57, 59-61, 63-65, 68, 71-78, 80, 83-85, 87-94, 96, 97, 99, 100, 103, 105, 107, 108, 110, 112-114, 116-123, 125-127) while 25 did not provide any definition.^(30, 31, 41, 45, 47, 54, 56, 62, 66, 67, 69, 70, 79, 81, 82, 86, 95, 98, 101, 102, 104, 106, 109, 111, 115) Of the 61 studies providing a definition, seven described time from last exposure to symptom onset,^(33, 65, 77, 78, 88, 105, 112) seven described time from first exposure to symptom onset,^(35, 48, 49, 53, 87, 99, 127) and 57 provided a definition of exposure to symptom onset without an inclusion of window for exposure.^(32, 34, 36-40, 42-44, 46, 50, 51, 53, 55, 57, 59-61, 63, 64, 68, 71-76, 80, 83-85, 89-94, 96, 97, 100, 103, 107, 108, 110, 113, 114, 116-123, 125, 126)

In terms of peer-review status, at the time of writing, 39 of the included studies were published as pre-prints and had yet to undergo formal peer-review raising additional concerns about overall quality and the potential for results to change prior to formal publication.^(30, 31, 33, 38, 39, 41, 45, 47, 51, 52, 54-56, 59, 69-71, 75-77, 81, 82, 88, 94, 95, 99-101, 105, 107, 110, 114, 117, 121, 122, 125-127)

Furthermore, as noted previously the vast majority of the studies included in this evidence summary pertain to data collected in China,^(30, 34-36, 40, 41, 44-57, 61, 62, 64, 67-73, 76-79, 81, 83-86, 88-92, 96-101, 104-127) in the first quarter of the year 2020,^(30-51, 53, 55-57, 59, 60, 62-73, 75-81, 83-94, 96-101, 104-123, 125-127) and predominantly relate to adult or mixed age populations, which may affect the overall generalisability of results to specific populations. A number of the included studies further cited the use of publicly available data, and while a conscious effort was made to check for duplication of datasets between studies, there is a possibility of some repeating data across studies.

Discussion

The results of this evidence summary included data from 98 studies; 95 of which contained information relevant to the incubation period of COVID-19, two provided limited evidence regarding asymptomatic populations, and one included both outcomes. For symptomatic populations, the median incubation period for COVID-19 is between five and six days; that is, 50% of cases will become symptomatic five to six days after exposure. On average, approximately 95% of individuals who experience symptoms will do so by day 14 indicating that approximately 1 in 20 may develop symptoms after this point. If a cut-off of 10 days from exposure is used, on average 82% to 87% of individuals will develop symptoms by this point, indicating that approximately 1 in 6 will do so at a later point. Some individuals may take 21 days or more to exhibit symptoms, however estimates of this proportion are associated with considerable levels of uncertainty.

To ensure clear and simple messaging, and to maximise public adherence, the duration of restriction of movements is likely to be a multiple of weeks (for example, seven days, 14 days) or 10 day blocks. If that is the case, a reduction in the duration of restricted movements from 14 to 10 or seven days will lead to a substantial increase in the proportion of pre-symptomatic individuals that are potentially released, and hence increase the risk transmission of COVID-19. Very limited evidence suggests that the incubation period of COVID-19 may be longer in children and older adults than the general population; which may denote additional caution when considering symptom-surveillance in these populations.

There is a lack of evidence regarding the time SARS-CoV-2 RNA is first detected in asymptomatic individuals; three studies highlighted that these individuals may typically be detected by day 10 since exposure, but that the time to a detected test may be substantially longer in some individuals. No clear evidence was identified to support reliable identification of days for opportune testing; studies tended to report results of multiple testing methods, but not clear results of serial days.

The overall quality of the studies included in this evidence summary was typically low, and the estimates presented were associated with a substantial degree of uncertainty. Additionally, the majority of studies were conducted in China within the first quarter of the year 2020, in predominantly adult populations with multiple exposure types included, which may limited the overall transferability and generalisability of these findings.

The term 'restriction of movements' (or quarantine) is frequently interchanged, and sometimes confused, with the term 'self-isolation', the differentiation between these concepts is crucially important for public understanding and appropriate implementation of public health strategies to reduce transmission of the SARS-CoV-2 virus. 'Self-isolation' refers to a person who has been diagnosed with COVID-19, or is

suspected of having the disease, strictly isolating from others to prevent onward transmission of the disease.^(3, 4, 15) The duration of self-isolation has recently been reduced in Ireland to 10 days; reflecting evidence which suggests those with mild-moderate disease are unlikely to be infectious beyond 10 days.⁽¹²⁹⁾ However, 'restriction of movements', sometimes referred to as 'quarantine' or 'self-quarantine', precedes self-isolation as a time period when an individual who has been exposed, or potentially exposed, to SARS-CoV-2 reduces their interaction with others as much as possible on a precautionary basis that they may have the disease.^(3, 4, 15) Should an individual subsequently become symptomatic, or be diagnosed through testing, they will then enter the 'self-isolation' period.^(3, 15) The implementation of restriction of movements is critical in the public health strategy for COVID-19 due to: ^(6-8, 12)

- the novelty of the virus,
- that an individual may be infectious before they show symptoms of the disease, or very soon after,
- and the existence of a potentially large proportion of asymptomatic individuals who will never show symptoms, but who are likely able to transmit the disease.

Restricting the movements of these individuals at the earliest possible time is crucial to reducing the spread of the disease; hence the emphasis placed on early and comprehensive contact-tracing within the context of the COVID-19 pandemic.

A rapid review conducted by the Cochrane collaboration⁽¹³⁰⁾ concludes that, although largely based on mathematical modelling, the evidence base consistently points to a reduction in incident cases of COVID-19 through the implementation of quarantine. Current guidance from large organisations including the WHO,⁽¹³⁾ and the CDC,⁽¹⁵⁾ advocates that 14 days of quarantine should be implemented for those exposed to SARS-CoV-2, with significant caution advised in terms of reducing this duration. The results of this evidence summary indicate that, on average, approximately 95% of individuals who will become symptomatic will do so within this time period; accordingly, depending on the risk environment in which a person was exposed, approximately 1 in 20 individuals may become symptomatic after the restricted movements period. Results from this evidence summary indicate that a reduction in the restriction of movements to 10 days, as implemented by a number of European countries,⁽¹⁸⁻²⁰⁾ could result in approximately one in six individuals potentially developing symptoms after this time point. In terms of absolute numbers, a reduction from 14 to 10 days could potentially lead to a three to four-fold increase in the proportion of pre-symptomatic individuals released into the community.

The findings from very limited evidence within this review regarding a potentially longer incubation period in children and older adults may be spurious, and there is a considerable lack of confidence in this evidence. However, it is plausible that the

longer duration in children may be reflective of their generally milder disease,⁽¹³¹⁾ potentially impeding early recognition by parents or guardians. Older adults may exhibit longer durations due to immunosenescence (gradual deterioration of the immune system) or secondary immunodeficiency (immune system already weakened by another disease or treatment).⁽¹³²⁾

The estimates of the incubation period within this evidence summary, and their role in informing the duration of the restriction of movements period for those exposed to SARS-CoV-2, are further complicated by the considerable proportion of infected asymptomatic individuals. The evidence base for these individuals is fragmented across the continuum of the disease process with many uncertainties including those related to prevalence, diagnostic accuracy, transmission capability, and infectiousness.^(5, 6, 10, 133) This evidence summary noted that studies relating to this population were severely limited in terms of time to a first SARS-CoV-2 RNA detected test identified through serial testing, and clear presentation of results by number of days since exposure. The availability of robust data regarding the accurate time to a first positive test in asymptomatic individuals would greatly inform decision-making regarding the most opportunistic time to identify this population in a setting with testing. This element is further compounded by the large uncertainty regarding the sensitivity of RT-PCR testing, specifically in asymptomatic individuals, and hence the possibility of considerable levels of false negatives, albeit potentially due to inappropriate timing of sample collection.⁽¹³³⁾

In the absence of robust data regarding testing of asymptomatic individuals, the widely recommended 14-day period of restricted movements, at a minimum, removes this population from circulating within the community for a substantial period of time. A growing evidence base suggests that asymptomatic individuals can transmit this disease; however, the magnitude at which this occurs is uncertain.^(7, 8, 10) While acknowledging a large degree of uncertainty and limitations of the data, Byrne et al.⁽¹³⁴⁾ estimate that asymptomatic individuals may be infectious on average for a period of six days. Significant caution should be used when interpreting this estimate as a variety of methods were used including duration of detection via RT-PCR testing, along with contact tracing and modelling approaches. Additionally, evidence of duration of infectiousness indicates that in symptomatic individuals the magnitude of infectiousness decreases with each day.^(129, 135) Collectively these estimates of infectiousness infer that the use of a 14-day time frame should reduce the risk of asymptomatic-yet-infectious individuals re-entering the community during peak periods of their infectiousness; however, it is unclear to what extent this risk is reduced and research on the specific viral dynamics of this population is needed.

The use of a 14-day restriction of movements period for COVID-19 is often cited in terms of an upper bound, or limit, of the incubation period when presented by organisations such as the WHO and the ECDC.⁽¹³⁶⁾ These estimates seem largely based on early epidemiological data from a small number of individual studies within the COVID-19 pandemic;^(34, 64) however, it is not clear what measure or percentile of individuals is used to inform this upper bound estimate. For example, results from this research indicate an upper bound considering the 99th percentile would necessitate a restricted movement period substantially longer than the currently recommended 14 days. Based on this evidence summary, the 14-day period is estimated to capture approximately 95% of individuals, or is reflective of the 95th percentile. The decision regarding what constitutes an acceptable rate of potentially missed cases, and possibly infectious individuals re-entering the community, is one which requires a balance between potential impact of the disease and the impact on the person and society.^(5, 137) Such decisions should reflect a form of risk-based assessment with careful consideration of elements, such as expected risk of infection and likelihood of onward transmission.⁽¹³⁷⁾ Many of these elements remain largely uncertain in the context of the COVID-19 pandemic; particularly with regard to factors such as secondary attack rates based on specific exposure risk.⁽¹²⁾ Plausibly, the likelihood of infection from exposure may be quite high for individuals within a household, or who are close contacts of a confirmed case,^(12, 138) but may be lower for those with travel-related exposure where the risk is based on the level of disease within the country from which travel originated, rather than knowledge of exposure at the level of the individual. In the absence of a reasonable degree of certainty around such key influences, compounded further by uncertainties related to those who are asymptomatic, decisions to reduce the current duration of restricted movements on a risk assessment basis could be based on theoretical modelling exercises based on assumptions; some such models have been put forward.^(139, 140) However, there will be inherent uncertainty associated with a number of the underlying assumptions given the evolving landscape of the variable nature of the COVID-19 disease.

Strengths and limitations of this evidence summary

An inherent limitation of estimates of incubation period is their reliance on accurate information provided by an individual with the disease, introducing the possibility of recall bias.⁽⁸⁵⁾ This is further compounded by how such accuracy is measured by studies and whether or not they exclude cases on the basis of these factors. This element is highlighted in the fact that many of the included studies were heterogeneous in their definition of the incubation period in terms of exposure windows; with most not defining first or last exposure, and many not presenting incubation period estimates for their whole sample. A number of the included studies

further cited the use of publicly available data, although a conscious effort was made to check for duplication of datasets, there is a possibility of some repeating data given the large proportion of cases analysed from China in the first quarter of the year 2020.

A further limitation is how the data related to incubation period were presented by the included studies. The majority of studies presented a measure of central tendency combined with information on dispersion, either as a standard deviation or as a range of percentiles. Such summary data points limit the ability to accurately estimate the parameters for a log-normal, Weibull or gamma distribution, or to determine the goodness of fit of these distributions. While these studies were not included in the main analysis, it did estimate the distribution parameters to understand whether those studies reporting distribution parameters might be systematically different in some way. We estimated goodness of fit based on the maximum difference between one of the supplied data points and the equivalent data point estimated by the fitted distribution. For a distribution defined only by central tendency and variance, there may be insufficient data to accurately determine the parameters of the distribution. Distribution parameters were separately pooled by study data type, and the differences found were minor for log-normal and Weibull distributions, but more pronounced for the gamma distribution. The findings indicate that the subset of studies used in the main analysis were not systematically biased in terms of the distribution of incubation periods of study participants.

It should be borne in mind that the analyses presented here are an evidence synthesis of an approximation of the incubation time as defined by statistical distributions. A statistical distribution may be a poor fit to the individual patient data. Studies almost exclusively used one of three distributions to summarise the data: log-normal, Weibull or gamma. In many cases the studies fit all three and reported a goodness of fit statistic for selecting the best fitting curve. However, 'best fitting' should not be conflated with 'well fitting'. As this analysis is intended to support policy in relation to quarantine, and given that quarantine is designed to minimise the number of potentially infected individuals who circulate in the community, the key information is in the right-hand tail of the distribution. The process of finding the best fit may bias in favour of a distribution that is well fitting with regard to central tendency, but may misrepresent the critical right-hand tail. A limited subset of studies have made the individual patient data available, but it was not feasible to extract and analyse those data. As such, it has not been possible to determine the extent to which the fitted distributions adequately describe the right-hand tail of the observed data. However, the relative consistency of the findings across the three

distribution types suggests that the right-hand tails may be sufficiently well-characterised to capture the frequency of longer incubation periods.

Lastly, for each of the distribution types, two parameters were pooled independently, which creates a potential bias if the two are correlated. For example, as the distributions used are confined to produce positive values, a lower mean may be associated with a higher variance to account for extreme high values. We assessed the impact of generating correlated random draws from the pooled distributions (Appendix 3), where the correlation was determined across studies. There was no evidence of a statistically significant correlation for any of the three distribution types, but with only 11 studies the analysis was potentially underpowered. Incorporating correlation did not change the key findings, although it did reduce uncertainty for the results generated using the gamma distribution. It is therefore likely that the simplifying assumption of independence of distribution parameters is unlikely to have biased the results in any meaningful way.

Conclusion

The duration of restriction of movements should be carefully informed with consideration of the benefits and risks in the context of the COVID-19 pandemic. The results of this review indicate that the widely recommended 14-day period is likely to capture approximately 95% of individuals who will become symptomatic. In contrast, a reduction to 10 or seven days would capture approximately 84% and 64% of individuals, respectively. Information regarding the time at which asymptomatic populations have detectable levels of disease is limited and uncertain; with only three studies of limited sample size reporting data from serial testing with limited evidence about specific days from exposure. The studies included in this review were typically of low quality design, and there were important limitations associated with the studies and the subsequent quantitative analysis undertaken; with considerable levels of uncertainty overall.

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Appendix 1. Summary of included studies for incubation period of COVID-19

Study Country Sample size (incubation only) Design DOI	Setting/Source Demographics Exposure type Disease severity	Incubation period estimate
Ai 2020 China N=44 Retrospective 10.1101/2020.02.19.20025023	<i>Setting:</i> Hospital <i>Demographics**:</i> Mean age (\pm SD) 50.38 (\pm 16.86), 52 males (51%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Mean (\pm SD) 8.09 (\pm 4.99)
Alshami 2020 Saudi Arabia N=59 Prospective 10.1101/2020.05.13.20100222	<i>Setting:</i> Quarantine <i>Demographics:</i> Mean age (\pm SD) 37.2 (\pm 13.25), 27 males (45.8%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mild/moderate	Median (IQR) 7 (8.25)
Alsofayan 2020 Saudi Arabia N=309 Retrospective 10.1016/j.jiph.2020.05.026	<i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> Median age (IQR) 37 (22), 747 males (54.2%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Subgroup aged 56-65 years:</i> Median (IQR) 7 (9.5) <i>Subgroup aged >65 years:</i> Median (IQR) 13 (16.3) <i>Total study population:</i> Median (IQR) 6 (7.5)
Ashraf 2020 Iran N=100 Retrospective 10.1101/2020.04.20.20072421	<i>Setting:</i> Hospital <i>Demographics:</i> Median age (IQR) 58 (20), 64 males (64.6%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Median (IQR) 7 (2)
Backer 2020 China N=88 Retrospective 10.2807/1560-7917.ES.2020.25.5.2000062	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> Age range 2-72, 57 males (64.7%) <i>Exposure type:</i> Travel <i>Disease severity:</i> Unclear	<i>Distribution:</i> Weibull* Mean 6.4 (95% CI 5.6-7.9) 2.5 th percentile 2.1 (95% CI 1.3-3.0), 5 th percentile 6.4 (95% CI 5.5-7.5), 50 th percentile 6.4 (95% CI 5.5-7.5), 95 th percentile

		10.3 (95% CI 8.6-14.1), 97.5 th percentile 11.1 (95% CI 9.1-15.5), 99 th percentile 11.9 (95% CI 9.7-17.2)
Bao 2020 China N=57 Retrospective 10.1111/tbed.13742	<i>Setting:</i> Outpatients <i>Demographics:</i> Mean age (\pm SD) 44 (\pm 16.30), 37 males (64.91%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Log normal Mean 1.83 (95% CI 1.60-2.06) 2.5 th percentile 1.7 (95% CI 1.2-2.1), 50 th percentile 5.4 (95% CI 4.5-6.3), 97.5 th percentile 17.7 (95% CI 12.6-22.9)
Bi 2020 China N=183 Retrospective 10.1101/2020.03.03.20028423	<i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> Mean age 45, 187 males (47.8%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	<i>Distribution:</i> Log normal Mean 5.95 (95% CI 4.94-7.11) 5 th percentile 1.64 (95% CI 1.33-2.04), 50 th percentile 4.8 (95% CI 4.22-5.44), 95 th percentile 14.04 (95% CI 12.19-15.9)
Bohmer 2020 Germany N=12 Prospective 10.1016/S1473-3099(20)30314-5	<i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> Median age (IQR) 35 (15), 12 males (75.0%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	Median (IQR) 4 (2.0)
Bui 2020 Vietnam N=19 Retrospective 10.1101/2020.05.09.20096800	<i>Setting:</i> Mixed <i>Demographics:</i> Median age (IQR) 37 (7.5), 7 males (36.84%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Weibull* Mean 6.4 (95% CI 4.9-8.5) 2.5 th percentile 1.4 (95% CI 0.4-2.7), 50 th percentile 6.1 (95% CI 4.4-8.0), 95 th percentile 11.9 (95% CI 9.1-12.0), 97.5 th percentile 13.0 (95% CI 9.1-20.7), 99 th percentile 14.4 (95% CI 10.6-24.0)
Chaw 2020 Brunei N=8 Retrospective 10.1101/2020.05.04.20090043	<i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> Median age (IQR) 33 (29), 46 males (64.8%) <i>Exposure type:</i> Close contacts <i>Disease severity:</i> Mixed	Median (IQR) 4.5 (2.75)
Chen (a) 2020	<i>Setting:</i> Hospital	Mean (\pm SD) 7.7 (\pm 4.1)

China N=136 Retrospective 10.1016/j.jfma.2020.04.019	<i>Demographics:</i> Median age (IQR) 47 (24), 69 males (50.7%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	
Chen (b) 2020 China N=70 Retrospective 10.21203/rs.3.rs-18007/v1	<i>Setting:</i> Hospital <i>Demographics**:</i> Mean age (\pm SD) 48.1 (\pm 17.5), 43 males (58.1%) <i>Exposure type:</i> Unclear <i>Disease severity:</i> Mixed	Median (IQR) 5 (4)
Cheng 2020 Mixed N=65 Prospective 10.1001/jamainternmed.2020.2020	<i>Setting:</i> Unclear <i>Demographics:</i> Unclear <i>Exposure type:</i> Unclear <i>Disease severity:</i> Unclear	<i>Distribution:</i> Gamma Shape 3.09 (95% CI 2.37-3.96), Scale 2.1 (95% CI 1.59-2.86) 50 th percentile 5.82 (95% CI 1.39-15.51), 95 th percentile 11.9 (95% CI 9.1-12.0), 97.5 th percentile 13.0 (95% CI 9.1-20.7), 99 th percentile 14.4 (95% CI 10.6-24.0)
Chun 2020 South Korea N=72 Retrospective 10.1016/j.ijid.2020.07.075	<i>Setting:</i> Unclear <i>Demographics:</i> Median age (IQR) 40 (61.79), 34 males (47%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Weibull* Shape 1.6 (95%CI 1.4-1.9), Scale 3.64 (95% CI 3.03-4.21) 50 th percentile 3.1 (95% CI 2.54-3.71)
Dai 2020 China N=180 Retrospective 10.2147/RMHP.S257907	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> Mean age (\pm SD) 46.1 (\pm 15.3), 97 males (53.9%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Weibull* <i>Subgroup aged <30 years (N=27):</i> Shape 1.3 (95% CI 0.8-1.8), Scale 5.3 (95% CI 3.5-7.1) 5 th percentile 0.5 (95% CI 0.2-0.9), 50 th percentile 4.0 (95% CI 3.5-4.4), 95 th percentile 12.3 (95% CI 11.7-12.8), 99 th percentile 17.1 (95% CI 16.5-17.6) <i>Subgroup aged 30-59 years (N=123):</i> Shape 1.6 (95% CI 1.4-1.9), Scale 7.3 (95% CI 6.4-8.2)

		<p>5th percentile 1.1 (95% CI 1.0-1.3), 50th percentile 5.8 (95% CI 5.6-6.0), 95th percentile 14.4 (95% CI 14.2-14.7), 99th percentile 18.9 (95% CI 18.6-19.2)</p> <p><i>Subgroup aged ≥60 years (N=30):</i> Shape 2.4 (95% CI 1.6-3.2), Scale 8.9 (95% CI 7.4-10.4) 5th percentile 2.6 (95% CI 2.0-3.2), 50th percentile 7.7 (95% CI 6.9-8.4), 95th percentile 14.1 (95% CI 13.2-15.0), 99th percentile 16.9 (95% CI 15.9-17.8)</p> <p><i>Total study population (N=180):</i> Shape 1.6 (95% CI 1.4-1.9), Scale 7.3 (95% CI 6.6-7.9) Mean 6.5 (95% CI 5.9-7.1) 5th percentile 1.2 (95% CI 0.9-1.5), 50th percentile 5.8 (95% CI 5.2-6.4), 95th percentile 14.3 (95% CI 13.0-15.7), 99th percentile 18.7 (95% CI 16.7-20.9)</p>
<p>Ding 2020 Hefei, China N=543 Retrospective 10.1101/2020.02.18.20024661</p>	<p><i>Source:</i> Government/Health Authority Data <i>Demographics subgroup Hefei region (N=157):</i> Mean age (±SD) 44.4 (±15.6), 83 males (52.9%)</p> <p><i>Demographics subgroup Shenzhen region (N=386):</i> Mean age (±SD) 45.15 (±17.99), 184 males (47.7%)</p> <p><i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear</p>	<p><i>Subgroup Hefei region (N=157):</i> Median (IQR) 4 (4)</p> <p><i>Subgroup Shenzhen region (N=386):</i> Median (IQR) 9 (9)</p>
<p>Du (a) 2020[^] China N=109 Retrospective 10.3760/cma.j.cn112338-20200313-00331</p>	<p><i>Setting:</i> Mixed <i>Demographics:</i> Mean age (±SD) 39.83 (±13.75), 65 males (59.63%) <i>Exposure type:</i> Unclear <i>Disease severity:</i> Unclear</p>	<p><i>Distribution:</i> Gamma*</p> <p>Shape 3.83 (95% CI 2.99-5.33), Beta/Scale 1.52 (95%CI 1.08-2.04)</p> <p>25th percentile 1.44, 50th percentile 5.06 (95% CI 3.49-7.30), 97.5th percentile 12.50</p>

Du (b) 2020 China N=75 Retrospective 10.21203/rs.3.rs-57472/v1	<i>Setting:</i> Mixed <i>Demographics:</i> Median age (IQR) 45 (23.0), 44 males (61.10%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	<i>Subgroup imported cases (N=33):</i> Median (IQR) 7.0 (5.2) <i>Subgroup secondary cases (N=42):</i> Median (IQR) 11.5 (7) <i>Total study population (N=75):</i> Median (IQR) 8.5 (6)
Guan (a) 2020 China N=291 Retrospective 10.1056/NEJMoa2002032	<i>Setting:</i> Mixed <i>Demographics**:</i> Median age (IQR) 47 (23.0), 637 males (58.10%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Median (IQR) 4 (5)
Guan (b) 2020 China N=1590 Retrospective 10.1101/2020.02.25.20027664	<i>Setting:</i> Hospital <i>Demographics:</i> Mean age (\pm SD) 39.83 (\pm 13.75), 904 males (57.3%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Mean (\pm SD) 3.6 (\pm 4.2)
Guo 2020 China N=85 Retrospective 10.1186/s12916-020-01719-2	<i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> Median age (range) 7 (4-14), 183 males (53.6%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mild/moderate	Median (IQR) 9 (7)
Hu 2020 China N=268 Retrospective 10.1101/2020.07.23.20160317	<i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> 601 males (51.0%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Weibull* Shape 1.58 (0.09), Scale 7.11 (0.33) Mean 6.4 (95% CI 0.7-16.6)
Hua 2020 China N=43 Retrospective 10.1002/jmv.26180	<i>Setting:</i> Hospital <i>Demographics:</i> Mean age (\pm SD) 8.16 (\pm 4.07), 26 males (60.5%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Mean (\pm SD) 9.1 (\pm 3.7)
Ji 2020 China N=12	<i>Setting:</i> Outpatients <i>Demographics:</i> Unclear <i>Exposure type:</i> Mixed	Mean (\pm SD) 15.25 (\pm 4.88)

Retrospective 10.21203/rs.3.rs-36516/v1	<i>Disease severity:</i> Unclear	
Jiang (a) 2020 China N=132 Retrospective 10.1101/2020.04.14.20065896	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> Unclear <i>Exposure type:</i> Unclear <i>Disease severity:</i> Unclear	<i>Distribution:</i> Log normal <i>Subgroup aged 15-64 years (N=110):</i> Mean 6.85 (95% CI 6.09-7.62) 50 th percentile 7 (95% CI 6.1-8.1), 95 th percentile 15.4 (95% CI 14.7-15.9) <i>Subgroup aged ≥65 years (N=22):</i> Mean 10.07 (95% CI 8.75-11.54) 50 th percentile 10.9 (95% CI 8.9-12.6), 95 th percentile 16.4 (95% CI 16.3-16.6)
Jiang (b) 2020 China N=55 Retrospective 10.1101/2020.04.10.20060335	<i>Setting:</i> Unclear <i>Demographics:</i> Median age (IQR) 45 (33.0), 27 males (49.10%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Median (IQR) 7 (6.5)
Jin 2020 China N=216 Retrospective 10.1136/gutjnl-2020-320926	<i>Setting:</i> Hospital <i>Demographics subgroup with GI symptoms (N=21):</i> Median age (IQR) 46.14 (14.19), 37 males (50%) <i>Demographics subgroup without GI symptoms (N=195):</i> Median age (IQR) 45.09 (14.45), 294 males (50.95%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	<i>Subgroup with GI symptoms (N=21):</i> Median (IQR) 4 (4) <i>Subgroup without GI symptoms (N=195):</i> Median (IQR) 5 (5)
Khonyongwa 2020 England N=44 Retrospective	<i>Setting:</i> Hospital <i>Demographics**:</i> 29 males (50.0%) <i>Exposure type:</i> Hospital <i>Disease severity:</i> Mixed	Median (IQR) 6.4 (1.6)

10.1101/2020.07.24.20148262		
Kong (a) 2020 South Korea N=8 Prospective 10.24171/j.phrp.2020.11.1.03	<i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> Mean age 42.6, 15 males (53.6%) <i>Exposure type:</i> Close contacts <i>Disease severity:</i> Unclear	Mean (\pm SD) 4.1 (\pm 1.85)
Kong (b) 2020 China N=136# Retrospective 10.1002/agm2.12114	<i>Source:</i> Government/Health Authority Data <i>Demographics subgroup aged 15-64 years (N=110):</i> Median age (IQR) 49 (44) <i>Demographics subgroup aged >65 years (N=22):</i> Median age (IQR) 69 (21) <i>Demographics total population (N=136):</i> Median age (IQR) 50.5 (23.7), 72 males (53%) <i>Exposure type:</i> Travel <i>Disease severity:</i> Unclear	<i>Distribution:</i> Unclear <i>Subgroup aged 15-64 years (N=110):</i> 5 th percentile 2.0 (90% CI 1.6-2.9), 25 th percentile 5.0 (90% CI 4.2-5.9), 50 th percentile 7.6 (90% CI 6.7-8.6), 75 th percentile 10.5 (90% CI 9.4-10.3), 90 th percentile 13.2 (90%CI 11.8-13.8) <i>Subgroup aged >65 years (N=22):</i> 5 th percentile 3.1 (90% CI 2.9-7.0), 25 th percentile 7.8 (90% CI 6.5-11.0), 50 th percentile 11.2 (90% CI 9.0-13.5), 75 th percentile 14.4 (90% CI 11.5-15.6), 90 th percentile 17.0 (90%CI 13.8-17.6) <i>Total study population (N=136):</i> 5 th percentile 2.3 (90% CI 1.7-3.0), 25 th percentile 5.3 (90% CI 4.6-6.3), 50 th percentile 8.3 (90% CI 7.4-9.2), 75 th percentile 11.3 (90% CI 10.3-12.1), 90 th percentile 14.2 (90%CI 12.8-14.6)
Kong (c) 2020 China N=10 Retrospective 10.1111/irv.12773	<i>Setting:</i> Mixed <i>Demographics:</i> Unclear <i>Exposure type:</i> Close contact <i>Disease severity:</i> Unclear	Median (IQR) 6 (6)
Lai 2020 Hong Kong N=40 Retrospective 10.1093/ije/dyaa106	<i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> 46 males (48%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Log normal* 2.5 th percentile 1 (95% CI 0.9-1.1), 50 th percentile 4.2 (95% CI 4-4.5), 95 th percentile 14 (95% CI 13.1-15.3), 97.5 th percentile 17.6 (95% CI 16.2-19.4)
Lauer 2020	<i>Source:</i> Government/Health Authority Data	<i>Distribution:</i> Log normal

China N=181 Retrospective 10.7326/M20-0504	<i>Demographics:</i> Median age (IQR) 44.5 (21.5), 108 males (60%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	Parameter 1 = 1.62 (1.50-1.76), Parameter 2 = 0.42 (0.27-0.54) 2.5 th percentile 2.2 (95% CI 1.8-2.9), 50 th percentile 5.1 (95% CI 4.5-5.8), 97.5 th percentile 11.5 (95% CI 8.2-15.6)
Le 2020 Vietnam N=11 Retrospective 10.3201%2Feid2607.200591	<i>Setting:</i> Hospital <i>Demographics:</i> Mean age 31.2, 3 males (27%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Not reported	Mean (\pm SD) 9.9 (\pm 5.4)
Lee 2020 South Korea N=47 Retrospective 10.1016/j.jiac.2020.06.018	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> Median age range 9-83 <i>Exposure type:</i> Unclear <i>Disease severity:</i> Unclear	<i>Distribution:</i> Log normal 50 th percentile 3.0 (95% CI 0.6-8.2)
Li (a) 2020 China N=74** Retrospective 10.1017/s0950268820001491	<i>Setting:</i> Mixed <i>Demographics**:</i> Mean age (\pm SD) 45.26 (\pm 15.68), 35 males (47.3%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	<i>Subgroup sporadic cases (N=43):</i> Median (IQR) 4 (5) <i>Subgroup Family cases (N=17):</i> Median (IQR) 6 (3) <ul style="list-style-type: none"> • <i>Family index cases (N=14):</i> Median (IQR) 4.5 (3.75) • <i>Family 2nd/3rd generation cases (N=31):</i> Median (IQR) 7 (2) <i>Total study population (N=74):</i> Median (IQR) 5 (3)
Li (b) 2020 China N=10 Prospective 10.1056/NEJMoa2001316	<i>Setting:</i> Mixed <i>Demographics**:</i> Median age (IQR) 59 (74), 240 males (56%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Log normal Mean 5.2 (95% CI 4.1-7.0) 95 th percentile 12.5 (95% CI 9.2-18.0)
Li (c) 2020 China N=NR	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> NR <i>Exposure type:</i> Unclear	<i>Distribution:</i> Gamma Mean 7.2 (95% CI 6.8-7.6)

Retrospective 10.1101/2020.02.26.20028431	<i>Disease severity:</i> Unclear	Shape 3.07 (95% CI 2.62-3.56), Scale 2.35 (95% CI 2.00-2.75)
Liang 2020 China N=12 Retrospective 10.1101/2020.02.25.20027763	<i>Setting:</i> Hospital <i>Demographics**:</i> Median age (IQR) 42 (31.5), 11 males (52.4%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Median (IQR) 6.5 (5)
Liau 2020 China N=11 Retrospective 10.1101/2020.03.10.20032136	<i>Setting:</i> Hospital <i>Demographics**:</i> 24 males (52.2%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	<i>Distribution:</i> Weibull Mean 7.2 50 th percentile 6.6 (95% CI 4.4-9.6), 95 th percentile 14.8 (95% CI 10.4-22.0)
Linton 2020 China N=210 Retrospective 10.3390/jcm9020538	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> NR <i>Exposure type:</i> Mixed <i>Disease severity:</i> NR	<i>Distribution:</i> Log normal <i>Subgroup excluding Wuhan residents (N=52):</i> Mean 5.00 (95% CI 4.2-6.0) 50 th percentile 4.3 (95% CI 3.5-5.1), 95 th percentile 10.6 (95% CI 8.5-14.1), 99 th percentile 15.4 (95% CI 11.7-22.5) <i>Subgroup including Wuhan residents (N=158):</i> Mean 5.8 (95% CI 5.2-6.5) 50 th percentile 5.3 (95% CI 4.7-6.0), 95 th percentile 11 (95% CI 9.6-12.9), 99 th percentile 14.2 (95% CI 12.1-17)
Liu (a) 2020 China N=65 Retrospective 10.1038/s41598-020-70387-2	<i>Setting:</i> Hospital <i>Demographics:</i> Mean age (\pm SD) 48.4 (\pm 18.46), 36 males (55.38%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Median (IQR) 6 (6)
Liu (b) 2020 Taiwan N=27	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> 26 males (47.3%) <i>Exposure type:</i> Mixed	Mean (\pm SD) 6.04 (\pm 3.11)

Retrospective 10.1097/JCMA.0000000000000411	<i>Disease severity:</i> Unclear	
Lopez Bernal 2020 UK N=41 Prospective 10.1101/2020.08.19.20177188	<i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> 231 males (48.9%) <i>Exposure type:</i> Household <i>Disease severity:</i> Unclear	<i>Subgroup confirmed cases (N=12):</i> Mean (\pm SD) 4.75 (\pm 2.34); Median (IQR) 4 (1.25) <i>Subgroup probable and confirmed cases (N=41):</i> Mean (\pm SD) 4.51 (\pm 2.66); Median (IQR) 4 (5)
Lu 2020 China N=37 Retrospective 10.1101/2020.02.19.20025031	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> NR <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Weibull Mean 6.4 (95% CI 5.3-7.6) 95 th percentile 13.1
Luo 2020 China N=121 Prospective 10.1101/2020.03.24.20042606	<i>Setting:</i> Quarantine <i>Demographics:</i> NR <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	Median (IQR) 1 (4)
Men 2020 China N=59 Retrospective 10.1101/2020.02.24.20027474	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> Mean age (\pm SD) 41.9 (\pm 13.2), 34 males (58.6%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	Mean (\pm SD) 5.84 (\pm 2.93)
Nie 2020 China N=2907 Retrospective 10.1093/infdi/jiaa211	<i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> Mean age (\pm SD) 44.24 (\pm 16.24), 3695 males (54.12%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Median (IQR) 5 (6)
Pan 2020^ China N=52 Retrospective 10.3760/cma.j.cn112338-20200330-00466	<i>Setting:</i> Mixed <i>Demographics:</i> Mean age (\pm SD) 56.27 (\pm 19.59), 16 males (30.7%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	Mean (\pm SD) 6.11 (\pm 3.38)

Patrikar 2020 India N=268 Retrospective 10.1177/1010539520956427	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> Mean age (\pm SD) 36.45 (\pm 17.27), males 60.3% <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Weibull* Mean 8.17 (95% CI 7.04-9.3) 5 th percentile 0.4, 50 th percentile 5.68, 97 th percentile 26.57
Ping 2020 China N=93 Retrospective 10.1101/2020.03.01.20028944	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> Median age (IQR) 42 (28), 48 males (52.0%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Log normal 2.5 th percentile 2.46 (95% CI 1.72-3.57), 50 th percentile 8.07 (95% CI 6.90-9.36), 95 th percentile 21.90 (95% CI 18.22-25.45), 97.5 th percentile 26.52 (95% CI 21.36-31.78)
Pongpirul 2020 Thailand N=83 Retrospective 10.1101/2020.06.24.20139642	<i>Setting:</i> Hospital <i>Demographics**:</i> Median age (IQR) 37 (24), 113 males (58.5%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Median (IQR) 5.5 (5)
Pung 2020 Singapore N=36 Prospective 10.1016/S0140-6736(20)30528-6	<i>Setting:</i> Mixed <i>Demographics**:</i> Median age (IQR) 40 (15), 7 males (41.0%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	Median (IQR) 4 (3)
Qian 2020 China N=91 Retrospective 10.1093/qjmed/hcaa089	<i>Setting:</i> Hospital <i>Demographics:</i> Median age (IQR) 50 (20.5), 37 males (40.66%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Median (IQR) 6 (5)
Qin 2020 China N=1084 Retrospective 10.1126/sciadv.abc1202	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> Mean age 41.31, 614 males (57.1%) <i>Exposure type:</i> Travel <i>Disease severity:</i> Unclear	<i>Distribution:</i> Weibull* Mean 8.29 (95% CI 7.67-8.9) 50 th percentile 7.76 (95% CI 7.02-8.53), 95 th percentile 16.32 (95% CI 15.62-17.04), 99 th percentile 20.31 (95% CI 19.15-21.47)

Ren 2020 China N=98 Retrospective 10.1111/irv.12787	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> Unclear <i>Exposure type:</i> Work <i>Disease severity:</i> Unclear	<i>Distribution:</i> Log normal Mean 5.3 (95% CI 4.6-6.0) 50 th percentile 4.6 (95% CI 4.0-5.2), 95 th percentile 11.1 (95% CI 9.3-12.8), 99 th percentile 16.1 (95% CI 12.9-19.2)
Sanche 2020 China N=24 Retrospective 10.3201/eid2607.200282	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> NR <i>Exposure type:</i> Unclear <i>Disease severity:</i> Unclear	Mean 4.2 (95% CI 3.5-5.1)
Shi 2020 China N=46 Retrospective 10.21203/rs.3.rs-25895/v1	<i>Setting:</i> Mixed <i>Demographics**:</i> Median age (IQR) 45 (79), 35 males (50.7%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	<i>Distribution:</i> Log normal Mean 4.77 (95% CI 3.61-5.94) 95 th percentile 12.0 (95% CI 10.09-13.91)
Song 2020 [^] China N=NR Retrospective 10.3760/cma.j.cn112338-20200205-00069	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> NR <i>Exposure type:</i> Unclear <i>Disease severity:</i> Unclear	<i>Distribution:</i> Gamma* Shape 2.22, Scale 0.44 Mean 5.01 (95% CI 4.31-5.69)
Sun (a) 2020 China N=55 Retrospective 10.1002/jmv.25966	<i>Setting:</i> Hospital <i>Demographics:</i> Median age (IQR) 44 (22), 31 males (56.4%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Median (IQR) 7.5 (6.8)
Sun (b) 2020 China N=33 Retrospective 10.1016/S2589-7500(20)30026-1	<i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> Median age (IQR) 46 (25), 281 males (55.0%) <i>Exposure type:</i> Travel <i>Disease severity:</i> Unclear	Median (IQR) 4.5 (2.5)
Tian 2020	<i>Setting:</i> Hospital	Mean (\pm SD) 6.7 (\pm 5.2)

China N=262 Retrospective 10.1016/j.jinf.2020.02.018	<i>Demographics:</i> Median age (IQR) 47.5 (93), 127 males (48.5%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	
Tindale 2020 China and Singapore N=228 Retrospective 10.7554/eLife.57149	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> NR <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Gamma* <i>Subgroup China (N=135):</i> Shape 4.74 (95% CI 3.35-5.72), Scale 1.83 (95%CI 1.29-2.04) Mean 8.68 (95% CI 7.72-9.7) 50 th percentile 8.06 <i>Subgroup Singapore (N=93):</i> Shape 3.05 (95% CI 2.0-3.84), Scale 1.95 (95% CI 1.23-2.34) Mean 5.99 (95% CI 4.97-7.14) 50 th percentile 5.32
Tomie 2020 Japan N=24 Retrospective 10.1101/2020.05.23.20110908	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> NR <i>Exposure type:</i> Close contact <i>Disease severity:</i> Unclear	<i>Distribution:</i> Log normal Mean 6.8 (10-90% values 2-12 days) 50 th percentile 5.7
Viego 2020 Argentina N=12 Retrospective 10.1101/2020.06.18.20134825	<i>Setting:</i> Unclear <i>Demographics:</i> NR <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Log normal Mean 7.5 (95% CI 4.11-10.89) 50 th percentile 5.76 (95% CI 3.59-9.33)
Wang (a) 2020 China N=219 Retrospective 10.1186/s12879-020-05251-9	<i>Setting:</i> Hospital <i>Demographics**:</i> Median age (IQR) 39 (29), 268 males (45.8%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	Monte Carlo simulation to estimate mean. Mean 6.3 (95% CI 6-6.6) 2.5 th percentile 5.2, 50 th percentile 5.2, 97.5 th percentile 6.1
Wang (b) 2020 China N=275	<i>Setting:</i> Hospital <i>Demographics:</i> Median age (IQR) 28 (34), 128 males (46.5%)	Median (IQR) 6 (6)

Retrospective 10.1093/ofid/ofaa187	<i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	
Wang (c) 2020 China N=14 Prospective 10.1183/13993003.00544-2020	<i>Setting:</i> Mixed <i>Demographics**:</i> Median age (IQR) 37 (63), 13 males (37.1%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mild/moderate	<i>Distribution:</i> Log normal Mean 4.5 (95% CI 2.0-20.0) 95 th percentile 11.4 (95% CI 4.0-12.0)
Wang (d) 2020 China N=120** Retrospective 10.1101/2020.04.20.20064899	<i>Setting:</i> Hospital <i>Demographics**:</i> Median age (IQR) 33.5 (28), 60 males (50.0%) <i>Exposure type:</i> Healthcare <i>Disease severity:</i> Mixed	Median (\pm SD) 5.2 (\pm 1.8)
Wang (e) 2020 China N=483 Retrospective 10.1101/2020.02.21.20026112	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> 81% aged 21-60 years, 637** males (55.0%) <i>Exposure type:</i> Unclear <i>Disease severity:</i> Unclear	<i>Distribution:</i> Log normal* Mean 7.43 (95% CI 3.0-6.4) Median (IQR) 7 (7)
Wen 2020 China N=92 Retrospective 10.1101/2020.03.22.20035246	<i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> Mean age 45.4, 197 males (47.2%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	<i>Distribution:</i> Log normal* Median (IQR) 5.02 (5.1) 2.5 th percentile 1.21, 97.5 th percentile 20.73
Wi 2020 South Korea N=66 Retrospective 10.1093/cid/ciaa967	<i>Setting:</i> Hospital <i>Demographics**:</i> Mean age (\pm SD) 41.3 (\pm 19.0), 54 males (48.6%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Mean (\pm SD) 6.5 (\pm 4.3)
Wong 2020 Brunei N=15 Prospective 10.4269/ajtmh.20-0771	<i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> Median age (IQR) 31.5 (26), 42 males (51.2%) <i>Exposure type:</i> Close contact <i>Disease severity:</i> Mixed	Median (IQR) 5 (5)
Wu (a) 2020	<i>Setting:</i> Quarantine	<i>Distribution:</i> Log normal

China N=48 Prospective 10.1093/cid/ciaa557	<i>Demographics:</i> Median age (IQR) 43.5 (26.5), 19 males (39.6%) <i>Exposure type:</i> <i>Disease severity:</i>	Mean 5.8 (95% CI 4.2-6.0) 5 th percentile 1.2 (95% CI 0.76-1.8), 50 th percentile 4.3 (95% CI 3.4-5.3), 95 th percentile 15.3 (95% CI 10.4-21.1)
Wu (b) 2020 China N=47 Retrospective 10.21203/rs.3.rs-30375/v1	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> Mean age (\pm SD) 50.7 (\pm 15.78), 22 males 44.9% <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	Median (IQR) 5 (4)
Xia (a) 2020 China N=10 Prospective 10.1016/j.jcv.2020.104360	<i>Setting:</i> Hospital <i>Demographics:</i> Mean age (\pm SD) 56.5 (\pm 11.6), 6 males 60.0% <i>Exposure type:</i> Close contact <i>Disease severity:</i> Mixed	Mean (\pm SD) 7.0 (\pm 2.59)
Xia (b) 2020 China N=106 Retrospective 10.1101/2020.03.06.20031955	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> Median age (range) 41 (19-73), 70 males (66.0%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Weibull Mean 4.9 (95% CI 4.4-5.4) 2.5 th percentile 0.8 (95% CI 0.5-1.1), 50 th percentile 4.5 (95% CI 4.0-5.1), 95 th percentile 9.9 (95% CI 8.9-11.2), 97.5 th percentile 11.1 (95% CI 9.9-12.6), 99 th percentile 12.5 (95% CI 11.0-14.4)
Xiao (a) 2020 China N=2555 Retrospective 10.3855/JIDC.12718	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> NR <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Distribution:</i> Weibull Shape 1.88, Scale 9.69 Mean 8.98 (95% CI 7.98-9.9) 50 th percentile 8.61
Xiao (b) 2020 China N=217**	<i>Source:</i> Government/Health Authority Data <i>Demographics</i> ** <i>:</i> 268 males (49.0%) <i>Exposure type:</i> Mixed	Mean (\pm SD) 8.58 (\pm 4.65)

Retrospective 10.21203/rs.3.rs-40003/v1	<i>Disease severity:</i> Unclear	
Xu (a) 2020 China N=69 Retrospective 10.1101/2020.03.08.20031658	<i>Setting:</i> Hospital <i>Demographics:</i> Median age (IQR) 57 (26), 35 males (50.7%) <i>Exposure type:</i> Unclear <i>Disease severity:</i> Mixed	Median (IQR) 4 (5)
Xu (b) 2020 China N=56 Retrospective 10.1136/bmj.m606	<i>Setting:</i> Hospital <i>Demographics**:</i> Median age (IQR) 41 (20), 35 males (56.0%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Median (IQR) 4 (2)
Xu (c) 2020 China N=51 Retrospective 10.1016/j.ijid.2020.03.022	<i>Setting:</i> Hospital <i>Demographics subgroup imported cases (N=15):</i> Median age (IQR) 35 (22), 10 males (66.7%) <i>Demographics subgroup secondary cases (N=17):</i> Median age (IQR) 37 (23.5), 7 males (41.2%) <i>Demographics subgroup tertiary cases (N=19):</i> Median age (IQR) 53 (30), 8 males (42.1%) <i>Exposure type:</i> Travel <i>Disease severity:</i> Mild/moderate	<i>Subgroup imported cases (N=15):</i> Median (IQR) 8 (6) <i>Subgroup secondary cases (N=17):</i> Median (IQR) 8 (7) <i>Subgroup tertiary cases (N=19):</i> Median (IQR) 12 (5)
Yang (a) 2020 China N=10 Retrospective 10.1080/23744235.2020.1800814	<i>Setting:</i> Quarantine <i>Demographics:</i> Median age (IQR) 32.5 (15.7), 3 males (30.0%) <i>Exposure type:</i> Close contact <i>Disease severity:</i> Unclear	Median (IQR) 3 (5)
Yang (b) 2020 China N=88 Prospective	<i>Source:</i> Government/Health Authority Data <i>Demographics:</i> NR <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	<i>Subgroup aged <14 years (N=3):</i> Median (IQR) 8 (1.5) <i>Subgroup aged 14-34 years (N=43):</i> Median (IQR) 5 (4.5)

10.1017/S0950268820001338		<p><i>Subgroup aged 35-64 years (N=17):</i> Median (IQR) 6 (5)</p> <p><i>Subgroup aged >64 years (N=25):</i> Median (IQR) 9 (5)</p>
<p>Yang (c) 2020 China N=31 Prospective 10.1101/2020.02.28.20028068</p>	<p><i>Setting:</i> Hospital <i>Demographics**:</i> Median age (IQR) 44 (20.0), 33 males (60.0%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed</p>	<p>Mean 8.42 (95% CI 6.55-10.29)</p>
<p>Yu 2020 China N=132 Retrospective 10.1111/tbed.13604</p>	<p><i>Source:</i> Government/Health Authority Data <i>Demographics**:</i> Median age (IQR) 50 (28.0), 172 males (51.7%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mild/moderate</p>	<p><i>Distribution:</i> Gamma</p> <p><i>Subgroup single exposure (N=11):</i> 50th percentile 7.5 (95% CI 4.4-11.8)</p> <p><i>Subgroup multiple exposure (N=57):</i> 50th percentile 7.0 (95% CI 5.9-8.1)</p> <p><i>Subgroup Travel to high-risk area (N=64):</i> 50th percentile 7.2 (95% CI 6.1-8.4)</p> <p><i>Total study population (N=132):</i> 50th percentile 7.2 (95% CI 6.4-7.9), 95th percentile 16.0, 99th percentile 20.4</p>
<p>Zhang (a) 2020 subgroup a China N=188 (mild) Retrospective 10.1186/s40249-020-00710-6</p>	<p><i>Setting:</i> Hospital <i>Demographics subgroup mild (N=17)**:</i> Median age (IQR) 37.5 (26.5), 26 males (50.0%)</p> <p><i>Demographics subgroup moderate (N=156)**:</i> Median age (IQR) 45 (20.0), 329 males (50.0%)</p> <p><i>Demographics subgroup severe (N=14)**:</i> Median age (IQR) 55 (18.0), 39 males (63.9%)</p> <p><i>Demographics subgroup critical (N=1)**:</i> Median age (IQR) 70 (18.0), 13 males (76.5%)</p>	<p><i>Subgroup mild (N=17):</i> Median (IQR) 7 (8.5)</p> <p><i>Subgroup moderate (N=156):</i> Median (IQR) 6 (6)</p> <p><i>Subgroup severe (N=14):</i> Median (IQR) 3 (3.5)</p> <p><i>Subgroup critical (N=1):</i> Median 7</p>

	<i>Exposure type:</i> Unclear	
Zhang (b) 2020 China N=26 Retrospective 10.1101/2020.05.16.20103796	<i>Setting:</i> Hospital <i>Demographics:</i> Median age (IQR) 24 (23.0), 12 males (46.2%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mild/moderate	Median (IQR) 7 (14)
Zhang (c) 2020 China N=49 Retrospective 10.1016/S1473-3099(20)30230-9	<i>Setting:</i> Mixed <i>Demographics:</i> Mean age (\pm SD) 41.9 (\pm 18.4), 22 males 45.0% <i>Exposure type:</i> Unclear <i>Disease severity:</i> Unclear	<i>Distribution:</i> Log normal* Mean 5.2 (95% CI 1.8-12.4) 95 th percentile 10.5
Zhang (d) 2020 China N=34 Retrospective 10.1101/2020.03.12.20034686	<i>Setting:</i> Hospital <i>Demographics:</i> Median age (IQR) 2.75 (7.02), 14 males (41.18%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Median (IQR) 10.5 (17.5)
Zhao (a) 2020 China N=45 Retrospective 10.1016/j.jiph.2020.06.013	<i>Setting:</i> Hospital <i>Demographics**:</i> Median age (IQR) 49 (30.0), 68 males (50.0%) <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Median (IQR) 6 (7.0)
Zhao (b) 2020 China N=23 Retrospective 10.1101/2020.03.13.20035436	<i>Setting:</i> Hospital <i>Demographics**:</i> Mean age (\pm SD) 52.0 (\pm 20.0), 34 males 44.2% <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Median (IQR) 4 (4.0)
Zhong (a) 2020 [^] China N=62 Retrospective 10.11855/j.issn.0577-7402.2020.04.05	<i>Setting:</i> Hospital <i>Demographics:</i> Mean age (\pm SD) 51.8 (\pm 13.5), 40 males 64.5% <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	Mean (\pm SD) 6.85 (\pm 4.45)

Zhong (b) 2020 China N=48 Retrospective 10.12998/wjcc.v8.i12.2554	<i>Setting:</i> Hospital <i>Demographics:</i> Mean age (\pm SD) 44.35 (\pm 15.76), 31 males 64.6% <i>Exposure type:</i> Mixed <i>Disease severity:</i> Unclear	Mean (\pm SD) 6.86 (\pm 3.57)
Zhou (b) 2020 China N=20 Retrospective 10.21203/rs.3.rs-30405/v1	<i>Setting:</i> Hospital <i>Demographics:</i> Median age (IQR) 42.5 (20.5), 10 males (50.0%) <i>Exposure type:</i> Unclear <i>Disease severity:</i> Mixed	Median (IQR) 6.5 (5.75)
Zhou (c) 2020 China N=197 Retrospective 10.1101/2020.03.26.20041426	<i>Setting:</i> Hospital <i>Demographics:</i> Mean age (\pm SD) 55.94 (\pm 18.83), 99 males 50.3% <i>Exposure type:</i> Mixed <i>Disease severity:</i> Mixed	Mean (\pm SD) 6.14 (\pm 9.27)

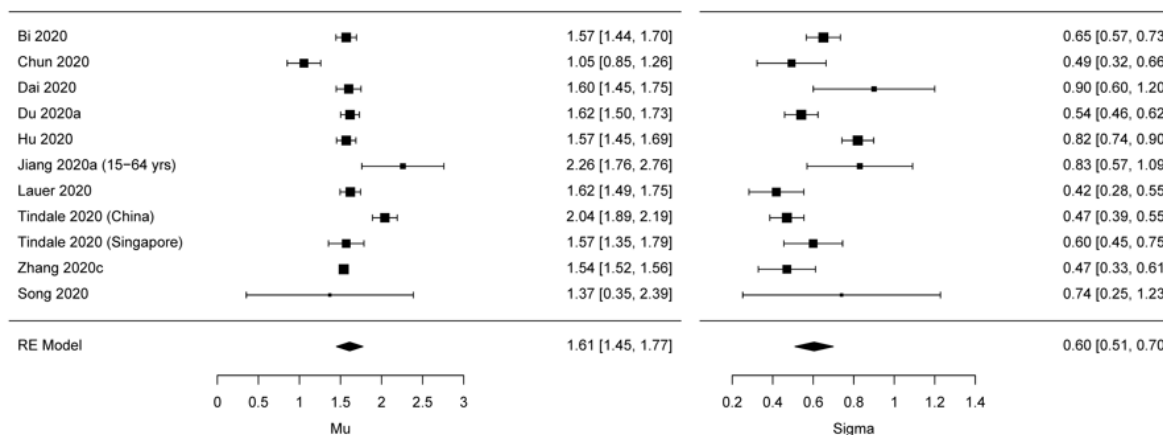
Appendix 2. Summary of included studies for time to first positive test in asymptomatic populations

Study Country Sample size DOI	Setting Demographics Exposure Serial sampling	Outcome
Zhou 2020a China N=26 10.1016/j.jinf.2020.03.028	<i>Setting:</i> Isolated observation <i>Demographics:</i> Mean age 37 years (range 3-90). 10 males (38.5%) <i>Exposure:</i> Close contact <i>Serial sampling:</i> Assumed yes (as indicated by repeat testing in some cases)	<i>Time from exposure to positive test:</i> Mean 8 days (range 5-22) Note: 9 individuals subsequently developed respiratory symptoms
Luo 2020 China N=8 10.1101/2020.03.24.20042606	<i>Setting:</i> Quarantine (surveillance) <i>Demographics:</i> NR <i>Exposure:</i> Close contact <i>Serial sampling:</i> Yes (every two days)	<i>Time from exposure to positive test:</i> All within 10 days <ul style="list-style-type: none"> • 2 on day 0 • 2 on day 1 • 1 on day 2 • 1 on day 3 • 1 on day 7 • 1 on day 10 Note: median delay of 2 days between last contact and quarantine
Jung 2020 South Korea N= 2 https://doi.org/10.3346/jkms.2020.35.e314	<i>Setting:</i> Active surveillance following self-quarantine <i>Demographics:</i> <i>Exposure:</i> Unclear <i>Serial sampling:</i> Active surveillance	<i>Time after quarantine to positive test:</i> Two individuals who were negative at day 14 (mandatory testing) and released from quarantine subsequently tested positive on day 2 and day 4 after release. One remained asymptomatic while one became symptomatic. Further caused 4 secondary cases.

Appendix 3. Supplementary analyses for distribution parameters

Log-normal

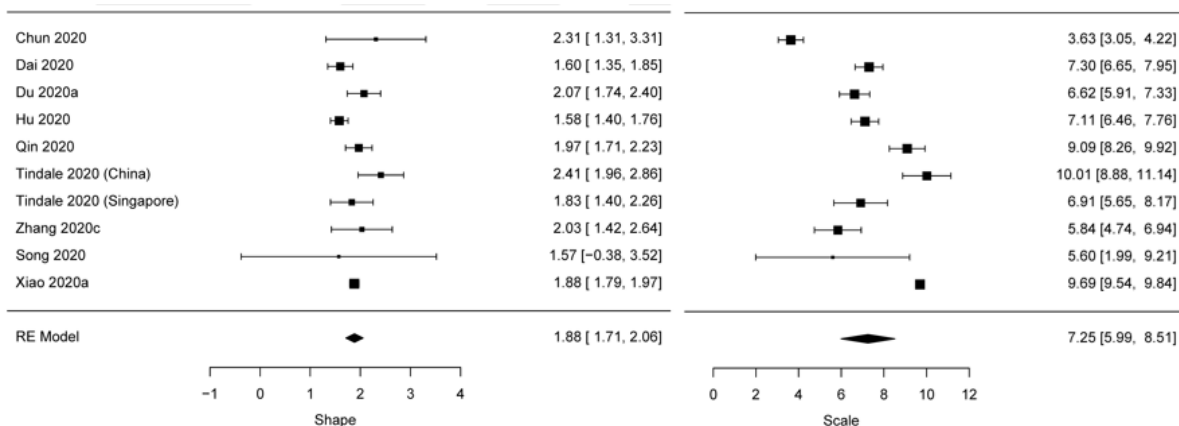
Figure 3.1 Forest plot of mu and sigma values for the log-normal distribution



There was substantial heterogeneity with an I^2 statistic of 95% for the mu parameter and 83% for the sigma parameter. One study (Tindale 2020, China subset) was considered influential in the meta-analysis of mu values, and one (Hu 2020) in the meta-analysis of sigma values.

Weibull

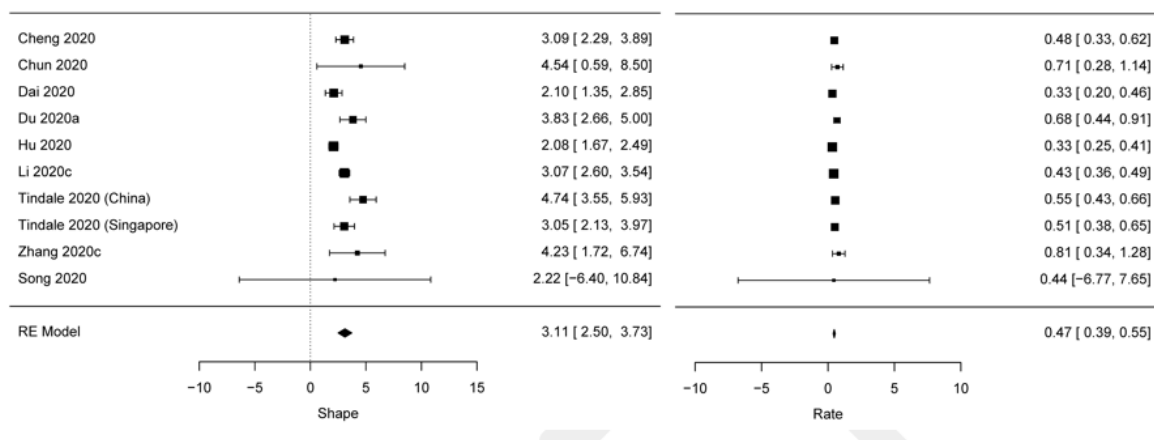
Figure 3.2 Forest plot of shape and scale values for the Weibull distribution



There was substantial heterogeneity with an I^2 statistic of 68% for the shape parameter and 97% for the scale parameter. No study was considered influential in the meta-analysis of the shape parameter, and one (Chun 2020) in the meta-analysis of the scale parameter.

Gamma

Figure 3.3 Forest plot of shape and rate values for the Gamma distribution



There was substantial heterogeneity with an I^2 statistic of 76% for the shape parameter and 64% for the rate parameter. One study (Tindale 2020, China subset) was considered influential in the meta-analysis of the shape parameter, and no studies for the meta-analysis of the scale parameter.

Table 3.1 Comparison of results with distribution parameters treated as independent and correlated

	Log-normal				Weibull				Gamma			
	Independent		Correlated		Independent		Correlated		Independent		Correlated	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
Mean (days)	6.0	(5.1 to 7.1)	6.0	(5.0 to 7.2)	6.4	(5.3 to 7.5)	6.4	(5.3 to 7.5)	6.7	(5.1 to 8.7)	6.7	(5.9 to 7.4)
Median (days)	5.0	(4.3 to 5.9)	5.0	(4.3 to 5.9)	6.0	(4.9 to 7.0)	6.0	(4.9 to 7.0)	6.0	(4.4 to 7.9)	6	(5.2 to 6.7)
95 %ile (days)	13.6	(10.8 to 16.9)	13.7	(10.6 to 17.3)	13.0	(10.7 to 15.4)	13.0	(10.7 to 15.3)	13.9	(11.0 to 17.5)	13.8	(12.6 to 15.3)
97.5%ile (days)	16.5	(12.8 to 20.9)	16.5	(12.6 to 21.5)	14.5	(11.9 to 17.3)	14.5	(12.0 to 17.2)	15.9	(12.7 to 19.9)	15.9	(14.4 to 17.5)
99 %ile (days)	20.6	(15.5 to 26.8)	20.7	(15.2 to 27.6)	16.4	(13.4 to 19.5)	16.4	(13.4 to 19.4)	18.5	(14.9 to 22.9)	18.4	(16.7 to 20.4)
At day 7 (%)	71%	(61% to 80%)	71%	(61% to 81%)	61%	(50% to 74%)	61%	(50% to 74%)	61%	(42% to 78%)	61%	(53% to 69%)
At day 10 (%)	87%	(80% to 93%)	87%	(79% to 94%)	84%	(74% to 98%)	84%	(74% to 93%)	82%	(67% to 93%)	83%	(77% to 88%)
At day 14 (%)	95%	(91% to 98%)	95%	(91% to 99%)	96%	(92% to 99%)	97%	(92% to 99%)	95%	(87% to 99%)	95%	(93% to 97%)

Appendix 4. Subgroup analyses for children and older adults

Table 4.1 Pooled incubation period in children (n=3 studies)

Studies included in quantitative analysis: Guo 2020, Hua 2020, Yang 2020b

	Log-normal		Weibull		Gamma	
	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)
Mean (days)	9.2	(8.1 to 10.5)	9.8	(8.7 to 11.9)	10.9	(2.9 to 32.5)
Median (days)	8.5	(7.7 to 9.3)	9.2	(6.7 to 10.5)	10.3	(2.4 to 31.1)
95%ile (days)	16.0	(10.6 to 23.3)	16.0	(12.1 to 41.3)	18.6	(6.4 to 50.0)
97.5%ile (days)	18.2	(11.2 to 28.3)	17.2	(12.5 to 53.8)	20.5	(7.3 to 53.4)
99%ile (days)	21.1	(11.7 to 35.4)	18.6	(13.0 to 71.0)	22.9	(8.6 to 58.8)
At day 7 (%)	29%	(8% to 42%)	23%	(6% to 51%)	39%	(0% to 97%)
At day 10 (%)	69%	(57% to 90%)	56%	(41% to 68%)	60%	(0% to 100%)
At day 14 (%)	91%	(78% to 100%)	90%	(69% to 100%)	77%	(1% to 100%)

Table 4.2 Pooled incubation period in older adults (n=3 studies)

Studies included in quantitative analysis: Dai 2020, Kong 2020b, Yang 2020b

	Log-normal		Weibull		Gamma	
	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)
Mean (days)	9.2	(8.1 to 10.5)	8.8	(7.9 to 9.7)	6.3	(3.0 to 13.5)
Median (days)	8.4	(7.4 to 9.6)	8.6	(7.7 to 9.5)	6.0	(2.8 to 12.9)
95%ile (days)	17.0	(14.1 to 20.5)	15.2	(13.3 to 17.3)	11.0	(5.5 to 23.3)
97.5%ile (days)	19.5	(15.8 to 23.9)	16.5	(14.3 to 19.0)	12.2	(6.1 to 25.7)
99%ile (days)	22.8	(17.9 to 28.6)	18.0	(15.5 to 21.1)	13.7	(7.0 to 28.7)
At day 7 (%)	34%	(22% to 45%)	34%	(26% to 42%)	70%	(7% to 99%)
At day 10 (%)	66%	(54% to 77%)	64%	(55% to 74%)	88%	(26% to 100%)
At day 14 (%)	88%	(80% to 95%)	91%	(84% to 97%)	96%	(58% to 100%)

Appendix 5. Methodological quality of included studies

Figure 5.1 Summary of quality of included studies

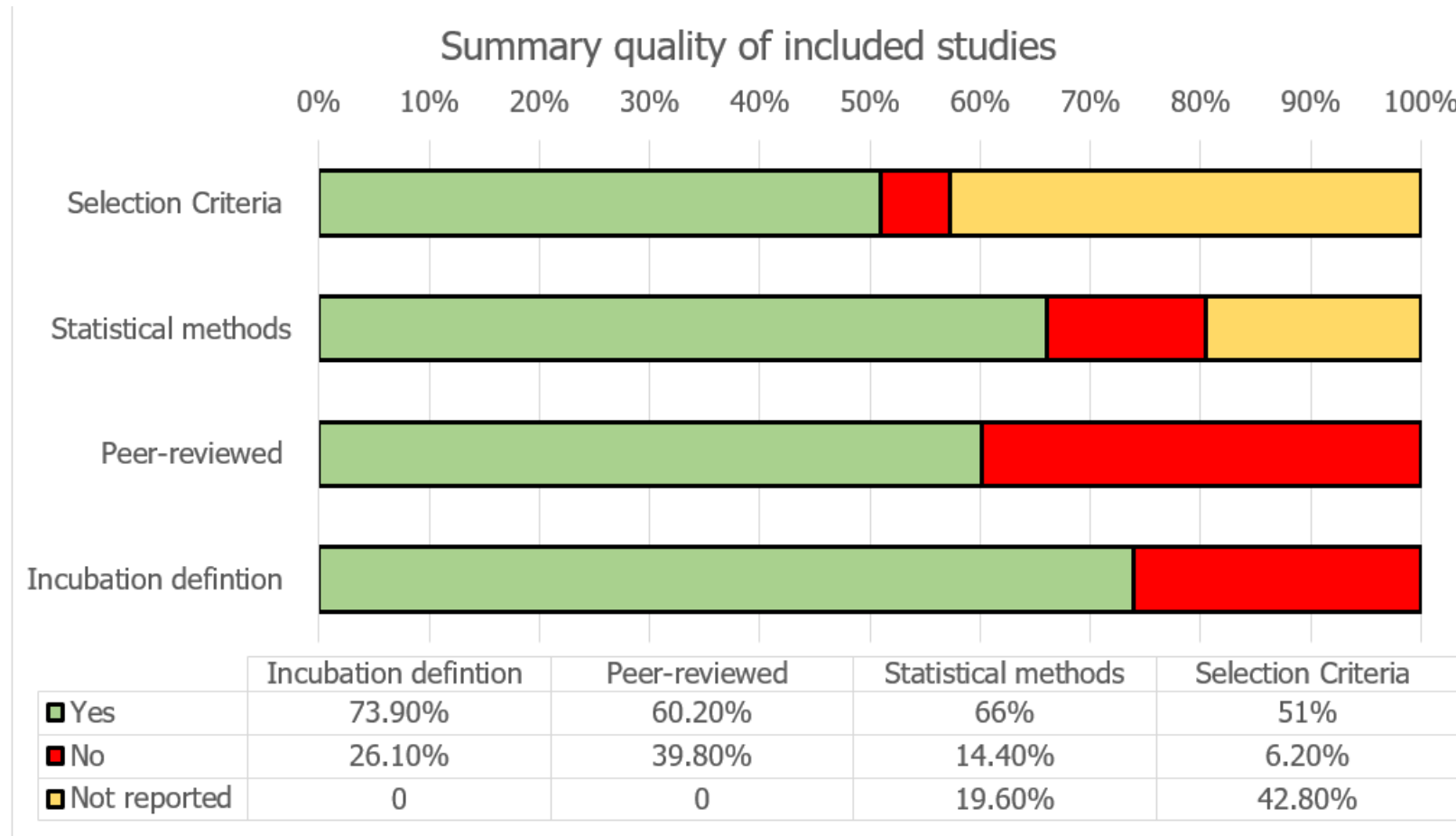


Table 5.1 Methodological quality of included studies

Study	Inclusion criteria reported and avoided inappropriate exclusion	Used appropriate statistical methods which were adequately described	Peer-reviewed	Defined incubation period	Definition of incubation period used
Ai 2020	Not reported	Yes	No	No	Non-applicable
Alshami 2020	Yes	Yes	No	No	Non-applicable
Alsofayan 2020	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Ashraf 2020	Yes	Yes	No	Yes	Last exposure to symptom onset
Backer 2020	Not reported	Not reported	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Bao 2020	Yes	No	Yes	Yes	First exposure to symptom onset
Bi 2020	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Bohmer 2020	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Bui 2020	Yes	Yes	No	Yes	Exposure to symptom onset (time of exposure not reported)
Chaw 2020	Yes	Yes	No	Yes	Exposure to symptom onset (time of exposure not reported)
Chen 2020a	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Chen 2020b	Yes	Yes	No	No	Non-applicable
Cheng 2020	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Chun 2020	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Dai 2020	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Ding 2020	Yes	No	No	No	Non-applicable
Du 2020a	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Du 2020b	Yes	Yes	No	No	Non-applicable
Guan 2020a	Yes	Yes	Yes	Yes	First exposure to symptom onset
Guan 2020b	Yes	Yes	Yes	Yes	First exposure to symptom onset
Guo 2020	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Hu 2020	Yes	Yes	No	Yes	Exposure to symptom onset (time of exposure not reported)
Hua 2020	Yes	Yes	Yes	Yes	First exposure to symptom onset
Ji 2020	Not reported	Not reported	No	No	Non-applicable

Jiang 2020a	Yes	Yes	No	Yes	Exposure to symptom onset (time of exposure not reported)
Jiang 2020b	Not reported	Yes	No	No	Non-applicable
Jin 2020	Not reported	No	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Khonyongwa 2020	Yes	No	No	Yes	Exposure to symptom onset (time of exposure not reported)
Kong 2020a	No	Not reported	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Kong 2020b	No	No	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Kong 2020c	Yes	Not reported	Yes	No	Non-applicable
Lai 2020	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Lauer 2020	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Le 2020	Yes	Not reported	Yes	Yes	Last exposure to symptom onset
Lee 2020	Not reported	Yes	Yes	No	Non-applicable
Li 2020a	Yes	Yes	Yes	No	Non-applicable
Li 2020b	Not reported	Not reported	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Li 2020c	Not reported	Not reported	No	No	Non-applicable
Liang 2020	Yes	Yes	No	No	Non-applicable
Liao 2020	Not reported	No	No	Yes	Exposure to symptom onset (time of exposure not reported)
Linton 2020	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Liu 2020a	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Liu 2020b	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Lopez Bernal 2020	No	Yes	No	Yes	Exposure to symptom onset (time of exposure not reported)
Lu 2020	Yes	Not reported	No	Yes	Exposure to symptom onset (time of exposure not reported)
Luo 2020**	Yes	Yes	No	Yes	Last exposure to symptom onset
Men 2020	Not reported	Yes	No	Yes	Exposure to symptom onset (time of exposure not reported)
Nie 2020	Not reported	Yes	Yes	Yes	Last exposure to symptom onset
Pan 2020	Not reported	No	Yes	No	Non-applicable
Patrikar 2020	Not reported	No	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Ping 2020	Not reported	Not reported	No	No	Non-applicable
Pongpirul 2020	Yes	Yes	No	No	Non-applicable
Pung 2020	Yes	Not reported	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Qian 2020	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)

Qin 2020	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Ren 2020	Not reported	No	Yes	No	Non-applicable
Sanche 2020	Not reported	No	Yes	Yes	First exposure to symptom onset
Shi 2020	Yes	Not reported	No	Yes	Last exposure to symptom onset
Song 2020	Not reported	Not reported	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Sun 2020a	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Sun 2020b	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Tian 2020	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Tindale 2020	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Tomie 2020	Yes	Not reported	No	Yes	Exposure to symptom onset (time of exposure not reported)
Viego 2020	Not reported	Not reported	No	No	Non-applicable
Wang 2020a	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Wang 2020b	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Wang 2020c	Yes	Not reported	Yes	No	Non-applicable
Wang 2020d	Not reported	No	No	Yes	First exposure to symptom onset
Wang 2020e	Not reported	Not reported	No	Yes	Exposure to symptom onset (time of exposure not reported)
Wen 2020	Not reported	Yes	No	No	Non-applicable
Wi 2020	Not reported	Yes	Yes	No	Non-applicable
Wong 2020	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Wu 2020a	Yes	Yes	Yes	No	Non-applicable
Wu 2020b	Not reported	Yes	No	Yes	Last exposure to symptom onset
Xia 2020a	No	Not reported	Yes	No	Non-applicable
Xia 2020b	Yes	No	No	Yes	Exposure to symptom onset (time of exposure not reported)
Xiao 2020a	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Xiao 2020b	Yes	No	No	Yes	First exposure to symptom onset
Xu 2020a	No	Yes	No	No	Non-applicable
Xu 2020b	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Xu 2020c	Not reported	Yes	Yes	No	Non-applicable
Yang 2020a	Yes	Yes	Yes	Yes	Last exposure to symptom onset
Yang 2020b	Not reported	Not reported	Yes	Yes	Exposure to symptom onset (time of exposure not reported)

Yang 2020c	Yes	Yes	No	Yes	Exposure to symptom onset (time of exposure not reported)
Yu 2020	Yes	No	Yes	No	Non-applicable
Zhang 2020a	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Zhang 2020b	Not reported	Yes	No	Yes	Exposure to symptom onset (time of exposure not reported)
Zhang 2020c	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Zhang 2020d	Yes	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Zhao 2020a	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Zhao 2020b	Yes	Yes	No	Yes	Exposure to symptom onset (time of exposure not reported)
Zhong 2020a	No	Yes	No	Yes	Exposure to symptom onset (time of exposure not reported)
Zhong 2020b	Not reported	Yes	Yes	Yes	Exposure to symptom onset (time of exposure not reported)
Zhou 2020b	Yes	Yes	No	Yes	Exposure to symptom onset (time of exposure not reported)
Zhou 2020c	Yes	Yes	No	Yes	Exposure to symptom onset (time of exposure not reported)
Zhou 2020a**	Not reported	Not reported	Yes	Non-applicable	Non-applicable
Jung 2020**	Yes	Non-applicable	Yes	Non-applicable	Non-applicable

**Denotes inclusion of asymptomatic populations

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