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Assessment of SARS-CoV-2 Seroprevalence by Community Survey and Residual Specimens, Denver, Colorado, July–August 2020

Kiersten J. Kugeler, PhD, MPH[1]; Laura J. Podewils, PhD[2]; Nisha B. Alden, MPH[3]; Tori L. Burket, MS[2]; Breanna Kawasaki, MPH[3]; Brad J. Biggerstaff, PhD[1]; Holly M. Biggs, MD[1]; Rachael Zacks, MD[1]; Monique A. Foster, MD, MPH[1]; Travis Lim, DrPH[1]; Emily McDonald, MD[1]; Jacqueline E. Tate, PhD[1]; Rachel K. Herlihy, MD, MPH[3]; Jan Drobeniuc, MD, PhD[1]; and Margaret M. Cortese, MD[1]; the Denver Community Seroprevalence Assessment Team

Abstract

Objectives: The number of SARS-CoV-2 infections is underestimated in surveillance data. Various approaches to assess the seroprevalence of antibodies to SARS-CoV-2 have different resource requirements and generalizability. We estimated the seroprevalence of antibodies to SARS-CoV-2 in Denver County, Colorado, via a cluster-sampled community survey.

Methods: We estimated the overall seroprevalence of antibodies to SARS-CoV-2 via a community seroprevalence survey in Denver County in July 2020, described patterns associated with seroprevalence, and compared results with cumulative COVID-19 incidence as reported to the health department during the same period. In addition, we compared seroprevalence as assessed with a temporally and geographically concordant convenience sample of residual clinical specimens from a commercial laboratory.

Results: Based on 404 specimens collected through the community survey, 8.0% (95% CI, 3.9%-15.7%) of Denver County residents had antibodies to SARS-CoV-2, an infection rate of about 7 times that of the 1.1% cumulative reported COVID-19 incidence during this period. The estimated infection-to-reported case ratio was highest among children (34.7; 95% CI, 11.1-91.2) and males (10.8; 95% CI, 5.7-19.3). Seroprevalence was highest among males of Black race or Hispanic ethnicity and was associated with previous COVID-19–compatible illness, a previous positive SARS-CoV-2 test result, and close contact with someone who had confirmed SARS-CoV-2 infection. Testing of 1598 residual clinical specimens yielded a seroprevalence of 6.8% (95% CI, 5.0%-9.2%); the difference between the 2 estimates was 1.2 percentage points (95% CI, −3.6 to 12.2 percentage points).

Conclusions: Testing residual clinical specimens provided a similar seroprevalence estimate yet yielded limited insight into the local epidemiology of COVID-19 and might be less representative of the source population than a cluster-sampled community survey. Awareness of the limitations of various sampling strategies is necessary when interpreting findings from seroprevalence assessments.

Keywords

SARS-CoV-2, seroprevalence, antibodies, COVID-19

Understanding the epidemiology of COVID-19 and trajectory of the COVID-19 pandemic depends on knowledge of the SARS-CoV-2 infection rate in the population.[1] Reported case data in the United States underestimate the SARS-CoV-2 infection rate because (1) a substantial proportion of infections are asymptomatic or sufficiently mild such that

Corresponding Author:
Margaret M. Cortese, MD, Centers for Disease Control and Prevention, COVID-19 Response Team, 1600 Clifton Rd NE, MS H24-5, Atlanta, GA 30333, USA.
Email: mcortese@cdc.gov

health care is not sought, (2) access to testing has varied, and (3) barriers to care and testing exist in some populations.[1-3] Assessments of the SARS-CoV-2 seroprevalence using various methods are necessary to understand the extent of transmission and the degree to which reported case numbers underestimate the number of infections and to inform prevention strategies.[1,4]

Different sampling approaches for assessing seroprevalence are associated with varying cost and representativeness; knowledge of the context of each assessment is required for correct interpretation of findings.[5] Sampling strategies that use randomization, such as cluster sampling, yield results that are most representative of the source population yet require substantial time and resources.[4,5] In contrast, seroprevalence assessments based on residual routine clinical sera offer ease of assessment on a broad scale yet may not be representative of their source populations.[1,4-7]

Building on a pilot community serosurvey implemented in Atlanta, Georgia, in May 2020,[8] we conducted a community serosurvey in Denver, Colorado, during late July 2020. This project aimed to estimate the seroprevalence of antibodies to SARS-CoV-2 among Denver residents, describe patterns associated with seropositivity, and compare the estimated SARS-CoV-2 infection rate with the cumulative reported COVID-19 incidence. In addition, we compared findings based on a different sampling strategy, a convenience sample of residual clinical specimens.

Methods

Community Serosurvey

We implemented a 2-stage cluster-sampled community seroprevalence survey using the Centers for Disease Control and Prevention's (CDC's) Community Assessment for Public Health Response framework.[9] Among 8054 census blocks in the City and County of Denver with occupied households in the 2010 US Census, we randomly selected 35 census blocks, or "clusters," with probability proportional to household number.[10] In the field, survey teams selected 7 households per census block by approaching every nth house, where n equals the number of households divided by 7. We excluded institutional settings such as long-term care and correctional facilities.

During July 22–August 8, 2020, survey teams approached selected households to describe the project and request participation. In addition to fluent Spanish-speaking team members, a telephone language line was available if preferred communication was in a language other than English or Spanish. If no one answered the door, survey teams left letters with project and contact information. Household replacement with the adjacent household in the predefined direction of selection occurred for households unable to be contacted after 3 visits and those that declined to participate. Upon encountering inaccessible multiunit buildings, teams approached residents who were entering or departing the complex.

For a household to be enrolled, ≥1 household member had to agree to provide a blood specimen for SARS-CoV-2 antibody testing. We defined a household member as someone who spent an average of ≥2 nights per week in the home. Participants (or parents/guardians of those aged <18 y) provided written consent. A verbal questionnaire queried demographic characteristics; number and details of illness episodes since January 15, 2020; previous SARS-CoV-2 real-time reverse transcription–polymerase chain reaction (RT-PCR) testing and results (antigen testing was not in use at the time); and close contact with people who had received a positive test result by RT-PCR.

Trained personnel collected blood at the home of each participant. Specimens were stored at ambient temperature overnight; the following morning, separated plasma was frozen at −20 °C. Specimens were batch-shipped to CDC Atlanta on dry ice. A CDC laboratory certified under the Clinical Laboratory Improvement Amendments of 1988 tested plasma specimens for antibodies using the Ortho-Clinical VITROS anti–SARS-CoV-2 total antibody assay. Assay performance characteristics assessed at CDC included sensitivity (93.2%) and specificity (99.0%).[8] Individual results were mailed to participants.

Commercial Laboratory Residual Sera

We obtained an age-stratified convenience sample of deidentified residual sera collected for routine clinical care (eg, cholesterol testing) of Denver-area residents during the dates of the community survey from a commercial laboratory. We sought at least 300 specimens from each age group (<18, 18-49, 50-64, and ≥65 y); specimens were deduplicated and almost all were from outpatients. We prioritized specimens from Denver County residents for selection and, once exhausted, incorporated specimens from residents of counties bordering Denver County. Data on age, sex, and residential zip code accompanied the specimens; data on race and ethnicity were unavailable. The same laboratory tested the specimens using the assay described previously.

Analysis

We adjusted initial survey weights reflecting household selection probabilities by raking calibration to more closely align the demographic characteristics of participants with the sex, age, and racial and ethnic composition of the population according to 2019 estimated county population distributions.[11-13] We compared demographic characteristics

[1]COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, GA, USA
[2]Denver Public Health, Denver, CO, USA
[3]Colorado Department of Public Health and Environment, Denver, CO, USA

of participants postweighting with the demographic characteristics of Denver County residents using the F-test for goodness-of-fit.[14] We weighted residual clinical specimens similarly (with only sex and age) using census data from 5 Denver-area counties. We calculated Denver County–specific SARS-CoV-2 seroprevalence to provide direct comparison with community survey findings. We implemented jackknife variance estimation and used 95% Wilson (score) CIs. Unweighted frequencies and weighted proportions are presented unless otherwise stated; we calculated differences in SARS-CoV-2 seroprevalence with 95% CIs to compare seroprevalence among subgroups. We compared SARS-CoV-2 seroprevalence estimates from the 2 sampling strategies by calculating the difference in proportion for 2 independent samples and 95% CIs around that difference.[15] We estimated SARS-CoV-2 infection-to-reported COVID-19 case ratios in Denver by dividing the estimated seroprevalence and 95% CIs by the cumulative reported SARS-CoV-2 incidence as of July 22, 2020, as provided by public health officials. These reported case data were captured through public health surveillance processes according to standardized case definitions.[16,17] We categorized survey responses according to past reported illnesses that met criteria of the Council of State and Territorial Epidemiologists (CSTE) surveillance case definition.[17] We conducted analyses using SAS version 9.4 (SAS Institute, Inc) and Stata version 13 (StataCorp). CDC and the Colorado Department of Public Health and Environment reviewed and considered this activity to be nonresearch public health surveillance; conduct was consistent with applicable federal law and CDC policy.

Table 1. Demographic characteristics of participants in a survey on community seroprevalence of SARS-CoV-2 antibodies and 2019 population estimates, Denver County, Colorado, July–August 2020

Characteristic	No. (%) of participants (N = 404)	Denver County residents (n = 727 211)[a]	*P* value[b]
Age group, y			<.001
0-17	21 (5.2)	138 625 (19.1)	
18-49	267 (66.1)	392 985 (54.0)	
50-64	69 (17.1)	108 766 (15.0)	
≥65	47 (11.6)	86 835 (11.9)	
Gender			.20
Male	189 (46.8)	364 478 (50.1)	
Female	214 (53.0)	362 733 (49.9)	
Other (nonbinary)	1 (0.2)	NA	
Race and ethnicity			<.001
Non-Hispanic White	301 (74.5)	399 284 (54.9)	
Non-Hispanic Black	12 (3.0)	64 632 (8.9)	
Hispanic	65 (16.1)	212 984 (29.3)	
Non-Hispanic Asian/ Pacific Islander, American Indian/ Alaska Native	16 (4.0)	33 056 (4.5)	
Multiple races/ unknown	10 (2.5)	17 255 (2.4)	

Abbreviation: NA, not available.
[a]2019 US Census Bureau population estimates from 2 data sources: single-year age data used to obtain population estimates for single-year age groups[13] and race and ethnicity data including multiple races.[14] All values are number (percentage).
[b]Using the F-test for goodness-of-fit of participants according to household selection probability.[15] $P < .05$ indicates significant differences.

Results

Community Serosurvey

We approached 476 households in 35 census blocks for participation in the community seroprevalence survey, of which 251 (53%) were enrolled. Of the 225 approached households that were not enrolled, 137 (61%) declined, 62 (28%) did not respond, 18 (8%) were vacant or residents were away, 4 (2%) initially expressed interest but did not respond to follow-up visits, 3 (1%) agreed to participate but blood specimens could not be obtained, and 1 (<1%) had a hearing disability that precluded effective communication.

The median participating household size was 2 people (range, 1-7). We obtained blood specimens from 404 participants (range, 1-7 participants per household). Compared with the county population, community survey participants were more frequently adults aged ≥18 and non-Hispanic White (Table 1).

Seroprevalence Estimates Overall and by Demographic Characteristics

Twenty-three of 404 survey participants had detectable anti–SARS-CoV-2 antibodies (weighted seroprevalence: 8.0% [95% CI, 3.9%-15.7%]; Table 2). The 23 seropositive people resided in 16 households located in 13 census blocks; we estimated that 6.4% (95% CI, 3.8%-10.6%) of Denver households had ≥1 seropositive person. Household size among households with ≥1 seropositive person was similar (mean, 2.6 [95% CI, 1.8-3.3] people) to households with no seropositive people (mean, 2.1 [95% CI, 1.8-2.3] people).

SARS-CoV-2 seroprevalence point estimates were higher among the younger age groups compared with the older age groups; none of the 47 enrolled adults aged ≥65 had detectable antibodies. The mean age was 28 (95% CI, 14-42) among people with detectable antibodies and 38 (95% CI, 34-42) among seronegative people. Seroprevalence among adults aged ≥18 (6.8%; 95% CI, 3.7%-12.1%) did not differ significantly from seroprevalence among people aged <18 years (13.1%; 95% CI, 4.2%-34.4%; difference in seroprevalence: 6.3 percentage points; 95% CI, −8.2 to 21.0 percentage points).

Seroprevalence was higher among males than among females (difference in seroprevalence: 8.8 percentage points; 95% CI, 0.5-16.9 percentage points). Seroprevalence was

Table 2. Weighted SARS-CoV-2 seroprevalence estimates overall and by demographic characteristics, as assessed by a community survey of SARS-CoV-2 seroprevalence, and cumulative laboratory-confirmed COVID-19 cases reported through surveillance, Denver County, Colorado, July–August 2020[a]

	Community seroprevalence survey			Cumulative COVID-19 cases reported through surveillance[b]		
Characteristic	Participants with SARS-CoV-2 antibodies, no. (%)	Participants without SARS-CoV-2 antibodies, no. (%)	Estimated seroprevalence, % (95% CI)	No. of cases	Incidence proportion, %[b]	Estimated infection-to-reported case ratio[c]
Total	23 (100.0)	381 (100.0)	8.0 (3.9-15.7)	8142	1.1	7.1 (3.5-14.0)
Gender						
Male	13 (77.2)	176 (47.4)	12.4 (6.5-22.2)	4185	1.1	10.8 (5.7-19.3)
Female	10 (22.8)	204 (52.2)	3.6 (1.8-7.1)	3957	1.1	3.3 (1.7-6.5)
Other (nonbinary)	0	1 (0.4)	—			—
Age group, y						
0-17	2 (31.5)	19 (18.0)	13.1 (4.2-34.4)	473	0.4	34.7 (11.1-91.2)
18-49	18 (56.7)	249 (53.8)	8.4 (4.3-15.7)	4733	1.2	7.0 (3.6-13.0)
50-64	3 (11.8)	66 (15.2)	6.3 (1.8-19.9)	1689	1.5	4.1 (1.2-12.9)
≥65	0	47 (13.0)	0 (0-7.6)	1207	1.4	—
Race and ethnicity						
Non-Hispanic White	11 (23.0)	290 (57.7)	3.3 (1.8-6.0)	2137	0.5	6.2 (3.4-11.2)
Non-Hispanic Black	2 (14.6)	10 (8.4)	13.1 (1.5-60.6)	660	1.0	12.8 (1.5-59.3)
Hispanic	9 (60.2)	56 (26.6)	16.4 (6.5-35.6)	3808	1.8	9.2 (3.6-19.9)
Non-Hispanic Asian/Pacific Islander, American Indian/ Alaska Native	1 (2.2)	15 (4.8)	3.8 (0.3-37.1)	330	1.0	3.8 (0.3-37.2)
Multiple races/ unknown[d]	0	10 (2.6)	0 (0-27.8)	114	0.7	—

[a]Survey respondent data weighted by selection probability and then calibrated by raking to more closely align with the demographic characteristics of the 2019 population distribution of Denver County.

[b]Cumulative laboratory-confirmed COVID-19 cases reported to Denver Public Health as of July 22, 2020, the first day of enrollment in the community survey. Incidence proportion = (cumulative reported case counts/2019 estimated population) × 100, rounded. Denominator population overall and per subgroup according to 2019 census population estimates.[13,14]

[c]Seroprevalence point estimate divided by cumulative reported incidence; range obtained by dividing upper and lower 95% CIs of seroprevalence estimate by cumulative reported incidence.

[d]Multiple/other includes "unknown" race; surveillance data reflect only participants of multiple-race or other race categories and exclude 1093 cases reported with unknown race and ethnicity.

substantially higher among males of other race or Hispanic ethnicity (24.7%; 95% CI, 10.0%-49.4%) than among non-Hispanic White males (1.9%; 95% CI, 0.6%-5.7%), non-Hispanic White females (4.7% 95% CI, 2.4%-9.2%), and females of other race or Hispanic ethnicity (2.2%; 95% CI, 0.5%-10.4%). The difference in these seroprevalence estimates was significant when comparing males of other races or Hispanic ethnicity with (1) non-Hispanic White males (difference in seroprevalence: 22.8 percentage points; 95% CI, 0.7-44.7 percentage points) and (2) females of other races or Hispanic ethnicity (difference in seroprevalence: 22.5 percentage points; 95% CI, 1.9-43.0 percentage points).

As of July 22, 2020, a total of 8142 cases meeting the confirmed surveillance case definition occurred among Denver County residents, a cumulative incidence proportion of 1.1% (Table 2). The estimated SARS-CoV-2 infection rate was 7.1 (95% CI, 3.5-14.0) times the reported COVID-19 incidence, with higher point estimates for rate differences among males and children than among other groups.

Illnesses, SARS-CoV-2 RT-PCR Testing, and Other Characteristics

Overall, seroprevalence estimates were higher among people with (1) previous illness compatible with COVID-19, (2) a previous positive test result for SARS-CoV-2 by RT-PCR, (3) previous compatible illness and an isolation recommendation without RT-PCR testing, and (4) close contact with a confirmed COVID-19 case, compared with people without these characteristics (Tables 3 and 4).

Table 3. Clinical, exposure, occupational, and residential characteristics overall and by SARS-CoV-2 antibody status, as assessed through a community survey of SARS-CoV-2 seroprevalence, Denver County, Colorado, July–August 2020[a]

Characteristic	Overall frequency of characteristic as weighted % (95% CI)	Participants with SARS-CoV-2 antibodies (n = 23)		Participants without SARS-CoV-2 antibodies (n = 381)	
		No.	Weighted % (95% CI)	No.	Weighted % (95% CI)
Acute illness[b]					
CSTE clinical criteria	18.6 (14.5-23.6)	13	53.3 (33.8-71.8)	70	15.6 (11.0-21.7)
Fever, cough, or loss of smell or taste	15.1 (11.4-19.8)	13	53.3 (33.8-71.8)	54	11.8 (8.0-17.1)
Any loss of smell or taste	3.6 (2.0-6.3)	5	20.7 (6.8-48.5)	9	2.4 (1.2-4.7)
Acute illness and tested	6.1 (3.8-9.5)	6	28.5 (13.1-51.3)	21	4.1 (2.4-7.1)
Compatible illness (CSTE COVID-19 clinical), not tested but asked to isolate	2.1 (0.9-4.8)	6	23.0 (7.9-50.1)	2	0.3 (0.1-1.6)
RT-PCR testing					
Ever tested by RT-PCR	19.4 (12.6-28.5)	8	46.3 (20.4-74.4)	68	17.0 (10.4-26.8)
RT-PCR positive	1.2 (0.4-3.5)	5	12.8 (3.6-36.9)	1	0.2 (0-1.4)
RT-PCR positive when ill	1.0 (0.3-3.3)	5	12.8 (3.6-36.9)	0	—
Exposure history[c]					
Close contact: RT-PCR–positive person	9.1 (5.0-15.8)	10	61.3 (33.1-83.5)	23	4.5 (2.8-7.3)
RT-PCR–positive person: household member/partner	3.2 (1.0-9.7)	4	48.1 (19.3-78.2)	1	0.2 (0-1.4)
RT-PCR–positive person: other	6.2 (3.9-9.8)	6	39.7 (17.7-66.9)	22	4.4 (2.7-7.0)
Occupational characteristics[d]					
Worked outside the home	70.4 (62.8-77.1)	15	64.4 (33.0-87.0)	266	70.9 (63.4-77.3)
Worked or volunteered in health care setting	10.6 (6.9-15.9)	2	5.9 (1.2-24.3)	46	11.0 (7.1-16.5)
Residential setting					
Currently living in single-family home	43.8 (27.9-61.1)	5	28.4 (7.5-66.0)	152	45.1 (28.3-63.2)

Abbreviations: CSTE, Council of State and Territorial Epidemiologists; RT-PCR, reverse transcription–polymerase chain reaction.
[a]Survey respondent data weighted by selection probability and then calibrated by raking to more closely align with the demographic characteristics of the 2019 population distribution of Denver County. Weighted percentages are overall and among the total of those with each antibody status.[12,13]
[b]First 3 categories refer to illnesses with onset on March 1, 2020, or later; others reflect illness onset on January 15, 2020, or later. Excludes 4 illnesses with non–COVID-19 diagnosis (eg, myocardial infarction). CSTE clinical criteria reflect an illness meeting the clinical criteria of CSTE COVID-19 surveillance case definition[17]: (1) any 1 of the following: cough, shortness of breath, difficulty breathing, new olfactory disorder, new taste disorder (note: only loss of smell or taste was used in the survey) or (2) at least 2 of fever (measured or subjective), chills, rigors, myalgia, headache, sore throat, nausea or vomiting, diarrhea, fatigue, congestion/runny nose. Any loss of smell or taste includes data only from people aged ≥14 years.
[c]Close contact with RT-PCR–positive person and the 2 exclusive subsets: questionnaire queried close contact with someone who received a positive test result while that contact was ill (first 10 days of illness) or around the time the testing was performed (2 days before to 10 days after swab). For health care workers, any patient contact lacking 6 feet of separation was considered close contact. For all others, close contact was defined as within 6 feet for 15 minutes or more or direct physical contact.
[d]Occupational and volunteer history reflects adults only.

Based on extrapolation from weighted survey findings, an estimated 19% of Denver residents experienced an illness meeting the clinical criteria of the CSTE COVID-19 surveillance case definition with onset on March 1, 2020, or later; 53.3% of people with detectable antibodies experienced such an illness, as did 15.6% of people without antibodies (Table 3). When the disease onset period was expanded to January 15, 2020, the same proportion (53.3%) of people with antibodies experienced a compatible illness during the time frame but so did 30.9% of people without antibodies. An estimated 3.6% of people aged ≥14 years experienced loss of smell or taste since March 2020; 20.7% of people with antibodies had experienced loss of smell or taste, but only 2.4% of people without antibodies had had this symptom. These values changed minimally when onset was expanded to January 15, 2020, or later. Three respondents reported non–COVID-19–related hospitalizations.

An estimated 19.4% of Denver residents received an RT-PCR test for SARS-CoV-2 at some point before the survey; 6.1% were tested because of acute illness and 14.3% were tested while asymptomatic. An estimated 1.2% of residents received a positive test result for SARS-CoV-2 by RT-PCR; 12.8% of people with antibodies received such a test result, but only 0.2% of people without antibodies had received this test result (Table 3).

Table 4. Seroprevalence estimates among people with or without the characteristic and difference in seroprevalence, as assessed through a community survey of SARS-CoV-2 seroprevalence, Denver County, Colorado, July–August 2020

Characteristic	Seroprevalence among those with characteristic, % (95% CI)	Seroprevalence among those without characteristic, % (95% CI)	Percentage-point difference in seroprevalence (95% CI)
Acute illness[a]			
CSTE clinical criteria	22.9 (10.2-43.8)	4.6 (2.0-10.3)	18.3 (1.8 to 34.8)
Fever, cough, or loss of smell or taste	28.2 (12.8-51.2)	4.4 (1.9-10.0)	23.8 (4.0 to 43.6)
Any loss of smell or taste	36.4 (13.9-67.1)	5.2 (2.7-9.9)	31.3 (−4.5 to 67.0)
Acute illness and tested	37.5 (13.0-70.1)	6.1 (3.1-11.4)	31.4 (−4.1 to 67.0)
Compatible illness (CSTE COVID-19 clinical), not tested but asked to isolate	86.4 (51.8-97.4)	6.3 (2.7-14.2)	80.1 (54.0 to 100.0)
RT-PCR testing			
Ever tested by RT-PCR	19.0 (6.1-46.0)	5.3 (2.6-10.5)	13.7 (−7.1 to 34.6)
RT-PCR positive	85.1 (45.2-97.5)	7.1 (3.3-14.6)	78.0 (39.2 to 100.0)
RT-PCR positive when ill	100.0	7.0 (3.2-14.5)	93.0 (87.5 to 98.4)
Exposure history[b]			
Close contact: RT-PCR–positive person	53.9 (25.4-80.1)	3.4 (1.8-6.3)	50.5 (16.6 to 84.4)
RT-PCR–positive person: household member/partner	94.1 (50.3-99.6)	3.4 (1.8-6.3)	90.7 (73.2 to 100.0)
RT-PCR–positive person: other	33.6 (13.8-61.7)	3.4 (1.8-6.3)	30.2 (1.6 to 58.9)
Occupational characteristics[c]			
Worked outside the home	6.2 (3.5-10.8)	8.1 (2.6-22.8)	−1.9 (−11.5 to 7.7)
Worked or volunteered in health care setting	3.8 (1.0-13.4)	7.1 (3.7-13.1)	−3.3 (−10.4 to 3.7)
Residential setting			
Currently living in single-family home	5.2 (1.3-18.9)	10.2 (5.1-19.3)	−5.0 (−14.9 to 4.9)

Abbreviations: CSTE, Council of State and Territorial Epidemiologists; RT-PCR, reverse transcription–polymerase chain reaction.
[a]First 3 categories refer to illnesses with onset on March 1, 2020, or later; others reflect illness onset on January 15, 2020, or later. Excludes 4 illnesses with non–COVID-19 diagnosis (eg, myocardial infarction). CSTE clinical criteria reflect an illness meeting the clinical criteria of CSTE COVID-19 surveillance case definition[17]: (1) any 1 of the following: cough, shortness of breath, difficulty breathing, new olfactory disorder, new taste disorder (note: only loss of smell or taste was used in the survey) or (2) at least 2 of the following: fever (measured or subjective), chills, rigors, myalgia, headache, sore throat, nausea or vomiting, diarrhea, fatigue, or congestion/runny nose. Any loss of smell or taste includes data only from people aged ≥14 years.
[b]Close contact with RT-PCR–positive person and the 2 exclusive subsets: questionnaire queried close contact with someone who received a positive test result while that contact was ill (first 10 days of illness) or around the time the testing was performed (2 days before to 10 days after swab). For health care workers, any patient contact lacking 6 feet of separation was considered close contact. For all others, close contact was defined as within 6 feet for 15 minutes or more or direct physical contact.
[c]Occupational and volunteer history reflects adults only.

Overall, we estimated that 2.1% of residents experienced an illness with clinical manifestations consistent with the surveillance case definition, were not tested by RT-PCR, but were advised to isolate by health care or public health personnel; this occurred among 23.0% of people with detectable antibodies and 0.3% of people without detectable antibodies (Table 3). In total, 9.1% of residents reported close contact with someone who had SARS-CoV-2 infection; this was reported by 61.3% of people with detectable antibodies and 4.5% of people without detectable antibodies. Among people whose close contact was with a household member or partner, 94.1% had detectable antibodies; among people with a close contact outside the household, 33.6% had detectable antibodies (Table 4).

Commercial Laboratory Residual Sera

Of 1598 residual clinical sera tested from the Denver area, 462 (28.9%) were from residents of Denver County, 1102 (68.9%) were from 4 contiguous counties, and the remaining 34 (2.1%) were from other nearby counties. Specimens were from 66 people aged <18 years (unweighted 4.1%), 515 adults aged 18-49 (unweighted 32.2%), 442 adults aged 50-64 (unweighted 27.7%), and 575 adults aged ≥65 (unweighted 36.0%). The median patient age was 58 (range, 2-98); most participants (57.9%) were female. The overall weighted seroprevalence was 6.8% (95% CI, 5.0%-9.2%); the estimated seroprevalence with only Denver County specimens was 6.5% (95% CI, 3.5%-11.9%). The mean age among people with detectable antibodies was 30 (95% CI, 34-36) and among those without detectable antibodies was 39 (95% CI, 38-41). The seroprevalence estimate among adults aged ≥65 was 1.9% (95% CI, 1.1%-3.4%). Seropositivity was similar between the sexes (males: 7.4% [95% CI, 4.7%-11.3%]; females: 6.2% [95% CI, 4.0%-9.5%]; difference in seroprevalence: 1.1 percentage point [95% CI, −3.0 to 5.4 percentage points]). The overall estimate did not differ significantly from that of the community

seroprevalence survey (difference in seroprevalences: 1.2 percentage points; 95% CI, −3.6 to 12.2 percentage points).

Discussion

Using a community serosurvey, we estimated that 8% of Denver residents had antibodies to SARS-CoV-2 by late July 2020, an infection rate approximately 7 times that of the reported cumulative COVID-19 incidence at that time. This local seroprevalence estimate is comparable with other seroprevalence estimates of <10% during this period across the United States.[1,6] Similarly, the SARS-CoV-2 infection-to-reported COVID-19 case ratio supports findings from a modeling effort conducted independently of SARS-CoV-2 seroprevalence data that estimated 7.7 times more SARS-CoV-2 infections among the US population than identified and cumulatively reported through September 2020.[18] Denver County is included in the Coronavirus Disease 2019 (COVID-19)–Associated Hospitalization Surveillance Network (COVID-NET) surveillance system, which monitors population-based rates of COVID-19–related hospitalization and death; our findings provide additional data that inform an understanding of the dynamics of SARS-CoV-2 at the population level.[19] Testing residual clinical specimens yielded a weighted seroprevalence comparable with the community survey and is a reasonable approach to obtaining a single seroprevalence estimate.[20] However, the community survey additionally provided information on demographic, clinical, and exposure factors associated with seroprevalence often unavailable through testing of residual clinical specimens and provided additional insight into the local epidemiology of SARS-CoV-2.

Elevated survey-based seroprevalence estimates among Hispanic or non-Hispanic Black people compared with non-Hispanic White people are consistent with other US data indicating higher COVID-19 incidence among racial and ethnic minority populations.[21] In Denver, Hispanic people have a disproportionately high incidence of COVID-19 cases, hospitalizations, and deaths.[16] In this survey, males who were Hispanic or of other race had a higher SARS-CoV-2 seroprevalence than females of the same race and ethnicity and non-Hispanic White males. This finding highlights the potential for complex interactions among sex, race, ethnicity, and the risk of SARS-CoV-2 infection. SARS-CoV-2 seroprevalence estimates from both the community survey and the commercial specimens tended to be higher among younger age groups than among older age groups, as noted elsewhere.[6,22] This finding could reflect better adherence to recommended prevention behaviors among older age groups living in noncongregate settings than among other subgroups of the population.[23]

Survey findings indicated that 1% of Denver County residents had received a positive RT-PCR test result for SARS-CoV-2 at some point before the survey. Despite the nature of self-report, this figure was similar to the 1.1% reported cumulative COVID-19 incidence reported through surveillance at the time of the survey. Our results suggest that children may have a higher SARS-CoV-2 infection-to-reported COVID-19 case ratio compared with other age groups, a finding consistent with reports that children are more likely to have asymptomatic or mild SARS-CoV-2 infections than adults, may be less likely than adults to be tested, and may be underrepresented in case-based surveillance figures.[2,18]

SARS-CoV-2 seropositivity was associated with having a clinically compatible illness since March 2020, previously receiving a positive test result for SARS-CoV-2 by RT-PCR, previous recommendation to isolate without SARS-CoV-2 testing, and close contact with someone with confirmed SARS-CoV-2 infection. Only 13% of seropositive people had previously received a positive RT-PCR test result, but among people who received a positive RT-PCR test result while ill, 100% had detectable antibodies. Close contact with a person with confirmed SARS-CoV-2 infection, and especially a household contact, had the strongest bivariate association with seropositivity. Increased secondary transmission of SARS-CoV-2 among household contacts as compared with other contacts is noted elsewhere.[24-26] Sample size and relatively low seroprevalence limited our ability to reliably discern independent associations with seropositivity in multivariable analyses, but these findings provide focus for future investigation.

We observed that in the Denver area, residual clinical specimens yielded a similar seroprevalence estimate to that of a random community survey. This comparability between a resource-intensive sampling strategy designed to be representative of the source population (community survey) and one far easier to obtain yet subject to obvious selection bias (residual clinical specimens) was also seen in the Atlanta metropolitan area. The evaluation in Atlanta is the only other published evaluation to date that directly compares both approaches using specimens collected during the same weeks and tested using the same assay at the same laboratory.[20] Local population-based assessment, such as with a community survey, provides additional insight into effects of the SARS-CoV-2 pandemic on certain populations on a local scale.[22] Residual clinical specimens lack information on patient race and ethnicity, as well as risk factors that can provide additional insight into local epidemiology of SARS-CoV-2 transmission. Furthermore, screening residual clinical specimens is likely to underrepresent populations with limited health care access and overrepresent older people or people with underlying health conditions, who may have been more likely than younger people to be subject to blood draws amid a pandemic; however, this approach provides a reasonable, rapid, and resource-light insight into the degree of transmission in a community. Various sampling strategies for seroprevalence assessments should be implemented to balance available resources with a desire to draw inference on local SARS-CoV-2 transmission dynamics and disproportionately affected populations.

Limitations

This assessment had several limitations. First, the impact of nonresponse bias on the survey-based seroprevalence estimate is unknown. Second, children and racial and ethnic minority populations were underrepresented in the survey despite the sampling design, although the raking adjustment generated bias-reduced estimates for these populations. Nevertheless, small sample sizes yielded wider CIs around seroprevalence estimates compared with CIs of more well-represented demographic subgroups. Advanced and thoughtful community engagement is likely to improve participation and acceptance of public health activities among racial and ethnic minority groups. Third, the community survey design excluded people who were unhoused or living in congregate settings, settings with demonstrated high SARS-CoV-2 transmission risk; seroprevalence and patterns associated with seropositivity in these settings may differ from the general population. In addition, the community survey was not powered to detect seroprevalence differences among subgroups; as such, those analyses have low precision. The comparison of sampling approaches was not powered to detect small differences in seroprevalence. Lastly, the prevalence and duration of detectable antibodies following asymptomatic SARS-CoV-2 infection may be lower than following symptomatic infection, and the correlation of detectable antibodies with protective immunity is unknown.[27-29] Therefore, seroprevalence assessments may underestimate infection rates, especially among people with asymptomatic infection. In contrast, the potential for false-positive results is higher when a condition is rare in the population and, despite the devastating toll of the pandemic, SARS-CoV-2 appeared to have infected a relatively small proportion of the population at the time of this survey.

Conclusion

We estimated that SARS-CoV-2 infection among Denver residents was 7 times that documented through case surveillance as of late summer 2020. The community survey provided estimates of seroprevalence in a defined geographic area and allowed for exploratory examination into transmission dynamics, including patterns associated with sex, age, and race and ethnicity, but its execution was resource intensive. Various strategies to assess seroprevalence balance representativeness with resource requirements. Implementation of various strategies on different geographic scales will continue to be important to understand transmission dynamics as the pandemic evolves and vaccination is broadly implemented.

Disclaimer

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Authors' Notes

Denver Community Seroprevalence Assessment Team: Olivia Almendares, MSPH; Catherine C. Espinosa, MPH; Erik Foster, MS (COVID-19 Response Team, Centers for Disease Control and Prevention); Thomas W. Gray, MSW, MPH (Denver Public Health); and Jennifer A. Lehman, BS; Grace E. Marx, MD, MPH; David W. McCormick, MD, MPH; Benjamin P. Monroe, MPH; Yoshinori J. Nakazawa, PhD; Amy M. Schwartz, MPH; Sarah W. Sheldon, MS; Shelby L. Ford, BS; Jean Randolph, MPA, RN; and Adam K. Wharton, MS (COVID-19 Response Team, Centers for Disease Control and Prevention).

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ORCID iD

Kiersten J. Kugeler, PhD, MPH https://orcid.org/0000-0002-5702-6688

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