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Seroprevalence of Antibodies to SARS-CoV-2 in 10 Sites in the United States, March 23-May 12, 2020

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IMPORTANCE Reported cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection likely underestimate the prevalence of infection in affected communities. Large-scale seroprevalence studies provide better estimates of the proportion of the population previously infected.

OBJECTIVE To estimate prevalence of SARS-CoV-2 antibodies in convenience samples from several geographic sites in the US.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional study performed serologic testing on a convenience sample of residual sera obtained from persons of all ages. The serum was collected from March 23 through May 12, 2020, for routine clinical testing by 2 commercial laboratory companies. Sites of collection were San Francisco Bay area, California; Connecticut; south Florida; Louisiana; Minneapolis-St Paul-St Cloud metro area, Minnesota; Missouri; New York City metro area, New York; Philadelphia metro area, Pennsylvania; Utah; and western Washington State.

EXPOSURES Infection with SARS-CoV-2.

MAIN OUTCOMES AND MEASURES The presence of antibodies to SARS-CoV-2 spike protein was estimated using an enzyme-linked immunosorbent assay, and estimates were standardized to the site populations by age and sex. Estimates were adjusted for test performance characteristics (96.0% sensitivity and 99.3% specificity). The number of infections in each site was estimated by extrapolating seroprevalence to site populations; estimated infections were compared with the number of reported coronavirus disease 2019 (COVID-19) cases as of last specimen collection date.

RESULTS Serum samples were tested from 16 025 persons, 8853 (55.2%) of whom were women; 1205 (7.5%) were 18 years or younger and 5845 (36.2%) were 65 years or older. Most specimens from each site had no evidence of antibodies to SARS-CoV-2. Adjusted estimates of the proportion of persons seroreactive to the SARS-CoV-2 spike protein antibodies ranged from 1.0% in the San Francisco Bay area (collected April 23-27) to 6.9% of persons in New York City (collected March 23-April 1). The estimated number of infections ranged from 6 to 24 times the number of reported cases; for 7 sites (Connecticut, Florida, Louisiana, Missouri, New York City metro area, Utah, and western Washington State), an estimated greater than 10 times more SARS-CoV-2 infections occurred than the number of reported cases.

CONCLUSIONS AND RELEVANCE During March to early May 2020, most persons in 10 diverse geographic sites in the US had not been infected with SARS-CoV-2 virus. The estimated number of infections, however, was much greater than the number of reported cases in all sites. The findings may reflect the number of persons who had mild or no illness or who did not seek medical care or undergo testing but who still may have contributed to ongoing virus transmission in the population.

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The first case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in the US was reported in Washington State on January 20, 2020. The first US case linked to community transmission was reported in California on February 26, 2020, followed by subsequent cases resulting from community transmission reported in Washington on February 28 and New York on March 3.[1-5] Since January 2020, states have been recommended to report all laboratory-confirmed cases to the Centers for Disease Control and Prevention (CDC).[6] Reported cases, however, likely represent only a fraction of SARS-CoV-2 infections, as an unknown proportion of cases are mild or asymptomatic, or they are otherwise not diagnosed or ascertained through passive public health reporting.[7-9] Furthermore, viral testing has been limited in many sites and was often reserved for severely ill patients early in the US outbreak, and testing availability has changed rapidly. Each of these issues could confound estimates of incident cases and epidemic dynamics that use only case-based reporting data.

Detection of antibodies to SARS-CoV-2 in a person's blood likely indicates that they were infected at some point since the start of the pandemic. Thus, serologic assays can be used to provide population-based estimates of infection that include people who had mild or asymptomatic infection or who were never tested despite having symptoms.

We used convenience samples of residual clinical specimens obtained from 2 commercial diagnostic laboratories to conduct a serologic survey. Our goal was to estimate the seroprevalence in the population—that is, the proportion of the population with evidence of previous infection with SARS-CoV-2, by age group, in 10 geographically diverse US sites with known community transmission.

Key Points

Question What proportion of persons in 10 US sites had detectable antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from March 23 to May 12, 2020?

Findings In this cross-sectional study of 16 025 residual clinical specimens, estimates of the proportion of persons with detectable SARS-CoV-2 antibodies ranged from 1.0% in the San Francisco Bay area (collected April 23-27) to 6.9% of persons in New York City (collected March 23-April 1). Six to 24 times more infections were estimated per site with seroprevalence than with coronavirus disease 2019 (COVID-19) case report data.

Meaning For most sites, it is likely that greater than 10 times more SARS-CoV-2 infections occurred than the number of reported COVID-19 cases; most persons in each site, however, likely had no detectable SARS-CoV-2 antibodies.

Methods

We obtained convenience samples of deidentified residual patient sera collected for routine screening (eg, cholesterol screening) or clinical management by 2 commercial clinical laboratories (Lab A and Lab B) from 10 sites. For Lab A, data on the breakdown between inpatients and outpatients were not available. For Lab B, almost all the samples were from outpatients. The samples were collected during discrete periods from March 23 through May 12 (**Table 1**; **Figure 1**). Sites and dates of collection included western Washington State (WA) (defined broadly; March 23-April 1); the New York City metro area (NY) (defined broadly; predominantly Manhattan, Bronx, Brooklyn, Queens, and Nassau counties; March 23-April 1); south Florida (FL) (restricted to Miami-Dade, Broward, Palm Beach, and Martin counties; April 6-10); Philadelphia metro statistical area counties and Lancaster and Cumberland counties (PA) (April 13-25); San Francisco Bay area, including San Jose (CA) (April 23-27); Minneapolis-St Paul-St Cloud combined statistical areas (MN) (April 30-May 12); and all of Missouri (MO) (April 20-26), Utah (UT) (April 20-May 3), Connecticut (CT) (April 26-May 3), and Louisiana (LA) (April 1-8) (eFigure 1 in the Supplement). Age or age group, patient sex, and collection date were available for all specimens; we aimed to have at least 300 specimens per age group. Specimens from all sites were deduplicated through laboratory records, except for specimens provided by Lab B from WA and NY. Both laboratories provided specimens from NY and WA; Lab A also provided specimens from CA, FL, and LA, and Lab B provided specimens from CT, MO, PA, MN, and UT. The zip code of patient residence was known for all Lab A specimens and for Lab B specimens from CT, MO, PA, MN, and UT, but not for Lab B specimens from NY and WA. Based on information from Lab B, which indicated that the majority of specimens from its facilities in WA and NY were drawn from the areas of greatest population density in western WA and NY metro areas, respectively, we assumed that Lab B specimens from WA and NY were from a similar geographic distribution to those received from Lab A for those sites. For individual specimens, no information on the reason for specimen collection was available.

After reviewing the protocol, CDC human subjects research officials determined that the testing represented nonresearch activity in the setting of a public health response to the coronavirus disease 2019 (COVID-19) pandemic and exempted it from further review. Informed consent was waived as deidentified data were used. On June 26, 2020, data from 6 sites (CT, FL, MO, NY, UT, and WA) were released on CDC's website,[18] and an early version of the non-peer-reviewed manuscript was posted on a preprint server.[19]

Laboratory Methods

Sera were tested at CDC in a 2-step process—a screening assay followed by a confirmatory assay for presumptive reactive specimens identified through screening. The CDC developed and validated an enzyme-linked immunosorbent assay (ELISA) that was used as the confirmatory assay, as has been previously described.[20] A specimen was considered reactive if, on confirmatory testing, at a background corrected optical density of 0.4 and at a serum dilution of 1:100, it had a signal to threshold ratio greater than 1. The screening assay was similar to the confirmatory assay. Sera were screened at a 1:100 dilution using a qualitative pan immunoglobulin (Ig) ELISA

Table 1. Number of Residual Clinical Specimens From Commercial Laboratories Tested for Antibodies to Severe Acute Respiratory Syndrome Coronavirus 2 in 10 Geographic Sites, by Sex, Age Group, and Location, With Dates of Specimen Collection for Each Site

Characteristic	No. (%)										
	All sites	Western Washington State	New York City metro area (New York)	Louisiana	South Florida	Philadelphia metro area (Pennsylvania)	Missouri	Utah	San Francisco Bay area (California)	Connecticut	Minneapolis-St Paul-St Cloud metro area (Minnesota)
Dates of specimen collection	March 23-May 12, 2020	March 23-April 1, 2020	March 23-April 1, 2020	April 1-8, 2020	April 6-10, 2020	April 13-25, 2020	April 20-26, 2020	April 20-May 3, 2020	April 23-27, 2020	April 26-May 3, 2020	April 30-May 12, 2020
Date of first case of community transmission[a]	NA	February 28, 2020	February 27, 2020	March 9, 2020	March 1, 2020	March 9, 2020	March 13, 2020	March 14, 2020	February 26, 2020	March 11, 2020	March 9, 2020
Sex											
Female	8853 (55.2)	1930 (59.1)	1333 (53.7)	677 (57.2)	964 (55.3)	422 (51.2)	1018 (54.1)	673 (59.5)	653 (53.4)	729 (50.9)	454 (52.8)
Male	7178 (44.8)	1334 (40.9)	1149 (46.3)	507 (42.8)	778 (44.7)	402 (48.8)	864 (45.9)	465 (41.1)	571 (46.7)	702 (49.1)	406 (47.2)
Age group, y											
0-18	1203 (7.5)	219 (6.7)	311 (12.5)	33 (2.8)	69 (4.0)	75 (9.1)	158 (8.4)	25 (2.2)[b]	45 (3.7)	219 (15.3)	49 (5.7)
19-49	5327 (33.2)	1213 (37.2)	909 (36.6)	619 (52.3)	491 (28.2)	193 (23.4)	394 (20.9)	470 (41.5)	371 (30.3)	297 (20.8)	370 (43.0)
50-64	3701 (23.1)	782 (24.0)	455 (18.3)	322 (27.2)	326 (18.7)	221 (26.8)	405 (21.5)	328 (29.0)	323 (26.4)	300 (21.0)	239 (27.8)
≥65	5802 (36.2)	1050 (32.2)	807 (32.5)	212 (17.9)	856 (49.1)	335 (40.7)	925 (49.2)	315 (27.8)	485 (39.6)	615 (43.0)	202 (23.5)
Total[c]	16 025	3264	2482	1184	1742	824	1882	1132	1224	1431	860

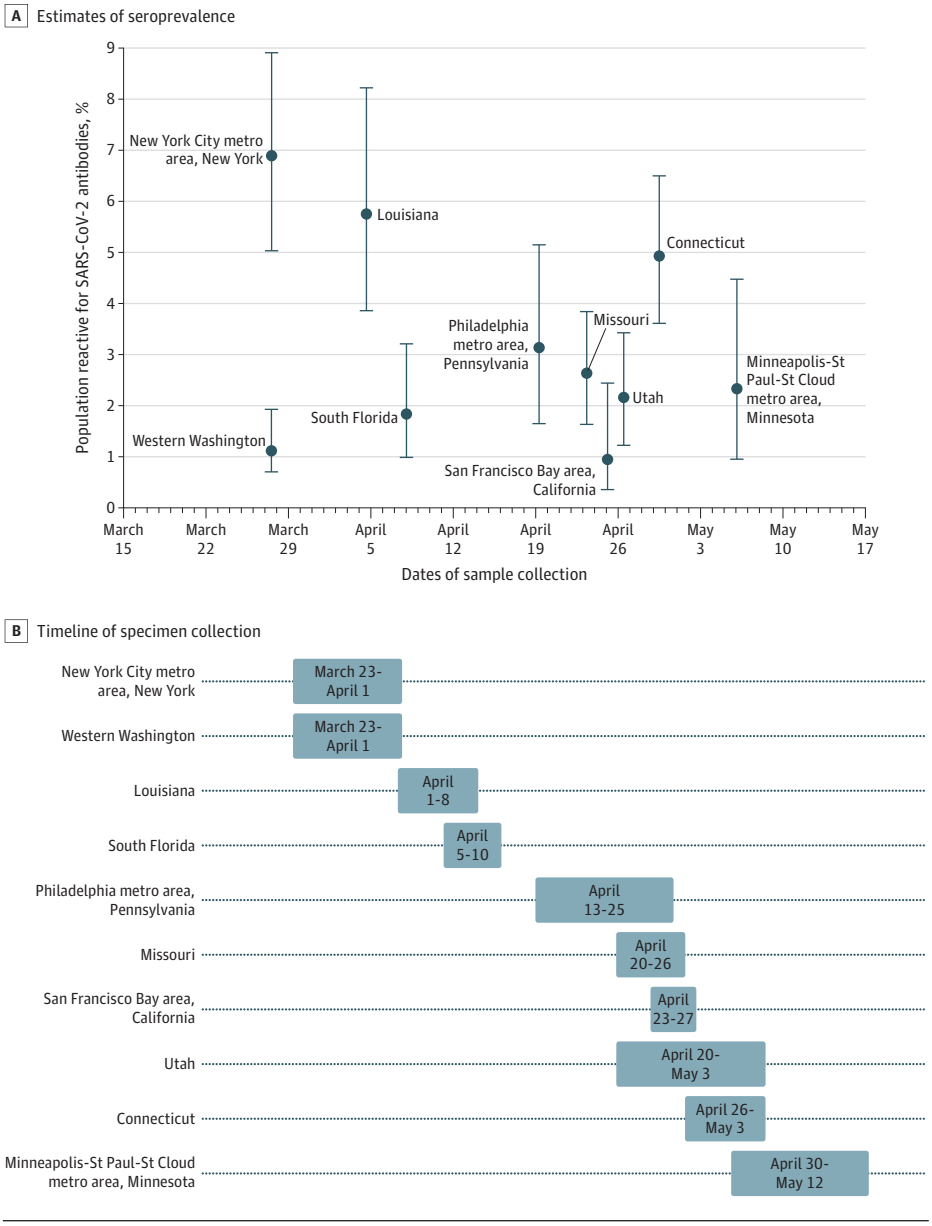
Abbreviation: NA, not applicable.

[a] Sources for dates of community transmission were state and city health departments and Centers for Disease Control and Prevention data.[5,10-17]

[b] Excluded from analysis owing to small sample size.

[c] The total number of specimens that had complete data for both age and sex.

Figure 1. Estimates of Seroprevalence to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Antibodies and Timeline of Specimen Collection



A, Estimates are shown with 95% CIs for 10 geographic sites from which residual clinical specimens were collected. Seroprevalence estimate is shown at the midpoint of the specimen collection date range. B, Timeline with specimen collection dates for each site.

against the prefusion stabilized ectodomain of the SARS-CoV-2 spike protein.[21] However, a greater coating concentration of spike protein was used, only 1 dilution was tested for each serum sample (1:100), and different optical density cutoffs were first used to identify presumptive reactive specimens, which were then referred for confirmatory testing.[20] Using the above definition of reactivity, specificity was 99.3% (95% CI, 98.3%-99.9%) and sensitivity was 96.0% (95% CI, 90.0%-98.9%).[20] Results of testing against sera from polymerase chain reaction–confirmed infections with other coronaviruses indicate that antibodies to commonly circulating human coronaviruses exhibited some cross-reactivity, but the level of cross-reactivity was below the limits of detection for this assay.[20]

Analysis

We calculated seroprevalence as the proportion of specimens that were confirmed reactive, stratified by sex and age group (0 to ≤18 years, 19 to ≤49 years, 50 to ≤64 years, and ≥65 years). We calculated age-standardized and sex-standardized seroprevalence estimates using weights derived from US census county-level population projections for the most sampled counties for CA, FL, MN, NY, PA, and WA, and from US census state-level data for CT, LA, MO, and UT. We estimated 95% CIs by generating 10 000 bootstrapped samples with replacement (eMethods in the Supplement). We conducted additional analyses with bootstrapping to account for assay test performance, using sensitivity and specificity parameters described above. We defined estimates that were age-

standardized and sex-standardized and adjusted for test characteristics as fully adjusted estimates. To assess for potential differences in populations using different laboratories, we compared seroprevalence in specimens from Lab A with those from Lab B for NY and WA, the 2 sites where both laboratories collected specimens.

To estimate the degree of underascertainment of reported cases for all sites, we assumed that the presence of SARS-CoV-2 antibodies represented infections that occurred prior to the last date of specimen collection. We applied the estimated age-adjusted and sex-adjusted seroprevalence estimates to the respective populations to estimate total infections. We then divided these numbers by the cumulative case counts reported to health departments[22] as of the last date of specimen collection for each site. Because antibodies may take an average of 10 to 14 days to be detectable after infection,[23-25] and collection periods were 6 to 14 days in length, we accounted for a lag in the development of antibodies in a scenario analysis using the cumulative number of reported cases as of 7 days prior to the start of specimen collection. The specimen collection period in relationship to reported cases is shown for each site in eFigure 2 in the Supplement, and the number of cases reported daily in the US is shown in eFigure 3 in the Supplement.

R (version 3.6.1) and Rstudio (version 1.2.1335) (R Foundation for Statistical Computing) were used to perform statistical analyses. Two-sided *P* values less than .05 were considered statistically significant.

Results

We tested 16 025 residual sera specimens from 10 sites collected from March 23 through May 12, with discrete collection periods for each site (Table 1). A total of 6320 (39.4%) specimens were from Lab A, and 9705 (60.6%) specimens were from Lab B. Of all specimens, 8853 (55.2%) were from women. The age group of 0-18 years comprised the smallest number of specimens (n = 1205, 7.5%), with the age group of 65 years and older comprising the largest number (n = 5845, 36.5%). Laboratory catchment areas as determined by the number of specimens were predominantly major cities and their metro areas, including some suburban or exurban counties for CA, FL, MN, NY, PA, and WA. Laboratories receiving specimens from the entire state (CT, LA, MO, and UT) received specimens from areas in numbers approximately proportionate to state population density (eFigure 1 in the Supplement).

Table 2 shows the seroprevalence estimates by sex and age as well as fully adjusted estimates. Seroprevalence ranged from 1.0% (95% CI, 0.3%-2.4%) in CA to 6.9% (95% CI, 5.0%-8.9%) in NY. Seroprevalence estimates fell within this range for the remaining 8 sites. There was no clear association between seroprevalence by age and sex across sites (**Figure 2**). In NY, there was a significant difference in fully adjusted seroprevalence between specimens obtained from Lab A (11.5%) and Lab B (5.7%) ($P < .01$). In WA, there was no difference in fully adjusted seroprevalence between specimens obtained from Lab A or Lab B (1.9% vs 1.5%; $P = .47$) (eTable 1 in the Supplement).

Table 3 shows estimates of the number of SARS-CoV-2 infections suggested by seroprevalence estimates in each site and compares these with the number of reported cases as of the last date of specimen collection (eFigure 2 in the Supplement). Our estimate for underascertainment was lowest in CT, where the estimation of 176 012 infections was 6.0 (range, 4.3-7.8) times greater than the 29 287 reported cases as of May 3, 2020, and highest for MO, where the estimation of 161 936 infections was 23.8 (range, 14.8-34.7) times greater than the 6794 reported cases as of April 25, 2020. Estimated numbers of infections for 7 sites—CT, FL, LA, MO, NY, UT, and WA—were at least 10 times greater than the number of reported cases.

Estimates of underascertainment using the date 7 days prior to start of specimen collection are shown in eTable 2 in the Supplement. Using these earlier dates, our point estimate for underascertainment was lowest in CT, where the number of estimated infections was 8.9 times greater than the number of cases reported as of April 19, 2020, and highest in NY, where the estimation of 641 778 infections was more than 1000 times greater than the 545 cases reported as of March 16, 2020. These estimates do not account for delays in reporting results, which may have been longer earlier in the pandemic.

Discussion

Our study estimated seroprevalence of antibodies to SARS-CoV-2 in 10 diverse geographic sites in the US, with discrete collection periods from late March through mid-May 2020. Seroprevalence estimates varied from 1.0% in the San Francisco Bay area in late April to 6.9% in the New York City metro area in late March. Our results for each site suggest that the number of infections was much greater than the number of reported cases throughout the study period; these infections likely include asymptomatic and mild infections for which health care was not sought, as well as symptomatic infections in persons who either did not seek care or in whom SARS-CoV-2 viral testing was not performed. It is possible that false-positive ELISA results could lead us to overestimate seroprevalence and infections. The estimates are the first reported from these 10 sites, from which specimens are to be collected at a variety of time points.[26]

The results of several US seroprevalence studies have been released, including those conducted in Santa Clara County (California), Idaho, Los Angeles (California), and New York.[27-31] As of early July 2020, 3 of these 4 studies had only been posted as preprints without peer review.[27-30] Studies have used different assays and participant selection methods. The Santa Clara County study, conducted April 3 and 4, 2020, approximately 5 weeks after the first case of community transmission of COVID-19 was detected in the San Francisco Bay area, estimated a seroprevalence rate of 2.5% to 4.2%.[27] The authors noted that seroprevalence estimates were largely driven by estimates of test performance characteristics, which is to be expected, particularly in a low-prevalence setting. A study in New York City conducted between late February and mid-April 2020 showed seroprevalence estimates of 2.2% and 10.1% for the weeks ending March 29 and April 5, respectively[30]; the

Table 2. Sex-Specific, Age-Specific, and Age- and Sex-Standardized Seroprevalence Estimates, Adjusted for Assay Performance Characteristics, for Specimens Collected in 10 Geographic Sites[a,b]

Characteristic	Persons reactive, % (95% CI)[a]									
	Western Washington State	New York City metro area (New York)	Louisiana	South Florida	Philadelphia metro area (Pennsylvania)	Missouri	Utah	San Francisco Bay area (California)	Connecticut	Minneapolis-St Paul-St Cloud metro area (Minnesota)
Sex										
Male	1.4 (0.8-2.4)	5.9 (4.5-7.6)	6.8 (4.2-9.3)	2.2 (1.1-3.6)	3.0 (1.3-5.2)	3.1 (1.8-4.6)	2.2 (0.9-3.6)	1.2 (0.4-2.7)	5.7 (3.8-7.6)	0.7 (0-2.3)
Female	1.7 (0.7-1.9)	5.7 (4.2-7.0)	7.0 (4.7-9.4)	2.2 (1.2-3.4)	1.9 (0.7-3.7)	2.6 (1.5-3.7)	2.5 (1.2-4.1)	0.7 (0.2-1.9)	4.1 (2.6-5.9)	2.7 (1.2-4.8)
Age group, y										
0-18	0.7 (0-2.5)[c]	2.7 (0.9-5.0)[c]	2.8 (0-11.5)	2.4 (0-7.8)	2.2 (0-6.9)	1.4 (0-4.1)	NA[d]	1.7 (0-7.7)	0.8 (0-2.9)	5.8 (0-14.3)
19-49	1.3 (0.7-2.3)[c]	8.3 (6.2-10.2)[c]	7.4 (4.7-10.0)	0.9 (0.2-2.2)	5.9 (2.4-9.8)	3.4 (1.4-5.5)	1.8 (0.6-3.5)	1.1 (0-2.6)	6.1 (3.1-9.3)	2.3 (0.8-4.2)
50-64	0.9 (0.3-1.9)	6.5 (4.3-9.6)	8.3 (4.5-11.9)	2.0 (0.3-4.0)	0.8 (0-2.8)	2.0 (0.5-3.8)	2.9 (0.9-5.2)	0.7 (0-2.4)	8.1 (4.8-11.6)	0.7 (0-2.8)
≥65	1.7 (0.9-2.7)	3.7 (2.2-5.2)	4.4 (1.5-8.0)	3.0 (1.7-4.5)	1.6 (0.3-3.5)	3.2 (1.9-4.6)	2.7 (0.9-5.0)	0.9 (0.2-2.5)	4.2 (2.3-6.0)	1.0 (0-3.2)
Overall estimate, age and sex standardized[b]	1.1 (0.7-1.9)[e]	6.9 (5.0-8.9)[e]	5.8 (3.9-8.2)[f]	1.9 (1.0-3.2)[e]	3.2 (1.7-5.2)[e]	2.7 (1.7-3.9)[f]	2.2 (1.2-3.4)[f]	1.0 (0.3-2.4)[e]	4.9 (3.6-6.5)[f]	2.4 (1.0-4.5)[e]

Abbreviation: NA, not available.

[a] A specimen was considered reactive if, on confirmatory testing with the assay described in Freeman et al,[20] at a background corrected optical density of 0.4, at a serum dilution of 1:100, it had a signal to threshold ratio of >1.

[b] All estimates are adjusted for test performance characteristics (specificity, 99.3%; 95% CI, 98.3%-99.9%; sensitivity, 96.0%; 95% CI, 90.0%-98.9%).

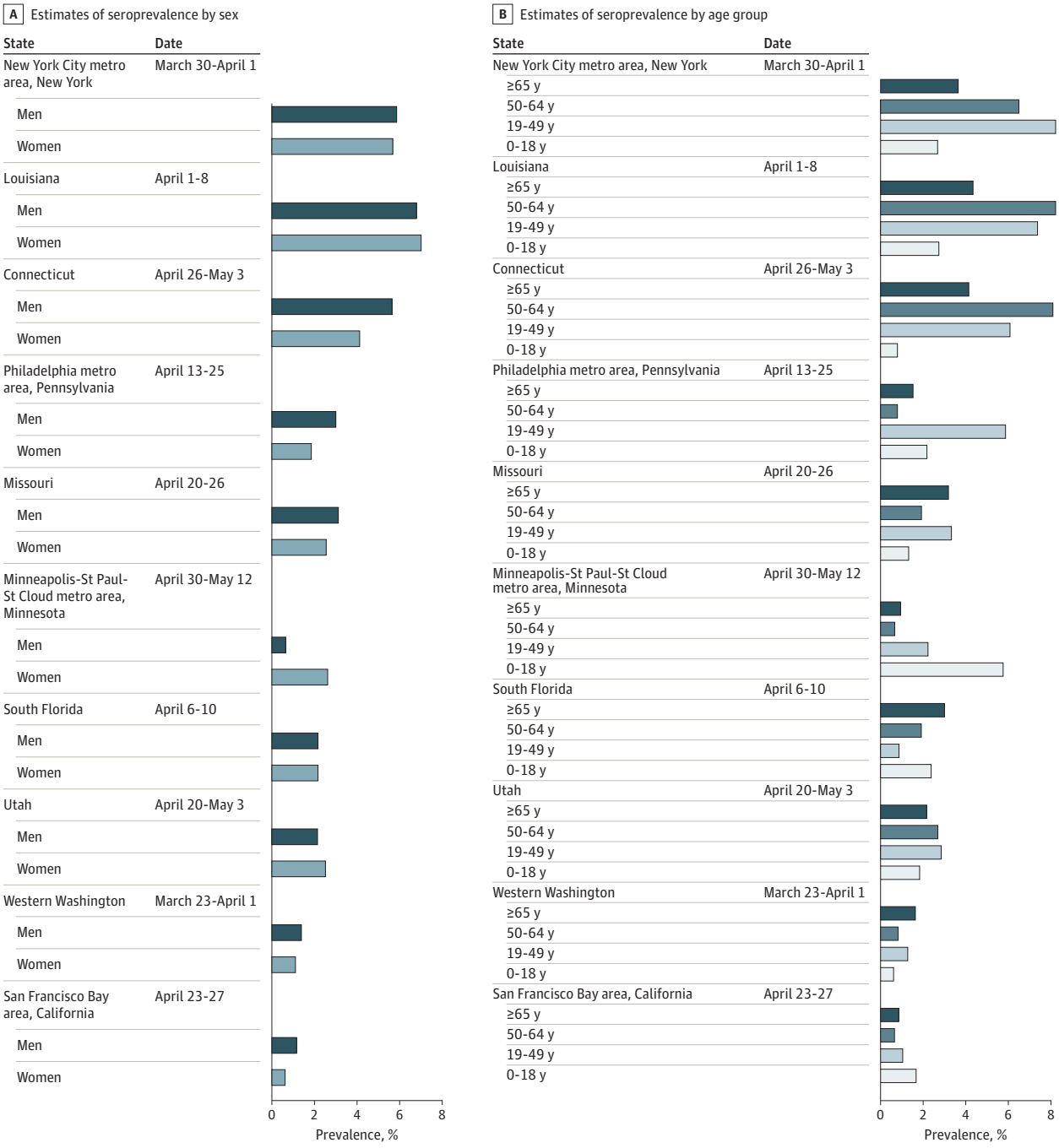
[c] A subset of samples did not have age by year available and were instead classified as age 5-17, 18-49, 50-64, and ≥65 y. The 5-17 and 19-49 y age groups were combined with those aged 5-18 and 19-49 y, respectively.

[d] The number of specimens for persons aged 0-18 y was inadequate, and those aged ≤18 y were excluded from the analysis.

[e] Standardized to the age and sex distribution of the counties in each area from which most specimens originated and adjusted for test performance characteristics as described above.

[f] Standardized to the age and sex distribution of the state and adjusted for test performance characteristics as described above.

Figure 2. Strata-Specific Estimates of Seroprevalence to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Antibodies in 10 Geographic Sites



A, Estimates of seroprevalence to SARS-CoV-2 antibodies by sex, from highest to lowest overall seroprevalence. B, Strata-specific estimates of seroprevalence to SARS-CoV-2 antibodies by age group, from highest to lowest overall seroprevalence.

NY specimen collection period in our study was March 23 to April 1. Another study in New York state used sera collected from April 19 to April 28, approximately 8 weeks after community transmission was first identified in New York City. A seroprevalence of 22.7% was estimated.[31] The higher seroprevalence found in this study compared with our results may reflect a different study population and specimen collection occurring several weeks later, during a period when SARS-CoV-2 was circulating widely in New York City.

At present, the relationship between detectable antibodies to SARS-CoV-2 and protective immunity against future infection is not known.[25] Extrapolating these estimates to make assumptions about population immunity should not be done until more is known about the correlations between the

Table 3. Estimated Number of Infections Based on Seroprevalence Estimates and Comparison With the Number of Reported Cases as of the Last Date of Specimen Collection for 10 Sites

Site	Catchment description	Catchment population, No.	Estimated seroprevalence, % (95% CI)[a]	Cases reported by date of last specimen collection, No.[b,c]	Estimated cumulative infections, No. (95% CI)	Estimated infections/reported cases, No. (range)[d]
Western Washington	King, Snohomish, Pierce, Kitsap, Grays Harbor counties	4 273 548	1.1 (0.7-1.9)	4308	48 291 (29 915-82 907)	11.2 (6.9-19.2)
New York City metro area (New York)	Manhattan, Bronx, Queens, Kings, Nassau counties	9 260 870	6.9 (5.0-8.9)	53 803	641 778 (464 896-826 070)	11.9 (8.6-15.4)
Louisiana	Statewide	4 644 049	5.8 (3.9-8.2)	17 030	267 033 (179 725-382 205)	15.7 (10.6-22.4)
South Florida	Miami-Dade, Broward, Palm Beach, Martin counties	6 345 345	1.9 (1.0-3.2)	10 525	117 389 (63 453-204 955)	11.2 (6.0-19.5)
Philadelphia metro area (Pennsylvania)	Bucks, Chester, Cumberland, Delaware, Lancaster, Montgomery, Philadelphia counties	4 910 139	3.2 (1.7-5.2)	22 987	156 633 (82 981-254 836)	6.8 (3.6-11.1)
Missouri	Statewide	6 110 800	2.7 (1.7-3.9)	6794	161 936 (100 828-235 877)	23.8 (14.8-34.7)
Utah	Adults aged ≥19 y (statewide)	2 173 082	2.2 (1.2-3.4)	4493[e]	47 373 (26 294-74 537)	10.5 (5.5-15.5)
San Francisco Bay area (California)	Alameda, Contra Costa, San Francisco, San Mateo, Marin, Santa Clara counties	6 662 454	1.0 (0.3-2.4)	7151	64 626 (22 652-162 564)	9.0 (3.2-22.7)
Connecticut	Statewide	3 562 989	4.9 (3.6-6.5)	29 287	176 012 (128 624-232 307)	6.0 (4.3-7.8)
Minneapolis-St Paul-St Cloud metro area (Minnesota)	Anoka, Benton, Carver, Chisago, Dakota, Goodhue, Hennepin, Isanti, Le Sueur, McLeod, Mille Lacs, Ramsey, Rice, Scott, Sherburne, Stearns, Steele, Washington, Wright counties	3 857 479	2.4 (1.0-4.5)	8880	90 651 (37 803-173 587)	10.2 (4.3-19.5)

[a] Standardized to the age and sex distribution of the counties in each region from which most specimens originated. All estimates are adjusted for test performance characteristics (specificity, 99.3%; 95% CI, 98.3%-99.9%; sensitivity, 96.0%; 95% CI, CI 90.0%-98.9%).

[b] Information from USA Facts.[22]

[c] Dates of last specimen collection, by site, were western Washington: April 1, 2020; New York City metro area: April 1, 2020; Louisiana: April 8, 2020; south Florida: April 10, 2020; Philadelphia metro area: April 25, 2020; Missouri: April 25, 2020; Utah: May 3, 2020; San Francisco Bay area: April 27, 2020; Connecticut: May 3, 2020; Minneapolis-St. Paul-St. Cloud metro area: May 12, 2020.

[d] Estimated number of times greater for infections suggested by seroprevalence estimates compared with reported cases. Range derived from 95% CIs of seroprevalence estimates.

[e] The number of specimens for persons aged 0-18 y was inadequate, and those aged <18 y were excluded from the analysis. Estimates are for adults aged ≥19 y. Case report data were not available by age in all cases and were estimated by publicly reported age grouping.

presence, titer, and duration of antibodies and protection against this novel, emerging disease.

The timing of the development of SARS-CoV-2–specific antibodies is variable; it is unknown when infection occurred for individuals in this study. Although humoral response kinetics to SARS-CoV-2 infection are not well understood, reactive IgA, IgM, and IgG antibodies have been detected as soon as 1 day after symptom onset.[32] In other studies, neutralizing antibodies were detected 10 to 15 days after symptom onset; the median time to development of total antibody, IgM, and IgG has been estimated as 11, 12, and 14 days, respectively.[23,25]

We compared the number of estimated cases in the population based on our seroprevalence estimates with the reported cases as of the last day of specimen collection. From this comparison, we estimated that there were from 6 times as many SARS-CoV-2 infections as reported cases in CT to 24 times the number of infections as reported cases in MO. Specimen collection in CT started later than other sites, and lower underascertainment estimates for CT may reflect increasing availability of testing as the pandemic progressed. These estimates of underascertainment are conservative; they would be higher if an earlier date had been used to take into account infected persons who had not yet developed detectable antibodies at the time of specimen collection. Our seroprevalence estimates are more likely to reflect infections that occurred a minimum of 1 to 2 weeks prior to the specimen collection.

Limitations

Our study has limitations that are associated with both the samples and with the tests used. The specimens were collected for clinical purposes from persons seeking health care and were shared with the CDC with minimal accompanying data. No data on recent symptomatic illness, underlying conditions, or possible COVID-19 exposures were available. It is possible that specimens were drawn from patients seeking care for suspected COVID-19 symptoms, potentially biasing results, particularly in settings such as NY where disease incidence was higher. Lab B sampled sera from metabolic panels taken at routine outpatient visits; Lab A sampled randomly with respect to clinical test type and admission status. Residual clinical specimens from screening or routine care are more likely to come from persons who require monitoring for chronic medical conditions despite the ongoing pandemic. These persons may not be representative of the general population, including in their health care seeking and social distancing behavior, immune response to infection, and disease exposure risk. Representativeness may vary by age group as well. Therefore, our seroprevalence estimates should be confirmed and extended by other studies, including serosurveys that use targeted sampling frames to enroll more representative populations.[33] For Lab B samples from NY and WA, it is possible that more than 1 specimen was from the same individual, as samples were not deduplicated. Given the large numbers of specimens from each site and that the potential for duplication should be unbiased with respect to SARS-CoV-2 infection, the influence on seroprevalence estimates is likely minimal. In addition, although the overall sample size was large, in some sites, there were few specimens from persons 18 years or younger, which limited our ability to estimate seroprevalence among children. Furthermore, at this stage in the pandemic, infections may not be evenly distributed even within these geographic sites. Thus, seroprevalence estimates for large geographic sites may not be accurate if the majority of samples come from specific areas with higher infection rates. We also had limited geographic data on a subset of specimens from Lab B for NY and WA, which may have been drawn from a larger geographic site than those from Lab A with zip code–level data. The inclusion of some specimens from other sites in WA and NY states, especially sites of lower seroprevalence around NY, may lead to inaccurate seroprevalence estimates for these areas and may explain the differences in the seroprevalence estimates between Lab A and Lab B for NY. Finally, the representation of specific geographic pockets may not be the same between the 2 commercial laboratories, and underlying patient populations may differ between the laboratories; therefore, combining results from Lab A and Lab B is problematic. Follow-up serosurveys will include zip code data for all specimens.

It is possible that the ELISA may exhibit cross-reactivity with antibodies to other common human coronaviruses; therefore, some results may represent a false-positive result for SARS-CoV-2, potentially leading to overestimation of the actual seroprevalence. The assay used has high specificity for SARS-CoV-2, and cross-reactivity with common coronaviruses generated results below the cutoff used for this assay.[20] However, even with a highly specific test, the effect of false-positive test results may be more marked in lower prevalence settings, including CA, FL, and WA. We did consider the performance characteristics of the ELISA when making seroprevalence estimates. Although the assay has high sensitivity (96%), it is not 100% sensitive and thus will not detect all persons with antibodies. Finally, several early reports indicate that not all persons with SARS-CoV-2 infection mount an antibody response, and antibody titers may be lower in those with milder disease; furthermore, levels of IgG and neutralizing antibodies decrease in some persons within 2 to 3 months after infection.[25,33-35] For these reasons, seroprevalence estimates may underestimate the proportion of persons with prior infection in any population.

Tracking population seroprevalence for SARS-CoV-2 infection serially, in a variety of specific geographic sites, should inform models of transmission dynamics and policy decisions regarding the effects of social distancing and other preventive measures. To inform understanding of the epidemiology of COVID-19, the CDC plans to conduct repeated sampling in these and other geographic sites around the US on an ongoing basis.[26]

Conclusions

In conclusion, the seroprevalence estimates we report suggest that at the time of specimen collection from March to early May 2020, a large majority of persons in 10 diverse geo-

graphic sites in the US had not been infected with SARS-CoV-2. The estimated number of infections, however, was much greater than the number of reported cases in all sites. This finding may reflect persons who had mild or no illness or who did not seek medical care or undergo testing but who still may have contributed to ongoing virus transmission in the population. Because persons often do not know if they are infected with SARS-CoV-2, the public should continue to take steps to help prevent the spread of COVID-19, such as wearing cloth face coverings when outside the home, remaining 6 feet apart from other people, washing hands frequently, and staying home when sick.

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