

SARS-CoV-2 Seroprevalence Studies: A Rapid Review

Kathryn Chess

Northwestern University Feinberg School of Medicine

Tyler A Jacobson

Northwestern University Feinberg School of Medicine

Lauren E Smith

Northwestern University Feinberg School of Medicine

Corinne Miller

Northwestern University Feinberg School of Medicine

Lisa R Hirschhorn

Northwestern University Feinberg School of Medicine

Mark D Huffman (✉ m-huffman@northwestern.edu)

Northwestern University <https://orcid.org/0000-0001-7412-2519>

Research article

Keywords: Covid-19, SARS-CoV-2, seroprevalence, rapid review

Posted Date: September 18th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-56014/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: During the COVID-19 pandemic, SARS-CoV-2 serology tests have been used to understand the extent to which populations have been infected. The objective of this study was to synthesize literature on SARS-CoV-2 seroprevalence studies, including sampling frames, study characteristics, assay test performance characteristics, and proportion of participants with IgG and IgM SARS-CoV-2 antibodies.

Methods: Bibliometric databases, trial registers, pre-print servers, and grey literature were searched through May 27, 2020 using a published protocol to identify eligible studies. Title and abstract screening and full-text reviewing were performed in duplicate. Study-level data were extracted, and a narrative synthesis was performed.

Results: Of the 4,049 studies screened for inclusion, 27 published reports were included, and 85 studies are ongoing. Most (52%) published reports were available through pre-print servers. Sample sizes ranged from 200 to 113,033 participants. Healthcare worker (n=9 studies, 33%) and non-representative, general population (n=10 studies, 37%) sampling frames were more commonly used than representative, general population sampling frames (n=7, 26%). Mean age ranged from 18 up to 69 years, and the proportion of females ranged from 25% to 85%. Test performance characteristics varied, including IgG sensitivity (range: 63.3% to 100%) and IgG specificity (range: 97.0% to 100%). IgG seroprevalence estimates ranged from 0.5% to 21.0%, and IgM seroprevalence ranged from 1.1% to 18.9%.

Conclusion: More high-quality SARS-CoV-2 seroprevalence studies using validated assays with larger sample sizes from representative and targeted sampling frames are needed to better understand the true burden of disease, differential spread of the virus, and infection fatality rate.

Background

As of July 7, 2020, the World Health Organization (WHO) reported 11,787,953 confirmed cases of COVID-19 and 542,463 deaths globally due to the virus.(1) According to the WHO, these statistics primarily reflect the results of one type of viral surveillance: reverse transcriptase polymerase chain reaction (RT-PCR) tests. Given that RT-PCR test results provide information about active infections, these data may be used to estimate the point prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus infection.(2) Serological testing, which involves detecting the presence or absence of antibodies in serum, can be used to detect past infection, as well as a proportion of active infections, depending on timing and serologic test used. Serological testing is useful for identifying infected individuals who were mildly symptomatic or asymptomatic, those who may not have sought testing during the period of viral shedding, and those who were not able to access diagnostic testing. SARS-CoV-2 seroconversion has been estimated to occur around 13 days after symptom onset, and unlike most other viral antibody responses, IgM and IgG titers to SARS-CoV-2 may be produced nearly simultaneously.(3)(4)

A reliable estimate of community-level seroprevalence of SARS-CoV-2, including among key subgroups such as healthcare workers and other essential workers, is necessary to define the true burden of COVID-

19. These data are also needed to define the SARS-CoV-2 infection fatality rate, which has been widely debated, by identifying individuals with asymptomatic or minimally symptomatic infection who are less likely to receive RT-PCR testing.(5) Moreover, seroprevalence data can aid in assessing equity and effectiveness of policies related to tightening and loosening shelter-in-place orders, lockdown, self-isolation, quarantine, and other physical distancing measures, and public mask use on disease burden. Seroconversion rates and longitudinal data on antibody responses will be needed to understand temporal trends in COVID-19 within and across populations and the length of time that antibodies remain present.

Based on these fundamental epidemiological needs to understand COVID-19, we sought to synthesize all available literature related to SARS-CoV-2 seroprevalence studies, including the populations studied, sampling frames used, assay test performance characteristics, and proportion of participants with IgG and IgM SARS-CoV-2 antibodies through this rapid review.

Methods

The protocol for this rapid review was posted online in April 2020, and its methods are outlined below.(6) The protocol follows recommendations outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)(7) with integration of the principles outlined in the PRISMA Rapid Review Extension Protocol.(8)

Data Sources

The study team included a research librarian (CM) who developed a comprehensive search strategy. The search strategy incorporated keywords and subject headings (when available) for the seroprevalence of SARS-CoV-2, including search terms for COVID-19, as the disease COVID-19 was officially named prior to the naming of the virus SARS-CoV-2. A complete list of search terms used is in the **Supplemental Table 1**. We adapted and performed the search in the following databases: PubMed MEDLINE 1946–, Embase 1947–, Cochrane Library (dates vary), CORD-19 (via Covidex search engine), Google, ClinicalTrials.gov, and Cochrane COVID-19 Study Register. We searched for published reports from November 2019 until the date of the search. We did not apply limits to language or location. We sought to include unpublished and grey literature by searching included pre-print servers, news articles, and clinical trial registries during our search. We reviewed the reference lists of included studies for additional relevant citations. We ran our initial search on April 9, 2020, deduplicated results in Endnote, and uploaded the results into Covidence, an online screening platform. We then ran a secondary, subsequent search on May 27, 2020 using the same approach.

In addition to the articles identified through database searches, the research team also hand-selected articles for inclusion in the rapid review that met our search criteria but were not identified through our database searches.

Study Eligibility

Our eligibility criteria were linked to the research question: What are the methods, results, and potential sources of bias of the subnational, national, and international seroprevalence studies of COVID-19 that have been published to estimate the seroprevalence of SARS-CoV-2? We consequently used the following elements to build our eligibility criteria: Population, Outcomes/Seroprevalence Rates, and Study Design.

Population:

We included surveillance studies that included participants at risk of contracting COVID-19 through any mode of transmission, such as community transmission, work-related exposure, or through contact with a confirmed case. We only included studies with participants who were selected or enrolled in the study from an identifiable sampling frame, including the general population, healthcare workers, patients receiving medical care, and residents of a given location. We relied upon authors' reporting of sampling frames as being representative of the population under study, which included methods such as multi-stage probability sampling, or non-representative, which included methods such as convenience sampling.

Outcomes/Seroprevalence Rates:

We included studies that assessed the seroprevalence of COVID-19 using a serological test administered to study participants.

Study Design:

We included cross-sectional studies, case-control studies, and cohort studies, as well as randomized controlled trials (RCTs) and quasi-experimental RCTs.

Exclusion Criteria

Exclusion criteria consisted of case reports, case series, assay validation studies, and opinion-driven reports (i.e., editorials and letters), and models. We excluded studies published prior to November 2019 and studies with fewer than 100 participants.

Screening and Data Extraction

Two reviewers (KC, TAJ, LES, or MDH) independently screened abstracts, titles, and full texts of retrieved studies in duplicate to identify studies to be evaluated further. Discrepancies were resolved through consensus. One review author (KC, TAJ, or LES) independently extracted data using a structured data extraction form with spot checking by another author (KC, TAJ, or LES). Data extracted from the studies included: publication date, study design, location, setting, sampling frame, sample size, antibody test name, measured seroprevalence, reported IgG and IgM sensitivity and specificity, and measured IgG and IgM titers.

Data Synthesis

We prepared descriptive tables to report the included study characteristics (i.e., with the following data presented for all included studies: authors, location, sampling frame, study design). We report characteristics of the assays used and measured seroprevalence reported in each study. We summarized the findings using a narrative synthesis given the expected heterogeneity across study locations, populations, and assays used.

Results

Included Studies

The flowchart of included studies is reported in the **Supplemental Fig. 1**. We identified 4,321 studies for screening through our search, and 17 additional studies were independently identified through hand searching. After removing duplicates, we screened 4,049 articles, evaluated 234 full reports, pre-prints, and ongoing studies at the full-text stage, and included 27 reports or pre-prints that met eligibility criteria. We also identified 85 ongoing studies listed whose titles and characteristics are listed **Supplemental Table 2 and Supplemental Table 3**.

Characteristics of Included Studies

The characteristics of the included studies are shown in Table 1. At the time of the search, 14 of the articles were in the pre-print stage, 12 articles were full reports, and 1 article was a published protocol. Nearly all (n = 26 studies, 96%) were cross-sectional study designs, and 1 study (4%) used a longitudinal cohort design. Seven (26%) studies were performed in the United States, 4 (15%) in China, 1 (4%) in Iran, 1 (4%) in Japan, and the remaining 14 (52%) studies were conducted in European countries (Spain, Denmark, Luxemburg, Switzerland, Belgium, Germany, Italy, Scotland, France, and the Czech Republic). No published studies were reported from lower-middle- or low-income countries. Among 85 ongoing studies identified from 22 countries, only 3 (4%) studies were from 2 upper-middle-income countries (Brazil [n = 2 studies], China [n = 1 study]), 3 (4%) studies were 2 lower-middle-income countries (Egypt [n = 2 studies], India [n = 1 study]), and none (0%) were from low-income countries.

Healthcare workers (n = 9 studies, 33%) and non-representative, general population (n = 11 studies, 41%) samples were the most commonly used sampling frames. Representative samples of the general population (n = 7, 26%) and close contacts of RT-PCR-confirmed COVID-19 patients (n = 4, 15%) were also used. The sample size in the included studies ranged from 200 to 113,033 participants. The reported mean or median age ranged from 18 years in a non-representative, general population sample study from France(9) to 60–69 years in a non-representative, general population sample study from Japan.(10) The proportion of females in each study ranged from 25% in a non-representative, general population sample in Italy(11) to 85% in a healthcare worker study in Germany.(12)

Assay Characteristics

Results of reported assay characteristics are shown in Table 2. Of the 27 included studies, 15 (56%) reported IgG sensitivity of the assay used for serological testing, which ranged from 63.3–100%. Sixteen

(59%) studies reported the IgG specificity of the assays used for serological testing, which ranged from 97.0–100%. Fifteen (56%) studies reported both IgG sensitivity and IgG specificity of the assays used for serological testing. The sensitivity (n = 9 studies, 33%) and specificity (n = 10 studies, 37%) of IgM assays had similar ranges compared to the IgG assays. Nine (33%) studies reported both IgM sensitivity and IgM specificity of the assays used for serological testing. Nine (33%) studies reported both IgG and IgM sensitivity and specificity of the assays used for serological testing. While some studies (n = 6, 22%) reported the optical density ratio used to define the cutoff value for negative, borderline, or positive serological assay results, no study reported measured IgG or IgM titers within its study sample in the presence of a positive or negative test result. One study (4%) evaluated neutralizing antibodies and reported concordance between the assay used to detect neutralizing antibodies and the detection of anti-spike IgG antibody by enzyme-linked immunosorbent assay (ELISA) but did not specify the sensitivity nor specificity of the assay used.(13)

Measured Seroprevalence

The proportions of study samples that were positive for IgG and IgM titer are reported in Table 3. Overall, 22 (81%) studies reported the proportion of participants who tested positive for IgG titers, and 11 (41%) studies reported the proportion of participants who tested positive for IgM titers. The proportion of participants who tested positive for IgG titers ranged from 0.5% for a study using non-representative (convenience) sampling of 10,449 members of the general population in 3 Chinese cities (Wuhan, Chengdu, and Guangzhou), including hotel staff, healthcare workers' relatives, community residents, and factory workers,(14) to 36.1% in a small study with a non-representative (convenience), general population sample of 202 participants in Chicago, United States using an IgG dried blood spot assay.(15) This estimate includes individuals classified as high seropositive (n = 33, 16%) and individuals classified as low seropositive (n = 40, 20%). The highest proportion of participants who tested positive for IgG titers amongst studies reporting an aggregate IgG seropositivity rate was 21.0% in a representative, general population study with 528 participants from the Guilan Province in Iran.(16)

Of the 11 (41%) studies that reported the proportion of study participants that tested positive for IgM SARS-CoV-2 titers, the reported proportions ranged from 0.6% in a study of 1,000 blood donors in Scotland(13) to 32.0% in a study with a non-representative, general population sample of 200 participants from Chelsea, Massachusetts in the United States.(17) The studies on the ends of this range reported aggregate proportions of patients who tested positive for IgG titers, IgM titers, or both titers rather than separately. The lowest proportion of study participants that tested positive for IgM titers amongst studies reporting IgM specifically was derived from a sample of 525 healthcare workers in Bari, Italy (1.1%).(18) The highest proportion of study participants that tested positive for IgM titers amongst studies reporting IgM specifically was from a representative sample of the general population containing 528 participants in the Guilan Province in Iran (18.9%).(16)

One study (4%) evaluated neutralizing antibodies and detected these antibodies in 1% (5/500) of the study sample.(13)

Discussion

This rapid review summarizes the methods, sampling frames, results, and potential sources of bias of the subnational, national, and international serology studies that have been used to estimate the seroprevalence of SARS-CoV-2. Our review builds on a previously published seroprevalence review(19) by using a more comprehensive search strategy that identified more published studies, as well as pre-prints and ongoing studies. In accordance with prior work,(19) we found substantial diversity in seroprevalence study characteristics, including their sampling frames, assay sensitivity and specificity, and study locations. For example, most studies (n = 20, 77%) derived seroprevalence estimates from a single sampling frame, such as healthcare workers or close contacts of patients with RT-PCR-confirmed COVID-19. Few studies were able to provide reliable and precise estimates of the burden of COVID-19: only 7 studies (26%) used representative sampling frames of the general population, and only 9 studies (33%) had samples of 1,000 participants or more. Most studies recruited participants whose mean age was < 65 years old, despite the predominance of non-representative sampling frames and higher risk of COVID-19-related complications among older adults. There were also very limited reports of studies or ongoing studies from middle-income countries, and none from low-income countries despite an increasing burden of disease in these large populations.(1) The lone study from the Guilan Province in Iran, an upper-middle-income country with an early onset of the pandemic, had the highest reported seroprevalence estimate (21%, n = 528) among studies that used a representative, general population sampling frame, though the study's relatively small sample size limits the precision of this estimate (calculated 95% Confidence Intervals: 18–25%).

These overall results suggest that both representative and more targeted studies, stratified by participants' risk of exposure, geography, and symptomology, with larger sample sizes across more countries, are needed to more accurately estimate SARS-CoV-2 seroprevalence, differential spread of the virus across groups, and infection fatality rate. These findings will prove useful to inform future policy creation and implementation. Researchers and health departments should focus on integrating biospecimen collection into demographic health surveys and routine blood tests at the state or county level to obtain sufficient sample sizes for generalizability at the local or regional levels.(20) To collect representative samples, investigators will need to use household enumeration data to identify eligible participants and adapt testing at sites that are convenient and safe for local community members, such as parks, libraries, schools, or community centers. Home-based, dried-blood-spot (DBS) assays may also be used for data collection either by the individual or community health workers for either targeted or population representative sampling.(21) Researchers and national health statistics agencies should leverage existing infrastructure for population surveillance, such as national census and demographic health surveys where blood tests are already integrated, given the importance and urgency in ascertaining the true COVID-19 seroprevalence across and between regions and populations.(20)

To derive a more complete picture of individuals' immune response to SARS-CoV-2, future research should also characterize lasting T cell responses in parallel to serological responses. Early evidence suggests that SARS-recovered patients can possess long-lasting memory T cells reactive to SARS-CoV-2

Nucleocapsid protein and that SARS-CoV-2 specific T cells may be detected in individuals with no known history of SARS, COVID-19, or contact with SARS or COVID-19 patients.(22) Likewise, only 1 study was identified that evaluated seroprevalence of neutralizing antibodies; therefore, further research is needed to understand the prevalence and importance of neutralizing antibody seroprevalence estimates compared with other antibody assay types. Results from such studies may shift management strategies for the pandemic by impacting forecasts about patients' susceptibility to SARS-CoV-2 infection from serosurveys.

Similarly, when considering how to generate more accurate forecasts of future SARS-CoV-2 pandemic curves, these findings suggest the potential utility of additional longitudinal cohort studies using quantitative assays. These studies are needed to explore the effects of containment measures and to understand the degree to which SARS-CoV-2 antibodies confer protective immunity, at what antibody threshold, and for how long. For example, some evidence suggests that asymptomatic individuals have waning levels of antibodies or may become seronegative over time.(23)

To achieve more accurate seroprevalence estimates, more studies using assays with high diagnostic accuracy, including high IgM and IgG sensitivity and specificity, are also needed. More high quality, independently-conducted validation studies assessing the diagnostic accuracy of these assays is also urgently needed.(24)

This review has potential limitations. First, there is a rapid influx of new information related to SARS-CoV-2 serology studies. It is possible that some published or ongoing studies may not have been included in this review. However, we used a comprehensive search strategy and identified 85 ongoing studies, the results of which may be included in future updates to this review. Second, data from this review include studies that were published on pre-print servers and have not undergone peer review. Thus, estimates from these reports may change. Third, epidemiological studies are often not prospectively registered, so this review may underestimate the number of ongoing studies and may not fully represent the characteristics of such ongoing studies, including study design, sampling frame, and sample size.

Conclusion

More high-quality SARS-CoV-2 serology studies using validated assays with larger sample sizes from representative as well as targeted sampling frames are needed to better understand the true burden of disease, differential spread of the virus, and infection fatality rate. Longitudinal data are also needed to understand temporal trends in seroprevalence, to evaluate the effectiveness of containment measures, and to perform more accurate pandemic forecasts. Given the need for rapid, reliable, and precise estimates of SARS-CoV-2 seroprevalence, such data collection should be integrated within the infrastructure of existing population health surveillance systems.

Abbreviations

ELISA: enzyme-linked immunosorbent assay

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RCTs: randomized controlled trials

RT-PCR: reverse transcriptase polymerase chain reaction

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

WHO: World Health Organization

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors' contributions

CM developed the database search strategy used for this review. KC, TAJ, LES, and MDH screened the abstracts, titles, and full texts of retrieved studies in duplicate to identify studies to be evaluated further. KC, TAJ, and LES independently extracted data from included studies using a structured data extraction form. KC was a major contributor in writing the manuscript. TAJ, LES, MDH, and LH all provided substantial edits and comments on the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

References

1. World Health O. Coronavirus disease (COVID-19): situation report, 169. Geneva: World Health Organization; 2020 2020-07-07.
2. Hadaya J, Schumm M, Livingston EH. Testing Individuals for Coronavirus Disease 2019 (COVID-19). *JAMA*. 2020;323(19):1981-.
3. Long Q-X, Liu B-Z, Deng H-J, Wu G-C, Deng K, Chen Y-K, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. *Nature Medicine*. 2020;26(6):845-8.
4. Interim Guidelines for COVID-19 Antibody Testing: Centers for Disease Control and Prevention; 2020 [Available from: <https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html>].
5. Bryant JE, Azman AS, Ferrari MJ, Arnold BF, Boni MF, Boum Y, et al. Serology for SARS-CoV-2: Apprehensions, opportunities, and the path forward. *Science Immunology*. 2020;5(47):eabc6347.
6. Chess K, Hirschhorn LR, Huffman MD. SARS-CoV-2 Serology Studies: A Rapid Review Proposal. DigitalHub. Galter Health Sciences Library & Learning Center; 2020.
7. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009;339:b2535.
8. Stevens A, Garritty C, Hersi M, Moher D. Developing PRISMA-RR, a reporting guideline for rapid reviews of primary studies (Protocol). 2018.
9. Grzelak L, Temmam S, Planchais C, Demeret C, Huon C, Guivel F, et al. SARS-CoV-2 serological analysis of COVID-19 hospitalized patients, pauci-symptomatic individuals and blood donors. *medRxiv*. 2020:2020.04.21.20068858.
10. Doi A, Iwata K, Kuroda H, Hasuike T, Nasu S, Kanda A, et al. Estimation of seroprevalence of novel coronavirus disease (COVID-19) using preserved serum at an outpatient setting in Kobe, Japan: A cross-sectional study. *medRxiv*. 2020:2020.04.26.20079822.
11. Valenti L, Bergna A, Pelusi S, Facciotti F, Lai A, Tarkowski M, et al. SARS-CoV-2 seroprevalence trends in healthy blood donors during the COVID-19 Milan outbreak. *medRxiv*. 2020:2020.05.11.20098442.
12. Brandstetter S, Roth S, Harner S, Buntrock-Döpke H, Toncheva AA, Borchers N, et al. Symptoms and immunoglobulin development in hospital staff exposed to a SARS-CoV-2 outbreak. *Pediatric Allergy and Immunology*.n/a(n/a).
13. Thompson C, Grayson N, Paton R, Lourenço J, Penman B, Lee LN, et al. Neutralising antibodies to SARS coronavirus 2 in Scottish blood donors - a pilot study of the value of serology to determine population exposure. *medRxiv*. 2020:2020.04.13.20060467.
14. Xu X, Sun J, Nie S, Li H, Kong Y, Liang M, et al. Seroprevalence of immunoglobulin M and G antibodies against SARS-CoV-2 in China. *Nature Medicine*. 2020.
15. McDade TW, McNally E, Zelikovich A, D'Aquila R, Mustanski B, Miller A, et al. High seroprevalence for SARS-CoV-2 among household members of essential workers detected using a dried blood spot assay. *medRxiv*. 2020:2020.06.01.20119602.

16. Shakiba M, Hashemi Nazari SS, Mehrabian F, Rezvani SM, Ghasempour Z, Heidarzadeh A. Seroprevalence of COVID-19 virus infection in Guilan province, Iran. medRxiv. 2020:2020.04.26.20079244.
17. Saltzman J. Nearly a third of 200 blood samples taken in Chelsea show exposure to coronavirus. The Boston Globe. 2020.
18. Paradiso AV, De Summa s, Silvestris N, Tommasi S, Tufaro A, De Palma G, et al. RAPID SEROLOGICAL TESTS HAVE A ROLE IN ASYMPTOMATIC HEALTH WORKERS COVID-19 SCREENING. medRxiv. 2020:2020.04.15.20057786.
19. Bobrovitz N, Arora RK, Yan T, Rahim H, Duarte N, Boucher E, et al. Lessons from a rapid systematic review of early SARS-CoV-2 serosurveys. medRxiv. 2020:2020.05.10.20097451.
20. Subramanian SV, James KS. Use of the Demographic and Health Survey framework as a population surveillance strategy for COVID-19. Lancet Glob Health. 2020;8(7):e895-e.
21. McDade TW, McNally E, D'Aquila RT, Mustanski B, Miller A, Vaught L, et al. Enzyme immunoassay for SARS-CoV-2 antibodies in dried blood spot samples: A minimally-invasive approach to facilitate community- and population-based screening. medRxiv. 2020:2020.04.28.20081844.
22. Le Bert N, Tan AT, Kunasegaran K, Tham CYL, Hafezi M, Chia A, et al. SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls. Nature. 2020.
23. Long Q-X, Tang X-J, Shi Q-L, Li Q, Deng H-J, Yuan J, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. Nature Medicine. 2020.
24. Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Spijker R, Taylor-Phillips S, et al. Antibody tests for identification of current and past infection with SARS-CoV-2. Cochrane Database of Systematic Reviews. 2020(6).
25. Garcia-Basteiro AL, Moncunill G, Tortajada M, Vidal M, Guinovart C, Jimenez A, et al. Seroprevalence of antibodies against SARS-CoV-2 among health care workers in a large Spanish reference hospital. medRxiv. 2020:2020.04.27.20082289.
26. Korth J, Wilde B, Dolff S, Anastasiou OE, Krawczyk A, Jahn M, et al. SARS-CoV-2-specific antibody detection in healthcare workers in Germany with direct contact to COVID-19 patients. J Clin Virol. 2020;128:104437-.
27. Madsen T, Levin N, Niehus K, Law K, Mayer J, Chapman M, et al. Prevalence of IgG antibodies to SARS-CoV-2 among emergency department employees. Am J Emerg Med. 2020:S0735-6757(20)30306-5.
28. Steensels D, Oris E, Coninx L, Nuyens D, Delforge M-L, Vermeersch P, et al. Hospital-Wide SARS-CoV-2 Antibody Screening in 3056 Staff in a Tertiary Center in Belgium. JAMA. 2020;324(2):195-7.
29. Bendavid E, Mulaney B, Sood N, Shah S, Ling E, Bromley-Dulfano R, et al. COVID-19 Antibody Seroprevalence in Santa Clara County, California. medRxiv. 2020:2020.04.14.20062463.
30. de Lusignan S, Lopez Bernal J, Zambon M, Akinyemi O, Amirthalingam G, Andrews N, et al. Emergence of a Novel Coronavirus (COVID-19): Protocol for Extending Surveillance Used by the

- Royal College of General Practitioners Research and Surveillance Centre and Public Health England. *JMIR Public Health Surveill.* 2020;6(2):e18606.
31. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, Oteo J, Hernán MA, Pérez-Olmeda M, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *The Lancet.*
 32. Snoeck CJ, Vaillant M, Abdelrahman T, Satagopam VP, Turner JD, Beaumont K, et al. Prevalence of SARS-CoV-2 infection in the Luxembourgish population: the CON-VINCE study. *medRxiv.* 2020:2020.05.11.20092916.
 33. Sood N, Simon P, Ebner P, Eichner D, Reynolds J, Bendavid E, et al. Seroprevalence of SARS-CoV-2–Specific Antibodies Among Adults in Los Angeles County, California, on April 10-11, 2020. *JAMA.* 2020;323(23):2425-7.
 34. Stringhini S, Wisniak A, Piumatti G, Azman AS, Lauer SA, Baysson H, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study. *The Lancet.*
 35. Bryan A, Pepper G, Wener MH, Fink SL, Morishima C, Chaudhary A, et al. Performance Characteristics of the Abbott Architect SARS-CoV-2 IgG Assay and Seroprevalence in Boise, Idaho. *Journal of Clinical Microbiology.* 2020:JCM.00941-20.
 36. Erikstrup C, Hother CE, Pedersen OBV, Mølbak K, Skov RL, Holm DK, et al. Estimation of SARS-CoV-2 infection fatality rate by real-time antibody screening of blood donors. *medRxiv.* 2020:2020.04.24.20075291.
 37. Havers FP, Reed C, Lim TW, Montgomery JM, Klena JD, Hall AJ, et al. Seroprevalence of Antibodies to SARS-CoV-2 in Six Sites in the United States, March 23-May 3, 2020. *medRxiv.* 2020:2020.06.25.20140384.
 38. Krátká Z, Luxová Š, Malíčková K, Fürst T, Šimková H. Testing for COVID-19: a few points to remember. *Cas Lek Cesk.* 2020;159(2):72-7.
 39. Zhao R, Li M, Song H, Chen J, Ren W, Feng Y, et al. Early detection of SARS-CoV-2 antibodies in COVID-19 patients as a serologic marker of infection. *Clinical Infectious Diseases.* 2020.
 40. Long Q-x, Deng H-j, Chen J, Hu J, Liu B-z, Liao P, et al. Antibody responses to SARS-CoV-2 in COVID-19 patients: the perspective application of serological tests in clinical practice. *medRxiv.* 2020:2020.03.18.20038018.
 41. Zhang J, Liu J, Li N, Liu Y, Ye R, Qin X, et al. Serological detection of 2019-nCoV respond to the epidemic: A useful complement to nucleic acid testing. *medRxiv.* 2020:2020.03.04.20030916.

Tables

Table 1
Characteristics of Included Studies.

Study ID	Country	Publication Date	Article Type	Sample size	Mean (SD) or median (IQR) age or age range, years	Female, %
Sample: Healthcare workers (HCW)						
Brandsetter 2020(12)	Germany	May 2020	Full report	201	18–65*	85.1%
Garcia-Basteiro 2020(25)	Spain	May 2020	Pre-print	578	42.1 ± 11.6	72.1%
Korth 2020(26)	Germany	May 2020	Full report	316	High-risk HCW: 36.7 ± 10.7; Low-risk HCW: 42.3 ± 13.2	65.0%
Madsen 2020(27)	USA	May 2020	Full report	279	NR	NR
Paradiso 2020(18)	Italy	Apr 2020	Pre-print	525	48 (20–73)*	62.1%
Steensels 2020(28)	Belgium	June 2020	Full report	3,056	IgG positive: 39.5 ± 13.1; IgG negative: 41.3 ± 12.4	IgG positive: 81.0%; IgG negative: 79.0%
Sample: Representative selection from the general population						
Bendavid 2020(29)	USA	Apr 2020	Pre-print	3,330	NR	63.1%
de Lusignan 2020(30)	England	Apr 2020	Protocol	1,000 at baseline, then 800 monthly	NR	NR
Pollan 2020(31)	Spain	July 2020	Full report	113,033	35–49†	52.1%
Shakiba 2020(16)	Iran	May 2020	Pre-print	528	18–60†	51.0%
Snoeck 2020(32)	Luxemburg	May 2020	Pre-print	1,862	47 ± 15	50.1%

*=interquartile range (IQR) not reported, total range provided, †=median reported, NR = not reported

Study ID	Country	Publication Date	Article Type	Sample size	Mean (SD) or median (IQR) age or age range, years	Female, %
Sood 2020(33)	USA	May 2020	Full report	863	55% aged 35–54	60.0%
Stringhini 2020(34)	Switzerland	June 2020	Full report	2,766	5–65+*	52.6%
Sample: Non-representative sample from the general population						
Bryan 2020(35)	USA	May 2020	Full report	4,856	40–49†	54.2%
Doi 2020(10)	Japan	May 2020	Pre-print	1,000	60–69†	51.0%
Erikstrup 2020(36)	Denmark	Apr 2020	Pre-print	9,496	40–49†	50.7%
Grzelak 2020(9)	France	Apr 2020	Full report	409	18†(NR)	65.0%
Havers 2020(37)	USA	June 2020	Pre-print	11,933	NR (50–64)	55.7%
Iafrate 2020(17)	USA	Apr 2020	Pre-print	200	NR	NR
McDade(15)	USA	June 2020	Pre-print	202	37	50.0%
Thompson 2020(13)	Scotland	Apr 2020	Pre-print	1,000	NR	NR
Valenti 2020(11)	Italy	May 2020	Pre-print	789	IgG/IgM positive: 42.6 ± 13.4; IgG/IgM negative: 40.7 ± 13.2	IgG/IgM positive: 25.0%; IgG/IgM negative: 35.6%
Sample: HCW and close contacts to patients with COVID-19						
Krátká 2020(38)	Czech Republic	Apr 2020	Full report	269	46 (21–71)*	59.5%
Zhao 2020(39)	China	May 2020	Full-report	281	NR	NR
Sample: Close contacts to patients with COVID-19 and patients with suspected COVID-19						

*=interquartile range (IQR) not reported, total range provided, †=median reported, NR = not reported

Study ID	Country	Publication Date	Article Type	Sample size	Mean (SD) or median (IQR) age or age range, years	Female, %
Long 2020(40)	China	Mar 2020	Pre-print	216	NR	NR
Sample: HCW, patients without COVID-19, non-representative sample from the general population						
Xu 2020(14)	China	Mar 2020	Full report	17,368	HCW and patients: 41 (31–56); Community: 50 (35–49)	HCW and patients: 63.1%; Community: 51.9%
Sample: Patients with COVID-19, patients without COVID-19, non-representative sample from the general population						
Zhang 2020(41)	China	Mar 2020	Pre-print	736	NR	63.0%
*=interquartile range (IQR) not reported, total range provided, †=median reported, NR = not reported						

Table 2
SARS-CoV-2 Serological Assay Test Performance Characteristics.

Study ID	Reported Assay IgG Sensitivity	Reported Assay IgG Specificity	Reported Assay IgM Sensitivity	Reported Assay IgM Specificity
Bendavid 2020	82.8%	99.5%	82.8%	99.5%
Brandsetter 2020	NR	NR	NR	NR
Bryan 2020	100.0%	99.9%	NR	NR
de Lusignan 2020	NR	NR	NR	NR
Doi 2020	NR	NR	NR	NR
Erikstrup 2020	82.6%	99.5%	82.6%	99.5%
Garcia-Basteiro 2020	97.0%	100.0%	75.0%	100.0%
Grzelak 2020	NR	NR	NR	NR
Havers 2020	96.0%	99.3%	NR	NR
Iafrate 2020	NR	NR	NR	NR
Korth 2020	NR	NR	NR	NR
Krátká 2020	100.0%	99.0%	NR	NR
Long 2020	NR	NR	NR	NR
Madsen 2020	95.4%	98.3%	NR	NR
McDade 2020	NR	NR	NR	NR
Paradiso 2020	NR	NR	NR	NR

NR = not reported

Study ID	Reported Assay IgG Sensitivity	Reported Assay IgG Specificity	Reported Assay IgM Sensitivity	Reported Assay IgM Specificity
Pollan 2020	Point-of-care: 97.2%; Chemiluminescent immunoassay: 100.0%	Point-of-care: 100.0%; Chemiluminescent immunoassay: 99.6%	Point-of-care: 87.9%	Point-of-care: 100.0%
Shakiba 2020	63.3%	100.0%	63.3%	100.0%
Snoeck 2020	85.7%	97.8%	NR	NR
Sood 2020	82.7%	99.5%	82.7%	99.5%
Steensels 2020	92.2%	97.0%	NR	NR
Stringhini 2020	93.0%	100.0%	NR	NR
Thompson 2020	97.1%	98.7%	97.1%	98.7%
Valenti 2020	100.0%	98.0%	85.0%	96.0%
Xu 2020	NR	99.3%	NR	100.0%
Zhang 2020	100.0%	99.0%	100.0%	98.5%
Zhao 2020	NR	NR	NR	NR
NR = not reported				

Table 3
Proportions of Study Samples Who Tested Positive for IgG and IgM Titers.

Study ID	IgG Positive Proportion	IgM Positive Proportion
Sample: Healthcare workers (HCW)		
Brandsetter 2020	36/201 (17.6%)	NR
Garcia-Basteiro 2020	44/578 (7.6%)	36/578 (6.2%)
Korth 2020	5/316 (1.6%)	NR
Madsen 2020	16/270 (5.9%)	NR
Paradiso 2020	NR	6/525 (1.1%)
Steensels 2020	197/3056 (6.4%)	NR
Sample: Representative selection from the general population		
Bendavid 2020	50/3330* (1.5%)	50/3330* (1.5%)
de Lusignan 2020	NR	NR
Pollan 2020	5,444/113,033 (4.8%)	NR
Shakiba 2020	111/528 (21.0%)	100/528 (18.9%)
Snoeck 2020	35/1,862 (1.9%)	NR
Sood 2020	35/836* (4.2%)	35/836* (4.2%)
Stringhini 2020	219/2,766 (7.9%)	NR
Sample: Non-representative sample from the general population		
Bryan 2020	87/4,856 (1.8%)	NR
Doi 2020	33/1,000 (3.3%)	NR
Erikstrup 2020	NR	63/9,496 (1.8%)
Grzelak 2020	NR	NR
Havers 2020	386/11933* (3.2%)	NR
Iafrate 2020	64/200* (32.0%)	64/200* (32.0%)
McDade 2020	73/202 (36.1%)	NR
Thompson 2020†	6/1000* (0.6%)	6/1000* (0.6%)
Valenti 2020	40/789* (5.1%)	40/789* (5.1%)

*=study reports a combined proportion for testing positive for IgM and/or IgG titers, †=study evaluated neutralizing antibodies, NR = not reported

Study ID	IgG Positive Proportion	IgM Positive Proportion
Sample: HCW and close contacts to patients with COVID-19		
Krátká 2020	5/269 (0.8%)	NR
Zhao 2020	29/281* (10.3%)	29/281* (10.3%)
Sample: Close contacts to patients with COVID-19 and patients with suspected COVID-19		
Long 2020	Close contacts: 23/164* (14.0%); Patients: 3/52 (5.8%)*	Close contacts: 23/164* (14.0%); Patients: 3/52 (5.8%)*
Sample: HCW, patients without COVID-19, non-representative sample from the general population		
Xu 2020	HCW and patients: 141/6,919 (2.0%) Community: 48/10,449 (0.5%)	NR
Sample: Patients with COVID-19, patients without COVID-19, non-representative sample from the general population		
Zhang 2020	NR	NR
* = study reports a combined proportion for testing positive for IgM and/or IgG titers, † = study evaluated neutralizing antibodies, NR = not reported		

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [APPENDIX.docx](#)
- [PRISMA2009checklistSARSCoV2seroprevalenceRR.doc](#)