Social vulnerability and rurality associated with higher SARS-CoV-2 infection-induced seroprevalence: a nationwide blood donor study, United States, July 2020 – June 2021

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SUMMARY

This nationwide study demonstrated continuously increasing SARS-CoV-2 seroprevalence in the U.S. across all geographic, demographic, and social sectors, during July 2020 – June 2021. The findings illustrated consistent disparities by race-ethnicity, rurality, and social vulnerability.

ABSTRACT

Background: Most studies on health disparities during COVID-19 pandemic focused on reported cases and deaths, which are influenced by testing availability and access to care. This study aimed to examine SARS-CoV-2 antibody seroprevalence in the U.S. and its associations with race/ethnicity, rurality, and social vulnerability over time.

Methods: This repeated cross-sectional study used data from blood donations in 50 states and Washington, D.C. from July 2020 through June 2021. Donor ZIP codes were matched to counties and linked with Social Vulnerability Index (SVI) and urban-rural classification. SARS-CoV-2 antibody seroprevalences induced by infection and infection-vaccination combined were estimated. Association of infection-induced seropositivity with demographics, rurality, SVI, and its four themes were quantified using multivariate regression models.

Findings: Weighted seroprevalence differed significantly by race/ethnicity and rurality, and increased with increasing social vulnerability. During the study period, infection-induced seroprevalence increased from 1.6% to 27.2% and 3.7% to 20.0% in rural and urban counties, respectively, while rural counties had lower combined infection- and vaccination-induced seroprevalence (80.0% vs. 88.1%) in June 2021. Infection-induced seropositivity was associated with being Hispanic, non-Hispanic Black, and living in rural or higher socially vulnerable counties, after adjusting for demographic and geographic covariates.

Conclusion: The findings demonstrated increasing SARS-CoV-2 seroprevalence in the U.S. across all geographic, demographic, and social sectors. The study illustrated disparities by race-ethnicity, rurality, and social vulnerability. The findings identified areas for targeted vaccination strategies and can inform efforts to reduce inequities and prepare for future outbreaks.

KEYWORDS

SARS-CoV-2, COVID-19, serological survey, seroprevalence, rural, social vulnerability, health equity

INTRODUCTION

Health equity is when all people have the opportunity to attain their full health potential, and no one is disadvantaged from achieving this potential because of social position or other socially determined circumstances. However, members of racial and ethnic minority groups have long experienced health disparities due to inequities in social determinants of health (SDOH), including socioeconomic status (SES) and social and community context [1]. The COVID-19 pandemic has brought longstanding social and racial injustice and health inequity to the forefront of public health. Compared to non-Hispanic Whites, some racial/ethnic minority groups, such as Hispanic and non-Hispanic Black, have experienced disproportionately higher rates of reported COVID-19 case incidence, associated severe illness, and death [2-4]. In addition, rural communities have experienced higher incidence and mortality rates than metropolitan communities beginning in early August 2020 [5].

Although multiple studies have analyzed trends in the race/ethnicity distribution of COVID-19 cases, most have used COVID-19 case data, which do not effectively capture all infections due to a large proportion of mild or asymptomatic cases that are not detected or reported [6]. Additionally, national surveillance data often lacks complete race/ethnicity information. As of July 2021, nearly 40% of reported U.S. COVID-19 cases and 20% of deaths did not have data for race or ethnicity [7].

Serological surveys have been valuable tools used to detect infections of SARS-CoV-2, the virus that causes COVID-19 [8, 9]. Previous serosurveys have observed substantial disparities in SARS-CoV-2 infection prevalence among racial and ethnic minority groups [10-12], yet samples have been limited to special populations or specific geographic areas (e.g., individual cities or states) in the United States [13, 14].

Since July 2020, CDC has been conducting a nationwide seroprevalence study in blood donors [15, 16]. We analyzed data from blood donor specimens collected from July 2020 to June 2021. The objectives were: 1) to study the weighted SARS-CoV-2 seroprevalence in the United States over time by demographics, rurality, and social vulnerability as measured by CDC's Social Vulnerability Index (SVI) [17]; 2) to model the associations between the infection-induced seropositivity and key demographics, rurality, and social vulnerability.

METHOD

Study Design

Antibody seroprevalence data were collected as part of a nationwide blood donor seroprevalence study, described in detail elsewhere [18]. In brief, data collection began in July 2020. Catchment areas from 17 blood collection organizations were combined into 65 study regions defined by state and metropolitan borders, representing 50 states and Washington D.C. Each month, approximately 500–4,000 anonymous blood donation specimens from each study region were selected, after excluding donations made specifically to provide COVID-19 convalescent plasma and samples with missing donor demographic data (2.85% excluded for missing race/ethnicity). Donor demographic information collected by the blood centers included age, gender, race/ethnicity, and residential ZIP code. Blood collection organizations were not able to select specimens from specific racial or ethnic populations. To increase representation from racial and ethnic minorities, sample size was increased for regions with larger racial and ethnic minority populations.

The study was approved by CDC as non-research public health surveillance based on anonymization of data and routine consent for blood donation testing that includes use of residual samples for research purposes. The study does not require human-subject research review nor clearance by the Office of Management and Budget and was conducted consistent with applicable federal law[1] and CDC policy.

[1] 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 2fsi341(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

Serological Testing

SARS-CoV-2 infection results in production of antibodies against the spike protein (anti-S) and the nucleocapsid protein (anti-N). All anonymous blood donation specimens were tested for the anti-S glycoprotein using the Ortho Vitros chemiluminescent S1 Total Immunoglobulin Assay (Vitros CoV2T; Ortho Clinical Diagnostics, Raritan, New Jersey). During July–December 2020, specimens with borderline positivity (signal-to-cutoff ratio S/Co = 1–10) were also tested for anti-N antibody using the Roche Elecsys chemiluminescent Total Immunoglobulin Assay (Elecsys CoV2T; Roche Diagnostics, Basel, Switzerland) to confirm infection. Specimens with high positivity (Vitros CoV2T S/Co >10) were not tested using the Elecsys CoV2T [15]. Validation of the antibody assays have been published previously [19].

COVID-19 vaccination began in the United States after the first COVID-19 vaccine received Emergency Use Authorization on December 14, 2020. Because COVID-19 vaccines lead to the formation of antibodies against SARS-CoV-2 spike protein but not anti-N antibody [20], presence of anti-S antibodies reflects the combined infection- and vaccination-induced seroprevalence. Therefore, beginning in January 2021, all specimens with positive anti-S antibodies were also tested for anti-N antibodies to distinguish infection-induced antibodies from the vaccine-induced antibodies (See Appendix 1 for details).

Conversion from ZIP codes to Counties and Linkage with SVI and Urban-Rural Classification

The blood donor residential locations were described by ZIP codes, while SVI, rurality, and other key information (e.g., case reporting) are defined by census tracts or counties. We applied the U.S. Department of Housing and Urban Development's (HUD) USPS ZIP Code Crosswalk files and established the percentage of residential addresses for each ZIP code located within a census tract [21]. Once a tract was assigned to a donor, the corresponding county was also assigned since census tracts nest completely within individual counties. We then linked the antibody results with county-level overall SVI and four SVI themes (SES, household composition and disability, minority status and language, housing and transportation) [17]. We also applied CDC's 2013 National Center for Health Statistics (NCHS) Urban-Rural Classification scheme to determine rurality (metropolitan/urban vs. nonmetropolitan/rural) [22]

Statistical Analyses

Chi-square test was conducted to examine demographic differences between this study's blood donor population and the general U.S. population. Because blood donor demographic characteristics differ from those of the U.S. population, monthly estimation weights were created based on the 2018 American Community Survey [23] estimates for age, gender, race/ethnicity. Furthermore, monthly sets of 50 pseudo-replicate weights were created to compute weighted seroprevalence standard errors. We conducted descriptive analyses on the demographic characteristics for donors and social vulnerability characteristics for all counties where donors were matched.

Following a repeated cross-section study design, monthly weighted combined (infection- and vaccine-induced) and infection-induced seroprevalences with 95% confidence intervals (95% CI) were calculated for the entire study population, and stratified by age group, sex, race/ethnicity, region, rurality, SVI, and the four SVI themes.

To visualize the spatial-temporal distributions, we mapped the study area by SVI and infection-induced seroprevalence. For the maps, we estimated weighted county-level infection-induced seroprevalences over 3-month periods for counties with more than 10 donors. All maps were generated using Esri's ArcGIS Pro version 2.8.0.

Multivariate logistic regression models were applied to assess the association of infection-induced seropositivity with factors of interest (race/ethnicity, rurality, and social vulnerability), adjusting for all other available covariates that may be related to seropositivity (age, gender, and region). To track trends in associations, the regression models were applied on monthly data to produce monthly odds ratios (ORs) and 95% CIs. The first model used the overall SVI as a measure for social vulnerability. A second model used the four themes of SVI as individual variables in order to identify associations of individual SVI themes and infection-induced seropositivity. All statistical analyses were conducted with R version 4.1.0 using the 'survey' package 4.0[2]. We used the survey design function jackknife (JK1) weighting with 50 replicate weights and the survey weighted generalized linear model function utilizing a quasibinomial distribution.

RESULTS

The number of donor specimens with linked county from 50 U.S. states and Washington D.C. increased from 115,312 in July 2020 to 131,913 in November 2020, and remained at approximately 133,000 per month since then, totaling 1,555,745 specimens during the study period (Supplemental Table S1). Overall, donors were evenly distributed by sex, regions, and social vulnerability, but were primarily 30-64 years of age (67.5%), non-Hispanic White (86.2%), and residents of urban counties (85.4%) (Table 1). Compared with the U.S. population aged 16 years and older, more blood donors were aged 50-64 years or non-Hispanic White, and fewer donors resided in socially vulnerable counties (Table 1).

The study area included 1,990 counties (63.3% of 3,142 counties in 50 states and Washington D.C.) that spanned the spectrum of social vulnerability for the overall SVI (Figure S1), its 4 themes, and 15 social factors (Supplemental Table S2). The median SVI in study counties was 0.44, slightly lower than that of all U.S. counties (0.5). The spatial-temporal distribution of SVI and infection-induced seroprevalence are visualized in seroprevalence (Figure S2) and bivariate seroprevalence-SVI maps (Figure 1). During the study period, seroprevalence increased significantly across all geographic, demographic, and social sectors (Table 2).

Before wide-spread vaccination, monthly weighted seroprevalence in the study increased from 3.5% (95% CI: 3.2%-3.9%) in July 2020 to 11.6% (95% CI: 11.3%-11.9%) in December 2020

[2] Lumley T (2021). Survey: analysis of complex survey samples. The R 'survey' package 4.0 is a freeware library which provides facilities in R for analyzing data from complex survey samples. Available at https://cran.r-project.org/web/packages/survey/index.html

(Figure 2, Table 2). Starting January 2021, largely driven by the country-wide vaccination efforts, the combined seroprevalence increased rapidly, reaching 87.4% in the study population and ranging from 83.1% to 95.3% among age, gender, racial/ethnic, and region groups in June 2021 (Supplemental Table S3). The infection-induced seroprevalence also increased, reaching 20.7% overall in June 2021 (Table 2). There was no significant difference by sex, consistent with other U.S.-based seroprevalence studies [8]. Infection-induced seroprevalence was consistently higher in younger age groups, Hispanic people, and non-Hispanic Black people, although the racial/ethnic differences narrowed over the study period (Figure 3).

Although seroprevalence in rural counties (1.6%, 95% CI: 1.1%-2.0%) was less than half of that in urban counties (3.7%, 95% CI: 3.4%-4.1%) in July 2020, the infection-induced seroprevalence in rural counties increased rapidly and reached 27.2% (95% CI: 26.1%-28.4%) in June 2021, significantly higher than in urban counties (20.0%; 95% CI: 19.6%-20.4%). In contrast, the June 2021 combined vaccine and infection-induced seroprevalence was significantly lower in rural counties (80.0%, 95% CI: 78.9%-81.2%) than in urban counties (88.1%, 95% CI: 87.8%-88.5%), indicating lower vaccine-induced seroprevalence in rural areas (Figure 2). Areas with increasing social vulnerability had increasingly higher infection-induced seroprevalence throughout the study period (Figure 3). Among the four SVI themes (Table 2, Figure S3), SES and household composition/disability exhibited similar trends as for the overall SVI.

Race/ethnicity, rurality, and the overall SVI were significantly associated with infection-induced seropositivity, after controlling for all available demographic and geographic covariates (Figure 4 and Supplemental Table S4). In July 2020, Hispanic and non-Hispanic Black donors had 2.6 (95%CI: 2.1-3.3) and 2.5 (95%CI: 1.8-3.6) times the odds of infection-induced seropositivity, respectively, compared with non-Hispanic Whites; the ORs decreased to 1.7 (95%CI: 1.6-1.8) and 1.3 (95%CI: 1.1-1.4), respectively, in June 2021. Infection-induced seropositivity increased with increasing social vulnerability and the effect size also decreased over time. OR for counties with the highest social vulnerability compared to those with the lowest SVI was 2.2 in July 2020 and gradually reduced to 1.2-1.3 by November 2020 until the end of study period ($p<0.001$ for all 12 months).

Notably, the OR for rural compared with urban counties increased from 0.57 (95%CI: 0.43-0.75) in July 2020 to 1.5 (95%CI: 1.4-1.6) in June 2021. The second model with the four SVI themes as individual variables (Supplemental Table S5) found a consistent association between the SES theme and infection-induced seropositivity (ORs highest vs. lowest: 2.9 [1.9-4.4] in July 2020 to 1.5 [1.3-1.7] in June 2021), which was stronger than the associations between overall SVI and seropositivity in the first model.

DISCUSSION

This study found that rural counties and counties with higher social vulnerability had experienced higher burdens of SARS-CoV-2 infection, but with significantly lower combined infection- and vaccine-induced seroprevalence in June 2021, likely because of differing vaccination rates. After adjusting for all available demographic and geographic factors, higher infection-inducted seropositivity was significantly associated with age, racial/ethnic, rurality, and social vulnerability. Although improving health equity has been an important national goal for decades, health disparities were evident and exacerbated during the COVID-19 pandemic. To reduce health disparities, it is important to understand the social and geographic factors that contribute to differential risk and identify which communities are most in-need of enhanced public health interventions.

The racial and ethnic disparities in infection-induced seropositivity, even after adjusting for all available covariate, were consistent with other studies reporting higher infection rates and case rates among Hispanic and non-Hispanic Black groups [2, 4, 24]. Furthermore, our model highlighted that the racial-ethnic disparities could not be explained entirely by SVI, its themes, and other key factors (age and geographic differences), indicating additional structural factors that drive racial/ethnic differences in infection rates. While the relative importance of social vulnerability and race/ethnicity appeared to decrease over time, consistent with a previous study analyzing case rates [25], disparities persisted. Infection-induced seroprevalence increased substantially, and the observed decrease in relative risks appears to be related to large increases in counties with lowest SVI and largely non-Hispanic White populations, rather than a decrease in incident infections in racial and ethnic minority populations. Focused research and efforts are needed to understand the underlying drivers of health disparities and optimize public health interventions that address environmental, place-based, occupational, policy and systemic factors that impact health outcomes.

The SVI's SES theme incorporates measures of income, unemployment, poverty, and education. We found that individuals living in areas with high levels of socioeconomic vulnerability had higher odds of seropositivity across all months of the study, although, similar to race/ethnicity, the size of this association decreased over time. Part of this shift was likely due to the relative increase in seroprevalence in the Midwest over time, which had the lowest levels of socioeconomic vulnerability in our sample. People with lower income are more likely to take public transportation, work in roles that cannot be performed remotely, and live in densely populated areas or communal housing [26, 27]. Each of these factors may have contributed to the higher levels of infection-induced seropositivity observed in our study. High socioeconomic vulnerability has also been associated with lower levels of COVID-19 vaccination uptake [28], which may further exacerbate disparities from the pandemic. Improving access to and uptake of COVID-19 vaccines among low-income populations are critical to reverse this pattern. Further, policies and practices aimed at reducing poverty levels may reduce the disparate burden of disease during future public health crises.

Since the onset of the pandemic in the United States, rural populations have been at higher risk of developing severe disease due to their disproportionately older age, lack of health insurance, lower SES, and higher risk of chronic diseases and disabilities compared to urban residents [5, 29]. Rural residents have also been less likely to take preventive measures (e.g., COVID-19 vaccine administration and mask-wearing) that would curtail the spread of SARS-CoV-2 [29, 30]. To address this differential risk, numerous efforts had been implemented to increase the availability of COVID-19 testing sites, availability of medical care during onset of severe COVID-19 illness, and availability of vaccine allocation sites in rural areas [29, 30]. Still, our study highlights the rapid increase in infection-induced seroprevalence in rural counties during the study period. Other researchers have found similar evidence based on comparison of reported case incidence and mortality rates in rural vs.

urban areas [5, 31]. Further, this study found that the vaccination-induced seroprevalence in rural counties was lower compared to urban counties, reflective of the reported lower vaccination rates in rural areas [30]. Reducing disparities in COVID-19 vaccination (e.g., measures to reduce vaccine hesitancy) will be vital in reducing the effects of COVID-19 in rural communities.

Our study has several notable strengths. First, this nationwide serological survey with complete race/ethnicity and location information can provide a more thorough assessment of infection rate and distribution of past infections compared with case surveillance data. Second, the study used highly sensitive and specific assays for the serological testing [19], which maximized consistency in antibody testing across time and across geographic regions. Third, we applied two serological tests, one for anti-S antibody and one for anti-N antibody, to track the seropositivity induced by infection and by vaccination. Fourth, the study had a large sample size with over 1.5 million specimens.

However, our study also had several limitations. First, blood donors are usually healthier than the general population. Acutely ill persons, children aged <16 years, and others with exclusionary criteria cannot donate blood; elderly (aged >75 years) and institutionalized persons (from nursing homes, prisons, etc.) are unlikely to donate blood and are therefore under-represented in this study [32]. Racial/ethnic minority groups were also under-represented compared to the U.S. general population [32]. To address this, appropriate weights and standardization were applied to all participants to account for age and race/ethnicity factors as possible. In 2022, CDC is planning to conduct a modified blood donor serosurveillance study that can oversample from racial and ethnic populations. Second, we transformed 29% of the records from ZIP code to county based on probabilities, which was subject to error. Third, the use of aggregated indices on rurality and social vulnerability at community levels reduces the capability of detecting true effects when compared with studies with individual-level data on participants' SES, housing, and related factors. Fourth, waning antibodies can influence prevalence estimates, especially those based on anti-nucleocapsid serologic tests [33]. Lastly, we could not include Puerto Rico and other U.S. territories in this study due to issues with data availability and compatibility. Information and research are needed for territories as they may present unique challenges with regards to health equity.

CONCLUSIONS

This nationwide seroprevalence study demonstrated rapidly increasing seroprevalence in the United States with distinct demographic and regional heterogeneity during July 2020 – June 2021. Evidence of prior SARS-CoV-2 infection was highest among Hispanic and non-Hispanic Black donors. Infection-induced seroprevalence in rural counties increased rapidly and the observed rural-urban difference continued to increase, while the combined infection- and vaccination-induced seroprevalence was lower among blood donors from rural counties as compared to those from urban counties. Counties with high social vulnerability, and low SES particularly, were significantly associated with SARS-CoV-2 infection-induced seroprevalence. The findings illustrate the disparities in SARS-CoV-2 infections in the United States independent of case-based surveillance and testing availability biases, identified areas/populations for targeted vaccination strategies to combat the COVID-19 pandemic, and can inform efforts to reduce inequities and prepare for future outbreaks.

NOTES

AUTHOR CONTRIBUTIONS

ZL developed the study concept, led the study, and drafted the manuscript. JMJ led the blood donor seroprevalence study (parent study) and provided the serological testing data. KB and EH conducted data linkage, cleaning, and preparation of final analysis data file. BL conducted statistical analyses. AMW conducted confirmatory data analyses. EH conducted GIS mapping. JDO provided sample weights and statistical consultation. ZL, JMJ, KB, EH, BL, AMW, LOR, AW and MPB contributed to study design and development. All coauthors contributed to the manuscript preparation, revision, and finalization.

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DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention/Agency for Toxic Substances and Disease Registry. Use of trade names is for identification only and does not imply endorsement by the Centers for Disease Control and Prevention or the U.S. Department of Health and Human Services.

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DECLARATION OF INTERESTS

All coauthors declare no conflict of interests. MPB reports Contract from the Centers for Disease Control and Prevention (CDC Contract 75D30120C08170) for the present study.

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FIGURE LEGENDS

Figure 1. Quarterly infection-induced seroprevalence and CDC's Social Vulnerability Index (SVI) bivariate maps in 1,990 counties in 50 U.S. states and Washington DC, United States, July 2020 – June 2021. Seroprevalence is weighted by demographic characteristics. Classification ranges are based on prevalence rates for counties with >10 donor samples during the study periods. SVI ranges are based on scores for all 1,990 counties in the study area.

Figure 2: Monthly weighted infection-induced seroprevalence and combined seroprevalence from infection and vaccination in U.S. blood donors, July 2020 – June 2021, by rurality level and social vulnerability.

Figure 3: Monthly weighted infection-induced seroprevalence in U.S. blood donors, July 2020 – June 2021, by rurality level, social vulnerability (as measured by CDC's Social Vulnerability Index or SVI), race/ethnicity, age group, sex, and census region . Error bars denote the 95% confidence intervals.

Figure 4. Results of multivariate regression model evaluating association of infection-induced seropositivity with race/ethnicity, sex, age, region, rurality level, and social vulnerability (as measured by CDC's Social Vulnerability Index or SVI). Model was run on monthly data from July 2020 to June 2021 to give a set of odds ratios with 95% confidence intervals (indicated by error bars) for all factors each month.

Table 1. Demographic characteristics of blood donors from 50 states and Washington D.C., U.S., July 2020 - June 2021. U.S. population (aged 16 years and older) are provided as a comparison. Results are presented as numbers (N, in thousands) and unweighted percentage (%).

Characteristics	**Blood donors in this study**		**U.S. Population (aged 16 years and older)**[1]	
	N (in thousands)	Percent[2,3]	N (in thousands)	Percent[2,3]
Total	1,556	100%	257,755	100%
Sex				
Male	764	49.1%	125,699	48.8%
Female	792	50.9%	132,056	51.2%
Age Category				
16-29 years	185	11.9%	62,088	24.1%
30-49 years	481	30.9%	83,380	32.3%
50-64 years	569	36.6%	63,048	24.5%
65+ years	321	20.6%	49,239	19.1%
Race/Ethnicity				
Non-Hispanic White	1,341	86.2%	164,240	63.7%
Non-Hispanic Black	40.4	2.6%	30,976	12%
Hispanic	96.9	6.2%	41,091	15.9%
Asian	46.2	3.0%	14,322	5.6%
Other[4]	31.5	2.0%	7,148	2.8%

U.S. Census Regions				
Northeast	276	17.7%	45,691	17.7%
Midwest	355	22.8%	54,231	21%
South	510	32.8%	97,142	37.7%
West	415	26.7%	60,692	23.5%
Social Vulnerability[5]				
Lowest Vulnerability	363	23.3%	34,282	13.3%
Low Vulnerability	424	27.3%	64,214	24.9%
High Vulnerability	484	31.1%	83,468	32.4%
Highest Vulnerability	284	18.2%	75,760	29.4%
Rurality Level				
Urban	1,328	85.4%	220,611	85.6%
Rural	228	14.6%	37,144	14.4%

1. Blood donors must be aged 16 years in most U.S. states. Data for U.S. Population aged 16 years and older, with the exception of race/ethnicity, are from 2018 American Community Survey 5-year estimates (https://data.census.gov/cedsci/). Race/Ethnicity estimates are from a custom table created from 2018 Public Use Microdata Sample (PUMS) 5-year estimates (https://www.census.gov/programs-surveys/acs/microdata.html).
2. Due to rounding, the sum for some groupings do not equal 100.0%.
3. Chi-square test p-values between this study population and U.S. population are <0.05 for all characteristics.
4. “Other” category includes more than one race, American Indian, and other race/ethnicity.
5. Lowest, low, high, and highest vulnerability defined as the 1st, 2nd, 3rd and 4th quartiles of the social vulnerability index in this study.

Table 2. Weighted infection-induced seroprevalence rates (95% CI, in percent) in blood donors from 50 states and Washington D.C., U.S., July 2020-June 2021, by age, sex, race/ethnicity, census region, rurality level, social vulnerability (as measured by CDC's Social Vulnerability Index or SVI), and the four SVI themes.

Characteristics	Jul-20	Aug-20	Sep-20	Oct-20	Nov-20	Dec-20
Total	3.5 (3.2, 3.8)	4.7 (4.5, 4.9)	4.9 (4.7, 5.1)	5.8 (5.5, 6.1)	7.9 (7.6, 8.2)	11.6 (11.3, 11.9)
Sex						
Female	3.4 (3, 3.8)	4.5 (4.2, 4.8)	4.8 (4.5, 5.1)	5.5 (5.2, 5.8)	7.8 (7.4, 8.2)	11.6 (11.1, 12.1)
Male	3.7 (3.1, 4.3)	4.9 (4.6, 5.2)	5.1 (4.8, 5.4)	6 (5.6, 6.4)	8.1 (7.7, 8.5)	11.6 (11.2, 12)
Age Category						
16-29 years	5.6 (4.7, 6.5)	6.8 (6.1, 7.5)	7.5 (7, 8)	8.9 (8.1, 9.7)	12.4 (11.5, 13.3)	17.1 (16.2, 18)
30-49 years	3.7 (3.3, 4.1)	5.2 (4.8, 5.6)	5.3 (4.9, 5.7)	5.9 (5.5, 6.3)	8.2 (7.7, 8.7)	12.4 (11.9, 12.9)
50-64 years	3 (2.4, 3.6)	3.8 (3.4, 4.2)	4 (3.6, 4.4)	4.8 (4.5, 5.1)	6.5 (6.2, 6.8)	9.5 (9.1, 9.9)
65+ years	1.4 (1, 1.8)	2.5 (2, 3)	2.3 (1.9, 2.7)	2.8 (2.4, 3.2)	3.9 (3.4, 4.4)	6.1 (5.6, 6.6)
Race/Ethnicity						
Non-Hispanic White	2.2 (2, 2.4)	2.8 (2.6, 3)	3.3 (3.2, 3.4)	4.1 (3.9, 4.3)	6.6 (6.4, 6.8)	10.2 (10, 10.4)
Non-Hispanic Black	6.6 (4.4, 8.8)	7.3 (6.2, 8.4)	7.8 (6.6, 9)	9.1 (7.8, 10.4)	10.1 (9, 11.2)	14 (12.1, 15.9)
Hispanic	6.9 (5.8, 8)	10.5 (9.4, 11.6)	9.3 (8.6, 10)	10.8 (9.9, 11.7)	12.9 (12, 13.8)	17.8 (16.4, 19.2)
Asian	3.3 (2.1, 4.5)	4.4 (3.5, 5.3)	4.2 (3.3, 5.1)	3.6 (2.8, 4.4)	4.2 (3.3, 5.1)	6.8 (5.6, 8)
Other[1]	3 (2.1, 3.9)	3.7 (2.7, 4.7)	4.5 (3.5, 5.5)	4.6 (3.7, 5.5)	8.1 (6.8, 9.4)	8.6 (7.1, 10.1)

Census Regions						
Northeast	6.8 (5.4, 8.2)	6.7 (6.1, 7.3)	5.9 (5.3, 6.5)	6.5 (5.9, 7.1)	7.3 (6.6, 8)	10.9 (10, 11.8)
Midwest	2.4 (1.9, 2.9)	2.8 (2.4, 3.2)	3.8 (3.4, 4.2)	5.4 (4.9, 5.9)	9.7 (9.1, 10.3)	16 (15.3, 16.7)
South	3.2 (2.9, 3.5)	5.7 (5.3, 6.1)	6.1 (5.7, 6.5)	6.9 (6.6, 7.2)	9.2 (8.8, 9.6)	12 (11.4, 12.6)
West	1.8 (1.6, 2)	3.2 (2.9, 3.5)	3.2 (2.8, 3.6)	3.8 (3.5, 4.1)	5.4 (5, 5.8)	8.2 (7.7, 8.7)
Rurality Level						
Urban	3.7 (3.3, 4.1)	5 (4.7, 5.3)	5 (4.8, 5.2)	5.8 (5.5, 6.1)	7.6 (7.3, 7.9)	11.1 (10.7, 11.5)
Rural	1.5 (1.1, 1.9)	2.1 (1.7, 2.5)	3.8 (3.4, 4.2)	5.8 (5.3, 6.3)	10.7 (10.1, 11.3)	16.7 (15.8, 17.6)
Social Vulnerability[2]						
Lowest Vulnerability	2.4 (2, 2.8)	2.6 (2.2, 3)	3.3 (2.9, 3.7)	4.2 (3.8, 4.6)	7.3 (6.7, 7.9)	10.8 (10.2, 11.4)
Low Vulnerability	2.4 (2, 2.8)	3 (2.6, 3.4)	3.5 (3.2, 3.8)	4.1 (3.7, 4.5)	6 (5.5, 6.5)	9.8 (9.3, 10.3)
High Vulnerability	4 (3.4, 4.6)	5.8 (5.3, 6.3)	6.1 (5.7, 6.5)	6.9 (6.5, 7.3)	8.4 (7.9, 8.9)	12.7 (12.2, 13.2)
Highest Vulnerability	5.3 (4.1, 6.5)	7 (6.4, 7.6)	6.3 (5.8, 6.8)	7.4 (6.8, 8)	10.1 (9.3, 10.9)	12.9 (12, 13.8)
SVI Theme 1 (Socioeconomic Status) [2]						
Lowest Vulnerability	2.6 (2.2, 3)	3 (2.7, 3.3)	3.5 (3.2, 3.8)	4.1 (3.8, 4.4)	6.3 (5.9, 6.7)	9.8 (9.3, 10.3)
Low Vulnerability	3.1 (2.6, 3.6)	4.3 (3.9, 4.7)	4.4 (4.1, 4.7)	5.3 (4.9, 5.7)	7 (6.6, 7.4)	10.8 (10.3, 11.3)
High Vulnerability	4.4 (3.8, 5)	6.5 (6, 7)	6.7 (6.2, 7.2)	7.1 (6.7, 7.5)	9.3 (8.8, 9.8)	13.2 (12.5, 13.9)
Highest Vulnerability	5.6 (3.7, 7.5)	6 (5.2, 6.8)	5.3 (4.6, 6)	8.3 (7.3, 9.3)	12.2 (10.9, 13.5)	15.1 (13.8, 16.4)

SVI Theme 2 (Household Composition and Disability) [2]						
Lowest Vulnerability	3.9 (3.4, 4.4)	5.1 (4.7, 5.5)	5.1 (4.8, 5.4)	5.5 (5.2, 5.8)	7.5 (7.1, 7.9)	10.6 (10.2, 11)
Low Vulnerability	2.8 (2.4, 3.2)	4.1 (3.7, 4.5)	5 (4.7, 5.3)	5.8 (5.4, 6.2)	7.3 (6.9, 7.7)	11.7 (11.1, 12.3)
High Vulnerability	2.4 (2, 2.8)	3.7 (3.3, 4.1)	4.3 (3.9, 4.7)	5.7 (5.2, 6.2)	8.6 (8, 9.2)	13.1 (12.1, 14.1)
Highest Vulnerability	4.9 (2.7, 7.1)	5.4 (4.4, 6.4)	4.7 (4.1, 5.3)	7.8 (6.8, 8.8)	12 (10.6, 13.4)	15.9 (14.7, 17.1)
SVI Theme 3 (Minority Status and Language) [2]						
Lowest Vulnerability	0.5 (0.3, 0.7)	1.5 (1.1, 1.9)	2 (1.5, 2.5)	3.9 (3.4, 4.4)	8.5 (7.6, 9.4)	14.3 (12.9, 15.7)
Low Vulnerability	1.2 (0.8, 1.6)	2 (1.7, 2.3)	2.8 (2.4, 3.2)	4.2 (3.7, 4.7)	8.2 (7.6, 8.8)	14.7 (13.9, 15.5)
High Vulnerability	1.9 (1.6, 2.2)	2.3 (2, 2.6)	3.5 (3.1, 3.9)	4.2 (3.8, 4.6)	7.4 (6.9, 7.9)	10.8 (10.3, 11.3)
Highest Vulnerability	4.4 (3.9, 4.9)	5.9 (5.6, 6.2)	5.7 (5.5, 5.9)	6.5 (6.2, 6.8)	8 (7.7, 8.3)	11.3 (10.9, 11.7)
SVI Theme 4 (Housing and Transportation) [2]						
Lowest Vulnerability	2.3 (1.9, 2.7)	2.4 (2, 2.8)	3.4 (2.9, 3.9)	4.8 (4.3, 5.3)	8.2 (7.4, 9)	12.2 (11.5, 12.9)
Low Vulnerability	2.7 (2.2, 3.2)	3.3 (2.9, 3.7)	3.7 (3.2, 4.2)	4.7 (4.2, 5.2)	7.1 (6.6, 7.6)	11.3 (10.6, 12)
High Vulnerability	2.7 (2.3, 3.1)	4.1 (3.8, 4.4)	4.9 (4.6, 5.2)	5.3 (5, 5.6)	7.4 (7, 7.8)	11.1 (10.5, 11.7)
Highest Vulnerability	4.9 (4.1, 5.7)	6.4 (5.9, 6.9)	5.9 (5.5, 6.3)	6.9 (6.5, 7.3)	8.7 (8.2, 9.2)	12 (11.4, 12.6)

Characteristics	Jan-21	Feb-21	Mar-21	Apr-21	May-21	Jun-21
Total	16.1 (15.8, 16.4)	18.5 (18.2, 18.8)	19.9 (19.5, 20.3)	20.8 (20.5, 21.1)	20.4 (20, 20.8)	20.7 (20.3, 21.1)

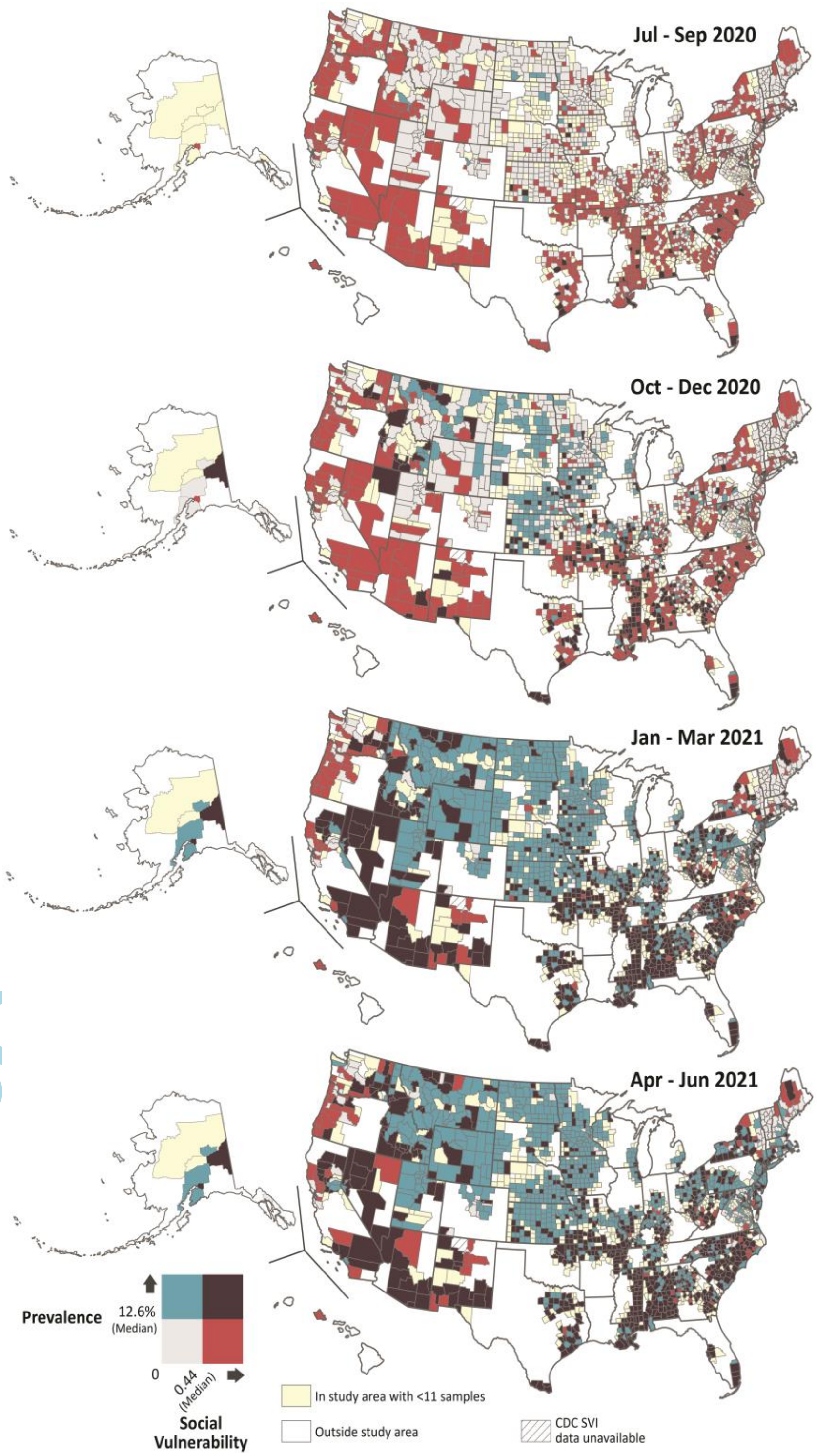
Sex						
Female	15.5 (15.1, 15.9)	18.5 (18, 19)	19.2 (18.7, 19.7)	20.8 (20.3, 21.3)	20.5 (20, 21)	20.4 (19.8, 21)
Male	16.6 (16.1, 17.1)	18.6 (18.1, 19.1)	20.6 (20.1, 21.1)	20.7 (20.2, 21.2)	20.3 (19.8, 20.8)	21 (20.6, 21.4)
Age Category						
16-29 years	22.2 (21.2, 23.2)	23.7 (22.8, 24.6)	27.3 (26.1, 28.5)	28 (26.9, 29.1)	27.2 (25.9, 28.5)	27.4 (26.3, 28.5)
30-49 years	17.1 (16.5, 17.7)	20.3 (19.6, 21)	21.3 (20.7, 21.9)	22.3 (21.7, 22.9)	21.9 (21.2, 22.6)	22.1 (21.5, 22.7)
50-64 years	14.1 (13.6, 14.6)	16.6 (16.1, 17.1)	18 (17.5, 18.5)	18.9 (18.4, 19.4)	18.5 (18, 19)	19.2 (18.7, 19.7)
65+ years	9.1 (8.4, 9.8)	11.6 (11, 12.2)	11 (10.4, 11.6)	11.8 (11.2, 12.4)	11.8 (11.3, 12.3)	12 (11.5, 12.5)
Race/Ethnicity						
Non-Hispanic White	14.4 (14.1, 14.7)	16.4 (16.1, 16.7)	18 (17.7, 18.3)	18.5 (18.3, 18.7)	18.5 (18.2, 18.8)	18.7 (18.4, 19)
Non-Hispanic Black	17.2 (15.6, 18.8)	21.3 (19.7, 22.9)	19.6 (17.8, 21.4)	23.6 (22.2, 25)	21.1 (19.4, 22.8)	23.6 (21.5, 25.7)
Hispanic	23.7 (22.6, 24.8)	27.1 (25.9, 28.3)	30.3 (29.1, 31.5)	30.6 (29.3, 31.9)	30 (28.6, 31.4)	29.9 (28.7, 31.1)
Asian	11.4 (10.1, 12.7)	12.6 (11.2, 14)	12.7 (11.4, 14)	12.6 (11.1, 14.1)	13 (11.7, 14.3)	12.3 (10.9, 13.7)
Other[1]	14.5 (12.1, 16.9)	16.8 (15, 18.6)	19.7 (17.7, 21.7)	20 (18.1, 21.9)	20.1 (18.5, 21.7)	20.4 (18.6, 22.2)
Census Regions						
Northeast	14.2 (13.3, 15.1)	15.2 (14.4, 16)	17.2 (16.4, 18)	18.9 (18.1, 19.7)	19.3 (18.2, 20.4)	20.4 (19.5, 21.3)
Midwest	19.7 (19, 20.4)	22 (21.3, 22.7)	23.7 (22.9, 24.5)	24.1 (23.4, 24.8)	23.6 (22.9, 24.3)	23.4 (22.6, 24.2)
South	17.5 (16.9, 18.1)	20.9 (20.3, 21.5)	21.8 (21.2, 22.4)	22.9 (22.4, 23.4)	22.2 (21.6, 22.8)	22.1 (21.5, 22.7)

West	12.8 (12.3, 13.3)	15.4 (14.9, 15.9)	16.8 (16.1, 17.5)	17 (16.3, 17.7)	16.4 (15.8, 17)	17 (16.4, 17.6)
Rurality Level						
Urban	15.4 (15.1, 15.7)	17.8 (17.5, 18.1)	19 (18.6, 19.4)	19.9 (19.5, 20.3)	19.6 (19.2, 20)	20 (19.6, 20.4)
Rural	22.4 (21.4, 23.4)	25.1 (24.1, 26.1)	28.7 (27.7, 29.7)	28.5 (27.6, 29.4)	27.5 (26.6, 28.4)	27.2 (26.1, 28.3)
Social Vulnerability[2]						
Lowest Vulnerability	14.6 (14, 15.2)	16.5 (15.9, 17.1)	18.6 (17.9, 19.3)	18.8 (18.2, 19.4)	19.2 (18.3, 20.1)	20 (19.3, 20.7)
Low Vulnerability	13.7 (13.2, 14.2)	15.7 (15.1, 16.3)	17.5 (16.8, 18.2)	18.4 (17.7, 19.1)	18 (17.3, 18.7)	17.8 (17.1, 18.5)
High Vulnerability	17.2 (16.6, 17.8)	19.9 (19.3, 20.5)	20.2 (19.6, 20.8)	21.9 (21.3, 22.5)	21 (20.4, 21.6)	21.6 (21.1, 22.1)
Highest Vulnerability	18.4 (17.7, 19.1)	21.6 (20.6, 22.6)	23.7 (22.7, 24.7)	23.6 (22.8, 24.4)	23.5 (22.6, 24.4)	23.6 (22.7, 24.5)
SVI Theme 1 (Socioeconomic Status) [2]						
Lowest Vulnerability	13.2 (12.7, 13.7)	14.4 (14, 14.8)	16.2 (15.6, 16.8)	17.1 (16.6, 17.6)	17 (16.3, 17.7)	17.3 (16.7, 17.9)
Low Vulnerability	14.7 (14.2, 15.2)	17.7 (17.1, 18.3)	19.2 (18.6, 19.8)	20.2 (19.6, 20.8)	19.4 (18.8, 20)	19.9 (19.2, 20.6)
High Vulnerability	19.1 (18.4, 19.8)	21.6 (20.8, 22.4)	22.4 (21.6, 23.2)	23.2 (22.5, 23.9)	23.1 (22.4, 23.8)	23.5 (22.6, 24.4)
Highest Vulnerability	19.8 (18.5, 21.1)	24.6 (23.2, 26)	26.6 (25, 28.2)	26.6 (25.4, 27.8)	25.9 (24.6, 27.2)	25.8 (24.4, 27.2)
SVI Theme 2 (Household Composition and Disability) [2]						
Lowest Vulnerability	14.4 (14, 14.8)	16.2 (15.7, 16.7)	17.3 (16.8, 17.8)	18.4 (17.9, 18.9)	18 (17.4, 18.6)	18.6 (18.1, 19.1)
Low Vulnerability	16.5 (15.8, 17.2)	19.9 (19.2, 20.6)	21.6 (21, 22.2)	22.4 (21.7, 23.1)	21.6 (20.9, 22.3)	21.7 (21.1, 22.3)
High Vulnerability	19.1 (18.2, 20)	22 (21.1, 22.9)	23.2 (22.2, 24.2)	23.4 (22.4, 24.4)	24 (23, 25)	24.1 (23.1, 25.1)

Highest Vulnerability	21.1 (19.7, 22.5)	24.6 (23, 26.2)	28 (26.5, 29.5)	28.4 (27.3, 29.5)	27.9 (26.7, 29.1)	26.9 (25.4, 28.4)
SVI Theme 3 (Minority Status and Language) [2]						
Lowest Vulnerability	19.8 (18.6, 21)	24.1 (22.6, 25.6)	26.3 (25, 27.6)	26.2 (24.8, 27.6)	26.9 (25.7, 28.1)	26.6 (24.9, 28.3)
Low Vulnerability	19.7 (18.6, 20.8)	21.3 (20.1, 22.5)	23.9 (23, 24.8)	23.6 (22.7, 24.5)	23.5 (22.5, 24.5)	23.2 (22.1, 24.3)
High Vulnerability	16.2 (15.5, 16.9)	17.5 (16.9, 18.1)	19 (18.3, 19.7)	20.8 (20.1, 21.5)	20.4 (19.4, 21.4)	20.8 (19.9, 21.7)
Highest Vulnerability	15.4 (15, 15.8)	18.1 (17.7, 18.5)	19.3 (18.9, 19.7)	20.1 (19.7, 20.5)	19.6 (19.2, 20)	20 (19.6, 20.4)
SVI Theme 4 (Housing and Transportation) [2]						
Lowest Vulnerability	17.1 (16.3, 17.9)	19 (18.2, 19.8)	21 (20.2, 21.8)	21.4 (20.6, 22.2)	22.4 (21.1, 23.7)	22.3 (21.3, 23.3)
Low Vulnerability	16 (15.3, 16.7)	18.8 (18, 19.6)	20.6 (19.8, 21.4)	21.4 (20.6, 22.2)	20.9 (20.1, 21.7)	21.1 (20.4, 21.8)
High Vulnerability	15.5 (14.9, 16.1)	18.7 (18.2, 19.2)	20.3 (19.8, 20.8)	21.1 (20.6, 21.6)	20.2 (19.6, 20.8)	20.5 (19.9, 21.1)
Highest Vulnerability	16.2 (15.6, 16.8)	18.1 (17.4, 18.8)	19.1 (18.5, 19.7)	20.1 (19.5, 20.7)	19.8 (19.1, 20.5)	20.3 (19.6, 21)

1. "Other" category includes more than one race, American Indian, and other race/ethnicity.
2. Lowest, low, high, and highest vulnerability defined as the 1st, 2nd, 3rd and 4th quartiles of the social vulnerability index in this study.

Figure 1



Jul - Sep 2020
Oct - Dec 2020
Jan - Mar 2021
Apr - Jun 2021
Prevalence
12.6%
(Median)
0
0.44
(Median)
Social
Vulnerability
In study area with <11 samples
Outside study area
CDC SVI
data unavailable

Figure 2

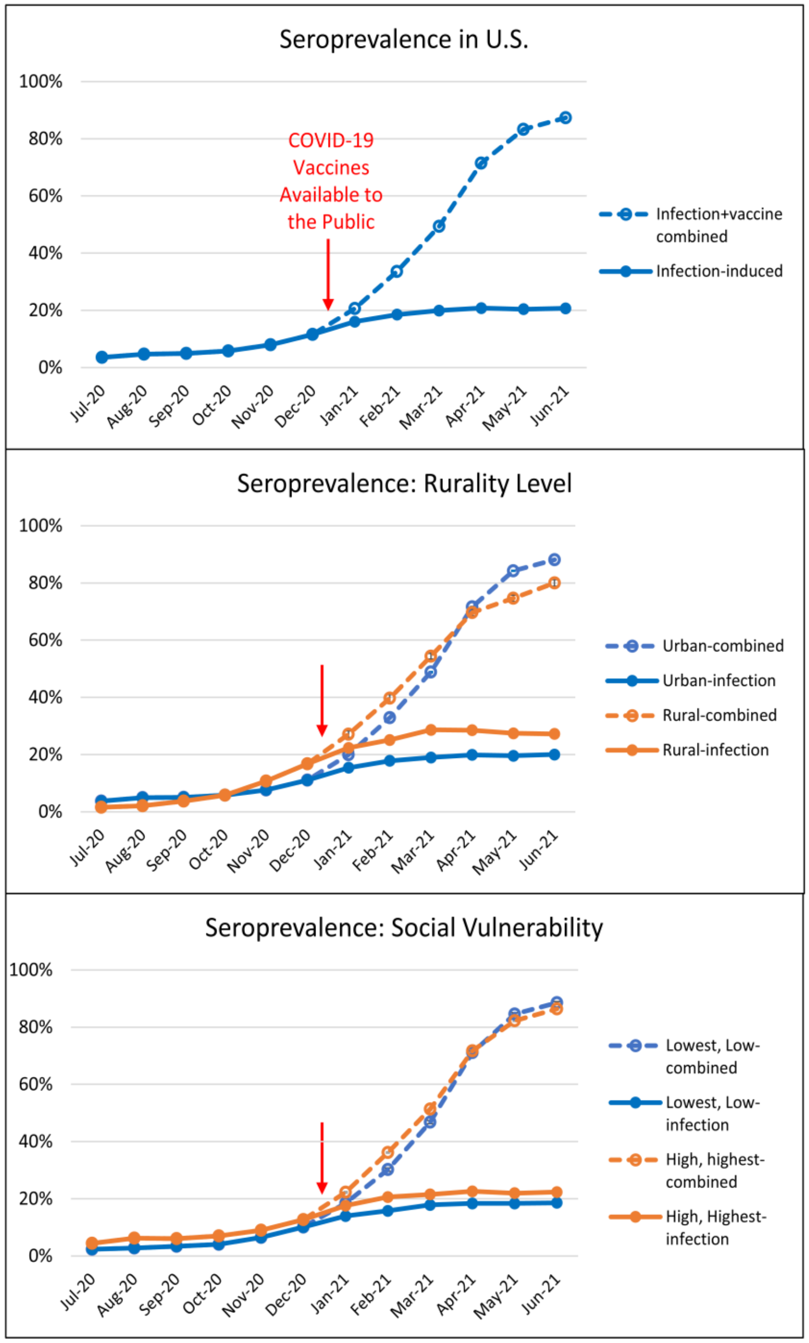
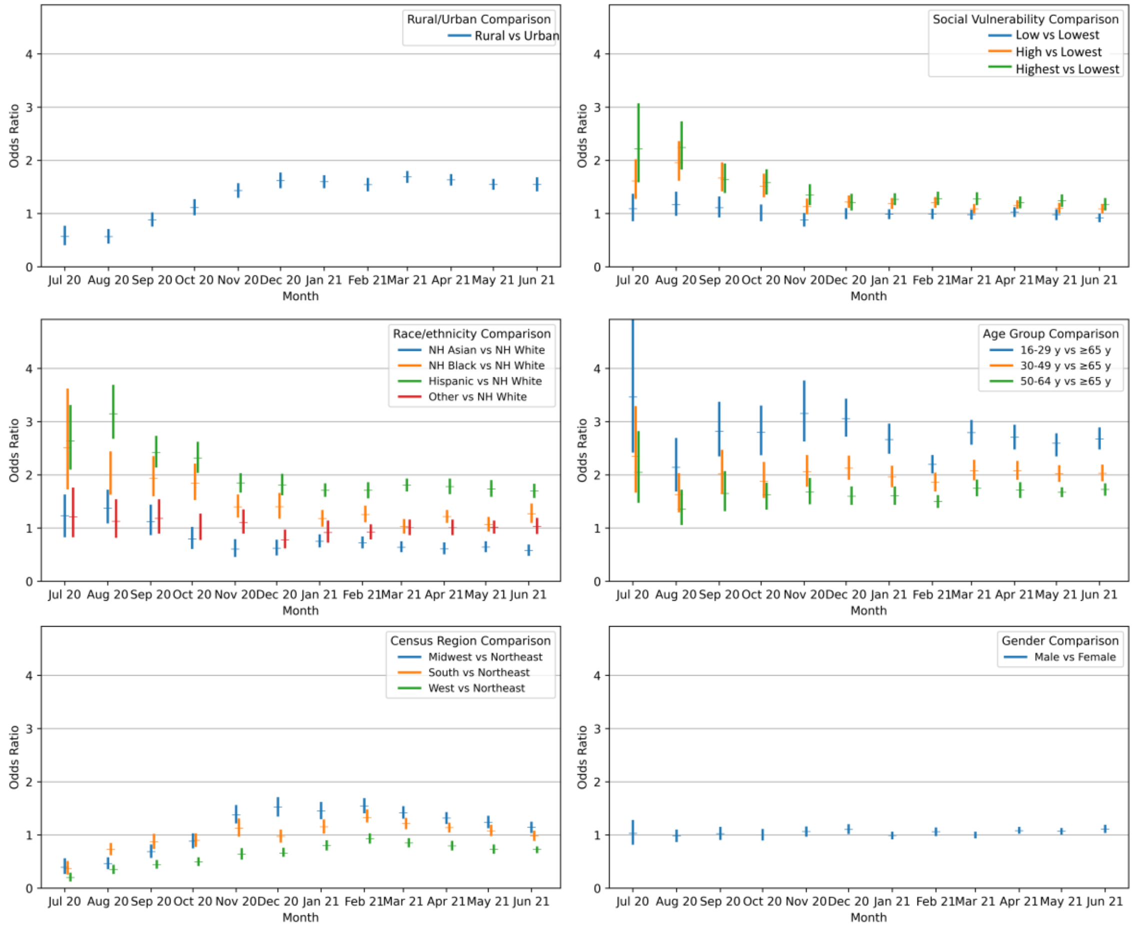

Seroprevalence in U.S.
100%
80%
60%
40%
20%
0%
COVID-19 Vaccines Available to the Public
Jul-20
Aug-20
Sep-20
Oct-20
Nov-20
Dec-20
Jan-21
Feb-21
Mar-21
Apr-21
May-21
Jun-21
Infection+vaccine combined
Infection-induced
Seroprevalence: Rurality Level
Urban-combined
Urban-infection
Rural-combined
Rural-infection
Seroprevalence: Social Vulnerability
Lowest, Low-combined
Lowest, Low-infection
High, highest-combined
High, Highest-infection

Figure 3


Rurality Level
35%
30%
25%
20%
15%
10%
5%
0%
Jul-20
Aug-20
Sep-20
Oct-20
Nov-20
Dec-20
Jan-21
Feb-21
Mar-21
Apr-21
May-21
Jun-21
Urban
Rural
Social Vulnerability
30%
25%
20%
15%
10%
5%
0%
Lowest
Low
High
Highest
Race/ethnicity
35%
30%
25%
20%
15%
10%
5%
0%
NH White
NH Black
Hispanic
Asian
Age Group
35%
30%
25%
20%
15%
10%
5%
0%
16-29
30-49
50-64
65+
Census Region
30%
25%
20%
15%
10%
5%
0%
Northeast
Midwest
South
West
Sex
25%
20%
15%
10%
5%
0%
Female
Male

Figure 4


Rural/Urban Comparison
Rural vs Urban
Social Vulnerability Comparison
Low vs Lowest
High vs Lowest
Highest vs Lowest
Race/ethnicity Comparison
NH Asian vs NH White
NH Black vs NH White
Hispanic vs NH White
Other vs NH White
Age Group Comparison
16-29 y vs ≥65 y
30-49 y vs ≥65 y
50-64 y vs ≥65 y
Census Region Comparison
Midwest vs Northeast
South vs Northeast
West vs Northeast
Gender Comparison
Male vs Female
Odds Ratio
0
1
2
3
4
Jul 20
Aug 20
Sep 20
Oct 20
Nov 20
Dec 20
Jan 21
Feb 21
Mar 21
Apr 21
May 21
Jun 21
Month