A Rapid Review and Meta-Analysis of the Asymptomatic Proportion of PCR-Confirmed SARS-CoV-2 Infections in Community Settings

Authors: Sarah Beale[1,2], Andrew Hayward[2], Laura Shallcross[1], Robert W Aldridge[1], Ellen Fragaszy*[1,3]

[1] UCL Institute of Health Informatics, 222 Euston Rd, London NW1 2DA

[2] UCL Research Department of Epidemiology & Public Health, 1-19 Torrington Place, London WC1E 7HB

[3] LSHTM Department of Infectious Disease Epidemiology, Keppel Street, London WC1E 7HT

*corresponding author: Ellen Fragaszy (ellen.fragaszy@ucl.ac.uk)

Abstract

Background: Up to 80% of active SARS-CoV-2 infections are proposed to be asymptomatic based on cross-sectional studies. However, accurate estimates of the asymptomatic proportion require systematic detection and follow-up to differentiate between truly asymptomatic and pre-symptomatic cases. We conducted a rapid review and meta-analysis of the asymptomatic proportion of PCR-confirmed SARS-CoV-2 infections based on methodologically-appropriate studies in community settings.

Methods: We searched Medline and EMBASE for peer-reviewed articles, and BioRxiv and MedRxiv for pre-prints published before 25/08/2020. We included studies based in community settings that involved systematic PCR testing on participants and follow-up symptom monitoring regardless of symptom status. We extracted data on study characteristics, frequencies of PCR-confirmed infections by symptom status, and (if available) cycle threshold/genome copy number values and/or duration of viral shedding by symptom status, and age of asymptomatic versus (pre)symptomatic cases. We computed estimates of the asymptomatic proportion and 95% confidence intervals for each study and overall using random effect meta-analysis.

Findings: We screened 1138 studies and included 21. The pooled asymptomatic proportion of SARS-CoV-2 infections was 23% (95% CI 16%-30%). When stratified by testing context, the asymptomatic proportion ranged from 6% (95% CI 0-17%) for household contacts to 47% (95% CI 21-75%) for non-outbreak point prevalence surveys with follow-up symptom monitoring. Estimates of viral load and duration of viral shedding appeared to be similar for asymptomatic and symptomatic cases based on available data, though detailed reporting of viral load and natural history of viral shedding by symptom status were limited. Evidence into the relationship between age and symptom status was inconclusive.

Conclusion: Asymptomatic viral shedding comprises a substantial minority of SARS-CoV-2 infections when estimated using methodologically-appropriate studies. Further investigation into variation in the asymptomatic proportion by testing context, the degree and duration of infectiousness for asymptomatic infections, and demographic predictors of symptom status are warranted.

Background

Reports of asymptomatic SARS-CoV-2 infection and potential transmission[1,2,3] have generated concern regarding the implications of undetected asymptomatic transmission on the effectiveness of public health interventions in the current COVID-19 pandemic[4]. However, estimating the proportion of asymptomatic SARS-CoV-2 infections with viral shedding is challenging as the majority of testing is carried out on symptomatic individuals[5]. Furthermore, longitudinal designs that include symptom follow-up are required to differentiate truly asymptomatic cases, i.e. those that never develop symptoms during infection, from pre-symptomatic cases, i.e. those that shed virus and therefore test positive prior to symptom onset (see Figure 1). While asymptomatic viral shedding has been suggested to comprise up to ~80% of SARS-CoV-2 infections [6,7,8], data informing these figures are largely confined to cross-sectional reports that cannot distinguish truly asymptomatic cases from those who are pre-symptomatic at the point of testing (see Figure 1). Interchangeable use of these concepts, i.e. asymptomatic and pre-symptomatic, precludes accurate estimation of the asymptomatic proportion of potentially infectious SARS-CoV-2 cases. Detectable SARS-CoV-2 shedding based on reverse transcriptase polymerase chain reaction (PCR) testing cannot conclusively establish infectiousness in the absence of viral culture [9,10]. However, PCR cycle threshold values provide an informative estimate of viral load and, by extension, probable infectiousness [9]; consequently, PCR-confirmed infection can provide a useful and accessible indicator of potentially infectious cases, including those without symptoms, for epidemiological modelling.

Differences in demographic characteristics of asymptomatic versus symptomatic individuals are also poorly understood. Age is an important risk factor for COVID-19 severity, with greater risk of poor prognostic outcomes including mortality in older adults[11,12]. Consequently, asymptomatic infection may be less common with increasing age. Understanding the relationship between age and symptom status has important implications for public health interventions.

Given the widespread discussion and potential implications of asymptomatic transmission of SARS-CoV-2, we aimed to rapidly synthesize studies to estimate the asymptomatic proportion of PCR-confirmed cases in community settings (primary outcome). We also aimed to synthesize available data from these studies regarding viral load and duration of viral shedding in asymptomatic community cases compared to pre-symptomatic cases or those symptomatic from baseline (secondary outcome), and the relationship between symptom status and age (secondary outcome). We limited the review to include studies from community settings rather than hospitals and other medical facilities to prevent selection bias towards symptomatic cases. Only studies reporting PCR-confirmed cases rather than exclusive serological studies were included to estimate the proportion of asymptomatic SARS-CoV-2 infection with viral shedding. The review was not extended to estimate the overall asymptomatic proportion including non-shedding serological cases due to the limited number of serological studies, varying interpretation, and ongoing development of valid serological assays for SARS-CoV-2.

Methodology

This review was reported in line with the PRISMA guidelines[13]. A protocol was not registered due to its status as a rapid review.

Search Strategy

We used Ovid to search the Medline and EMBASE databases of peer-reviewed literature (2019- May 05 2020 and search repeated to include period of May 06 2020 to June 10 2020, and subsequently to include June 11 2020 to August 25 2020) using the following search terms for titles and abstracts: *(Coronavirus* OR Covid-19 OR SARS-CoV-2 OR nCoV) AND (asymptomatic)* AND (*polymerase chain reaction OR PCR OR laboratory-confirmed OR confirmed*). We also searched BioRxiv and MedRxiv for titles and abstracts of pre-print manuscripts using the terms *"Covid-19" + "asymptomatic"*. We hand-searched the reference lists of all included studies to identify any additional relevant literature.

Selection Criteria

We included studies that met all of the following criteria: 1) human study; AND 2) presented original research or public health COVID-19 surveillance data; AND 3) available in English; AND 4) presented data on polymerase chain reaction (PCR) confirmed COVID-19 cases; AND 5) presented data on PCR testing of exposed or potentially exposed individuals regardless of symptom status (to avoid bias towards symptomatic cases); AND 6) had systematic follow-up at ≥ 1 time-point and reporting of symptom status among PCR confirmed cases (to differentiate pre-clinical shedding from truly asymptomatic cases); AND 7) presented data from a community setting (i.e. community and home contact tracing, population screening, traveller screening, community institutional settings such as care homes, schools, or workplaces, occupational exposure including healthcare workers). Studies were excluded if they met any of the following criteria: 1) studies or case series with <5 positive cases and/or <20 total cases (small sample size) due to likely low generalisability of asymptomatic proportions; OR 2) not possible to consistently ascertain the symptomatic status of participants across follow-up; OR 3) inadequate detail about testing strategy (i.e. not possible to discern if all cases were tested systematically); OR 4) recruitment/reporting of patients from acute healthcare settings (e.g. hospitals, medical facilities) due to selection bias towards symptomatic cases.

Data Extraction and Analysis

One researcher performed the search and deduplication using Ovid, screened and selected studies, and extracted study details. Two researchers extracted primary outcome data independently and resolved any disagreement by consensus. We extracted the following variables of interest to assess the primary and secondary outcomes and the characteristics and quality of included studies: author names, year of publication, publication type (peer-reviewed article or pre-print), study design, study setting, study country of location, participant age (mean, median, or range as available), participant sex distribution, symptoms comprising symptomatic case definition, duration of symptom history at PCR-confirmation, duration of follow-up symptom monitoring, testing criteria, sample size, number of participants who underwent PCR testing, number of PCR-confirmed cases, number of confirmed cases who remained asymptomatic throughout follow-up, and cycle threshold or genome copy number values, viral culture results, duration of

viral shedding for asymptomatic and pre-/symptomatic cases, and any available data regarding age or age distribution of asymptomatic versus (pre)symptomatic cases if reported.

We performed random-effects meta-analysis using the *metaprop* programme[14] in Stata Version 15 to compute the study-specific and pooled asymptomatic proportion - the primary outcome of this review - with its 95% confidence intervals (Wilson score method) and 95% prediction intervals [15], applying the Freeman-Tukey transformation. We decided a-priori to use a random effects model to address heterogeneity. The asymptomatic proportion is given as the number of consistently asymptomatic confirmed cases divided by the total number of PCR-confirmed cases who received follow-up (Figure 2). It is important to note that the term asymptomatic proportion is sometimes used to alternatively refer to the asymptomatic proportion of all infections including those that do not shed virus and would not be PCR-confirmed (see Figure 2). To account for potential exposure-driven heterogeneity in asymptomatic proportion, we present findings stratified by testing context as well as overall. Testing context was subdivided into studies comprising exclusive household contacts of an index case, studies comprising contacts from other settings or those (potentially) exposed to an outbreak (including travellers returning from high-prevalence regions), and point prevalence surveys not specifically linked to an outbreak that had follow-up symptom monitoring.

We reported available findings regarding the viral load, duration of viral shedding, and age of asymptomatic and (pre)symptomatic cases, but did not conduct meta-analysis due to sparse reporting and inconsistencies in data presented.

Risk of Bias Assessment

We assessed risk of bias based using criteria relevant to the topic of this review adapted from the Joanna Briggs Institute critical appraisal tool for prevalence studies[16] (Table 1). Two researchers independently assessed the risk of bias for each included study and resolved any disagreement by consensus. Bias was assessed according to criteria described in Table 1, with studies graded as very low risk of bias if they were unlikely to have been affected by bias on any of the criteria, low if one criterion may have been affected, moderate if two may have been affected, and high if all three may have been affected. Risk of publication bias across included studies was assessed using a funnel plot and Egger's test.

Results

Records Identified

Figure 3 presents an adapted PRISMA flow diagram[13] of the study selection procedure. The search yielded 1077 published articles indexed on OVID and 473 pre-prints. Following deduplication, we screened the titles and abstracts of 1138 published articles and pre-prints, of which we assessed the 133 full texts – including a relevant text identified through hand-search of the literature – and included 21 in the present review [17-37]. Three of the 21 included studies comprised household contacts of confirmed cases[26,28,29]. A further 3 included studies were point prevalence surveys with symptom monitoring follow-up[34,35,36], one of which was conducted in a general population sample[36] and the remaining two in nursing

home samples[34,35]. The remaining 15 studies involved participants with other epidemiological links to confirmed or suspected cases/outbreaks[17,18,19,20,21,22, 23,24,25,27,30,31,32,33], including 5 studies based in nursing homes [18,19,24,32,37], and 1 study of healthcare workers with occupational exposure to confirmed cases[30]. The healthcare worker study was included as it comprised whole-facility testing following occupational exposure in healthcare workers rather than patients presenting to healthcare settings due to symptoms (see inclusion criteria). Studies were conducted across the following range of countries in Asia, Europe, and North America: China[22,25,26,27,29], USA[18,19,28,32,36], UK[24,35,37], South Korea[17], France[20], Vietnam[21], Brunei[23], Italy[30], Japan[31], Hong Kong[33], and Ireland[34]. Risk of bias was rated as very low for 2 studies [30,33], low for 15 studies[17-20,22,23,25-29,32,34-36], and moderate for 4 studies[21,24,31,37].

Asymptomatic Proportion of PCR-Confirmed SARS-CoV-2 Infections in Community Settings

Estimates of the asymptomatic proportion of PCR-positive SARS-CoV-2 infections for included studies ranged from 0% (95% CI 0-0.8%; Yousaf et al., 2020[28]) to 91% (95% CI 73%-98%; Starling et al., 2020[35]). Table 2 reports all asymptomatic proportions with 95% confidence intervals for as well as details of included studies. Based on random-effects meta-analysis (Figure 4), the pooled estimate for the asymptomatic proportion was 23% (95% CI 16%-30%; 95% prediction interval 0.01-57%). There was high heterogeneity: $Q(20)= 253.06$, $p<.001$, $\tau^2= 0.11$, $I^2= 92.10\%$. Heterogeneity appeared to be partly influenced by testing context (test for subgroup heterogeneity: $Q(2) = 10.49$, $p=0.01$), but remained substantial within these subgroups. Household contact studies demonstrated the lowest asymptomatic proportion estimate of 6% (95% CI 0-17%; heterogeneity $Q(2)= 12.09$, $p<.001$ $\tau^2= 0.07$, $I^2= 83.46\%$), rising to 23% (95% CI 14-32%; $Q(14)= 139.86$, $p<.001$ $\tau^2= 0.12$, $I^2= 89.99\%$) for studies comprising participants with other epidemiological links to SARS-CoV-2 cases or outbreaks, and 47% (95% CI 21-75%; $Q(2)= 47.16$, $p<.001$ $\tau^2= 0.23$, $I^2= 95.76\%$) for point prevalence surveys with symptom follow-up and without direct links to outbreaks/cases. Data were limited for studies exclusively involving household contacts or point prevalence surveys (both *n*=3 studies).

The funnel plot (Figure 5) and Egger's test did not indicate publication bias across studies included in the meta-analysis: *t*=0.23, *p*=0.82, 95% CI: -0.97, 1.20.

Viral Load and Duration of Viral Shedding

Eight of the twenty-one included studies reported data regarding the CT values/viral load and/or duration of viral shedding for asymptomatic cases versus pre-symptomatic cases and/or those symptomatic from baseline. Differences in methodology and reporting precluded meta-analysis.

Five studies reported CT values and/or genome copy number by symptom status. One of these studies, Hung et al. (2020)[33], found lower median baseline genome copy number in asymptomatic (3.86 log10 copies/mL) than symptomatic participants (7.62 log10 copies/mL). The remaining four studies all reported similar CT values for asymptomatic and symptomatic participants. Arons et al. (2020)[18] reported similar

baseline median cycle threshold values (CT) for asymptomatic (CT =25.5), pre-symptomatic (CT=23.1), and symptomatic (CT=24.5) cases. Infectious virus was isolated by viral culture from 33% (1/3) of available asymptomatic case specimens, 70.8% (17/24) of pre-symptomatic case specimens, and 65.0% (16/20) for symptomatic case specimens[18]. Chamie et al. (2020)[36] also found that median CT values across samples were not significantly different between asymptomatic (CT=24, IQR: 19-26) and symptomatic individuals (CT=24, IQR: 19-25). Pre-symptomatic individuals appeared to have higher median CT values if seronegative and similar values if seropositive, but numerical detail was not reported overall for this group. Ladhani et al. (2020)[37] also found no significant difference in baseline CT values between asymptomatic, pre-symptomatic, symptomatic, and post-symptomatic (i.e. reported symptoms in the two weeks prior to positive PCR result) participants; exact values were not provided. Chau et al. (2020)[21] also reported similar baseline cycle threshold values for asymptomatic and symptomatic cases, though further numeric detail was not reported. When including all PCR results across follow-up for asymptomatic versus symptomatic cases (including negative PCR results), asymptomatic cases appeared to demonstrate lower CT values overall, which was proposed to indicate faster viral clearance[21].

Direct investigation of duration of viral shedding was limited. Lombardi et al. (2020)[30] found that median duration from positive test to first negative test was shorter in asymptomatic participants (22 days; IQR: 15–30) than symptomatic ones (29 days; IQR: 24–31), but the difference was not statistically significant. Danis et al. (2020)[20] reported that the single asymptomatic case demonstrated the same viral load dynamics as one of the five symptomatic cases, with respective viral shedding periods of 7 and 6 days.

Age of Symptomatic versus Asymptomatic Cases

Six studies[21,27,29,31,33,37] reported information regarding the age of asymptomatic versus symptomatic cases. Variation in measurement and reporting precluded meta-analysis. Findings are reported in Table 3. Three studies indicated no significant difference in age between symptomatic and asymptomatic cases, while three studies suggested that asymptomatic cases tended to be younger than those with symptoms. Five studies were conducted in general population samples (contacts/potential contacts of confirmed cases or returning travellers), and one study was conducted in nursing home residents and staff with results stratified for these groups. Only one study[29] reported a substantial child sub-sample (<14 years old), and found a higher asymptomatic proportion for infected children (23% *n*=10/43) than adults (7%, *n*=8/108).

Discussion

Accurate estimates of the asymptomatic proportion of SARS-CoV-2 infections depend on appropriate study designs that systematically detect asymptomatic viral shedding and follow these cases up to differentiate truly asymptomatic infections from pre-clinical shedding. We calculated that an overall estimate of 23% of PCR-confirmed SARS-CoV-2 infections in community settings were asymptomatic, with a 95% confidence interval between 16%-30%. These findings do not support claims [6,7,8] of a very

high asymptomatic proportion for PCR-confirmed infections (up to 80%) and highlight the importance of distinguishing between asymptomatic and pre-symptomatic cases. Heterogeneity in estimates of the asymptomatic proportion, however, was partly influenced by variation between testing contexts. Subgroup estimates range from 6% (95%CI 0-17%) for household contacts, increasing to 23% (95% CI 14-32%) for participants with other epidemiological links to case(s) or outbreaks, and the highest estimate of 47% (95% CI 21-74%) for point prevalence studies not directly linked to contact(s)/outbreaks.

These findings should be interpreted with caution in terms of the relationship between exposure and symptom status[38]. The assumption that household contacts of index cases may experience frequent and intense exposure with limited protection compared to other groups, and conversely that participants in non-outbreak studies may have more limited exposure, could not be empirically verified in the present review. Confidence intervals for subgroup asymptomatic proportions overlapped substantially, and data were limited for both the household contact and the point prevalence survey with symptom follow-up categories (both *n*=3 included studies). Furthermore, the estimate for point prevalence surveys was affected by one study[35] with a very high asymptomatic proportion (91%); this estimate was likely influenced by the limited symptomatic case definition of new-onset cough or fever. Estimates for the other two studies were similar to the 'other epidemiological link' category (26% and 29%). Only one of the point prevalence studies with symptom follow-up[36] was conducted in a general population sample. Furthermore, the 'other epidemiological link' category comprised a variety of study testing contexts, including studies that combined household contacts with participants with less intensive exposure, which likely contributed to substantial within-category heterogeneity. Despite these substantial limitations, further investigation is warranted into variability in the asymptomatic proportion across testing contexts as more data become available.

This effect of study context may partially account for differences between the overall estimate of the asymptomatic proportion in the current review and higher estimates from other studies. Notably, early population-based data collected from English households by the Office for National Statistics suggested that only 22% (95% CI 14-32%) of the 88 individuals who tested positive for COVID-19 thus far reported any symptoms, rising to 29% (95% CI 19-40%) of the 76 individuals tested repeatedly[8]. Similarly, 69% of another English community sample recruited regardless of symptom status reported no symptoms in the seven days up to their positive PCR result[39]. However, neither of these studies systematically followed-up cases regarding their symptoms across the course of infection, potentially overestimating the asymptomatic proportion and precluding inclusion in this review. Furthermore, findings were affected by the small sample size and consequently wide confidence intervals due to testing at a period of relatively low COVID-19 incidence in the population, as well as potential false positive PCR tests leading to an overestimate of asymptomatic cases. While some of these issues may have impacted studies included in the present review, the careful screening of study design and methodology done as part of this review was reflected in the overall very low or low risk of bias on assessed criteria for all but four included studies. An additional strength of our review is the systematic search of both peer-reviewed published literature and preprint studies which has enabled us to capture the most up to date estimates available.

Although this review identifies PCR-confirmed cases, PCR-confirmation and symptom-status alone cannot establish whether cases are infectious and, if so, the degree or duration of their infectiousness. Case reports, however, have indicated potential transmission of SARS-CoV-2 from some asymptomatic index cases [1,2,9,21]. The balance of evidence regarding viral load in the present review indicates that asymptomatic cases had similar baseline or overall median viral loads to pre-symptomatic and symptomatic cases. Virological evidence suggests that infectious SARS-CoV-2 can be isolated by viral culture from samples with cycle threshold values up to 33, though the proportion of infectious virus decreases at higher cycle threshold values (i.e. lower viral load)[40]. While median baseline cycle threshold values for all symptom status groups (23.1-25.5) reported by Arons et al. (2020)[18] fell well within this limit, infectious virus was isolated from only 33% of asymptomatic baseline samples, compared to 71% of pre-symptomatic and 65% of symptomatic samples. These findings should be interpreted with caution given the very small sample of asymptomatic specimens (n=3). Overall, clear reporting of cycle threshold values across follow-up by symptom status was lacking in included studies. This is an important area for further research given that the degree and duration of the infectious period for asymptomatic cases, as well as the overall proportion of virus-shedding cases that are asymptomatic, influence the contribution of asymptomatic cases to SARS-CoV-2 transmission at a population level.

Evidence regarding the duration of SARS-CoV-2 shedding by symptom status was very limited, with two studies suggesting no substantial difference in viral clearance times for asymptomatic and symptomatic cases. Duration of shedding varied widely between participants across all symptom status groups in included studies. The sample of asymptomatic cases in studies that reported duration of viral shedding also tended to be small, and the natural history of viral excretion by symptom status remains unclear. Further inquiry into the degree of preclinical shedding for pre-symptomatic cases, although not the focus of this review, is also warranted. The contribution of asymptomatic and pre-symptomatic cases to the overall spread of infection cannot be accurately inferred in the absence of high-quality evidence assessing the infectiousness of such cases[41].

Evidence was also split regarding age and symptom status, with three studies indicating no difference in age between asymptomatic and symptomatic cases and three studies indicating that asymptomatic cases may tend to be younger than those with symptoms. Samples in the present study – both within the age-related analysis and in the meta-analysis overall – tended to comprise primarily or exclusively of adults, and one study with a substantial child subsample[29] found that a larger proportion of infected children were asymptomatic (23%) than adults (7%). Further comparison of the asymptomatic proportion for children and adults is required.

An important limitation of this review was the variability between symptomatic case definitions across included studies. Only eight of the twenty-one included studies[18,22-24,30,32,35,37] described the full range of symptoms included within their symptomatic case definitions, while a further ten studies[19,20,23,25-29,33,34] reported details of symptoms endorsed by participants but did not specify whether or which additional

symptoms were assessed as part of their case definitions and three[17,31,36] provided no detail. While a similar range of symptoms appear to have been monitored/endorsed across most included studies, it is possible that symptomatic case identification may have been affected by reporting bias and consequently that the true proportion of symptomatic cases was underestimated. Notably, Starling et al. (2020) [35] – the study with the highest reported asymptomatic proportion (91%) – used a very limited case definition of new-onset cough or fever. The reported proportion likely reflects individuals not meeting this case definition and excludes cases with other symptom profiles. This issue is particularly relevant given that unusual symptoms such as dysosmia/anosmia - only explicitly investigated by four studies[21,28,30,37] - and dysgeusia/ageusia -only explicitly investigated by two studies[28,30] - may be the primary or sole symptom for some COVID-19 cases [42-44]. Demographic reporting across studies was also limited and it was not possible to stratify findings by further demographic characteristics. Estimates of the asymptomatic proportion may vary across population subgroups and this is a relevant area for future enquiry.

We included only studies with symptom-related follow-up to prevent symptom status misclassification. However, overestimation of the asymptomatic proportion may still occur in contact tracing studies initiated during established outbreaks, such as Graham et al. (2020)[24.], if baseline symptomatic participants are classified as index cases and systematically excluded from the asymptomatic proportion. This review was also limited to estimating the asymptomatic proportion of virologically-confirmed infections. The asymptomatic proportion of infection varies depending on whether infections are identified using virological or serological methods[45]. PCR confirmation, which identifies infection with viral shedding, is informative for modelling transmission potential. However, review of the asymptomatic proportion of total infections based on emerging serological evidence – which identifies infections regardless of viral shedding – will be informative to understand how far SARS-CoV-2 has spread within populations and investigate evidence of immunity following asymptomatic infection[46].

Overall, this review provides preliminary evidence that, when investigated using methodologically-appropriate studies, a substantial minority of SARS-CoV-2 infections with viral shedding are truly asymptomatic. These findings indicate that testing should not be exclusively limited to symptomatic individuals. Further research identifying distinguishing features (e.g. age) and testing contexts for truly asymptomatic cases, as well as their transmission potential, is recommended to inform testing programmes. These findings also highlight the importance of other public health measures, such as promoting social distancing and wearing face coverings in public places, regardless of symptom status.

Competing Interests: AH serves on the UK New and Emerging Respiratory Virus Threats Advisory Group. The other authors declare no competing interests.

Data Availability Statement:

University College London Research Data Repository: http://doi.org/10.5522/04/12344135

This project contains the following underlying data:

Asymptomatic meta-analysis V2.csv (data used to conduct meta-analysis of asymptomatic proportion)

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

References:

* indicates inclusion in current meta-analysis

1   Pan X, Chen D, Xia Y, et al. Asymptomatic cases in a family cluster with SARS-CoV-2 infection. The Lancet Infectious Diseases. 2020; **20**: 410–1.

2   Bai Y, Yao L, Wei T, et al. Presumed Asymptomatic Carrier Transmission of COVID-19. JAMA 2020; **323**: 1406–7.

3   Chan JF-W, Yuan S, Kok K-H, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020; **395**: 514–23.

4   Gandhi M, Yokoe DS, Havlir DV. Asymptomatic Transmission, the Achilles' Heel of Current Strategies to Control Covid-19. N Engl J Med 2020; published online April 24. DOI:10.1056/NEJMe2009758.

5   Department of Health and Social Care. Coronavirus (COVID-19): getting tested. 2020; published online April 15 2020. https://www.gov.uk/guidance/coronavirus-covid-19-getting-tested (accessed May 11, 2020).

6   Day M. Covid-19: four fifths of cases are asymptomatic, China figures indicate. BMJ 2020; **369**. DOI:10.1136/bmj.m1375.

7   COVID-19: What proportion are asymptomatic? - CEBM. CEBM. https://www.cebm.net/covid-19/covid-19-what-proportion-are-asymptomatic/ (accessed May 17, 2020).

8   Office for National Statistics. Coronavirus (COVID-19) Infection Survey Pilot: 5 June 2020; published online June 5 2020. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/coronaviruscovid19infectionsurveypilot/5june2020.

9   Furukawa NW, Brooks JT, Sobel J. Early Release - Evidence Supporting Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 While Presymptomatic or Asymptomatic - Volume 26, Number 7—July 2020 - Emerging Infectious Diseases Journal - CDC. DOI:10.3201/eid2607.201595.

10   Joynt GM, Wu WK. Understanding COVID-19: what does viral RNA load really mean? Lancet Infect Dis 2020; published online March 27. DOI:10.1016/S1473-3099(20)30237-1.

11   Wu C, Chen X, Cai Y, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med 2020; published online March 13. DOI:10.1001/jamainternmed.2020.0994.

12   Fang X, Li S, Yu H, et al. Epidemiological, comorbidity factors with severity and prognosis of COVID-19: a systematic review and meta-analysis. Aging 2020; **12**: 12493.

13   Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009; **339**. DOI:10.1136/bmj.b2535.

14   Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. Arch Public Health 2014; **72**: 1–10.

15   IntHout J, Ioannidis JPA, Rovers MM, Goeman JJ. Plea for routinely presenting prediction intervals in meta-analysis. BMJ Open 2016; **6**: e010247.

16   Munn Z, Moola S, Riitano D, Lisy K. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. International Journal of Health Policy and Management 2014; **3**: 123.

17   *Park SY, Kim Y-M, Yi S, et al. Coronavirus Disease Outbreak in Call Center, South Korea. Emerg Infect Dis 2020; **26**. DOI:10.3201/eid2608.201274.

18   *Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. N Engl J Med 2020; published online April 24. DOI:10.1056/NEJMoa2008457.

19   *Roxby AC, Greninger AL, Hatfield KM, et al. Detection of SARS-CoV-2 Among Residents and Staff Members of an Independent and Assisted Living Community for Older Adults - Seattle, Washington, 2020. MMWR Morb Mortal Wkly Rep 2020; **69**: 416–8.

20   *Danis K, Epaulard O, Bénet T, et al. Cluster of coronavirus disease 2019 (Covid-19) in the French Alps, 2020. Clin Infect Dis 2020; published online April 11. DOI:10.1093/cid/ciaa424.

21   *Chau NVV, Lam VT, Dung NT, et al. The natural history and transmission potential of asymptomatic SARS-CoV-2 infection. medRxiv 2020; : 2020.04.27.20082347.

22   *Luo L, Liu D, Liao X-L, et al. Modes of contact and risk of transmission in COVID-19 among close contacts. medRxiv 2020; : 2020.03.24.20042606.

23   *Chaw L, Koh WC, Jamaludin SA, et al. SARS-CoV-2 transmission in different settings: Analysis of cases and close contacts from the Tablighi cluster in Brunei Darussalam. medRxiv. 2020 : 2020.05.08. 20090043.

24   *Graham NS, Junghans C, Downes R, et al. SARS-CoV-2 infection, clinical features and outcome of COVID-19 in United Kingdom nursing homes. medRxiv. 2020.05.26.20105460

25   *Wang Y, Tong J, Qin Y, et al. Characterization of an asymptomatic cohort of SARS-COV-2 infected individuals outside of Wuhan, China. Clin Inf Dis 2020; **ciaa629**.

26   * Wu J, Huang Y, Tu C, et al. Household Transmission of SARS-CoV-2, Zhuhai, China, 2020. Clin Inf Dis 2020; **ciaa557**.

27   *Yang N, Shen Y, Shi C, *et al.* In-flight transmission cluster of COVID-19: a retrospective case series. *Infect Dis* 2020; 1–11.

28   *Yousaf AR, Duca LM, Chu V, et al. A prospective cohort study in non-hospitalized household contacts with SARS-CoV-2 infection: symptom profiles and symptom change over time. *Clin Infect Dis* 2020; published online July 28. DOI:10.1093/cid/ciaa1072.

29   *Hua C, Miao Z, Zheng J, et al. Epidemiological features and viral shedding in children with SARS-CoV-2 infection. *Journal of Medical Virology*. 2020. DOI:10.1002/jmv.26180.

30   *Lombardi A, Consonni D, Carugno M, et al. Characteristics of 1573 healthcare workers who underwent nasopharyngeal swab testing for SARS-CoV-2 in Milan, Lombardy, Italy. *Clin Microbiol Infect* 2020; published online June 20. DOI:10.1016/j.cmi.2020.06.013.

31   *Tabata S, Imai K, Kawano S, et al. Clinical characteristics of COVID-19 in 104 people with SARS-CoV-2 infection on the Diamond Princess cruise ship: a retrospective analysis. *The Lancet Infectious Diseases*. 2020; **20**: 1043–50.

32   *Patel MC, Chaisson LH, Borgetti S, et al. Asymptomatic SARS-CoV-2 Infection and COVID-19 Mortality During an Outbreak Investigation in a Skilled Nursing Facility. *Clinical Infectious Diseases.* 2020. DOI:10.1093/cid/ciaa763.

33   *Hung IF-N, Cheng VC-C, Li X, et al. SARS-CoV-2 shedding and seroconversion among passengers quarantined after disembarking a cruise ship: a case series. *The Lancet Infectious Diseases*. 2020; **20**: 1051–60.

34   *Kennelly SP, Dyer AH, Martin R, et al. Asymptomatic carriage rates and case-fatality of SARS-CoV-2 infection in residents and staff in Irish nursing homes. *medRxiv*. 2020. 06.12. DOI:10.1101/2020.06.11.20128199.

35   *Starling A, White E, Showell D, Wyllie D, Kapadia S, Balakrishnan R. Whole Care Home Testing for Covid-19 in a Local Authority Area in the United Kingdom. *medRxiv*. 2020. 08.11. DOI:10.1101/2020.08.06.20162859.

36   *Chamie G, Marquez C, Crawford E, et al. SARS-CoV-2 Community Transmission During Shelter-in-Place in San Francisco. *medRxiv*. 2020. 06.17. DOI:10.1101/2020.06.15.20132233.

37   *Ladhani S, Yimmy Chow J, Janarthanan R, et al. Investigation of SARS-CoV-2 Outbreaks in Six Care Homes in London, April 2020: The London Care Home Investigation. *SSRN Electronic Journal*. DOI:10.2139/ssrn.3638267.

38   Wang Y, Zhang L, Sang L, Ye F, Ruan S, Zhong B, Song T, Alshukairi AN, Chen R, Zhang Z, Gan M. Kinetics of viral load and antibody response in relation to COVID-19 severity. *The Journal of Clinical Investigation*. 2020 Aug 31;**130**(10).

39   Riley S, Ainslie KE, Eales O, Jeffrey B, Walters CE, Atchison CJ, Diggle PJ, Ashby D, Donnelly CA, Cooke G, Barclay W. Community prevalence of SARS-CoV-2 virus in England during May 2020: REACT study. *medRxiv*. 2020 Jan 1. DOI: 10.1101/2020.07.10.20150524.

40   La Scola B, Le Bideau M, Andreani J, *et al.* Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards. *Eur J Clin Microbiol Infect Dis* 2020; **39**: 1059–61.

41   Patrozou E, Mermel LA. Does Influenza Transmission Occur from Asymptomatic Infection or Prior to Symptom Onset? *Public Health Reports. 2009;* **124**: 193–6.

42   Spinato G, Fabbris C, Polesel J, *et al.* Alterations in Smell or Taste in Mildly Symptomatic Outpatients With SARS-CoV-2 Infection. *JAMA* 2020; published online April 22. DOI:10.1001/jama.2020.6771.

43   Eliezer M, Hautefort C, Hamel A-L, *et al.* Sudden and Complete Olfactory Loss Function as a Possible Symptom of COVID-19. *JAMA Otolaryngol Head Neck Surg* 2020; published online April 8. DOI:10.1001/jamaoto.2020.0832.

44   Menni C, Valdes AM, Freidin MB, *et al.* Real-time tracking of self-reported symptoms to predict potential COVID-19. *Nat Med* 2020; : 1–4.

45   Leung NHL, Xu C, Ip DKM, Cowling BJ. The fraction of influenza virus infections that are asymptomatic: a systematic review and meta-analysis. *Epidemiology* 2015; **26**: 862.

46   Winter AK, Hegde ST. The important role of serology for COVID-19 control. *Lancet Infect Dis* 2020; published online April 21. DOI:10.1016/S1473-3099(20)30322-4.

Tables and Figures

Figure 1. *Timeline of Symptom Development and Viral Shedding in Relation to Timing of Virological Testing*
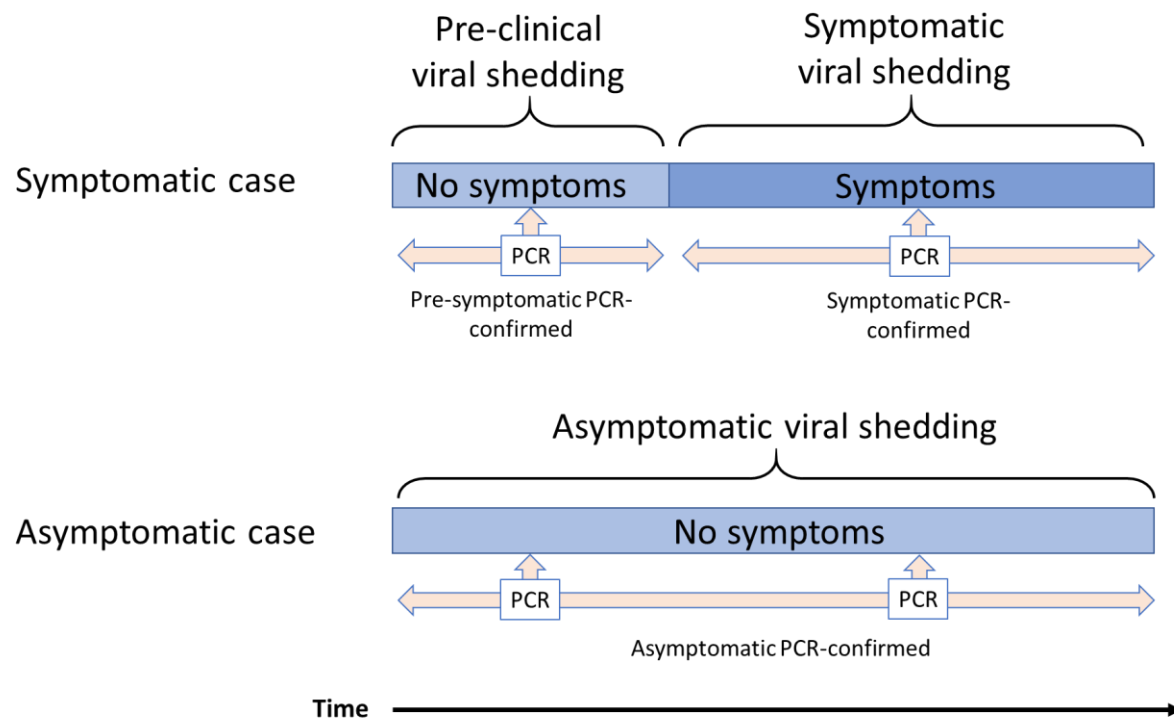
Figure 1 Note: This figure demonstrates two trajectories of symptom development in cases with detectable viral shedding. The symptomatic case trajectory comprises a period of pre-clinical viral shedding, in which the individual demonstrates no symptoms but tests PCR positive (pre-symptomatic PCR-confirmed). These individuals subsequently develop symptoms and continue to shed virus (symptomatic PCR-confirmed). Consequently, cases with a symptomatic trajectory may appear to be asymptomatic if tested in the pre-clinical shedding period and not followed-up. Asymptomatic cases with viral shedding, conversely, test PCR positive and never go on to develop symptoms across the course of infection (asymptomatic PCR-confirmed).

Figure 2. *Summary Classification of Clinical and PCR Outcomes and Calculation of Asymptomatic Proportions*
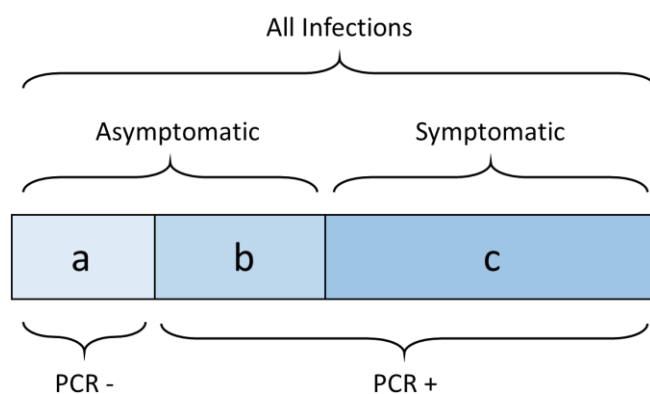
$$\text{Asymptomatic Proportion among PCR+ cases} = \frac{b}{b+c}$$

$$\text{Asymptomatic Proportion among all infections (requires serology)} = \frac{a+b}{a+b+c}$$

Figure 3. *Adapted PRISMA Flow Diagram of Study Selection*
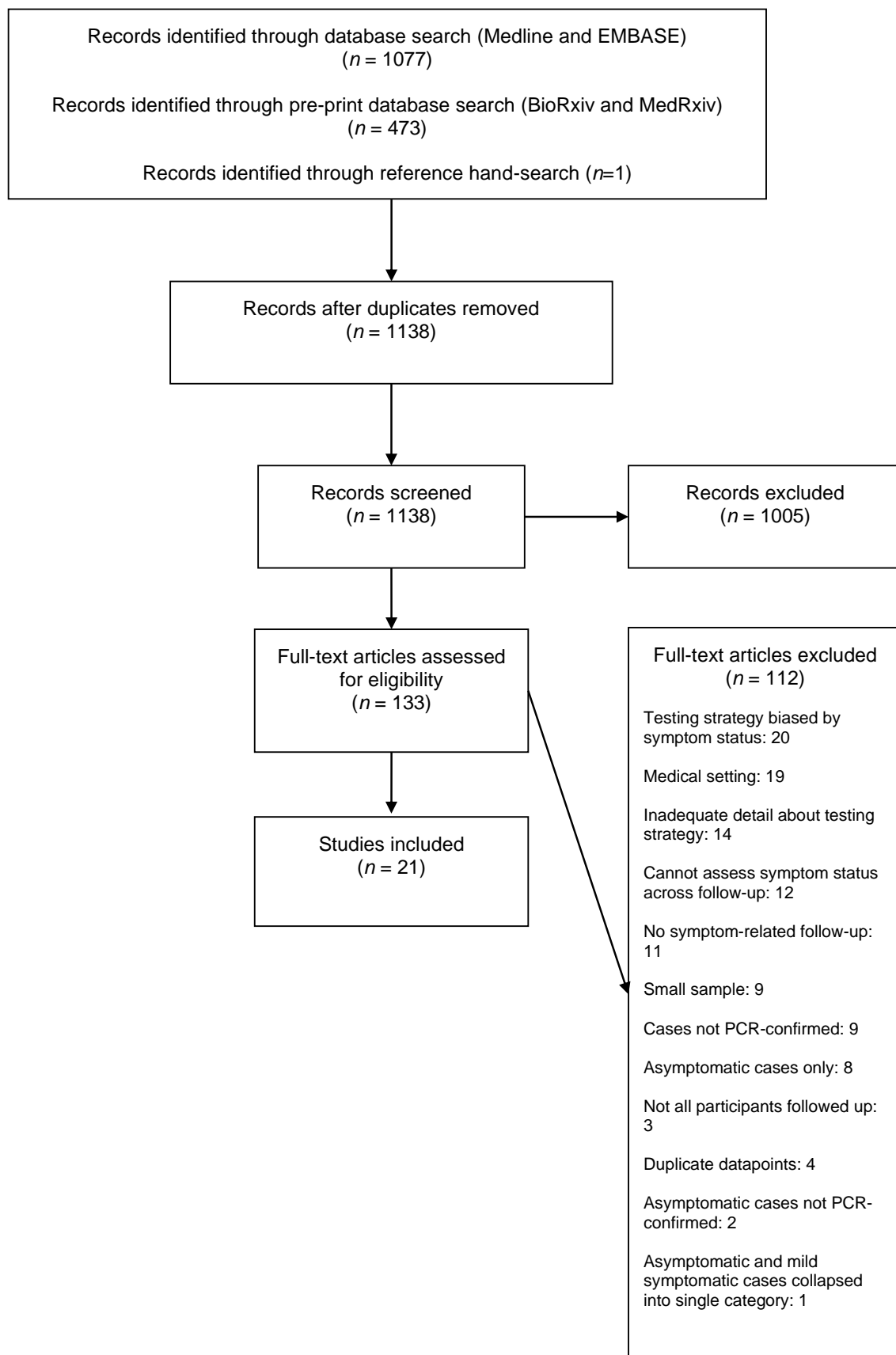
Figure 4. *Meta-Analysis Results for COVID-19 Asymptomatic Proportion in Community Studies*
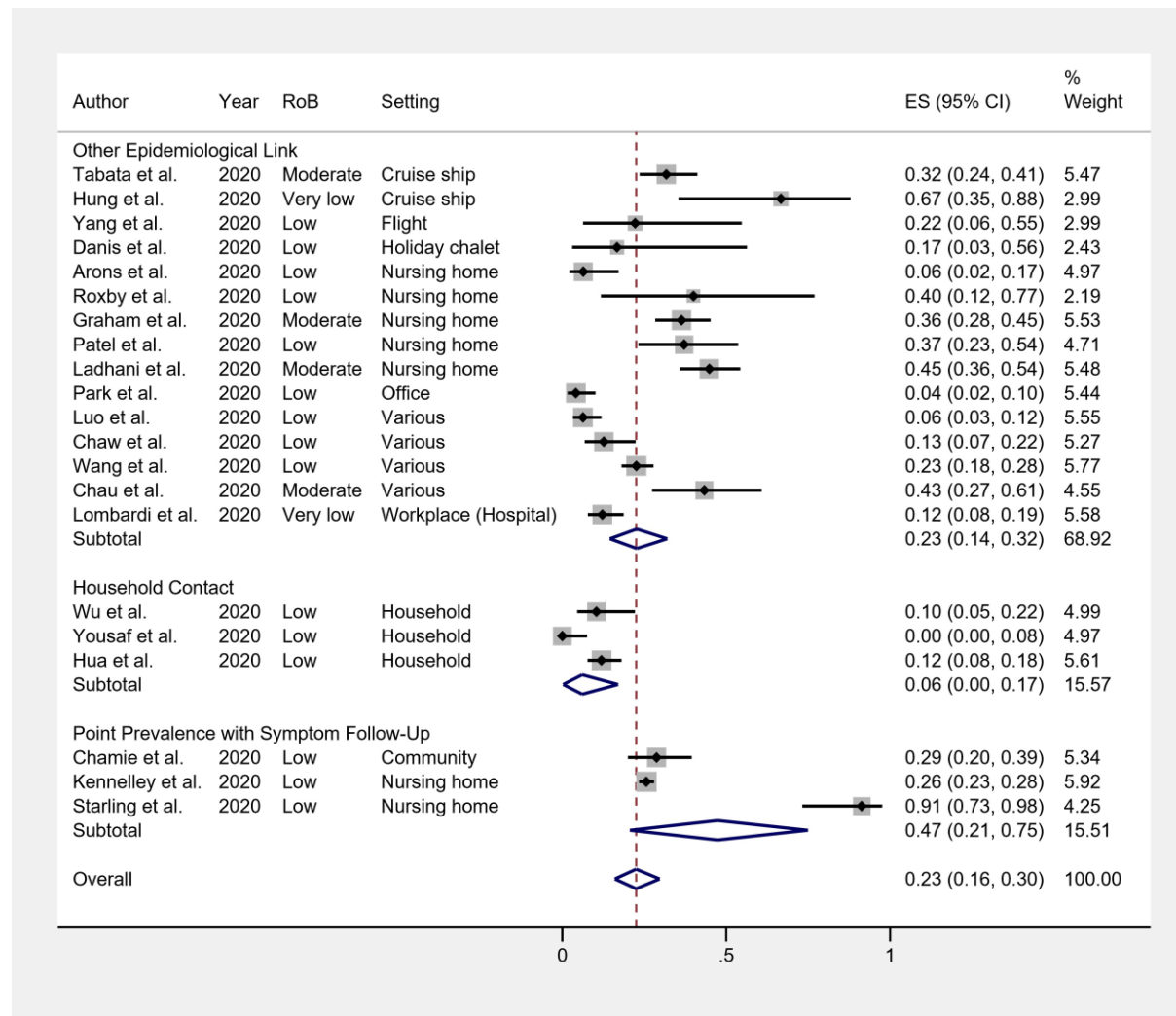
Figure 4 Note: ES (effect size) = asymptomatic proportion; I^2 = heterogeneity; asymptomatic proportions are given in decimal form

Figure 5. *Funnel Plot for Meta-Analysis of COVID-19 Asymptomatic Proportion in Community Studies*
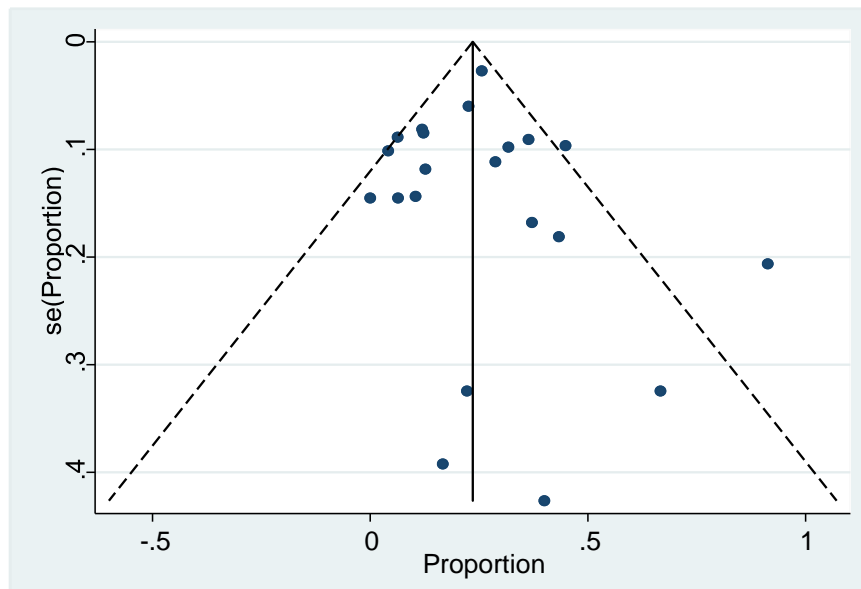
Table 1. *Risk of Bias Assessment*

Potential Issue	Direction of Bias
Information Bias: Initial testing does not identify all infected people shedding virus	Effect estimate could be biased downwards if PCR testing is more likely to detect symptomatic shedders compared to asymptomatic shedders. This could be because asymptomatic cases shed less virus or shed for a shorter duration.
Information Bias: Difficulty distinguishing pre-clinical versus truly asymptomatic	Effect estimate could be biased upwards if pre-symptomatic cases are misclassified as asymptomatic (see figure 1)
Non-Participation Bias: Individuals opt out of initial PCR testing or out of symptom follow-up	Effect estimate could be biased in either direction if participation is influenced on symptom-status

Table 2. *Descriptive Summary of Studies Included in Meta-Analysis*

Reference	Country of study	Participant group description	Study design	Testing criteria	Symptom assessment method	Symptoms included in symptomatic case definition	Length of baseline symptom history	Length of symptom follow-up	Tested *n*	Test Specimen and Frequency	PCR+ Cases *n*	Asymptomatic Proportion % (95% CI, *n/N*)	Risk of Bias
Park et al. (2020)	South Korea	General public: mean age 38 (range 20-80); 72% female (620/857 with demographic data)	Surveillance	Exposed to index case(s)	Standardised assessment form based on patient interviews	Unspecified	From date of first symptom onset (if any)	14 days	1143	Nasopharyngeal and oropharyngeal swabs daily. Collection method (self- vs healthcare worker) unspecified	97	4% (2-10%, 4/97)	Low
Arons et al. (2020)	USA	Residents of one nursing home: mean age: 76 ±10; 63% female (48/76)	Serial point prevalence survey	Exposed to index case(s)	Standardised assessment form based on interviews and medical records	Fever, cough, shortness of breath, chills, myalgia, malaise, sore throat, runny nose or congestion, confusion or sleepiness, dizziness, headache, diarrhoea, and nausea and/or vomiting.	Within previous 14 days	7 days	76	Nasopharyngeal and oropharyngeal swabs twice one week apart. Collection method (self- vs healthcare worker) unspecified	47[b]	6% (2-17%, 3/47)	Low

Study	Country	Population	Study design	Exposure	Assessment	Symptoms	Symptom timing	Follow-up	N	Sample collection	n	Secondary attack rate	Risk
Roxby et al. (2020)	USA	Residents of one nursing home: mean age = 86 (range 69-102); 77% female (62/80) Staff of one nursing home: mean age 40 (range 16-70); 72% female (45/62)	Surveillance	Exposed to index case(s)	Standardised assessment form based on patient self-report with or without staff assistance	Fever, cough, and other symptoms inc. sore throat, chills, confusion, body aches, dizziness, malaise, headaches, cough, shortness of breath, and/or diarrhoea	Within previous 14 days	7 days	142	Nasopharyngeal swabs twice one week apart. Collection method (self- vs healthcare worker) unspecified	5	40% (12-77%, 2/5)	Low
Danis et al. (2020)	France	General public (demographic details unknown)	Surveillance	Exposed to index case(s)	Bespoke (to study) assessment forms based on patient interviews	Full list unspecified but included fever, dry cough, wet cough, asthenia/fatigue, chills, sweats, rhinorrhoea, and/or myalgia	From date of first symptom onset (if any)	14 days	11[a]	Nasopharyngeal swabs or endotracheal aspirates daily. Collection method (self- vs healthcare worker) unspecified	6	17% (3-56%, 1/6)	Low
Chau et al. (2020)	Vietnam	General public: median age 29 (range 16-60); 50% female (15/30 with follow-up)	Prospective cohort	Exposed to index case(s) and returning travellers from high-risk areas	Standardised assessment forms based on participant report	Full list unspecified but included fever, cough, rhinorrhoea, fatigue, diarrhoea, sore throat, muscle pain, headache, abdominal pain, and/or lost sense of smell	From date of first symptom onset (if any)	14+ days	14000	Nasopharyngeal swabs daily and saliva at baseline. Collection method (self- vs healthcare worker) unspecified	30[d]	43% (27-61%, 13/30)	Moderate

Study	Country	Population	Design	Exposure	Symptom assessment	Symptoms	Follow-up start	Follow-up duration	N	Testing	n	Proportion asymptomatic	Risk of bias
Luo et al. (2020)	China	General public: median age 38.0 (IQR: 25.0 - 52.0); 50% female (2466/4950)	Prospective cohort	Exposed to index case(s)	Standardised assessment forms from participant self-report	Fever, cough, chill, sputum production, nasal congestion, rhinorrhoea, sore throat, headache, fatigue, myalgia, arthralgia, shortness of breath, difficulty breathing, chest tightness, chest pain, conjunctival congestion, nausea, vomit, diarrhoea, stomach-ache, and/or other	From date of first symptom onset (if any)	Until 2 consecutive negative swabs – up to 30 days	495	Oropharyngeal swabs every two days. Swabbing conducted by public health workers.	129	6% (3-12%, 8/129)	Low
Chaw et al. (2020)	Brunei	General public: median age 33 (IQR = 29.5); 35% female (*n*=25/71) **ᵉ**	Surveillance	Exposed or epidemiological link to outbreak	Digital records on the national health information system database	Fever, cough, runny nose, sore throat	From date of first symptom onset (if any)	14 days	127	Nasopharyngeal swab. Those with positive swab or who developed symptoms re-tested until two consecutive negative tests (for positives) at unreported frequency.	71	13% (7-22%, 9/71)	Low

											Collection method (self- vs healthcare worker) unspecified.			
Graham et al. (2020)	United Kingdom	Residents of four nursing homes: median age 83 (IQR= 15); 62% female (*n*=246/394) [g]	Serial point prevalence survey	Exposed to nursing home outbreak	Case note review and information from medical and nursing team	New fever, cough and/or breathlessness, newly altered mental status or behaviour, anorexia, diarrhoea or vomiting	Within previous 14 days	7 days	313	Nasopharyngeal and oropharyngeal swabs collected at baseline, with previously unavailable or test-negative participants (re)tested one week later. Collected by healthcare workers.	126*	35% (27-44%, 44/126)	Moderate
Wang et al. (2020)	China	General population: mean age 39.3 (SD=16.5); 46% female (*n*=29/63) [h]	Surveillance	Exposed to index case(s)	Medical reports	Full list unspecified but including cough, fever, short of breathless and muscle soreness	From 2 days after exposure event	Until discharge from quarantine (median 10-13 days for those with and without normal chest x-ray respectively	Unclear (only 279 positives reported on)	Nasopharyngeal swabs daily. Collection method (self- vs healthcare worker) unspecified.	279	23% (18-28%, 63/279)	Low
Wu et al. (2020)	China	General population: median age 43.5 (IQR= 35.8-62.3) for secondary cases and 37 (IQR= 14.5-58)	Surveillance	Exposed to index case(s)	Internet-based questionnaires	Fever, cough, shortness of breath, diarrhoea or other common symptoms (including expectoration, haemoptysis, sore throat, nasal	Since exposure event	21 days	143	Nasopharyngeal and/or oropharyngeal swabs (at Day 1, 7, and 14 for asymptomatic cases and up to	48	10% (5-22%, 5/48)	Low

		for non-cases. 56% female *n*=80/143)				obstruction, runny nose, sneeze, headache, muscle ache or fatigue)				3-day intervals if showed symptoms). Collected by healthcare workers.			
Yang et al. (2020)	China	General population: median age 32 (IQR:26-33); 78% female (7/9)[e]	Retrospective cohort	Exposed to confirmed case on flight	Medical records	Full list unspecified but including cough, expectoration, myalgia, headache, sore throat, anorexia, fatigue, diarrhoea, nausea, vomiting, chest distress, and dyspnoea	From date of first symptom onset (if any)	14 days	325	Throat swab at baseline. Subsequent frequency and collection method (self- vs healthcare worker) unspecified.	9 [j]	22% (6-55%, 2/9)	Low
Yousaf et al. (2020)	USA	General population: 35% (69/195) <18 years, 46% (89/195) 18-49 years, 15% (29/195) 50-64 years, 4% (8/195) 65+ years; 51% female (99/195)	Prospective cohort	Household contacts of confirmed case(s)	Standardised questionnaire and symptom diary	Full list unspecified but including fever, chills, myalgia, or fatigue, runny nose, nasal congestion, or sore throat, cough, difficulty breathing, shortness of breath, wheezing, or chest pain, headache, loss of taste, or loss of smell, nausea/vomiting, diarrhoea, and abdominal pain	From date of first symptom onset (if any)	14 days	195	Nasopharyngeal swab on first and last day of study and if new symptoms were reported	47	0% (0-0.08%, 0/9)	Low

Hua et al. (2020)	China	General population: mean age 8.16 (SD: 4.07); 39% female (17/43) [k]; 39% children (<14 years, 325/835), 61% (510/835) adults	Retrospective cohort	Family contacts of confirmed case(s) or returning from high-risk areas	Medical and public health records	Full list unspecified but including fever, cough, stuffy/runny nose, fatigue, diarrhoea, vomiting/abdominal pain, shortness of breath, chest tightness, and headache	Since exposure to index case(s)	Until discharge from quarantine (mean=20.2, SD: 7.9, range 3-32 days)	835	Respiratory specimens. Further details of collection unspecified.	151	12% (8-18%, 18/151)	Low
Lombardi et al. (2020)	Italy	Healthcare workers: mean age 44.5 years; 64% female (1010/1573)	Surveillance	Exposed occupationally to confirmed case(s)	Infectious disease notification form	Fever, cough, dyspnoea, asthenia, myalgia, coryza, sore throat, headache, ageusia or dysgeusia, anosmia or parosmia, ocular symptoms, diarrhoea, nausea, and vomiting	14 days	Until end of study for patients asymptomatic at baseline	1573	Nasopharyngeal swabs at baseline and subsequently for positive cases at unspecified frequency. Collection method (self vs healthcare workers) unspecified.	139	12% (8-19%, 17/139)	Very low
Tabata et al. (2020)	Japan	General population: median age 68 (IQR: 47-75); 48% female (50/104) [e]	Surveillance/ Retrospective cohort	Exposed to confirmed case(s) on cruise ship – whole ship screening	Medical records based on clinical interviews	Unspecified	From beginning of quarantine period	Until discharge or end of study (whichever was earliest); median 10 days (IQR: 7-10)	Unclear for study. 3711 tested on ship but not all isolated in study facility.	Pharyngeal swabs or sputum specimens. Further details of collection unspecified.	104	32% (24-41%, 33/104)	Moderate

Patel et al. (2020)	USA	Residents of one nursing home: median age 82 (IQR: 72-92); 69% female (24/35)	Surveillance	Exposed to nursing home outbreak	Interview by nursing staff	Fever, cough, shortness of breath, hypoxia, sore throat, nasal congestion, diarrhoea, decreased appetite, chills, myalgias, headaches, new onset confusion	From baseline	30 days	118	Nasopharyngeal swab at single time-point. Collected by healthcare workers.	35	37% (23-54%, 13/35)	Low
Hung et al. (2020)	Hong Kong	General population: median age 58 (IQR: 56–61) for positive participants and for negative 64 (IQR: 56–70); 59% female (127/215)	Prospective cohort	Exposed to confirmed case(s) on cruise ship	Questionnaire	Full list unspecified but including chills and rigors, cough, sputum, malaise, myalgia, diarrhoea, rhinorrhoea, and fever	From baseline	14+ days	215	Nasopharyngeal, throat, and rectal swabs at baseline, and Days 4, 8, and 12. Collected by healthcare workers.	9	67% (35-88%, 6/9)	Very low
Kennelley et al. (2020)	Ireland	Residents and staff of 28 nursing homes. Further demographic detail unspecified.	Surveillance	National point-prevalence testing programme for nursing homes	Survey	Cough, fever, dyspnoea, and any new-onset symptoms deemed notable by medical officer/general practitioner	7 days	7 days	2718	Nasopharyngeal swab at single time-point. Further details of collection unspecified.	1374	26% (23-28%, 352/1374)	Low
Starling et al. (2020)	UK	Residents of 15 nursing homes [m]: median age ranged across homes from 36.0-90.5 (range 18-106); sex distribution	Surveillance	Local authority point-prevalence testing programme for nursing homes	Interview with care home managers	New continuous cough or fever	From baseline	14 days	441	Upper respiratory tract specimens at single time-point. Collected by healthcare workers.	23	91% (73-98%, 21/23)	Low

		ranged across homes from 40.0-78.6% female											
Chamie et al. (2020)	USA	General population: 3% 4-10 years (118/3953), 4% 11-17 years (141/3953), 64% 18-50 years (2532/3953), 24% 51-70 years (951/3953); 5% > 70 years (211/3953); 43% female (1699/3953)	Prospective cohort	Resident, bordering, or employed within a local inner-city census-tract area	In-person interview at baseline and follow-up by community team if positive	Unspecified	Unspecified but includes symptoms prior to testing	14 days	3953	Oropharyngeal or mid-turbinate nasal swab at single time-point. Collected by healthcare workers.	80[n]	29% (20-39%, 23/80)	Low
Ladhani et al. (2020)	UK	Residents and staff of 6 nursing homes: median age for positive participants 85 (78-90) for residents and 47 (38-57) for staff; for negative participants 85 (80-91) for residents and 47 (35-56) for staff; 74% female (386/518)	Surveillance	Exposed to nursing home outbreak	Datasheet and daily phone call with research worker	Fever, persistent cough, sore throat, shortness of breath, anosmia, new-onset confusion, reduced alertness, fatigue, lethargy, reduced mobility, diarrhoea	14 days	14 days	518	Nasal swabs at single time-point. Collected by healthcare workers for residents and self-collected by staff.	158	45% (36-54%, 77/158)	Moderate

Table 2 Notes: [a] includes only high-risk contacts isolated and followed-up in France; [b] excludes one case that had history of previous positive test but was negative at facility-wide study testing; [c] excludes one case with negative PCR at baseline and positive PCR at follow-up PCR, as symptom monitoring not possible; [d] not including 19 PCR-positive cases that refused follow-up; [e] demographics only reported for PCR- positive cases; [f] includes one case excluded from present analyses as identified via symptoms and not systematic PCR-testing; [g] only residents included as staff testing was not systematic and was partially based on symptom status; [h] demographics reported for asymptomatic participants only; [i] demographics reported for PCR-positive cases or those with clinical abnormalities only; [j] excludes index case and two PCR-positive case without symptom follow-up; [k] demographics for children only but adults included in clinical outcomes; [l] 8 participants excluded because of insufficient data; [m] staff excluded due to requirement to be 'fit to work' biasing sample towards asymptomatic participants; [n] excluding 3 PCR-positive participants without symptom status classification/follow-up

Table 3. *Reported Findings for Age of Asymptomatic versus Symptomatic Cases*

Study	Sample	Findings
Chau et al. (2020)	General public (contacts of confirmed case or returning travellers)	Median age of asymptomatic versus symptomatic participants: 30 (range 16-60) versus 27 (range 18-58)
Yang et al. (2020)	General public exposed to index case on flight	Median age of asymptomatic and symptomatic participants: 26 (IQR: 25.5-26.5) versus 33 (IQR: 29-45) *note: very small asymptomatic sample (n=2)
Hua et al. (2020)	General public exposed to household cases or returning from high-risk areas	23% of infected children (≤14 years, n=10/43) were asymptomatic versus 7% of infected adults (n=8/108), with children comprising 56% (n= 10/18) of asymptomatic cases and adults 44% (n= 8/18)
Tabata et al. (2020)	General public exposed to outbreak on cruise ship	Median age of asymptomatic versus symptomatic participants: 70 (IQR: 57-75) versus 68 (IQR: 56-74)
Hung et al. (2020)	General public exposed to outbreak on cruise ship	Median age of asymptomatic and symptomatic participants: 57 (IQR: 47–59) versus 68 (IQR: 59–68)
Ladhani et al. (2020)	Nursing home residents and staff	Median age of asymptomatic, post-symptomatic, pre-symptomatic, and symptomatic residents: 84 (IQR: 78-90); 88 (IQR: 85-91); 84 (IQR: 80-91); 87 (IQR: 80-91) Median age of asymptomatic, post-symptomatic, pre-symptomatic, and symptomatic staff: 50 (IQR: 40-56); 54, (41-59); 38 (IQR 34-49); 40 (IQR: 26-55)