Prevalence of SARS-CoV-2 antibodies in a large nationwide sample of patients on dialysis in the USA: a cross-sectional study

Shuchi Anand, Maria Montez-Rath, Jialin Han, Julie Bozeman, Russell Kerschmann, Paul Beyer, Julie Parsonnet, Glenn M Chertow

Summary

Background Many patients receiving dialysis in the USA share the socioeconomic characteristics of underserved communities, and undergo routine monthly laboratory testing, facilitating a practical, unbiased, and repeatable assessment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seroprevalence.

Methods For this cross-sectional study, in partnership with a central laboratory that receives samples from approximately 1300 dialysis facilities across the USA, we tested the remainder plasma of 28 503 randomly selected adult patients receiving dialysis in July, 2020, using a spike protein receptor binding domain total antibody chemiluminescence assay (100% sensitivity, 99·8% specificity). We extracted data on age, sex, race and ethnicity, and residence and facility ZIP codes from the anonymised electronic health records, linking patient-level residence data with cumulative and daily cases and deaths per 100 000 population and with nasal swab test positivity rates. We standardised prevalence estimates according to the overall US dialysis and adult population, and present estimates for four prespecified strata (age, sex, region, and race and ethnicity).

Findings The sampled population had similar age, sex, and race and ethnicity distribution to the US dialysis population, with a higher proportion of older people, men, and people living in majority Black and Hispanic neighbourhoods than in the US adult population. Seroprevalence of SARS-CoV-2 was 8·0% (95% CI 7·7–8·4) in the sample, 8·3% (8·0–8·6) when standardised to the US dialysis population, and 9·3% (8·8–9·9) when standardised to the US adult population. When standardised to the US dialysis population, seroprevalence ranged from 3·5% (3·1–3·9) in the west to 27·2% (25·9–28·5) in the northeast. Comparing seroprevalent and case counts per 100 000 population, we found that 9·2% (8·7–9·8) of seropositive patients were diagnosed. When compared with other measures of SARS-CoV-2 spread, seroprevalence correlated best with deaths per 100 000 population (Spearman's ρ=0·77). Residents of non-Hispanic Black and Hispanic neighbourhoods experienced higher odds of seropositivity (odds ratio 3·9 [95% CI 3·4–4·6] and 2·3 [1·9–2·6], respectively) compared with residents of predominantly non-Hispanic white neighbourhoods. Residents of neighbourhoods in the highest population density quintile experienced increased odds of seropositivity (10·3 [8·7–12·2]) compared with residents of the lowest density quintile. County mobility restrictions that reduced workplace visits by at least 5% in early March, 2020, were associated with lower odds of seropositivity in July, 2020 (0·4 [0·3–0·5]) when compared with a reduction of less than 5%.

Interpretation During the first wave of the COVID-19 pandemic, fewer than 10% of the US adult population formed antibodies against SARS-CoV-2, and fewer than 10% of those with antibodies were diagnosed. Public health efforts to limit SARS-CoV-2 spread need to especially target racial and ethnic minority and densely populated communities.

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Division of Nephrology (S Anand MD, M Montez-Rath PhD, J Han MS, Prof G M Chertow MD) **and Division of Infectious Diseases & Geographic Medicine** (Prof J Parsonnet MD), **Department of Medicine, and Department of Epidemiology and Population Health** (Prof J Parsonnet, Prof G M Chertow), **Stanford University, Palo Alto, CA, USA; and Ascend Clinical Laboratory, Redwood City, CA, USA** (J Bozeman CLS, R Kerschmann MD, P Beyer MBA)

Correspondence to: Shuchi Anand, Division of Nephrology, Department of Medicine, Stanford University School of Medicine, Palo Alto, California 94304, USA **sanand2@stanford.edu**

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus stimulates a rapid antibody response in people with symptomatic[1–5] and asymptomatic[2,6,7] infection. Seroprevalence of SARS-CoV-2 antibodies in a population thus serves as a reasonable measure of exposure and spread. Seroprevalence surveys in the USA, however, have been restricted to single hotspots[8–10] or under-represented high-risk or vulnerable populations.[9,11] Moreover, these studies face challenges to timely repetition and longitudinal follow-up, limiting their utility for surveillance.[8–10]

Patients receiving dialysis might be considered an ideal sentinel population in which to study the evolution of the COVID-19 public health crisis. Patients receiving dialysis in the USA undergo routine monthly laboratory studies to gauge the effectiveness of therapy and to screen for associated complications. In haemodialysis, regular access to the bloodstream abrogates the need for phlebotomy to acquire blood samples. Risk factors for acquisition of SARS-CoV-2 and for severe COVID-19, including advanced age, non-white race, poverty, and diabetes, are the rule rather than the exception in the US dialysis population.[12]

Research in context

Evidence before this study

Measuring the seroprevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies provides a comprehensive assessment of its community spread. Community seroprevalence surveys require considerable infrastructure and expense, and face implementation challenges during the COVID-19 pandemic due to restricted outreach in the worst-affected communities. Of the two largest seroprevalence surveys in the USA, one was limited only to New York state (n=15 101) and used convenience sampling at grocery stores. A second survey used remainder plasma from people visiting commercial laboratories in six cities (n=11 933), but lacked details on race and ethnicity and other community-level risk factors.

Added value of this study

We tested the remainder plasma of 28 503 patients receiving dialysis throughout the USA, using a chemiluminescence assay with high sensitivity and specificity. To our knowledge, we provide the first nationally representative estimate of SARS-CoV-2 seroprevalence in the US dialysis and US adult population, and estimates for differences in seroprevalence by neighbourhood race and ethnicity, poverty, population density, and mobility restriction. We also evaluate which of the existing measures of COVID-19 incidence most closely correlate with seroprevalence. Most importantly, we show that as patients receiving dialysis have monthly blood draws, without fail and without bias, and are a population with increased representation of racial and ethnic minorities, repeated cross-sectional analyses of seroprevalence within this sentinel population can be implemented as a practical and unbiased surveillance strategy in the USA.

Implications of all the available evidence

Similar to data from other highly affected countries and regions (eg, Spain and Wuhan, China), despite the intense strain on resources and unprecedented excess mortality being experienced in the USA during the COVID-19 pandemic, fewer than 10% of US adults had formed antibodies to SARS-CoV-2 as of July, 2020. There was significant regional variation from less than 5% prevalence in the west to more than 25% in the northeast. Public health efforts to curb the spread of the virus need to continue, with focus on some of the highest-risk communities that we identified, such as majority Black and Hispanic neighbourhoods, poorer neighbourhoods, and densely populated metropolitan areas. A surveillance strategy relying on monthly testing of remainder plasma of patients receiving dialysis can produce unbiased estimates of SARS-CoV-2 spread inclusive of hard-to-reach, disadvantaged populations in the USA. Such surveillance can inform disease trends, resource allocation, and effectiveness of community interventions during the COVID-19 pandemic.

Testing remainder plasma from monthly samples obtained for routine care of patients on dialysis for SARS-CoV-2 antibodies therefore represents a practical approach to a population-representative surveillance strategy,[13] informing risks faced by a susceptible population while ensuring representation from racial and ethnic minorities. In addition, seroprevalence surveys in patients receiving dialysis can be linked to patient-level and community-level data to enable evaluation and quantification of differences in SARS-CoV-2 prevalence by demographic and neighbourhood strata, and thus facilitate effective mitigation strategies targeting the highest-risk individuals and communities.

In partnership with a commercial clinical laboratory, we tested seroprevalence of SARS-CoV-2 antibodies in a randomly selected representative sample of patients. Our goal was to provide a nationwide estimate of exposure to SARS-CoV-2 during the first wave of COVID-19 in the USA, up to July, 2020, with stratification by region, age, sex, and race and ethnicity. We also harnessed population data on SARS-CoV-2 cases and deaths and percentage testing positive using nasal swab testing to assess how seroprevalence estimates correlated with other epidemiological measures of COVID-19 incidence. Finally, to inform preventive strategies for the high-risk dialysis population as well as the general population, we investigated community-level correlates for seropositivity.

Methods

Study design and participants

We did a cross-sectional analysis of adult (≥18 years) patients undergoing monthly laboratory testing at Ascend Clinical using samples obtained for routine clinical care that otherwise would have been discarded. Ascend Clinical is a commercial clinical laboratory based in Redwood City, California, that receives samples from a nationwide network of around 1300 dialysis facilities, serving approximately 65 000 patients. We randomly selected patients from the patient list on June 15, 2020, for seroprevalence testing to be done in July, 2020, using implicit stratification by region, age, sex, and race and ethnicity followed by systematic sampling with fractional polynomials.[14] After sample selection and processing, Ascend Clinical sent anonymised data on patient age, sex, race and ethnicity, and residence and facility ZIP codes to Stanford University investigators for analyses. Stanford University investigators further linked patient geographical information (ZIP code) to census data and publicly available COVID-19 burden and community mobility data. The study received expedited approval from the Stanford University of Medicine Institutional Review Board; informed consent was waived.

Procedures

We used the US Food and Drug Administration-approved Siemens Healthineers SARS-CoV-2 spike protein receptor

binding domain (S1RBD) total antibody (immunoglobulin) chemiluminescence assay, which has 100% sensitivity (≥14 days after a positive PCR test) and 99·8% specificity.[5] We chose this assay on the basis of its Emergency Use Authorization in June, 2020, in the context that S1RBD is also the target of vaccine development efforts.[15] Sample processing is detailed in the appendix (p 3).

We linked patient-level residence data with cumulative and daily cases and deaths per 100 000 population as compiled on a county level by the Center for Systems Science and Engineering at Johns Hopkins University[16] and with nasal swab test positivity rates, as compiled on a state level by the Covid Tracking Project.[17] For Utah, we followed the Utah Department of Health groupings of several smaller counties and extracted data directly.[18] New York City data are not available by county within the Johns Hopkins University dataset; therefore, we directly extracted data from the New York City Dashboard.[19] For county-level mobility restrictions, we used Google Mobility Data that report an average percentage change in the number of workplace visits over the period March 1–15, 2020, before the implementation of shelter-in-place restrictions in the majority of the country. Percentage changes in the Google Mobility data are indexed to a corresponding weekday (eg, Tuesdays are matched to Tuesdays) from Jan 3 to Feb 6, 2020.[20]

We also linked patient-level residence data with ZIP code tabulation area (ZCTA) data from the 2018 American Community Survey (ACS) 5-year estimates[21] to ascertain patient neighbourhood proportion living below the poverty level and race and ethnicity mix, and with American Census Bureau 2010 estimates[22] to ascertain population density. We defined ZCTA majority race and ethnicity as Hispanic, non-Hispanic Black, or non-Hispanic white if the population in the ZCTA was at least 60% Hispanic, non-Hispanic Black, or non-Hispanic white, respectively; where this was not the case, if the Hispanic and Black population combined was at least 60% of the population, the ZCTA majority was defined as Hispanic and Black, otherwise as other. For urban versus rural ZCTA status, we used the 2010 Rural Urban Commuting Area codes by census tract, categorising a ZCTA as dense urban, metropolitan, micropolitan, or small town or rural area if more than 50% of the population in the ZCTA was living in one of these area codes.[23]

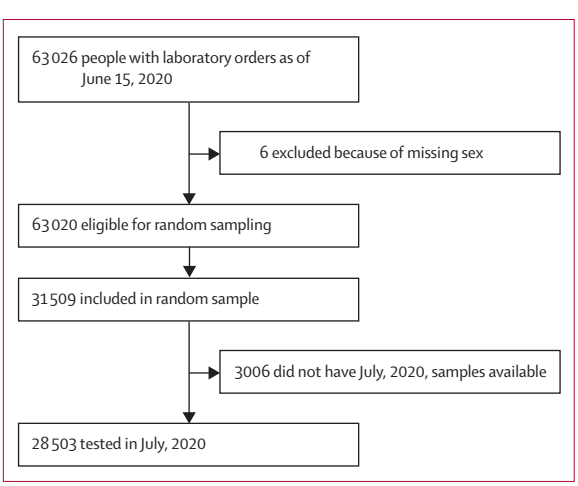

Figure 1: **Patient sampling and analytic cohort**

See **Online** for appendix

Statistical analysis

We assumed a nationwide prevalence of SARS-CoV-2 antibody of 5%.[8,24] To generate prevalence estimates for patients on dialysis using preselected regional strata with precision within 0·5%, a sample of 27 364 was required (appendix p 2). Based on previous trends, we expected 15% of selected samples to be unavailable in July, 2020, due to death, move to other facilities, or other reasons for missing laboratory data (eg, hospitalisation or non-adherence). Accounting for this potential dropout, we randomly selected 31 509 patients.

We present prevalence estimates with 95% CIs in our sample, standardised to the US adult dialysis population and to the US adult population. For the US adult dialysis

	Selected sample (n=28 503)	US adult dialysis population (n=499 150)	US adult population (n=253 815 197)
Age, years			
18–44	3303 (11·6%)	60 540 (12·1%)	117 499 477 (46·3%)
45–64	11 541 (40·5%)	207 022 (41·5%)	83 892 606 (33·1%)
65–79	10 220 (35·9%)	174 341 (34·9%)	39 949 825 (15·7%)
≥80	3439 (12·1%)	57 247 (11·5%)	12 473 289 (4·9%)
Sex			
Female	12 155 (42·6%)	213 869 (42·8%)	130 236 328 (51·3%)
Male	16 348 (57·4%)	285 281 (57·2%)	123 578 869 (48·7%)
Race and ethnicity*†			
Hispanic	3187 (11·2%)	87 611 (17·6%)	60 861 275 (18·7%)
Non-Hispanic white	6533 (22·9%)	203 421 (40·8%)	197 202 727 (60·4%)
Non-Hispanic Black	4894 (17·2%)	173 190 (34·7%)	39 717 152 (12·2%)
Other	2479 (8·7%)	34 928 (7·0%)	28 493 202 (8·7%)
Unknown	11 410 (40·0%)	0	0
ZCTA majority race and ethnicity*‡			
Non-Hispanic white	8733 (30·6%)	206 678 (41·4%)	189 968 192 (58·2%)
Non-Hispanic Black	2585 (9·1%)	54 999 (11·0%)	12 550 083 (3·8%)
Hispanic	4568 (16·0%)	52 953 (10·6%)	26 310 796 (8·1%)
Hispanic and Black	2878 (10·1%)	43 396 (8·7%)	17 238 911 (5·3%)
Other	9737 (34·2%)	140 781 (28·2%)	80 206 374 (24·6%)
Region			
Northeast	4536 (15·9%)	78 619 (15·8%)	44 519 465 (17·5%)
South	10 939 (38·4%)	214 974 (43·1%)	96 250 597 (37·9%)
Midwest	3763 (13·2%)	94 490 (18·9%)	52 876 708 (20·8%)
West	9265 (32·5%)	111 067 (22·3%)	60 168 427 (23·7%)

US adult population given is for 2018 and US adult patients dialysis population as of Jan 1, 2017. ZCTA=ZIP code tabulation area. *Computed for total US 2018 population (n=326 274 356). †When excluding people with unknown race and ethnicity, the proportions were 18·6% Hispanic, 38·2% non-Hispanic white, 28·6% non-Hispanic Black, and 14·5% non-Hispanic other. ‡343 people in the US Renal Data System and two people in the sample populations were missing data on ZCTA majority race and ethnicity due to missing ZIP code.

Table 1: **Comparison of sampled population, US adult dialysis population, and US adult population**

For the **United States Renal Data System database** see https://www.usrds.org

population, we used the distribution of all adults receiving maintenance dialysis, excluding those living in the territories, on Jan 1, 2017, identified through the United States Renal Data System database. For the US adult population, we used 2018 ACS 1-year estimates.[21] Based on the test sensitivity range obtained by Schnurra and colleagues in their external validation,[25] we also provide test characteristic-adjusted sample population estimates, ranging sensitivity from 85% to 98%.[10] To compute the percentage of estimated seroprevalent cases that were likely to be diagnosed cases,[10,26] we compared the estimated seroprevalent cases per 100 000 adult population with Johns Hopkins University estimates of cumulative diagnosed cases per 100 000 US adult population as of June 15, 2020.

To standardise estimates, we assigned weights to each person based on their membership to each of 32 strata of census regions (northeast, south, midwest, and west), age (18–44, 45–64, 65–79, and ≥80 years), and sex. We defined post-stratification weights as the proportion of each stratum represented in the US dialysis population or US adult population divided by the analogous proportion in the sample.[27–29] We then computed weighted frequencies and 95% CIs according to four prespecified strata (region, age, sex, and race and ethnicity) with differences evaluated using Rao-Scott χ^2 tests.[30,31] Due to the missingness of race and ethnicity data in the electronic health records, we used the additional measure of ZCTA race and ethnicity distribution with categories adapted from Moore and colleages.[32,33]

Next, we correlated five measures of COVID-19 incidence—cumulative cases on June 15, 2020 (or first available date between June 15 and June 30, 2020); cumulative deaths on June 30, 2020 (or last available date between June 15 and June 30, 2020); 15-day averages of daily cases and daily deaths; and percentage testing positive on nasal swab tests between June 15 and June 30, 2020—with SARS-CoV-2 seroprevalence in patients on dialysis in July, 2020. To do this, we first collapsed all measures to a state level and then assessed the Spearman's correlation coefficient ρ for the association of each measure with seroprevalence. Because of the high density of Ascend Clinical facilities in New York, Texas, and California, we also chose those states to present county-level correlations.

Finally, using logistic regression, we determined the age-adjusted and sex-adjusted correlates of seropositivity for patient ZCTA race and ethnicity distribution, percentage living below poverty level, rural or urban classification, population density, and county mobility restriction.

We assumed statistical significance at $\alpha<0{\cdot}05$. All statistical analyses were done with SAS Enterprise Guide (version 7.1) and Stata (version 15.1).

	Unweighted sample		Standardised to US adult dialysis population*	
	Count	Seropositive	Seropositive	Seropositive people per 100 000 population†
Age, years‡				
18–44	291	8·8% (7·9–9·9)	8·9% (8·0–10·0)	8921
45–64	958	8·3% (7·8–8·8)	8·6% (8·1–9·2)	8632
65–79	807	7·9% (7·4–8·5)	7·9% (7·4–8·5)	7934
≥80	236	6·9% (6·0–7·8)	7·3% (6·5–8·3)	7337
Sex				
Female	970	8·0% (7·5–8·5)	8·2% (7·7–8·7)	8162
Male	1322	8·1% (7·7–8·5)	8·4% (7·9–8·8)	8359
Race and ethnicity§				
Hispanic	201	6·3% (5·5–7·2)	6·3% (5·5–7·3)	3808
Non-Hispanic Black	467	9·5% (8·7–10·4)	9·3% (8·5–10·1)	5004
Non-Hispanic white	229	3·5% (3·1–4·0)	3·4% (3·0–3·9)	1991
Other	103	4·2% (3·4–5·0)	4·9% (4·1–5·9)	4796
Unknown	1292	11·3% (10·7–12·0)	11·8% (11·1–12·4)	..
ZCTA majority race and ethnicity§				
Hispanic	412	9·0% (8·2–10·0)	9·4% (8·5–10·3)	13 387
Non-Hispanic Black	380	14·7% (13·3–16·3)	14·1% (12·9–15·5)	13 575
Hispanic and Black	420	14·6% (13·3–16·1)	14·5% (13·2–15·9)	17 333
Non-Hispanic white	367	4·2% (3·8–4·7)	4·3% (3·8–4·7)	3438
Integrated	713	7·3% (6·8–7·9)	8·0% (7·4–8·6)	8610
Region§				
Northeast	1231	27·1% (25·7–28·7)	27·2% (25·9–28·5)	27 207
South	474	4·3% (4·0–4·7)	4·4% (4·0–4·8)	4358
Midwest	265	7·0% (6·2–7·9)	7·1% (6·3–7·9)	7062
West	322	3·5% (3·1–3·9)	3·5% (3·1–3·9)	3487
Overall	2292	8·0% (7·7–8·4)	8·3% (8·0–8·6)	8275

SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. ZCTA=ZIP code tabulation area. *Standardised to the US dialysis population using all adults receiving dialysis for the treatment of end-stage kidney disease on Jan 1, 2017, identified through the United States Renal Data System database (n=499 150). †Seropositivity per 100 000 people calculated as (standardised count/category count) × 100 000. ‡Different at $\alpha<0{\cdot}05$ by the Rao-Scott χ^2 test. §Different at $\alpha<0{\cdot}0001$ by the Rao-Scott χ^2 test.

Table 2: **Seroprevalence of SARS-CoV-2 antibodies in patients receiving dialysis in the USA**

Role of the funding source

Ascend Clinical Laboratories supported the remainder plasma testing for SARS-CoV-2 antibodies. SA, MM-R, and JH had complete access to all data in the study and SA, MM-R, JH, JP, and GMC were responsible for the decision to submit for publication.

Results

Of the 31 509 people selected for testing on June 15, 2020, 28 503 were tested in July, 2020 (figure 1), with 25 217 (88·5%) tested in the first 2 weeks (appendix p 4). The sampling was representative of the US dialysis patient distribution by age, sex, race and ethnicity (when excluding patients without race and ethnicity data), and region, except sampled patients were less likely to be non-Hispanic Black (table 1). Compared with the US adult population, our sampled patient population was older, had more men, and was more likely to be non-Hispanic Black and living in non-white neighbourhoods

	Seropositivity standardised to US adult population*	Seropositive people per 100 000 population†
Age, years‡		
18–44	9·8% (8·7–10·9)	9006
45–64	9·5% (8·9–10·1)	9516
65–79	8·3% (7·8–8·9)	8315
≥80	7·4% (6·5–8·5)	7436
Sex		
Female	9·3% (8·6–10·2)	9022
Male	9·3% (8·6–10·0)	8954
Race and ethnicity§		
Hispanic	8·0% (6·6–9·6)	3526
Non-Hispanic Black	9·9% (8·7–11·3)	12035
Non-Hispanic white	4·3% (3·5–5·2)	1102
Other	5·7% (4·2–7·7)	3342
Unknown	12·5% (11·6–13·5)	..
ZCTA majority race and ethnicity§		
Hispanic	11·3% (9·8–12·9)	16041
Non-Hispanic Black	13·9% (12·1–16·0)	31061
Hispanic and Black	16·3% (14·3–18·5)	24923
Non-Hispanic white	4·8% (4·1–5·5)	1919
Other	8·9% (8·0–9·8)	8423
Region§		
Northeast	27·6% (25·7–29·7)	26697
South	5·1% (4·5–5·7)	4894
Midwest	7·4% (6·3–8·8)	7157
West	4·2% (3·6–4·9)	4048
Overall	9·3% (8·8–9·9)	8989

ZCTA=ZIP code tabulation area. *Standardised to the US population using American Community Survey 2018 data. †Seropositivity per 100 000 people calculated as (standardised count/category count) × 100 000. ‡Different at α<0·05 by the Rao-Scott χ^2 test. §Different at α<0·0001 by the Rao-Scott χ^2 test.

Table 3: **Seroprevalence estimates for the US adult population**

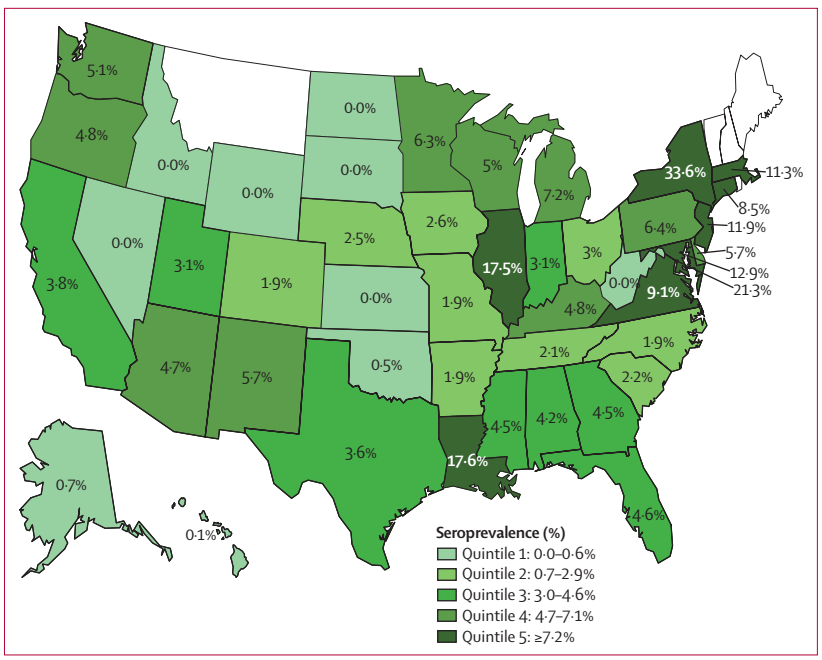

Figure 2: **Prevalence of SARS-CoV-2 antibodies in sampled population, by state**
Bolded borders represent states with more than 100 patients in the sample. The median number of patients sampled by state was 176 (IQR 83–536). States in white were not sampled. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

(table 1). A greater proportion of our sampled population and the US dialysis population lived in the west, and a lower proportion lived in the midwest, compared with the US adult population. Patients in our sample lived in 46 states and in 1013 (32%) of 3141 US counties (appendix p 6).

Overall, sample seroprevalence was 8·0% (95% CI 7·7–8·4). Accounting for the externally validated test sensitivity,[25] seroprevalence ranged from 8·2% (7·9–8·5) to 9·4% (9·1–9·8) in our sampled population (appendix p 7). When standardised to the US dialysis population, seroprevalence was 8·3% (8·0–8·6), with high regional variation in seroprevalence (ranging from 3·5% [3·1–3·9] in the west to 27·2% [25·9–28·5] in the northeast; table 2). Seroprevalence was similar by sex and modestly lower in people aged 80 years or older compared with those aged 45–64 years (table 2). Differences in seroprevalence by race and ethnicity were similar using both our patient-level (electronic health record) and neighbourhood-level (ZCTA majority race and ethnicity) measures, with non-Hispanic Black patients having the highest seropositivity, followed by Hispanic patients, and non-Hispanic white patients having the lowest.

We estimated the SARS-CoV-2 standardised seroprevalence in the US population to be 9·3% (95% CI 8·8–9·9; table 3). Based on the Johns Hopkins University cumulative case data as of June 15, 2020, the prevalence of (nasal swab) diagnosed cases was 826 per 100 000 US adult population, compared with our estimate of 8989 seropositive people per 100 000 population, meaning that 9·2% (8·7–9·8) of seropositive people were diagnosed.

Using data from our sampled population, variation by state was high, ranging from 0·0% in seven states to 33·6% (31·7–35·6) in New York, with the highest regional variation occurring in the northeast (figure 2; appendix pp 8–9). When comparing state seroprevalence against cumulative cases and deaths per 100 000 population, deaths correlated best (ρ=0·66 for cases *vs* 0·77 for deaths; figure 3). The percentage of people testing positive by nasal swab test and 15-day average of daily deaths in the latter half of June, 2020, showed a weaker correlation (ρ=0·58 and 0·66, respectively), whereas 15-day average of daily cases did not correlate with seroprevalence (ρ=–0·14). On a county level in California, New York, and Texas, there was even more heterogeneity in the correlation between seroprevalence and other disease measures (ρ≤0·51 for all correlations for all three states' county-level data; appendix p 10).

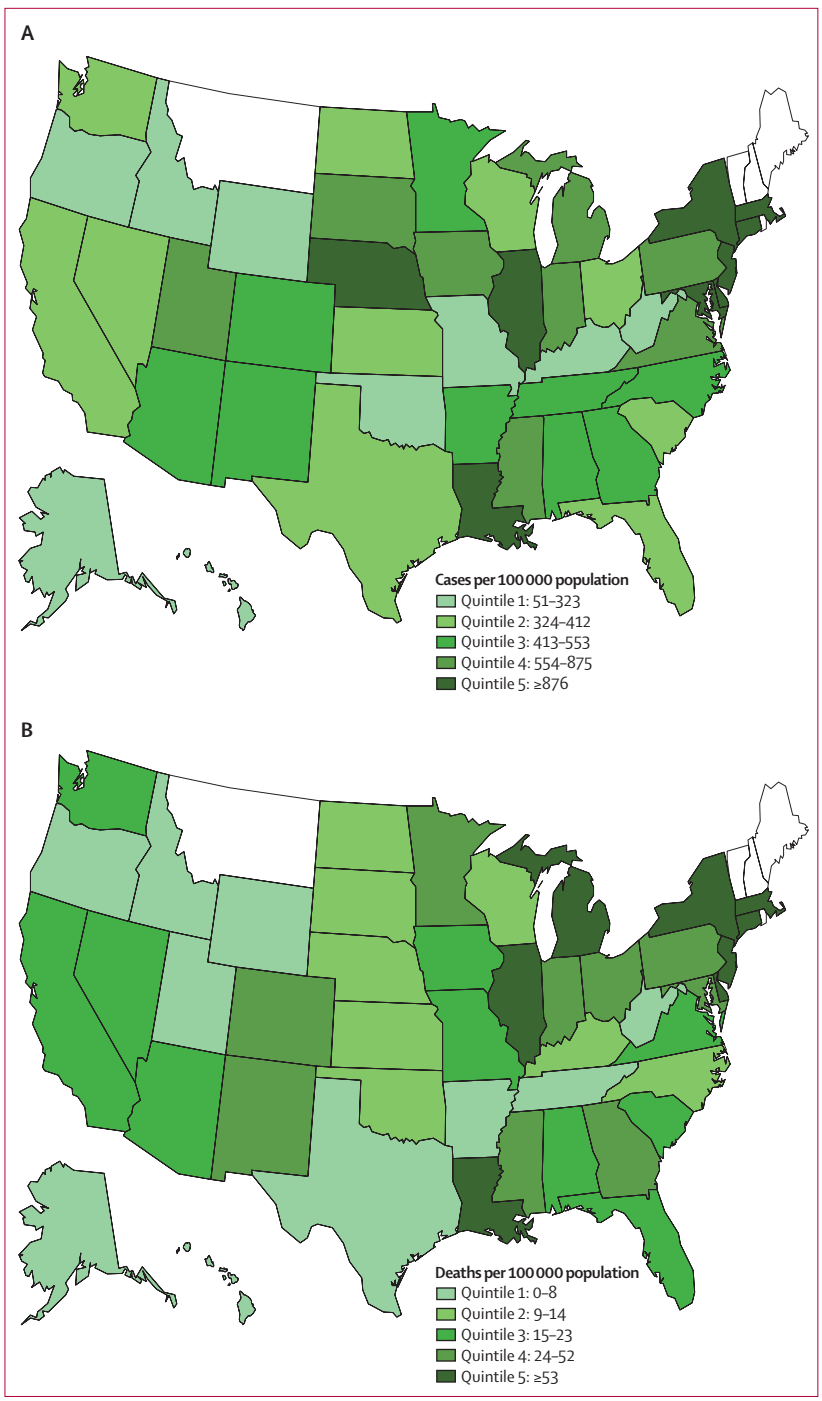

Figure 3: **Cumulative cases (A) and cumulative deaths (B) per 100 000 population, by state**
Data are in the US population as of June 15 (A) and June 30 (B), 2020.[16,18,19,21] States in white were not included in the sample.

Likelihood of SARS-CoV-2 seropositivity was lower among older people (odds ratio 0·8 [95% CI 0·7–0·9] for people aged 80 years or older *vs* people aged 45–64 years), but did not differ by sex (1·0 [0·9–1·1] for women *vs* men). In age-adjusted and sex-adjusted models, neighbourhood racial and ethnic distribution, poverty level, dense urbanisation, population density, and percentage change in workplace visits in early March, 2020, were all strongly associated with seropositivity (figure 4).

Discussion

In our analysis of seroprevalence of SARS-CoV-2 spike protein receptor binding antibodies from a nationwide representative sample of patients receiving dialysis, we find that despite the USA contemporaneously leading the world in the numbers of diagnosed cases, overall, fewer than 10% of US adults had evidence of seroconversion in July, 2020. A vast majority of US adults, including people receiving dialysis who are among the highest risk for mortality upon contracting SARS-CoV-2,[34] do not have evidence of exposure or immune response. Furthermore, we find increased likelihood of SARS-CoV-2 seropositivity in residents of predominantly Black and Hispanic neighbourhoods (two to three times higher), poorer areas (two times higher), and the most densely populated areas (ten times higher). Early reduction in community mobility in March, 2020, was associated with 60% lower likelihood of individual-level seroconversion by July that year.

Unlike most published estimates of SARS-CoV-2 seroprevalence from the USA,[8,10,11] patients included in our study sample had antibodies measured from blood collected as part of routine medical care. Thus, our prevalence estimates should not be subject to selection bias due to presence versus absence of symptoms, availability of testing materials, local or regional testing strategies, geography, income, educational attainment, language proficiency, immigration status, mobility, anxiety, fear, or other factors. Moreover, since end-stage kidney disease qualifies affected patients for Medicare insurance, and since end-stage kidney disease disproportionately affects Black, Hispanic, and other disadvantaged populations,[12,35,36] we are able to determine—with a high level of precision—differences in seroprevalence among patient groups within and across regions of the USA. Of the two larger seroprevalence surveys published from the USA thus far, one was confined to New York state (n=15 101), employed a convenience sampling technique at grocery stores, and relied on a microsphere immunoassay with lower sensitivity.[10] The second, the Centers for Disease Control and Prevention (CDC) Six Sites study (n=11 933), used remainder plasma from people getting testing for undefined clinical indications, and did not have detailed sociodemographic information about the tested people.[11]

Uncertainty exists as to whether seroprevalence estimates in the dialysis population can be extrapolated to the US population more broadly. A recent analysis of SARS-CoV-2 IgG antibodies in two dialysis units in London, UK, reported seroprevalence of 36%, higher than in healthy blood donors (15%) but lower than in healthcare workers (45%) sampled within a similar time frame.[37] Our data might overestimate overall seroprevalence in

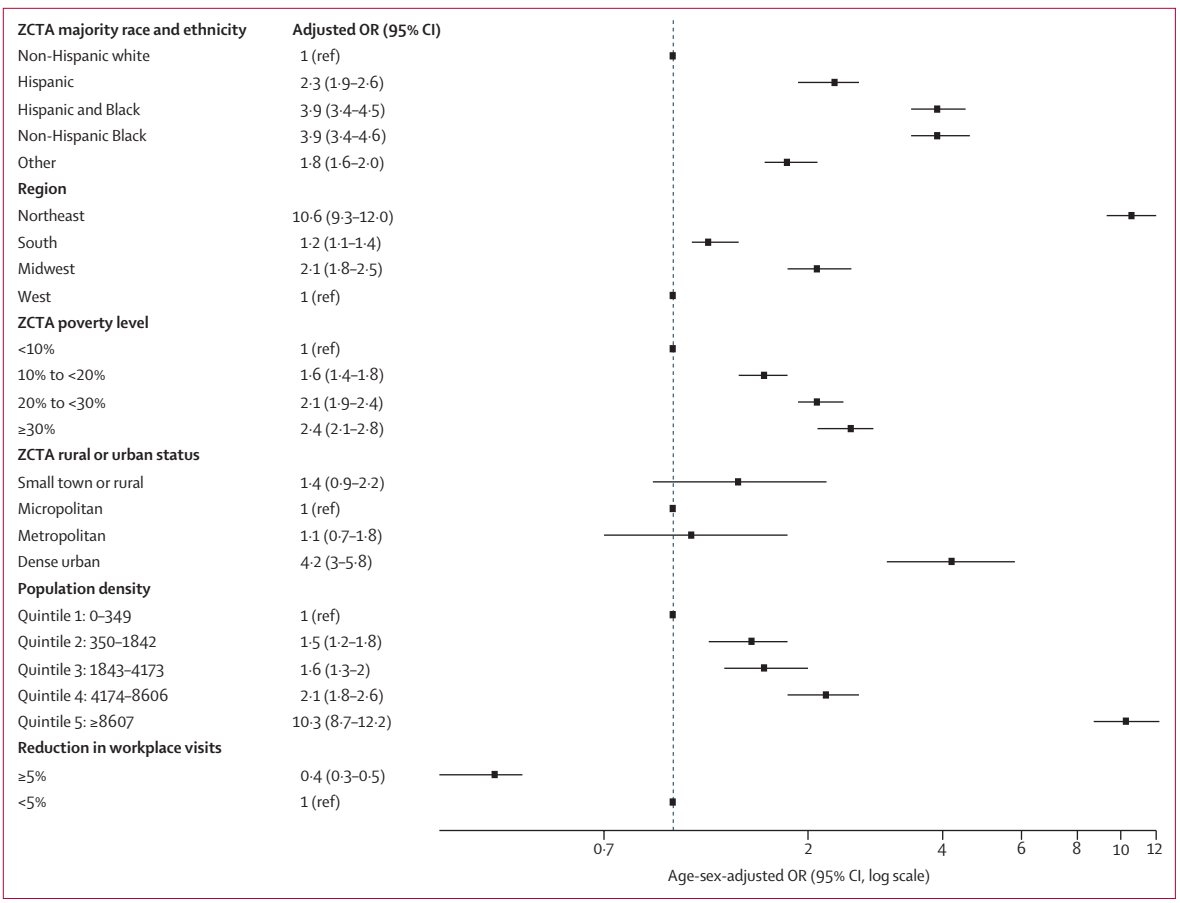

Figure 4: **Forest plot for odds of SARS-CoV-2 seropositivity**
All variables are at a neighbourhood (ie, ZCTA) level, except for reduction in workplace visits, which is at a county level, and are modelled separately, accounting for age and sex. Poverty level is defined as percentage of people living below the federal poverty level in the ZCTA. Population density quintiles are derived from the ZCTA (median 2884 people per square mile [IQR 603–6800]). Reductions in workplace visits were measured during the first 2 weeks of March, 2020, compared with a baseline in January–February, 2020. OR=odds ratio. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. ZCTA=ZIP code tabulation area.

the general population since patients on dialysis are disproportionately from racial and ethnic minorities;[38,39] for example, Black Americans have a nearly four-times higher risk of end-stage kidney disease than white Americans.[12] Moreover, the process of undergoing in-centre haemodialysis might include the use of public or non-public shared transportation to and from the facility, and 10–12 h of care delivered in indoor facilities.

Conversely, these data might underestimate overall seroprevalence in the general population. Patients receiving dialysis are less likely to be employed[40] and more likely to restrict their mobility and social activity due to advanced age and frailty;[41] therefore, they might have fewer opportunities to acquire the infection, particularly from asymptomatic individuals. Extrapolating from multiple prospective hepatitis B immunisation studies—in which 50–75% of vaccinated patients receiving dialysis mounted a response compared with 95% or more people from the general population—patients receiving dialysis might mount a weaker immune response and thus be less likely to seroconvert.[42] Finally, patients receiving dialysis might have been more likely to die or have been hospitalised due to complications of SARS-CoV-2 infection. If so, these patients would not have been present for testing in the dialysis facilities, creating a survival bias and yielding lower estimates of exposure.

Nonetheless, the ten-times difference we observed between diagnosed cases per 100 000 population and our estimates of seropositive people per 100 000 has been similarly reported in studies from New York,[10] the CDC Six Sites study,[11] and in a population-representative analysis from Geneva.[26] Thus, our findings comport with other seroprevalence estimates. We confirm that as in other studies from COVID-19 hotspots,[1,26,43] a minority of the population has evidence of exposure and immune response, and a vast majority, including people at high risk for mortality (ie, the population on dialysis), remain vulnerable. In fact, even if the seroprevalence estimates derived from the US dialysis population overestimated true seroprevalence in the overall US adult population, our data nonetheless support that fewer than 10% of the US population has seroconverted as of July, 2020, and

herd immunity remains out of reach, as has been the conclusion from large international surveys from the UK[44] and Spain,[1] where intense outbreaks of COVID-19 occurred during the spring and summer of 2020.

Furthermore, the seroprevalence differences captured by region, age, sex, and community-level risk factors (ie, internal comparisons) are expected to be similar in the US dialysis and US general adult population. Our study provides convincing evidence that the COVID-19 pandemic has dramatically amplified existing health disparities. Data from the CDC highlighting SARS-CoV-2 health disparities evaluate hospitalisations and deaths by race and ethnicity,[45,46] calling into question whether Black and Hispanic populations are experiencing more severe illness versus facing higher likelihoods of exposure. Some US state dashboards also report higher cumulative cases among Black and Hispanic people compared with non-Hispanic white people,[47] but none have as precisely quantified differences on a national level.

Neighbourhood poverty and population density were also highly correlated with seroprevalence, with a possible threshold effect for population density, such that there was a ten-times higher risk in the highest density ZCTAs (>8607 people per square mile). Population density is recognised as a crucial factor, driving the spread in metropolitan areas, in confined spaces (eg, the *Diamond Princess* cruise ship), large gatherings (eg, the New Orleans' Mardi Gras),[48,49] and in populous regions across the world.[50] Rocklöv and Sjödin suggest that the basic reproduction number (R_0) of SARS-CoV-2 increases linearly with population density.[51] Our data also show slightly lower likelihood of seropositivity among older people, as was seen in a recent report from Geneva[26] and attributed to better adherence to physical distancing measures by the authors. A higher competing risk from hospitalisations or mortality after SARS-CoV-2 exposure might be a larger contributing factor in the observed lower seroprevalence in older compared with younger age groups.

In addition to providing an overall estimate of SARS-CoV-2 seroprevalence and quantifying differences by patient and community characteristics, our study puts forth a viable surveillance strategy for SARS-CoV-2 spread in the USA. WHO and other experts[13,52] advocate for repeated cross-sectional analyses of seroprevalence as a disease tracking system able to most completely measure the true incidence of SARS-CoV-2, since these can more likely capture incidence of exposure in both symptomatic and asymptomatic individuals. In fact, we observed substantial heterogeneity in the correlation between seroprevalence and other measures of SARS-CoV-2 that are currently being used—with the exception of deaths per 100 000, which are a late outcome[53]—supporting the use of rapidly instituted seroprevalence surveys as a complementary surveillance tool. Additional public health implications of seroprevalence surveys include assessing testing adequacy. For example, in states where the difference between seropositive and diagnosed cases is decreasing over time, testing capacity is likely to be increasing. Furthermore, following seroconversion rates over time can presage hospitalisations and intensive care unit stays, since the time between exposure and seroconversion is relatively short (median 10 days),[26] and can therefore facilitate resource allocation. Finally, as we show by assessing community mobility restrictions, seroprevalence surveys can measure the effects of interventions to treat or prevent infection with SARS-CoV-2.[13] Repeated serological surveys, if done in a community setting, would require extensive resources and yet remain subject to selection bias. However recurring monthly testing of remainder plasma of randomly selected sets of people—as is practically feasible in patients receiving dialysis—can serve as a representative surveillance system in the USA, with minimal phlebotomy or infrastructure requirement, and as our data show, include traditionally under-represented and socially disadvantaged groups.

This analysis has numerous strengths. We used a highly specific and sensitive immunoassay, one which has been robustly linked to SARS-CoV-2 exposure.[13,25,54,55] The study sample was highly representative of the US dialysis population and, as noted, we used remainder plasma from specimens used in routine clinical care. The sample size and sampling scheme allowed us to estimate with precision prevalence across several patient characteristics. Moreover, linking to US Census and other publicly available data sources assembled during the pandemic provides valuable context when considering the implications of these data to the general population. There are also several important limitations. As noted previously, it is plausible that seroprevalence estimates from the US dialysis population overestimate seroprevalence in the US adult population. We do not have patient-level data on symptoms nor nasal swab testing results, and thus cannot test whether the likelihood of seroconversion differs in patients receiving dialysis from generally healthy adults, although preliminary data from London, UK, suggest no differences.[37] We also do not have patient-level data on health status, employment status, income, household size, living space, and other sociodemographic factors, and so relied on neighbourhood proxies for some of these domains. Dialysis units are more often located in urban areas, and thus we have under-representation of rural areas. Finally, while large, our study was designed for precise regional, not state-level or county-level, estimates.

In conclusion, we present SARS-CoV-2 seroprevalence data in a broadly representative sample of patients receiving dialysis across the USA and show striking differences in seroprevalence by several patient characteristics, with higher seroprevalence in younger patients, Black and Hispanic patients, and patients living in poorer and majority-minority neighbourhoods. These data can help to inform surveillance and management strategies during the next phase of the pandemic. Serial sampling of dialysis

remainder plasma should be used to determine trends in disease prevalence and the effect of various strategies being implemented around the USA to reduce the burden of COVID-19 on the general population.

Contributors

SA assisted with data cleaning and analysis planning, and manuscript writing. MM-R developed the analysis plan, generated census data tables, supervised data analysis, and contributed to manuscript writing. JH undertook data cleaning and analysis, including linkage to external data and figure generation, and contributed to manuscript writing. JB undertook sample processing and data preparation and contributed to manuscript writing. RK selected seroprevalence testing, supervised sample processing, and contributed to manuscript writing. PB co-conceived the study, secured seroprevalence testing, and supervised sample processing and data preparation. JP supervised the study analysis plan, identified relevant external data, contributed to data interpretation, and supervised manuscript writing. GMC co-conceived the study, supervised the study analysis plan, and co-wrote the manuscript.

Declaration of interests

JB, RK and PB are employed by Ascend Clinical Laboratories. GMC is on the Board of Directors of Satellite Healthcare, a not-for-profit dialysis organisation. All remaining authors declare no competing interests.

Data sharing

De-identified cross-sectional data from the analysis can be made available after authors' review of request and might require compilation of specific categories (eg, at the older age groups) to protect patient privacy.

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