Rapid Evidence Product

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Antibody Response Following SARS-CoV-2 Infection and Implications for Immunity: A Rapid Living Review

Contents

Background and Purpose

As Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) antibody tests become widely available, clinicians and patients have questions about their interpretation and clinical use. Who should receive an antibody test and when is this testing clinically indicated? Does antibody testing provide information about reinfection risk among individuals who have recovered from COVID-19 (the disease caused by SARS-CoV-2)? For patients with detectable antibodies, should testing be repeated periodically to monitor the durability of their antibody response?

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For clinicians to properly use and interpret SARS-CoV-2 serologic tests, up-to-date guidance is needed. Understanding how to interpret antibody testing and whether past infection protects against future infection is also necessary to develop successful public health interventions to reduce disease spread. Interpreting positive antibody test results as indicative of immunity (i.e., protection from reinfection or disease), without understanding the degree of protection conferred by antibodies, could be harmful if positive antibody results lead individuals to stop recommended practices such as wearing masks and social distancing. Guidelines from the Centers for Disease Control and Prevention (CDC)[1] and the Infectious Diseases Society of America (IDSA)[2] do not currently recommend antibody testing to help guide individual healthcare decisions; rather, antibody testing is only recommended for community seroprevalence surveys and in select cases to confirm SARS-CoV-2 infection.

While antibody presence is popularly equated with immunity, the actual relationship between antibodies and immunity varies among viral diseases. Reinfection frequently occurs with human coronaviruses that cause the common cold (hCoV-229N, hCoV-NL63, and hCoV-OC43), even though infection with these coronaviruses generates a host antibody response. For these coronaviruses, reinfection risk may be related to insufficient quantity or persistence of antibodies, insufficient antibodies at the site of infection, or frequent viral mutations that render host antibodies ineffective (similar to seasonal influenza).[3,4] Because SARS-CoV has not reemerged since 2004, and MERS-CoV cases remain sporadic, experience from these two prior coronavirus outbreaks provides minimal insight into the reinfection risk with SARS-CoV-2.

Documented cases of SARS-CoV-2 reinfection have been relatively rare compared with the overall number of new COVID-19 cases worldwide.[5] Case reports have generated speculation regarding the role of antibodies in the risk and severity of reinfection but have not demonstrated clear trends. While case reports and small case series are helpful to generate hypotheses regarding reinfection risk in SARS-CoV-2, larger studies that follow patients over time are needed to provide estimates of reinfection risk. For example, longitudinal studies of recovered COVID-19 patients or large prospective electronic health record database studies of infection rates among patients with and without prior COVID-19 and with and without antibodies could improve understanding of whether antibodies confer protective immunity.

The aims of this rapid systematic review are to synthesize evidence on the prevalence, levels, and durability of the antibody response to SARS-CoV-2 infection among adults and how antibodies correlate with protective immunity. Given the rapidly evolving evidence within this field, the Agency for Healthcare Research and Quality's Evidence-based Practice Center (AHRQ EPC) Program will maintain this report as a living review with planned ongoing literature surveillance and critical appraisal. We will provide regular report updates as additional evidence becomes available, modifying the scope of the review as new directions in SARS-CoV-2 immunity research emerge. This review was conducted in coordination with the American College of Physicians (ACP) as part of AHRQ's standing work to provide health professional organizations and systems with evidence reviews to support the development of clinical guidance for their clinician members.

Key Questions

1. What is the prevalence, level, and durability of detectable anti-SARS-CoV-2 antibodies among adults infected with or recovered from reverse transcription polymerase chain reaction (RT-PCR) -diagnosed SARS-CoV-2 infection?
    a. Do the levels and durability of detectable antibodies vary by patient characteristics (e.g., age, sex, race/ethnicity, and comorbidities), COVID-19 severity, presence of symptoms, time from symptom onset, or as measured by different types of immunoassays (e.g., immunoassay sensitivity/specificity)?
2. Do anti-SARS-CoV-2 antibodies confer natural immunity against reinfection?
    a. Does conferred immunity vary by factors such as initial antibody levels, patient characteristics, presence of symptoms, or severity of disease?

    b. Is there a threshold level of detectable anti-SARS-CoV-2 antibodies necessary to confer natural immunity, and if so, does this threshold vary by patient characteristics (e.g., age, sex, race/ethnicity, and comorbidities)?
3. If anti-SARS-CoV-2 antibodies confer natural immunity against reinfection, how long does this immunity last?
    a. Does immunity vary by factors such as initial antibody levels, patient characteristics, presence of symptoms, or severity of disease?
4. What are the unintended consequences of antibody testing after SARS-CoV-2 infection?

Evidence Summary

Characteristics of the Antibody Response to SARS-CoV-2 Infection

- Evidence suggests that the majority of adults develop detectable levels of immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies following infection with SARS-CoV-2 (moderate strength of evidence* [SoE]).
- IgM levels peak approximately 20 days after symptom onset or RT-PCR diagnosis and subsequently decline. IgG levels peak approximately 25 days after symptom onset or RT-PCR diagnosis and may remain detectable for at least 120 days (moderate SoE*).
- Almost all adults develop neutralizing antibodies in response to SARS-CoV-2 infection, and these antibodies may remain detectable for at least 152 days (low SoE*).
- A small percentage of people do not develop antibodies in response to SARS-CoV-2 infection for reasons that are largely unclear but may be related to less severe disease or absence of symptoms.
- Antibody prevalence does not appear to vary by age or sex, but older age may be associated with higher antibody levels (low SoE*). Non-White race may be associated with higher antibody prevalence and levels (low SoE*). COVID-19 severity and presence of symptoms may also be associated with higher antibody prevalence or levels (low SoE*). More evidence is needed to draw stronger conclusions regarding how the antibody response varies by patient characteristics and disease factors.
- Studies to date have not established the relationship between the development of antibodies after RT-PCR-diagnosed SARS-CoV-2 infection and the risk of reinfection. Studies based on index serologic testing suggest that the presence of antibodies is associated with a lower risk of a subsequent positive SARS-CoV-2 RT-PCR test.

*Strength of evidence (SoE) ratings are based on criteria that assess methodologic study quality, how directly studies evaluated the outcomes of interest, precision of effect estimates, and the consistency of findings across studies. See the Methods section and Appendixes D–E for more detail.

Methods

This review followed standard methods and guidelines for conducting and reporting of systematic reviews.[6,7] The review protocol was developed with input from ACP and AHRQ staff and was publicly posted on the AHRQ Effective Health Care (EHC) Program website.[8] The protocol is also registered with PROSPERO International Prospective Register of Systematic Reviews (registration number CRD42020207098).[9]

Data Sources and Searches

A research librarian conducted a search for English-language articles in the following databases: Ovid MEDLINE ALL, Elsevier Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index to Nursing and Allied Health Literature (CINAHL), ClinicalTrials.gov, WHO COVID, and COVID19reviews.org. The original search was conducted from January 1 to August 5, 2020. Later hand-searching of relevant citations revealed gaps in the search strategies as written for MEDLINE ALL, Embase, CENTRAL, and CINAHL and these search strategies were revised for an updated search that captured citations from January 1 to December 15, 2020. The revised and original search strategies are available in Appendix A, which also includes more information about changes made for the updated search. The search was limited to peer-reviewed publications and excluded studies published only in preprint (not peer-reviewed) databases.

Study Selection

We included studies of adults (18 years or older) with RT-PCR-diagnosed SARS-CoV-2 infection who underwent serologic testing if the study addressed our key questions and included at least one of our outcomes of interest. See Appendix Table B-1 for detailed study inclusion and exclusion criteria. We included immunoassay validation studies identified in our first round of searching but subsequently focused on selection of studies that directly addressed our key questions. While we retained immunoassay validation studies to illustrate what they added to the evidence base, these studies provided indirect and less reliable evidence regarding antibody dynamics given that seroprevalence had to be extrapolated from sensitivity and specificity estimates. Using a sequential process, one reviewer screened titles and abstracts for inclusion and reviewed full texts, and a second reviewer verified inclusion and exclusion decisions. Disagreements were resolved through consensus.

Data Extraction

Similarly, using a sequential process, one reviewer extracted data on study characteristics and outcomes of interest, and a second reviewer verified accuracy of the extraction. For studies that did not report the prevalence of antibodies among patients, but instead reported the percentage of serum samples with antibodies, we calculated seroprevalence, defined as the percentage of individuals in the population who had detectable antibodies at a specific time after infection.

Quality Assessment

Two reviewers sequentially assessed methodologic study quality. For each study design, we used adapted criteria from an appropriate quality assessment tool (Appendix D). Specifically, we used the Joanna Briggs Institute Checklist for Prevalence Studies for seroprevalence studies,[10] the Newcastle-Ottawa Quality Assessment Scales for cross-sectional and cohort studies,[11] and the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) for immunoassay validation studies.[12]

Data Synthesis and Analysis

We synthesized evidence qualitatively and did not perform meta-analyses due to variability in study populations, immunoassays used, test timing, and outcomes. We employed a "best evidence" approach to qualitative synthesis, meaning that we focused on studies that most directly addressed our key questions and were of highest methodological quality.[13]

Grading the Strength of the Body of Evidence

Two reviewers rated the overall strength of evidence for each outcome using criteria that assessed study methodologic quality (risk of bias), how directly studies evaluated the outcomes and populations of interest, precision of effect estimates, and the consistency of findings across studies (Appendix E).[14] In the absence of large, long-term clinical trials that may have produced high-strength evidence, we used the following standards for strength of evidence assessments: evidence comprising multiple large methodologically sound observational studies with consistent findings received a rating of "moderate"; evidence from fewer studies or studies with smaller sample sizes but mostly consistent results received a rating of "low"; and this same type of evidence with inconsistent results received a rating of "insufficient." We focused strength of evidence assessments regarding antibody prevalence on results from seroprevalence, cross-sectional, and cohort studies, rather than on results from immunoassay validation studies (which provide less reliable estimates, for reasons discussed above). For the remaining outcomes of interest, we incorporated results from all studies into strength of evidence assessments.

External Peer Review

Two content experts and one methodologist reviewed the draft report, and it was revised to address their comments.

Literature Surveillance

AHRQ will maintain this report as a living systematic review with planned ongoing literature surveillance and critical appraisal through December 2021, adjusting the timeline as needed depending on when we can conclusively answer the review's key questions. We will consider modifying the scope of the review to address new developments in SARS-CoV-2 immunity research, such as the growing understanding of the protective role of cell-mediated immunity. New evidence that does not substantively change the review conclusions will be summarized in bimonthly surveillance reports. We will produce report updates whenever we identify new evidence that would change the nature or strength of our conclusions, or every 4 months (whichever is sooner). Surveillance reports and review updates will be publicly posted on the AHRQ EHC Program website.

Evidence Base

The literature flow diagram (Figure 1) summarizes the results of the search and study selection process.[15] After screening 3,937 citations identified through database searching and 87 additional citations found through hand-searching, we included 66 observational studies.[15-80]

Study Characteristics

Characteristics of included studies are summarized in Appendix Table C-1. Overall, the evidence base comprises the following: (1) four studies[15,30,36,50] estimating seroprevalence among a given population that includes a smaller subpopulation known to have SARS-CoV-2 infection; (2) 45 cross-sectional or cohort studies[18-23,25,26,29,31,32,35,37,39-44,47,48,51-56,58-64,67-69,71, 74-80] characterizing the antibody response (i.e., antibody types, levels, and duration) among adults with SARS-CoV-2 infection; and (3) 17 studies validating the diagnostic performance of one or more immunoassays.[16,17,24,27,28,33,34,38,45,46,49,57,65,66,70,72,73] Most studies were relevant to key questions regarding the prevalence, levels, durability, and variability of the antibody response by patient and clinical factors and did not directly address whether antibodies are associated with protective immunity.

About half of the studies (52%) included fewer than 100 participants with RT-PCR diagnosed SARS-CoV-2; sample sizes ranged from 29 to 2,547 (median 98). Most studies (64%) included participants with a range of disease severity and symptoms. Nine studies (14%) only included participants with asymptomatic or mild disease, 10 (15%) only included participants with moderate, severe, or critical disease, and five (7%) did not report disease severity. Twenty-five studies (38%) were conducted in China, 22 (33%) in Europe, 12 (18%) in the United States and Canada, and the remaining seven studies (11%) were from other countries (Korea, Japan, Thailand, Singapore, India, and Brazil). Thirty-four studies (51%) were conducted in hospital settings, 15 (23%) in outpatient settings, another 15 (23%) within a mix of inpatient and outpatient settings, and two (3%) did not report the setting. Most studies evaluated antibody prevalence or levels within the first 28 days from symptom onset or RT-PCR diagnosis. A longitudinal prospective study of neutralizing antibody titers among 32 recovered adults collected samples up to 152 days after symptom onset, the longest duration of followup among included studies.[25] With a few exceptions,[15,22,51,54,64] most other studies followed participants for less than 100 days.

Studies measured IgM and IgG most frequently, followed by neutralizing antibodies and IgA. Studies used a variety of immunoassays, including commercially available immunoassays and those developed "in house" by academic or research institutions. Appendix Table C-2 presents immunoassay manufacturer information, performance characteristics, and authorization status in the United States and Europe.

Overall, 15 studies (23%) had a low risk of bias, 16 (24%) had a high risk of bias, and reporting gaps made risk of bias for the remaining 35 (53%) unclear. Appendix D presents risk of bias assessments for each study, as well as the criteria used in assessments. Three of the four seroprevalence studies had a low risk of bias.[15,30,36] The exception was a study of U.S. Navy service members aboard the USS Theodore Roosevelt carrier during a SARS-CoV-2 outbreak with a high risk of bias due to low participation (27% of eligible participants were included in the sample), differences in the age and racial distribution of participants compared to nonparticipants, and use of participant self-report for RT-PCR and serology test results.[50] Among

cross-sectional and cohort studies with high risk of bias, the most serious methodologic issues were unclear patient selection methods (i.e., whether selection was random or consecutive) and lack of adjustment for confounding factors, like age, that could influence subgroup comparisons.[18,20,41,43,47,52,55,58,67,69,77,78,80] In the immunoassay validation studies, inadequate reporting of patient selection methods and unclear or inconsistent criteria for interpreting immunoassay results meant we could not rule out high risk of bias and limited the clinical applicability of results.[16,17,24,27,28,33,34,38,45,46,49,57,65,66,70,72,73]

Key Question 1: Prevalence, Levels, and Duration of Detectable Antibodies in SARS-CoV-2 Infection

Summary prevalence estimates are presented in Table 1, and an overview of how antibody levels trend over time is presented in Table 2. Detailed prevalence results from seroprevalence, cross-sectional, and cohort studies are presented in Appendix Table C-3 and prevalence results from immunoassay validation studies are presented in Appendix Table C-4. Strength of evidence assessments are summarized in Appendix E.

Table 1. IgM, IgG, IgA and neutralizing antibody prevalence

Antibody Subtype	Peak Prevalence Estimate (%)	Number of Studies; Total Number (N) of RT-PCR+ Participants
IgM	**Median 80* (Range: 9-98)** when measured approximately 20 days post- symptom onset or RT-PCR diagnosis	**21 Studies (Total N=6,073)**: Dave, 2020[26]; Fafi-Kremer, 2020[29]; Gudbjartsson, 2020[15]; Hou, 2020[31]; Huang, 2020[32]; Iversen, 2020[36]; Iyer, 2020[37]; Ko, 2020[39]; Li, 2020[42]; Liu X, 2020[47]; Lynch, 2020[48]; Qu, 2020[52]; Seow, 2020[55]; Shu, 2020[58]; Stock da Cunha, 2020[60]; Sun, 2020[61]; Xu, 2020[75]; Young, 2020[76]; Zhang, 2020[77]; Zhao, 2020[78]; Zhao, 2020[79]
IgG	**Median 95* (Range: 15-100)** when measured approximately 25 days post- symptom onset or RT-PCR diagnosis	**24 Studies (Total N=9,136)**: Bruni, 2020[20]; Dave, 2020[26]; Fafi-Kremer, 2020[29]; Gudbjartsson, 2020[15]; Hou, 2020[31]; Iversen, 2020[36]; Iyer, 2020[37]; Ko, 2020[39]; Li, 2020[42] ; Liu X, 2020[47]; Lynch, 2020[48]; Petersen, 2020[51]; Qu, 2020[52]; Seow, 2020[55]; Shang, 2020[56]; Shu, 2020[58]; Sun, 2020[61]; Suthar, 2020[62]; Wang B, 2020[68]; Xu, 2020[75]; Young, 2020[76]; Zhang, 2020[77]; Zhao, 2020[78]; Zhao, 2020[79]
IgA	**Median 83 (Range: 75-89)** when measured from days 2-122 post-symptom onset or RT-PCR diagnosis	**5 Studies (Total N=747)**: Bruni, 2020[20]; Chirathaworn, 2020[23]; Iyer, 2020[37]; Schaffner, 2020[54]; Seow, 2020[55]
NAb	**Median 99* (Range: 76-100)** when measured approximately 30 days after symptom onset or RT-PCR diagnosis	**8 Studies (Total N=979)**: Crawford, 2020[25]; Fafi-Kremer, 2020[29]; Iyer, 2020[37]; Ko, 2020[39]; Koblischke, 2020[40]; Suthar, 2020[62]; Wang, 2020[69]; Wendel, 2020[71]

Abbreviations: IgM/G/A = immunoglobulin M/G/A; Nab = neutralizing antibody; RT-PCR+ = reverse transcription polymerase chain reaction positive result; RT-PCR = reverse transcription polymerase chain reaction.

*Calculation based on results of studies that evaluated antibody prevalence close to their estimated peak (20, 25, and 30 days after symptom onset or positive RT-PCR, for IgM, IgG, and neutralizing antibodies respectively) excluding studies that did not provide estimates within +/- 10 days of the peak. If studies reported antibody prevalence as measured by more than one immunoassay, the highest prevalence estimate was included. Calculations do not include results of total antibody immunoassays (e.g. IgM and IgG).

Table 2. Antibody kinetics (timing and duration)*

Antibody Subtype	Earliest Detected	Peak	Starts To Decline	Maximum Followup (Studies to Date)
IgM	**Median 7 Days (Range: 3-14)** **12 Studies (Total N: 1,715)**: Bao, 2020[18]; Dave, 2020[26]; Hou, 2020[31]; Infantino, 2020[34]; Liu X, 2020[47]; Qu, 2020[52]; Shu, 2020[58]; Sun, 2020[61]; Young, 2020[76]; Xie, 2020[74]; Zhang, 2020[77]; Zhao, 2020[79]	**Median 20 Days (Range: 10-35)** **15 Studies (Total N: 5,474)**: Bao, 2020[18]; Chen, Y. 2020[21]; Dave, 2020[26]; de la Iglesia, 2020[27]; Hou, 2020[31]; Huang, 2020[32]; Isho, 2020[35]; Kwon, 2020[41]; Li, 2020[42]; Liu X, 2020[47]; Qu, 2020[52]; Seow, 2020[55]; Shu, 2020[58]; Sun, 2020[61]; Zhang, 2020[77]	**Median 27 Days (Range: 14-35)** **7 Studies (Total N: 2,413)**: Bao, 2020[18]; Chen, Y. 2020[21]; Crawford, 2020[25]; Dave, 2020[26]; Isho, 2020[35]; Qu, 2020[52]; Sun, 2020[61]	**115 Days** Isho, 2020[35]
IgG	**Median 12 Days (Range: 3-41)** **16 Studies (Total N= 4,348)**: Bao, 2020[18]; Chen, Y. 2020[21]; Dave, 2020[26]; Jaaskelainen, 2020[38]; Kwon, 2020[41]; Liu J, 2020[43]; Liu X, 2020[47]; Lynch, 2020[48]; Qu, 2020[52]; Shang, 2020[56]; Shu, 2020[58]; Van Elslande, 2020[67]; Xie, 2020[74]; Young, 2020[76]; Zhang, 2020[77]; Zhao, 2020[79]	**Median 25 Days (Range: 14-42)** **11 Studies (Total N= 5,032)**: Bao, 2020[18]; Gudbjartsson, 2020[15]; Huang, 2020[32]; Isho, 2020[35]; Iyer, 2020[37]; Li, 2020[42] ; Liu X, 2020[47]; Qu, 2020[52]; Shu, 2020[58]; Van Elslande, 2020[67]; Zhang, 2020[77]	**Median 60 Days (Range: 30-100)** **4 Studies (Total N=3,286)**: Chen, Yuezhou 2020[22]; Isho, 2020[35]; Li, 2020[42]; Shang, 2020[56]	**120 Days** Gudbjartsson, 2020[15]
IgA	**11 Days** **1 Study (Total N=40)**: Jaaskelainen, 2020[38]	**Median Days Not Calculated (Range: 16-30)** **2 Studies (Total N=632)**: Isho, 2020[35]; Seow, 2020[55]	**Median 30 Days (Range: 28-48)** **4 Studies (Total N= 1,977)**: Gudbjartsson, 2020[15]; Isho, 2020[35]; Schaffner, 2020[54]; Seow, 2020[55]	**140 Days** Chirathaworn, 2020[23]
NAb	**Median Days Not Calculated (Range: 6-7 Days)** **3 studies (Total N= 103)**: Koblischke, 2020 [40]; Suthar, 2020 [62]; Wang, 2020 [69]	**Median 31 Days (Range: 15-45)** **6 studies (Total N=921)**: Fafi-Kremer, 2020 [29]; Isho, 2020 [35]; Ko, 2020 [39]; Koblischke, 2020[40]; Seow, 2020 [55]; Wang, 2020 [69]	**Median 30 Days (Range: 22-60)** **3 studies (Total N=126)**: Crawford, 2020 [25]; Koblischke, 2020 [40]; Seow, 2020 [55]	**152 Days** Crawford, 2020[25]

Abbreviations: IgM/G/A = immunoglobulin M/G/A; N = number; Nab = neutralizing antibody.
*Studies included in this table reported trends in antibody levels by specific day (e.g. first detected on day 7). Additional studies evaluated antibody kinetics but described results more generally (e.g. IgM peaked early in the disease course, then declined). All studies that were incorporated into strength of evidence assessments for each outcome are listed in Appendix E.

The best evidence regarding seroprevalence is from large studies that explicitly aimed to characterize the antibody response (i.e., antibody types and levels) over time. An example of a

comprehensive and methodically sound study is one conducted in Iceland[15] (hereafter referred to as the Icelandic study) designed to estimate population seroprevalence (including among those with *undiagnosed* SARS-CoV-2 infection) that included a population-based cohort of 1,263 patients with RT-PCR-diagnosed SARS-CoV-2. Using two pan-Ig immunoassays (i.e., immunoassays detecting a composite of IgM, IgG and IgA antibodies), this study found that 2–35 days after diagnosis, 93.8 percent (95% CI 84.6–98.4) of hospitalized patients (N=48) had positive results for both tests (the study's definition of seropositivity). Among a larger sample of recovered patients (N=1,215) tested an average of 100 days after diagnosis, 91.1 percent had positive results for both tests (95% CI 89.4–92.6). Strengths of this study include population-level sampling, use of multiple antibody tests, and the overall study duration, which monitored the levels and durability of antibody response for up to 120 days. Limitations include a relatively homogeneous population from a single geographic region and a lack of information regarding disease severity among the sample of recovered patients.

IgM Prevalence, Levels, and Duration

Evidence suggests that most adults with RT-PCR confirmed SARS-CoV-2 (80%) develop IgM antibodies. We derived this estimate from results of 21 seroprevalence, cross-sectional, and cohort studies (N=6,073, range 32–1,850) that reported IgM prevalence at or around 20 days post-symptom onset or RT-PCR diagnosis (Table 1).[15,26,29,31,32,36,37,39,42,47,48,52,55,58,60,61,75-79] We chose to examine IgM prevalence at or around 20 days because this is when IgM levels are estimated to peak based on a subset of studies describing trends in IgM levels over time (Table 2). Results from studies that trended IgM levels over time also suggest that IgM is first detected at a mean of seven days and starts to decline at 27 days (Table 2). Figure 2 illustrates the distribution IgM prevalence estimates.

We have moderate confidence in findings regarding IgM peak prevalence and trends in IgM levels over time. Although some studies had serious methodological limitations and nearly all used different immunoassays and collected samples at different frequencies and time points, findings that most individuals develop IgM and that these levels decline over time are consistent across most studies.

IgG Prevalence, Levels, and Duration

Evidence suggests that nearly all adults with RT-PCR-diagnosed SARS-CoV-2 (95%) develop IgG antibodies. In the same way that we derived an overall estimate for IgM prevalence, we derived an estimate for IgG based on results from 24 seroprevalence, cross-sectional, and cohort studies (N=9,136, range 32-2,547) that reported IgG prevalence at or around 25 days, when IgG levels are estimated to peak (Table 1).[15,20,26,29,31,36,37,39,42,47,48,51,52,55,56,58,61,62,68, 75-79] Studies that trended IgG levels over time also found that IgG is first detected at a mean of 12 days (slightly later than IgM), peaks at 25 days, then plateaus and may decline after 60 days (Table 2). Figure 3 illustrates the distribution IgG prevalence estimates. We have moderate confidence in findings regarding IgG peak prevalence and trends in IgG levels over time. Findings are consistent even though studies were conducted in different regions and settings and had a range of quality.

IgA Prevalence, Levels, and Duration

Only five cross-sectional and cohort studies (N=747, range 40–343) evaluated IgA prevalence.[20,23,37,54,55] These studies varied widely in test timing, finding that IgA prevalence ranged from 75-89% when measured from days 2-122 post-symptom onset or RT-PCR diagnosis. Like IgG, IgA may remain detectable for months past SARS-CoV-2 infection. The Icelandic study found that IgA antibodies peaked within a month of SARS-CoV-2 diagnosis and then declined but remained detectable for at least 100 days.[15] Similar findings were reported in two other studies that trended IgA levels over time.[23,55] We have low confidence in these findings given the smaller number of studies (with small sample sizes) with estimates for IgA prevalence and levels at different time points.

Neutralizing Antibody Seroprevalence, Levels, and Duration

Evidence from eight cross-sectional and cohort studies (N=979, range 29–567) suggests that almost all individuals (99%) develop neutralizing antibodies (Tables 1 provides a summary estimate, and Table 3 presents individual study results).[25,29,37,39,40,62,69,71] Studies had different findings regarding the durability of neutralizing antibodies. While some found that neutralizing antibody levels declined following the acute phase of illness, other studies found that neutralizing antibodies plateaued and remained detectable for several months (Table 2).[25,40,55] Several studies found that neutralizing activity correlates with presence of IgG antibodies to the spike, nucleocapsid and RBD proteins.[22,37,40] We have low confidence in findings regarding neutralizing antibody prevalence and changes in levels over time. Although results are consistent, studies of neutralizing antibody activity were small, used different neutralization tests, and collected samples at different frequencies and time points, limiting our ability to draw stronger conclusions.

Table 3. Prevalence of neutralizing antibodies

	Test Timing in Days Post Symptom Onset (PSO) or RT-PCR Diagnosis	Number Antibody Positive/ Number Tested (%)
Crawford, 2020[25]	~30 days (range 22-48) PSO	32/32 (100)
	104 days (range 58-152) PSO	27/32 (84)
Fafi-Kremer, 2020[29]	13-20 days PSO	23/29 (79)*
	21-27 days PSO	76/83 (92)
	≥28 days PSO	47/48 (98)
Iyer, 2020[37]	0-75 days PSO	15/15 (100)
Ko, 2020[39]	Median 20 - 36 days post RT-PCR+	64/70 (91)
Koblischke, 2020[40]	Median 7 (IQR 4-11) days PSO	16/29 (55)
	15-22 days PSO	29/29 (100)
Suthar, 2020[62]	3-30 days PSO and 2-19 days post RT-PCR+	40/44 (91)
Wang, 2020[69]	90 days PSO	30 (100)
Wendel, 2020[71]	NR	189/250 (76)

Abbreviations: NR = not reported; RT-PCR = reverse transcription polymerase chain reaction.
*Data presented is for medium concentration of neutralizing antibodies (ID50>50).

Lack of an Antibody Response

Nearly all studies found that a certain proportion of patients with RT-PCR-diagnosed SARS-CoV-2 did not have detectable antibodies. For example, in the Icelandic study, among 489 patients who underwent antibody testing at two different time points (once at least 3 weeks after

diagnosis and again at least one month after the first sample), 19 (4%) had negative results for both pan-Ig immunoassays. Few studies evaluated whether patient factors or COVID-19 severity were associated with seronegativity. An exception is a U.S. study of 2,547 frontline healthcare workers and first responders, which found that about 6 percent of participants remained seronegative from 14 to 90 days after symptom onset.[51] This result was strongly associated with disease severity and presence of symptoms. While 11 percent of 308 asymptomatic patients did not develop antibodies, none of the 79 previously hospitalized patients were seronegative.

Key Question 1a: Variation in Prevalence, Levels, and Duration of Anti-SARS-CoV-2 Antibodies by Patient Characteristics and Disease Severity

Appendix Table C-5 provides an overview of results regarding variation in the antibody response by patient characteristics. A summary of these findings is presented below.

Variation in Anti-SARS-CoV-2 Antibodies by Age, Sex, and Race/Ethnicity

We identified 14 observational studies that assessed variation in the antibody response by patient age, sex, and/or race/ethnicity.[15,21,22,29,32,40,42,51,56,57,59,63,64,71]

Four cross-section and cohort studies[29,51,56,59] that controlled for comorbidities and markers of COVID-19 severity (such as the number or type of symptoms) and one immunoassay validation study[57] evaluated the association of age and seroprevalence and found no difference (Appendix Table C-5). Separately from prevalence, eight studies[15,21,22,32,40,42,59,64] compared antibody levels by age. Six[15,22,32,42,59,64] found that older age was associated with higher antibody levels while two studies[21,40] found no difference. Overall, the ability to synthesize results is limited by variability in the definitions of older age as well as by variability in outcomes (IgG levels were studied most frequently, followed by IgM and neutralizing antibodies).

The same five studies [29,51,56,57,59] that evaluated variation in antibody prevalence by age also evaluated variation by sex and did not detect a difference. With regard to variation in antibody levels by sex, six studies found no difference.[32,40,59,63,64,71] However, two studies detected a statistically significant difference: the Icelandic study,[15] which found that levels of anti–S1-RBD pan-Ig and anti-S1 IgA were lower in women, and a large Chinese study[21] of hospitalized adults which found that found that anti-S and anti-N IgM titers were higher in men compared with women (but IgG titers were no different).

Only two studies[51,59] evaluated the association of antibody prevalence and levels by race/ethnicity and results suggest that non-White race may be associated with higher antibody prevalence and levels. The large U.S. study[51] of healthcare workers and first responders described above found that non-Hispanic White participants were more than twice as likely to *lack* IgG antibodies compared with non-Hispanic Blacks. A smaller study of predominantly hospitalized adults conducted in the United Kingdom[59] also found that higher IgG antibody levels were associated with non-White race.

We have low confidence in findings for variation in the anti-SARS-CoV-2 antibody response by age, sex, and race/ethnicity, given that few studies examined these outcomes and most studies were small (fewer than 300 participants). Although most results are based on adjusted analyses (that controlled for potential confounders), evidence synthesis is limited by variation in study methods. Not all studies evaluated the same antibody type, used the same immunoassay, or

compared antibody prevalence or levels with the same frequency and at the same intervals. These inconsistencies limit our ability to draw stronger conclusions regarding study results.

Variation in Anti-SARS-CoV-2 Antibodies by Comorbidities

Evidence is unclear regarding whether comorbidities are associated with variation in antibody prevalence, levels, or durability as most studies did not conduct these analyses. Moreover, studies that stratified results by patient comorbidities often did not evaluate the same comorbidities or outcomes. Studies that did evaluate the same comorbidities and outcomes had inconsistent findings (Appendix Table C-5).

Specifically, among six studies[15,24,29,48,51,59] that considered whether weight (body mass index or obesity) was associated with antibody prevalence or levels, four[15,29,51,59] found an association with higher weight and higher neutralizing antibody activity, higher seroconversion rates, or higher IgM, IgG and IgA antibody levels. Two studies[24,48] found no difference. Among four studies[29,48,51,59] examining the association between hypertension and antibody prevalence and levels, one study[59] found that hypertension was associated with a higher seroconversion rate and three[29,48,51] found no difference. Similarly, among three studies[32,48,51] that stratified antibody results by pre-existing diabetes mellitus, one study[32] found that diabetes was associated with higher IgG levels and two studies[48,51] found no difference. Future larger studies are needed to draw stronger conclusions regarding these associations.

In addition, although immunosuppressive conditions such as malignancy and human immunodeficiency virus (HIV) and use of immunosuppressive treatments may influence the antibody response to viral infection, studies infrequently evaluated these associations or excluded immunosuppressed participants from analysis. The largest study to evaluate these associations found that use of immunosuppressive medication, but not diagnosis of an immunosuppressive condition, was associated with IgG seronegativity.[51]

Variation in Anti-SARS-CoV-2 Antibodies by Disease Severity

Evidence suggests that antibody responses vary by disease severity (Table 4). Studies most frequently evaluated variation in antibody levels (rather than prevalence) by disease severity. Overall, 25 studies compared antibody levels among participants with more and less severe disease and had conflicting findings (Table 4). However, the best evidence from five studies with larger sample sizes (more than 100 participants) and low risk of bias found that disease severity was associated with a more robust antibody response in terms of antibody levels.[15,23,32,64,79] Among these, the Greek study[64] of 259 convalescing adults found that COVID-19 related hospitalization history was significantly correlated with higher total (IgM, IgG, and IgA) antibody levels, while the absence of symptoms was associated with lower antibody levels. The same study also reported significantly higher neutralizing antibody levels and activity among previously hospitalized patients compared with those who did not require inpatient care.

Evidence also suggests that disease severity is associated with differences in antibody kinetics (Table 4). Five studies noted that participants with more severe disease had a delayed time to seroconversion compared to participants with milder disease.[32,42,52,57,78] However, a sixth study had opposite conclusions.[76]

Table 4. Variation in Anti-SARS-CoV-2 antibodies by disease severity

Outcome	Total Number of Studies; Total Number (N) of RT-PCR+ participants (Range) Summary of Findings
Antibody Prevalence	**10 Studies (Total N=876)**: • 3 studies found an association between disease severity and higher seroprevalence (Bruni, 2020[20]; Chirathaworn, 2020[23]; Liu, 2020[47]) • 2 studies found that disease severity is associated with lower seroprevalence (Dave, 2020[26]; Stock da Cunha, 2020[60]) • 5 studies found no difference (Liu, 2020[46]; Theel, 2020[65]; Traugott, 2020[66]; Van Elslande, 2020[67]; Wolff, 2020[72])
Antibody Levels	**25 Studies (Total N=8,228)**: • 17 studies found an association between disease severity and higher antibody levels (Chirathaworn, 2020[23]; Theel, 2020[65]; Chen, 2020[22]; Crawford, 2020[25]; Kwon, 2020[41]; Lynch, 2020[48]; Qu, 2020[52]; Seow, 2020[55]; Sun, 2020[61]; Terpos, 2020[64]; Young, 2020[76]; Zhang, 2020[77]; Zhao G, 2020[78]; Zheng, 2020[80]; Gudbjartsson, 2020[15]; Huang, 2020[32]; Li, 2020[42]) • 3 studies found that disease severity is associated with lower antibody levels (Stock da Cunha, 2020[60]; Chen, 2020[21]; Bruni, 2020[20]); in 2 studies this finding was specific to critical illness (Chen, 2020[21]; Bruni, 2020[20]) • 1 study had mixed findings (Hou, 2020[31]); and 4 found no difference (Liu R, 2020[46]; Van Elslande, 2020[67]; Wolff, 2020[72]; Xie, 2020[74])
Antibody Kinetics (Timing and Duration)	**6 Studies (Total N=2,627)**: • 5 studies found that disease severity was associated with a delay in detectable antibodies compared to cases of less severe disease (Huang, 2020[32] Li, 2020[42]; Qu, 2020[52]; Shen, 2020[57]; Zhao G, 2020[78]) • 1 study found that disease severity was associated with earlier seroconversion (Young, 2020[76])

Studies often did not measure the same antibodies at the same time or using comparable immunoassays, include the same outcome (e.g., antibody prevalence, levels, or duration), or consistently define clinical categories of disease severity, thereby limiting comparisons across studies. Overall, more studies found that antibody prevalence and levels are positively associated (rather than inversely associated) with disease severity, and several studies suggest that antibody kinetics vary between patients with more and less severe disease. Our confidence in these findings is low given methodologic limitations such as small study sizes, inconsistent adjustment for confounding factors, and lack of precision in estimates. Future larger studies are needed to draw stronger conclusions.

Variation in Anti-SARS-CoV-2 Antibodies in Asymptomatic Versus Symptomatic Patients

Evidence suggest that presence of symptoms is associated with higher antibody prevalence and levels. The U.S. study of 2,547 frontline healthcare workers and first responders that investigated patient and disease factors associated with a lack of antibody generation found that more asymptomatic participants were seronegative compared to symptomatic participants (11% vs 5.6%, P-value ≤0.001).[51] A smaller U.S. study of 92 participants with mild disease mostly treated as outpatients found a significant association between clinical symptoms, illness duration, and levels of anti-S, anti-N, and anti-RBD antibodies.[22] Three immunoassay validation studies had inconsistent results.[33,49,72] Similar to findings regarding disease severity, we have low confidence in findings related to variation in the antibody response by presence/absence of symptoms.

Four observational studies[15,29,59,64] evaluated the association between antibody prevalence and levels and different symptom types and had inconsistent results. The Greek study described above[64] that enrolled adults convalescing from symptomatic SARS-CoV-2 infection found a statistically significant association between anti-S, anti-N and anti-RBD antibody levels and fever, anosmia, and ageusia. However, a French study[29] of 160 healthcare workers with mild RT-PCR diagnosed infection found that presence of cough was associated with higher neutralizing antibody activity, while ageusia, anosmia, and fever were not. Similarly, a U.K.-based study[59] of 177 adults with mostly moderate to severe disease found that higher seroconversion frequency was associated with respiratory symptoms. The Icelandic study found that fever, maximum temperature reading, cough, and loss of appetite were associated with higher levels of Anti–S1-RBD pan-Ig (IgM, IgG and IgA) and Anti-S1 IgA antibodies.[15]

Variation in Anti-SARS-CoV-2 Antibodies as Measured by Different Immunoassays

Ten studies[15-17,27,29,39,65-67,72] (total N=1,996) assessed differences in seroconversion rates, timing, and antibody levels as measured by different immunoassays. Five studies[16,17,27,29,66] compared the diagnostic accuracy of rapid diagnostic tests (RDTs) designed to detect anti-SARS-CoV-2 IgM and IgG antibodies compared with common commercial immunoassays including enzyme-linked immunosorbent assay (ELISA), immunofluorescence assay (IFA), and lateral flow immunochromatographic assay (LFA). One study[27] assessed the agreement between two different RDTs. These studies generally found that RDTs had inferior sensitivity and specificity characteristics and lower diagnostic accuracy compared with laboratory-based immunoassays. A complete assessment of the diagnostic accuracy of immunoassays for SARS-CoV-2 antibodies is beyond the scope of this review but has been addressed recently by others.[81]

Key Questions 2–3: Role of Anti-SARS-CoV-2 Antibodies in Immunity From Reinfection and Duration of Immunity

Studies included in this review primarily aimed to estimate seroprevalence and characterize the antibody response following SARS-CoV-2 infection and did not directly evaluate the association of antibodies with immunity. A retrospective study of 47 hospitalized patients in China with moderate to severe COVID-19 mentions a potential case of reinfection in one patient during the "convalescence stage" of the disease.[78] Notably, the patient did not have detectable antibodies (either IgM or IgG) at 4-week followup following discharge but the study does not provide more detail or describe how reinfection was determined. Otherwise, we did not identify any studies of individuals with RT-PCR-diagnosed SARS-CoV-2 directly linking the presence or absence of antibodies with incidence of reinfection. A Danish study is investigating immunity among healthcare workers by following SARS-CoV-2 antibody-positive participants at 1, 5, 10, and 20 years but so far has only reported initial antibody test results.[36] Population seroprevalence studies, such as the Icelandic study discussed above,[15] could also provide insight into reinfection risk if study periods were extended and incidence of reinfection was compared among participants with and without antibodies. An ongoing study conducted by the Finnish Institute for Health and Welfare is also following a cohort of individuals recovered from COVID-19 to assess persistence of virus specific IgG and neutralizing antibodies for five years after recovery from SARS-CoV-2.[82]

While studies of adults with RT-PCR-diagnosed SARS-CoV-2 would provide the most direct and reliable results to address our key questions, longitudinal studies of adults with known SARS-CoV-2 serology results (but not necessarily a history of RT-PCR diagnosis) may also provide insight into reinfection risks. While we did not formally include or critically appraise studies in which the index test was an antibody test (rather than RT-PCR), we note that several recent studies based on index serologic testing suggest that antibody presence is associated with protective immunity. A prospective study following 12,541 healthcare workers in the U.K. for up to 31 weeks found that baseline anti-S IgG seropositivity was associated with a lower risk of subsequent positive SARS-CoV-2 RT-PCR (223/11364 vs. 2/1265, adjusted incidence rate ratio 0.11).[83,84] Only 37 percent (466/1265) of the seropositive workers had a prior RT-PCR-diagnosed infection. Two small retrospective studies also suggest that prior SARS-CoV-2 infection, as measured by positive antibody results, is associated with a reduced risk of reinfection.[85,86] One of these studies described a SARS-CoV-2 outbreak among attendees and staff at a summer school retreat.[85] Among 152 participants, 76 percent (116) had confirmed or presumed SARS-CoV-2 infection, while none of the 24 individuals who had documented seropositive results in the 3 months prior to the retreat developed symptoms. In another study, three individuals with positive neutralizing antibody results (and negative SARS-CoV-2 RT-PCR) prior to departing on a fishing vessel did not subsequently test positive for SARS-COV-2 despite an outbreak affecting 85 percent (104/122) of the onboard population.[86] Although they provide indirect evidence regarding protective immunity that results from SARS-CoV-2 infection, studies based on index serologic testing are likely to become more common and we will consider updating our scope to include them in future versions of this review.

Given that the association of anti-SARS-CoV-2 antibodies and immunity has not yet been established (KQ 2), we did not identify any studies providing evidence on variation in immunity by patient or antibody characteristics (KQ 2a and KQ 2b). Similarly, we did not identify any evidence on immunity duration (KQ 3 and KQ 3a).

Key Question 4: Unintended Consequences of Antibody Testing After SARS-CoV-2 Infection

Abandoning recommended practices to reduce virus exposure and transmission risks (such as wearing masks and social distancing) is a potential unintended consequences of antibody testing. In a survey of 560 British healthcare workers, 15 percent of whom had a history of RT-PCR confirmed SARS-CoV-2, 11 percent (61) indicated that they would view social distancing as less important and 31 percent (175) would be "happier to visit friends and relatives."[53] No studies have documented actual behavior change related to knowledge of antibody status.

Conclusions

This rapid systematic review synthesizes currently available evidence (based on a literature search through December 2020) on the prevalence of anti-SARS-CoV-2 antibodies following COVID-19 and whether antibodies confer immunity against reinfection. Understanding the clinical significance of SARS-CoV-2 antibody tests is necessary for clinician and patient decision-making as well as health policy formulation.

Moderate-strength evidence suggests that the majority of adults with SARS-CoV-2 infection develop IgM and IgG antibodies. Moderate-strength evidence also suggests that IgM peaks

approximately 20 days after symptom onset or RT-PCR diagnosis and then declines, while IgG levels peak at approximately 25 days and remain detectable for at least 120 days (the longest they have been studied). Low-strength evidence suggests neutralizing antibody activity may also persist for several months.

Low-strength evidence also suggests that antibody prevalence does not vary by age or sex, but older age may be associated with higher antibody levels. In addition, low-strength evidence suggests that antibody prevalence and levels are positively associated with disease severity. However, patient characteristics and disease factors may be mutually confounding and not all studies adjusted results accordingly. Future larger studies of high methodologic quality are needed to draw stronger conclusions regarding these associations.

Most studies published on or before December 15, 2020, have not been designed to evaluate whether the presence of anti-SARS-CoV-2 antibodies confers immunity against reinfection. Several studies are underway to help answer some of these questions and the AHRQ EPC Program will update this report as new evidence becomes available.

The existing evidence base has several limitations. Most studies are small, single center and geographically specific, and included hospitalized patients with COVID-19, potentially limiting applicability to other populations and settings. Another limitation is that the U.S. Food and Drug Administration (FDA) (or another similar regulatory body) has not yet evaluated the diagnostic accuracy of several immunoassays. The regulatory standard for emergency use authorization from the FDA is different from FDA's typical review standard. Tests that have been authorized for emergency use generally have less evidence supporting the point estimates, which are derived from studies intended to validate serologic tests used in an emergency use setting. Antibody test results may be falsely negative due to the known biological limitations of antibody tests, including cases in which the quantity of antibodies present in a specimen is below the detection limit of the assay, when the virus has undergone minor mutations, and when tests are used in immunocompromised individuals. Antibody test results may also be falsely positive due to past non-SARS-CoV-2 viral exposures and cross-reactivity, endogenous and exogenous substance interferences, or other causes. The degree to which false positive or negative results impact prevalence estimates is unclear and was rarely commented on by study authors. A third general limitation of studies examining SARS-CoV-2 reinfection rates is the chance of persistently positive RT-PCR testing due to viral RNA shedding that does not represent active infection, a recently recognized phenomenon. The U.S. Centers for Disease Control and Prevention have developed guidelines to distinguish persistent viral shedding from new infections, which should be taken into account in future studies of reinfection risk.[87]

Limitations of our review methods include use of sequential rather than independent dual review to complete study selection, data extraction, and quality assessment. Given the large volume of studies and our rapid review timeline, we may have missed subgroup data (such as seroprevalence comparisons by age or sex) if the information was in an online appendix or otherwise not prominently featured in the text. A second limitation is our exclusion of preprints (non-peer-reviewed publications). We acknowledge that online publication of studies prior to the journal peer-review process has become more common in the era of COVID-19 and we may have excluded pertinent studies. As this is a living review with ongoing literature surveillance, we will continue to monitor the evidence base for relevant studies as they are published. Finally, our scope was limited to studies of adults with RT-PCR-diagnosed SARS-CoV-2, and findings may not apply to those diagnosed clinically based on other criteria (such as imaging findings) or those with subclinical disease who did not seek medical care.

Future Research

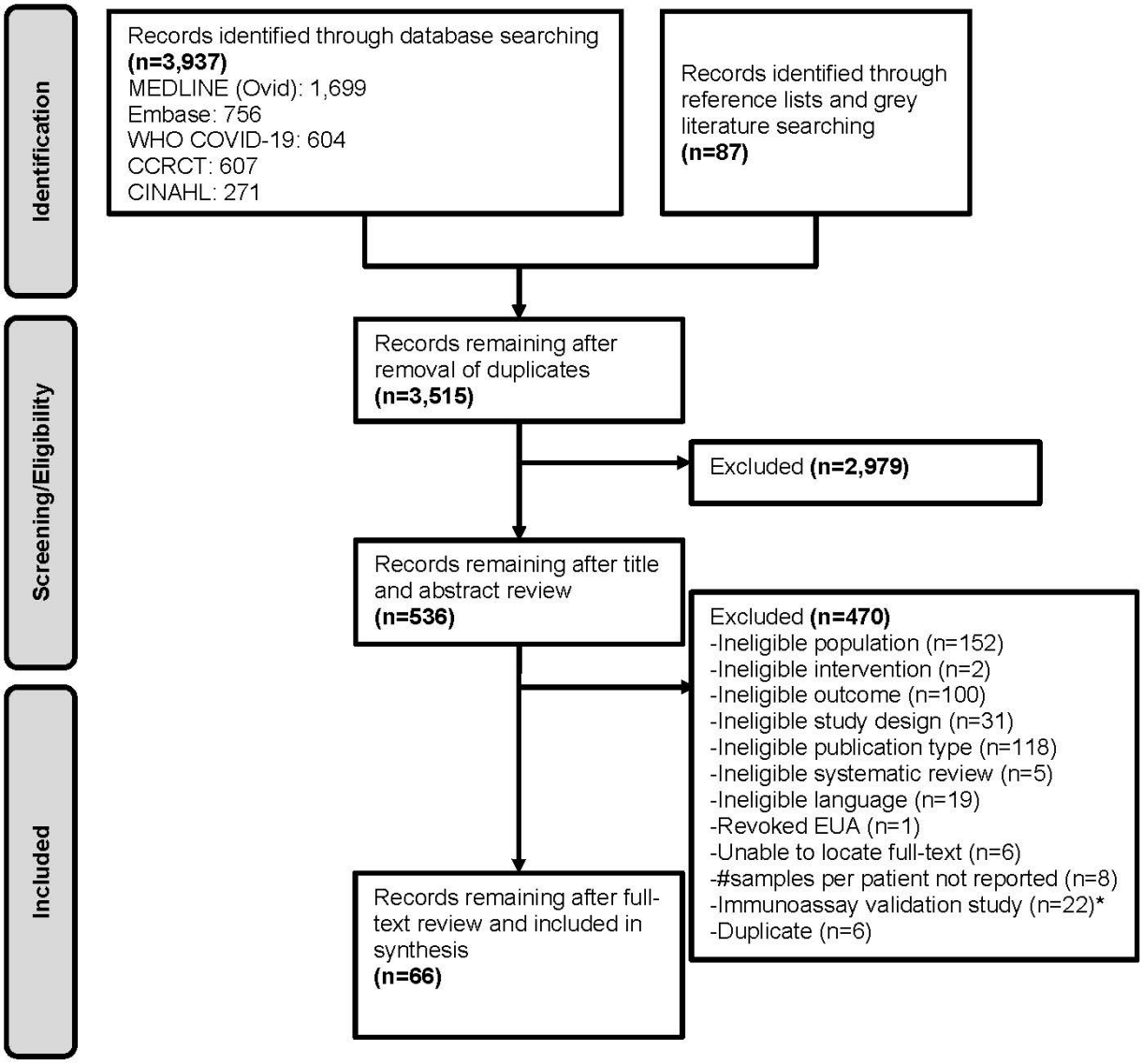
Although this systematic review focused on studies of SARS-CoV-2 antibodies, the immune system's overall response to infection includes both antibody formation (antibody-mediated immunity) and cell-mediated immunity (immunity dependent on the recognition of antigen by T cells). Host factors and properties of the virus itself determine how effectively the immune system responds (Table 5). While these factors must be considered in vaccine development, they also apply when considering whether infection protects against reinfection. More broadly, community infection rates, exposures due to occupation or population density, poverty, and other social determinants of health may also affect rates of reinfection with SARS-CoV-2 (Table 5).[88]

Table 5. Factors influencing immunity

Host	Age, Sex, Race/Ethnicity, Genetic Susceptibility, Comorbidities, Prior Infection
Virus	Viral Replication/Mutation Rate, Reactogenicity
Disease Course	Viral Load/Exposure Intensity, Disease Severity and Complications
Exposure & Environment	Community Infection Prevalence, Occupational and Environmental Exposure Risks

Studies designed to evaluate the roles of both antibody-mediated and cell-mediated immunity in preventing SARS-CoV-2 reinfection are underway. One such study from the National Institute of Allergy and Infectious Diseases is a prospective observational study of immunity and long-term health sequela after SARS-CoV-2 infection.[89] The study is enrolling adults who recovered from past RT-PCR-diagnosed SARS-CoV-2 infection or had a history of exposure to someone with COVID-19 symptoms but did not develop an infection. The prospective study will monitor serum markers of antibody and T cell-mediated immunity over a 3-year period and will evaluate incidence of SARS-CoV-2 reinfection over time. Additional selected in-progress studies are detailed in Appendix Table F-1.

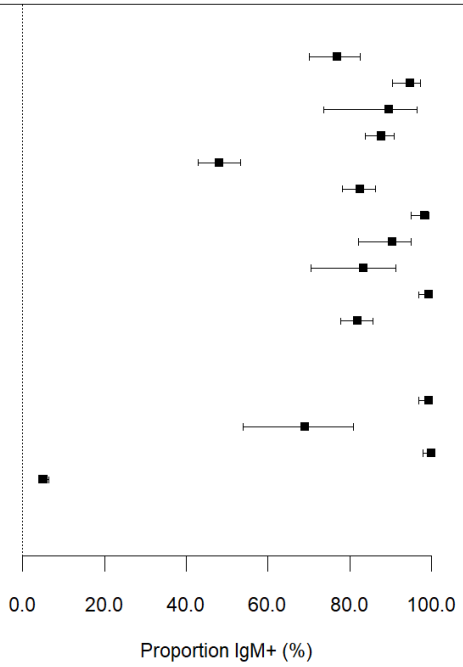
Figure 1. Literature flow diagram



*Exclusion applied to update search only.

Figure 2. IgM Prevalence at 0–30 days and after 30 days*

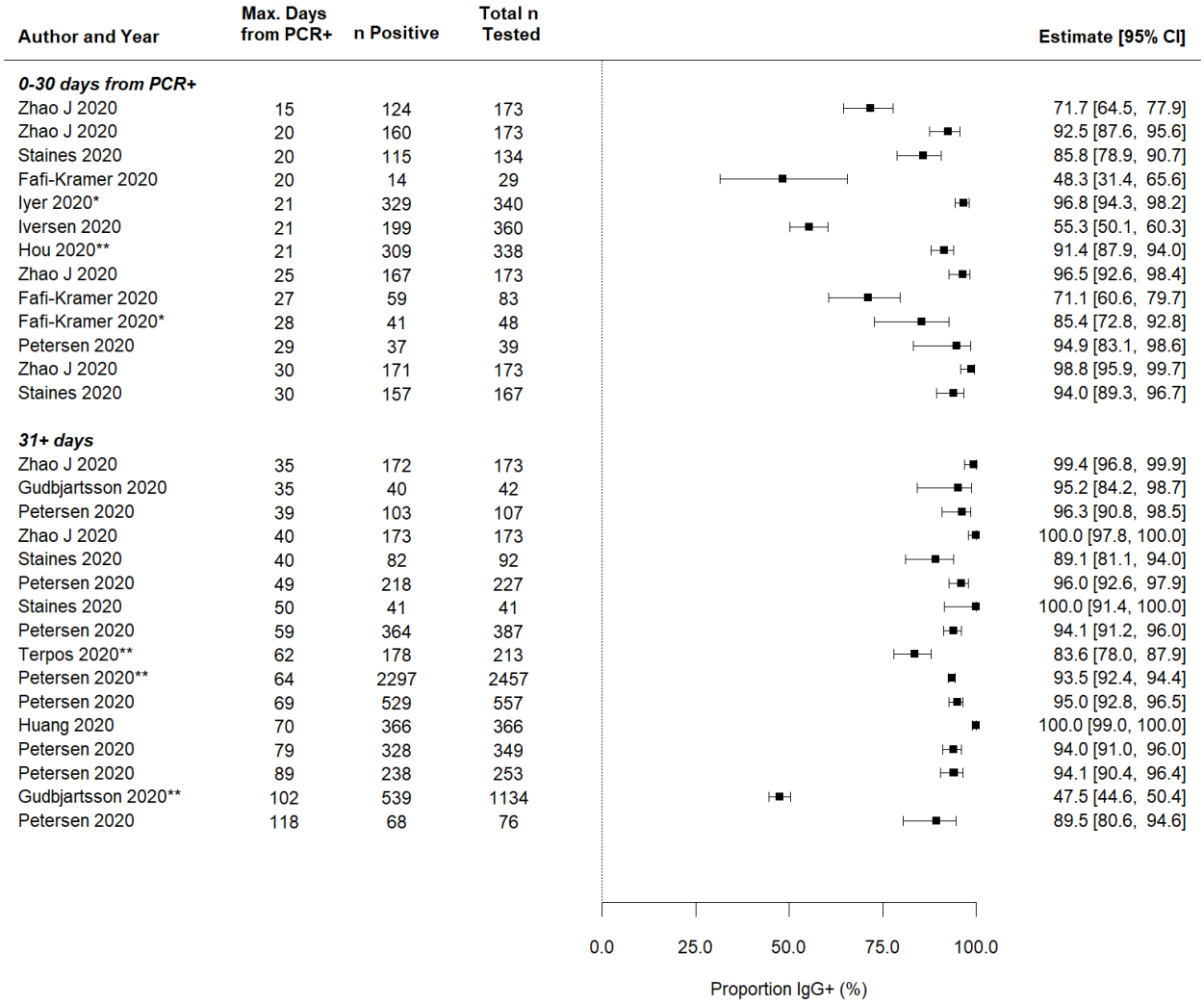
Author and Year	Max. Days from PCR+	n Positive	Total n Tested	Estimate [95% CI]
0-30 days from PCR+				
Zhao J 2020	15	133	173	76.9 [70.1, 82.5]
Zhao J 2020	20	164	173	94.8 [90.4, 97.2]
Fafi-Kramer 2020	20	26	29	89.7 [73.6, 96.4]
Iyer 2020*	21	301	343	87.8 [83.9, 90.8]
Iversen 2020	21	173	360	48.1 [42.9, 53.2]
Hou 2020**	21	279	338	82.5 [78.1, 86.2]
Zhao J 2020	25	170	173	98.3 [95.0, 99.4]
Fafi-Kramer 2020	27	75	83	90.4 [82.1, 95.0]
Fafi-Kramer 2020*	28	40	48	83.3 [70.4, 91.3]
Zhao J 2020	30	172	173	99.4 [96.8, 99.9]
Huang 2020	30	300	366	82.0 [77.7, 85.6]
31+ days				
Zhao J 2020	35	172	173	99.4 [96.8, 99.9]
Gudbjartsson 2020	35	29	42	69.0 [54.0, 80.9]
Zhao J 2020	40	173	173	100.0 [97.8, 100.0]
Gudbjartsson 2020**	102	57	1145	5.0 [3.9, 6.4]



CI = confidence interval.
*Number of days from RT-PCR+ is minimum of unbounded range (e.g., >20 days).
**Study provided mean or median number of days from RT-PCR+.

Note. Studies represented had well-characterized patient populations and settings, measured antibodies using validated immunoassays, and lacked serious methodological problems.

Figure 3. IgG Prevalence at 0–30 days and after 30 days



CI = confidence interval.
*Number of days from RT-PCR+ is minimum of unbounded range (e.g., >20 days).
**Study provided mean or median number of days from RT-PCR+.

Note. Studies represented had well-characterized patient populations and settings, measured antibodies using validated immunoassays, and lacked serious methodological problems.

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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help health care decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Afterword

Recognized for excellence in conducting comprehensive systematic reviews, the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) program is developing a range of rapid evidence products to assist end-users in making specific decisions in a limited timeframe.

The AHRQ EPC Program recognizes that people are struggling with urgent questions on how to control the COVID-19 pandemic. To shorten timelines, reviewers make strategic choices about which review processes to abridge. However, the adaptations made for expediency may limit the certainty and generalizability of the findings from the review, particularly in areas with a large literature base. Transparent reporting of the methods used and the resulting limitations of the evidence synthesis are extremely important.

Given the rapidly evolving field, the AHRQ EPC Program will update this review regularly to keep the medical community and public up to date as new evidence becomes available with a planned end date 1 year from initial searches. If you have comments or have unpublished data to share related to this report, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov and will be considered in the next version of the report.

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Appendix Contents

Appendix A. Search Strategies

Searches

The research librarian searched for published, unpublished, and ongoing studies, utilizing a modified Ovid MEDLINE ALL COVID-19 hedge, study design filters, and select publication type limits. The original search was conducted in August 2020; however, later handsearching of relevant citations revealed inadequacies in the search strategies as written for Medline ALL, Embase.com, CCRCT, and CINAHL. These search strategies were revised in December 2020 and rerun from January 1 to December 15, 2020 to capture missed records. Revisions included supplementing named tests (line 12), altering some keywords and Boolean logic in lines 11 and 19, and adding MMWR as a journal term search. The revised and original search strategies are below.

The search strategy is reported in accordance with Cochrane Collaboration Information Specialist Searching: Recording and Reporting website guidance. To improve readability, database search syntax legends providing the abbreviated field codes commands with their respective definitions.

Updated Search Strategies: December 2020

Ovid MEDLINE ALL

Date searched: December 16, 2020
1 exp Coronavirus/ (46285)
2 exp Coronavirus Infections/ (50775)
3 (coronavirus* or corona-virus* or OC43 or NL63 or 229E or HKU1 or HCoV* or ncov* or covid* or sars-cov* or sarscov* or Sars-coronavirus* or "Severe Acute Respiratory Syndrome").ti,ab,kf. (99841)
4 or/1-3 (106962)
5 4 not (SARS or MERS or MERS-CoV or "Middle East respiratory syndrome" or camel* or dromedar* or equine or coronary or coronal or covidence* or covidien or "influenza virus" or HIV or bovine or calves or TGEV or feline or porcine or BCoV or PED or PEDV or PDCoV or FIPV or FCoV or SADS-CoV or canine or CCov or zoonotic or "avian influenza" or H1N1 or H5N1 or H5N6 or IBV or murine).ti,ab,kf. (93114)
6 ((pneumonia or covid* or coronavirus* or corona virus* or ncov* or 2019-ncov or sars*).mp. or exp pneumonia/) and Wuhan.mp. (3983)
7 (2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19 or covid 2019 or ((novel or new or nouveau) adj2 (CoV or nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or ((covid or covid19 or covid-19) and pandemic*2) or (coronavirus* and pneumonia)).ti,ab,kf. (84518)
8 COVID-19.rx,px,ox. or severe acute respiratory syndrome coronavirus 2.os. (40897)
9 or/5-8 (98540)
10 exp Antibodies/ or exp Immunity/ (1106277)
11 (((active or adaptive or assay* or assess* or humoral or long-term or natural or protective or response or test or tests or testing) adj2 (immune or immunity or immunolog*)) or ((antibody or anti-body or antibodies or anti-bodies) adj3 ("Anti-SARS-CoV-2" or assay* or attenuat* or complete or detect* or level or levels or neutral* or positive or "SARS-CoV-2" or test or tests or testing)) or "Anti-SARS-CoV-2" or convalescent or "false immunity" or IgA or IgG or IgM or immunoglobulin or immunoassay* or immuno-assay* or postinfection or post-infection or reactivate or reactivated or reactivation or recurrent

or recurrence or reinfect* or re-infect* or repositive or re-positive or "second infection*" or seroepidemiolog* or serologic* or seronegativ* or seropositiv* or seroprevalence or "subsequent infection*" or T-cell or T-cells).ti,ab,kf. (1649742)
12 ("Alinity i SARS-CoV-2 IgG" or "Architect SARS-CoV-2 IgG" or "Assure COVID-19 IgG/IgM" or "Anti-SARS-CoV-2 Rapid Test" or "Babson Diagnostics aC19G1" or "Beckman Coulter Access SARS-CoV-2 IgG" or "WANTAI SARS-CoV-2" or "Platelia SARS-CoV-2" or "Biohit SARS-CoV-2 IgM/IgG" or "qSARS-CoV-2 IgG/IgM" or "LIAISON SARS-CoV-2 S1/S2 IgG" or "Diazyme DZ-Lite SARS-CoV-2 IgG" or "SARS-CoV-2 RBD IgG" or "SARS-COV-2 ELISA" or "RightSign COVID-19" or "LYHER Novel Coronavirus" or "COVID-19 IgG/IgM Rapid Test Cassette" or "SCoV-2 Detect IgG ELISA" or "SCoV-2 Detect IgM ELISA" or "Mt. Sinai Laboratory COVID-19 ELISA" or "VITROS Anti-SARS-CoV-2 IgG" or "VITROS Immunodiagnostic Products Anti-SARS-CoV" or "Elecsys Anti-SARS-CoV-2" or "ADVIA Centaur SARS-CoV-2" or COV2T or "Atellica IM SARS-CoV-2" or "Dimension EXL SARS-CoV-2 Total antibody" or "Dimension Vista SARS-CoV-2 Total antibody" or "Vibrant COVID-19 Ab" or "New York SARS-CoV Microsphere Immunoassay" or "SARS-CoV-2 antibody" or "anti-SARS-CoV-2 antibody" or "Enzyme linked immunosorbent" or "Chemiluminescence immunoassay" or "Enzyme linked fluorescence" or "Immunochromatographic assay" or "Microneutralization assay" or "Neutralization assay" or "SARS-Cov-2 RT-PCR").ti,ab,kf. (95905)
13 or/10-12 (2319708)
14 and/9,13 (10069)
15 14 and (202*.dp. or 20200101:20301231.ep.) (7476)
16 exp clinical trial/ or exp cohort studies/ or exp epidemiologic studies/ (3229715)
17 ("controlled clinical trial" or meta-analysis or "observational study" or "randomized controlled trial" or "systematic review").pt. (902690)
18 (cohort or cohorts or (control and (group* or study)) or cross-sectional or follow-up or longitudinal or meta-analy* or metaanaly* or observational or ((evidence or rapid or systematic) adj3 (review or synthesis)) or prospective or prospectively or ((random* or control*) adj3 trial) or retrospective or retrospectively).ti,ab,kf. (4540608)
19 (((antibody or anti-body or antibodies or anti-bodies or immune or immunity or immunolog*) adj3 (active or adaptive or assess* or detect* or humoral or IgA or IgG or IgM or immunoglobulin or long-term or natural or protective or response* or "SARS-CoV-2" or convalescent or postinfection or post-infection or reactivate or reactivated or reactivation or recurrent or recurrence or reinfect* or re-infect* or repositive or re-positive or second-infection* or seronegativ* or seropositiv* or seroprevalence or subsequent-infection*)) or Anti-SARS-CoV-2 or false-immunity).ti. or MMWR.jw. (103468)
20 or/16-19 (5825607)
21 and/15,20 (2787)
22 21 not ((exp animals/ not humans/) or (animal* or primate*).ti.) (2751)
23 22 not ("in vitro techniques"/ or (case or "in vitro" or man or report or patient or woman).ti. or ("case reports" or comment or editorial or letter).pt.) (2319)

Ovid Medline Syntax
.ab = Abstract
.dp = Date of publication
.ep = Election publication date
.kf = Keyword heading word
.mp = Default field searching (includes all of the following fields automatically: ti,ab,ot,nm,hw,fx,kf,ox,px,rx,ui,sy)
.pt = Publication type (e.g., journal article, randomized controlled trial, editorial, etc.)
.px = Protocol supplementary concept [word indexed]
.os = Organism supplementary concept [phrase indexed]
.ox = Organism supplementary concept [word indexed]

.rx = Rare disease supplementary concept
.ti = Title
exp = Explode (retrieves all MeSH subject terms underneath it in the tree hierarchy)
/ = MeSH subject term search
(#...) Ending each search line, it indicates the number of retrieved records for that search on the date of the search

Elsevier Embase

Date searched: December 16, 2020
#1 'coronavirus infection'/de OR 'coronavirus disease 2019'/de (81,600)
#2 coronavirus*:ti,ab,kw OR 'corona virus*':ti,ab,kw OR oc43:ti,ab,kw OR nl63:ti,ab,kw OR 229e:ti,ab,kw OR hku1:ti,ab,kw OR hcov*:ti,ab,kw OR ncov*:ti,ab,kw OR covid*:ti,ab,kw OR 'sars cov*':ti,ab,kw OR sarscov*:ti,ab,kw OR 'sars coronavirus*':ti,ab,kw OR 'severe acute respiratory syndrome':ti,ab,kw (96,362)
#3 #1 OR #2 (103,048)
#4 #3 NOT (sars:ti,ab,kw OR mers:ti,ab,kw OR 'mers cov':ti,ab,kw OR 'middle east respiratory syndrome':ti,ab,kw OR camel*:ti,ab,kw OR dromedar*:ti,ab,kw OR equine:ti,ab,kw OR coronary:ti,ab,kw OR coronal:ti,ab,kw OR covidence*:ti,ab,kw OR covidien:ti,ab,kw OR 'influenza virus':ti,ab,kw OR hiv:ti,ab,kw OR bovine:ti,ab,kw OR calves:ti,ab,kw OR tgev:ti,ab,kw OR feline:ti,ab,kw OR porcine:ti,ab,kw OR bcov:ti,ab,kw OR ped:ti,ab,kw OR pedv:ti,ab,kw OR pdcov:ti,ab,kw OR fipv:ti,ab,kw OR fcov:ti,ab,kw OR 'sads cov':ti,ab,kw OR canine:ti,ab,kw OR ccov:ti,ab,kw OR zoonotic:ti,ab,kw OR 'avian influenza':ti,ab,kw OR h1n1:ti,ab,kw OR h5n1:ti,ab,kw OR h5n6:ti,ab,kw OR ibv:ti,ab,kw OR murine:ti,ab,kw) (61,709)
#5 (covid*:ti,ab,kw OR coronavirus*:ti,ab,kw OR 'corona virus*':ti,ab,kw OR ncov*:ti,ab,kw OR '2019 ncov':ti,ab,kw OR sars*:ti,ab,kw OR 'pneumonia'/exp) AND wuhan:ti,ab,kw (4,018)
#6 '2019 ncov':ti,ab,kw OR ncov19:ti,ab,kw OR 'ncov 19':ti,ab,kw OR '2019-novel cov':ti,ab,kw OR 'sars cov2':ti,ab,kw OR 'sars cov 2':ti,ab,kw OR sarscov2:ti,ab,kw OR 'sarscov 2':ti,ab,kw OR 'sars coronavirus2':ti,ab,kw OR 'sars coronavirus 2':ti,ab,kw OR 'sars-like coronavirus*':ti,ab,kw OR 'coronavirus 19':ti,ab,kw OR covid19:ti,ab,kw OR 'covid 19':ti,ab,kw OR 'covid 2019':ti,ab,kw OR (((novel OR new OR nouveau) NEAR/2 (cov OR ncov OR covid OR coronavirus* OR 'corona virus' OR pandemi*2)):ti,ab,kw) OR ((covid:ti,ab,kw OR covid19:ti,ab,kw OR 'covid 19':ti,ab,kw) AND pandemic*2:ti,ab,kw) OR (coronavirus*:ti,ab,kw AND pneumonia:ti,ab,kw) (77,672)
#7 #4 OR #5 OR #6 (90,359)
#8 'antibodies,antisera and immunoglobulins'/exp OR 'immunity'/exp (2,755,112)
#9 (active:ti,ab,kw OR adaptive:ti,ab,kw OR assay*:ti,ab,kw OR assess*:ti,ab,kw OR humoral:ti,ab,kw OR 'long term':ti,ab,kw OR natural:ti,ab,kw OR protective:ti,ab,kw OR response:ti,ab,kw OR test:ti,ab,kw OR tests:ti,ab,kw OR testing:ti,ab,kw) AND adj2:ti,ab,kw AND (immune:ti,ab,kw OR immunity:ti,ab,kw OR immunolog*:ti,ab,kw) OR (((antibody OR 'anti body' OR antibodies OR 'anti bodies') NEAR/3 ('anti-sars-cov-2' OR assay* OR attenuat* OR complete OR detect* OR level OR levels OR neutral* OR positive OR 'sars-cov-2' OR test OR tests OR testing)):ti,ab,kw) OR 'anti-sars-cov-2':ti,ab,kw OR convalescent:ti,ab,kw OR 'false immunity':ti,ab,kw OR iga:ti,ab,kw OR igg:ti,ab,kw OR igm:ti,ab,kw OR immunoglobulin:ti,ab,kw OR immunoassay*:ti,ab,kw OR 'immuno assay*':ti,ab,kw OR postinfection:ti,ab,kw OR 'post infection':ti,ab,kw OR reactivate:ti,ab,kw OR reactivated:ti,ab,kw OR reactivation:ti,ab,kw OR recurrent:ti,ab,kw OR recurrence:ti,ab,kw OR reinfect*:ti,ab,kw OR 're infect*':ti,ab,kw OR repositive:ti,ab,kw OR 're positive':ti,ab,kw OR 'second infection*':ti,ab,kw OR seroepidemiolog*:ti,ab,kw OR serologic*:ti,ab,kw OR seronegativ*:ti,ab,kw OR seropositiv*:ti,ab,kw OR seroprevalence:ti,ab,kw OR 'subsequent infection*':ti,ab,kw OR 't cell':ti,ab,kw OR 't cells':ti,ab,kw (2,080,042)
#10 'alinity i sars-cov-2 igg':ti,ab,kw OR 'architect sars-cov-2 igg':ti,ab,kw OR 'assure covid-19 igg/igm':ti,ab,kw OR 'anti-sars-cov-2 rapid test':ti,ab,kw OR 'babson diagnostics ac19g1':ti,ab,kw OR

'beckman coulter access sars-cov-2 igg':ti,ab,kw OR 'wantai sars-cov-2':ti,ab,kw OR 'platelia sars-cov-2':ti,ab,kw OR 'biohit sars-cov-2 igm/igg':ti,ab,kw OR 'qsars-cov-2 igg/igm':ti,ab,kw OR 'liaison sars-cov-2 s1/s2 igg':ti,ab,kw OR 'diazyme dz-lite sars-cov-2 igg':ti,ab,kw OR 'sars-cov-2 rbd igg':ti,ab,kw OR 'sars-cov-2 elisa':ti,ab,kw OR 'rightsign covid-19':ti,ab,kw OR 'lyher novel coronavirus':ti,ab,kw OR 'covid-19 igg/igm rapid test cassette':ti,ab,kw OR 'scov-2 detect igg elisa':ti,ab,kw OR 'scov-2 detect igm elisa':ti,ab,kw OR 'mt. sinai laboratory covid-19 elisa':ti,ab,kw OR 'vitros anti-sars-cov-2 igg':ti,ab,kw OR 'vitros immunodiagnostic products anti-sars-cov':ti,ab,kw OR 'elecsys anti-sars-cov-2':ti,ab,kw OR 'advia centaur sars-cov-2':ti,ab,kw OR cov2t:ti,ab,kw OR 'atellica im sars-cov-2':ti,ab,kw OR 'dimension exl sars-cov-2 total antibody':ti,ab,kw OR 'dimension vista sars-cov-2 total antibody':ti,ab,kw OR 'vibrant covid-19 ab':ti,ab,kw OR 'new york sars-cov microsphere immunoassay':ti,ab,kw OR 'sars-cov-2 antibody':ti,ab,kw OR 'anti-sars-cov-2 antibody':ti,ab,kw OR 'enzyme linked immunosorbent':ti,ab,kw OR 'chemiluminescence immunoassay':ti,ab,kw OR 'enzyme linked fluorescence':ti,ab,kw OR 'immunochromatographic assay':ti,ab,kw OR 'microneutralization assay':ti,ab,kw OR 'neutralization assay':ti,ab,kw OR 'sars-cov-2 rt-pcr':ti,ab,kw (110,025)
#11 #8 OR #9 OR #10 (3,973,743)
#12 #7 AND #11 (15,081)
#13 #12 AND (2020:py OR 2021:py) (13,726)
#14 'clinical trial'/de OR 'randomized controlled trial'/de OR 'randomization'/de OR 'single blind procedure'/de OR 'double blind procedure'/de OR 'crossover procedure'/de OR 'placebo'/de OR 'prospective study'/de OR ('randomi?ed controlled' NEXT/1 trial*) OR rct OR 'randomly allocated' OR 'allocated randomly' OR 'random allocation' OR (allocated NEAR/2 random) OR (single NEXT/1 blind*) OR (double NEXT/1 blind*) OR ((treble OR triple) NEAR/1 blind*) OR placebo* (2,416,261)
#15 'meta analysis'/exp OR 'systematic review'/de OR 'observational study'/de (577,404)
#16 cohort:ti,ab,kw OR cohorts:ti,ab,kw OR ((control NEAR/3 (group* OR study)):ti,ab,kw) OR 'cross sectional':ti,ab,kw OR 'follow up':ti,ab,kw OR longitudinal:ti,ab,kw OR 'meta analy*':ti,ab,kw OR metaanaly*:ti,ab,kw OR observational:ti,ab,kw OR (((evidence OR rapid OR systematic) NEAR/3 (review OR synthesis)):ti,ab,kw) OR prospective:ti,ab,kw OR prospectively:ti,ab,kw OR (((random* OR control*) NEAR/3 trial):ti,ab,kw) OR retrospective:ti,ab,kw OR retrospectively:ti,ab,kw OR survey:ti,ab,kw (6,116,304)
#17 (((antibody OR 'anti body' OR antibodies OR 'anti bodies' OR immune OR immunity OR immunolog*) NEAR/3 (active OR adaptive OR assess* OR detect* OR humoral OR iga OR igg OR igm OR immunoglobulin OR 'long term' OR natural OR protective OR response* OR 'sars-cov-2' OR convalescent OR postinfection OR 'post infection' OR reactivate OR reactivated OR reactivation OR recurrent OR recurrence OR reinfect* OR 're infect*' OR repositive OR 're positive' OR 'second infection*' OR seronegativ* OR seropositiv* OR seroprevalence OR 'subsequent infection*')):ti) OR 'anti sars cov 2':ti OR 'false immunity':ti OR mmwr:ta (121,681)
#18 #14 OR #15 OR #16 OR #17 (7,381,231)
#19 #13 AND #18 (3,995)
#20 #19 NOT ('animal'/exp NOT 'human'/exp OR animal*:ti OR primate*:ti) (3,954)
#21 #20 NOT ('in vitro study'/exp OR case:ti OR 'in vitro':ti OR man:ti OR report:ti OR patient:ti OR woman:ti OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'case report'/de) (2,542)
#22 #21 AND [embase]/lim NOT ([embase]/lim AND [medline]/lim) (684)

Embase.com
.ab = Abstract
.kw = Keyword
.py = Publication year
.ti = Title
/de = Subject term search
/exp = Explode subject term (retrieves all Embase subject terms underneath it in the tree hierarchy)

(#...) Ending each search line, it indicates the number of retrieved records for that search on the date of the search

Ovid EBM Reviews – Cochrane Central Register of Controlled Trials

Date searched: December 16, 2020
1 exp Coronavirus/ (10)
2 exp Coronavirus Infections/ (513)
3 (coronavirus* or corona-virus* or OC43 or NL63 or 229E or HKU1 or HCoV* or ncov* or covid* or sars-cov* or sarscov* or Sars-coronavirus* or "Severe Acute Respiratory Syndrome").ti,ab. (4865)
4 or/1-3 (4891)
5 4 not (MERS or MERS-CoV or "Middle East respiratory syndrome" or camel* or dromedar* or equine or coronary or coronal or covidence* or covidien or "influenza virus" or HIV or bovine or calves or TGEV or feline or porcine or BCoV or PED or PEDV or PDCoV or FIPV or FCoV or SADS-CoV or canine or CCov or zoonotic or "avian influenza" or H1N1 or H5N1 or H5N6 or IBV or murine).ti,ab. (4343)
6 ((pneumonia or covid* or coronavirus* or corona virus* or ncov* or 2019-ncov or sars*).mp. or exp pneumonia/) and Wuhan.mp. (148)
7 (2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19 or covid 2019 or ((novel or new or nouveau) adj2 (CoV or nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or ((covid or covid19 or covid-19) and pandemic*2) or (coronavirus* and pneumonia)).ti,ab. (3530)
8 or/5-7 (4603)
9 (((active or adaptive or assay* or assess* or humoral or long-term or natural or protective or response or test or tests or testing) adj2 (immune or immunity or immunolog*)) or ((antibody or anti-body or antibodies or anti-bodies) adj3 ("Anti-SARS-CoV-2" or assay* or attenuat* or complete or detect* or level or levels or neutral* or positive or "SARS-CoV-2" or test or tests or testing)) or "Anti-SARS-CoV-2" or convalescent or "false immunity" or IgA or IgG or IgM or immunoglobulin or immunoassay* or immuno-assay* or postinfection or post-infection or reactivate or reactivated or reactivation or recurrent or recurrence or reinfect* or re-infect* or repositive or re-positive or "second infection*" or seroepidemiolog* or serologic* or seronegativ* or seropositiv* or seroprevalence or "subsequent infection*" or T-cell or T-cells).ti,ab. (104719)
10 ("Alinity i SARS-CoV-2 IgG" or "Architect SARS-CoV-2 IgG" or "Assure COVID-19 IgG/IgM" or "Anti-SARS-CoV-2 Rapid Test" or "Babson Diagnostics aC19G1" or "Beckman Coulter Access SARS-CoV-2 IgG" or "WANTAI SARS-CoV-2" or "Platelia SARS-CoV-2" or "Biohit SARS-CoV-2 IgM/IgG" or "qSARS-CoV-2 IgG/IgM" or "LIAISON SARS-CoV-2 S1/S2 IgG" or "Diazyme DZ-Lite SARS-CoV-2 IgG" or "SARS-CoV-2 RBD IgG" or "SARS-COV-2 ELISA" or "RightSign COVID-19" or "LYHER Novel Coronavirus" or "COVID-19 IgG/IgM Rapid Test Cassette" or "SCoV-2 Detect IgG ELISA" or "SCoV-2 Detect IgM ELISA" or "Mt. Sinai Laboratory COVID-19 ELISA" or "VITROS Anti-SARS-CoV-2 IgG" or "VITROS Immunodiagnostic Products Anti-SARS-CoV" or "Elecsys Anti-SARS-CoV-2" or "ADVIA Centaur SARS-CoV-2" or COV2T or "Atellica IM SARS-CoV-2" or "Dimension EXL SARS-CoV-2 Total antibody" or "Dimension Vista SARS-CoV-2 Total antibody" or "Vibrant COVID-19 Ab" or "New York SARS-CoV Microsphere Immunoassay" or "SARS-CoV-2 antibody" or "anti-SARS-CoV-2 antibody" or "Enzyme linked immunosorbent" or "Chemiluminescence immunoassay" or "Enzyme linked fluorescence" or "Immunochromatographic assay" or "Microneutralization assay" or "Neutralization assay" or "SARS-Cov-2 RT-PCR").ti,ab. (3815)
11 or/9-10 (107109)
12 and/8,11 (647)

13 limit 12 to yr="2020 -Current" (595)

Ovid EBM Reviews Cochrane Central Register of Controlled Trials
.ab = Abstract
.mp = Default field searching (includes all of the following fields automatically: ti,ab,hw)
.ti = Title
(#...) Ending each search line, it indicates the number of retrieved records for that search on the date of the search

CINAHL Plus With Fulltext (EBSCOHost)

Date searched: December17, 2020
S1 (MH "Coronavirus") OR (MH "Coronavirus Infections") OR (MH "COVID-19") (20,834)
S2 TI (coronavirus* OR corona-virus* OR OC43 OR NL63 OR 229E OR HKU1 OR HCoV* OR ncov* OR covid* OR sars-cov* OR sarscov* OR Sars-coronavirus* OR "Severe Acute Respiratory Syndrome") OR AB (coronavirus* OR corona-virus* OR OC43 OR NL63 OR 229E OR HKU1 OR HCoV* OR ncov* OR covid* OR sars-cov* OR sarscov* OR Sars-coronavirus* OR "Severe Acute Respiratory Syndrome") (29,363)
S3 S1 OR S2 (32,613)
S4 TI (SARS OR MERS OR MERS-CoV OR "Middle East respiratory syndrome" OR camel* OR dromedar* OR equine OR coronary OR coronal OR covidence* OR covidien OR "influenza virus" OR HIV OR bovine OR calves OR TGEV OR feline OR porcine OR BCoV OR PED OR PEDV OR PDCoV OR FIPV OR FCoV OR SADS-CoV OR canine OR CCov OR zoonotic OR "avian influenza" OR H1N1 OR H5N1 OR H5N6 OR IBV OR murine) OR AB (SARS OR MERS OR MERS-CoV OR "Middle East respiratory syndrome" OR camel* OR dromedar* OR equine OR coronary OR coronal OR covidence* OR covidien OR "influenza virus" OR HIV OR bovine OR calves OR TGEV OR feline OR porcine OR BCoV OR PED OR PEDV OR PDCoV OR FIPV OR FCoV OR SADS-CoV OR canine OR CCov OR zoonotic OR "avian influenza" OR H1N1 OR H5N1 OR H5N6 OR IBV OR murine) (238,041)
S5 S3 NOT S4 (29,811)
S6 (TI (pneumonia OR covid* OR coronavirus* OR corona virus* OR ncov* OR 2019-ncov OR sars*) OR AB (pneumonia OR covid* OR coronavirus* OR corona virus* OR ncov* OR 2019-ncov OR sars*) OR (MH "Pneumonia+")) AND Wuhan (896)
S7 TI ((2019-ncov OR ncov19 OR ncov-19 OR 2019-novel CoV OR sars-cov2 OR sars-cov-2 OR sarscov2 OR sarscov-2 OR Sars-coronavirus2 OR Sars-coronavirus-2 OR SARS-like coronavirus* OR coronavirus-19 OR covid19 OR covid-19 OR covid 2019 OR ((novel OR new OR nouveau) N2 (CoV OR nCoV OR covid OR coronavirus* OR corona virus OR Pandemi*2)) OR ((covid OR covid19 OR covid-19) and pandemic*2) OR (coronavirus* AND pneumonia))) OR AB ((2019-ncov OR ncov19 OR ncov-19 OR 2019-novel CoV OR sars-cov2 OR sars-cov-2 OR sarscov2 OR sarscov-2 OR Sars-coronavirus2 OR Sars-coronavirus-2 OR SARS-like coronavirus* OR coronavirus-19 OR covid19 OR covid-19 OR covid 2019 OR ((novel OR new OR nouveau) N2 (CoV OR nCoV OR covid OR coronavirus* OR corona virus OR Pandemi*2)) OR ((covid OR covid19 OR covid-19) and pandemic*2) OR (coronavirus* AND pneumonia))) (25,928)
S8 S5 OR S6 OR S7 (31,257)
S9 (MH "Antibodies+") OR (MH "Immunity+") (111,464)
S10 TI (((active OR adaptive OR assay* OR assess* OR humoral OR long-term OR natural OR protective OR response OR test OR tests OR testing) N2 (immune OR immunity OR immunolog*)) OR ((antibody OR anti-body OR antibodies OR anti-bodies) N3 ("Anti-SARS-CoV-2" OR assay* OR attenuat* OR complete OR detect* OR level OR levels OR neutral* OR positive OR "SARS-CoV-2" OR test OR tests OR testing)) OR "Anti-SARS-CoV-2" OR convalescent OR "false immunity" OR IgA OR IgG OR IgM OR immunoglobulin OR immunoassay* OR immuno-assay* OR postinfection OR post-

infection OR reactivate OR reactivated OR reactivation OR recurrent OR recurrence OR reinfect* OR re-infect* OR repositive OR re-positive OR "second infection*" OR seroepidemiolog* OR serologic* OR seronegativ* OR seropositiv* OR seroprevalence OR "subsequent infection*" OR T-cell OR T-cells) OR AB (((active OR adaptive OR assay* OR assess* OR humoral OR long-term OR natural OR protective OR response OR test OR tests OR testing) N2 (immune OR immunity OR immunolog*)) OR ((antibody OR anti-body OR antibodies OR anti-bodies) N3 ("Anti-SARS-CoV-2" OR assay* OR attenuat* OR complete OR detect* OR level OR levels OR neutral* OR positive OR "SARS-CoV-2" OR test OR tests OR testing)) OR "Anti-SARS-CoV-2" OR convalescent OR "false immunity" OR IgA OR IgG OR IgM OR immunoglobulin OR immunoassay* OR immuno-assay* OR postinfection OR post-infection OR reactivate OR reactivated OR reactivation OR recurrent OR recurrence OR reinfect* OR re-infect* OR repositive OR re-positive OR "second infection*" OR seroepidemiolog* OR serologic* OR seronegativ* OR seropositiv* OR seroprevalence OR "subsequent infection*" OR T-cell OR T-cells) (182,780)
S11 TI ("Alinity i SARS-CoV-2 IgG" OR "Architect SARS-CoV-2 IgG" OR "Assure COVID-19 IgG/IgM" OR "Anti-SARS-CoV-2 Rapid Test" OR "Babson Diagnostics aC19G1" OR "Beckman Coulter Access SARS-CoV-2 IgG" OR "WANTAI SARS-CoV-2" OR "Platelia SARS-CoV-2" OR "Biohit SARS-CoV-2 IgM/IgG" OR "qSARS-CoV-2 IgG/IgM" OR "LIAISON SARS-CoV-2 S1/S2 IgG" OR "Diazyme DZ-Lite SARS-CoV-2 IgG" OR "SARS-CoV-2 RBD IgG" OR "SARS-COV-2 ELISA" OR "RightSign COVID-19" OR "LYHER Novel Coronavirus" OR "COVID-19 IgG/IgM Rapid Test Cassette" OR "SCoV-2 Detect IgG ELISA" OR "SCoV-2 Detect IgM ELISA" OR "Mt. Sinai Laboratory COVID-19 ELISA" OR "VITROS Anti-SARS-CoV-2 IgG" OR "VITROS Immunodiagnostic Products Anti-SARS-CoV" OR "Elecsys Anti-SARS-CoV-2" OR "ADVIA Centaur SARS-CoV-2" or COV2T OR "Atellica IM SARS-CoV-2" OR "Dimension EXL SARS-CoV-2 Total antibody" OR "Dimension Vista SARS-CoV-2 Total antibody" or "Vibrant COVID-19 Ab" or "New York SARS-CoV Microsphere Immunoassay" or "SARS-CoV-2 antibody" OR "anti-SARS-CoV-2 antibody" OR "Enzyme linked immunosorbent" OR "Chemiluminescence immunoassay" OR "Enzyme linked fluorescence" OR "Immunochromatographic assay" OR "Microneutralization assay" OR "Neutralization assay" OR "SARS-Cov-2 RT-PCR") OR AB ("Alinity i SARS-CoV-2 IgG" OR "Architect SARS-CoV-2 IgG" OR "Assure COVID-19 IgG/IgM" OR "Anti-SARS-CoV-2 Rapid Test" OR "Babson Diagnostics aC19G1" OR "Beckman Coulter Access SARS-CoV-2 IgG" OR "WANTAI SARS-CoV-2" OR "Platelia SARS-CoV-2" OR "Biohit SARS-CoV-2 IgM/IgG" OR "qSARS-CoV-2 IgG/IgM" OR "LIAISON SARS-CoV-2 S1/S2 IgG" OR "Diazyme DZ-Lite SARS-CoV-2 IgG" OR "SARS-CoV-2 RBD IgG" OR "SARS-COV-2 ELISA" OR "RightSign COVID-19" OR "LYHER Novel Coronavirus" OR "COVID-19 IgG/IgM Rapid Test Cassette" OR "SCoV-2 Detect IgG ELISA" OR "SCoV-2 Detect IgM ELISA" OR "Mt. Sinai Laboratory COVID-19 ELISA" OR "VITROS Anti-SARS-CoV-2 IgG" OR "VITROS Immunodiagnostic Products Anti-SARS-CoV" OR "Elecsys Anti-SARS-CoV-2" OR "ADVIA Centaur SARS-CoV-2" or COV2T OR "Atellica IM SARS-CoV-2" OR "Dimension EXL SARS-CoV-2 Total antibody" OR "Dimension Vista SARS-CoV-2 Total antibody" or "Vibrant COVID-19 Ab" or "New York SARS-CoV Microsphere Immunoassay" or "SARS-CoV-2 antibody" OR "anti-SARS-CoV-2 antibody" OR "Enzyme linked immunosorbent" OR "Chemiluminescence immunoassay" OR "Enzyme linked fluorescence" OR "Immunochromatographic assay" OR "Microneutralization assay" OR "Neutralization assay" OR "SARS-Cov-2 RT-PCR") (10,132)
S12 S9 OR S10 OR S11 (268,156)
S13 S8 AND S12 (1,487)
S14 TI ((cohort OR cohorts OR (control AND (group* OR study)) OR cross-sectional OR follow-up OR longitudinal OR meta-analy* OR metaanaly* OR observational OR ((evidence OR rapid OR systematic) N3 (review OR synthesis)) OR prospective OR prospectively OR ((random* or control*) N3 trial) OR retrospective OR retrospectively OR survey)) OR AB ((cohort OR cohorts OR (control AND (group* OR study)) OR cross-sectional OR follow-up OR longitudinal OR meta-analy* OR metaanaly* OR observational OR ((evidence OR rapid OR systematic) N3 (review OR synthesis)) OR prospective OR

prospectively OR ((random* or control*) N3 trial) OR retrospective OR retrospectively OR survey)) (1,485,298)
S15 TI (((antibody OR anti-body OR antibodies OR anti-bodies OR immune OR immunity OR immunolog*) N3 (active OR adaptive OR assess* OR detect* OR humoral OR IgA OR IgG OR IgM OR immunoglobulin OR long-term OR natural OR protective OR response* OR "SARS-CoV-2" OR convalescent OR postinfection OR post-infection OR reactivate OR reactivated OR reactivation OR recurrent OR recurrence OR reinfect* OR re-infect* OR repositive OR re-positive OR second-infection* OR seronegativ* OR seropositiv* OR seroprevalence OR subsequent-infection*)) OR Anti-SARS-CoV-2 OR false-immunity) OR AB (((antibody OR anti-body OR antibodies OR anti-bodies OR immune OR immunity OR immunolog*) N3 (active OR adaptive OR assess* OR detect* OR humoral OR IgA OR IgG OR IgM OR immunoglobulin OR long-term OR natural OR protective OR response* OR "SARS-CoV-2" OR convalescent OR postinfection OR post-infection OR reactivate OR reactivated OR reactivation OR recurrent OR recurrence OR reinfect* OR re-infect* OR repositive OR re-positive OR second-infection* OR seronegativ* OR seropositiv* OR seroprevalence OR subsequent-infection*)) OR Anti-SARS-CoV-2 OR false-immunity) (30,041)
S16 S14 OR S15 (1,505,434)
S17 S13 AND S16 (706)
S18 TI (case OR "in vitro" OR man OR report OR patient OR woman) OR MH ("In Vitro Studies") OR MH("Case Studies") (458,589)
S19 S17 NOT S18 Limiters: Published Date: 20200101-20210631; Exclude MEDLINE records (208)

CINAHL (Current Index to Nursing and Allied Health Literature)
AB = Abstract
MH = Major Heading (major subject of the publication)
TI = Title
(#...) Ending each search line, it indicates the number of retrieved records for that search on the date of the search

Original Search Strategy: August 2020

Ovid MEDLINE ALL

Date searched: August 5, 2020
1 exp Coronavirus/ (24702)
2 exp Coronavirus Infections/ (25370)
3 (coronavirus* or corona-virus* or OC43 or NL63 or 229E or HKU1 or HCoV* or ncov* or covid* or sars-cov* or sarscov* or Sars-coronavirus* or "Severe Acute Respiratory Syndrome").ti,ab,kf. (54179)
4 or/1-3 (60361)
5 4 not (SARS or MERS or MERS-CoV or "Middle East respiratory syndrome" or camel* or dromedar* or equine or coronary or coronal or covidence* or covidien or "influenza virus" or HIV or bovine or calves or TGEV or feline or porcine or BCoV or PED or PEDV or PDCoV or FIPV or FCoV or SADS-CoV or canine or CCov or zoonotic or "avian influenza" or H1N1 or H5N1 or H5N6 or IBV or murine).ti,ab,kf. (32966)
6 ((pneumonia or covid* or coronavirus* or corona virus* or ncov* or 2019-ncov or sars*).mp. or exp pneumonia/) and Wuhan.mp. (2362)
7 (2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19 or covid 2019 or ((novel or new or nouveau) adj2 (CoV or nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or ((covid or covid19 or covid-19) and pandemic*2) or (coronavirus* and pneumonia)).ti,ab,kf. (40627)
8 COVID-19.rx,px,ox. or severe acute respiratory syndrome coronavirus 2.os. (15787)
9 or/5-8 (47964)
10 exp Antibodies/ or exp Immunity/ (1092488)
11 (((active or adaptive or assess* or humoral or long-term or natural or protective or response) adj2 (immune or immunity or immunolog*)) or ((antibody or antibodies) adj5 (attenuat* or complete or detect or detected or detection or detections or level or levels or neutral* or positive)) or convalescent or "false immunity" or "false positive" or "false negative" or IgG or "immunoglobulin G" or IgM or "immunoglobulin M" or immunoassay* or immuno-assay* or postinfection or post-infection or reactivate or reactivated or reactivation or recurrent or recurrence or reinfect* or re-infect* or repositive or re-positive or "second infection*" or seroepidemiolog* or serological or seronegativ* or seropositiv* or seroprevalence or "subsequent infection*" or T-cell or T-cells).ti,ab,kf. (1571174)
12 ("Alinity i SARS-CoV-2 IgG" or "Architect SARS-CoV-2 IgG" or "Assure COVID-19 IgG/IgM" or "Anti-SARS-CoV-2 Rapid Test" or "Babson Diagnostics aC19G1" or "Beckman Coulter Access SARS-CoV-2 IgG" or "WANTAI SARS-CoV-2" or "Platelia SARS-CoV-2" or "Biohit SARS-CoV-2 IgM/IgG" or "qSARS-CoV-2 IgG/IgM" or "LIAISON SARS-CoV-2 S1/S2 IgG" or "Diazyme DZ-Lite SARS-CoV-2 IgG" or "SARS-CoV-2 RBD IgG" or "SARS-COV-2 ELISA" or "RightSign COVID-19" or "LYHER Novel Coronavirus" or "COVID-19 IgG/IgM Rapid Test Cassette" or "SCoV-2 Detect IgG ELISA" or "SCoV-2 Detect IgM ELISA" or "Mt. Sinai Laboratory COVID-19 ELISA" or "VITROS Anti-SARS-CoV-2 IgG" or "VITROS Immunodiagnostic Products Anti-SARS-CoV" or "Elecsys Anti-SARS-CoV-2" or "ADVIA Centaur SARS-CoV-2" or COV2T or "Atellica IM SARS-CoV-2" or "Dimension EXL SARS-CoV-2 Total antibody" or "Dimension Vista SARS-CoV-2 Total antibody" or "Vibrant COVID-19 Ab" or "New York SARS-CoV Microsphere Immunoassay").ti,ab,kf. (19)
13 or/10-12 (2223243)
14 and/9,13 (4373)
15 14 and (202*.dp. or 20200101:20301231.ep.) (2647)
16 exp clinical trial/ or exp cohort studies/ or exp epidemiologic studies/ (3153243)
17 ("controlled clinical trial" or meta-analysis or "observational study" or "randomized controlled trial" or "systematic review").pt. (875867)

18 (cohort or cohorts or (control and (group* or study)) or cross-sectional or follow-up or longitudinal or meta-analy* or metaanaly* or observational or ((evidence or rapid or systematic) adj3 (review or synthesis)) or prospective or prospectively or ((random* or control*) adj3 trial) or retrospective or retrospectively or survey).ti,ab,kf. (4731249)
19 (assess* or ((active or adaptive or assess* or humoral or long-term or natural or protective or response) adj2 (immune or immunity or immunolog*)) or ((antibody or antibodies) adj3 (attenuat* or complete or detect or detected or detection or detections or level or levels or neutral* or positive)) or convalescent or "false immunity" or "false positive" or "false negative" or IgG or "immunoglobulin G" or IgM or "immunoglobulin M" or immunoassay* or immuno-assay* or inciden* or postinfection or post-infection or reactivate or reactivated or reactivation or recurrent or recurrence or reinfect* or re-infect* or repositive or re-positive or "second infection*" or seroepidemiolog* or serological or seronegativ* or seropositiv* or seroprevalence or "subsequent infection*").ti. (776693)
20 or/16-19 (6379286)
21 and/15,20 (1049)
22 21 not ((exp animals/ not humans/) or (animal* or primate*).ti.) (1035)
23 22 not ("in vitro techniques"/ or (case or "in vitro" or man or report or patient or woman).ti. or ("case reports" or comment or editorial or letter).pt.) (801)

Elsevier Embase

Date searched: August 5, 2020
#1 'coronavirus infection'/de OR 'coronavirus disease 2019'/de (38,075)
#2 coronavirus*:ti,ab,kw OR 'corona virus*':ti,ab,kw OR oc43:ti,ab,kw OR nl63:ti,ab,kw OR 229e:ti,ab,kw OR hku1:ti,ab,kw OR hcov*:ti,ab,kw OR ncov*:ti,ab,kw OR covid*:ti,ab,kw OR 'sars cov*':ti,ab,kw OR sarscov*:ti,ab,kw OR 'sars coronavirus*':ti,ab,kw OR 'severe acute respiratory syndrome':ti,ab,kw (53,792)
#3 #1 OR #2 (57,579)
#4 #3 NOT (sars:ti,ab,kw OR mers:ti,ab,kw OR 'mers cov':ti,ab,kw OR 'middle east respiratory syndrome':ti,ab,kw OR camel*:ti,ab,kw OR dromedar*:ti,ab,kw OR equine:ti,ab,kw OR coronary:ti,ab,kw OR coronal:ti,ab,kw OR covidence*:ti,ab,kw OR covidien:ti,ab,kw OR 'influenza virus':ti,ab,kw OR hiv:ti,ab,kw OR bovine:ti,ab,kw OR calves:ti,ab,kw OR tgev:ti,ab,kw OR feline:ti,ab,kw OR porcine:ti,ab,kw OR bcov:ti,ab,kw OR ped:ti,ab,kw OR pedv:ti,ab,kw OR pdcov:ti,ab,kw OR fipv:ti,ab,kw OR fcov:ti,ab,kw OR 'sads cov':ti,ab,kw OR canine:ti,ab,kw OR ccov:ti,ab,kw OR zoonotic:ti,ab,kw OR 'avian influenza':ti,ab,kw OR h1n1:ti,ab,kw OR h5n1:ti,ab,kw OR h5n6:ti,ab,kw OR ibv:ti,ab,kw OR murine:ti,ab,kw) (32,173)
#5 (covid*:ti,ab,kw OR coronavirus*:ti,ab,kw OR 'corona virus*':ti,ab,kw OR ncov*:ti,ab,kw OR '2019 ncov':ti,ab,kw OR sars*:ti,ab,kw OR 'pneumonia'/exp) AND wuhan:ti,ab,kw (2,347)
#6 '2019 ncov':ti,ab,kw OR ncov19:ti,ab,kw OR 'ncov 19':ti,ab,kw OR '2019-novel cov':ti,ab,kw OR 'sars cov2':ti,ab,kw OR 'sars cov 2':ti,ab,kw OR sarscov2:ti,ab,kw OR 'sarscov 2':ti,ab,kw OR 'sars coronavirus2':ti,ab,kw OR 'sars coronavirus 2':ti,ab,kw OR 'sars-like coronavirus*':ti,ab,kw OR 'coronavirus 19':ti,ab,kw OR covid19:ti,ab,kw OR 'covid 19':ti,ab,kw OR 'covid 2019':ti,ab,kw OR (((novel OR new OR nouveau) NEAR/2 (cov OR ncov OR covid OR coronavirus* OR 'corona virus' OR pandemi*2)):ti,ab,kw) OR ((covid:ti,ab,kw OR covid19:ti,ab,kw OR 'covid 19':ti,ab,kw) AND pandemic*2:ti,ab,kw) OR (coronavirus*:ti,ab,kw AND pneumonia:ti,ab,kw) (37,049)
#7 #4 OR #5 OR #6 (45,302)
#8 'antibodies,antisera and immunoglobulins'/exp OR 'immunity'/exp (2,692,035)
#9 (((active OR adaptive OR assess* OR humoral OR 'long term' OR natural OR protective OR response) NEAR/2 (immune OR immunity OR immunolog*)):ti,ab,kw) OR (((antibody OR antibodies) NEAR/5 (attenuat* OR complete OR detect OR detected OR detection OR detections OR level OR levels OR neutral* OR positive)):ti,ab,kw) OR convalescent:ti,ab,kw OR 'false immunity':ti,ab,kw OR 'false positive':ti,ab,kw OR 'false negative':ti,ab,kw OR igg:ti,ab,kw OR 'immunoglobulin g':ti,ab,kw OR

igm:ti,ab,kw OR 'immunoglobulin m':ti,ab,kw OR immunoassay*:ti,ab,kw OR 'immuno assay*':ti,ab,kw OR postinfection:ti,ab,kw OR 'post infection':ti,ab,kw OR reactivate:ti,ab,kw OR reactivated:ti,ab,kw OR reactivation:ti,ab,kw OR recurrent:ti,ab,kw OR recurrence:ti,ab,kw OR reinfect*:ti,ab,kw OR 're infect*':ti,ab,kw OR repositive:ti,ab,kw OR 're positive':ti,ab,kw OR 'second infection*':ti,ab,kw OR seroepidemiolog*:ti,ab,kw OR serological:ti,ab,kw OR seronegativ*:ti,ab,kw OR seropositiv*:ti,ab,kw OR seroprevalence:ti,ab,kw OR 'subsequent infection*':ti,ab,kw OR 't cell':ti,ab,kw OR 't cells':ti,ab,kw (2,159,420)
#10 'alinity i sars-cov-2 igg':ti,ab,kw OR 'architect sars-cov-2 igg':ti,ab,kw OR 'assure covid-19 igg/igm':ti,ab,kw OR 'anti-sars-cov-2 rapid test':ti,ab,kw OR 'babson diagnostics ac19g1':ti,ab,kw OR 'beckman coulter access sars-cov-2 igg':ti,ab,kw OR 'wantai sars-cov-2':ti,ab,kw OR 'platelia sars-cov-2':ti,ab,kw OR 'biohit sars-cov-2 igm/igg':ti,ab,kw OR 'qsars-cov-2 igg/igm':ti,ab,kw OR 'liaison sars-cov-2 s1/s2 igg':ti,ab,kw OR 'diazyme dz-lite sars-cov-2 igg':ti,ab,kw OR 'sars-cov-2 rbd igg':ti,ab,kw OR 'sars-cov-2 elisa':ti,ab,kw OR 'rightsign covid-19':ti,ab,kw OR 'lyher novel coronavirus':ti,ab,kw OR 'covid-19 igg/igm rapid test cassette':ti,ab,kw OR 'scov-2 detect igg elisa':ti,ab,kw OR 'scov-2 detect igm elisa':ti,ab,kw OR 'mt. sinai laboratory covid-19 elisa':ti,ab,kw OR 'vitros anti-sars-cov-2 igg':ti,ab,kw OR 'vitros immunodiagnostic products anti-sars-cov':ti,ab,kw OR 'elecsys anti-sars-cov-2':ti,ab,kw OR 'advia centaur sars-cov-2':ti,ab,kw OR cov2t:ti,ab,kw OR 'atellica im sars-cov-2':ti,ab,kw OR 'dimension exl sars-cov-2 total antibody':ti,ab,kw OR 'dimension vista sars-cov-2 total antibody':ti,ab,kw OR 'vibrant covid-19 ab':ti,ab,kw OR 'new york sars-cov microsphere immunoassay':ti,ab,kw (18)
#11 #8 OR #9 OR #10 (3,903,483)
#12 #7 AND #11 (6,621)
#13 #12 AND (2020:py OR 2021:py) (5,292)
#14 'clinical trial'/de OR 'randomized controlled trial'/de OR 'randomization'/de OR 'single blind procedure'/de OR 'double blind procedure'/de OR 'crossover procedure'/de OR 'placebo'/de OR 'prospective study'/de OR ('randomi?ed controlled' NEXT/1 trial*) OR rct OR 'randomly allocated' OR 'allocated randomly' OR 'random allocation' OR (allocated NEAR/2 random) OR (single NEXT/1 blind*) OR (double NEXT/1 blind*) OR ((treble OR triple) NEAR/1 blind*) OR placebo* (2,349,364)
#15 'meta analysis'/exp OR 'systematic review'/de OR 'observational study'/de (542,335)
#17 assess*:ti OR (((active OR adaptive OR assess* OR humoral OR 'long term' OR natural OR protective OR response) NEAR/2 (immune OR immunity OR immunolog*)):ti) OR (((antibody OR antibodies) NEAR/3 (attenuat* OR complete OR detect OR detected OR detection OR detections OR level OR levels OR neutral* OR positive)):ti) OR convalescent:ti OR 'false immunity':ti OR 'false positive':ti OR 'false negative':ti OR igg:ti OR 'immunoglobulin g':ti OR igm:ti OR 'immunoglobulin m':ti OR immunoassay*:ti OR 'immuno assay*':ti OR inciden*:ti OR postinfection:ti OR 'post infection':ti OR reactivate:ti OR reactivated:ti OR reactivation:ti OR recurrent:ti OR recurrence:ti OR reinfect*:ti OR 're infect*':ti OR repositive:ti OR 're positive':ti OR 'second infection*':ti OR seroepidemiolog*:ti OR serological:ti OR seronegativ*:ti OR seropositiv*:ti OR seroprevalence:ti OR 'subsequent infection*':ti (1,023,676)
#16 cohort:ti,ab,kw OR cohorts:ti,ab,kw OR ((control NEAR/3 (group* OR study)):ti,ab,kw) OR 'cross sectional':ti,ab,kw OR 'follow up':ti,ab,kw OR longitudinal:ti,ab,kw OR 'meta analy*':ti,ab,kw OR metaanaly*:ti,ab,kw OR observational:ti,ab,kw OR (((evidence OR rapid OR systematic) NEAR/3 (review OR synthesis)):ti,ab,kw) OR prospective:ti,ab,kw OR prospectively:ti,ab,kw OR (((random* OR control*) NEAR/3 trial):ti,ab,kw) OR retrospective:ti,ab,kw OR retrospectively:ti,ab,kw OR survey:ti,ab,kw (5,907,213)
#18 #14 OR #15 OR #16 OR #17 (7,720,648)
#19 #13 AND #18 (1,561)
#20 #19 NOT ('animal'/exp NOT 'human'/exp OR animal*:ti OR primate*:ti) (1,545)
#21 #20 NOT ('in vitro study'/exp OR case:ti OR 'in vitro':ti OR man:ti OR report:ti OR patient:ti OR woman:ti OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'case report'/de) (918)
#22 #21 AND [embase]/lim NOT ([embase]/lim AND [medline]/lim) (265)

Cochrane Central Register of Controlled Trials (Ovid EBM Reviews)

Date searched: August 5, 2020
1 (coronavirus* or corona-virus* or OC43 or NL63 or 229E or HKU1 or HCoV* or ncov* or covid* or sars-cov* or sarscov* or Sars-coronavirus* or "Severe Acute Respiratory Syndrome").ti,ab. (2228)
2 ((pneumonia or covid* or coronavirus* or corona virus* or ncov* or 2019-ncov or sars*) and Wuhan).ti,ab. (85)
3 (2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19 or covid 2019 or ((novel or new or nouveau) adj2 (CoV or nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or ((covid or covid19 or covid-19) and pandemic*2) or (coronavirus* and pneumonia)).ti,ab. (938)
4 or/1-3 (2252)
5 (((active or adaptive or assess* or humoral or long-term or natural or protective or response) adj2 (immune or immunity or immunolog*)) or ((antibody or antibodies) adj5 (attenuat* or complete or detect or detected or detection or detections or level or levels or neutral* or positive)) or convalescent or "false immunity" or "false positive" or "false negative" or IgG or "immunoglobulin G" or IgM or "immunoglobulin M" or immunoassay* or immuno-assay* or postinfection or post-infection or reactivate or reactivated or reactivation or recurrent or recurrence or reinfect* or re-infect* or repositive or re-positive or "second infection*" or seroepidemiolog* or serological or seronegativ* or seropositiv* or seroprevalence or "subsequent infection*" or T-cell or T-cells).ti,ab. (97064)
6 ("Alinity i SARS-CoV-2 IgG" or "Architect SARS-CoV-2 IgG" or "Assure COVID-19 IgG/IgM" or "Anti-SARS-CoV-2 Rapid Test" or "Babson Diagnostics aC19G1" or "Beckman Coulter Access SARS-CoV-2 IgG" or "WANTAI SARS-CoV-2" or "Platelia SARS-CoV-2" or "Biohit SARS-CoV-2 IgM/IgG" or "qSARS-CoV-2 IgG/IgM" or "LIAISON SARS-CoV-2 S1/S2 IgG" or "Diazyme DZ-Lite SARS-CoV-2 IgG" or "SARS-CoV-2 RBD IgG" or "SARS-COV-2 ELISA" or "RightSign COVID-19" or "LYHER Novel Coronavirus" or "COVID-19 IgG/IgM Rapid Test Cassette" or "SCoV-2 Detect IgG ELISA" or "SCoV-2 Detect IgM ELISA" or "Mt. Sinai Laboratory COVID-19 ELISA" or "VITROS Anti-SARS-CoV-2 IgG" or "VITROS Immunodiagnostic Products Anti-SARS-CoV" or "Elecsys Anti-SARS-CoV-2" or "ADVIA Centaur SARS-CoV-2" or COV2T or "Atellica IM SARS-CoV-2" or "Dimension EXL SARS-CoV-2 Total antibody" or "Dimension Vista SARS-CoV-2 Total antibody" or "Vibrant COVID-19 Ab" or "New York SARS-CoV Microsphere Immunoassay").ti,ab. (0)
7 or/5-6 (97064)
8 and/4,7 (199)
9 limit 8 to yr="2020 -Current" (120)

CINAHL Plus With Full Text

Date searched: August 7, 2020
S1 (MH "Coronavirus") OR (MH "Coronavirus Infections") OR (MH "COVID-19") (9,838)
S2 TI (coronavirus* OR corona-virus* OR OC43 OR NL63 OR 229E OR HKU1 OR HCoV* OR ncov* OR covid* OR sars-cov* OR sarscov* OR Sars-coronavirus* OR "Severe Acute Respiratory Syndrome") OR AB (coronavirus* OR corona-virus* OR OC43 OR NL63 OR 229E OR HKU1 OR HCoV* OR ncov* OR covid* OR sars-cov* OR sarscov* OR Sars-coronavirus* OR "Severe Acute Respiratory Syndrome") (12,901)
S3 S1 OR S2 (14,816)
S4 TI (SARS OR MERS OR MERS-CoV OR "Middle East respiratory syndrome" OR camel* OR dromedar* OR equine OR coronary OR coronal OR covidence* OR covidien OR "influenza virus" OR HIV OR bovine OR calves OR TGEV OR feline OR porcine OR BCoV OR PED OR PEDV OR PDCoV OR FIPV OR FCoV OR SADS-CoV OR canine OR CCov OR zoonotic OR "avian influenza" OR H1N1

OR H5N1 OR H5N6 OR IBV OR murine) OR AB (SARS OR MERS OR MERS-CoV OR "Middle East respiratory syndrome" OR camel* OR dromedar* OR equine OR coronary OR coronal OR covidence* OR covidien OR "influenza virus" OR HIV OR bovine OR calves OR TGEV OR feline OR porcine OR BCoV OR PED OR PEDV OR PDCoV OR FIPV OR FCoV OR SADS-CoV OR canine OR CCov OR zoonotic OR "avian influenza" OR H1N1 OR H5N1 OR H5N6 OR IBV OR murine) (231,787)
S5 S3 NOT S4 (12,643)
S6 (TI (pneumonia OR covid* OR coronavirus* OR corona virus* OR ncov* OR 2019-ncov OR sars*) OR AB (pneumonia OR covid* OR coronavirus* OR corona virus* OR ncov* OR 2019-ncov OR sars*) OR (MH "Pneumonia+")) AND Wuhan (482)
S7 TI ((2019-ncov OR ncov19 OR ncov-19 OR 2019-novel CoV OR sars-cov2 OR sars-cov-2 OR sarscov2 OR sarscov-2 OR Sars-coronavirus2 OR Sars-coronavirus-2 OR SARS-like coronavirus* OR coronavirus-19 OR covid19 OR covid-19 OR covid 2019 OR ((novel OR new OR nouveau) N2 (CoV OR nCoV OR covid OR coronavirus* OR corona virus OR Pandemi*2)) OR ((covid OR covid19 OR covid-19) and pandemic*2) OR (coronavirus* AND pneumonia))) OR AB ((2019-ncov OR ncov19 OR ncov-19 OR 2019-novel CoV OR sars-cov2 OR sars-cov-2 OR sarscov2 OR sarscov-2 OR Sars-coronavirus2 OR Sars-coronavirus-2 OR SARS-like coronavirus* OR coronavirus-19 OR covid19 OR covid-19 OR covid 2019 OR ((novel OR new OR nouveau) N2 (CoV OR nCoV OR covid OR coronavirus* OR corona virus OR Pandemi*2)) OR ((covid OR covid19 OR covid-19) and pandemic*2) OR (coronavirus* AND pneumonia))) (10,325)
S8 S5 OR S6 OR S7 (13,330)
S9 (MH "Antibodies+") OR (MH "Immunity+") (108,403)
S10 TI ((((active OR adaptive OR assess* OR humoral OR long-term OR natural OR protective OR response) N2 (immune OR immunity OR immunolog*)) OR ((antibody OR antibodies) N5 (attenuat* OR complete OR detect OR detected OR detection OR detections OR level OR levels OR neutral* OR positive)) OR convalescent OR "false immunity" OR "false positive" OR "false negative" OR IgG OR "immunoglobulin G" OR IgM OR "immunoglobulin M" OR immunoassay* OR immuno-assay* OR postinfection OR post-infection OR reactivate OR reactivated OR reactivation OR recurrent OR recurrence OR reinfect* OR re-infect* OR repositive OR re-positive OR "second infection*" OR seroepidemiolog* OR serological OR seronegativ* OR seropositiv* OR seroprevalence OR "subsequent infection*" OR T-cell OR T-cells)) OR AB ((((active OR adaptive OR assess* OR humoral OR long-term OR natural OR protective OR response) N2 (immune OR immunity OR immunolog*)) OR ((antibody OR antibodies) N5 (attenuat* OR complete OR detect OR detected OR detection OR detections OR level OR levels OR neutral* OR positive)) OR convalescent OR "false immunity" OR "false positive" OR "false negative" OR IgG OR "immunoglobulin G" OR IgM OR "immunoglobulin M" OR immunoassay* OR immuno-assay* OR postinfection OR post-infection OR reactivate OR reactivated OR reactivation OR recurrent OR recurrence OR reinfect* OR re-infect* OR repositive OR re-positive OR "second infection*" OR seroepidemiolog* OR serological OR seronegativ* OR seropositiv* OR seroprevalence OR "subsequent infection*" OR T-cell OR T-cells)) (172,897)
S11 TI (("Alinity i SARS-CoV-2 IgG" OR "Architect SARS-CoV-2 IgG" OR "Assure COVID-19 IgG/IgM" OR "Anti-SARS-CoV-2 Rapid Test" OR "Babson Diagnostics aC19G1" OR "Beckman Coulter Access SARS-CoV-2 IgG" OR "WANTAI SARS-CoV-2" OR "Platelia SARS-CoV-2" OR "Biohit SARS-CoV-2 IgM/IgG" OR "qSARS-CoV-2 IgG/IgM" OR "LIAISON SARS-CoV-2 S1/S2 IgG" OR "Diazyme DZ-Lite SARS-CoV-2 IgG" OR "SARS-CoV-2 RBD IgG" OR "SARS-COV-2 ELISA" OR "RightSign COVID-19" OR "LYHER Novel Coronavirus" OR "COVID-19 IgG/IgM Rapid Test Cassette" OR "SCoV-2 Detect IgG ELISA" OR "SCoV-2 Detect IgM ELISA" OR "Mt. Sinai Laboratory COVID-19 ELISA" OR "VITROS Anti-SARS-CoV-2 IgG" OR "VITROS Immunodiagnostic Products Anti-SARS-CoV" OR "Elecsys Anti-SARS-CoV-2" OR "ADVIA Centaur SARS-CoV-2" OR COV2T OR "Atellica IM SARS-CoV-2" OR "Dimension EXL SARS-CoV-2 Total antibody" OR "Dimension Vista SARS-CoV-2 Total antibody" OR "Vibrant COVID-19 Ab" OR "New York SARS-CoV

Microsphere Immunoassay")) OR AB (("Alinity i SARS-CoV-2 IgG" OR "Architect SARS-CoV-2 IgG" OR "Assure COVID-19 IgG/IgM" OR "Anti-SARS-CoV-2 Rapid Test" OR "Babson Diagnostics aC19G1" OR "Beckman Coulter Access SARS-CoV-2 IgG" OR "WANTAI SARS-CoV-2" OR "Platelia SARS-CoV-2" OR "Biohit SARS-CoV-2 IgM/IgG" OR "qSARS-CoV-2 IgG/IgM" OR "LIAISON SARS-CoV-2 S1/S2 IgG" OR "Diazyme DZ-Lite SARS-CoV-2 IgG" OR "SARS-CoV-2 RBD IgG" OR "SARS-COV-2 ELISA" OR "RightSign COVID-19" OR "LYHER Novel Coronavirus" OR "COVID-19 IgG/IgM Rapid Test Cassette" OR "SCoV-2 Detect IgG ELISA" OR "SCoV-2 Detect IgM ELISA" OR "Mt. Sinai Laboratory COVID-19 ELISA" OR "VITROS Anti-SARS-CoV-2 IgG" OR "VITROS Immunodiagnostic Products Anti-SARS-CoV" OR "Elecsys Anti-SARS-CoV-2" OR "ADVIA Centaur SARS-CoV-2" OR COV2T OR "Atellica IM SARS-CoV-2" OR "Dimension EXL SARS-CoV-2 Total antibody" OR "Dimension Vista SARS-CoV-2 Total antibody" OR "Vibrant COVID-19 Ab" OR "New York SARS-CoV Microsphere Immunoassay")) (0)
S12 S9 OR S10 OR S11 (255,093)
S13 S8 AND S12 [Limiters - Publication Type: Clinical Trial, Meta Analysis, Randomized Controlled Trial, Systematic Review] (6)
S14 TI ((cohort OR cohorts OR (control AND (group* OR study)) OR cross-sectional OR follow-up OR longitudinal OR meta-analy* OR metaanaly* OR observational OR ((evidence OR rapid OR systematic) N3 (review OR synthesis)) OR prospective OR prospectively OR ((random* or control*) N3 trial) OR retrospective OR retrospectively OR survey)) OR AB ((cohort OR cohorts OR (control AND (group* OR study)) OR cross-sectional OR follow-up OR longitudinal OR meta-analy* OR metaanaly* OR observational OR ((evidence OR rapid OR systematic) N3 (review OR synthesis)) OR prospective OR prospectively OR ((random* or control*) N3 trial) OR retrospective OR retrospectively OR survey)) (1,424,933)
S15 TI (assess* OR ((active OR adaptive OR assess* OR humoral OR long-term OR natural OR protective OR response) N2 (immune OR immunity OR immunolog*)) OR ((antibody OR antibodies) N3 (attenuat* OR complete OR detect OR detected OR detection OR detections OR level OR levels OR neutral* OR positive)) OR convalescent OR "false immunity" OR "false positive" OR "false negative" OR IgG OR "immunoglobulin G" OR IgM OR "immunoglobulin M" OR immunoassay* OR immuno-assay* OR inciden* OR postinfection OR post-infection OR reactivate OR reactivated OR reactivation OR recurrent OR recurrence OR reinfect* OR re-infect* OR repositive OR re-positive OR "second infection*" OR seroepidemiolog* OR serological OR seronegativ* OR seropositiv* OR seroprevalence OR "subsequent infection*") (212,433)
S16 S13 OR S14 OR S15 (1,568,048)
S17 S8 AND S12 AND S16 [Limiters - Published Date: 20200101-20201231; Exclude MEDLINE records] (41)
S18 TI (case OR "in vitro" OR man OR report OR patient OR woman) OR MH ("In Vitro Studies") OR MH("Case Studies") (446,398)
S19 S17 NOT S18 (35)

ClinicalTrials.gov

Date searched: August 5, 2020
AREA[OverallStatus] EXPAND[Term] COVER[FullMatch] ("Recruiting" OR "Active, not recruiting" OR "Completed") AND AREA[ConditionSearch] (2019-ncov OR ncov19 OR ncov-19 OR 2019-novel CoV OR sars-cov2 OR sars-cov-2 OR sarscov2 OR sarscov-2 OR Sars-coronavirus2 OR Sars-coronavirus-2 OR SARS-like coronavirus OR coronavirus-19 OR covid19 OR covid-19 OR covid 2019 OR (novel OR new OR nouveau) AND (CoV OR nCoV OR covid OR coronavirus OR corona virus OR Pandemic) OR (covid OR covid19 OR covid-19) AND pandemic OR coronavirus AND pneumonia) AND AREA[InterventionSearch] (immunity OR antibodies OR convalescent OR EXPAND[Concept] "false immunity" OR EXPAND[Concept] "false positive" OR EXPAND[Concept] "false negative" OR IgG OR immunoglobulin OR IgM OR immunoassay or immuno-assay OR postinfection OR post-

infection OR reactivated OR recurrent OR reinfection OR re-infection OR repositive OR re-positive OR EXPAND[Concept] "second infection" OR seroepidemiology OR serological OR seronegative OR seropositive OR seroprevalence OR EXPAND[Concept] "subsequent infection" OR T-cell) AND AREA[StudyFirstPostDate] EXPAND[Term] RANGE[01/01/2020, 08/05/2020] (171)

WHO COVID

Date searched: August 5, 2020
tw:((ti:(immunity OR antibody OR serological OR seroepidemiology OR seroprevalence OR seropositive OR seropositivity OR seronegative OR seronegativity OR post-infection OR postinfection OR convalescent OR recurrent OR recurrence OR reactivated OR reactivation OR immunoglobulin OR igg OR igm OR immune-assay OR immunoassay))) AND db:("COVIDWHO") AND year_cluster:("2020")

Covid19reviews.org

Date searched: August 5, 2020
Keyword searching: immunity, antibody, serological, seroepidemiology, seroprevalence, seropositive, seropositivity, seronegative, seronegativity, post-infection, postinfection, convalescent, recurrent, recurrence, reactivated, reactivation, false, secondary, immunoglobulin, IgG, IgM, immune-assay, immunoassay

Appendix B. Inclusion/Exclusion Criteria

Table B-1. Inclusion and exclusion criteria

PICOTS	Inclusion and Exclusion Criteria
Population	**Include**: **KQ 1,4**: Adults with RT-PCR-confirmed SARS-CoV-2 infection who underwent serologic testing for antibodies to SARS-CoV-2 (e.g. IgM, IgG, IgA, etc.) using an immunoassay. **KQ 2-3**: Adults with RT-PCR-confirmed SARS-CoV-2 infection who underwent serologic testing using an immunoassay and had detectable antibodies to SARS-CoV-2 (e.g. IgM, IgG, IgA, etc.). **Exclude**: Children less than 18 years of age; studies using serologic assays that have had Emergency Use Authorization revoked by the U.S. Food and Drug Administration.
Outcomes	**Include:** **KQ 1:** • Levels of antibodies to SARS-CoV-2 • Length of time that antibodies remain detectable **KQ 2:** • Incidence of reinfection (defined as new clinical or laboratory evidence of COVID-19 after a documented period of recovery, or according to the most recent definition of reinfection per the U.S. Centers for Disease Control and Prevention)[87] **KQ 3:** • Duration of immunity (i.e. length of time between an initial RT-PCR-confirmed SARS-CoV-2 infection with clinical recovery to another SARS-CoV-2 infection) **KQ 4:** • Unintended consequences of antibody testing after SARS-CoV-2 infection (*e.g.,* discontinuation of recommended safety practices such as wearing masks or social distancing due to misinterpretation of positive antibody test results as indicative of immunity) We will stratify outcomes by the following factors: • Patient characteristics (i.e. age, gender, race/ethnicity, comorbidities) • COVID-19 severity (i.e. mild, moderate, severe, and critical as defined in NIH COVID-19 treatment guidelines)[90] • Presence of symptoms (asymptomatic or symptomatic) • Time from symptom onset or RT-PCR diagnosis to antibody testing • Type of test and characteristics of the immunoassay (i.e., name, manufacturer, sensitivity and specificity, test methodology, test kit identifying information, lot number, expiration dates)
Eligible study designs	**Include:** Any study design that addresses the key questions and otherwise meets eligibility criteria, including systematic reviews, randomized controlled trials (RCTs), and controlled and uncontrolled observational studies. We will include intervention series (i.e., prospective studies that assess outcomes of interest among a series of patients. Systematic reviews that meet criteria for timeliness, relevance, and quality. **Exclude:** Descriptive case series with <25 subjects, case reports, non-peer reviewed articles, commentaries (i.e. editorials, non-systematic reviews), and systematic reviews that do not meet the criteria detailed above. Animal studies, in-vitro studies, and studies of infection with coronavirus other than SARS-CoV-2 (e.g., SARS-CoV-1, MERS-CoV, seasonal coronaviruses).
Study settings	**Include**: Any setting (*i.e.* nursing facility, community, acute care hospital, prison, public health clinic, private clinic, etc.). **Exclude**: None

Abbreviations: CDC = Centers for Disease Control and Prevention; CoV = coronavirus; COVID-19 = coronavirus disease 2019; EUA = emergency use authorization; FDA = Food and Drug Administration; IgG/M = immunoglobulin G/M; KQ = key question; MERS = Middle East respiratory syndrome; NIH = National Institutes of Health; PICOTS = population, intervention, comparator, outcome, timing, setting; RCT = randomized controlled trial; RT-PCR = reverse transcription polymerase chain reaction; SARS = severe acute respiratory syndrome; US = United States; WHO = World Health Organization.

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Appendix C. Evidence Tables

Table C-1. Characteristics of included studies

Author, Year, Country	Number of Participants (Number of RT-PCR+ participants)	RT-PCR+ Population Description	Age (Range or SD)	Sex: Male N (%)	Race/Ethnicity: N (%)	Comorbidities: N (%)
Andrey, 2020[16] Switzerland	91 (41)	Adults hospitalized with moderate to severe disease[a]	*RT-PCR+ participants*: Age (Median): 71 (IQR: 63-76)	*RT-PCR+ participants*: Male: 32 (78)	NR	NR
Andrey, 2020[17] Switzerland	91 (46)	Adults hospitalized with moderate to severe disease[a]	*RT-PCR+ participants*: Age (Median): 66 (IQR: 51-76)	*RT-PCR+ participants*: Male: 28 (61)	NR	NR
Bao, 2020[18] China	160 (103)	Hospitalized (67%) and recovered (33%) adults[a]	*RT-PCR+ participants:* Age (Median): 44 (Range: 21-83)	NR	NR	NR
Blain, 2020[19] France	113 (46)	79 nursing home residents and 34 healthcare workers with a range of asymptomatic to severe disease[a]	*Nursing home residents (NR for staff)*: Age (Mean): 86 (SD: 16)	NR	NR	DM: 9 (24) Obesity: 10 (26) CVD: 32 (84) Cerebrovascular disease. 10 (26) Chronic lung disease: 9 (23)
Bruni, 2020[20] Italy	98 (40)	Adults recovered from asymptomatic (8%), mild symptomatic (60%) and moderate to severe (32%) disease evaluated as potential convalescent plasma donors[a]	*Hospitalized*: Age (Mean): 64 (SD: 8) *Non-hospitalized*: Age (Mean): 53 (SD: 9)	*Hospitalized*: Male: 18 (75) *Non-hospitalized*: Male: 9 (56)	NR	*Hospitalized*: DM: 5 (21) Obesity: 3 (13) Cardiopulmonary: 7 (29) *Non-hospitalized*: Obesity: 1 (6) Cardiopulmonary: 2 (12)

Author, Year, Country	Number of Participants (Number of RT-PCR+ participants)	RT-PCR+ Population Description	Age (Range or SD)	Sex: Male N (%)	Race/Ethnicity: N (%)	Comorbidities: N (%)
Chen, 2020[21] China	1,578 (1,532)	Adults hospitalized with mild to moderate (43%), severe (51%) and critical (6%) disease[a]	*Total sample*: Age (Median): 60 (IQR: 51-68)	*Total sample*: Male: 779 (49)	NR	*Total sample*: DM: 250 (16) HTN: 492 (31) CAD: 104 (7) Cerebrovascular disease: 65 (4) COPD: 8 (<1) Malignancy: 35 (2)
Chen, 2020[22] U.S.	92 (91)	Outpatient (93%) and hospitalized (7%) adults with predominantly mild disease[b]	*Total sample*: Age (Mean): 43 (SD: 15)	*Total sample*: Male: 26 (29)	*Total sample*: AA/Black: 1 (1) Asian: 6 (7) Hispanic: 4 (4) NH White: 83 (90)	*Total sample*: DM: 1 (1) CVD: 9 (10) Lung Disease: 11 (12) Immunosuppressed: 2 (2)
Chirathaworn, 2020[23] Thailand	525 (217)	Adults recovered from asymptomatic (2%), mild (70%), and moderate- severe (28%) disease[c]	*RT-PCR+ participants:* Age (Median) 33 (IQR: 25-47)	*RT-PCR+ participants:* Male: 92 (42)	NR	NR
Choe, 2020[24] Republic of Korea	149 (70)	Adults quarantined in a COVID-19 hospital ward[a]	*RT-PCR+ participants*: Age (Mean): 68 (SD: 16)	*RT-PCR+ participants*: Male: 30 (43)	NR	*RT-PCR+ participants*: DM: 17 (24) HTN: 25 (36) CVD: 11 (16) CKD: 5 (7) Lung Disease: 14 (20)
Crawford, 2020[25] U.S.	32 (32)	Outpatients with asymptomatic (19%) and mild (57%) disease and hospitalized patients with moderate-severe (24%) disease[a]	Age (Median): 45 (22-79)	Male: 14 (44)	AA/Black: 0 (0) AI/AN: 1 (3) Asian: 4 (13) Hispanic: 1 (3) NH White: 26 (81)	DM: 1 (3) HTN: 3 (90 Asthma: 1 (3) COPD: 1 (3) Malignancy: 1 (3)
Dave, 2020[26] India	100 (100)	Adults with asymptomatic (76%), mild to moderate (17%) and severe (7%) disease admitted to a dedicated COVID-19 ward[a]	Age (Mean): 37 (Range: NR)	Male: 45 (45)	NR	DM, HTN, thyroid disorder, or malignancy: 22 (22)

Author, Year, Country	Number of Participants (Number of RT-PCR+ participants)	RT-PCR+ Population Description	Age (Range or SD)	Sex: Male N (%)	Race/Ethnicity: N (%)	Comorbidities: N (%)
de la Iglesia, 2020[27] Spain	110 (58)	Convenience sample of non-hospitalized adults with mild disease registered in the public health department database of Leon, Spain[a]	*Total sample*: Age (Mean): 48 (SD: 11)	*Total sample*: Male: 48 (48)	NR	NR
Delliere, 2020[28] France	102 (102)	A mix of hospitalized and outpatient adults with asymptomatic (2%), mild (36%), severe (34%) and critical (28%) disease[d]	Age (Mean): 52 (SD: 16)	Male: 59 (58)	NR	Malignancy: 4 (4)
Fafi-Kremer, 2020[29] France	160 (160)	Healthcare workers recovered from asymptomatic and mildly symptomatic infection[a]	Age (Median): 32 (IQR: 26-44)	Male: 50 (31)	NR	HTN: 10 (6) Obesity: 17 (11) Asthma: 11 (7)
Flannery, 2020[30] U.S.	1,293 (46)	Asymptomatic and mildly symptomatic parturient women presenting for child delivery at two urban hospitals in Philadelphia[a]	*Total sample*: Age (Median): 31 (IQR: 27-35)	*Total sample*: Male: 0 (0)	*Total sample*: AA/Black: 537 (42) Asian: 106 (8) Hispanic: 125 (10) NH White: 447 (35)	*Total sample*: Obesity: 337 (26) DM: 113 (9) HTN: 404 (31) Asthma: 194 (15)
Gudbjartsson, 2020[15] Iceland	30,576 (1,263)	Hospitalized and recovered patients with mild, moderate, and severe disease[e]	*Hospitalized (RT-PCR+ participants)*: Age (Mean): 66 (SD: 12) *Recovered (RT-PCR+ participants)*: Age (Mean): 43 (SD: 16)	*Hospitalized (RT-PCR+ participants)*: Male: 29 (60) *Recovered (RT-PCR+ participants)*: Male: 583 (48)	NR	NR
Hou, 2020[31] China	338 (338)	Hospitalized adults with mild (19%), severe (59%) and critical (22%) illness[f]	Age (Mean): 62 (SD: 16)	Male: 171 (51)	NR	DM: 63 (19) HTN: 140 (41) CVD: 18 (5) Malignancy: 17 (5)

Author, Year, Country	Number of Participants (Number of RT-PCR+ participants)	RT-PCR+ Population Description	Age (Range or SD)	Sex: Male N (%)	Race/Ethnicity: N (%)	Comorbidities: N (%)
Huang, 2020[32] China	366 (366)	Adults hospitalized with a mix of mild (61%) and severe (39%) disease[a]	Age (Median): 62 (IRQ: 51-69)	Male: 176 (48)	NR	DM: 65 (18) HTN: 136 (37)
Imai, 2020[33] Japan	112 (112)	Asymptomatic (34%) and symptomatic (66%) adults referred for evaluation at two urban hospitals[g]	Age (Median): 67 (IQR: 45-74)	Male: 64 (57)	NR	NR
Infantino, 2020[34] Italy	64 (64)	Adults hospitalized with mild-moderate (49%) and severe (51%) disease[a]	Age (Mean): 59 (SD: 23)	Male: 26 (43)	NR	NR
Isho, 2020[35] Canada	986 (567)	Adults with a mix of mild to severe illness[h]	*RT-PCR+ participants:* Age (Median range across cohorts): 58-61	*RT-PCR+ participants:* Male: 305 (54)	NR	NR
Iversen, 2020[36] Denmark	29,117 (360)	Healthcare workers recovered from asymptomatic (22%) and mildly symptomatic (78%) infection participating in seroprevalence survey[a]	*Total sample*: Male: 6,077 (21)	*Total sample*: Male: 6,077 (21)	NR	NR
Iyer, 2020[37] U.S.	1,891 (343)	Adults hospitalized with predominantly severe (93%) illness[a]	*RT-PCR+ participants:* Age (Median): 59 (IQR: 45-71)	*RT-PCR+ participants:* Male: 213 (62)	*RT-PCR+ participants:* AA/Black: 34 (10) Asian, AI/AN, or other: 30 (9) Hispanic: 121 (35) NH White: 125 (36)	*RT-PCR+ participants:* Immunosuppressed: 26 (8)
Jaaskelainen, 2020[38] Finland	40 (40)	Adults hospitalized with asymptomatic to mild (24%), moderate (41%), and severe- critical (35%) disease[a]	Age: 56 (Range: 24-77)	Male: 23 (58)	NR	NR

Author, Year, Country	Number of Participants (Number of RT-PCR+ participants)	RT-PCR+ Population Description	Age (Range or SD)	Sex: Male N (%)	Race/Ethnicity: N (%)	Comorbidities: N (%)
Ko, 2020[39] Republic of Korea	70 (70)	Hospitalized and outpatient adults with asymptomatic (21%), mildly symptomatic (70%) and severe (9%) disease[i]	Age (mean): Asymptomatic 25 (SD: 8); Mild 31 (SD: 9); Pneumonia 66 (SD: 13)	Male: 31 (44)	NR	DM: 6 (9) HTN: 2 (3) Malignancy: 1 (1)
Koblischke, 2020[40] Austria	29 (29)	Adults hospitalized with a mix of moderate (45%) and severe (55%) disease[a]	Age (mean): Moderate 72 (Range: 29-98); Severe 57 (Range: 12-77); Deceased 78 (Range: 63-84)	Male: 16 (55)	NR	DM: 8 (28) HTN: 12 (41) COPD: 2 (7)
Kwon, 2020[41] China	31 (31)	Adults hospitalized with asymptomatic (3%), mild (16%), moderate (55%), severe (19%) and critical (7%) disease[j]	Age (Mean): 50 (SD: 3)	Male: 13 (42)	NR	DM: 4 (13) HTN: 9 (29) COPD: 2 (6) Obesity: 1 (3)
Li, 2020[42] China	1850 (1850)	Adults hospitalized with mild to moderate (43%) and severe-critical (57%) disease[i]	*Mild-Moderate*: Age (Median): 47 (IQR: 57-65) *Severe-Critical*: Age (Median): 55 (IQR: 64-72)	*Mild-Moderate*: Male: 399 (50) *Severe-Critical*: Male: 530 (50)	NR	*Mild-Moderate*: HTN: 217 (27) DM: 107 (14) CVD: 68 (9) Cerebrovascular disease: 26 (3) Malignancy: 15 (2) *Severe-Critical*: HTN: 389 (37) DM: 181 (17) CVD: 164 (16) Cerebrovascular disease: 72 (7) Malignancy: 42 (4)

Author, Year, Country	Number of Participants (Number of RT-PCR+ participants)	RT-PCR+ Population Description	Age (Range or SD)	Sex: Male N (%)	Race/Ethnicity: N (%)	Comorbidities: N (%)
Liu, 2020[43] China	484 (484)	Previously hospitalized recovered adults[a]	*Antibody-positive*: Age (Median): 51 (SD: 14) *Antibody-negative*: Age (Median): 49 (SD: 17)	*Antibody-positive*: Male: 190 (48) *Antibody-negative*: Male: 43 (49)	NR	NR
Liu, 2020[45] China	238 (153)	Hospitalized adults[a]	*RT-PCR+ participants*: Age (Median): 54 (IQR: 39-64)	*RT-PCR+ participants*: Male: 93 (61)	NR	NR
Liu, 2020[46] China	133 (91)	Hospitalized patients with moderate (33%), severe (39%) and critical (28%) disease[l]	*RT-PCR+ participants*: Age (Median): Moderate 68 (IQR: 64-72); Severe: 68 (IQR: 61-74); Critical: 70 (IQR: 60-77)	*RT-PCR+ participants*: Male: 63 (47)	NR	NR
Liu, 2020[47] China	32 (32)	Hospitalized adults with mild (44%) and severe (56%) disease[m]	Age (Median): 55 (Range: NR)	Male: 21 (67)	NR	NR
Liu, 2020[44] China	151 (111)	Adults hospitalized with asymptomatic (27%), mild (20%) and moderate-severe (53%) disease[a]	*Asymptomatic RT-PCR+*: Age (Median): 56 (Range: 20-94) *Symptomatic RT-PCR+*: Age (Median): 56 (Range: 23-93)	*Asymptomatic RT-PCR+*: Male: 48 (59) *Symptomatic RT-PCR+*: Male: 48 (59)	NR	NR
Lynch, 2020[48] U.S.	153 (94 primary cohort; 59 screened for convalescent plasma donation)	Outpatient (34%) and hospitalized (66%) adults with a range of disease severity[a]	*Primary cohort*: Age (Median): 49 (IRQ: 39-58)	*Primary cohort*: Male: 64 (68)	*Primary cohort*: Hispanic: 71 (77)	*Primary cohort*: HTN: 36 (38) Diabetes: 37 (39) Obesity: 19 (20) CKD: 6 (6) HIV: 3 (3)

Author, Year, Country	Number of Participants (Number of RT-PCR+ participants)	RT-PCR+ Population Description	Age (Range or SD)	Sex: Male N (%)	Race/Ethnicity: N (%)	Comorbidities: N (%)
Pancrazzi, 2020[49] Italy	516 (73)	Asymptomatic/pauci-symptomatic (37%) and symptomatic (63%) adults presenting at local emergency departments[a]	*RT-PCR+ participants*: Age (Median): 53 (Range: NR)	*RT-PCR+ participants*: Male: 39 (53)	NR	NR
Payne, 2020[50] U.S.	382 (98)	Asymptomatic and mildly symptomatic U.S. Navy service members aboard the USS Theodore Roosevelt carrier during SARS-CoV-2 outbreak[a]	*Total sample*: Age (Median): 30 (IQR: 24-35)	*Total sample*: Male: 289 (76)	*Antibody or RT-PCR+ participants*: AA/Black: 25 (11) AI/AN/Native Hawaiian/PI: 9 (4) Asian: 13 (6) Hispanic: 47 (20) NH White: 142 (60)	*Antibody or RT-PCR+ participants*: DM, HTN, asthma, or immunosuppressed: 15 (6)
Petersen, 2020[51] U.S.	2,547 (2,547)	Healthcare workers recovered from predominantly asymptomatic and mild disease participating in seroprevalence survey[a]	*Antibody positive*: Age: 40 (SD: 10) *Antibody negative*: Age: 41 (SD: 10)	*Antibody positive*: Male: 1566 (94) *Antibody negative*: Male: 96 (6)	*Antibody positive*: AA/Black: 361 (97) Asian: 184 (93) Hispanic: 603 (92) NH White: 1037 (94) *Antibody negative*: AA/Black: 12 (3) Asian: 13 (7) Hispanic: 54 (8) NH White: 67 (6)	Immune-compromised: Antibody positive: 29 (94); Antibody negative: 2 (7)
Qu, 2020[52] China	41 (41)	Adults hospitalized with mild to moderate (36%), severe (40%) and critical (24%) disease[n]	Age (Median): 62 (IQR 42-66)	Male: 27 (66)	NR	>1 comorbidity (not further defined): 9 (22)
Robbins, 2020[53] U.K.	560 (84)	Healthcare workers recovered from SARS-CoV-2 infection of varying severity[a]	Age: NR	*Total sample*: Male: 112 (20)	*Total sample*: Black and minority ethnic background: 140 (25)	NR
Schaffner, 2020[54] Liechtenstein	82 (82)	Outpatient adults with a range of disease severity[a]	Age (Median): 39 (IQR: 29-58)	Male: 42 (51)	NR	DM: 2 (2) HTN: 8 (10) CVD: 5 (6) Cerebrovascular disease: 2 (2) Malignancy: 1 (1)

Author, Year, Country	Number of Participants (Number of RT-PCR+ participants)	RT-PCR+ Population Description	Age (Range or SD)	Sex: Male N (%)	Race/Ethnicity: N (%)	Comorbidities: N (%)
Seow, 2020[55] U.K.	96 (65)	Adults recovered from mild to moderate (33%) and severe-critical (67%) disease[o]	*RT-PCR+ participants*: Age (Mean): 55 (Range: 23-95)	*RT-PCR+ participants*: Male: 51 (79)	NR	*RT-PCR+ participants*: DM: 18 (30) HTN: 12 (20) Obesity: 16 (26) Malignancy: 3 (5) Immunosuppressed: 2 (3)
Shang, 2020[56] China	778 (778)	Adults hospitalized with severe disease[p]	Age (Median): 64 (IQR: 55-72)	Male: 367 (53)	NR	Malignancy: 26 (3)
Shen, 2020[57] China	150 (97)	Adults hospitalized with a mix of "ordinary" (78%) and severe (22%) disease[q]	*RT-PCR+ participants*: Age (Median): 38 (IRQ: 46-56)	*RT-PCR+ participants*: Male: 59 (61)	NR	*RT-PCR+ participants*: DM: 7 (7) HTN: 16 (17) Malignancy: 2 (2)
Shu, 2020[58] China	131 (131)	Hospitalized and recovered adults with a range of "normal" (11%), severe (63%), and critical (26%) disease[a]	Age (Mean): 51 (SD: 12)	Male: 90 (69)	NR	HTN: 31 (24) DM: 31 (24) CVD: 7 (5)
Staines, 2020[59] U.K.	177 (177)	Hospitalized patients, hospital staff, and outpatient adults, with a range of asymptomatic to critical disease severity[a]	Age (Median): 64 (IQR: 52-77)	Male: 101 (57)	White: 60 (34) Non-White: 62 (35)	>1 concurrent condition: 129 (73)
Stock da Cunha, 2020[60] Spain	200 (38)	Hospitalized (55%) and outpatient (45%) end-stage kidney disease patients on hemodialysis with a range of asymptomatic to severe COVID-19[a]	*RT-PCR+ participants*: Age (Mean): 73 (SD: 12)	*RT-PCR+ participants*: Male: 26 (68)	Race/ethnicity: NR	ESRD on dialysis: 200 (100)

Author, Year, Country	Number of Participants (Number of RT-PCR+ participants)	RT-PCR+ Population Description	Age (Range or SD)	Sex: Male N (%)	Race/Ethnicity: N (%)	Comorbidities: N (%)
Sun, 2020[61] China	38 (38)	Hospitalized adults (including ICU and non-ICU patients)[a]	*Non-ICU*: Age (Median): 44 (IQR 32-56) *ICU*: Age (Median): 58 (IQR 49-70)	*Non-ICU*: Male: 14/27 (52) Race/ethnicity: NR *ICU*: Male: ICU: 10/11 (91)	NR	*Non-ICU*: HTN: 5 (19) CVD: 1 (4) *ICU*: DM: 5 (45) HTN: 4 (36) Lung Disease: 2 (18)
Suthar, 2020[62] U.S.	44 (44)	Hospitalized adults[a]	Age: 25-87	Age: 25-87	NR	NR
Takahashi, 2020[63] U.S.	162 (98)	Hospitalized adults with severe and critical disease[r]	*RT-PCR+ participants*: Age (mean): Female 64 (SD: 17), Male 62 (SD: 17)	*RT-PCR+ participants*: Male: 47 (48)	*RT-PCR+ participants*: AA/Black: 29 (30) Hispanic: 14 (14) NH White: 53 (54)	*RT-PCR+ participants*: HTN: 50 (51) CVD: 24 (24) Chronic lung disease: 23 (24) Recent cancer treatment: 7 (7) Immunosuppressed: 5 (5)
Terpos, 2020[64] Greece	259 (259)	Hospitalized (32%) and outpatient (68%) adults with a spectrum of disease severity[a]	Age (≥50 years): 121 (47)	Male: 137 (53)	NR	NR
Theel, 2020[65] U.S.	56 (56)	Hospitalized (59%) and outpatient (41%) adults with a range of disease severity[a]	*Inpatient*: Age (Median): 61 (Range: 24-90) *Outpatient*: Age (Median): 37 (21-64)	*Inpatient*: Male: 20 (61) *Outpatient*: Male: 10 (43)	NR	NR
Traugott, 2020[66] Austria	77 (77)	A mix of hospitalized (50%) and outpatient adults with mild, moderate, and severe disease[s]	Age (Median): 63 (Range: 15-92)	Male: 48 (62)	NR	NR
Van Elslande, 2020[67] Belgium	227 (114)	Hospitalized patients with a range of moderate to severe and critical disease[a]	*RT-PCR+ participants*: Age (Median): 67 (Range: 23-90)	*RT-PCR+ participants*: Male: 81 (71)	NR	Comorbidities NR: Excluded Immunosuppressed participants

Author, Year, Country	Number of Participants (Number of RT-PCR+ participants)	RT-PCR+ Population Description	Age (Range or SD)	Sex: Male N (%)	Race/Ethnicity: N (%)	Comorbidities: N (%)
Wang, 2020[68] U.S.	58 (58)	Hospitalized and outpatient adults with multiple myeloma presenting with mild to critical COVID-19 disease[a]	Age (Median): 67 (SD: 12.5)	Male: 30 (52)	NR	Multiple Myeloma: 58 (100) Obesity: 21/57 (37) High CAD risk: 32 (55)
Wang, 2020[69] China	30 (30)	Previously hospitalized adults recovered from non-severe (90%) and severe (10%) disease[t]	Age (Median): 52 (IQR: 45-67)	Male: 12 (40)	NR	DM: 2 (7) HTN: 9 (30) CAD: 2 (7) COPD: 1 (3) CKD: 1 (3)
Wang, 2020[70] China	375 (141)	Hospitalized adults[a]	*RT-PCR+ participants*: Age (Median): 58 (Range: 21-95)	*RT-PCR+ participants*: Male: 65 (46)	NR	
Wendel, 2020[71] Brazil	271 (271)	Convalescent adults recovered from predominantly mild disease[a]	Age: Range 18-60 years	Male: 230 (85)	NR	NR
Wolff, 2020[72] Belgium	111 (111)	Asymptomatic (22%) and symptomatic (78%) adults[a]	Age (Median): Asymptomatic: 61 (Range: 20-85); Mild-Moderate: 60 (Range: 21-88); Severe: 59 (26-88)	Male: 63 (57)	NR	NR
Xiang, 2020[73] China	109 (85)	Adults hospitalized with a spectrum of "normal" (79%) to severe (21%) disease[u]	Age (Median): 51 (IRQ: 32-65)	Male: 31 (36)	NR	Comorbidity including DM, HTN, CKD, lung disease, malignancy: 33 (39)
Xie, 2020[74] China	373 (373)	Patients enrolled at the Shanghai Public Health Clinical Center (SPHCC) and its affiliated hospital, with mild (2%), moderate (84%), severe (9%) and critical (5%) disease[v]	Age: ≤39: 128 (34); 40-49: 62 (17); 50-59: 67 (18); 60-69: 77 (21); 70-79: 32 (9); ≥80: 7 (2)	Male: 197 (53)	NR	DM: 29 (8) HTN: 71 (19) CVD: 18 (5) COPD: 4 (1)

Author, Year, Country	Number of Participants (Number of RT-PCR+ participants)	RT-PCR+ Population Description	Age (Range or SD)	Sex: Male N (%)	Race/Ethnicity: N (%)	Comorbidities: N (%)
Xu, 2020[75] China	242 (242)	A mix of hospitalized and outpatient adults with moderate (87%) and severe (13%) disease[a]	Age (Median): 47 (Range: NR)	Male: 136 (56)	NR	NR
Young, 2020[76] Singapore	100 (100)	Hospitalized adults with a spectrum of disease severity[a]	Age (Mean): 44 (Range: 35-56)	Male: 56 (56)	Chinese ethnicity: 83 (83)	DM: 10 (10) HTN: 19 (19)
Zhang, 2020[77] China	222 (222)	Hospitalized adults with a mix of non-severe (68%), and severe (32%) disease[b]	Age (Median): 62 (IQR 52-69)	Male: 107 (48)	NR	Comorbidity (not defined): 80 (36)
Zhao, 2020[78] China	92 (47)	Previously hospitalized adults recovered from moderate (60%) and severe (40%) disease[a]	*RT-PCR+ participants*: Age (Median): 52 (IQR 35-63)	*RT-PCR+ participants*: Male: 19 (40)	NR	NR
Zhao, 2020[79] China	173 (173)	Adults hospitalized with moderate (68%) and critical (32%) disease[w]	Age (Median): 48 (IRQ: 35-61)	Male: 84 (49)	NR	HTN: 20 (12) DM: 11 (6) CAD 3 (2) Malignancy: 2 (1) Chronic bronchitis 1 (<1) CKD: 1 (<1)
Zheng, 2020[80] China	723 (693)	Hospitalized adults with mild (1%), moderate (73%), severe (23%) and critical (3%) disease[x]	*Total sample*: Age (Median): 61 (SD: 15)	*Total sample*: Male: 290 (40)	NR	NR

Abbreviations: AA = African-American; AI = American Indian; AN = Alaska Native; CAD = coronary artery disease; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; COVID-19 = coronavirus disease 2019; CVD = cardiovascular disease; DM = diabetes mellitus; ESRD = end-stage renal disease; HTN = hypertension; HIV = human immunodeficiency virus, IRQ = interquartile range; N = number; NH = non-Hispanic; NR = not reported; RT-PCR+ = polymerase chain reaction positive result; PI = Pacific Islander; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SD = standard deviation; U.K. = United Kingdom; U.S. = United States.

Footnotes:
[a] Disease severity classification not reported.

[b] The study categorized disease severity according to self-reporting of symptoms: "participants rated the severity of their COVID-19 symptoms on a 1-10 scale, with 1 describing very mild symptoms and 10 describing very severe symptoms".
[c] Disease severity was categorized between mild and severe based on a 1-10 point self-reported symptom scale.
[d] Severe disease was defined as "requiring hospitalization in a medical or intensive care unit".
[e] Patients were categorized as having either mild, moderate, or high illness severity. Low illness severity was defined as having mild symptoms, moderate severity defined as having mild dyspnea, cough, or fever for ≥5 days and high severity, was defined as severe dyspnea with worsening cough, high or persistent fever for five days or longer, or severe fatigue.
[f] Disease severity was categorized as either mild, severe, or critical. Mild severity was defined by the presence of either: (a) fever, (b) typical COVID-19 symptoms, or (c) radiographic evidence of COVID-19 pneumonia. Severe illness was by the presence of either: (a) respiratory distress (respiration rate ≥ 30 times/min); (b) blood oxygen saturation (SpO2) ≤ 93% in resting state; or (c) arterial partial pressure of O2 to fraction of inspired oxygen (PaO2/FiO2) ratio ≤ 300 mmHg. Critical illness by the presence of either: (a) respiratory failure requiring mechanical ventilation; (b) shock; or (c) multiple organ dysfunction requiring intensive care unit (ICU) treatment.
[g] Patients were categorized as either asymptomatic or symptomatic. Symptomatic cases met one or more of the following criteria: (a) Presence of clinical symptoms of COVID-19 (fever, cough, nasal discharge etc.), (b) peripheral capillary oxygen saturation <93%, and (c) need for supplemental oxygen.
[h] Disease severity was categorized as either mild, moderate, or severe disease. Mild severity was defined as disease not requiring hospitalization, moderate severity was defined as disease requiring hospitalization but not intensive care unit (ICU) admission, severe illness was defined as condition requiring ICU level of care.
[i] Patients were classified as having either asymptomatic, mildly symptomatic, or severe infection. Severe illness was defined as COVID-19 pneumonia requiring intensive care unit (ICU) level of care.
[j] Disease severity was classified as either mild, moderate, severe, or critical according to the World Health Organization (WHO) 2020 Clinical Management of COVID-19 Interim Guidance. WHO/2019-nCoV/Clinical/2020.5. (May 27, 2020 Interim Guidance).
[k] Disease severity was classified as either mild, moderate, or severe according to the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia released by the National Health Commission (Version 6 or Trail Version 7).
[l] Disease severity was classified as either moderate, severe, or critical according to the World Health Organization (WHO), Clinical Management of Severe Acute Respiratory Infection (SARI) When COVID-19 Disease is Suspected (2020).
[m] Patients were classified as having either mild or severe disease. Severe illness met one or more of the following conditions: (a) respiratory distress (≥30 breaths/min); (b) oxygen saturation ≤93% at rest; (c) arterial partial pressure of oxygen (PaO2)/fraction of inspiration O2 (FiO2) ≤300 mmHg (1 mmHg = 0.133 kPa); (d) respiratory failure requiring mechanical ventilation; (e) septic shock development; or (f) critical organ failure requiring ICU care. Illness not meeting any of the above criteria was considered mild.
[n] Patients were categorized as having mild, moderate, severe, or critical illness. Mild illness severity was categorized as mild clinical symptoms without radiographic evidence of COVID-19 pneumonia. Moderate illness was categorized by the presence of: (a) fever, (b) respiratory symptoms, and (c) radiographic evidence of COVID-19 pneumonia. Severe illness met one or more of the following criteria: (a) respiratory distress, hypoxia (SpO2 ≤93%), or abnormal blood gas analysis (PaO2 <60 mmHg, and (b) PaCO2 >50 mmHg). Critical severity was categorized as either respiratory failure requiring mechanical ventilation, shock, or other organ failure that requires intensive care unit (ICU) care.
[o] Patients were classified as having either asymptomatic, mild, moderate, severe, or critical illness according to the maximum level of respiratory support required during hospitalization.
[p] According to the study: "the severity of COVID-19 was defined according to the Chinese Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7).
[q] Patients were classified as having either "ordinary" or severe illness. Severe illness was defined as meeting any of the following criteria: (a) respiratory distress, RR≥30/min; (b) in resting state, oxygen saturation ≤93%; (c) partial arterial oxygen pressure (PaO2)/oxygen absorption concentration (FiO2) ≤300 mmHg.

[r] Disease severity was rated using an institutionally developed 1 – 5 point scale based on the following criterial Level 1: admitted and observed without supplementary oxygen; Level 2: requiring ≤ 3L supplementary oxygen via nasal canal to maintain SpO2 > 92%; Level 3: receiving tocilizumab, which per hospital treatment protocol required that the patient received>3L supplementary oxygen to maintain SpO2 > 92%, or, requiring >2L supplementary oxygen to maintain SpO2 > 92% and had a high-sensitivity C-reactive protein (CRP) > 70; Level 4: requiring ICU-level care; or Level 5: requiring intubation and mechanical ventilation.
[s] Disease severity were categorized as either mild, moderate, or severe according to the World Health Organization Guidelines for Diagnosing Coronavirus Disease 2019.
[t] Disease severity was categorized according to the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7:). Severe illness classified as meeting one or more of the following criteria : (a) respiratory distress (≥30 times/minutes), (b) the oxygen saturation ≤93% at rest, (c) the arterial partial pressure of oxygen (PaO2) / the fraction of inspired oxygen (FiO2) ≤ 300 mmHg.
[u] Disease severity was classified the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7).
[v] Patients were categorized as having either "normal" or severe illness. "Normal" illness severity was defined having fever and respiratory symptoms along with radiographic evidence of COVID-19 pneumonia. Severe cases met one or more of the following criteria: (a) respiratory distress (≥ 30 breaths/minute), (b) oxygen saturation ≤ 93% at rest, (c) arterial partial pressure of oxygen/fraction of inspired oxygen ratio ≤ 300 mm Hg (l mm Hg = 0.133 kPa), or (d) chest imaging with >50% progression of radiographic abnormalities within 24–48 hours.
[w] Patients were categorized as having mild, moderate, severe, and critical disease according to the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7). Mild illness was defined by the presence of mild respiratory symptoms without radiographic evidence of COVID-19 pneumonia. Moderate cases were defined by the presence of fever, respiratory symptoms, and radiographic findings of pneumonia. Severe cases met one or more of the following criteria: (a) respiratory distress (⩾30 breaths/ min); (b) oxygen saturation ⩽93% at rest; (c) arterial partial pressure of oxygen (PaO2)/fraction of inspired oxygen (FiO2)⩽300 mmHg (l mmHg = 0.133 kPa); and Critical cases: cases meeting any of the following criteria: (a) respiratory failure and requiring mechanical ventilation; (c) shock; (d) with other organ failure that requires ICU care.
[x] Patients were categorized as having either moderate or critical illness according to the Chinese New Coronavirus Pneumonia Prevention and Control Program (4th Edition) Critical illness severity was defined as meeting one or more of the following criteria: (a) the presence of ARDS or oxygen saturation less than 93% and (b) requiring invasive or noninvasive mechanical ventilation.
[y] Patients were categorized as having either mild, moderate, severe, or critical illness according to the Chinese Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Seventh Edition). Mild illness was defined by the presence of mild respiratory symptoms without radiographic evidence of COVID-19 pneumonia. Moderate illness was defined by the presence of fever, respiratory symptoms, and radiographic evidence of COVID-19 pneumonia. Severe illness was defined as meeting one or more of the following criteria: (a) shortness of breath with a respiratory rate over 33 breaths per min; (b) oxygen saturation ≤93% in a resting state; (c) PaO2/FiO2 ≤300 mm Hg (1 mm Hg = 0.133 kPa) or (d) chest imaging with >50% progression of radiographic abnormalities within 24–48 hours. Critical disease classified as meeting one or more of the following criteria: (a) respiratory failure requiring mechanical ventilation; (b) shock; and (c) other organ failure requiring intensive care unit (ICU) admission.

Table C-2. Immunoassays used in included studies

Immunoassay Manufacturer (Country)	Immunoassay Brand Name	Assay Type	Antibody(s) Detected	Sensitivity % (95% CI) [a]	Specificity % (95% CI) [a]	FDA EUA Status[b] (Y/N)	EU CE-IVD Status[c] (Y/N)	Studies Utilizing Immunoassays
Abbott Laboratories (Illinois, USA)	Alinity i SARS-CoV-2 IgG	CMIA	IgG	100 (89.9-100)	99 (94.6-99.8)	Y	Y[e]	Delliere[28]
	Architect SARS-CoV-2 IgG Assay	CMIA	IgG	100 (95.8-100)	99.6 (99-99.9)	Y	Y[e]	Crawford[25] Petersen[51] Schaffner[54] Theel[65] Van Elslande[67]
Acro Biotech, Inc. (California, USA)	2019-nCoV IgM/IgG Rapid Test Cassette	LFA	IgM/IgG	IgG: 100 (86-100) IgM: 85 (62.1-96.8)	IgG: 96 (89.4-99.9) IgM: 96 (86.3-99.5)	N	Y	Pancrazzi[49]
Artron Laboratories, Inc. (Burnaby, Canada)	One Step Novel Coronavirus (COVID-19) IgM/IgG Antibody Test	LFA	IgM/IgG	93.4 (NR)	97.7 (NR)	N	N	Imai[33]
Augurix SA (Valais, Switzerland)	SARS-CoV-2 IgM/IgG RDT	LFA	IgM/IgG	IgM: NR IgG: 98.3 (NR)	IgM: NR IgG: 96.3 (NR)	N	Y	Andrey, 2020[17]
Beijing Wantai Biological Pharmacy Enterprise Co., Ltd (Beijing, China)	SARS CoV-2 Ab Rapid Test	LFA	Total Ab	100 (88.7-100)	98.8 (93.3-99.8)	Y	Y	Traugott[66]
	SARS-CoV-2 IgM ELISA	ELISA	IgM	86.1 (NR)	99.4 (NR)	N	Y	Traugott[66]
	SARS-CoV-2 Total Ab ELISA	ELISA	Total Ab	96.7 (83.3-99.4)	97.5 (91.3-99.3)	Y	Y	Gudbjartsson[15] Traugott[66] Zhao[79]
BioMérieux SA (Craponne, France)	VIDAS SARS-CoV-2 IgG	ELFA	IgG	100 (88.3-100)	99.9 (99.4-100)	Y	Y[f]	Wolff[72]
	VIDAS SARS-CoV-2 IgM	ELFA	IgM	100 (85.7-100)	99.4 (97.7-99.8)	Y	Y[f]	Wolff[72]
Bioscience Diagnostic Technology Co., Ltd. (Tianjin, China)	COVID-19 BSS SARS-CoV-2IgM/IgG MCLIA	CLIA	IgM/IgG	NR NR	NR NR	N	N	Wang[69] Xu[75] Zheng[80]

Immunoassay Manufacturer (Country)	Immunoassay Brand Name	Assay Type	Antibody(s) Detected	Sensitivity % (95% CI) [a]	Specificity % (95% CI) [a]	FDA EUA Status[b] (Y/N)	EU CE-IVD Status[c] (Y/N)	Studies Utilizing Immunoassays
Biosynex (Illkirch-Graffenstaden, France)	COVID-19 BSS SARS-CoV-2 IgM/IgG RDT	LFA	IgM/IgG	IgM: 86.8 (71.9-95.6) IgG 97.4 (86.2-99.9)	IgM 98.6 (95-99.8) IgG 99.3 (96.2-99.9)	N	Y	Fafi-Kremer[29]
Boditech Med, Inc. (Republic of Korea)	AFIAS COVID-19 Ab IgG assay	FIA	IgG	95.8 (NR)	96.7 (NR)	N	Y	Ko[39]
Centers for Disease Control (Georgia, USA)	IgM/IgG/IgA ELISA	ELISA	IgM/IgG/IgA	NR	NR	N[d]	N	Payne[50] Petersen[51]
Chongqing Xinsaiya Biotechnology Company (Chongqing, China)	Anti-SARS-CoV-2 IgG kit	FIA	IgG	NR	NR	N	N	Liu[47]
	Anti-SARS-CoV-2 IgM kit	FIA	IgM	NR	NR	N	N	Liu[47]
DiaSorin (Saluggia, Italy)	LIAISON SARS-CoV-2 S1/S2 IgG	CMIA	IgG	97.6 (87.4-99.6)	99.3 (98.6-99.6)	Y	Y	Van Elslande[67] Wolff[72]
Dialab ZJG Biotech Co (Suzhou, China)	FIA for the detection of anti-S IgG and IgM	FIA	IgM/IgG	NR	NR	N	N	Bao[18]
Eagle Biosciences(New Hampshire, USA)	Anti-N IgG ELISA	ELISA	IgG	100 (NR)	100 (NR)	N[d]	Y[e]	Gudbjartsson[15]
	Anti-N IgM ELISA	ELISA	IgM	45 (NR)	100 (NR)	N[d]	Y[e]	Gudbjartsson[15]
Emory Medical Laboratories (Georgia, USA)	Anti-RBD IgG ELISA	ELISA	IgG	100 (88.7-100)	96.4 (94.6-97.6)	Y	N	Suthar[62]
Epitope Diagnostics, Inc. (California, USA)	EDI Novel Coronavirus COVID-19 IgG ELISA	ELISA	IgG	100 (NR)	100 (NR)	N	Y	Gudbjartsson[15] Theel[65]
	EDI Novel Coronavirus COVID-19 IgM ELISA	ELISA	IgM	73.1 (NR)	100 (NR)	N	Y	Gudbjartsson[15]
ET Healthcare (California, USA)	Pylon cTnI Immunoassay	NR	IgM/IgG	NR	NR	N	N	Lynch[48]

Immunoassay Manufacturer (Country)	Immunoassay Brand Name	Assay Type	Antibody(s) Detected	Sensitivity % (95% CI) [a]	Specificity % (95% CI) [a]	FDA EUA Status[b] (Y/N)	EU CE-IVD Status[c] (Y/N)	Studies Utilizing Immunoassays
Euroimmun (Lübeck, Germany)	SARS-CoV-2 IgG ELISA	ELISA	IgG	90 (74.4-96.5)	100 (95.4-100)	Y	Y	Andrey[16] Andrey[17] Chirathaworn[23] Gudbjartsson[15] Jaaskelainen[38] Schaffner[54] Terpos[64] Theel[65] Traugott[66] Wolff[72]
	SARS-CoV-2 IgA ELISA	ELISA	IgA	97.4 (90.9-99.5)	93.8 (89-96.6)	N	Y	Chirathaworn[23] Gudbjartsson[15] Jaaskelainen[38] Schaffner[54] Terpos[64] Traugott[66] Wolff[72]
Guangzhou Wondofo Biotech Co., Ltd. (Guangzhou, China)	Wondfo SARS-COV-2 Lateral Flow Assay	LFA	IgM/IgG	86.4 (82.5-89.6)	99.6 (97.6-99.9)	N	Y	de la Iglesia[27]
Hangzhou AllTest Biotech Co., Ltd. (Hangzhou, China)	All Test 2019-nCoV IgG/IgM Rapid Test	LFA	IgM/IgG	IgM: 85 (62.1-96.8) IgG: 100 (86.0-100)	IgM: 96 (86.3-99.5) IgG: 98 (89.4-99.9)	N	Y	de la Iglesia[27] Traugott[66]
Hunan Yuanjing Biotechnology Co., Ltd. (Hunan, China)	COVID-19 IgM Detection Kit (Magnetic Bead CLIA)	CLIA	IgM	NR	NR	N	N	Liu[44]
	COVID-19 IgG Detection Kit (Magnetic Bead CLIA)	CLIA	IgG	NR	NR	N	N	Liu[44]
ID.Vet (Montpellier, France)	ID Screen SARS-CoV-2-Anti-N IgG Indirect ELISA	ELISA	IgG	95.2 (95.5-100)	99.9 (99.5-100)	N	Y	Blain[19]

Immunoassay Manufacturer (Country)	Immunoassay Brand Name	Assay Type	Antibody(s) Detected	Sensitivity % (95% CI) [a]	Specificity % (95% CI) [a]	FDA EUA Status[b] (Y/N)	EU CE-IVD Status[c] (Y/N)	Studies Utilizing Immunoassays
Jiangsu Medomics Medical Technology Co. (Nanjing, China)	Point-of-Care Qualitative IgM/IgG LF Immunoassay	LFA	IgM/IgG	NR	NR	N	N	Shang[56]
Kyab Biotech Co., Ltd. (Wuhan, China)	IgM/IgG MaxiSorp Nunc-immuno ELISA	ELISA	IgM/IgG	NR	NR	N	N	Shu[58]
Lizhue Reagent Co., Ltd (Zhuhai, China)	Colloidal Gold ICG Assay	LFA	IgM/IgG	NR	NR	N	N	Zhao[78]
Mairui (Shenzhen, China)	BC-5800 Automatic Blood Cell Analyzer–Total Antibodies (IgM/IgG/IgA)	NR	Total Ab	NR	NR	N	N	Xie[74]
MEDsan GmbH, Biological Health Solutions (Hamburg, Germany)	MEDsan COVID-19 IgM/IgG Rapid Test	LFA	IgM/IgG	IgM: 90 (74.4-96.5) IgG: 90 (74.4-96.5) IgM+IgG 90 (74.4-96.5)	IgM: 93.8 (86.2-97.3) IgG: 93.8 (86.2-97.3) IgM+IgG 92.5 (84.6-96.5)	N	N	Andrey[16]
Mikrogen (Neuried, Germany)	RecomWell SARS-Cov-2 Anti-S/N IgG ELISA	ELISA	IgG	100 (70-100)	96.5 (91.0-98.9)	N	Y	Van Elslande[67]
Mologic Ltd. (Bedford, England)	COVID-19 IgG ELISA	ELISA	IgG	NR	NR	N[d]	N	Staines[59]
Mount Sinai Hospital Clinical Laboratory (New York, USA)	Mt. Sinai Laboratory COVID-19 ELISA	ELISA	IgG	92.5 (80.1-97.4)	100 (95.1-100)	Y	N	Takahashi[63] Wang[68]
NTBIO Diagnostics, Inc. (British Columbia, Canada)	NTBIO COVID-19 IgM/IgG Antibody Test Cassette	LFA	IgM/IgG	NR	NR	N	Y	Andrey[16]
Orient Gene Biotech (Zhejiang, China)	COVID-19 IgG/IgM LF Assay	LFA	IgM/IgG	IgM 100 (88.7-100) IgG 96.7 (83.3-99.4) IgM +IgG: 100 (88.7-100)	IgM 100 (95.4-100) IgG 97.5 (91.3-99.3) IgM+IgG: 97.5 (91.3-99.3)	Y[g]	Y	Andrey[16] Delliere[28]

Immunoassay Manufacturer (Country)	Immunoassay Brand Name	Assay Type	Antibody(s) Detected	Sensitivity % (95% CI) [a]	Specificity % (95% CI) [a]	FDA EUA Status[b] (Y/N)	EU CE-IVD Status[c] (Y/N)	Studies Utilizing Immunoassays
Ortho-Clinical Diagnostics, Inc. (New York, USA)	Vitros Immunodiagnostic Products Anti-SARS-CoV-2 IgG CLIA	CLIA	IgG	90 (76.9-96)	100 (99.1-100)	Y	N	Petersen[51] Theel[65]
PCL, Inc (Seoul, Republic of Korea)	PCL COVID-19 IgM/IgG Colloidal Gold Assay	LFA	IgM/IgG	IgM: 93.3 (78.7-98.2) IgG: 80 (62.7-90.5)	IgM: 100 (94.8-100) IgG: 100 (94.8-100)	N	Y	Choe[24]
	PCL COVID-19 Total Ab ELISA	ELISA	Total Ab	NR	NR	N	N	Ko[39]
ProtATonce (Athens, Greece)	ProTAtonce Multiplex assay	Luminex	Total Ab	NR	NR	N	N	Terpos[64]
Roche Diagnostics (Basel, Switzerland)	Elecsys SARS CoV-2 Ab CLIA	CLIA	Total Ab	100 (88.3-100)	99.8 (99.7-99.9)	Y	Y	Gudbjartsson[15] Schaffner[54] Van Elslande[67] Wolff[72]
Shanghai Outdo Biotech Co., Ltd. (Shanghai, China)	Novel Coronavirus (SARS-CoV-2) Total Ab (IgM/IgG) Colloidal Gold Assay	LFA	IgM/IgG	NR	NR	N	Y	Shen[57]
Shenzhen YHLO Biotech Co. Ltd (Shenzhen, China)	iFlash-SARS-CoV-2 IgG CLIA	CLIA	IgG	96.3 (NR)	97.4 (NR)	N	Y	Chen[21] Hou[31] Huang[32] Infantino[34] Li[42] Liu[46] Qu[52] Zhang[77]
	iFlash-SARS-CoV-2 IgM CLIA	CLIA	IgM	86.6 (NR)	98.3 (NR)	N	Y	Chen[21] Hou[31] Huang[32] Infantino[34] Li[42] Liu[46] Qu[52] Zhang[77]

Immunoassay Manufacturer (Country)	Immunoassay Brand Name	Assay Type	Antibody(s) Detected	Sensitivity % (95% CI) [a]	Specificity % (95% CI) [a]	FDA EUA Status[b] (Y/N)	EU CE-IVD Status[c] (Y/N)	Studies Utilizing Immunoassays
Shenzhen New Industries Biomedical Engineering Co, Ltd. (SNIBE) Diagnostic (Shenzen, China)	Maglumi 2019-nCoV IgM/IgG	CLIA	IgM/IgG	IgM: 77.5 (69.9-83.6) IgG: 100 (97.4-100)	IgM: 99.6 (97.5-99.9) IgG: 99.1 (96.8-99.8)	Y	Y	Van Elslande[67] Chirathaworn[23]
Vircell (Granada, Spain)	COVID-19 IgG ELISA	ELISA	IgG	85 (NR)	98 (NR)	N	Y	Stock da Cunha[60]
	COVID-19 IgM+IgA ELISA	ELISA	IgM/IgA	88 (NR)	99 (NR)	N	Y	Stock da Cunha[60]
SIDAK Lifecare, Ltd. (Bahadurgarh, India)	COVID-19 IgM/IgG Antibody Rapid Test	LFA	IgM/IgG	NR	NR	N	N	Dave[26]
WuXi Diagnostics (Shanghai, China)	2019-nCoV IgM/IgG Detection Kit	ELISA	IgM/IgG	NR	NR	N	N	Bao, 2020[18]
Xiamen Wantai Kairui Biological Technology Co., Ltd (Fujian, China)	IgG/Total Ab CMIA	CMIA	IgG/Total Ab	NR	NR	N	N	Wang[70]
Zhuhai Livzon Diagnostics Inc. (Zhuhai, China)	Livzon SARS-Cov-2 IgM/IgG) Lateral Flow Assay	LFA	IgM/IgG	IgM 86.7 (70.3-94.7) IgG: 66.7 (48.8-80.8) IgM+IgG: 86.7 (70.3-94.7)	IgM 97.5 (91.3-99.3) IgG: 100 (95.4-100) IgM+IgG: 97.5 (91.3-99.3)	N	Y	Iversen[36]
	IgM/IgG ELISA	ELISA	IgM/IgG	NR	NR	N	N	Liu[45] Xiang[73]
In-House or Non-Commercial Tests without Manufacturer Information	In-house ELISA	ELISA	IgM/IgG/ IgA	NR	NR	N	N	Bruni[20]
	Quantitative ELISA for Anti-N, -S, and -RBD IgM and IgG antibodies	ELISA	IgM/IgG	NR	NR	N	N	Chen[22]
	In-house ELISA	ELISA	IgM/IgG/ IgA	NR	NR	N	N	Crawford[25]
	SARS-CoV-2 Anti-Spike RBD IgM/IgG In-House ELISA	ELISA	IgM/IgG	NR	NR	N	N	Flannery[30]

Immunoassay Manufacturer (Country)	Immunoassay Brand Name	Assay Type	Antibody(s) Detected	Sensitivity % (95% CI) [a]	Specificity % (95% CI) [a]	FDA EUA Status[b] (Y/N)	EU CE-IVD Status[c] (Y/N)	Studies Utilizing Immunoassays
	In-house ELISA	ELISA	IgM/IgG/ IgA	NR	NR	N	N	Isho[35]
	Surrogate neutralization ELISA (snELISA)	snELISA	Neutralizing	NR	NR	N	N	Isho[35]
	In-house ELISA	ELISA	IgM/IgG/ IgA	NR	NR	N	N	Iyer[37]
	Laboratory-developed ELISA	ELISA	IgM/IgG	NR	NR	N	N	Koblischke[40]
	Laboratory-developed ELISA	ELISA	IgG/IgM	NR	NR	N	N	Kwon[41]
	Colloidal-based IgM Assay	LFA	IgG	NR	NR	N	N	Liu[43]
	In-house ELISA	ELISA	IgM/IgG/ IgA	NR	NR	N	N	Seow[55]
	In-house ELISA	ELISA	IgM/IgG	NR	NR	N	N	Sun[61]
	In-house ELISA	ELISA	Total Ab	NR	NR	N	N	Terpos[64]
	In-house ELISA	ELISA	Total Ab	NR	NR	N	N	Wendel[71]
	In-house ELISA	ELISA	IgM/IgG	NR	NR	N	N	Young[76]

Abbreviations: Abs = antibodies; Anti-N/S = anti-nucleotide/spike protein; CEFA = cyclic enhanced florescence assay; CE-IVD = CE-marked in-vitro diagnostic device; CI = confidence interval; CLIA = chemiluminescence immunoassay; CMIA = chemiluminescence microparticle immunoassay; COVID-19 = coronavirus disease 2019; ELFA = enzyme linked fluorescent assay; (sn)ELISA = (surrogate neutralization) enzyme-linked immunosorbent assay; EU = European Union; EUA = emergency use authorization; FDA = United States Food and Drug Administration; FIA = fluorescence immunoassay; FRNT = focus reduction neutralization test; ICG = immunochromatographic assay; IgA/G/M = immunoglobulin A/G/M; LF = lateral flow; MIA = microsphere immunoassay; NR = not reported; RBD = receptor binding domain; RDT = rapid diagnostic test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Footnotes:

[a] For all tests with FDA EUA, estimates of sensitivity and specificity were obtained from FDA sources[91]; for non-EUA tests, information was obtained from manufacturer's brochures when possible.

[b] FDA EUA status current as of 12/23/2020; table does not provide information for tests that have pending EUA requests.[91]

[c] EU CE-IVD mark status current as of 10/16/2020 and sourced from FindDx.org[92] unless otherwise specified; CE-IVD mark indicates adherence to protection standards (health, safety, and environmental) for in vitro diagnostic devices sold within the European Economic Area.

[d] Test has not been issued EUA or CE-IVD mark, but has been labeled "research use only."[93]

[e] CE mark status provided by manufacturer.

[f] CE mark status provided by Johns Hopkins Center for Health Security.[93]

[g] Orient Gene Biotech's wholly owned subsidiary, Healgen Scientific, developed the test (COVID-19 IgG/IgM Rapid Test Cassette), which received EUA on May 29, 2020.

Table C-3. IgM, IgG, and IgA prevalence (seroprevalence, cross-sectional, and cohort studies)

Author, Year	Test Timing in Days*	IgM N Antibody Positive/N Tested (%)	IgG N Antibody Positive/N Tested (%)	IgA N Antibody Positive/N Tested (%)	IgM, IgG, *and/or* IgA N Antibody Positive/N Tested (%)
Blain, 2020[19]	~42 post RT-PCR+	NR	Anti-N: 33/46 (72)	NR	NR
Bruni, 2020[20]	2-32 PSO	NR	*Hospitalized and non-hospitalized*: Anti-S: 40/40 (100) Anti-RBD:40/40 (100) Anti-N: 40/40 (100)	*Hospitalized:* NR *Non-Hospitalized:* Anti-RBD: 12/16 (75) Anti-N: 4/16 (25)	NR
Chirathaworn, 2020[23]	Median 54 (IQR: 45-61)	30/217 (14)	192/217 (89)	181/217 (83)	NR
Dave, 2020[26]	0-7 PSO	2/23 (9)	0/23 (0)	NR	NR
	8-14 PSO	11/27 (40)	9/27 (33)	NR	NR
	15-21 PSO	8/36 (22)	12/36 (33)	NR	NR
	>21 PSO	0/14 (0)	9/14 (64)	NR	NR
Fafi-Kremer, 2020[29]	13-20 PSO	Anti-RBD: 26/29 (90)	Anti-RBD: 14/29 (48)	NR	Anti-RBD IgM or IgG: 27/29 (93)
	21-27 PSO	Anti-RBD: 75/83 (71)	Anti-RBD: 59/83 (71)	NR	Anti-RBD IgM or IgG: 80/83 (96)
	≥28 PSO	Anti-RBD: 40/48 (83)	Anti-RBD: 41/48 (85)	NR	Anti-RBD IgM or IgG: 46/48 (96)
Flannery, 2020[30]	0-6 post RT-PCR+	NR	NR	NR	Anti-S/RBD IgM or IgG: 15/26 (58)
	7-13 post RT-PCR+	NR	NR	NR	Anti-S/RBD IgM or IgG: 5/5 (100)
	14-20 post RT-PCR+	NR	NR	NR	Anti-S/RBD IgM or IgG: 2/2 (100)
	≥21 post RT-PCR+	NR	NR	NR	Anti-S/RBD IgM or IgG: 14/14 (100)
Gudbjartsson, 2020[15]	2-35 post RT-PCR+	Anti-N: 29/42 (69)	Anti-N: 40/42 (95)	NR	Anti-N pan-Ig:46/48 (96) Anti-S1/RBD pan-Ig: 46/48 (96)
	Mean 100 post RT-PCR+	Anti-N: 57/1145 (5)	Anti-N: 539/1134 (48)	NR	Anti-N pan-Ig: 1120/1215 (92) Anti-S1/RBD pan-Ig: 1143/1215 (94)
Hou, 2020[31]	Median 22 (SD 8-9) PSO	Anti-S/N: 279/338 (83)	Anti-S/N: 309/338 (94)	NR	Anti-S/N IgM and IgG: 266/338 (79)

Author, Year	Test Timing in Days*	IgM N Antibody Positive/N Tested (%)	IgG N Antibody Positive/N Tested (%)	IgA N Antibody Positive/N Tested (%)	IgM, IgG, *and/or* IgA N Antibody Positive/N Tested (%)
Huang, 2020[32]	Median 20 (IQR 10-29) PSO	Anti-N/E: 300/366 (82)	NR	NR	NR
	Median 51 (IQR 42-60) PSO	NR	Anti-N/E: 366/366 (100)	NR	NR
Iversen, 2020[36]	7-21 PSO	173/360 (48)	199/360 (55)	NR	IgM and IgG: 141/360 (39) IgM or IgG: 231/360 (64)
Iyer, 2020 [37]	21-122 PSO	Anti-RBD: 140/159 (88)	Anti-RBD: 153/159 (96)	Anti-RBD: 142/159 (89)	NR
Ko, 2020[39]	Median 20-36 post RT-PCR+	Anti-RBD/N: 6/70 (9)	Anti-RBD/N: 69/70 (99)	NR	Anti-RBD/N IgM and IgG: 68/70 (97)
Li, 2020[42]	1-7 PSO	Anti-S/N: 19/48 (40)	Anti-S/N: 34/48 (71)	NR	NR
	8-14 PSO	Anti-S/N: 51/91 (56)	Anti-S/N: 67/91 (74)	NR	NR
	15-21 PSO	Anti-S/N: 82/160 (51)	Anti-S/N: 122/161 (76)	NR	NR
	22-28 PSO	Anti-S/N: 108/165 (66)	Anti-S/N: 137/165 (83)	NR	NR
	29-35 PSO	Anti-S/N: 257/339 (76)	Anti-S/N: 324/340 (95)	NR	NR
	36-42 PSO	Anti-S/N: 601/752 (80)	Anti-S/N: 728/756 (96)	NR	NR
	43-49 PSO	Anti-S/N: 369/462 (80)	Anti-S/N: 453/463 (98)	NR	NR
	50-56 PSO	Anti-S/N: 214/285 (75)	Anti-S/N: 282/286 (99)	NR	NR
	57-63 PSO	Anti-S/N: 102/171 (60)	Anti-S/N: 167/171 (98)	NR	NR
	64-70 PSO	Anti-S/N: 53/96 (55)	Anti-S/N: 94/96 (98)	NR	NR
	77-84 PSO	Anti-S/N: 21/37 (57)	Anti-S/N: 36/37 (97)	NR	NR
	85-91 PSO	Anti-S/N: 4/9 (44)	Anti-S/N: 9/9 (100)	NR	NR
Liu, 2020[43]	Median 51 (SD: 15) PSO	NR	397/484 (82)	NR	NR
Liu, 2020[47]	15-28 PSO	Anti-S 29/32 (91)[1]	Anti-S 30/32 (94)[2]	NR	NR
Lynch, 2020[48]	30 (IRQ 25-34) PSO	*ICU patients:* Anti-RBD/N: 15/16 (94)	*ICU patients:* Anti-RBD/N: 16/16 (100)	NR	NR
	33 (IRQ 28-38) PSO	*Non-ICU patients:* Anti-RBD/N: 13/21 (62)	*Non-ICU patients:* Anti-RBD/N: 16/21 (76)	NR	NR

Author, Year	Test Timing in Days*	IgM N Antibody Positive/N Tested (%)	IgG N Antibody Positive/N Tested (%)	IgA N Antibody Positive/N Tested (%)	IgM, IgG, *and/or* IgA N Antibody Positive/N Tested (%)
	48 (IRQ 44-52) PSO	*Non-ICU patients:* Anti-RBD/N: 18/42 (43)	*Non-ICU patients:* Anti-RBD/N: 38/42 (91)	NR	NR
Payne, 2020[50]	Median 22 (IQR: 15-26) PSO	NR	NR	NR	Anti-S pan-Ig 88/98 (90)
Petersen, 2020[51a]	14-29 PSO	NR	Anti-S1: 39/NR (95)	NR	NR
	30-39 PSO	NR	Anti-S1: 107/NR (96)	NR	NR
	40-49 PSO	NR	Anti-S1: 227/NR (96)	NR	NR
	50-59 PSO	NR	Anti-S1: 387/NR (94)	NR	NR
	60-69 PSO	NR	Anti-S1: 557/NR (95)	NR	NR
	70-79 PSO	NR	Anti-S1: 349/NR (94)	NR	NR
	80-89 PSO	NR	Anti-S1: 253/NR (94)	NR	NR
	90-118 PSO	NR	Anti-S1: 76/NR (89)	NR	NR
Qu, 2020[52]	3 – 43 PSO	Anti-S/N: 36/41 (88)	Anti-S/N: 40/41 (98)	NR	NR
Schaffner, 2020[54]	Median 48 (IQR 43-52) PSO	NR	Anti-S: 71/82 (87) Anti-N: 75/82 (91)	Anti-S: 64/82 (78)	NR
	Median 140 (IQR 133-144) PSO	NR	Anti-S: 68/82 (83) Anti-N: 52/82 (63)	Anti-S: 56/82 (68)	NR
Seow, 2020[55]	0-7 PSO	Anti-S: NR/65 (12) Anti-RBD: NR/65 (11) Anti-N: NR/65 (15)	Anti-S: NR/65 (11) Anti-RBD: NR/65 (11) Anti-N: NR/65 (15)	Anti-S: NR/65 (12) Anti-RBD: NR/65 (6) Anti-N: NR/65 (9)	NR
	8-14 PSO	Anti-S: NR/65 (52) Anti-RBD: NR/65 (49) Anti-N: NR/65 (62)	Anti-S: NR/65 (48) Anti-RBD: NR/65 (48) Anti-N: NR/65 (59)	Anti-S: NR/65 (49) Anti-RBD: NR/65 (32) Anti-N: NR/65 (48)	NR
	15-21 PSO	Anti-S: NR/65 (75) Anti-RBD: NR/65 (72) Anti-N:NR/65 (80)	Anti-S: NR/65 (68) Anti-RBD: NR/65 (69) Anti-N: NR/65 (77)	Anti-S: NR/65 (71) Anti-RBD: NR/65 (52) Anti-N: NR/65 (65)	NR
	22-28 PSO	Anti-S: NR/65 (85) Anti-RBD: NR/65 (82) Anti-N: NR/65 (91)	Anti-S: NR/65 (83) Anti-RBD: NR/65 (80) Anti-N: NR/65 (91)	Anti-S: NR/65 (86) Anti-RBD: NR/65 (65) Anti-N: NR/65 (77)	NR
	29-35 PSO	Anti-S: NR/65 (88) Anti-RBD: NR/65 (86) Anti-N: NR/65 (91%)	Anti-S: NR/65 (85) Anti-RBD:NR/65 (82) Anti-N: NR/65 (91)	Anti-S: NR/65 (87) Anti-RBD: NR/65 (68) Anti-N: NR/65 (79)	NR
	36-42 PSO	Anti-S: NR/65 (89) Anti-RBD: NR/65 (89) Anti-N: NR/65 (91)	Anti-S: NR/65 (86) Anti-RBD:NR/65 (83) Anti-N:NR/65 (91)	Anti-S: NR/65 (89) Anti-RBD: NR/65 (69) Anti-N: NR/65 (80)	NR
	43-49 PSO	Anti-S: NR/65 (91) Anti-RBD: NR/65 (91) Anti-N: NR/65 (94)	Anti-S: NR/65 (89) Anti-RBD:NR/65 (86) Anti-N:NR/65 (94)	Anti-S: NR/65 (91) Anti-RBD: NR/65 (71) Anti-N: NR/65 (83)	NR

Author, Year	Test Timing in Days*	IgM N Antibody Positive/N Tested (%)	IgG N Antibody Positive/N Tested (%)	IgA N Antibody Positive/N Tested (%)	IgM, IgG, *and/or* IgA N Antibody Positive/N Tested (%)
	50-56 PSO	Anti-S: NR/65 (92) Anti-RBD: NR/65 (92) Anti-N: NR/65 (94)	Anti-S: NR/65 (91) Anti-RBD:NR/65 (88) Anti-N:NR/65 (94)	Anti-S: NR/65 (92) Anti-RBD: NR/65 (72) Anti-N: NR/65 (83)	NR
	57-63 PSO	Anti-S: NR/65 (92) Anti-RBD: NR/65 (92) Anti-N: NR/65 (95)	Anti-S: NR/65 (92) Anti-RBD: NR/65 (92) Anti-N: NR/65 (95)	Anti-S: NR/65 (94) Anti-RBD: NR/65 (72) Anti-N: NR/65 (85)	NR
Shang, 2020[56]	Median 41 (range 21-81) PSO	NR	Anti-S/N: NR/778 (89)	NR	NR
Shu, 2020[58]	5-40 PSO	Anti-N 113/131 (86)	Anti-N 129/131 (99)	NR	NR
Staines, 2020[59]	NR, Study period: 55 days	NR	Anti-S/N: 162/177 (92)	NR	NR
Stock da Cunha, 2020[60]	13 post RT-PCR+[b]	17/29 (45)	17/29 (45)	NR	IgM and IgG: 15/29 (40)
Sun, 2020[61]	1-7 PSO	Anti-N: NR/27(42) Anti-S: NR/27(42)	Anti-N: NR/27(42) Anti-S: NR/27(58)	NR	Anti-N IgM and IgG: NR/27(58) Anti-S IgM and IgG: NR/27(67)
	8-14 PSO	Anti-N: NR/27(74) Anti-S: NR/27(68)	Anti-N: NR/27(84) Anti-S: NR/27(79)	NR	Anti-N IgM and IgG: NR/27(95) Anti-S IgM and IgG: NR/27(90)
	15-21 PSO	Anti-N: NR/27(74) Anti-S: NR/27(74)	Anti-N: 27/27(100) Anti-S: 27/27(100)	NR	Anti-N IgM and IgG: 27/27(100) Anti-S IgM and IgG: 27/27(100)
Suthar, 2020[62]	3-30 PSO and 2-19 post RT-PCR+	NR	Anti-RBD: 44/44 (100)	NR	NR
Terpos, 2020[64]	62 (14-104) PSO or RT-PCR+	NR	NR	NR	Anti-S1 IgG/A: NR/259 (88) Anti-S/N/RBD IgM/G/A: NR/259 (88)
Van Elslande, 2020[67]	First test at hospital admission	NR	Anti-N: NR/76 (30-37)[c] Anti-S/N: NR/76 (29-33)[d] Anti-S: NR/76 (21)[e]	NR	Anti-N IgM and IgG: NR/76 (34)

Author, Year	Test Timing in Days*	IgM N Antibody Positive/N Tested (%)	IgG N Antibody Positive/N Tested (%)	IgA N Antibody Positive/N Tested (%)	IgM, IgG, *and/or* IgA N Antibody Positive/N Tested (%)
	1 week into hospital admission	NR	Anti-N: NR (93-95)[f] Anti-S/N: NR (90-93)[g] Anti-S: NR (85-93)[h]	NR	Anti-N IgM and IgG: NR/41 (93)
Wang, 2020[68]	Median 32 post RT-PCR+	NR	22/23 (96)	NR	NR
Wendel, 2020[71]	NR	NR	NR	NR	Anti-N IgM/G/A: 250/271 (92)
Xu, 2020[75]	0-14	Anti-S/N: 184/242 (76)	Anti-S/N: 206/242 (85)	NR	NR
	15-20	Anti-S/N: 232/242 (96)	Anti-S/N: 242/242 (100)	NR	NR
	21-28	Anti-S/N: 242/242 (100)	Anti-S/N: 242/242 (100)	NR	NR
Young, 2020[76]	1-7 PSO	Anti-RBD: 5/30 (18)	Anti-RBD: 2/30 (8)	NR	NR
	8-14 PSO	Anti-RBD: 12/30 (39)	Anti-RBD: 8/30 (27)	NR	NR
	15-21 PSO	Anti-RBD: 11/30 (36)	Anti-RBD: 15/30 (50)	NR	NR
	>21 PSO	Anti-RBD: 2/30 (7)	Anti-RBD: 5/30 (15)	NR	NR
Zhang, 2020[77]	0-35 PSO	182/222 (82)	219/222 (99)	NR	NR
Zhao, 2020[78]	28 PSO	15/26 (58)	20/26 (77)	NR	IgM and IgG: 15/19 (58)
Zhao, 2020[79]	1-14 PSO	Anti-RBD 133/173 (77)	124/173 (72)	NR	NR
	15-20 PSO	164/173 (95)	160/173 (92)	NR	NR
	21-25 PSO	170/173 (98)	167/173 (97)	NR	NR
	26-30 PSO	172/173 (99)	171/173 (99)	NR	NR
	31-35 PSO	172/173 (99)	172/173 (99)	NR	NR
	36-40 PSO	173/173 (100)	173/173 (100)	NR	NR
Zheng, 2020[80]	NR	192/693 (28)	612/693 (88)	NR	185/693 (27)

*Days post symptom onset (PSO) or post RT-PCR+, if reported

Abbreviations: Anti-RBD = anti-receptor binding domain; Anti-N = anti-nucleocapsid, Anti-S = anti-spike; CLIA = chemiluminescence immunoassay; CMIA = chemiluminescent magnetic microparticle immunoassay; COVID-19 = coronavirus disease 2019; E = envelope protein; ELFA = enzyme linked fluorescent assay; ELISA = enzyme-linked immunosorbent assay; IgM/G/A = immunoglobulin M/G/A; ICG = immunochromatographic assay; LFA = lateral flow assay; N = number; NR = not reported; RT-PCR+ = polymerase chain reaction positive result; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; PSO = post-symptom onset; S = spike; S1 = S1 unit of spike protein.

Footnotes:

[a] Per Petersen et al, data presented excludes 308 persons without symptoms and 127 persons who did not report a date of symptom onset. The interval between symptom onset and antibody testing ranged from 4-118 days.

[b] Data not reported clearly. Timing of antibody testing is reported as mean 13 days from PCR testing for PCR negative participants. This timing was assumed to be the same for RT-PCR+ participants.

[c] Measured with Abbott IgG-N and Euro NCP IgG-N, range of results reported.

[d] Measured with Maglumi IgG-N/S and Mikrogen IgG-S/N, range of results reported.

[e] Measured with Diasorin IgG-S and Euro S1 IgG-S, range of results reported.

[f] Measured with Abbott IgG-N and Euro NCP IgG-N, range of results reported.

[g] Measured with Maglumi IgG-N/S and Mikrogen IgG-S/N, range of results reported.

[h] Measured with Diasorin IgG-S and Euro S1 IgG-S, range of results reported.

Table C-4. IgM, IgG, and IgA prevalence (immunoassay validation studies)

Author, Year Immunoassay Type(s)	Test Timing in Days*	IgM N Antibody Positive/N Tested (%)	IgG N Antibody Positive/N Tested (%)	IgA N Antibody Positive/N Tested (%)	IgM, IgG, *and/or* IgA N Antibody Positive/ N Tested (%)
Andrey, 2020[16] 1.**IgM/IgG RDT** 2.**IgM/IgG RDT** 3.**IgM/IgG RDT** 4.**Anti-S rIFA** 5.**Anti-S1 IgG ELISA**	0-14 post RT-PCR+	1. 4/14 (29) 2. 12/14 (86) 3. 12/14 (86)	1. 11/14 (79) 2. 13/14 (93) 3. 13/14 (93) 4. 12/14 (86) 5. 13/14 (93)	NR	NR
	>14 post RT-PCR+	1. 6/27 (22) 2. 22/27 (82) 3. 26/27 (96)	1. 25/27 (93) 2. 25/27 (93) 3. 26/27 (96) 4. 26/27 (96) 5. 24/27 (89)	NR	NR
Andrey, 2020[17] 1.**IgG/IgM RDT** 2.**Anti-S rIFA** 3.**Anti-S1 IgG ELISA**	0-6 post RT-PCR+	1. 1/20 (5)	1. 8/20 (40) 2. 9/20 (45) 3. 6/20 (30)	NR	NR
	7-14 post RT-PCR+	1. 2/14 (14)	1. 10/14 (71) 2. 10/14 (71) 3. 9/14 (64)	NR	NR
	>14 post RT-PCR+	1. 2/12 (17)	1. 12/12 (100) 2. 12/12 (100) 3. 12/12 (100)	NR	NR
Choe, 2020[24] **Anti-N/RBD IgG/IgM RDT**	Mean 24 (SD 10) post RT-PCR+	NR	NR	NR	IgM and IgG: 46/70 (66) IgM or IgG: 65/70 (93)
de la Iglesia, 2020[27] 1.**IgG/IgM RDT** 2.**IgM and IgG LFA (composite test)**	>14 PSO	1. NR/58 (18)	1. NR/58 (58)	NR	2. IgM and IgG: NR/58 (41)
Delliere, 2020[28] **IgM/IgG LFA**	≥28 PSO or RT-PCR+	NR	NR	NR	IgM and IgG: 102/102 (100)
Imai, 2020[33] IgM/IgG LFA	1-6 PSO	25/90 (28)	3/90 (3)	NR	IgM and IgG: 25/90 (28)
	7-14 PSO	12/25 (48)	2/25 (8)	NR	IgM and IgG:12/25 (48)
	>14 PSO	23/24 (96)	15/24 (63)	NR	IgM and IgG: 23/24 (96)

Author, Year Immunoassay Type(s)	Test Timing in Days*	IgM N Antibody Positive/N Tested (%)	IgG N Antibody Positive/N Tested (%)	IgA N Antibody Positive/N Tested (%)	IgM, IgG, *and/or* IgA N Antibody Positive/ N Tested (%)
Infantino, 2020[34] **Anti-S/N IgM/IgG CLIA**	8-17 PSO	NR	NR	NR	41/61 (67)
Jaaskelainen, 2020[38] **Anti-S1 IgG/IgA ELISA**	Median 11-12 PSO	NR	13/39 (33)	NR	IgA and IgG: 3/39 (33)
Liu, 2020[45] **Anti-N IgM/IgG ELISA**	0-5 PSO	NR	NR	NR	IgM or IgG: 5/9 (56)
	6-10 PSO	NR	NR	NR	IgM or IgG: 11/25 (44)
	>11 PSO	NR	NR	NR	IgM or IgG: 111/119 (93)
Liu, 2020[46] **IgM/IgG CLIA**	14-35 PSO	74/91 (81)	91/91 (100)	NR	NR
Pancrazzi, 2020[49] **IgM/IgG RDT**	On the day of RT-PCR+	3/73 (4)	15/73 (7)	NR	IgM and IgG: 9/73 (12)
Shen, 2020[57] **IgM/IgG immuno-chromatography assay**	0-7 PSO	NR	NR	NR	22/40 (55)
	8-14 PSO	NR	NR	NR	24/33 (73)
	15-28 PSO	NR	NR	NR	23/24 (96)
Theel, 2020[65] 1.**Anti-N IgG CMIA** 2.**Anti-N IgG ELISA** 3.**Anti-S1 IgG ELISA** 4.**Anti-S IgG CLIA**	<7 PSO (*Inpatients*) or RT-PCR+ (*Outpatients*)	NR	*Inpatients*: 1.4/38 (11) 2.1/38 (3) 3.0/38 (0) 4.1/38 (3) *Outpatients*: 1.2/11(18) 2.1/11(9) 3.2/11(18) 4.1/11 (9)	NR	NR
	8-14 PSO	NR	*Inpatients*: 1.45/91 (50) 2.41/91 (45) 3.25/91 (28) 4.35/91 (39)	NR	NR

Author, Year Immunoassay Type(s)	Test Timing in Days*	IgM N Antibody Positive/N Tested (%)	IgG N Antibody Positive/N Tested (%)	IgA N Antibody Positive/N Tested (%)	IgM, IgG, *and/or* IgA N Antibody Positive/ N Tested (%)
	≥15 PSO	NR	*Inpatients*: 1.56/61 (92) 2.61/61 (100) 3.61/61 (100) 4.61/61 (100)	NR	NR
	≥20 post RT-PCR+	NR	*Outpatients*: 1.22/23 (96) 2.13/23 (57) 3.21/23 (91) 4.22/23 (96)	NR	NR
Traugott, 2020[66] 1.**Anti-RBD IgM ELISA** 2.**Anti-S1 IgG ELISA** 3.**Anti-S1 IgA ELISA** 4.**Anti-RBD Total Ab ELISA** 5.**Total Ab RDT** 6.**IgM/IgG RDT**	1-5 PSO	1. 8/30 (27) 6. 6/30 (20)	2. 1/30 (3) 6. 4/30 (13)	3. 9/30 (30)	4.11/30 (37) 5. 6/30 (20)
	6-10 PSO	1. 23/25 (92) 6. 5/25 (20)	2. 10/25 (20) 6. 12/25 (48)	3. 21/25 (84)	4. 23/25 (92) 5. 20/25 (80)
	≥11 PSO	1. 22/22 (100) 6. 10/22 (46)	2. 22/22 (100) 6. 22/22 (100)	3. 22/22 (100)	4. 22/22 (100) 5. 22/22 (100)
Wang, 2020[70] **Anti-RBD IgM/IgG CMIA**	0-10 PSO	NR	NR	NR	58/61 (95)
	11-20 PSO	NR	NR	NR	70/82 (85)
	>20 PSO	NR	NR	NR	7/8 (88)
Wolff, 2020[72] 1.Anti-S IgM ELFA 2.Anti-S IgG CMIA 3.**Anti-S1 IgG ELISA** 4.**Anti-S IgG ELFA** 5.**Anti-S1 IgA ELISA** 6.**Anti-N Total Ab CLIA**	0-7 PSO or post RT-PCR+	1. 14/35 (40)	2. 18/35 (51) 3. 21/35 (60) 4. 20/35 (57)	5. 25/35 (71)	6. 24/35 (69)
	8-14 PSO or post RT-PCR+	1. 25/31 (81)	2. 21/31 (68) 3. 22/31 (71) 4. 22/31 (71)	5. 25/31 (81)	6. 26/31 (84)
	>15 PSO or post RT-PCR+	1. 33/45 (73)	2. 39/45 (88) 3. 41/45 (92) 4. 39/45 (87)	5. 42/45 (93)	6. 40/45 (89)
Xiang, 2020[73] **Anti-N IgM/IgG ELISA**	3-40 PSO	51/66 (77)	55/66 (83)	NR	NR

Abbreviations: Anti-RBD = anti-receptor binding domain; Anti-N = anti-nucleocapsid, Anti-S = anti-spike; CLIA = chemiluminescence immunoassay; CMIA = chemiluminescent magnetic microparticle immunoassay; COVID-19 = coronavirus disease 2019; E = envelope protein; ELFA = enzyme linked fluorescent assay; ELISA = enzyme-linked immunosorbent assay; IgM/G/A = immunoglobulin M/G/A; ICG = immunochromatographic assay; LFA = lateral flow assay; N = number; NR = not reported; RT-PCR+ = polymerase chain reaction positive result; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; PSO = post-symptom onset; S = spike; S1 = S1 unit of spike protein.

*Days post symptom onset (PSO) or post RT-PCR+, if reported

Table C-5. Variation in antibody prevalence and levels by patient characteristics

Patient characteristic: Outcome N Studies N RT-PCR+ Subjects	Author(s)	Study Results
Age: Seroprevalence 5 Studies Total N=3,759	Fafi-Kremer, 2020[29]	No difference for neutralizing antibody activity.
	Petersen, 2020[51]	No difference in IgG seronegative status.
	Shang, 2020[56]	No difference in IgG prevalence, levels, and kinetics.
	Shen, 2020[57]	Higher prevalence among adults >65, but not statistically significant (ordinal variable: age ≤35, 36-55, 56-65, and age >65).
	Staines, 2020[59]	No difference in seroconversion rates by patient age (dichotomous variable: age <70, >70 years of age).
Age: Antibody levels 8 Studies Total N=5,567	Chen Yong, 2020[21]	No difference in IgM or IgG levels (ordinal variable: age 14-49, 50-64, ≥65 years of age).
	Chen Yuezhou, 2020[22]	Statistically significant correlation between IgG levels and age (continuous variable).
	Gudbjartsson, 2020[15]	Among recovered group, antibody levels were higher in older individuals (continuous variable defined as “change in levels per 10 years of life”).
	Huang, 2020[32]	Patients with older age had higher IgM and IgG antibody levels (dichotomous variable: ≤60, >60 years of age).
	Koblischke, 2020[40]	No difference in the antibody response by age.
	Li, 2020[42]	IgG levels significantly higher in older patients (ordinal variable: <40 years, 40–65 years, and >65 years of age).
	Staines, 2020[59]	Age >70 associated with higher IgG concentration (dichotomous variable: age ≤70, >70).
	Terpos, 2020[64]	Age ≥50 correlated with higher IgG titers (dichotomous variable: age <50, ≥50).
Sex: Seroprevalence 5 Studies Total N=3,759	Fafi-Kremer, 2020[29]	No association with neutralizing antibody.
	Petersen, 2020[51]	No difference.
	Shang, 2020[56]	No statistical difference in antibody responses.
	Shen, 2020[57]	Non-statistically significant finding of higher prevalence among men.
	Staines, 2020[59]	No difference.
Sex: Antibody levels 8 Studies Total N=3,995	Chen Yong, 2020[21]	IgM titers were higher in male patients than female patients. No difference was observed for IgG.
	Gudbjartsson, 2020[15]	Among recovered group, Pan-Ig anti–S1-RBD and IgA anti-S1 levels were lower in female persons.
	Huang, 2020[32]	No difference in IgG or IgM.
	Koblischke, 2020[40]	No difference.
	Staines, 2020[59]	No difference in antibody concentrations.
	Takahashi, 2020[63]	No difference in IgG or IgM.
	Terpos, 2020[64]	No difference.
	Wendel, 2020[71]	No difference.
Race/ethnicity: Antibody prevalence 1 Study Total N=2,547	Petersen, 2020[51]	Non-Hispanic Whites were over twice as likely to lack IgG antibodies than non-Hispanic Blacks.

Patient characteristic: Outcome N Studies N RT-PCR+ Subjects	Author(s)	Study Results
Race/ethnicity: Antibody levels 1 Study Total N=177	Staines, 2020[59]	Higher IgG antibody concentrations were associated with nonwhite race.
Comorbidities: Seroprevalence 7 Studies Total N=3,860	Delliere, 2020[28]	No patients with malignancy (N=4) had detectable IgM or IgG [hematological malignancies (*n*=2) and metastatic lung carcinoma (*n*=1) and glioblastoma (*n*=1) undergoing chemotherapy and/or radiation].
	Fafi-Kremer, 2020[29]	Higher body mass index was associated with high neutralizing antibody activity, while tobacco use, pre-existing asthma or hypertension had no association with high neutralizing antibody activity.
	Petersen, 2020[51]	Immunosuppressive therapy or medications was associated with seronegativity. No difference related to pre-existing diabetes, hypertension, chronic heart disease, chronic kidney disease, chronic liver disease, or chronic obstructive pulmonary disease.
	Shang, 2020[56]	Higher prevalence of IgG among non-cancer patients 98% (95% CI 96 to 99) compared to cancer patients 65% (95% CI 44 to 82) (P=0.001).
	Staines, 2020[59]	Hypertension and body mass index were associated with seroconversion.
	Stock da Cunha, 2020[60]	Among patients with end-stage renal disease on hemodialysis, 13% of patients had not developed antibodies at a mean of 13 days after having a positive PCR.
	Wang B, 2020[68]	Among patients with multiple myeloma, 96% (22/23) had detectable IgG.
Comorbidities: Antibody levels 6 Studies Total N=3,617	Chen, Y. 2020[25]	No significant difference in IgM or IgG titers by underlying disease.
	Chen, Yuezhou 2020[24]	No correlations between initial virus-specific IgG level and body mass index.
	Gudbjartsson, 2020[15]	Among recovered group, body mass index associated with higher antibody levels, tobacco use associated with lower antibody levels.
	Huang, 2020[32]	IgG titers were significantly associated with diabetes.
	Lynch, 2020 [48]	No significant differences in antibody concentrations when stratifying patients by comorbidities (hypertension, type 2 diabetes, obesity, and chronic kidney disease).
	Wendel, 2020[51]	Weight positively correlated with IgM, IgG, and IgA titers.

Abbreviations: CI = confidence interval; IgA/G/G = immunoglobulin A/G/M; N = number; PCR = polymerase chain reaction; RBD = receptor binding domain; RT-PCR+ = polymerase chain reaction positive result; S1 = S1 subunit of spike protein.

Appendix D. Quality Assessment

Table D-1. Methods of quality assessment by study design

Study Design	Quality Assessment Tools*
Seroprevalence	Joanna Briggs Institute Checklist for Prevalence Studies[10]
Cross-sectional	Newcastle-Ottawa Quality Assessment Scale[11]
Cohort	Newcastle-Ottawa Quality Assessment Scale[11]
Immunoassay Validation	QUADAS-2[12]

*Adapted for use in this review.

Table D-2. Quality assessment of seroprevalence studies*

Author, Year	1	2	3	4	5	6	7	8	9	Comments	Risk of Bias
Flannery, 2020[30]	N	Y	Y	Y	Y	Y	Y	Y	Y	Participants are pregnant women (unique population) who may have more frequent care or more access to care than the general population; however, this finding would not be expected to affect seroprevalence results. Universal RT-PCR testing was implemented during the study period. 80% of eligible participants were included in the sample.	Low
Gudbjartsson, 2020[15]	Y	Y	Y	Y	Y	Y	Y	Y	U	Population-based sample. The number of individuals eligible for voluntary study participation is not reported; therefore, unable to evaluate adequacy of the response rate.	Low
Iversen, 2020[36]	Y	Y	Y	Y	Y	Y	Y	Y	Y	97% of eligible participants were included in the sample.	Low
Payne, 2020[50]	N	U	U	Y	N	U	U	Y	U	Participants were U.S. service members onboard a ship during a SARS-CoV-2 outbreak (unique population and setting). 27% of eligible participants were included in the sample. Survey participants were slightly older and had a different racial distribution than non-participants. RT-PCR and serology results based on participant self-report.	High

Abbreviations: N = no; NA = not applicable; RT-PCR = polymerase chain reaction; U = unclear; Y = yes.

***Criteria (Adapted from the Joanna Briggs Institute Checklist for Prevalence Studies[10]):**

1. Was the sample frame appropriate to address the target population?
    - Yes = the study includes participants representative of the overall population
    - No = the study includes participants with unique characteristics or treated in unique settings
    - Unclear
2. Were study participants recruited in an appropriate way?
    - Yes/No/Unclear
3. Was the sample size adequate?
    - Yes = the sample size is large enough to produce a reliable estimate of the measure(s) of interest
    - Unclear = authors did not report a sample size calculation and/or it is otherwise unclear if the sample was large enough to produce a reliable estimate of the measure(s) of interest
4. Were the study subjects and setting described in detail?
    - Yes/No

5. Was data analysis conducted with sufficient coverage of the identified sample? (i.e. Did subgroups within the identified sample, such as older and younger participants, respond at similar rates?)
    - Yes/No/Unclear
6. Were valid methods used for the identification of the condition?
    - Yes/No/Unclear
7. Was the condition measured in a standard, reliable way for all participants?
    - Yes/No/Unclear
8. Was there appropriate statistical analysis?
    - Yes/No/Unclear
9. Was the response rate adequate, and if not, was the low response rate managed appropriately?
    - Yes/No/Unclear

Table D-3. Quality assessment of cross-sectional studies*

Author	1	2	3	4	5	6	7	Applicability	Comments	Risk of Bias
Chirathaworn, 2020[23]	Y	U	U	Y	Y	Y	Y	Fair	Unclear whether participants were comparable to non-participants.	Low
Dave, 2020[26]	U	U	U	Y	U	U	N	Fair	Unclear sampling strategy. Excluded patients on immunosuppressing medications or with immune-deficient diseases. No details provided regarding performance characteristics of immunoassay used.	High
Fafi-Kremer, 2020[29]	Y	U	U	Y	Y	Y	Y	Fair	The number of individuals eligible for voluntary study participation is not reported; unclear if participants and non-participants were comparable.	Low
Robbins, 2020[53]	Y	U	U	Y	U	Y	N	Fair	Unclear if respondents and non-respondents were comparable.	Unclear
Suthar, 2020[62]	Y	U	U	Y	U	Y	N	Fair	Small sample of acutely ill individuals. No adjustment for potential confounders.	Unclear
Xu, 2020[75]	U	U	U	Y	U	Y	N	Fair	Sampling strategy not described for RT-PCR+ participants. No adjustment for potential confounders.	High

Abbreviations: N = no; NA = not applicable; P = partial; RT-PCR+ = polymerase chain reaction positive result; U = unclear; Y = yes.

***Criteria (Adapted from the Newcastle-Ottawa Scale for Cross-Sectional Studies[11]):**

Selection

1. Sample representative?
    - Yes = Truly representative of the average in the target population (all subjects or random sampling); or somewhat representative of the average in the target population (non-random sampling).
    - No = Selected group of users
    - Unclear = No description of the sampling strategy.
2. Sample size justified and satisfactory?
    - Yes/No/Unclear
3. Non-participants comparable to participants?
    - Yes = Comparability between participants and non-participants is established, and the participation rate is satisfactory.
    - No = The participation rate is unsatisfactory or the comparability between participants and non-participants is unsatisfactory.
    - Unclear = No description of the participation rate or the characteristics of participants and non-participants

4. Ascertainment of the exposure appropriate?
    - Yes = Adequately described, such as by medical record review or participant self-report.
    - Unclear = Ascertainment methods not described.

Comparability

5. Were subjects in different outcome groups comparable, based on the study design or analysis?
    - Yes/No/Unclear

Outcome

6. Were outcomes pre-specified and ascertained using appropriate methods?
    - Yes
    - Unclear
7. Appropriate statistical analyses on potential confounders?
    - Yes = Appropriate statistical analyses were conducted.
    - No = No statistical analyses were conducted to adjust for confounders.
    - Unclear = Statistical analysis was conducted but is not well-described and adjustment for confounders cannot be determined.

Table D-4. Quality assessment of cohort studies*

Author, Year	1	2	3	4	5	6	7	8	9	10	11	Applicability	Comments	Risk of Bias
Bao, 2020[18]	U	U	Y	Y	U	Y	Y	N	N	N	U	Low	No description of sampling strategy. Unclear if groups were comparable at baseline. No adjustment for potential confounders.	High
Blain, 2020[19]	Y	NA	Y	Y	NA	Y	Y	NA	NA	N	U	Low	Unique population and setting; results may not be applicable to broader population. Comorbidities and symptoms not reported for whole sample.	Unclear
Bruni, 2020[20]	Y	U	Y	Y	U	Y	Y	Y	N	N	U	Fair	Unclear if groups were comparable at baseline. No adjustment for potential confounders.	High
Chen, 2020[21]	Y	NA	Y	Y	NA	Y	Y	Y	U	N	U	Fair	No adjustment for potential confounders.	Unclear
Chen, 2020[22]	Y	NA	Y	Y	NA	Y	Y	Y	U	N	U	Fair	Participants included those with a range of disease severity. No adjustment for potential confounders.	Unclear
Crawford, 2020[25]	Y	NA	Y	Y	NA	Y	Y	Y	N	N	U	Fair	Small sample. Participants included those with a range of disease severity. Methods well-described.	Low
Hou, 2020[31]	Y	U	Y	Y	U	Y	Y	Y	N	N	U	Fair	Unclear if groups were comparable at baseline. No adjustment for potential confounders.	Unclear
Huang, 2020[32]	Y	NA	Y	Y	NA	Y	Y	Y	Y	N	U	Fair		Low
Isho, 2020	Y	U	Y	Y	U	Y	Y	Y	Y	Y	U	Fair	Unclear if groups were comparable at baseline.	Low
Iyer, 2020	Y	U	Y	Y	N	Y	Y	Y	U	N	U	Fair	Age and sex distribution differed between RT-PCR+ cases and pre-pandemic controls, but that finding is unlikely to influence antibody prevalence among RT-PCR+ cases.	Unclear
Ko, 2020[39]	Y	U	Y	Y	U	Y	Y	Y	N	N	U	Fair	Results are not adjusted for potential confounders such as age or comorbidities.	Unclear
Koblischke, 2020[40]	Y	U	Y	Y	U	Y	Y	Y	N	N	U	Fair	Small sample size. No adjustment for potential confounders.	Unclear
Kwon, 2020[41]	U	NA	Y	Y	NA	Y	Y	Y	N	N	U	Fair	Small sample size. Unclear sampling strategy. No adjustment for potential confounders.	High

Author, Year	1	2	3	4	5	6	7	8	9	10	11	Applicability	Comments	Risk of Bias
Li, 2020[42]	U	U	Y	Y	U	Y	Y	Y	N	N	U	Good	Large sample size. Unclear sampling strategy. No adjustment for potential confounders.	Unclear
Liu J, 2020[43]	U	NA	Y	Y	NA	Y	Y	N	N	N	Y	Fair	Unclear sampling strategy. Methods poorly described. No adjustment for potential confounders.	High
Liu J, 2020[44]	Y	NA	Y	Y	NA	Y	Y	Y	N	N	U	Fair	Small sample size. Some patients still hospitalized at end of study period. No adjustment for potential confounders.	Unclear
Liu X, 2020[47]	U	NA	Y	Y	NA	Y	Y	N	N	N	U	Fair	Unclear sampling strategy. No adjustment for potential confounders.	High
Lynch, 2020[48]	Y	NA	Y	Y	NA	U	Y	Y	Y	N	U	Unclear	May have limited applicability. Study uses an immunoassay that is not well-described for use in this context (performance characteristics NR).	Unclear
Petersen, 2020[51]	Y	NA	Y	Y	NA	Y	Y	Y	Y	N	U	Good	Large sample size.	Low
Qu, 2020[52]	U	NA	Y	Y	NA	Y	Y	N	N	N	U	Fair	Unclear sampling strategy. No adjustment for potential confounders.	High
Schaffner, 2020[54]	Y	NA	Y	Y	NA	Y	Y	N	N	N	U	Fair	No adjustment for potential confounders.	Unclear
Seow, 2020[55]	U	NA	Y	Y	NA	Y	Y	N	N	N	U	Fair	Unclear sampling strategy. Limited demographic information regarding two study cohorts. No adjustment for potential confounders.	High
Shang, 2020[56]	U	NA	Y	Y	NA	Y	Y	Y	Y	N	U	Fair	Unclear sampling strategy.	Unclear
Shu, 2020[58]	U	NA	Y	Y	NA	Y	Y	N	N	N	U	Fair	Unclear sampling strategy. No adjustment for potential confounders	High
Staines, 2020[59]	Y	NA	Y	Y	NA	Y	Y	Y	Y	N	U	Fair	Participants included those with a range of disease severity. Methods well-described.	Low
Stock da Cunha, 2020[60]	Y	NA	Y	Y	NA	Y	Y	Y	N	N	U	Low	Small sample. Population of patients undergoing hemodialysis; results may not be applicable to broader population. . No adjustment for potential confounders.	Unclear
Sun, 2020[61]	Y	Y	Y	Y	Y	Y	Y	N	U	N	U	Fair	Small sample. No adjustment for potential confounders.	Unclear
Takahashi, 2020[63]	Y	Y	Y	Y	Y	Y	Y	Y	U	N	Y	Fair	Sample of hospitalized patients.	Low

Author, Year	1	2	3	4	5	6	7	8	9	10	11	Applicability	Comments	Risk of Bias
Terpos, 2020[64]	Y	NA	Y	Y	NA	Y	Y	Y	Y	N	U	Good	Secondary analysis of participants in a clinical trial. Participants had a range of disease severity.	Low
Van Elslande, 2020[67]	N	U	Y	Y	U	Y	Y	N	N	N	U	Fair	Unclear sampling strategy. Excluded immunocompromised patients. No adjustment for potential confounders.	High
Wang B, 2020[68]	Y	NA	Y	Y	NA	Y	Y	Y	N	N	U	Low	Population of patients with multiple myeloma; results may not be applicable to broader population. No adjustment for potential confounders.	Unclear
Wang K, 2020[69]	U	NA	Y	Y	NA	Y	Y	N	N	N	U	Fair	Unclear sampling strategy. Small sample size. No adjustment for potential confounders.	High
Wendel, 2020[71]	Y	NA	Y	Y	NA	Y	Y	Y	Y	N	U	Fair		Low
Xie, 2020[74]	Y	NA	Y	Y	NA	Y	Y	N	N	N	U	Fair		Unclear
Young, 2020[76]	Y	NA	Y	Y	NA	Y	Y	Y	U	N	U	Fair		Low
Zhang, 2020[77]	U	NA	Y	Y	NA	Y	Y	N	N	N	U	Fair	Unclear sampling strategy. Small sample size. No adjustment for potential confounders.	High
Zhao G, 2020[78]	U	U	Y	Y	Y	Y	Y	N	N	N	U	Fair	Unclear sampling strategy. Small sample size. No adjustment for potential confounders.	High
Zhao J, 2020[79]	Y	NA	Y	Y	NA	Y	Y	Y	Y	N	U	Fair		Low
Zheng, 2020[80]	U	NA	Y	Y	NA	Y	Y	N	N	N	U	Fair	Unclear sampling strategy. No adjustment for potential confounders.	High

Abbreviations: N = no; NA = not applicable; RT-PCR+ = polymerase chain reaction positive result; U = unclear; Y = yes.

***Criteria (Adapted from the Newcastle-Ottawa Scale for Cohort Studies[11]):**

Selection

1. Was the exposed cohort representative?

    - Yes = Truly representative of the average in the target population (all subjects or random sampling); or, somewhat representative of the average in the target population (non-random sampling).
    - No = Selected group of users
    - Unclear = No description of the sampling strategy.

2. Was the non-exposed systematically selected? Criteria applies if the study included a control group distinct from controls used to validate immunoassay accuracy.
    - Yes = Random or consecutive sample.
    - No = Selected group of users.
    - Unclear = No description of the sampling strategy.
3. Does the study report how RT-PCR SARS-CoV-2 status was ascertained?
    - Yes/No/Unclear
4. Eligibility criteria pre-specified?
    - Yes = the eligible population is described.
    - No = the study provides no information regarding the eligible population or the study modifies eligibility without justification.

Comparability

5. Were the exposed and non-exposed groups comparable at baseline? Criteria applies if the study included a control group distinct from controls used to validate immunoassay accuracy (as for question 2).
    - Yes/No/Unclear/NA

Outcome

6. Were outcomes pre-specified and ascertained using appropriate methods?
    - Yes/No/Unclear
7. Was follow-up long enough for outcomes to occur?
    - Yes=follow-up duration was reasonably appropriate given the outcome of interest
    - No
    - Unclear
8. Were potential confounding factors identified? Criteria applies if the study included a control group distinct from controls used to validate immunoassay accuracy (as for question 2) or the study conducted subgroup analysis.
    - Yes/No
9. Appropriate statistical analyses on potential confounders?
    - Yes = Appropriate statistical analyses were conducted.
    - No = No statistical analysis was conducted to adjust for confounders.

- Unclear = Statistical analysis was conducted but is not well-described and adjustment for confounders cannot be determined.

10. Important differential loss to follow-up or overall high loss to follow-up?
    - Yes/No/Unclear
11. Reporting of an appropriate handling of missing data?
    - Yes = no missing data or the study appropriately reports missing data and handling.
    - No
    - Unclear = unclear whether data are missing or the study reports missing data but does not describe how missing data were handled.

Table D-5. Quality assessment of immunoassay validation studies*

Author	1	2	3	4	5	6	7	8	9	10	11	12	13	Risk of Bias
Andrey, 2020[16]	U	N	Y	U	Y	U	Y	U	U	Y	Y	Y	Y	Unclear
Andrey, 2020[17]	U	N	Y	Y	Y	U	Y	Y	U	Y	Y	Y	Y	Unclear
Choe, 2020[24]	Y	N	Y	U	Y	U	Y	U	U	Y	Y	Y	Y	Unclear
de la Iglesia, 2020[27]	Y	N	Y	U	Y	U	Y	U	U	Y	Y	Y	Y	Unclear
Delliere, 2020[28]	U	N	Y	N	U	U	Y	U	U	Y	Y	Y	Y	Unclear
Imai, 2020[33]	U	N	Y	U	Y	U	Y	U	U	Y	Y	Y	Y	Unclear
Infantino, 2020[34]	U	N	Y	U	Y	U	Y	U	U	Y	Y	Y	Y	Unclear
Jaaskelainen, 2020[38]	U	N	Y	U	U	U	Y	U	U	Y	Y	Y	Y	Unclear
Liu R, 2020[46]	U	Y	Y	U	Y	U	Y	U	U	Y	Y	Y	Y	Unclear
Liu L, 2020[45]	Y	N	Y	U	Y	U	Y	U	U	Y	Y	Y	Y	Unclear
Pancrazzi, 2020[49]	U	Y	Y	U	U	U	Y	U	U	Y	Y	Y	Y	Unclear
Shen, 2020[57]	U	N	Y	U	Y	U	Y	U	U	Y	Y	Y	Y	Unclear
Theel, 2020[65]	U	N	Y	U	Y	U	Y	U	U	Y	Y	Y	Y	Unclear
Traugott, 2020[66]	U	N	Y	U	Y	U	Y	U	U	Y	Y	Y	Y	Unclear
Wang P, 2020[70]	U	N	Y	U	Y	U	Y	U	U	Y	Y	Y	Y	Unclear
Wolff, 2020[72]	Y	N	Y	U	Y	U	Y	U	U	Y	Y	Y	Y	Unclear
Xiang, 2020[73]	U	N	Y	U	U	U	Y	U	U	Y	Y	Y	Y	Unclear

Abbreviations: N = no; U = unclear; Y = yes.

***Criteria (based on Modified QUADAS-2 Tool [12]):**

Patient Selection

1. Was a consecutive or random sample of patients enrolled?
    - Yes/No/Unclear
2. Did the study avoid a case-control design (i.e. enroll participants with known disease and a control group without the condition, which may exaggerate diagnostic accuracy)?
    - Yes/No/Unclear
3. Did the study avoid inappropriate exclusions?

- Yes/No/Unclear

Index Test(s)

4. Were the index test results interpreted without knowledge of the results of the reference standard?
    - Yes/No/Unclear
5. If a threshold was used, was it pre-specified?
    - Yes/No/Unclear
6. Could problems with the conduct of the test have significantly distorted the measurements?
    - Yes/No/Unclear

Reference Standard

7. Is the reference standard likely to correctly classify the target condition?
    - Yes/No/Unclear
8. Were the reference standard results interpreted without knowledge of the results of the index test?
    - Yes/No/Unclear
9. Could problems with the conduct of the reference standard have significantly distorted the measurements?
    - Yes/No/Unclear

Flow and Timing

10. Was there an appropriate interval between index test(s) and reference standard?
    - Yes/No/Unclear
11. Did all patients receive a reference standard?
    - Yes/No/Unclear
12. Did patients receive the same reference standard?
    - Yes/No/Unclear
13. Were all patients included in the analysis?
    - Yes/No/Unclear

Appendix E. Strength of Evidence Assessment

Table E-1. Summary of evidence by study outcome

Outcome	Outcome Sub-category	N Studies, N RT-PCR+ Subjects	Directness	Precision	Study Risk of Bias [a]	Consistency	Strength of Evidence
Antibody prevalence at estimated peak levels post-symptom onset or RT-PCR diagnosis*	IgM	**21 Studies (Total N=6,073)**: Dave, 2020[26]; Fafi-Kremer, 2020[29]; Gudbjartsson, 2020[15]; Hou, 2020[31]; Huang, 2020[32]; Iversen, 2020[36]; Iyer, 2020[37]; Ko, 2020[39]; Li, 2020[42] ; Liu X, 2020[47]; Lynch, 2020[48]; Qu, 2020[52]; Seow, 2020[55]; Shu, 2020[58]; Stock da Cunha, 2020[60]; Sun, 2020[61]; Xu, 2020[75]; Young, 2020[76]; Zhang, 2020[77]; Zhao, 2020[78]; Zhao, 2020[79]	Direct	Imprecise[b]	Low: 6 Unclear: 7 High: 8	Consistent[c]	**Moderate**
	IgG	**24 Studies (Total N=9,136)**: Bruni, 2020[20]; Dave, 2020[26]; Fafi-Kremer, 2020[29]; Gudbjartsson, 2020[15]; Hou, 2020[31]; Iversen, 2020[36]; Iyer, 2020[37]; Ko, 2020[39]; Li, 2020[42] ; Liu X, 2020[47]; Lynch, 2020[48]; Petersen, 2020[51]; Qu, 2020[52]; Seow, 2020[55]; Shang, 2020[56]; Shu, 2020[58]; Sun, 2020[61]; Suthar, 2020[62]; Wang B, 2020[68]; Xu, 2020[75]; Young, 2020[76]; Zhang, 2020[77]; Zhao, 2020[78]; Zhao, 2020[79]	Direct	Imprecise[b]	Low: 6 Unclear: 9 High: 9	Consistent[c]	**Moderate**
	IgA	**5 Studies (Total N=747)**: Bruni, 2020[20]; Chirathaworn, 2020[23]; Iyer, 2020[37]; Schaffner, 2020[54]; Seow, 2020[55]	Direct	Imprecise[b]	Low: 1 Unclear: 2 High: 2	Consistent[c]	**Low**
	NAb	**8 Studies (Total N=979)**: Crawford, 2020[25]; Fafi-Kremer, 2020[29]; Iyer, 2020[37]; Ko, 2020[39]; Koblischke, 2020[40]; Suthar, 2020[62]; Wang, 2020[69]; Wendel, 2020[71]	Direct	Imprecise[b]	Low: 3 Unclear: 4 High: 1	Consistent[c]	**Low**

Outcome	Outcome Sub-category	N Studies, N RT-PCR+ Subjects	Directness	Precision	Study Risk of Bias [a]	Consistency	Strength of Evidence
Antibody levels over time and duration	IgM	**22 Studies (Total N=6,704)**: Bao, 2020[18]; Chen, Yong 2020[21]; Chirathaworn, 2020[23]; Crawford, 2020[25]; Dave, 2020[26]; de la Iglesia, 2020[27]; Hou, 2020[31]; Huang, 2020[32]; Infantino, 2020[34] ; Isho, 2020[35]; Kwon, 2020[41]; Li, 2020[42] ; Liu X, 2020[47]; Qu, 2020[52]; Seow, 2020[55]; Shu, 2020[58]; Sun, 2020[61]; Wendel, 2020[71]; Xie, 2020[74]; Young, 2020 [76]; Zhang, 2020[77]; Zhao, 2020[79]	Direct	Imprecise[b]	Low: 7 Unclear: 7 High: 8	Consistent[c]	**Moderate**
	IgG	**25 Studies (Total N=9,269)**: Bao, 2020[18]; Chen, Yong 2020[21]; Chen, Yuezhou 2020[22]; Dave, 2020[26]; Gudbjartsson, 2020[15]; Hou, 2020[31]; Huang, 2020[32]; Isho, 2020[35]; Iyer, 2020[37]; Jaaskelainen, 2020[38]; Kwon, 2020[41]; Li, 2020[42] ; Liu J, 2020[43]; Liu X, 2020[47]; Lynch, 2020[48]; Qu, 2020[52]; Seow, 2020[55]; Shang, 2020[56]; Shu, 2020[58]; Sun, 2020[61]; Van Elslande, 2020[67]; Xie, 2020[74]; Young, 2020[76]; Zhang, 2020[77]; Zhao, 2020[79]	Direct	Imprecise[b]	Low: 5 Unclear: 10 High: 10	Consistent[c]	**Moderate**
	IgA	**6 Studies (Total N=2,234)**: Chirathaworn, 2020[23]; Gudbjartsson, 2020[15]; Isho, 2020[35]; Jaaskelainen, 2020[38]; Schaffner, 2020[54]; Seow, 2020[55]	Direct	Imprecise[b]	Low: 3 Unclear: 2 High: 1	Consistent[c]	**Low**
	NAb	**8 Studies (Total N=997)**: Crawford, 2020[25]; Fafi-Kremer, 2020[29]; Isho, 2020[35]; Ko, 2020[39]; Koblischke, 2020[40]; Seow, 2020[55]; Suthar, 2020[62]; Wang K, 2020[69]	Direct	Imprecise[b]	Low: 3 Unclear: 3 High: 2	Consistent[c]	**Low**

Outcome	Outcome Sub-category	N Studies, N RT-PCR+ Subjects	Directness	Precision	Study Risk of Bias [a]	Consistency	Strength of Evidence
Variation in antibody prevalence by patient characteristics	Age	**12 Studies (Total N=9,149)**: Chen, Yong, 2020[21]; Chen Yuezhou, 2020[22]; Fafi-Kremer, 2020[29]; Gudbjartsson, 2020[15]; Huang, 2020[32]; Koblischke, 2020[40]; Li, 2020[42]; Petersen, 2020[51]; Shang, 2020[56]; Shen, 2020[57]; Staines, 2020[59]; Terpos, 2020[64]	Direct	Imprecise[b]	Low: 6 Unclear: 6	Consistent[c]	**Low**
	Sex	**12 Studies (Total N=7,577)**: Chen Yong, 2020[21]; Fafi-Kremer, 2020[29]; Gudbjartsson, 2020[15]; Huang, 2020[32]; Koblischke, 2020[40]; Petersen, 2020[51]; Shang, 2020[56]; Shen, 2020[57]; Staines, 2020[59]; Takahashi, 2020[63]; Terpos, 2020[64]; Wendel, 2020[71]	Direct	Imprecise[b]	Low: 8 Unclear: 4	Consistent[c]	**Low**
	Race/Ethnicity	**2 Studies (Total N=2,724)**: Petersen, 2020[51]; Staines, 2020[59]	Direct	Imprecise[b]	Low: 2	Consistent[c]	**Low**
	Comorbidities	**13 Studies (Total N=7,477)**: Chen, Yong 2020[21]; Chen, Yuezhou 2020[22]; Delliere, 2020[28]; Fafi-Kremer, 2020[29]; Gudbjartsson, 2020[15]; Huang, 2020[32]; Lynch, 2020 [48]; Petersen, 2020[51]; Shang, 2020[56]; Staines, 2020[59]; Stock da Cunha, 2020[60]; Wang B, 2020[68]; Wendel, 2020[51]	Direct	Imprecise[b]	Low: 6 Unclear: 7	Inconsistent[d]	**Insufficient**
Variation in antibody prevalence/levels by symptoms	Asymptomatic versus Symptomatic	**9 Studies (Total N=4,793)**: Chen, 2020[22]; Fafi-Kremer, 2020[29]; Gudbjartsson, 2020[15]; Imai, 2020[33]; Pancrazzi, 2020[49]; Petersen, 2020[51]; Staines, 2020[59]; Terpos, 2020[64]; Wolff, 2020[72]	Direct	Imprecise[b]	Low: 5 Unclear: 4	Consistent[c]	**Low**

Outcome	Outcome Sub-category	N Studies, N RT-PCR+ Subjects	Directness	Precision	Study Risk of Bias [a]	Consistency	Strength of Evidence
Variation in antibody prevalence/levels by disease severity	Mild versus Severe/Critical	**30 Studies (Total N=8,900)**: Bruni, 2020[20]; Chen, 2020[21]; Chen, 2020[22]; Chirathaworn, 2020[23]; Crawford, 2020[25]; Dave, 2020[26]; Gudbjartsson, 2020[15]; Hou, 2020[31]; Huang, 2020[32]; Huang, 2020[32]; Kwon, 2020[41]; Li, 2020[42]; Liu R, 2020[46]; Liu X, 2020[47]; Lynch, 2020[48]; Qu, 2020[52]; Seow, 2020[55]; Shen, 2020[57]; Stock da Cunha, 2020[60] ;Sun, 2020[61]; Terpos, 2020[64] ; Theel, 2020[65];Traugott, 2020[66] ;Van Elslande, 2020[67]; Wolff, 2020[72] ; Xie, 2020[74]; Young, 2020[76]; Zhang, 2020[77]; Zhao G, 2020[78]; Zheng, 2020[80]	Direct	Imprecise[b]	Low: 7 Unclear: 13 High: 10	Consistent[c]	**Low**
Variation in antibody prevalence by immunoassay	NA	**10 studies (Total N= 1,996)**: Andrey, 2020[16]; Andrey, 2020[17]; de la Iglesia, 2020[27]; Fafi-Kremer, 2020[29]; Gudbjartsson, 2020[15]; Ko, 2020[39]; Theel, 2020[65]; Traugott, 2020[66]; Van Elslande, 2020[67]; Wolff, 2020[72]	Indirect	Imprecise[b]	Low: 2 Unclear: 7 High: 1	Inconsistent[d]	**Insufficient**
Incidence of reinfection in patients with antibodies	NA	NA (No studies addressed KQs)	NA	NA	NA	NA	**Insufficient**
Length of time between an initial infection and reinfection	NA	No findings	No findings	No findings	No findings	No findings	**Insufficient**
Unintended consequences of antibody testing	NA	**1 Study (N=84)**: Robbins[53]	Indirect	Imprecise[b]	Low	NA	**Insufficient**

Abbreviations: IgM/G/A = immunoglobulin M/G/A; KQ = key question; N = number; Nab = neutralizing antibody; NA = not applicable; RT-PCR = polymerase chain reaction.
*Includes seroprevalence, cross-sectional, and cohort studies. Immunoassay validation studies excluded from strength of evidence assessments for prevalence outcomes.

Note: Based on consensus among review authors, we applied the following general algorithm for strength of evidence assessments: Evidence comprised of multiple large methodologically sound observational studies with consistent findings received a rating of "moderate." Evidence from fewer studies or studies

with smaller sample sizes but mostly consistent results received a rating of "low," and this same type of evidence with inconsistent results received a rating of "insufficient." No reporting bias was detected.

Footnotes:
[a] See Appendix Table D: Quality Assessment.
[b] Results rated as imprecise if a) individuals studies had small sample sizes or a low number of data points to estimate trends or b) studies had a wide variation in estimates.
[c] Results are consistent in the direction of effect.
[d] Results are inconsistent in the direction or magnitude of effect.

Appendix F. Research In Progress

Table F-1. Ongoing trials relevant to key questions[a]

Study Title and ClinicalTrials.gov Identifier (NCT Number)	Study Design, Country	Population	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
Longitudinal serological study of the spread and course of COVID-19 infections; **NCT04377724**	Prospective Cohort Switzerland	Cohort of initially healthy adults composed of employees and students of the National Supercomputing Center (ETH) in Zürich, Switzerland	• Seroprevalence and serum titers of anti-SARS-CoV-2 IgM, IgG, and IgA antibodies • Characterization of mononuclear cells before and after SARS-CoV-2 infection • Immune response to seasonal Coronaviruses an Influenza virus in patients with SARS-CoV-2 infections	Active, not recruiting as of December 7, 2020	June 30, 2021
Study of the SARS-CoV-2 (COVID-19) serological profile of an Army training hospital staff; **NCT04387838**	Prospective Cohort France	Army training hospital staff from the Hopital d'Instuction des Armées Sainte-Anne	• Anti-SARS-CoV-2 seroconversion rates at 0, 30 and 60 days • Correlation between seroconversion and sex • Correlation between seroconversion and age • Correlation between seroconversion and occupational exposures • Correlation between seroconversion and PPE use • Correlation between seroconversion and COVID-19 exposures	Recruiting as of June 9, 2020	July 31, 2020
Immune RACE – Immune Response Action to COVID-19 Events; **NCT04494893**	Prospective Cohort US (Seattle, WA)	Cohort 1: Subjects exposed to SARS-CoV-2 infection Cohort 2: Subjects with active SARS-CoV-2 infection Cohort 3: Subjects recovered from SARS-CoV-2 infection	• Comparison of disease specific T cell repertoire signatures in patients and controls • Identification of the immunodominant antigens that elicit a T cell response to COVID-19 • Risk stratification based on an individual's immune signature • Determine whether an immune signature can be detected in individuals exposed to SARS-CoV-2 earlier than currently available tests	Recruiting as of July 31, 2020	January 31, 2021

Study Title and ClinicalTrials.gov Identifier (NCT Number)	Study Design, Country	Population	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
How Immune Responses Shape Virological and Clinical Characteristics of COVID-19; **NCT04329546**	Prospective Cohort Switzerland	Cohort A: Subjects with laboratory confirmed SARS-CoV-2 infection Cohort B: Household contacts of subjects with laboratory confirmed SARS-CoV-2, with and without symptoms and with and without laboratory SARS-CoV-2 confirmation	• Titers of anti-SARS-CoV-2 IgG antibodies at 28 days following PCR diagnosis • Peak viral load in the 56 days following PCR diagnosis	Recruiting as of April 13. 2020	March 31, 2021
Study of Clinical and Immune Severity Profiles of Patients Infected with SARS-CoV-2 (COVID-19) (REACOVIM); **NCT04365166**	Prospective Cohort France	Adults with PCR confirmed SARS-CoV-2 infection admitted to ICU	• Plasma cytokine profile – Th1/Th2/Th17/Treg balance and Type I Interferons • Phenotype of circulating T and B cells, NK cells and monocytes • Angiotensin Converting Enzyme Type II (ACE2) polymorphism • Disease severity (duration of ICU stay, duration of hospital stay, duration without mechanical ventilation, SOFA score, LIS score • SARS-CoV-2 viral load • Acquired co-infections (bacterial or fungal) • Associated comorbidities	Recruiting as of May 14, 2020	April 21, 2022
Predictive Immune Biomarkers for COVID-19 Pathogenesis; **NCT04385108**	Prospective Cohort France	Adults with PCR confirmed SARS-CoV-2 assembled into three cohorts: Cohort A: Patients with severe COVID-19 requiring ICU care Cohort B: Non-severe hospitalized patients with secondary clinical worsening requiring ICU management Cohort C: Non-severe hospitalized patients not requiring ICU management	• Seroprevalence and kinetics of anti-SARS-CoV-2 IgM and IgG antibodies on days 0, 2, 4, 8. 12 and 30 or at discharge • Phenotypic profiling of T cell subsets through the expression of a wide range of surface and intracellular markers on days 0, 2, 4, 8. 12 and 30 or at discharge	Recruiting as of May 14, 2020	December 31, 2021

Study Title and ClinicalTrials.gov Identifier (NCT Number)	Study Design, Country	Population	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
A Prospective Study of Acute Immune Responses to SARS-CoV-2 Infection; **NCT04431414**	Prospective Cohort USA (Burlingame, AL, San Francisco, CA, Miami, FL)	Cohort A: PCR confirmed SARS-CoV-2 positive subjects without symptoms Cohort B: PCR confirmed SARS-CoV-2 positive subjects with mild symptoms Cohort C: PCR confirmed SARS-CoV-2 positive subjects who are hospitalized	• Prevalence and titers of anti-SARS-CoV-2 antibodies • Prevalence and titers of anti-SARS-CoV-2 neutralizing antibodies • Prevalence and titers of SARS-CoV-2 specific B cells • Transcriptional profiles of peripheral blood leukocytes • Concentration of serum cytokines and other soluble factors • Prevalence and titers of anti-SARS-CoV-2 specific CD4+ and CD8+T cells	Recruiting as of December 7, 2020	January 2021
Understanding Immunity to SARS-CoV-2, the Coronavirus Causing COVID-19 **NCT04373148**	Prospective Cohort USA (Stanford, CA)	Adults with PCR confirmed SARS-CoV-2 infection Control: Adults who tested negative for SARS-CoV-2 (but may have viral symptoms)	• Testing immunity to SARS-CoV-2 for 1 year • Testing the SARS-CoV-2 virus overtime for 1 year	Recruiting as of November 16, 2020	April 30, 2022
Determinants of SARS-CoV-2 (COVID-19) Persistence after Convalescence; **NCT04448145**	Prospective Cohort USA (New York, NY)	Adults with PCR confirmed SARS-CoV-2 infection	• Duration of SARS-CoV-2 viral persistence • Prevalence of cell immune responses (B cell, CD4+, CD8+, NK and NK T cell immune responses • Prevalence of post-viral sequela	Recruiting as of June 25, 2020	March 1, 2021
Longitudinal COVID-19 Antibody Testing in Indiana University Undergraduate Students; **NCT04620798**	Prospective Cohort USA (Indiana)	College students	• Frequency of handwashing, face touching, hand sanitizer use, social event avoidance, staying home from work/school, mask wearing, physical distancing, avoiding people at high-risk for severe COVID-19 infections • Proportion of participants with detectable SARS-CoV-2 over 8 weeks	Active, not recruiting as of November 9, 2020	December 2020

Study Title and ClinicalTrials.gov Identifier (NCT Number)	Study Design, Country	Population	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
SARS-Cov2 (COVID-19) Infection and Reinfection Through the Analysis of a RT-PCR Results Database; **NCT04653844**	Prospective Cohort France	French population with a positive SARS-Cov2 diagnosis documented through a positive RT-PCR result	SARS-CoV-2 reinfection rate	Active, not recruiting as of December 7, 2020	February 20, 2021
COVID-19 and SARS-CoV-2 Antibodies in Multiple Sclerosis Patients: a Large Study in the Amsterdam MS Cohort **NCT04498286**	Prospective Cohort Netherlands	Adults with multiple sclerosis receiving care in the MS Center Amsterdam	• Correlation of COVID-19 course with MS immunomodulatory treatment • Correlation of COVID-19 course in MS patients with positive SARS-CoV-2 antibodies defined by questionnaires (asymptomatic, mild symptoms, severe symptoms, hospitalization) with MS immunomodulatory treatment	Active, recruiting as of December 30, 2020	November 1, 2021
Study of Seroprevalence Vis-À-Vis SARS-CoV-2 and Correlation with Clinical Forms of COVID-19 in Patients Followed by Pulmonology in the Grand-Est region. **NCT04528901**	Prospective Cohort France	Adults with chronic pulmonary conditions (including persistent asthma, lung cancer, history of lung transplantation and others)	Prevalence of anti-SARS-CoV-2 antibodies among patients with chronic pulmonary conditions	Active, recruiting, as of December 30, 2020	September 2020
Study All of Anti-SARS-CoV-2 Antibodies Seroprevalence among Lyon-Bron Military Health Schools Personnel **NCT04516928**	Prospective Cohort France	Personnel of the Military Health Schools of Lyon-Bron	• Proportion of participants with IgM and IgG anti-SARS-CoV-2 antibodies • Proportion of participants for detectable anti-SARS-CoV-2 antibodies who are asymptomatic • Correlation coefficient between medical risk factors and positive serology • Correlation coefficient between epidemiological risk factors and positive serology • Correlation coefficient between social risk factors and positive serology	Active, recruiting as of December 30, 2020	November 2, 2020

Study Title and ClinicalTrials.gov Identifier (NCT Number)	Study Design, Country	Population	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
The Prevalence of SARS-CoV-2 IgG Antibody Formation in Physicians at Advocate Lutheran General Hospital and Their Household Members **NCT04540484**	Prospective Cohort USA (Illinois)	Medical staff (attending physicians, fellows, residents) at Advocate Lutheran General Hospital Physician household members aged 18 years and above who tested positive for anti-SARS-CoV-2 antibodies	• Total prevalence of anti-SARS-CoV-2 IgG antibodies • Prevalence of anti-SARS-CoV-2 IgG antibodies among physicians • Prevalence of anti-SARS-CoV-2 IgG antibodies among household members • Prevalence of anti-SARS-CoV-2 IgG antibodies in household members of physicians tested positive for COVID-19 IgG • Differences in anti-SARS-CoV-2 IgG prevalence among physicians with minimal, moderate, and high COVID-19 exposure risk • Prevalence of asymptomatic SARS-CoV-2 infection • Anti-SARS-CoV-2 IgG antibody persistence for up to 12 months	Active, recruiting as of December 30, 2020	September 24, 2021
Evaluation of Cell-Mediated and Humoral Immunity Following COVID-19 in Pregnancy **NCT04568044**	Prospective Cohort UK	Cohort A: Nonpregnant adults with mild-moderate COVID-19 Cohort B: Nonpregnant adults with severe-critical COVID-19 Cohort C: Nonpregnant adults without history of COVID-19 Cohort D: Pregnant/postnatal women with COVID-19 Cohort E: Pregnant/postnatal women with diagnosis of influenza within 4 months Cohort F: Pregnant/postnatal women who have received the influenza vaccine	• Phenotyping of antibody secreting cells and memory B cells during COVID-19 infection and following recovery • Quantification of anti-SARS-CoV-2 IgG production by memory B cells to measure long-lasting immune protection against reinfection • Quantification of SARS-CoV-2 viral load with PCR • Phenotyping of circulatory T Follicular Helper cells • Assessment of T cell-mediated immune function after COVID-19 • Among pregnant subjects, comparison of antibody production in England phenotyping function between COVID-19 and influenza infection and influenza vaccination	Active, recruiting as of December 30, 2020	December 31, 2022

Study Title and ClinicalTrials.gov Identifier (NCT Number)	Study Design, Country	Population	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
T Cell Response to SARS-CoV-2 Peptides by MA test and IgG Antibody response to SARS COV-2 by commercial ELISA test **NCT04573348**	Observational Cohort Israel	Cohort A: Adults recovered from moderate to severe PCR confirmed SARS-CoV-2 Cohort B: C recovered from asymptomatic or mild PCR confirmed SARS-CoV-2 Cohort C: Household members of PCR confirmed adults without history of positive PCR Cohort D: Healthy adults who adhere to social distancing	T cell reactivity in SARS-CoV-2 infection Prevalence of detectable anti-SARS-CoV-2 antibodies among healthy volunteers	Active, recruiting as of December 30, 2020	May 10, 2021

Abbreviations: Ab = antibody; ARDS = acute respiratory distress syndrome; CLIA = chemiluminescence immunoassay; COVID-19 = coronavirus disease 2019; CT = computed tomography; CT.Gov = ClinicalTrials.gov; ELISA = enzyme linked immunosorbent assay; FP = false positive; HCW = healthcare worker; IgA/G/M = immunoglobulin A/G/M; ICU = intensive care unit; NR = not reported; RT-PCR = reverse transcription polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SOFA = Sepsis Related Organ Failure Assessment Score, LIS = Lung Injury Score.

Footnotes:
[a] ClinicalTrials.gov last accessed December 30, 2020

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