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Research Paper

Seroprevalence of SARS-CoV-2 IgG antibodies among health care workers prior to vaccine administration in Europe, the USA and East Asia: A systematic review and meta-analysis

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ABSTRACT

Background: Knowing the seroprevalence of SARS-CoV-2 IgG antibodies across geographic regions before vaccine administration is one key piece of knowledge to achieve herd immunity. While people of all ages, occupations, and communities are at risk of getting infected with SARS-CoV-2, the health care workers (HCWs) are possibly at the highest risk. Most seroprevalence surveys with HCWs conducted worldwide have been limited to Europe, North America, and East Asia. We aimed to understand how the seroprevalence of SARS-CoV-2 IgG antibodies varied across these geographic regions among HCWs based on the available evidences.

Methods: By searching through PubMed, ScienceDirect, and Google Scholar databases, eligible studies published from January 1, 2020 to January 15, 2021 were included for the systematic review and meta-analysis. The random-effects model was used to estimate the pooled proportion of IgG seropositive HCWs. Publication bias was assessed by funnel plot and confirmed by Egger's test. Heterogeneity was quantified using I² statistics. We performed sensitivity analyses based on sample size, diagnostic method and publication status. The study protocol was registered with PROSPERO (CRD42020219086).

Findings: A total of 53 peer-reviewed articles were selected, including 173,353 HCWs (32.7% male) from the United States, ten European, and three East Asian countries. The overall seropositive prevalence rate of IgG antibodies was 8.6% in these regions (95% CI= 7.2-9.9%). Pooled seroprevalence of IgG antibodies was higher in studies conducted in the USA (12.4%, 95% CI= 7.8-17%) than in Europe (7.7%, 95% CI=6.3-9.2%) and East Asia (4.8%, 95% CI=2.9-6.7%). The subgroup study also estimated that male HCWs had 9.4% (95% CI= 7.2-11.6%) IgG seroconversion, and female HCWs had 7.8% (95% CI=5.9-9.7%). The study exhibits a high prevalence of IgG antibodies among HCWs under 40 years in the USA, conversely, it was high in older HCWs (≥40 years of age) in Europe and East Asia. In the months February-April 2020, the estimated pooled seroprevalence was 5.7% (4.0-7.4%) that increased to 8.2% (6.2–10%) in April-May and further to 9.9% (6.9–12.9%) in the May-September time-period. Interpretation: In the view of all evidence to date, a significant variation in the prevalence of SARS-CoV-2 antibodies in HCWs is observed in regions of Europe, the United States, and East Asia. The patterns of IgG antibodies by time, age, and gender suggest noticeable regional differences in transmission of the virus. Based on the insights driven from the analysis, priority is required for effective vaccination for older HCWs from Europe and East Asia. A considerable high seroprevalence of IgG among HCWs from the USA suggests a high rate of past infection that indicates the need to take adequate measures to prevent hospital spread. Moreover, the seroprevalence trend was not substantially changed after May 2020, suggesting a slow progression of long-term SARS-CoV-2 immunity. Routine testing of HCWs for SARS-CoV-2 should be considered even after the rollout of vaccination to identify the areas of increased transmission. Funding: None

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Abbreviations: IGG, immunoglobulin-g; IGM, immunoglobulin-m; CMI, chemiluminescent microparticle immunoassay; ELISA, Enzyme-Linked Immunosorbent Assay; P, Proportion/Prevalence; CI, Confidence Interval

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Research in context

Evidence before this study

We searched in PubMed, ScienceDirect, and Google Scholar for peer-reviewed papers and research reports on seroprevalence of anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) IgG antibodies, using the search words 'seroprevalence', 'anti-SARS-CoV-2 IgG' and 'COVID antibodies' and similar terms up to January 15, 2021. We identified 53 peer-reviewed serosurveys. In this context, to assess the seroprevalence of anti-SARS-CoV-2 IgG antibodies among health care workers (HCWs), peer-reviewed studies published in high-indexed journals have been considered to reduce heterogeneity.

Added value of this study

This research used existing studies to analyze the pooled-prevalence of anti-SARS-CoV-2 IgG antibodies in HCWs employed in Europe, East Asia, and the United States, and the estimates varied across these geographic regions. Moreover, the seroprevalence of IgG was compared across age groups, gender, countrywise infection risk, work-place infection risk, and study period. Our research also uses statistical techniques to estimate the pooled seroprevalence of IgG antibodies in the HCWs while capturing heterogeneity in the estimates. In order to understand the global pattern of natural immunity against this obdurate virus, the study allowed us to visualize the progression of seropositive status of IgG antibodies among HCWs prior to vaccination.

Implications of all the available evidence

Our findings highlight that the immunological landscape has not been changed significantly over time, suggesting a slow progression of long-term SARS-CoV-2 immunity. The seroprevalence of SARS-CoV-2 IgG antibodies among HCWs from the USA is higher than in the countries from Europe or East Asia. As the world plans to find a new equilibrium between minimizing the direct impacts of COVID-19 on the infected and indirect impacts on society, such serological study is crucial to providing new insights into disease transmission.

1. Introduction

The ongoing pandemic of the 2019 novel coronavirus, known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported in late December 2019 in Wuhan, China [1]. It grew into a full-scale pandemic within weeks and is now continuing its spread across the world, with nearly 80 million reported cases in 190 countries and more than 1.7 million deaths [2]. A few countries have now approved coronavirus vaccines for use, but as people await their roll-out, cases keep rising in many parts of the world [2]. Hence, it is crucial to understand the vaccines' effectiveness in controlling a pandemic.

There are two ways through which a person may become immune to SARS-CoV-2 infection [3]. Catching the disease typically results in natural immunity to the disease for a certain period and another means of being resistant is vaccination. Comparing the above-mentioned groups would be informative to prove vaccine effectiveness, especially for understanding the gap of antibody duration. Many countries have approved and distributed vaccines across the world to control the pandemic [2]. Together with vaccination and natural protection will help to achieve herd immunity, a state where a proportion of a population needs to be immune to an infectious agent [4]. Therefore, it is essential to know the seroprevalence of natural antibodies that might help estimate the time required for a geographical region to achieve herd immunity as well as would partly explain transmission pattern of the disease in a region.

This ongoing pandemic is a significant burden to the health care services and the HCWs, such as doctors, nurses, hospital cleaners, laboratory technicians, etc., as they remain at the highest risk of exposure to the virus [5-9]. Moreover, HCWs in Europe and the USA are at increased risk of disease exposure as they live in high-risk transmission zone [8-10]. To plan an adequate public health response for HCWs and anticipate the disease dynamics, the measurement of anti-SARS-CoV-2 antibodies is of utmost importance.

Antibodies are one of our primary defenses against viruses, created to identify particular proteins on the surface of a virus and initiate processes that gradually neutralize and eventually remove them. The serological tests to detect the presence of IgG antibodies may provide a more reliable estimation of the prevalence of SARS-CoV-2 past infection in the population, as is likely to persist for a more extended period after cleaning up the viral infection [11]. The IgG represents the most robust and long-duration antibody against the SARS-CoV-2 virus and can be detected after a median of 14 days (IQR 10-18 days) from the onset of symptoms during infection [11–12].

Many seroprevalences of SARS-CoV-2 antibodies related studies have now become available [13–14]. The majority of seroprevalence surveys with HCWs conducted worldwide have been limited to Europe, North America, and East Asia. The prevalence of such antibodies from a large-scale serosurvey conducted over four collection periods in the US ranged from less than 1% to 23% [13]. To date, three meta-analyses of antibody prevalence among HCWs have been published, and the presence of IgG and/or IgM antibodies has been found to vary between 8% and 17% globally [15–17]. These articles included pre-print articles as well as accounted IgG and/or IgM antibodies. It was not possible to extract the information only on seroprevalence of IgG antibodies in the HCWs from the available meta-analyses which is essential to understand the global trend of persisting antibody rates over time produced by natural penetration. Thus, our objective was to estimate pooled seroprevalence of SARS-CoV-2 IgG antibodies across geographic regions and to investigate the pattern by agegroup, gender, infection risk of HCWs, and study period.

2. Methods

2.1. Search strategy

We searched the PubMed, Google Scholar, and ScienceDirect online databases to select peer-reviewed papers for systematic review and meta-analysis. We screened observational studies (crosssectional and cohort) to enunciate the seroprevalence of SARS-CoV-2 antibodies among the HCWs. Our search included only articles published from January 1, 2020, to January 15, 2021. The screening language was restricted to English. In Appendix A, a description of search terms is given. We used *Mendeley* citation management software to compile the results of the search. Henceforth, we manually explored references of selected studies to combine all relevant papers to construct the summary estimates. The study inclines with the Preferred Reporting Items for Systematic Review and meta-analysis (PRISMA) guidelines [18]. The protocol was registered in the PROS-PERO database (CRD42020219086).

2.2. Selection criteria

The principal outcome of the meta-analysis was the pooled-proportion of IgG antibodies in the HCWs. Our systematic review included studies that documented the serum SARS-CoV-2 IgG antibody status among the HCWs as the outcome of interest. The status was obtained as overall, positive, and borderline/negative determined by the respective serological technique, providing a clinical sensitivity and specificity of at least 80%, used in individual studies. Studies using multiple diagnostic tests to define seropositivity, however, not stratifying the HCWs by the methods were excluded. Studies that contained less than fifty HCWs were also not included which might lead to analysis heterogeneity. Research based at hospitals or healthcare centers were further selected for full-text review, excluding community-based studies that might have partly included HCWs. Additional to the above-mentioned criteria, the prospective studies were designated eligible if they were published in journals that were Q1 or Q2 indexed by the SCImago Journal & Country Rank portal (https://www.scimagojr.com). Although for pooled-prevalence estimation we excluded the grey literature (pre-prints, thesis, and dissertation), the pre-prints were followed to perform sensitivity analyses. We considered eliminating articles for more than one rationale. Titles and abstracts of the studies obtained from the database searches were screened independently by three reviewers-ZT, MKH, and SMN. Any discordance was addressed until an agreement was reached or by the arbitration of AH alone.

2.3. Data extraction and quality assessment

A pre-specified form was used for data abstraction. To estimate the seroprevalence of IgG antibodies against SARS-CoV-2, principal data were taken on the total number of HCWs quantitatively evaluated for SARS-CoV-2 IgG antibody levels, how many of them were seropositive and negative from the selected published studies as well as the pre-print articles. Additionally, data on the name of the first author, country, study period (start-end month), study design (crosssectional or cohort), testing method (any method having at least 80% clinical sensitivity or specificity), median or mean age of HCWs (in years), number of female HCWs, number of HCWs at high risk and infectivity risk of HCWs based on work-type (high, intermediate or low) were recorded from the published article only. We considered high-risk HCWs who were reported to have direct patient contact. We further stratified the articles based on country-wise infection level risk (high, moderate or low). A country was defined as high-risk when the infection crossed millions of cases, as moderate-risk when the infection reached between 500,000 cases and a million of cases. The remaining countries were considered as low-risk group. Moreover, HCWs cross-tabulated by age-group and seropositivity status were documented, whenever possible.

The Newcastle-Ottawa Scale (NOS) was used for the assessment of the included studies (Supplementary file 1). The NOS consists of three domains called selection, comparability, and exposure or outcome of interest. Scores reflect the articles' methodological stringency, lucidity, and clarity. We did not, however, exclude any papers based on quality scoring. Besides, the PRISMA statement consists of a 27-item checklist and is given in Supplementary File 2.

Data abstraction and quality assessment from individual studies was primarily executed by three investigators independently (ZT, MKH, and SMN), from October 2020 to January 2021. All the extracted data and respective evaluations were circumspectly verified by AH.

2.4. Statistical analysis

We performed data analysis using *meta* and *metafor* packages in the R statistical software (version 3.6.1). We calculated the seroprevalence of IgG antibodies with a 95% confidence interval (CI) for each study. Following, the pooled seroprevalence was estimated using a random-effects model that allows true effect size to vary from study to study. The calculated proportion from each study and the combined effect estimate with 95% CI were represented graphically by a *Forest Plot*. Publication bias was assessed by observing the symmetry of *funnel plots* visually and confirmed by *Egger's test.* Heterogeneity across the selected studies was investigated by I^2 *statistic.* The I^2 statistic represents the percentage of total variation across studies due to heterogeneity rather than chance.

Analysis of the subgroups was carried out to determine the pooled prevalence for each group and look for potential explanations of the heterogeneity. Geographical region (Europe, USA and East-Asia), gender (male and female), mean or median age (less than 40 years and 40 years or older), study period (February-April, April-May and May-September), infection risk based on work-place of the HCWs (high and intermediate/low) and country-wise infection risk level (high, moderate and low) were considered for sub-group analysis. Further, the regional differences by gender and age-group were also calculated. We also conducted sensitivity analyses after removing a few studies to evaluate the robustness of the findings based on sample size, diagnostic method and publication status. In addition, we investigated the associated factors for SARS-CoV-2 IgG sero-positive status by gender, age-group, country-wise risk and work-place risk of HCWs. The studies included in this analysis were, however, observational and could not provide evidence of causality.

2.5. Role of the funding source

There was no funding source for this study. All authors had full access to all the data in the study and the corresponding author had final responsibility for the decision to submit for publication.

3. Results

3.1. Identification and selection of studies

A flowchart of step-wise literature search to select the appropriate articles is summarized in the PRISMA format and is presented in Fig. 1. The initial search retrieved a total of 1486 studies from the pre-specified databases. After eliminating the duplicates, the titles and abstracts were scanned for further selection of probable articles. Subsequently, the investigators elected 128 articles based on eligibility criteria for full-text review. By manual searching through the included papers' reference lists, 7 studies were considered for scrutiny, resulting the total number of potential articles to be 135. Finally, 53 studies were included for systematic review and meta-analysis.

3.2. Characteristics of the studies

Table 1 outlines the main characteristics of the 53 studies included in our systematic review and meta-analysis. We selected ten countries from Europe, the USA, and three countries from East Asia in the meta-analysis. The majority of the studies (n = 34) were conducted in Europe, followed by 12 studies from the USA and 7 studies from East Asia. The East Asian studies were from China, Korea, and Japan. The meta-analysis included 173,353 HCWs, of which 32.7% were male.

Of the 53 studies, most (90%) of the research designs were cross-sectional, and the other 5 were cohort. Several different test methods have been used to detect the presence of IgG in the blood of health care workers. The enzyme-linked immunosorbent assay (ELISA) and chemiluminescent microparticle immunoassay (CMI) were used most frequently to identify IgG antibody in the included studies. The selected studies were conducted between January and September 2020.

3.3. Meta-analysis of the seroprevalence

The seroprevalence of antibodies against SARS-CoV-2 among HCWs ranged from 0.3% to 32.6% in the studies. Fig. 2 displays the forest plot showing the prevalence of IgG antibody seropositive from studies along with confidence intervals. Estimated by the random-



Fig. 1. PRISMA flow diagram for study selection.

effects model, the pooled serological prevalence of the antibodies was 8.5% (95% CI=7.1–9.9%; I²=99.4%). The pooled proportion of IgG seropositivity against the coronavirus was the highest in the USA with 12.4% (95% CI=7.5–17.2%; I²=99.7%). However, studies from Europe and East Asia were calculated to have the pooled seroprevalence 7.7% (95% CI=6.3–9.2%; I²=99%) and 4.8% (95% CI=2.9- 6.7%; I²=95.5%), respectively. There were no precise evidence of publication bias by visual examination of funnel plot symmetry, and further, the absence was supported by the Egger test and is shown in Supplementary file 6.

3.4. Subgroup analysis

The subgroup analysis of the seroprevalence by age, gender, study period and infection risk level is given in Table 2. The results indicate an increasing trend in the overall seroprevalence among HCWs over the months from February to September 2020. Globally, the pooled prevalence of antibodies against coronavirus infection in the study period between February and April was 5.7 percent (95% CI = 4.0-7.4%; I2 = 97.7%). During April to May, the prevalence of IgG antibodies increased to 8.2% (95% CI = 6.2-10.0%; I2 = 99.3%) and in

Table 1

Characteristics of the included studies in the meta-analysis (all the studies were done in 2020).

Andex de J.31Indy<	First author's name listed in alphabetical order	Country	Study Period	Study design	Test method	Total number of health care workers	Median/Mean age (years)	% of Female HCWs	% of high risk HCWs	Infection level
Bindpore cal, [34]UKMay-luneCons-sectionalConsident cal, SectionalCons Secti	Amendola et al. [33]	Italy	April	Cross-Sectional	ELISA	663	44.0*	83.7	NA	High
Binaliar ed. [3]SpainMayGras SectionalCons SectionalNameHighBlainer ed. [3]HeginMayGras SectionalName200A3.27.5NAHighBlainer ed. [17]HeginMayGras SectionalName200A3.27.5NAHighBlainer ed. [17]HeginMayGras SectionalName1.61Name7.1Name	Bampoe et al. [34]	UK	May-June	Cross-Sectional	Chemiluminescent Microparticle Immunoassay	200	37.0*	84	100	High
Biake et al, [59] UK May-August May-August Cross Sectional Construment et al. [50] NA Construct et al. [50] NA Pilate AL NA Pilate AL NA Pilate AL NA Pilate AL NA	Barallat et al. [35]	Spain	May	Cross Sectional	Chemiluminescent Microparticle Immunoassay	7563	43.8	75.0	NA	High
Bialine cal, J2) Belgiam May-June Cross Sectional Chernalluminescent Micropartice Immunosasy H85 NA 7.3.1 7.3.1 No.8. Brunz-awadisk et al, J8) USA May Cross Sectional Lateral Flow Immunosasy G01 NA 7.2.4 NA High Brunz-awadisk et al, J81 USA May Cross Sectional Lateral Flow Immunosasy G01 NA YA NA High Constructional L1 Inter Al, M91 Cross Sectional Max Chronanographic Assay 90114 40.1 YA NA NA <td>Black et al. [36]</td> <td>Ůĸ</td> <td>May-August</td> <td>Cross Sectional</td> <td>NA</td> <td>200</td> <td>45.3</td> <td>75</td> <td>NA</td> <td>High</td>	Black et al. [36]	Ůĸ	May-August	Cross Sectional	NA	200	45.3	75	NA	High
Bank Zwacksier al. [18] USA May func Cross Sectional M. M. State Fight Fight M. Cases Cases Fight M. Cases Cases M. M.<	Blairon et al. [37]	Belgium	May-June	Cross Sectional	Chemiluminescent Microparticle Immunoassay	1485	NA	73.1	37.03	Moderate
Brunner etal, [59]USAMayCross SectionalLateral Plow Immunoasay601NA72.4NAHighCorradiu et al, [41]RayAprilCross SectionalImmunochromatographic Asay23443.0°71.8NAHighDarims et al, [42]KAAprilCross SectionalImmunochromatographic Asay27.6NANANAHighDarims et al, [43]SpainAprilCross SectionalImmunochromatographic Asay17.6NANANAHighDarims et al, [46]SpainAprilCross SectionalImmunochromatographic Asay27.1NANANAHighPiophane etal, [46]SpainAprilCross SectionalILSASpainNANAHighCoros SectionalLisACross SectionalLisASpainNANAHighCoros SectionalJapo-Japa-Cross SectionalLisASpainSpainNAHighCoros SectionalLisACross SectionalLisASpainSpainNAHighHibbite etal, [51]USAAprilCross SectionalLisALisASpainNAHighKohler etal, [52]DemmarkAprilCross SectionalLisALisANANAHighKohler etal, [52]DemmarkAprilCross SectionalLisALisANANAHighKohler etal, [53]USAMarkCross SectionalLisALisANA <td>Brant-Zawadski et al. [38]</td> <td>USĂ</td> <td>May-June</td> <td>Cross-Sectional</td> <td>NA</td> <td>2924</td> <td>42.6</td> <td>72.7</td> <td>54.3</td> <td>High</td>	Brant-Zawadski et al. [38]	USĂ	May-June	Cross-Sectional	NA	2924	42.6	72.7	54.3	High
Chen et al, [40] China I, jamany-February Cross-Sectional LISA 105 30.0" 79.04 NA Low Corradii et al, [42] With A pril-May Cross Sectional NA 20.514 43.1 NA NA High Doins et al, [42] Spain April-May Cross Sectional NA 4607 41.8 74.4 NA NA High Doins et al, [43] Prance May-Jence Cross Sectional Expander Cross Sectional NA Fig.1 Fig.3 NA High Humer et al, [51] UK March-April Cross Sectional Expander Cross Sectional Expander Cross Sectional NA High Humer et al, [51] Kros April-May Cross Sectional	Brunner et al. [39]	USA	May	Cross Sectional	Lateral Flow Immunoassay	601	NA	72.4	NA	High
Corrading al. [41]IndiaAprilCross-SectionalImmunochromatographic Assay23443.071.8NAHighDacots 4.1.[42]SpainAprilCross SectionalImmunochromatographic Assay175NANANAHighDacots 4.1.[43]SpainAprilCross SectionalImmunochromatographic Assay175NANANAHighDacots 4.1.[45]BelgiumMay-SeptemberCohortELSA850NANANAHighDagots e1.1.[46]SianAprilCross SectionalLLSA850NANANAHighDodo e1.1.[46]SianMay-SeptemberCons SectionalManusersent Microparticle Immunoassay21722077.3NAHighPordbore e1.1.[46]GranMarchCross SectionalNaNaNAHighNAHighHinther e1.[51]JapanJunc-JuiyCross SectionalLateral Ploy Immunoassay237.9244.478.94.6LowHinther e1.[51]KoraAprilCross SectionalLateral Ploy Immunoassay237.9244.478.94.6LowKhall e1.[51]KoraAprilCross SectionalLateral Ploy Immunoassay237.9244.478.94.6LowKhall e1.[51]KoraAprilCross SectionalLateral Ploy Immunoassay237.9244.478.9A.6LowKhall e1.[51]KoraMaranaCross SectionalLateral Ploy Imm	Chen et al. [40]	China	January-February	Cross-Sectional	ELISA	105	30.0*	79.04	NA	Low
D. Sims et al. (2) UK April May Cross Sectional NA May May High Decostal-Urbette et al. (4) France May-June Cross Sectional Na 4607 41.8 74.9 NA High Deubsards et al. (4) France May-June Cross Sectional Na 4607 41.8 74.9 NA Maderate Funder et al. (4) Japon April-May Cross Sectional ElEMa 850 NA 46.1 100 Low Gadoout et al. (4) LisA Cross Sectional Chemiuminescent Microparticle Immunoassay 213 22.1 72.4 A3 A0 High Interacter et al. (4) USA April-May Cross Sectional Chemiuminescent Microparticle Immunoassay 76.1 71.4 74.8 NA High Interacter et al. (5) Korea February Cross Sectional Na	Corradini et al. [41]	Italy	April	Cross-Sectional	Immunochromatographic Assay	234	43.0*	71.8	NA	High
Dacksdt.lubierd el. [4]SpainAprilCross SectionaNANANANAHighDusybargh et.l. [45]BelgiumMay-SeptemberColortELSAS50NANANAModerateDusybargh et.l. [45]BelgiumApril-MayCross SectionaILSAS50NA64.1NAMaderateFernandez et.l. [47]SpainApril-MayCross SectionaILSAS20NA64.1NAHighHibro et.l. [50]JapinJapinApril-MayCross SectionaILSAS217S2877.3NAHighHibro et.l. [50]JapinJapinMarch-JuneColortELSAS217S2877.6NAHighHibro et.l. [50]JapinJapinCross SectionaNAHighS21742.870.30NAHighHibro et.l. [51]USAApril-MayCross SectionaNAEter How Immunoassay23423.073.6NAHighJapin et.l. [51]UKMayCross SectionaILSAS3.073.6NANAHighJapin et.l. [51]GermanyMarch-AprilCross SectionaILSAS3.0NANAHighJahreet et.l. [52]GermanyMarch-AprilCross SectionaILSAS3.0NANANAHighJahreet et.l. [53]GermanyApril-MayCross SectionaILSAS3.0NANANAHighJahreet et.l. [54] <td< td=""><td>D. Sims et al. [42]</td><td>UK</td><td>April-May</td><td>Cross Sectional</td><td>NA</td><td>20,614</td><td>43.1</td><td>NA</td><td>NA</td><td>High</td></td<>	D. Sims et al. [42]	UK	April-May	Cross Sectional	NA	20,614	43.1	NA	NA	High
Delmase tal, [44]FranceMay-luneCross SectionalNA460741.874.9NAHighFujito et al, [46]JapanAprilCross SectionalELBAS50NA64.110.0LowFrandacc et al, [47]SpainAprilCross SectionalELBA92NA64.110.0LowGodbourt et al, [48]USAJuly-OctoberCross SectionalChemiluminescent Microparticle Immunoassa243971.228.277.3NAHighHibmo et al, [50]JapanJune-JulyCross SectionalChemiluminescent Microparticle Immunoassa87133.071.5NALowHibmo et al, [51]JapanJune-JulyCross SectionalChemiluminescent Microparticle Immunoassa87133.071.3NALowJeremiser al, [53]USAAprilCross SectionalChemiluminescent Microparticle Immunoassa1690A2.874.1NAHighJeremiser al, [54]UKMayCross SectionalChemiluminescent Microparticle Immunoassa1090NANANANAHighLackermair et al, [55]KoreaFebruaryCross SectionalChemiluminescent Microparticle Immunoassa101238.3775.220.7LowLackermair et al, [56]GermanyMarch-AprilCross SectionalNA108446.0°NANAHighLackermair et al, [56]KoreaFebruary-March-AprilCross SectionalNA108446.0° <td>Dacosta-Urbieta et al. [43]</td> <td>Spain</td> <td>April</td> <td>Cross Sectional</td> <td>Immunochromatographic Assay</td> <td>175</td> <td>NA</td> <td>NA</td> <td>NA</td> <td>High</td>	Dacosta-Urbieta et al. [43]	Spain	April	Cross Sectional	Immunochromatographic Assay	175	NA	NA	NA	High
Dysbyging et.al. [45]BeigiumMus_SeptembrCohortEUSAB50NANANANAModerateFernandez et.al. [47]SpainApril-MuyCross SectionalChemliuminescemt Microparticle Immunossa243942.178.4NAHighFernandez et al. [49]GermanyMarch-JuneCross SectionalAbobt immunossa211722.277.3NAHighHigh et al. [50]JapanJune JulyCross SectionalChemliuminescemt Microparticle Immunossa80633.071.6NALowHinner et al. [51]USAApril-MuyCross SectionalChemliuminescemt Microparticle Immunossa80.533.071.6NAHighHuner et al. [51]USAApril-MuyCross SectionalChemliuminescemt Microparticle Immunossa180.9NANANANAHighHuner et al. [51]USAAprilCross SectionalChemliuminescemt Microparticle Immunossa190.9NANANANAHighKohler et al. [56]SwitterlandMach-AprilCross SectionalChemliuminescemt Microparticle Immunossa191.6NANANANAHighLaberer at al. [51]WadeApril-AprilCross SectionalChemliuminescemt Microparticle Immunossa196.9NANANANAHighLaberer at al. [51]WadeApril-AprilCross SectionalChemliuminescemt Microparticle Immunossa196.9NANANANAHigh <t< td=""><td>Delmas et al. [44]</td><td>France</td><td>May-June</td><td>Cross Sectional</td><td>NA</td><td>4607</td><td>41.8</td><td>74.9</td><td>NA</td><td>High</td></t<>	Delmas et al. [44]	France	May-June	Cross Sectional	NA	4607	41.8	74.9	NA	High
Fujine ardia (4a)japanAprilCross SectionalELISA92NA64.110.0LowGradbout et al. (44)USAJuly-OctoberCross SectionalAbbott immunassay241942.178.4NAHighHolmer et al. (46)USAJuly-OctoberCross SectionalChemlluminescent Microparticle Immunoassay87133.0NA70.1HighHibme et al. (50)JapanJune-JulyCross SectionalChemlluminescent Microparticle Immunoassay87633.0°71.6NALowPiermias et al. (52)DenmarkAprilCross SectionalChemlluminescent Microparticle Immunoassay10942.870.03NAHighRhainer et al. (53)USAAprilCross SectionalChemlluminescent Microparticle Immunoassay109NANANAHighKohler et al. (54)Kohren FebruaryCross SectionalELISACross SectionalELISA101.238.3°75.220.7LowKohren et al. (54)SwitzerdandMacth-AprilCross SectionalELISA101.238.0°83.4NAHighLackermair et al. (54)GermanyMarch-AprilCross SectionalELISA101.438.0°83.4NAHighLackermair et al. (54)GermanyMarch-AprilCross SectionalKohren et al. (54)SolNANANANANALackermair et al. (54)GermanyMarch-AprilCross SectionalNANANA <td>Duysburgh et al. [45]</td> <td>Belgium</td> <td>May-September</td> <td>Cohort</td> <td>ELISA</td> <td>850</td> <td>NA</td> <td>NA</td> <td>NA</td> <td>Moderate</td>	Duysburgh et al. [45]	Belgium	May-September	Cohort	ELISA	850	NA	NA	NA	Moderate
Frimance et al. [47]SpainApril-MayCross SectionalChemiluminescent Microparticle Immunossay243942.178.4NAHighCordbort et al. [50]JapanJunc-JuncCools SectionalELSAS7139.0NA70.1HighHerzberg et al. [49]CemanyMarch-JuncCools SectionalChemiluminescent Microparticle Immunoassay73442.870.3NAHighHumer et al. [51]USAApril-MayCross SectionalElsaBisno73442.870.3NAHighJeremias et al. [53]USAAprilCross SectionalElsaBisno30931.184.5NAHighKohler et al. [54]UKMayCross SectionalElsaBisno316NANANAHighKohler et al. [56]SwitzelandMarch-AprilCross SectionalElsaBisno31.6NANANAHighLakermair et al. [56]GermanyAprilCross SectionalElsaBisnoBisnoNANANAHighLakermair et al. [56]GermanyAprilCross SectionalElsaBisnoNANANAHighLakermair et al. [56]SwedenAprilCross SectionalNANANAHighLakermair et al. [56]SwedenAprilCross SectionalNANANAHighLakermair et al. [56]SwedenAprilCross SectionalNANANA <td< td=""><td>Fujita et al. [46]</td><td>Japan</td><td>April</td><td>Cross Sectional</td><td>ELISA</td><td>92</td><td>NA</td><td>64.1</td><td>100</td><td>Low</td></td<>	Fujita et al. [46]	Japan	April	Cross Sectional	ELISA	92	NA	64.1	100	Low
Condboart et al. [48] USA July-October Cross Sectional Abbott immunoassay 2217 282 77.3 NA High Herzberg et al. [49] Germany March-June Cohort EISA 871 30.0 NA 70.1 Bigh Humer et al. [51] USA April Cross Sectional Chemiluminescent Microparticle Immunoassay 806 33.0° 71.6 NA Low Jermiase et al. [52] Demark April Color Sectional Literal Row Immunoassay 199 NA NA MA High Koat al. [53] USA April Cross Sectional EISA 109 NA NA NA High Koat al. [55] Switzerland March-April Cobor Coross Sectional EISA 101 38.3° 75.2 20.7 Low Kohth et al. [56] Switzerland March-April Cross Sectional EISA 106 NA NA NA High Laharet al. [56] Switzerland April Cross Sec	Fernandez et al. [47]	Spain	April-May	Cross Sectional	Chemiluminescent Microparticle Immunoassay	2439	42.1	78.4	NA	High
Herberg et al. [49] Gemany March-gune Cohort ELSA S71 39.0 NA 70.1 High Hunner et al. [51] USA April-May Cross Sectional NA Torss Sectional NA Torss Sectional NA Torss Sectional NA Torss Sectional ELso No Jeremias et al. [53] USA April Cross Sectional ELso No ELso No ELso No NA NA NA High Kohler et al. [54] UK May Cross Sectional ELSA 309 31.1 84.5 NA High Kohler et al. [55] Korea February Cross Sectional ELSA 309 31.1 84.5 NA High Labermair et al. [56] Korea April Cross Sectional ELSA 306 NA NA NA NA High Labermair et al. [57] Korea April Cross Sectional ELSA 1084 Kore NA NA NA NA High March	Godbout et al. [48]	USA	July-October	Cross Sectional	Abbott immunoassay	2217	282	77.3	NA	High
Hiblio et al. [50] Jpan June-Juy Cross Sectional Chemiltaminescent Microparticle Immunoassay 806 33.0" 71.6 NA Low Numere al. [51] USA April Cross-Sectional Na Figh Na High Ipermiase al. [53] USA April Cross Sectional ELSA 1699 42.8 74.1 NA High Koalt cal. [54] UKA May Cross Sectional ELSA 1699 42.8 74.1 NA	Herzberg et al. [49]	Germany	March-June	Cohort	ELISA	871	39.0	NA	70.1	High
Hunter et al. [51]USAApril-MaryCross-SectionalNA744.2.870.03NAHighJeremis et al. [52]DenmarkAprilCross SectionalLateral Flow Immunoassay28,79244.478.94.6.LowJeremis et al. [54]UKMayCross SectionalELISA169942.874.1NAHighKoret al. [55]KoreaFebruaryCross SectionalChemiluminescent Microparticle Immunoassay30931.184.5NALowKorlh et al. [57]GermanyMarch-AprilCross-SectionalILENA316NANANAHighLahrer et al. [59]ItalyMarch-AprilCross-SectionalELISA15138.0°83.4NAHighLidstrom et al. [51]SwedenAprilCross-SectionalNA108446.0°NANANAHighLidstrom et al. [61]SwedenAprilCross-SectionalNANANANAModerateLidstrom et al. [63]USAAprilCross-SectionalNANANANANAHighMarson et al. [63]USAAprilCross-SectionalNANANANAHighMarson et al. [64]USAMarch-AprilCross-SectionalNA326NANANAHighMarson et al. [65]USAMarch-AprilCross-SectionalNAAd22ModerateLidstrom et al. [64]USAAprilCr	Hibino et al. [50]	Japan	June-July	Cross Sectional	Chemiluminescent Microparticle Immunoassay	806	33.0*	71.6	NA	Low
jeresme et al. [52] Demark April Color Lateral Flow Immunoassay 28,792 44.4 78,9 4.6 Low premias et al. [54] UK Mar Cross Sectional ELSA 1699 42.8 74.1 NA Macharei (15) Six NA NA NA NA NA Macharei (16) Six NA	Hunter et al. [51]	USA	April-May	Cross-Sectional	NA	734	42.8	70.03	NA	High
jeremiaset al. [5]USAÁprilCross SectionalELSA16942.874.1NAHighKolalit et al. [55]KoreaFebruaryCross SectionalClemiluminescent Microparticle Immunoassay190NANANANAHighKohler et al. [57]KoreaFebruaryCostorCholminescent Microparticle Immunoassay101238.375.220.7LowKorth et al. [57]CermanyMarch-AprilCross SectionalELSA316NANANAHighLackermair et al. [58]GermanyMarch-AprilCross SectionalELSA105NANANAHighLindahi et al. [60]SwedenAprilCross SectionalNANA1005NANANAHighLindahi et al. [61]SwedenMarch-AprilCross SectionalCross SectionalCross SectionalELSA270NANANAHighMassour et al. [63]USAAprilCross SectionalELSA28538.445.9NAHighMassour et al. [64]BelgiumAprilCross SectionalELSA28538.445.9NAHighMascour et al. [65]USAMarch-AprilCross SectionalELSA28538.445.9NAHighJose ChornNANAS26NANANANA16.916.9NA16.9NA16.9NA16.9NA16.9NA16.91	Iversen et al. [52]	Denmark	April	Cohort	Lateral Flow Immunoassay	28,792	44.4	78.9	4.6	Low
The ball et al. [54]UKMayCress SectionalChemiluminescent Microparticle Immunoassay190NANANAHighKohler et al. [55]KorreaFebruaryCress SectionalChemiluminescent Microparticle Immunoassay30931.8A.NALowKohler et al. [57]GermanyMarch-AprilCross-SectionalELSA316NANANAHighLakermait et al. [58]GermanyAprilCross-SectionalELSA316NANANAHighLahner et al. [59]ItalyMarch-AprilCross-SectionalNA108446.0°NANANAMaLindral et al. [61]SwedenMay-JuneCross SectionalChemiluminescent Microparticle Immunoassay867942.076.725.6ModerateMarsin et al. [62]USAMarch-AprilCross SectionalChemiluminescent Microparticle Immunoassay87942.076.725.6ModerateMarsin et al. [63]USAMarch-AprilCross SectionalNANA40.32938.445.9NAHighMarsin et al. [64]BelgiumAprilCross SectionalImmunochromatographic Assay49841.57.1.NAHighPleate et al. [67]UKApril-JuneCohortLISA644041.57.2.00.2.HighPleate et al. [67]UKApril-JuneCohortELSA644041.57.1.NAHighPleate et al. [68]<	leremias et al. [53]	USA	April	Cross Sectional	ELISA	1699	42.8	74.1	NA	High
Ko et al. [55]KoreaFeinaryCross SectionalELISAand construction30931.184.5NALowKohler et al. [57]GermanyMarch-AprilCross SectionalELISA316NANANAHighLackernair et al. [58]GermanyAprilCross SectionalELISA15138.0°83.4NAHighLindhi et al. [60]SwedenAprilCross SectionalNA1005NANANANAModerateLidstrom et al. [61]SwedenAprilCross SectionalNA1005NANANAModerateMansour et al. [62]USAAprilCross SectionalNA28538.445.9NAHighMarsour et al. [63]USAMarch-AprilCross SectionalNA286NANANAHighMarsour et al. [63]USAMarch-AprilCross SectionalNA28.538.445.9NAHighMarsour et al. [64]BelgiumAprilCross SectionalNA40.32942.073.745.5HighOlalla et al. [65]USAMarch-JuneCohortNAAA40.32942.071.1NAHighPalcot et al. [65]UKApril-JuneCohortELISA47.641.166.320.8LowOlalla et al. [66]SpainAprilCross SectionalNA47.841.168.446.445.7High <td< td=""><td>Khalil et al. [54]</td><td>UK</td><td>Mav</td><td>Cross Sectional</td><td>Chemiluminescent Microparticle Immunoassay</td><td>190</td><td>NA</td><td>NA</td><td>NA</td><td>High</td></td<>	Khalil et al. [54]	UK	Mav	Cross Sectional	Chemiluminescent Microparticle Immunoassay	190	NA	NA	NA	High
I I I I NormalSinterlandMarch-ÁprilCohortChemiluminescent Microparticle Immunoassay101238.3"7.5.22.0.7LowKorth et al. [57]GermanyMarch-AprilCross-SectionalEUSA1518.0"8.14N.AHighLaherer et al. [59]ItalyMarch-AprilCross-SectionalNA108446.0"NA55.1HighLindhal et al. [60]SwedenAprilCross-SectionalNA108446.0"NANANAModerateLidstrom et al. [61]SwedenAprilCross-SectionalNA108446.0"NANANAModerateLidstrom et al. [62]USAAprilCross-SectionalNA200NANANAHighMarstour et al. [63]USAMarch-AprilCross SectionalNA226NANA82.2ModerateMoscola et al. [65]USAMarch-AprilCross SectionalNA40.32942.0"73.745.5HighMartin et al. [66]SpainAprilCross SectionalImmunochromatographic Assay49841.571.1NAHighPictori et al. [68]SwetenApril-AprilCross SectionalNA472641.168.320.8LowPictori et al. [69]ItalyApril-AprilCross SectionalNA472641.168.469.73.8LowPictori et al. [61]UKApril-MayCross Sectional <td>Ko et al. [55]</td> <td>Korea</td> <td>February</td> <td>Cross Sectional</td> <td>ELISA</td> <td>309</td> <td>31.1</td> <td>84.5</td> <td>NA</td> <td>Low</td>	Ko et al. [55]	Korea	February	Cross Sectional	ELISA	309	31.1	84.5	NA	Low
Korth etal.SprintCross-SectionalELISASprintSprintCross-SectionalELISASprint <th< td=""><td>Kohler et al. [56]</td><td>Switzerland</td><td>March-April</td><td>Cohort</td><td>Chemiluminescent Microparticle Immunoassay</td><td>1012</td><td>38.3*</td><td>75.2</td><td>20.7</td><td>Low</td></th<>	Kohler et al. [56]	Switzerland	March-April	Cohort	Chemiluminescent Microparticle Immunoassay	1012	38.3*	75.2	20.7	Low
Lackernarie et al. [58]GremanyAprilCross SectionalELISA15138.0"83.4NAHughLahner et al. [69]ItalyMarch-AprilCross-SectionalNA108446.0"NANANAModerateLindah et al. [61]SwedenAprilCross-SectionalNA1005NANANAModerateLindah et al. [62]USAAprilCross SectionalNACross SectionalNANANANAModerateMadsen et al. [63]USAAprilCross SectionalNA270NANANAHighMarch et al. [63]USAMarch-AprilCross SectionalNA28538.445.9NAHighMarch et al. [63]USAMarch-AprilCross SectionalNA266NANANA82.2ModerateMoscola et al. [65]USAMarch-guneCohortNANA40.32942.0"73.745.5HighPletat et al. [67]UKApril-JuneCohortNASectional644041.572.020.2HighPletat et al. [68]WitzerlandAprilCross SectionalNA472641.168.320.8LowPublicklos et al. [70]UKMayCross SectionalNA472641.168.344.8ModerateSchindt et al. [71]UKMayCross SectionalNAMacerate472641.084.644.8<	Korth et al. [57]	Germany	March-April	Cross-Sectional	ELISA	316	NA	NA	NA	High
Lahner et al. [59]ItalyMarch-AprilCross-SectionalNA108446.0°NAS5.1High ModerateLindahl et al. [60]SwedenAprilCross-SectionalNA1005NANANANAModerateMalsour et al. [61]WsdenMay-JuneCross SectionalNA270NANANANAHighMansour et al. [63]USAAprilCross SectionalNA270NANANAHighMarch -JaneCross SectionalNASectionalNA28538.445.9NAHighMarch -JaneCross SectionalNASectionalNA28538.445.9NAHighMarch -JaneCross SectionalNANA326NANANA82.2ModerateMoscola et al. [65]USAMarch-JuneCohortNA40.32942.0°73.745.5HighPaltet et al. [67]UKApril-ICross SectionalImmunochromatographic Assay49841.571.1NAHighPaltet et al. [67]UKMarch-JuneCohortELISA644041.572.020.2HighPoulikakos et al. [70]UKMaryCross SectionalNAMarch-JuneCross-SectionalNA449546.469.73.8LowPoulikakos et al. [71]GreeceApril-MayCross-SectionalImmunochromatographic Assay214644.084.6 <td< td=""><td>Lackermair et al. [58]</td><td>Germany</td><td>April</td><td>Cross Sectional</td><td>ELISA</td><td>151</td><td>38.0*</td><td>83.4</td><td>NA</td><td>High</td></td<>	Lackermair et al. [58]	Germany	April	Cross Sectional	ELISA	151	38.0*	83.4	NA	High
Lindahl et al. [60]SwedenAprilCross-SectionalNANANANAMaMaderateLindstrom et al. [61]SwedenMay-JuneCross-SectionalChemiluminescent Microparticle Immunoasay867942.076.725.6ModerateMadsen et al. [62]USAAprilCross SectionalNANANANAHighMarsne et al. [63]USAMarch-AprilCross SectionalELISA28538.445.9NAHighMartin et al. [64]BelgiumAprilCross SectionalELISA286NANANAHighPollal et al. [66]SpainAprilCross SectionalImmunochromatographic Assay49841.571.1NAHighPallett et al. [67]UKApril-JuneCohortELISA644041.572.020.2HighPiccoli et al. [68]SwitzerlandAprilCross SectionalNA472641.168.320.8LowPolichakos et al. [70]UKMayCross SectionalNACross SectionalNANA82543.271.6NAHighPolichakos et al. [71]UKMayCross SectionalNaCross SectionalNa149546.469.73.8LowRudberg et al. [72]SwedenApril-MayCross SectionalMultinescent Microparticle Immunoassay281NANANAHighSoldky et al. [73]GermanyAprilCross-	Lahner et al. [59]	Italy	March-April	Cross-Sectional	NA	1084	46.0*	NA	55.1	High
Lidstrom et al. [61]SwedenMay-juneCross Sectional Cross SectionalChemiluminescent Microparticle Immunoassay867942.076.725.6ModerateMadsen et al. [62]USAAprilCross SectionalNAAndHighMansour et al. [64]BelgiumAprilCross SectionalRL28588.445.9NAHighMarch-derilCross SectionalNANA326NANA82.2ModerateMoscola et al. [65]USAMarch-lucCross SectionalNA40.32042.075.745.5HighOlalla et al. [66]SpainAprilCross SectionalImmunochromatographic Assay49841.571.1NAHighPleicel et al. [67]UKApril-JuneCohortELSA644041.572.020.2HighPleicel et al. [68]SwitzerlandApril-JuneCohortELSA644041.571.1NAHighPolitikos et al. 701UKMayCross SectionalChemiluminescent Microparticle Immunoassay281543.271.6NAHighPolitikos et al. 701UKMayCross SectionalChemiluminescent Microparticle Immunoassay2815NA80.0NAHighSocket al. 711GreeceApril-MayCross-SectionalImmunochromatographic Assay149546.469.73.8LowSotigue et al. [75]KayCross-SectionalLiteral Flow Immunoassay244	Lindahl et al. [60]	Sweden	April	Cross-Sectional	NA	1005	NA	NA	NA	Moderate
Madsen et al. [62]USAAprilCross SectionalNANAHighMansour et al. [63]USAMarch-AprilCross SectionalEUSA28538.445.9NAHighMartin et al. [64]BelgiumAprilCross SectionalNA326NANANA82.2ModerateMoscola et al. [65]USAMarch-JuneCohortNAAA40.32942.0°73.745.5HighOlala et al. [66]SpainAprilCross-SectionalImmunochromatographic Assay49841.571.1NAHighPictori et al. [67]UKApril-JuneCohortEUSA644041.572.020.2HighPictori et al. [68]SwitzerlandAprilCross SectionalNA472641.168.320.8LowPiebani et al. [69]ItalyFebruary-MayCross-SectionalChemiluminescent Microparticle Immunoassay281NA72.9NAHighPoulikakos et al. [70]UKMayCross-SectionalChemiluminescent Microparticle Immunoassay281NA72.9NAHighSoldy et al. [71]GreeceApril-MayCross-SectionalEUSA385NA80.0NAHighSoldy et al. [74]UKMarch-AprilCross-SectionalEUSA385NA80.0NAHighSoldy et al. [76]BelgiumAprilCross-SectionalLetral Flow Immunoassay20245.0°65.5 </td <td>Lidstrom et al. [61]</td> <td>Sweden</td> <td>Mav-June</td> <td>Cross Sectional</td> <td>Chemiluminescent Microparticle Immunoassay</td> <td>8679</td> <td>42.0</td> <td>76.7</td> <td>25.6</td> <td>Moderate</td>	Lidstrom et al. [61]	Sweden	Mav-June	Cross Sectional	Chemiluminescent Microparticle Immunoassay	8679	42.0	76.7	25.6	Moderate
Mansour et al. [53]USAMarch-AprilCross SectionalELISA28538.445.9NAHighMartin et al. [64]BelgiumAprilCross SectionalNA326NANA82.2ModerateMoscola et al. [65]USAMarch-IuneCohortNA40.32942.0°73.745.5HighOlalla et al. [66]SpainAprilCross SectionalImmunochromatographic Assay49841.571.1NAHighPlettet et al. [67]UKAprilCross SectionalNA472641.168.320.8LowPlebani et al. [69]ItalyFebruary-MayCross SectionalChemiluminescent Microparticle Immunoassay281NA72.9NAHighPosichogiou et al. [71]GreeceApril-MayCross SectionalImmunochromatographic Assay214NA72.9NAHighPosichogiou et al. [71]GreemanyAprilCross SectionalImmunochromatographic Assay214644.084.644.8ModerateSchmidt et al. [73]GermanyAprilCross SectionalLateral Flow Immunoassay20245.0°65.378.2HighStochogi et al. [74]UKMarch-AprilCross SectionalLateral Flow Immunoassay20245.0°65.378.2HighStoche et al. [76]BelgiumAprilCross SectionalLateral Flow Immunoassay20245.0°65.378.2HighStoche et al. [76	Madsen et al. [62]	USA	April	Cross Sectional	NA	270	NA	NA	NA	High
Martin et al. [64]BelgiumAprilCross SectionalNA326NANA82.2ModerateMoscola et al. [65]USAMarch-JuneCohortNA40.32942.0°73.745.5HighJollal et al. [65]SpainAprilCross-SectionalImmunochromatographic Assay49841.571.1NAHighPallett et al. [67]UKApril-JuneCohortELISA644041.572.020.2HighPictoli et al. [68]SwitzerlandAprilCross SectionalChemiluminescent Microparticle Immunoassay828543.271.6NAHighPolikakos et al. [70]UKMayCross-SectionalChemiluminescent Microparticle Immunoassay281NA72.9NAHighPsichogiou et al. [71]GreeceAprilCross-SectionalChemiluminescent Microparticle Immunoassay281NA72.9NAHighSolddy et al. [72]SwedenAprilCross-SectionalImmunochromatographic Assay149546.469.73.8LowSolddy et al. [73]GermanyAprilCross-SectionalLateral Flow Immunoassay244NANANAHighSotogiu et al. [75]ItalyAprilCross-SectionalLateral Flow Immunoassay20245.0°65.378.2HighStock et al. [76]BelgiumAprilCross-SectionalLateral Flow Immunoassay244NANANAHighStock et a	Mansour et al. [63]	USA	March-April	Cross Sectional	ELISA	285	38.4	45.9	NA	High
Moscola et al. [65]USAMarch-JuneCohortNA40,32942.0°73.745.5HighOlalla et al. [66]SpainAprilCross-SectionalImmunochromatographic Assay49841.571.1NAHighPlaltett et al. [67]UKAprilCross-SectionalNA472641.168.320.2HighPliccoli et al. [68]SwitzerlandAprilCross SectionalNA472641.168.320.8LowPlebani et al. [69]I talyFebruary-MayCross SectionalChemiliuminescent Microparticle Immunoassay828543.271.6NAHighPoulikakos et al. [70]UKMayCross-SectionalChemiliuminescent Microparticle Immunoassay281NA72.9NAHighPoulikakos et al. [70]UKMayCross-SectionalChemiliuminescent Microparticle Immunoassay149546.469.73.8LowRudberg et al. [72]SwedenApril-MayCross-SectionalLateral Flow Immunoassay214644.084.644.8ModerateSolodky et al. [74]UKMarch-AprilCross-SectionalLateral Flow Immunoassay20245.0°65.378.2HighSotes et al. [76]BelgiumAprilCross-SectionalLateral Flow Immunoassay20245.0°65.378.2HighStock et al. [77]USAAprilCross-SectionalLateral Flow Immunoassay20245.0°65.5100Hi	Martin et al. [64]	Belgium	April	Cross Sectional	NA	326	NA	NA	82.2	Moderate
Olalla et al. [66]SpainAprilCross-SectionalImmunochromatographic Assay49841.571.1NAHighPallett et al. [67]UKApril-JuneCohortELISA644041.572.020.2HighPiccoli et al. [68]SwitzerlandAprilCross SectionalNA472641.168.320.8LowPlebani et al. [69]ItalyFebruary-MayCross SectionalChemiluminescent Microparticle Immunoassay828543.271.6NAHighPoulikakos et al. [70]UKMayCross-SectionalChemiluminescent Microparticle Immunoassay281NA72.9NAHighPoulikakos et al. [71]GreeceApril-MayCross-SectionalImmunochromatographic Assay149546.646.044.8ModerateSchmidt et al. [73]GermanyAprilCross-SectionalELISA385NA80.0NAHighSoldky et al. [74]UKMarch-AprilCross-SectionalLateral Flow Immunoassay244NANANAHighSoldky et al. [75]ItalyAprilCross-SectionalLateral Flow Immunoassay20245.0°65.378.2HighSteensels et al. [76]BelgiumAprilCross-SectionalLateral Flow Immunoassay244NANANAHighStubblefield et al. [79]USAAprilCross-SectionalELISA9837.650.0NAHighStubblefield et al.	Moscola et al. [65]	USA	March-Iune	Cohort	NA	40.329	42.0*	73.7	45.5	High
Pallett et al. [67]UKApril-JuneCohortELISA644041.572.020.2HighPiccoli et al. [68]SwitzerlandAprilCross SectionalNA472641.168.320.8LowPlebani et al. [69]ItalyFebruary-MayCross SectionalChemiluminescent Microparticle Immunoasay828543.271.6NAHighPoulikakos et al. [70]UKMayCross-SectionalChemiluminescent Microparticle Immunoasay828543.271.6NAHighPoulikakos et al. [71]GreeceApril-MayCross-SectionalChemiluminescent Microparticle Immunoasay281NA72.9NAHighPoulikakos et al. [72]SwedenApril-MayCross-SectionalImmunochromatographic Assay149546.469.73.8LowRudberg et al. [73]GermanyAprilCross-SectionalLateral Flow Immunoassay214644.084.644.8ModerateSoldky et al. [74]UKMarch-AprilCross-SectionalLateral Flow Immunoassay20245.0°65.378.2HighSoldky et al. [75]ItalyAprilCross-SectionalLateral Flow Immunoassay3056NANANAHighStock et al. [76]BelgiumAprilCross SectionalELISA24934.0°65.5100HighStock et al. [79]USAAprilCross SectionalELISA24934.0°65.5100High <tr< td=""><td>Olalla et al. [66]</td><td>Spain</td><td>April</td><td>Cross-Sectional</td><td>Immunochromatographic Assav</td><td>498</td><td>41.5</td><td>71.1</td><td>NA</td><td>High</td></tr<>	Olalla et al. [66]	Spain	April	Cross-Sectional	Immunochromatographic Assav	498	41.5	71.1	NA	High
Piccoli et al. [63]SwitzerlandAprilCross SectionalNA472641.168.320.8LowPlebani et al. [69]ItalyFebruary-MayCross SectionalChemiluminescent Microparticle Immunoassay828543.271.6NAHighPoulikakos et al. [70]UKMayCross SectionalChemiluminescent Microparticle Immunoassay828543.271.6NAHighPoilkakos et al. [71]GreeceApril-MayCross SectionalChemiluminescent Microparticle Immunoassay281NA72.9NAHighPsichogiou et al. [71]GreeceApril-MayCross SectionalImmunochromatographic Assay149546.469.73.8LowRudberg et al. [72]SwedenAprilCross-SectionalELISA385NA80.0NAHighSolodky et al. [74]UKMarch-AprilCross-SectionalLateral Flow Immunoassay20245.0°65.378.2HighSolodky et al. [75]ItalyAprilCross-SectionalLateral Flow Immunoassay3056NANANA35.7ModerateStock et al. [76]BelgiumAprilCross-SectionalELISA9837.650.0NAHighStubblefield et al. [78]USAAprilCross-SectionalELISA244NANANALowSydney et al. [79]USAAprilCross-SectionalELISA9837.650.0NAHighSydney	Pallett et al. [67]	UK	April-Iune	Cohort	ELISA	6440	41.5	72.0	20.2	High
Plebani et al. [69]ItalyFebruary-MayCross SectionalChemiluminescent Microparticle Immunoassay828543.271.6NAHighPoulikakos et al. [70]UKMayCross SectionalChemiluminescent Microparticle Immunoassay281NA72.9NAHighPsichogiou et al. [71]GreeceApril-MayCross SectionalImmunochromatographic Assay149546.469.73.8LowRudberg et al. [72]SwedenApril-MayCross-SectionalImmunochromatographic Assay214644.084.644.8ModerateSchmidt et al. [73]GermanyAprilCross-SectionalELISA385NA80.0NAHighSolodky et al. [74]UKMarch-AprilCross-SectionalLateral Flow Immunoassay20245.0°65.378.2HighSolodky et al. [75]ItalyAprilCross-SectionalLateral Flow Immunoassay3056NANANAMederateStock et al. [77]USAAprilCross SectionalELISA24934.0°65.5100HighStubblefield et al. [78]USAAprilCross SectionalELISA24934.0°65.5100HighSymbolic et al. [79]USAApril-MayCross SectionalChemiluminescent Microparticle Immunoassay1700NANANAMederateSymbolic et al. [79]USAApril-MayCross SectionalChemiluminescent Microparticle Immunoassay1700N	Piccoli et al. [68]	Switzerland	April	Cross Sectional	NA	4726	41.1	68.3	20.8	Low
Poulikakos et al. [70]UKMayCross-SectionalChemiluminescent Microparticle Immunoassay281NA72.9NAHighPsichogiou et al. [71]GreeceApril-MayCross SectionalImmunochromatographic Assay149546.469.73.8LowRudberg et al. [72]SwedenApril-MayCross SectionalMultiplex Assay214644.084.644.8ModerateSchmidt et al. [73]GermanyAprilCross-SectionalELISA385NA80.0NAHighSolodky et al. [74]UKMarch-AprilCross-SectionalLateral Flow Immunoassay244NANANAHighSotgiu et al. [75]ItalyAprilCross-SectionalLateral Flow Immunoassay20245.0°65.378.2HighStock et al. [76]BelgiumAprilCross-SectionalLateral Flow Immunoassay3056NANA35.7ModerateStock et al. [77]USAAprilCross-SectionalELISA9837.650.0NAHighStubblefield et al. [78]USAAprilCross-SectionalELISA24934.0°65.5100HighSydney et al. [79]USAApril-MayCross SectionalChemiluminescent Microparticle Immunoassay1700NANANALowVenugopal et al. [80]JapanApril-MayCross SectionalChemiluminescent Microparticle Immunoassay325NANANALow	Plebani et al. [69]	Italy	February-May	Cross Sectional	Chemiluminescent Microparticle Immunoassay	8285	43.2	71.6	NA	High
Psichogiou et al. [71]GreeceApril-MayCross SectionalImmunochromatographic Assay149546.469.73.8LowRudberg et al. [72]SwedenApril-MayCross-SectionalMultiplex Assay214644.084.644.8ModerateSchmidt et al. [73]GermanyAprilCross-SectionalELISA385NA80.0NAHighSolodky et al. [74]UKMarch-AprilCross-SectionalLateral Flow Immunoassay244NANANAHighSotgiu et al. [75]ItalyAprilCross-SectionalLateral Flow Immunoassay20245.0°65.378.2HighSteensels et al. [76]BelgiumAprilCross-SectionalLateral Flow Immunoassay3056NANA35.7ModerateStock et al. [77]USAAprilCross-SectionalELISA9837.650.0NAHighStubblefield et al. [78]USAAprilCross-SectionalELISA24934.0°65.5100HighSydney et al. [79]USAApril-MayCross SectionalChemiluminescent Microparticle Immunoassay1700NANANALowYungopal et al. [81]ChinaMarchCross SectionalELISA325NANANALowVenugopal et al. [82]USAApril-MayCross SectionalChemiluminescent Microparticle Immunoassay175NANANALowVenugopal et al. [83]G	Poulikakos et al. [70]	UK	Mav	Cross-Sectional	Chemiluminescent Microparticle Immunoassay	281	NA	72.9	NA	High
Rudberg et al. [72]SwedenApril-MayCross-SectionalMultiplex Assay214644.084.644.8ModerateSchmidt et al. [73]GermanyAprilCross-SectionalELISA385NA80.0NAHighSolodky et al. [74]UKMarch-AprilCross-SectionalLateral Flow Immunoassay244NANANAHighSotgiu et al. [75]ItalyAprilCross-SectionalLateral Flow Immunoassay20245.0°65.378.2HighSteensels et al. [76]BelgiumAprilCross-SectionalLateral Flow Immunoassay3056NANANAHighStock et al. [77]USAAprilCross-SectionalELISA9837.650.0NAHighStubblefield et al. [78]USAAprilCross-SectionalELISA24934.0°65.5100HighSydpey et al. [79]USAApril-MayCross SectionalELISA24934.0°65.5100HighSydpey et al. [79]USAApril-MayCross SectionalChemiluminescent Microparticle Immunoassay1700NANANALowVenugopal et al. [81]ChinaMarchCross SectionalELISA325NANANALowVenugopal et al. [82]USAMarch-MayCross SectionalChemiluminescent Microparticle Immunoassay47841.568.813.6HighVacha et al. [84]ChinaMarch-April<	Psichogiou et al. 71	Greece	April-May	Cross Sectional	Immunochromatographic Assay	1495	46.4	69.7	3.8	Low
Schmidt et al. [73]GermanyAprilCross-SectionalELISA385NA80.0NAHighSolodky et al. [74]UKMarch-AprilCross SectionalLateral Flow Immunoassay244NANANAHighSotgiu et al. [75]ItalyAprilCross-SectionalLateral Flow Immunoassay20245.0°65.378.2HighSteensels et al. [76]BelgiumAprilCross-SectionalLateral Flow Immunoassay3056NANA35.7ModerateStock et al. [77]USAAprilCross-SectionalELISA9837.650.0NAHighStubblefield et al. [78]USAAprilCross-SectionalELISA24934.0°65.5100HighSydney et al. [79]USAApril-MayCross SectionalClista24934.0°65.5100HighTakita et al. [80]JapanApril-MayCross SectionalImmunochromatographic Assay175NANANALowTu et al. [81]ChinaMarchCross SectionalELISA325NANANALowVenugopal et al. [82]USAMarch-MayCross SectionalELISA32142.767.9NALowVachoyiannopoulos et al. [83]CreeceApril-MayCross SectionalELISA21142.767.9NALowVachoyiannopoulos et al. [84]ChinaMarch-AprilCross SectionalELISA321<	Rudberg et al. [72]	Sweden	April-May	Cross-Sectional	Multiplex Assav	2146	44.0	84.6	44.8	Moderate
Solodky et al. [74]UKMarch-AprilCross SectionalLateral Flow Immunoassay244NANANAHighSotgiu et al. [75]ItalyAprilCross-SectionalLateral Flow Immunoassay20245.0°65.378.2HighSteensels et al. [76]BelgiumAprilCross-SectionalLateral Flow Immunoassay3056NANA35.7ModerateStock et al. [77]USAAprilCross SectionalELISA9837.650.0NAHighStubblefield et al. [78]USAAprilCross SectionalELISA24934.0°65.5100HighSydney et al. [79]USAApril-MayCross SectionalChemiluminescent Microparticle Immunoassay175NANANAHighSydney et al. [80]JapanApril-MayCross SectionalELISA325NANANALowTu et al. [81]ChinaMarch-MayCross SectionalELISA325NANANALowVenugopal et al. [82]USAMarch-MayCross SectionalELISA325NANANALowVaendet al. [84]ChinaMarch-AprilCross SectionalELISA32142.767.9NALowVaundet al. [84]ChinaMarch-AprilCross SectionalELISA32142.767.9NALowVaundet al. [84]ChinaMarch-AprilCross SectionalChemiluminescent Microparticle Immunoa	Schmidt et al. [73]	Germany	April	Cross-Sectional	ELISA	385	NA	80.0	NA	High
Sotgiu et al. [75]ItalyAprilCross-SectionalLateral Flow Immunoassay20245.0*65.378.2HighSteensels et al. [76]BelgiumAprilCross-SectionalLateral Flow Immunoassay3056NANA35.7ModerateStock et al. [77]USAAprilCross SectionalELISA9837.650.0NAHighStubblefield et al. [78]USAAprilCross SectionalELISA24934.0*65.5100HighSydney et al. [79]USAApril-MayCross SectionalChemiluminescent Microparticle Immunoassay170NANANAHighTakita et al. [80]JapanApril-MayCross SectionalELISA325NANANALowTu et al. [81]ChinaMarchCross SectionalELISA325NANANALowVenugopal et al. [82]USAMarch-MayCross SectionalChemiluminescent Microparticle Immunoassay47841.568.813.6HighVlachoyiannopoulos et al. [83]GreeceApril-MayCross SectionalELISA32142.767.9NALowXu et al. [84]ChinaMarch-AprilCross SectionalNA4384NA73.5NALowVarma et al. [85]SpainApril-MayCross SectionalChemiluminescent Microparticle Immunoassay603843.871.162.7High	Solodky et al. [74]	UK	March-April	Cross Sectional	Lateral Flow Immunoassay	244	NA	NA	NA	High
Steensels et al. [76]BelgiumAprilCross-SectionalLateral Flow Immunoassay3056NANA35.7ModerateStock et al. [77]USAAprilCross SectionalELISA9837.650.0NAHighStubblefield et al. [78]USAAprilCross-SectionalELISA24934.0°65.5100HighSydney et al. [79]USAApril-MayCross SectionalChemiluminescent Microparticle Immunoassay1700NANANAHighTakita et al. [80]JapanApril-MayCross SectionalELISA325NANANALowTu et al. [81]ChinaMarchCross-SectionalELISA325NANANALowVenugopal et al. [82]USAMarch-MayCross SectionalChemiluminescent Microparticle Immunoassay47841.568.813.6HighVlachoyiannopoulos et al. [83]GreeceApril-MayCross SectionalELISA32142.767.9NALowXu et al. [84]ChinaMarch-AprilCross SectionalNA4384NA73.5NALowVarona et al. [85]SpainApril-MayCross SectionalChemiluminescent Microparticle Immunoassay603843.871.162.7High	Sotgiu et al. [75]	Italy	April	Cross-Sectional	Lateral Flow Immunoassav	202	45.0*	65.3	78.2	High
Stock et al. [77]USAAprilCross SectionalELISA9837.650.0NAHighStubblefield et al. [78]USAAprilCross-SectionalELISA24934.0*65.5100HighSydney et al. [79]USAApril-MayCross SectionalChemiluminescent Microparticle Immunoassay1700NANANAHighTakita et al. [80]JapanApril-MayCross SectionalChemiluminescent Microparticle Immunoassay175NANANALowTu et al. [81]ChinaMarchCross-SectionalELISA325NANANALowVenugopal et al. [82]USAMarch-MayCross SectionalChemiluminescent Microparticle Immunoassay47841.568.813.6HighVlachoyiannopoulos et al. [83]GreeceApril-MayCross SectionalELISA32142.767.9NALowXu et al. [84]ChinaMarch-AprilCross SectionalNA4384NA73.5NALowVarona et al. [85]SpainApril-MayCross SectionalChemiluminescent Microparticle Immunoassay603843.871.162.7High	Steensels et al. [76]	Belgium	April	Cross-Sectional	Lateral Flow Immunoassay	3056	NA	NA	35.7	Moderate
Stubblefield et al. [78]USAAprilCross-SectionalELISA24934.0°65.5100HighSydney et al. [79]USAApril-MayCross SectionalChemiluminescent Microparticle Immunoassay1700NANANAHighTakita et al. [80]JapanApril-MayCross SectionalImmunochromatographic Assay175NANANALowTu et al. [81]ChinaMarchCross-SectionalELISA325NANANALowVenugopal et al. [82]USAMarch-MayCross SectionalChemiluminescent Microparticle Immunoassay47841.568.813.6HighVlachoyiannopoulos et al. [83]GreeceApril-MayCross SectionalELISA32142.767.9NALowXu et al. [84]ChinaMarch-AprilCross SectionalNANA4384NA73.5NALowVarona et al. [85]SpainApril-LuneCross SectionalChemiluminescent Microparticle Immunoassay603843.871.162.7High	Stock et al. [77]	USA	April	Cross Sectional	ELISA	98	37.6	50.0	NA	High
Sydney et al. [79]USAApril-MayCross SectionalChemiluminescent Microparticle Immunoassay1700NANANAHighTakita et al. [80]JapanApril-MayCross SectionalImmunochromatographic Assay175NANANANALowTu et al. [81]ChinaMarchCross-SectionalELISA325NANANALowVenugopal et al. [82]USAMarch-MayCross SectionalChemiluminescent Microparticle Immunoassay47841.568.813.6HighVlachoyiannopoulos et al. [83]GreeceApril-MayCross SectionalELISA32142.767.9NALowXu et al. [84]ChinaMarch-AprilCross SectionalNA4384NA73.5NALowVarona et al. [85]SpainApril-luneCross SectionalChemiluminescent Microparticle Immunoassay603843.871.162.7High	Stubblefield et al. [78]	USA	April	Cross-Sectional	ELISA	249	34.0*	65.5	100	High
Takita et al. [80]JapanApril-MayCross SectionalImmunochromatographic Assay175NANANALowTu et al. [81]ChinaMarchCross-SectionalELISA325NANANALowVenugopal et al. [82]USAMarch-MayCross SectionalChemiluminescent Microparticle Immunoassay47841.568.813.6HighVlachoyiannopoulos et al. [83]GreeceApril-MayCross SectionalELISA32142.767.9NALowXu et al. [84]ChinaMarch-AprilCross SectionalNA4384NA73.5NALowVarona et al. [85]SpainApril-luneCross SectionalChemiluminescent Microparticle Immunoassay603843.871.162.7High	Sydney et al. [79]	USA	April-Mav	Cross Sectional	Chemiluminescent Microparticle Immunoassav	1700	NA	NA	NA	High
Tu et al. [81]China MarchMarchCross-Sectional Cross-SectionalELISA325NANANALowVenugopal et al. [82]USAMarch-MayCross SectionalChemiluminescent Microparticle Immunoassay47841.568.813.6HighVlachoyiannopoulos et al. [83]GreeceApril-MayCross SectionalELISA32142.767.9NALowXu et al. [84]ChinaMarch-AprilCross SectionalNA4384NA73.5NALowVarona et al. [85]SpainApril-JuneCross SectionalChemiluminescent Microparticle Immunoassay603843.871.162.7High	Takita et al. [80]	Japan	April-Mav	Cross Sectional	Immunochromatographic Assav	175	NA	NA	NA	Low
Venugopal et al. [82]USAMarch-MayCross SectionalChemiluminescent Microparticle Immunoassay47841.568.813.6HighVlachoyiannopoulos et al. [83]GreeceApril-MayCross SectionalELISA32142.767.9NALowXu et al. [84]ChinaMarch-AprilCross SectionalNA4384NA73.5NALowVarona et al. [85]SpainApril-luneCross SectionalChemiluminescent Microparticle Immunoassay603843.871.162.7High	Tu et al. [81]	China	March	Cross-Sectional	ELISA	325	NA	NA	NA	Low
Vlachoyiannopoulos et al. [83] Greece April-May Cross Sectional ELISA 321 42.7 67.9 NA Low Xu et al. [84] China March-April Cross Sectional NA 4384 NA 73.5 NA Low Varona et al. [85] Spain April-June Cross Sectional Chemiluminescent Microparticle Immunoassay 6038 43.8 71.1 62.7 High	Venugopal et al. [82]	USA	March-Mav	Cross Sectional	Chemiluminescent Microparticle Immunoassav	478	41.5	68.8	13.6	High
Xu et al. [84] China March-April Cross Sectional NA 4384 NA 73.5 NA Low Varona et al. [85] Spain April-June Cross Sectional Chemiluminescent Microparticle Immunoassay 6038 43.8 71.1 62.7 High	Vlachoviannopoulos et al. [83]	Greece	April-May	Cross Sectional	ELISA	321	42.7	67.9	NA	Low
Varona et al [85] Spain April-lune Cross Sectional Chemiluminescent Microparticle Immunoassay 6038 43.8 71 1 62.7 High	Xu et al. [84]	China	March-April	Cross Sectional	NA	4384	NA	73.5	NA	Low
- a span - April jane eros sectional enermanmescent meroparticle minitunoasay 0050 - 75,0 - 71,1 - 02,7 - 11gli	Varona et al. [85]	Spain	April-June	Cross Sectional	Chemiluminescent Microparticle Immunoassav	6038	43.8	71.1	62.7	High

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* Median age.



Fig. 2. Forest plot of the seroprevalence of SARS-CoV-2 IgG antibodies with corresponding 95% confidence intervals.

Summary results of subgroup analysis.						
Subgroup		No of studies	Pooled seroprevalence	95% CI	$I^{2}(\%)$	
Regions	USA	12	0.124	0.078-0.170	99.6	
	Europe	34	0.077	0.063-0.092	99.0	
	East Asia	07	0.048	0.029-0.067	95.5	
Country wise infection level	High	34	0.093	0.073-0.113	99.4	
	Moderate	09	0.095	0.065-0.127	98.8	
	Low	10	0.039	0.024-0.054	97.9	
Gender	Male	25	0.094	0.072-0.116	98.4	
	Female	26	0.078	0.059 - 0.097	99.3	
Mean/Median Age	Less than 40 years	12	0.058	0.042 - 0.074	95.6	
	40 years or more	25	0.087	0.068-0.105	99.1	
Study period	February-April	10	0.057	0.040 - 0.074	97.7	
	April-May*	28	0.082	0.062 - 0.100	99.3	
	May-September	15	0.099	0.069-0.129	99.4	
Work types of HCWs	High risks	18	0.119	0.084-0.154	99.1	
	Low or intermediate risks	15	0.086	0.060-0.112	99.6	
Overall		53	0.086	0.071 - 0.099	99.4	

* Two of the studies were conducted between March-June.

the months between May and September, it further increased to 9.9% (95% CI = 6.9-12.9%; I2 = 99.4%) among the HCWs.

Table 2

It appears from Table 2 that compared to the female participants (7.8%, 95% CI=5.9–9.7%), the pooled prevalence of IgG antibodies was moderately higher among the male HCWs (9.4%, 95% CI=7.2–11.6%). Regional differences in the pooled serological prevalence of SARS-CoV-2 IgG antibodies by gender and age groups is given in Fig. 3. It demonstrates that 12.7% (95% CI=7.12–18.31%) of male and 11.2% (95% CI=5.87–16.67%) of female HCWs in the USA were seropositive. Moreover, in the European zone, 8.6% (95% CI=6.3–10.9%) of male and 6.7% (95% CI=4.8–8.7%) of female HCWs had IgG antibodies. In East Asia, differences in the seroprevalence of HCWs by gender was found negligible.

Based on the work type of the HCWs, the high-risk group was found to have a seroprevalence of 11.9% (95% CI=8.4%–15.4) while intermediate- or low-risk HCWs had 8.6% (95% CI=6%–11.2%). HCWs from high and moderate-risk countries were observed to have a high seroprevalence of IgG antibodies relative to low-risk countries (Table 2).

In the three regions, the study focused on whether the participants' average or median age showed heterogeneous prevalence. In Europe, about 8.5% (95% CI=6.2–10.8%) of HCWs aged 40 years or older were IgG-positive compared to 4.8% (95% CI=1.5–8.0%) of HCWs aged less than 40 years. The difference between the age-groups was greater in East Asia, estimating an 8.53% (95% CI=0.3–24.5%) IgG seroprevalence among older (\geq 40 years of age)



Fig. 3. Regional differences of pooled serological prevalence of SARS-CoV-2 IgG antibodies by gender (top) and age group (bottom).

HCWs, while only 1.6% (95% CI=0.4–2.8%) of the young were infected. In contrast, in the United States, the pooled prevalence of IgG antibodies developed in the young HCWs was 17.7% (95% CI=9.5–26.0%) which was almost double compared to the older group (9.5%, 95% CI=5.1–13.9%). We intended to compare the two age groups (less than 40 years or 40 years and above) and thus, we assumed symmetry in the age distribution of each sample, which allowed us to take the mean and median age simultaneously in the analysis.

3.5. Sensitivity analyses for seroprevalence

We conducted sensitivity analyses that included each of the following types of studies: studies with more than 500 HCWs, regional differences from the studies with more than 500 HCWs, testing conducted with ELISA and pre-print studies. Forest plots are reported in Supplementary File 4. When considering studies of more than 500 participants, the overall seroprevalence among HCWs tends to be 8.02% (95% CI=6.23–9.82%). The seroprevalence was 9.3% (95% CI=5.5–13.2%) considering studies that conducted testing with ELISA. We also found the regional trend of seroprevalence between Europe, the USA, and East Asia was similar to the original studies after including studies that considered at least 500 HCWs. Moreover, we analyzed frequencies to estimate proportions from the 18 pre-print studies. The results from the supplements provide the seroprevalence was 8.0% (95% CI=5.6–10.4%). The findings are, therefore, similar to the meta-analysis of 53 studies.

3.6. Factors associated with SARS-CoV-2 IGG antibodies positivity

We investigated the associated factors for SARS-CoV-2 IgG seropositive status by gender, age-group, country-wise risk and workplace risk of HCWs. Forest plots are given in Supplementary File 5. The overall pooled odds ratio of 25 studies for the association between gender and IgG antibody status was 1.18 (OR=1.18, 95% CI= 1.06–1.31) indicating the odds of catching an infection in male HCWs was higher by 18% than female. In most research, the prevalence of IgG antibodies per age-group was absent. We combined four studies to compare HCWs below the age of 50 and HCWs at the age of 50 and above. The odds between these two age groups were not significantly different (OR=1.09, 95% CI=0.67-1.77, reference: 50 years and over). In addition, we observed that high-risk HCWs were 1.62 times more likely to develop IgG antibodies than low or intermediate-risk HCWs, indicating that high-risk HCWs were 62% more at risk of infection than low or intermediate-risk HCWs (OR=1.62, 95% CI=1.04-2.58).

4. Discussion

This study investigated serum SARS-CoV-2 IgG antibody status of 173,353 HCWs of 14 countries obtained from 53 studies, which could help explain vaccine seroconversion effectiveness. Based on reported antibody findings, we investigated the variations in pooled seroprevalence of Europe, the USA, and East Asia.

Many national and regional studies have performed to estimate the seroprevalence of SARS-CoV-2 IgG antibodies in the general population [19–22]. In a meta-analysis, SARS-CoV-2 seroprevalence ranged from 0.37% to 22.1% for the general population and found a pooled estimate of 3.38% [19]. Another meta-analysis of 338 studies involving 2.3 million individuals from 50 countries found that in the general population, SARS-CoV-2 antibody seroprevalence was as low as 3.2% [20]. Studies reported HCWs to suffer a significant risk from COVID-19, with the most vulnerable population being those employed in hospital environments [23-26]. Our study calculated the pooled seroprevalence of SARS-CoV-2 IgG antibodies among the HCWs 8.6%, which is higher than the general population. Similar meta researches find different seroprevalences in the HCWs, varying from 7% to 11% [15–17].

The differences in the future precautions taken against the virus could be based on the regional variations of seroprevalence of SARS-CoV-2 IgG antibodies. It appears from our analysis that seroprevalence was higher in studies that were conducted in the USA compared to those in Europe and East Asia. The result is consistent with a meta-analysis that found that the proportion of SARS-CoV-2-positive HCWs was about a one-third of all COVID-19 patients of China compared to the USA and a half to Europe [16]. This reflects the strong adherence of HCWs in East Asia to infection prevention and control measures and the appropriate use of personal protective equipment's. The USA also seemed unprepared to cope with the surge in patients that led to a severe shortage of personal protective equipment leading to increased number of cases at the health care centers. [27].

Moreover, our pooled estimates indicate that younger HCWs were infected more compared to older HCWs in the United States. At the

early stage of pandemic, an analysis of cases by the Center for Disease Control and Prevention from the USA revealed that 38% of those who were ill enough to be treated in hospital were younger than 55 [28]. It depicts that the virus might not be taken seriously by younger generations of the USA [29]. The US data also showed a dramatic rise in cases among the under-40 age-group who perceived themselves as less likely to contract a serious case of illness, and such second-wave behavior had let their guard down [30]. In our meta-analysis, the scenario was opposite in the case of Europe and East Asia where the elderly HCWs exhibited a higher prevalence of seropositive IgG antibodies than the USA. All except one (Japan) of the top 30 countries with the highest number of older citizens are from Europe and thus were affected most by the pandemic [31]. This partly explains why higher number of older HCWs developed IgG antibodies compared to younger group in Europe. Further analysis did not indicate a significant association between the age-group association with serum SARS-CoV-2 IgG antibody positivity. However, since we combined only four studies to measure the pooled odds ratio, the relationship between age and infection requires further investigation.

We also found the HCWs who worked in inpatient settings had a high prevalence of IgG antibodies. Studies also found that compared with the low or intermediate risk of HCWs, there was an increased risk of transmission in all health care settings for front-line HCWs [22]. The odds ratio also suggests a significant association between high-risk HCWs and catching infection. This highlights the importance of ensuring the availability of the patient care equipment and other aspects of following hospital safety protocols, including proper application and removal of the PPE. Thus, the likelihood of HCWs contributing to the spread of infections to the community is high, particularly when they are asymptomatic or mildly symptomatic.

Over time, we observed an increase in seroprevalence from about 5% in February-April to about 10% in May-September, which was anticipated for seroconversion in given time. The findings also resonate with the expectation that, relative to low-infection level countries, most antibodies were produced in HCWs from high-risk countries. Community transmission thus played a crucial role in the data on seroprevalence.

It is also evident from our study that male HCWs had higher pooled prevalence of serum IgG antibodies against SARS-CoV-2 than the females. With few exceptions, the gender bias observed in COVID-19 infection is a worldwide phenomenon. Researches published demonstrates similar trend, nevertheless, they also indicate no statistically significant difference in the prevalence of antibodies by gender similar to our analysis when observed closely. [20,29,32] Gender differences have been previously studied in adaptive immune systems and may account for the female advantage in COVID-19 [30]. This explains why such difference in circulating antibodies is not significant, though males were more prone to be infected than females.

In our meta-analysis, high heterogeneity suggests variation in study outcomes between the included studies. The heterogeneity was not fully explained by geographical region, gender, age-group, workplace infection risk, or country-wise infection risk. We speculate that there may be heterogeneity within the population, caused by other variables such as socioeconomic status, lifestyle, culture, and hospital protocol coverage. It could be argued that the high heterogeneity across the included studies could render the estimates of pooled prevalence less useful; however, high heterogeneity may also suggest that there is a large variation in the seroprevalence of preexisting IgG antibodies across geogrphic regions, gender, age groups and country-wise risk level of infection.

In this study, the results are subjected to at least three limitations. First, the heterogeneity was very high across studies. However, to resolve this constraint, we conducted a random-effects model and subgroup analysis. Second, depending on the antibody tests applied, the seroprevalence reported in studies may be under or overestimated. The validity (sensitivity and specificity) of the antibody tests in most of the included studies has not been published. Third, many of the cross-sectional seroprevalence studies included in the metaanalysis aimed to evaluate immunity and were likely to underestimate the previous infection rates because antibodies tend to be detectable for a discrete period after infection.

This study showed an overall small proportion of HCWs from East Asia developed SARS-CoV-2 IgG antibodies. The high seroprevalence of antibodies in the United States suggests that the country has the most substantial evidence of challenges in high-risk countries. Herd immunity theory due to acute exposure to infection is questionable due to the slow progression of seroprevalence worldwide, and vaccination attempts to develop antibodies could be useful. Balanced resource allocation for East Asian, the US, and European countries should be considered to halt disease transmission, especially in male HCWs and increasing age. This outcome may have important implications for prioritizing vaccines' delivery and investigating the time needed by geographical regions for achieving herd immunity. Also, this study with study period evaluation gives us an understanding of the slow progression of long-term immunity against SARS-CoV-2.

Contributors

AH, and SMN contributed to the literature search and study concept and design. AH, SMN, ZN, MKH, and MMH contributed to the data acquisition. AH accessed the data and contributed to the data analysis. AH, SMN and ZN contributed to the data interpretation. AH, MKH and MMH drafted the manuscript. All authors contributed to critical revision to the manuscript.

Data sharing

Because this meta- analysis was based on data extracted from previously published research, most of the data and study materials are available in the public domain. For further discussions, we invite interested parties to contact the corresponding author.

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Declaration of Competing Interest

All other authors declare no competing interests.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eclinm.2021.100770.

Appendix A: Search Strategy

A. PubMed					
#1 ("Seroprevalence" OR "Prevalence" OR "Proportion") AN	ND 81,768				
("Antibody" OR "Antibodies" OR "IgG" OR "IgM"					
OR "Immunoglobulins" OR "Immunoglobulin")					
#2 ("COVID-19" OR "Coronavirus disease"	3377				
OR "Coronavirus" OR					
"SARS-CoV-2")					
AND ("Healthcare workers")					
#3 #1 AND #2	43				
Searching date starting from					
01/01/2020 to 15/01/2021					
All the entries were					
under 'All Fields' category					
B. Google Scholar					
#1	46,000				
	(continued)				

("Seroprevalence" OR				
"Prevalence"				
OR "Proportion")				
AND ("Antibody"				
OR "Antibodies"				
OR "IgG"				
OR "IgM"				
OR "Immunoglobulins"				
OR "Immunoglobulin")				
#2 ("COVID-19" OR "Coronavirus disease"	19,000			
OR "Coronavirus" OR "SARS-CoV-2")				
AND ("Healthcare workers")				
#3 #1 AND #2	30			
Searching date starting from				
01/01/2020 to 15/01/2021				
All the searches were filtered				
to find articles published in 2020 only				
C. ScienceDirect				
#1 ("Seroprevalence" OR "Prevalence")	13,847			
AND ("Antibodies"				
OR "lgG"				
OR "IgM"				
OR "Immunoglobulins")				
#2 ("COVID-19"	2175			
OR "SARS-CoV-2")				
AND ("Healthcare workers")				
#3 #1 AND #2	95			
Searching date starting from				
01/01/2020 to 15/01/2021				
All the searches were				
filtered to find articles with				
study period 2020 only				

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