

Predictors of Test Positivity, Mortality, and Seropositivity during the Early Coronavirus Disease Epidemic, Orange County, California, USA

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We conducted a detailed analysis of coronavirus disease in a large population center in southern California, USA (Orange County, population 3.2 million), to determine heterogeneity in risks for infection, test positivity, and death. We used a combination of datasets, including a population-representative seroprevalence survey, to assess the actual burden of disease and testing intensity, test positivity, and mortality. In the first month of the local epidemic (March 2020), case incidence clustered in high-income areas. This pattern quickly shifted, and cases next clustered in much higher rates in the north-central area of the county, which has a lower socioeconomic status. Beginning in April 2020, a concentration of reported cases, test positivity, testing intensity, and seropositivity in a north-central area persisted. At the individual level, several factors (e.g., age, race or ethnicity, and ZIP codes with low educational attainment) strongly affected risk for seropositivity and death.

In late 2019, an epidemic of coronavirus disease (COVID-19), a respiratory disease caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in Wuhan, China, and rapidly spread worldwide. COVID-19 has manifested in different ways across social, economic, and demographic groups, with regard to apparent risk for infection, disease severity, and death (1–3). The elderly and those with underlying conditions are at the highest risk

for severe disease (4). Many hospitalized patients require supplemental oxygen or ventilators (5), and a high mortality rate occurs among those who are hospitalized (6). In many places, healthcare facilities have been overwhelmed by a surge in cases and have had an insufficient supply of needed ventilators and intensive care unit beds, resulting in massive illness and death (7,8). Availability of tests and operational barriers were limiting factors for diagnosis in parts of the United States during the early months of the pandemic (9).

California is the most populous state in the United States, and it has an estimated 39.5 million inhabitants. Orange County (OC) is a coastal county in California and the sixth most populous county in the country, with an estimated 3.2 million inhabitants. The first confirmed case in California (the third US case) was reported from OC on January 25 (10). On January 30, the World Health Organization declared a global health emergency (11), and on January 31, the United States likewise declared a public health emergency (12). On February 26, local (i.e., community) transmission was first confirmed in the United States in northern California (13). Several counties by this time had already declared local public health emergencies, including Santa Clara (14), San Diego (15), and Orange (16) Counties, as had the city of San Francisco (17). By mid-March, an apparent surge in locally transmitted cases was occurring in OC (Figure 1) and other counties in California, triggering emergency shelter-in-place orders by the governor and the county health officer at the Orange County Health Care Agency (OCHCA), prohibiting public or private gatherings and also leading to school and business closures (18). Although many businesses were closed

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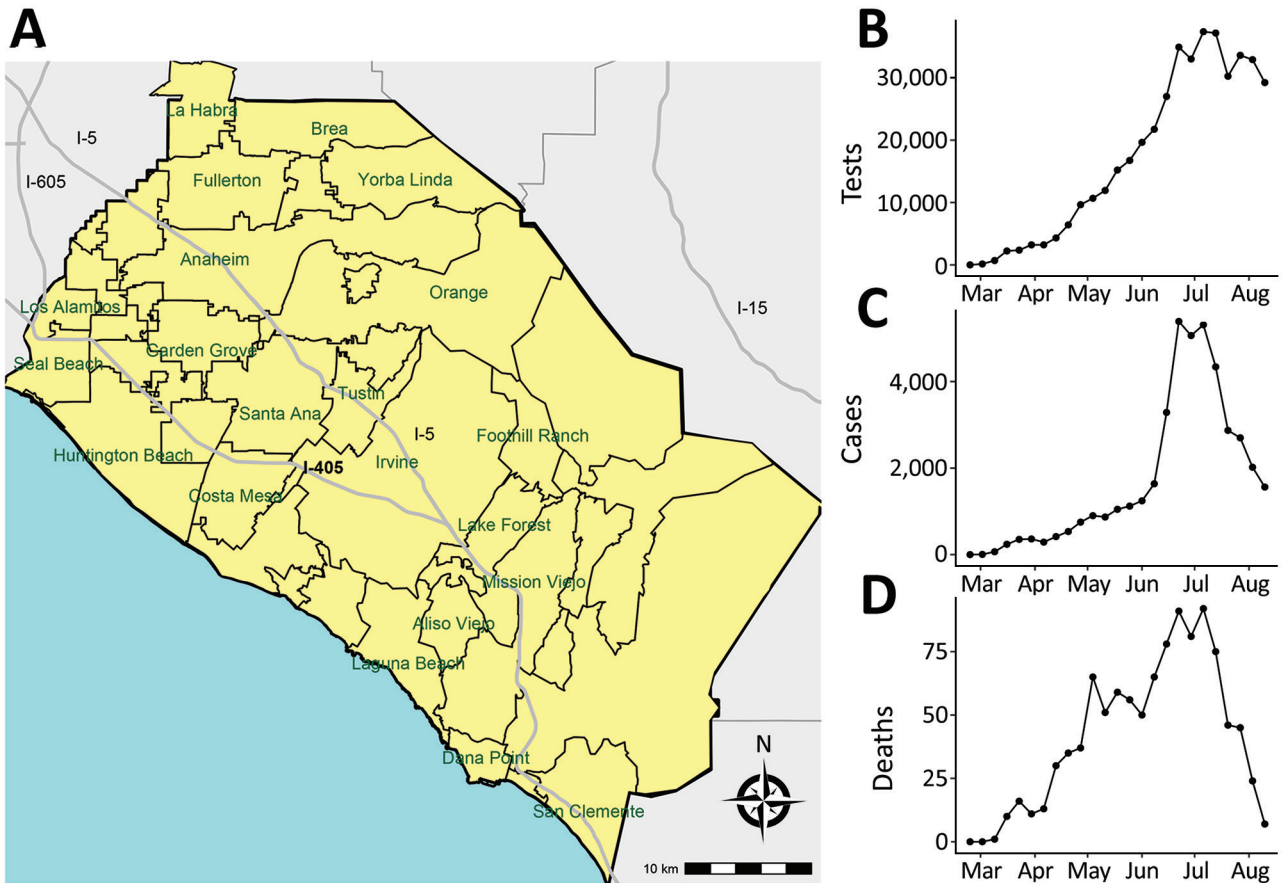


Figure 1. Locations of major cities (A), number of weekly severe acute respiratory syndrome coronavirus 2 tests (B), weekly confirmed coronavirus disease cases (C), and weekly coronavirus disease deaths (D), Orange County, California, USA, July–August 2020.

at this time, the mandated social distancing measures had exceptions in place for persons working in essential jobs, which was broadly defined and included medical professionals, food providers, delivery agencies, public officials, construction contractors, and building laborers (19). The social and economic characteristics of persons working essential jobs differs from the overall population (20).

Almost half of OC residents >5 years of age speak a language other than English at home. In

addition, many within the Hispanic/Latinx and Asian communities of OC live below the poverty level (17.9% and 12.0%, respectively) and face challenges in education, household income, access to healthcare, health disparities, and life expectancy (21,22). The relatively small land area, high population density, and diverse population of OC provides a unique opportunity to explore potentially important social, economic, and demographic correlates of COVID-19 epidemiology.

Table 1. Global Moran's *I* statistics for reported coronavirus disease case incidence, test positivity, and testing intensity for each month of the study period, Orange County, California, USA, March–August 2020*

Month	Case incidence		Test positivity		Testing intensity	
	<i>I</i>	p value	<i>I</i>	p value	<i>I</i>	p value
March	0.238	0.002	0.059	0.150	0.448	0.001
April	0.168	0.012	0.271	0.001	0.022	0.257
May	0.558	0.001	0.492	0.001	0.345	0.001
June	0.606	0.001	0.552	0.001	0.469	0.001
July	0.591	0.001	0.500	0.001	0.408	0.001
August	0.603	0.001	0.472	0.001	0.185	0.002

*The Moran's *I* statistic indicates the degree of spatial clustering whereas the simulated p-value gives an indication of statistical significance. Moran's *I* values roughly range from -1 to 1, with 1 indicating complete spatial clustering (i.e., all areas with high values are neighboring other areas with high values) and -1 indicating complete spatial dispersion (with high value areas always neighboring low value areas).

We conducted a detailed spatiotemporal epidemiologic analysis of COVID-19 in OC during March 1–August 16, 2020. We drew from reported tests and

mortality data from the county health agency. Given that passively detected cases are prone toward bias, in July 2020 we also conducted a seroprevalence

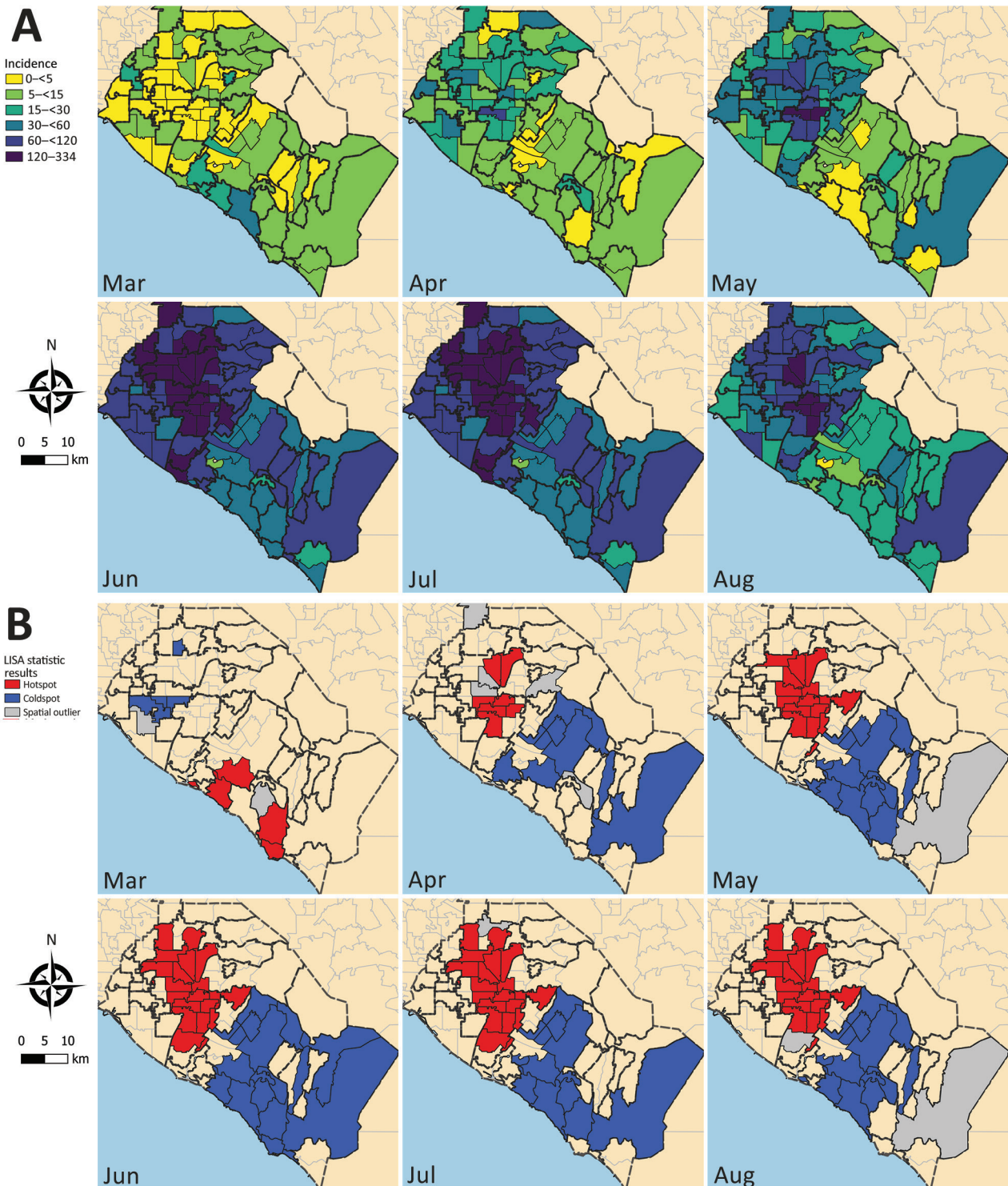


Figure 2. Coronavirus disease incidence, Orange County, California, USA, July–August 2020. A) Reported case incidence of coronavirus by month. Case incidence is calculated as the number of cases per 100,000 persons per week. B) Results from tests of statistical clustering (based on LISA statistics [24]). LISA, local indicators of spatial autocorrelation.

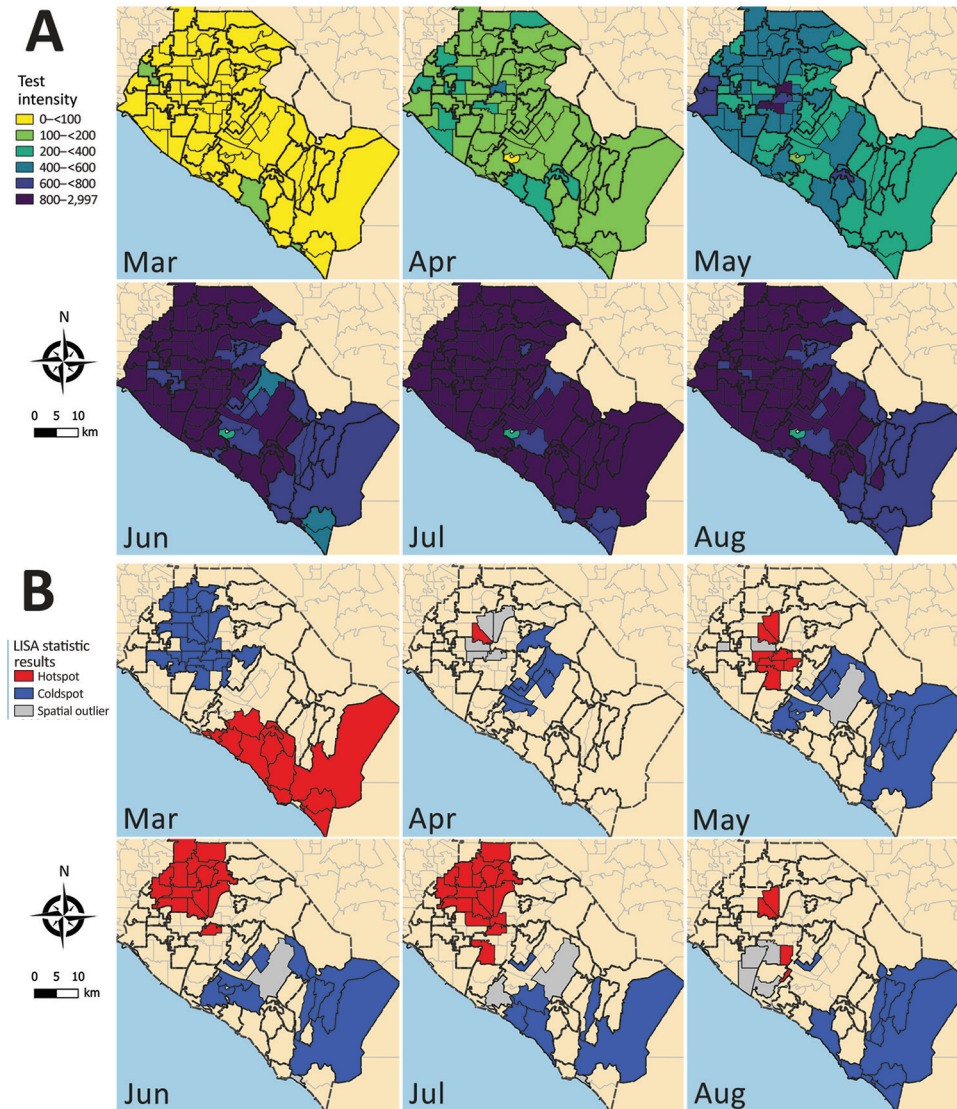


Figure 3. Severe acute respiratory syndrome coronavirus 2 test intensity, Orange County, California, USA, July–August 2020. A) Test intensity by month, calculated as the number of tests per 100,000 persons per week at the ZIP code level. B) Results from tests of statistical clustering (based on LISA statistics [24]). LISA, local indicators of spatial autocorrelation.

survey to assess the actual burden of disease in the county. We use both datasets to compare predictors of test positivity, death, and seropositivity over the first 6 months of the epidemic.

Methods

Data

Case and Mortality Data

Case data were provided by OCHCA and consisted of individual-level records of all negative and positive PCR tests conducted throughout the county during March 1–August 16, 2020; this date aligns with our cross-sectional seroprevalence survey completed on August 16. OCHCA receives testing data from the California Reportable Disease Information Exchange (CalREDIE), an infectious

disease surveillance system implemented by the California Department of Public Health (14). The data include test date, age, sex, race, ethnicity, and ZIP code of the person taking the test. For persons who had repeat PCR testing after testing positive, we included only the first positive diagnosis in our analyses; we retained multiple negative test results. Mortality data were also provided by OCHCA (also through CalREDIE) and consisted of individual-level records of deaths attributed to COVID-19. OCHCA likewise provided data on the number and percentage of hospital beds that were occupied by COVID-19 patients over time.

Seroprevalence Data

Participants in the serologic survey were recruited using a proprietary database (Appendix, <https://wwwnc.cdc.gov/EID/article/27/10/21-0103-App1>).

pdf), which is intended to be representative of the age, income, and racial and ethnic diversity of OC. We recruited 1 participant per household (by email or phone) to participate in a survey on their thoughts and opinions regarding COVID-19. The survey included questions on sociodemographics, occupation, social activities, any illness or symptoms in the past few months, and whether the person had been diagnosed with COVID-19. After completing this portion of the survey, each eligible participant was asked if they would be willing to participate in a drive-through blood test for SARS-CoV-2 antibodies. Eligibility for antibody testing was restricted to a quota sample designed to be demographically representative of the county as a whole. Recruitment to the antibody test was delayed to the end of the questionnaire to avoid biasing the serologic survey toward persons who believed that they were infected with SARS-CoV-2. A total of 10 field sites for

drive-through blood tests were dispersed throughout OC to minimize driving distances for participants. This cross-sectional survey was conducted July 10–August 16, 2020. The seroprevalence study design and overall findings for OC have been described previously (23).

Serologic Test Data

We used a coronavirus antigen microarray to classify participants from the serologic survey as seropositive or seronegative. The array tests for IgG and IgM and contains 12 antigens from SARS-CoV-2 (R.R. de Assis et al., unpub. data, <https://doi.org/10.1101/2020.04.15.043364>).

ZIP Code–Level Sociodemographic Data

At the ZIP code level, we included median household income, the percentage of adults >25 years of

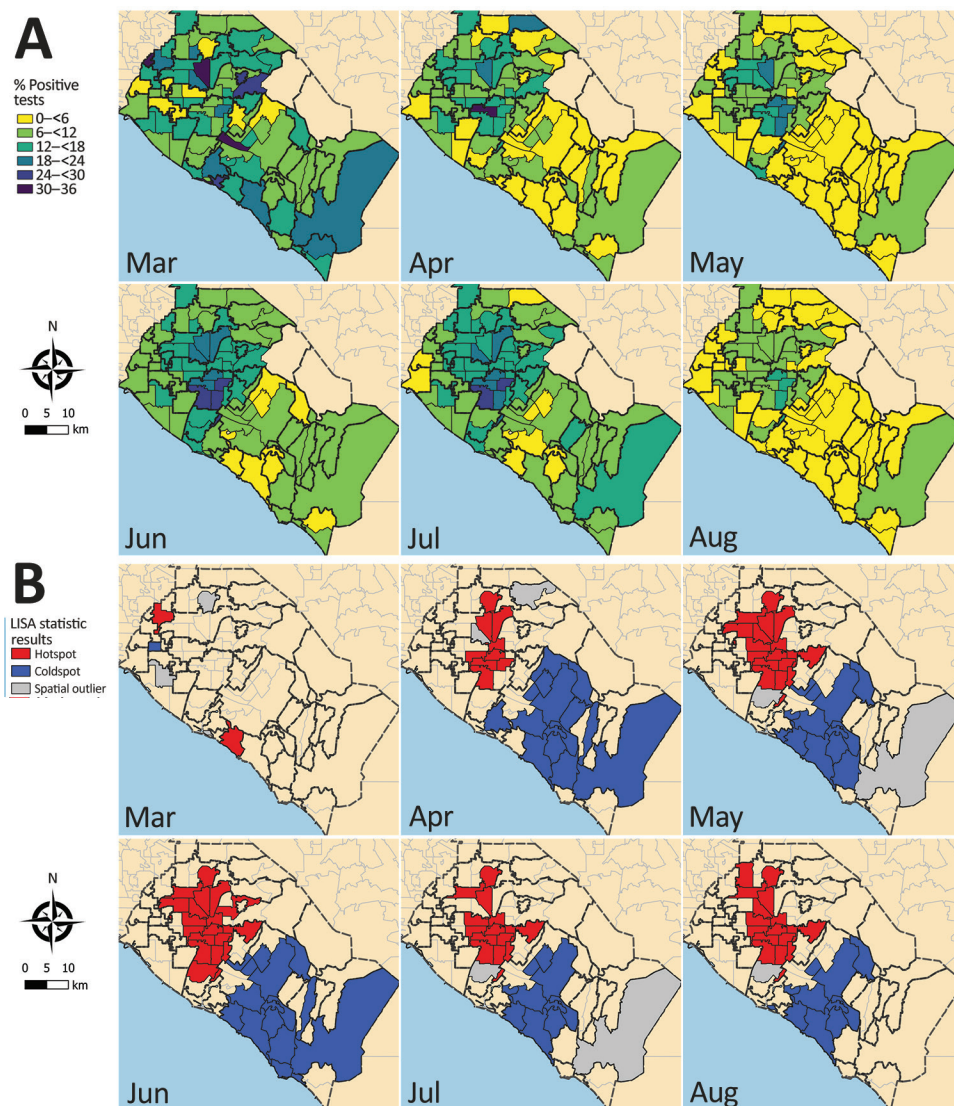


Figure 4. Severe acute respiratory syndrome coronavirus 2 test positivity, Orange County, California, USA, July–August 2020. A) Test positivity at ZIP code level by month. B) Results from tests of statistical clustering (based on LISA statistics [24]). LISA, local indicators of spatial autocorrelation.

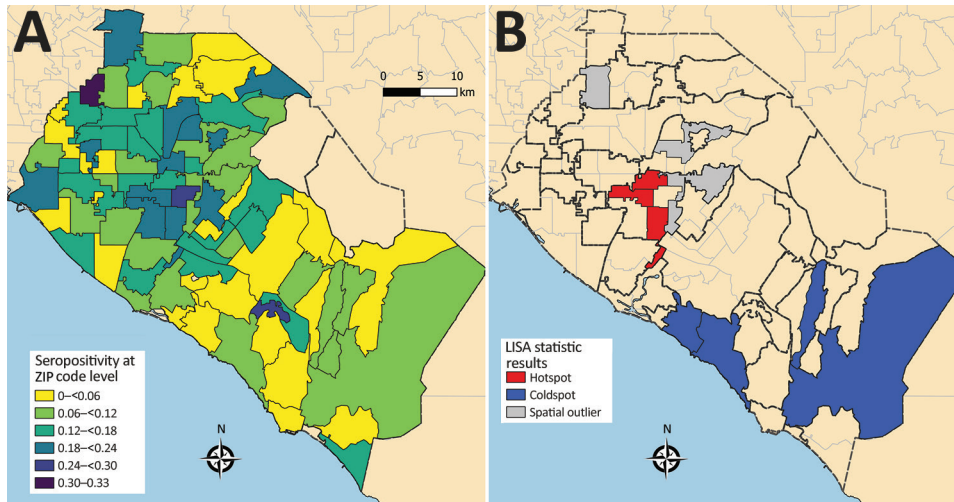


Figure 5. Severe acute respiratory syndrome coronavirus 2 seropositivity, Orange County, California, USA, July–August 2020. A) Seropositivity at ZIP code level. B) Results from tests of statistical clustering (based on LISA statistics [24]). LISA, local indicators of spatial autocorrelation.

age with at least a bachelor's degree, the percentage of adults who had health insurance in the previous 5 years, the number of persons per square kilometer, and the percentage of houses with >1 person per room. These data came from the 2018 American Community Survey (21).

Analysis

Descriptive Spatiotemporal Data Analysis

We aggregated reported cases and number of tests at the ZIP code level and by week. We included 86 ZIP codes in the analysis. For plotting cases on OC maps, we further aggregated the data by month (March–August). We calculated and mapped case incidence as positive cases per 100,000 population per week, testing intensity as total number of tests per 100,000 persons per week, and test positivity as the percentage of positive tests for each month.

We conducted formal testing of spatial autocorrelation by using the global Moran's *I* statistic and spatial correlograms. We then used local clustering statistics (local indicators of spatial autocorrelation [LISA] [24]) to visualize the location of clusters. We ran all tests for case incidence, test positivity, and test intensity. We also used LISA statistics to map and assess seropositivity.

Relational Analysis of COVID-19 Test Positivity, Risk for Death, and Seropositivity

We used logistic regressions to explore geographic, demographic, economic, and epidemiologic predictors of the odds of testing positive for COVID-19, of dying from COVID-19, and of being seropositive for SARS-CoV-2 antibodies. Predictors in our

models were age group, sex, and race or ethnicity at the individual level (Appendix Table 1). ZIP code-level predictors were median household income, the percentage of adults >25 years of age with at least a bachelor's degree, the percentage of adults who had health insurance in the previous 5 years, population density (persons/km²), and house crowding (the percentage of houses with >1 person per room).

We tested several specifications of the models. Through preliminary exploratory analyses, we noted that the first cases were reported from coastal ZIP codes but that this pattern had shifted inland over time. The best fitting model included a smoothed interaction term for time, coded by day (Appendix Table 1), and median household income at the ZIP code level.

We included the same predictors in the model for risk for death, except for the interaction between time and median household income, which did not improve model performance. Given reports of increased mortality rates related to hospital bed shortages, we also included as a predictor the number of intensive care unit beds occupied by suspected or confirmed COVID-19 patients on the day that any person tested positive for SARS-CoV-2. For all model results, we calculated model-adjusted odds ratios (aORs) with 95% CIs.

Software

We created maps by using QGIS 3.4.9 (<https://qgis.org>). We conducted tests for spatial autocorrelation by using GeoDa 1.14.0 (<https://geodacenter.github.io>) and all other analyses by using R statistical software 3.5.2 (R Project for Statistical Computing, <https://www.r-project.org>).

Table 2. Generalized additive logistic regression results for odds of testing positive for SARS-CoV-2, Orange County, California, USA, March–August 2020*

Characteristic	No. (%)		Adjusted odds ratio† (95% CI)
	SARS-CoV-2 positive	Total tests	
Age group, y			
0–4	487 (1.3)	4,835 (1.53)	Referent
5–9	490 (1.31)	3,855 (1.22)	1.62 (1.41–1.86)
10–14	855 (2.28)	5,064 (1.6)	2.26 (2.00–2.56)
15–19	2,124 (5.66)	13,814 (4.36)	2.32 (2.08–2.58)
20–24	4,646 (12.37)	31,727 (10.02)	2.04 (1.85–2.26)
25–29	4,640 (12.36)	34,695 (10.96)	1.74 (1.57–1.93)
30–34	3,791 (10.1)	29,900 (9.44)	1.62 (1.46–1.79)
35–39	3,291 (8.77)	25,776 (8.14)	1.67 (1.5–1.85)
40–49	5,950 (15.85)	44,835 (14.16)	1.75 (1.58–1.93)
50–59	5,747 (15.31)	48,502 (15.32)	1.54 (1.39–1.71)
60–69	3,045 (8.11)	36,294 (11.46)	1.04 (0.94–1.16)
70–79	1,404 (3.74)	22,190 (7.01)	0.77 (0.69–0.86)
>80	1,076 (2.87)	15,139 (4.78)	0.80 (0.72–0.9)
Sex			
F	19,076 (50.81)	173,723 (54.87)	Referent
M	18,470 (49.19)	142,903 (45.13)	1.20 (1.18–1.23)
Race or ethnicity			
White	12,195 (32.48)	63,050 (19.91)	Referent
Asian	1,573 (4.19)	13,858 (4.38)	0.55 (0.52–0.58)
Black	289 (0.77)	2,058 (0.65)	0.58 (0.51–0.65)
Hispanic	3,473 (9.25)	9,147 (2.89)	1.68 (1.6–1.76)
Native American	56 (0.15)	314 (0.1)	0.82 (0.62–1.09)
Pacific Islander	127 (0.34)	1,600 (0.51)	0.35 (0.29–0.42)
Unknown	19,833 (52.82)	226,599 (71.57)	0.32 (0.31–0.33)
% Persons with college degree in ZIP code			
1st quartile	20,665 (55.04)	120,279 (37.99)	Referent
2nd quartile	9,484 (25.26)	87,802 (27.73)	0.89 (0.77–1.03)
3rd quartile	4,560 (12.15)	64,604 (20.4)	0.70 (0.58–0.84)
4th quartile	2,837 (7.56)	43,941 (13.88)	0.68 (0.56–0.83)
% Persons with insurance in ZIP code			
1st quartile	19,749 (52.6)	111,798 (35.31)	Referent
2nd quartile	10,371 (27.62)	93,431 (29.51)	0.83 (0.73–0.95)
3rd quartile	3,824 (10.18)	53,201 (16.8)	0.67 (0.56–0.8)
4th quartile	3,602 (9.59)	58,196 (18.38)	0.58 (0.48–0.7)
Population density, × 1,000 persons/km ² ‡			0.97 (0.9–1.04)
House crowding			1.03 (1.02–1.04)

*Excludes the coefficients for ZIP code–level median income and time because of interaction between median income and time. A random intercept was included for ZIP code. The period covered in this analysis is March 1–August 16, 2020. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

†Adjusted for all covariates listed plus ZIP code estimated median income and time of test in days. Model intercept represents odds of a White female in the 0–4-y age group in a ZIP code in the first quartile of college degree and insured with the average population density. The odds of this person testing positive for SARS-CoV-2 is estimated to be 0.19 (95% CI 0.16–0.22).

‡Estimated percentage of population density in a person's ZIP code.

Ethics Considerations

This analysis constitutes a retrospective analysis of deidentified, anonymized epidemiologic records. Therefore, it is exempt from ethics review.

Results

A total of 597,922 tests were reported to OCHCA through August 16, 2020. After excluding repeated tests and those with incomplete data, 316,626 (53.0% of all records) persons were included in the test positivity analysis; 37,546 (12.0%) persons tested positive for COVID-19. A total of 42,383 persons with positive COVID-19 tests were included in the mortality analysis; 1,038 (2.5%) died from the disease. In the separate population-based serologic survey, 2,979 persons participated and 350 tested seropositive.

Spatial Patterns in Reported COVID-19 Cases, Testing Intensity, and Seropositivity

The tests for spatial autocorrelation indicated significant clustering in reported cases and testing intensity in the first month (March) of the local epidemic (Table 1; Appendix Figures 1, 2). Conversely, no detectable clustering of test positivity occurred in March (Table 1; Appendix Figure 3). The highest reported case incidence in March was along the central coast and southern portion of the county (Figure 2, panel A). The LISA statistics indicated statistically significant clustering of high-incidence ZIP codes in the central coast area (Figure 2, panel B). This clustering of case incidence overlaps with clustering of test intensity in March (Figure 3, panels A, B).

Clustering of reported cases and test positivity increased in magnitude in May (Table 1; Appendix Figures 1, 3). Although clustering in test intensity was high in March (Table 1; Appendix Figure 2), it decreased in May as access to testing spread throughout much of the county. Clustering in testing intensity increased again in June and July (centered on the hotspots in the north-central part of the county) (Figure 2, 4). By April, case incidence, testing intensity, and test positivity had all shifted to the north-central part of the county. ZIP code-level seropositivity also revealed a cluster in the north-central part of OC (Figure 5), especially in the city of Santa Ana (Figure 1).

Results from Generalized Additive Model Logistic Regression Analysis

Factors Associated with Testing Positive for SARS-CoV-2 Infection

Age was a strong predictor of testing positive. Persons in the 10–14- and 15–19-year age groups had

the highest odds of testing positive (both with ≈ 2.30 times the odds of testing positive compared with the 0–4 year age group) (Table 2; Figure 6). Men and boys had 1.20 times the odds of testing positive than women and girls (95% CI 1.18–1.23). Persons who identified as Hispanic or Latinx had 1.7 times the odds of testing positive (95% CI 1.60–1.76) than did non-Hispanic Whites, whereas Asian (aOR 0.55; 95% CI 0.52–0.58), Black (aOR 0.58; 95% CI 0.51–0.65), and Pacific Islander (aOR 0.35; 95% CI 0.29–0.42) persons had lower odds of testing positive than did non-Hispanic Whites. A large proportion of persons did not have attributable race or ethnicity data in the records (72% of all records through August 16). This unknown category includes persons who had no race or ethnicity categories recorded, those who had unknown or mixed listed for race or ethnicity, and those who listed multiple races.

ZIP code-level population density was not a significant predictor of testing positive (Table 2; Figure 6). However, education (percentage of adults >25 years

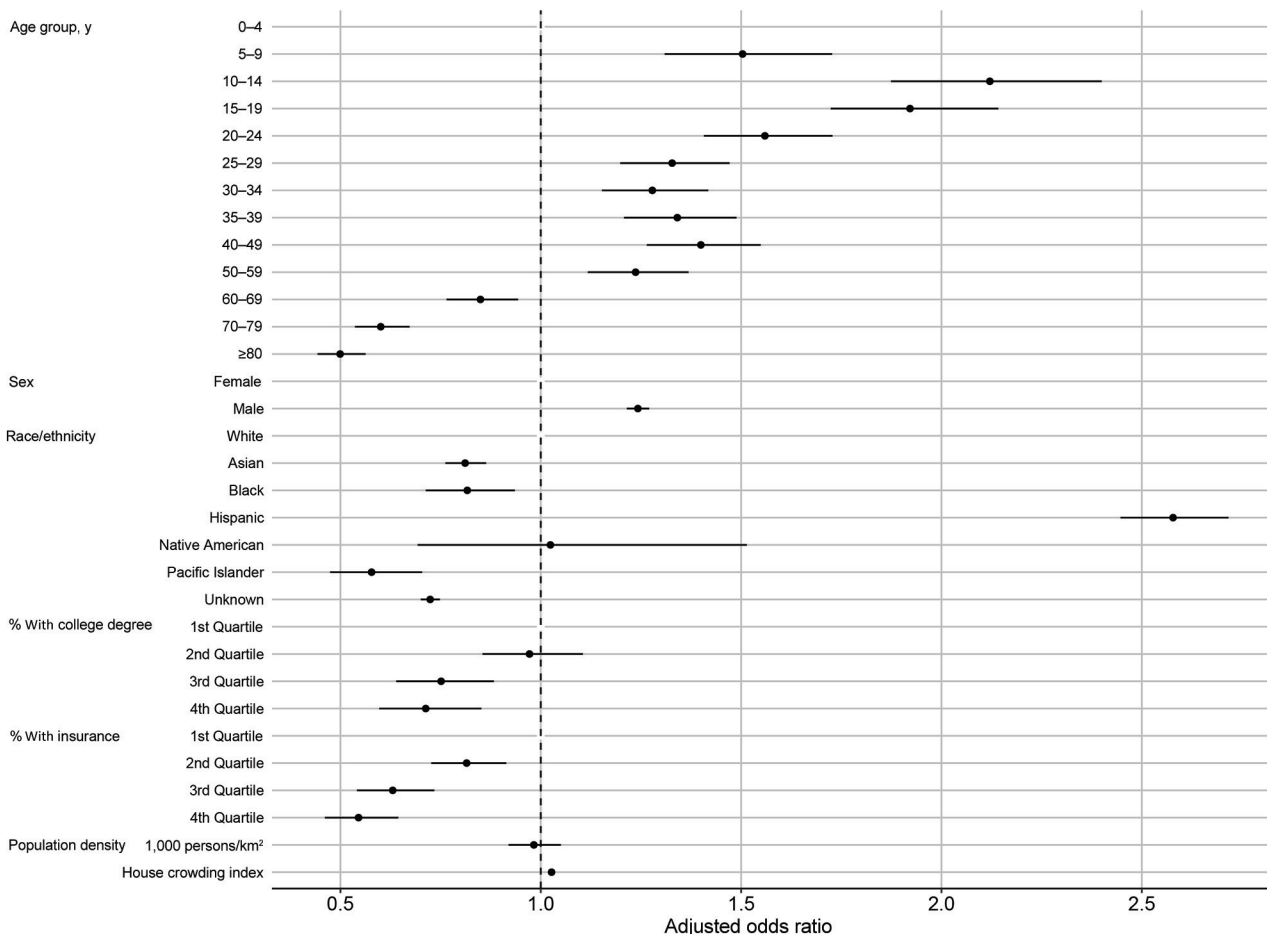


Figure 6. Model-adjusted odds ratios and 95% CIs from the logistic regression for odds of testing positive for severe acute respiratory syndrome coronavirus 2, Orange County, California, USA, July–August 2020. Corresponding data presented in Table 2.

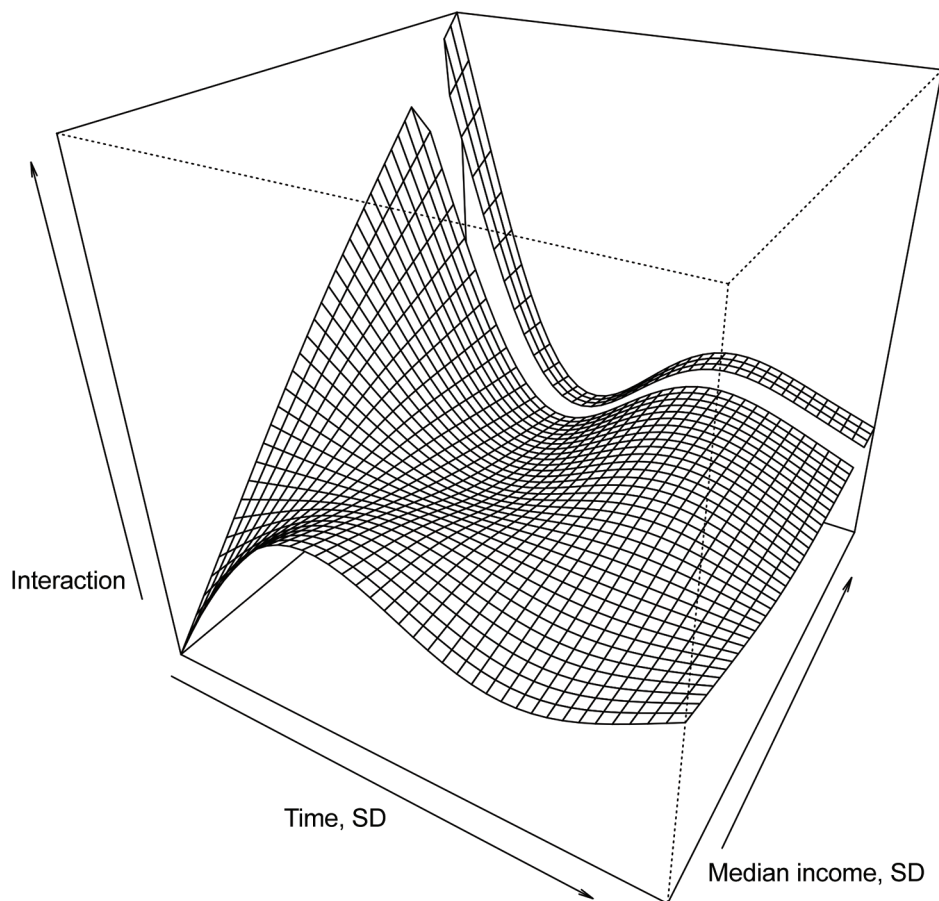


Figure 7. Three-dimensional plot of the smoothed interaction between ZIP code-level median household income and time as a predictor of testing positive for severe acute respiratory syndrome coronavirus 2, Orange County, California, USA, July–August 2020.

of age with at least a bachelor's degree), health insurance coverage (percentage of adults who had health insurance in the previous 5 years), median household income, and household crowding were all statistically significant predictors of testing positive. For example, persons who lived in ZIP codes with the highest education levels had 32% decreased odds of testing positive (aOR for the fourth quartile 0.68, 95% CI 0.56–0.83). In addition, the interaction between ZIP code-level median household income (Figure 7) indicates that persons from wealthier ZIP codes had increased risk for testing positive at the beginning of the epidemic in OC. However, this pattern quickly shifted, and persons from lower-income areas showed the highest odds of testing positive in subsequent months.

Factors Associated with Dying from COVID-19

For each increase in 10 years of age, we observed an associated 2.5-fold increase in the odds of death (aOR 2.56, 95% CI 2.45–2.67; Table 3; Figure 8). Infected men and boys were twice as likely to die from COVID-19 than were women and girls (aOR 2.00, 95% CI 1.73–2.31). Although persons who identified as

Asian were less likely to test positive for SARS-CoV-2 infection (Table 2), those who did test positive had higher odds of death. Compared with non-Hispanic Whites, this group had 54% increased odds of dying from COVID-19 (aOR 1.54, 95% CI 1.23–1.93).

Living in ZIP codes with high education levels and health insurance coverage was also predictive of mortality outcomes (Table 3; Figure 8). Persons who tested positive for COVID-19 and lived in ZIP codes with the highest levels of educational attainment had 49% lower odds of dying from COVID-19 (aOR for the fourth quartile 0.51, 95% CI 0.31–0.84). Persons who lived in ZIP codes with the highest levels of health insurance coverage had 21% lower odds of dying from COVID-19. ZIP code-level household crowding and the number of COVID-19 patients in hospital beds were both significant predictors of death. Risk for death from COVID-19 decreased over the study period.

Factors Associated with SARS-CoV-2 Seropositivity

ZIP code-level cumulative incidence was a significant predictor of individual-level seropositivity in

the absence of other ZIP code-level predictors. Every increase in 10% of the ZIP code cumulative incidence resulted in an approximately 50% increase in the odds that a person would be seropositive (Appendix Table 2).

ZIP code-level cumulative incidence was no longer a statistically significant predictor of seropositivity when other ZIP code-level predictors were added to the model (Table 4; Figure 9). In the full model (including all ZIP code-level covariates), median household income had a protective effect; persons coming from ZIP codes with higher median household income had lower odds of being seropositive for SARS-CoV-2 antibodies (aOR for every 1 SD increase 0.75, 95% CI 0.57–1.00).

We found no difference in age groups with regard to seropositivity. Although men and boys were more likely to test positive or to die from SARS-CoV-2 infection, they were less likely than women and girls to be seropositive (aOR 0.75, 95% CI 0.59–0.94). Hispanic and Latinx persons had 54% increased odds of being seropositive (aOR 1.54, 95% CI 1.17–2.03). Pacific

Islanders may also have had higher odds of being seropositive, but with small total numbers and broad 95% CIs (aOR 3.89, 95% CI 1.04–14.65); 3 of 12 Pacific Islanders tested were seropositive.

Discussion

Infectious disease data from passive case detection can be biased in various ways, including the well-documented challenge of uneven access to testing and diagnosis (25) and a general bias toward persons who are seeking clinical care for symptomatic disease. In our analysis of COVID-19 in OC, we used a rich set of complementary data that included those passively collected (e.g., reported cases and mortality records) and those from active screening (e.g., population-based serologic testing). Results indicate that, in the early days of the epidemic in OC, both testing intensity and test positivity were concentrated in wealthy and affluent areas along the central coast. After March, however, a large cluster of reported cases formed in lower-income north-central OC (especially the cities of Santa Ana and Anaheim)

Table 3. Logistic regression results for odds of dying from COVID-19 among persons who tested positive for SARS-CoV-2, Orange County, California, USA, March–August 2020*

Characteristic	No. (%)		Adjusted odds ratio (95% CI)†
	COVID-19 deaths, n = 1,038	Total cases, n = 42,383	
Age, decades			2.56 (2.45–2.67)
Sex			
F	450 (43.35)	21,694 (51.19)	Referent
M	588 (56.65)	20,689 (48.81)	2.00 (1.73–2.31)
Race or ethnicity			
White	345 (33.24)	6,390 (15.08)	Referent
Asian	186 (17.92)	1,963 (4.63)	1.54 (1.23–1.93)
Black	15 (1.45)	322 (0.76)	1.06 (0.56–2.02)
Hispanic	92 (8.86)	3,874 (9.14)	1.05 (0.79–1.38)
Native American	3 (0.29)	34 (0.08)	1.46 (0.46–4.58)
Pacific Islander	3 (0.29)	130 (0.31)	0.71 (0.22–2.26)
Unknown	394 (37.96)	29,670 (70)	0.47 (0.4–0.55)
% With college degree in ZIP code			
1st quartile	656 (63.2)	23,221 (54.79)	Referent
2nd quartile	190 (18.3)	10,223 (24.12)	0.67 (0.52–0.86)
3rd quartile	155 (14.93)	5,691 (13.43)	0.77 (0.54–1.08)
4th quartile	37 (3.56)	3,248 (7.66)	0.51 (0.31–0.84)
% With insurance in ZIP code			
1st quartile	566 (54.53)	21,989 (51.88)	Referent
2nd quartile	281 (27.07)	11,097 (26.18)	1.04 (0.83–1.29)
3rd quartile	123 (11.85)	5,185 (12.23)	1.36 (0.95–1.93)
4th quartile	68 (6.55)	4,112 (9.7)	0.79 (0.52–1.2)
Population density, × 1,000 persons/km ² ‡			0.83 (0.71–0.96)
House crowding index			1.04 (1.02–1.05)
Median income (SD)			0.86 (0.7–1.05)
Time (SD)			0.68 (0.62–0.75)
COVID-19 ICU patients (SD)§			1.18 (1.05–1.34)

*Values are no. (%) except where indicated. A random intercept was included for ZIP code. The period covered in this analysis is March 1–August 16, 2020. Total numbers of positive cases are larger than the total number reported in Table 2 because of more extensive data curation for mortality data than for general test data. More rows of data were dropped because of missing information (e.g., on age or sex) in the test positivity data than in the mortality data. COVID-19, coronavirus disease; ICU, intensive care unit; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

†Model intercept represents odds of death for a White female diagnosed with SARS-CoV-2 in the 0–4 years age group in a ZIP code in the first quartile of college degree and insured with the average population density in Orange County. The odds of this person testing dying from COVID-19 is estimated to be zero.

‡Estimated percentage of population density in a person's ZIP code.

§Percentage of hospital beds not being used by COVID-19 patients in Orange County.

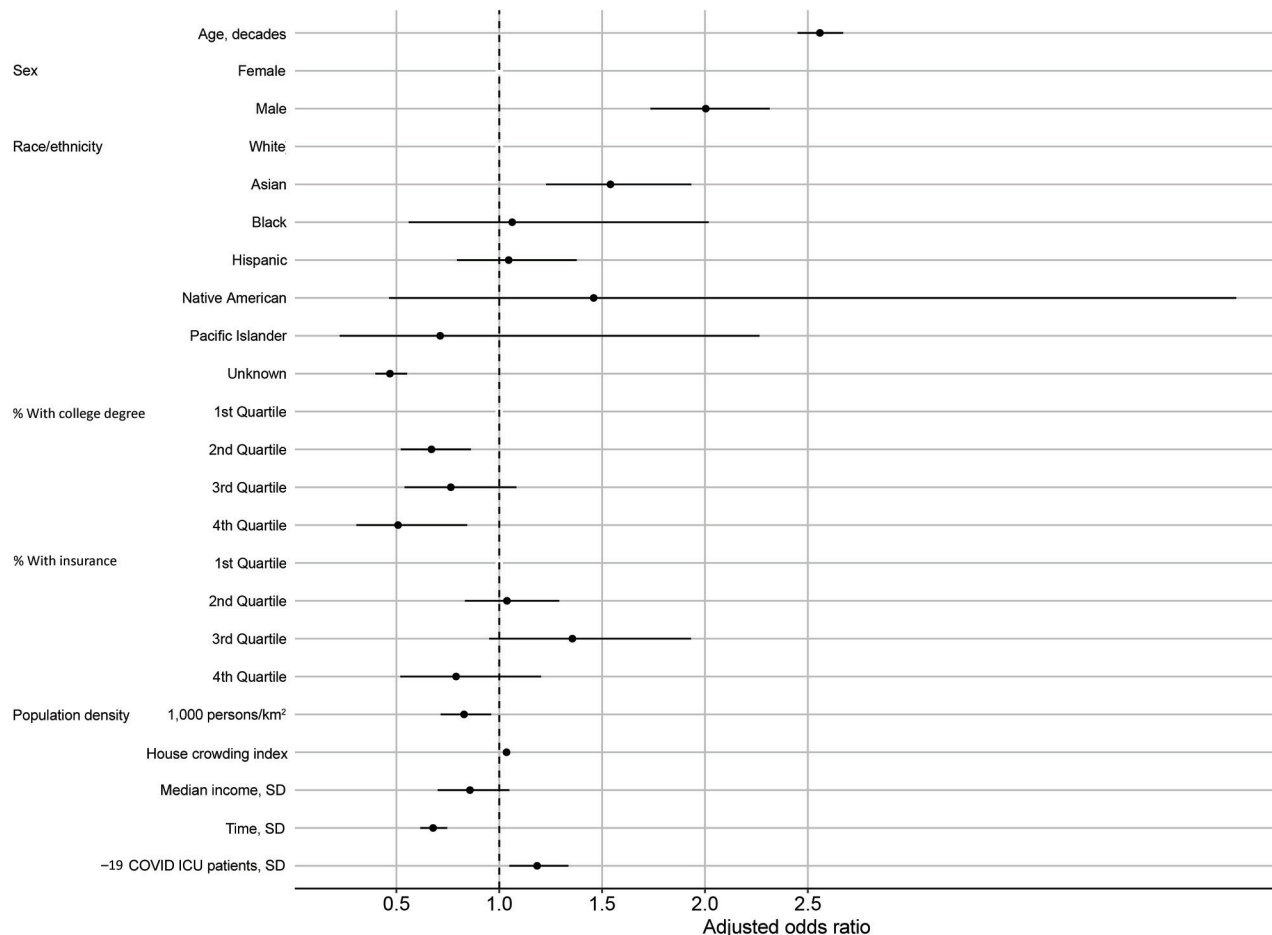


Figure 8. Model-adjusted odds ratios and 95% CIs from the logistic regression for the odds of dying from COVID-19, Orange County, California, USA, July–August 2020. Corresponding data presented in Table 3. COVID-19, coronavirus disease; ICU, intensive care unit.

(Figures 1, 2), growing in size in May and persisting over time. Testing intensity spread throughout the county during this same period.

Consistent with other reports, we also found that age and male sex strongly predict testing positive and COVID-19 associated death (26). Intriguingly, whereas older age groups and men and boys were more likely to have symptomatic disease, our population-based serologic survey found that women and girls were more likely than their male counterparts to be seropositive. Hispanic and Latinx persons had higher risk for infection and testing positive, even after controlling for several ZIP code-level socioeconomic factors. Given the consistency of this finding between the models for test positivity and seropositivity, the risk for being infected with SARS-CoV-2 rises above and beyond the risks of living in a ZIP code with high transmission or a ZIP code with low income and low levels of educational attainment. Other studies also note an increased risk for testing positive among

Hispanic and Latinx persons (27–29). Our seroprevalence survey indicates that in OC, this finding is not an artifact of passive case detection but instead represents an actual true greater risk for infection for Hispanic and Latinx persons.

Although persons identifying as Asian were less likely to test positive for SARS-CoV-2, they were more likely to die when infected. This disparity is consistent with national data, though its cause is uncertain (30). This pattern may reflect discrepancies in outreach communication to these communities or other socioeconomic and cultural factors (31,32) and warrants further detailed investigation.

Social determinants of health, defined as “conditions in which people are born, grow, work, live, age, and the wider set of forces and systems,” play a critical role in the creation of disparities related to illness, death, and quality of life (33). These social determinants include (among other factors) poverty, wealth, educational quality, household and neighborhood

conditions, childhood experience, and social support. Several speculative explanations have been proposed for these sociodemographic patterns related to COVID-19, including living in dense quarters (and this pattern is evident in our analyses). In addition, as the state and local shelter-in-place and social distancing policies were mandated, persons who are independently wealthy or who work in occupations where working from home was a viable option, were more capable of practicing social distancing. Persons from low socioeconomic status areas, by contrast, may have less ability to practice social distancing. Our analyses show that persons from ZIP codes with lower overall educational attainment and health

insurance coverage and with higher housing density were more likely to test positive for and die from COVID-19. The association with median household income was more complex and changed over time with regard to test positivity. However, we also find that persons from ZIP codes with lower median household income were also more likely to be seropositive for SARS-CoV-2. These findings underscore the importance of understanding contextual factors surrounding infectious disease outbreaks.

Study limitations include that county-reported testing and mortality data did not include individual-level information on income, education, and insurance. These variables were only available at the ZIP

Table 4. Logistic regression results for odds ratio of testing seropositive for SARS-CoV-2, Orange County, California, USA, July–August 2020*

Characteristic	No. (%)		Adjusted odds ratio (95% CI)†
	SARS-CoV-2 seropositive, n = 350	Total tested, n = 2,604	
Age group, y			
18–24	19 (5.43)	158 (5.35)	Referent
25–29	31 (8.86)	234 (7.92)	1.09 (0.58–2.04)
30–34	33 (9.43)	275 (9.31)	0.97 (0.52–1.81)
35–39	35 (10)	328 (11.1)	0.85 (0.46–1.56)
40–49	83 (23.71)	651 (22.04)	1.08 (0.62–1.87)
50–59	82 (23.43)	659 (22.31)	1.09 (0.62–1.89)
60–69	46 (13.14)	418 (14.15)	1.02 (0.56–1.86)
70–79	18 (5.14)	188 (6.36)	0.93 (0.45–1.91)
≥80	3 (0.86)	43 (1.46)	0.64 (0.18–2.32)
Sex			
F	222 (63.43)	1,668 (56.47)	Referent
M	128 (36.57)	1,286 (43.53)	0.75 (0.59–0.94)
Race or ethnicity‡			
White	108 (30.86)	1,228 (41.57)	Referent
Asian	47 (13.43)	435 (14.73)	1.25 (0.85–1.82)
Black	5 (1.43)	42 (1.42)	1.28 (0.48–3.37)
Hispanic	162 (46.29)	1,010 (34.19)	1.54 (1.17–2.03)
Pacific Islander	3 (0.86)	12 (0.41)	3.89 (1.04–14.65)
Unknown	25 (7.14)	227 (7.68)	1.25 (0.78–2)
% With college degree in ZIP code			
1st quartile	158 (45.14)	937 (31.72)	Referent
2nd quartile	92 (26.29)	893 (30.23)	0.98 (0.65–1.46)
3rd quartile	59 (16.86)	644 (21.8)	1.15 (0.64–2.04)
4th quartile	41 (11.71)	480 (16.25)	1.15 (0.59–2.22)
% With insurance in ZIP code			
1st quartile	154 (44)	928 (31.42)	Referent
2nd quartile	91 (26)	812 (27.49)	0.98 (0.67–1.43)
3rd quartile	54 (15.43)	597 (20.21)	0.99 (0.56–1.76)
4th quartile	51 (14.57)	617 (20.89)	0.95 (0.51–1.76)
Population density, × 1,000 persons/km ²			1.02 (0.81–1.29)
House crowding index			1.00 (0.96–1.04)
Median income (SD)			0.76 (0.57–1.00)
% Persons in ZIP code SARS-CoV-2 positive >10%§			1.25 (0.80–1.96)

*This cross sectional survey was conducted July 10–August 16, 2020. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

†Model intercept represents odds of testing seropositive for SARS-CoV-2 for a White female diagnosed with SARS-CoV2 in the 18–24 years age group in a ZIP code in the first quartile of college degree and insured with the average population density, and average percentage of SARS-CoV-2 positive persons in Orange County. The odds of this person testing seropositive is estimated to be 0.074 (95% CI 0.031–0.178). 95% CIs computed with robust SEs.

‡For comparison, the estimated race/ethnicity makeup of Orange County in 2021 is non-Hispanic White (38.6%, n = 1,223,157; Black/African American (1.6%, n = 52,696); American Indian or Alaskan Native (0.3%, n = 6,018); Asian (21.1%, n = 685,728); Native Hawaiian or Pacific Islander (0.3%, n = 8,885); other or multiple races (3.1%, n = 100,297); Hispanic or Latinx (35.0%, n = 1,115,740) (21). American Indian or Alaska Native race group not included in analysis because of lack of data; no person of this race group tested seropositive.

§Number of persons who tested positive in person's ZIP code reported to Orange County Public Health Department during March 1–August 16, 2020, divided by estimated population of ZIP code.

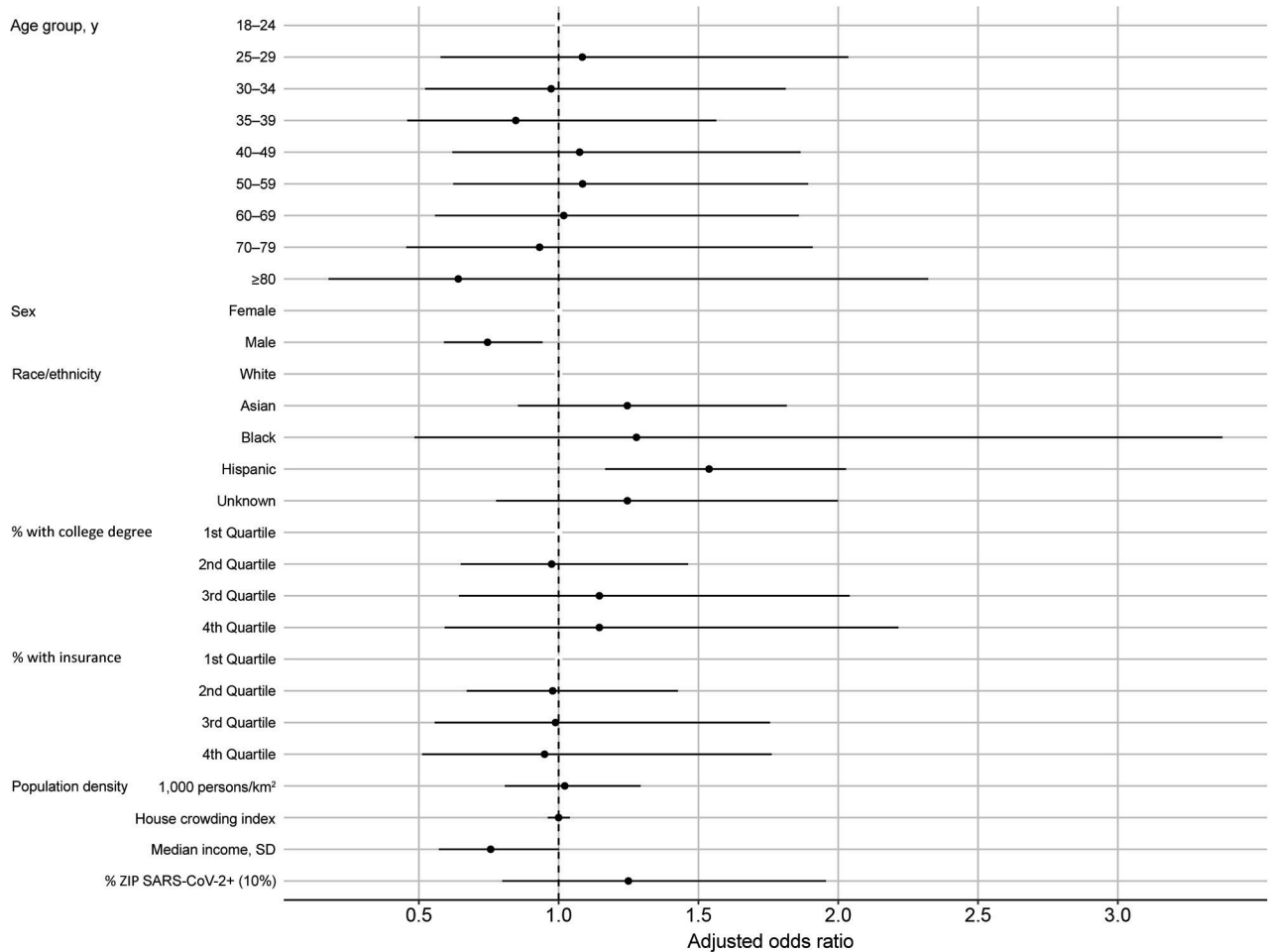


Figure 9. Model-adjusted odds ratios and 95% CIs from the logistic regression for the odds of being seropositive for severe acute respiratory syndrome coronavirus 2, Orange County, California, USA, July–August 2020. Corresponding data presented in Table 4. +, positive.

code-level, and ZIP codes are unlikely to adequately represent important spatial units. Our seroprevalence survey occurred during July 10–August 16, 2020. We limited our analyses of test positivity and risk for death to before August 16, to correspond with the end of the seroprevalence survey. However, the survey occurred over a period of just over a month, during which time the cumulative incidence was changing. Missing data on race and ethnicity (72% of all official test records) and small counts of some racial and ethnic groups may have affected our findings for groups with low counts in this analysis. Even when race or ethnicity data were available, they were broad categories (e.g., Asian rather than specific Asian ethnicities), which is a major limitation of these data, and efforts are being made to improve collection of race and ethnicity data. A major challenge over the course of this pandemic has been collecting data in a standardized format when test results are being reported from

a wide variety of laboratories that are affiliated with many different private and governmental entities. We do not believe that the race and ethnicity data are missing at random but also are not able to assess the magnitude of bias that this possibility would introduce, especially given that race and ethnicity appear to be risk factors for infection.

Study strengths include the diversity of OC in terms of socioeconomic and demographic predictors, which provide sufficient power to investigate these factors in our analyses. California was also one of the first states to issue an executive order for residents to stay home, providing data for several months when only essential workers were permitted to work outside the home. Our analyses were able to identify temporal shifts in the demographics of COVID-19 test positivity that likely reflect disparities related to occupation type that are further amplified by household characteristics. Finally, we are able to assess differences in

risk for infection and test positivity by comparing our population-level serologic survey to routinely collected (passive) data from county statistics.

The reasons for the spatial, sociodemographic, and economic patterns we discovered are likely complex and broadly related to issues of accessing healthcare and general social determinants of health. The clear disparities in how this disease has manifested in OC point toward the need for approaches that are socio-culturally appropriate and have a focus on health equity. The large amount of missing data and the collection of only broad categories of race and ethnicity information highlight the need for improved data collection. Finally, measures that focus on the hardest-hit communities, including those that involve working with community-based organizations who have experience working with hard-hit demographic and geographic groups to ensure equitable access to health services, may serve as efficient points of intervention for COVID-19.

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We acknowledge the actOC research manager, Emily Drum, and the logistical expertise of Bruce Albala, who set up and helped run the seroprevalence study. Many University of California–Irvine students and alumni were involved in collecting blood samples for the serologic survey, and we gratefully acknowledge their contributions. We are grateful to members of the Felgner Laboratory who made the serologic survey possible under sometimes trying conditions (especially Rie Nakajima, Aarti Jain, and Rafael Ramiro de Assis). Guiyun Yan and Xiaoming Wang provided space for cold storage. We also acknowledge conversations with colleagues and community leaders with regard to social determinants of health and health equity, including Sora Tanjasiri, Mary Anne Foo, Brittany Morey, Ahn Ellen, Tricia Nguyen, America Bracho, and many others.

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T.B. and B.B.A. were both principal investigators for the serologic survey. B.B.A. also oversaw the data exchange between University of California, Irvine and Orange County Health Care Agency.

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Dr. Parker is an infectious disease epidemiologist with expertise in spatial epidemiology, demography, and biomedical anthropology. He is an assistant professor in public health at the University of California, Irvine, and the director of the Global Health Research, Education, and Translation Initiative.

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Predictors of Test Positivity, Mortality, and Seropositivity during the Early Coronavirus Disease Epidemic, Orange County, California, USA

Appendix

Recruitment for Seroprevalence Survey

The SoapBoxSample database contains email addresses and phone numbers of individuals residing in Orange County. We invited (via email [36.4%] or random-digit telephone dialing [63.6%]) one resident per household to participate, without initial mention of SARS-CoV-2 antibody testing. We did not allow the opportunity to defer the survey to another household member. We recruited up to, but not over, targeted quotas for each sociodemographic stratum, according to the population distribution of each stratum in Orange County. Based on U.S. Census-derived population distributions in OC, we targeted recruitment to ensure adequate sample size of subjects from the following strata: age-by-gender (18 to 34 years, 35 to 54 years, 55 years or above; by male, female), race/ethnicity (Hispanic, Asian non-Hispanic, and other non-Hispanic including white and Black, and household income (<\$50,000, \$50,000–99,999, and \$100,000 or above).

In addition, we encouraged participation of racial/ethnic minorities and/or lower-income adults in several ways. First, for four of the 6 weeks of the survey, we offered the survey in the five most commonly spoken languages in OC (i.e., English, Spanish, Mandarin, Vietnamese, and Korean). Second, we invited all household members of underrepresented groups to receive testing at the drive-thru site. Third, for the last 2 weeks of the survey (given that the quotas for racial/ethnic minorities had not been reached) we targeted particular zip codes with a large proportion of racial/ethnic minorities.

Appendix Table 1. Description of covariates (predictors) used in logistic regressions

Variable	Description	Spatial scale	Transformation
Age	Age of individual	Individual level	Either age groups or 10 y units
Gender	Binary indicator for male or female	Individual level	
Race/ethnicity	Race or ethnicity of individual	Individual level	
% with College Degree	Percentage of adults over age 25 with at least a Bachelor's Degree	Zip code level	Aggregated into quartiles for multivariable regressions
% with Insurance	Percentage of adults over 18 with insurance in the past 5 y	Zip code level	Aggregated into quartiles for multivariable regressions
Population Density	Number of people (in thousands) per square kilometer	Zip code level	Centered on its mean and standardized by standard deviation
House Crowding	Percentage of households with more than 1.0 person per room	Zip code level	
Median Income	Median household income in zip code	Zip code level	Centered on its mean and standardized by standard deviation
% Zip Code SARS-CoV-2+	Cumulative incidence of reported COVID-19 cases in zip code, up to August 16th	Zip code level	
COVID ICU patients (std. dev.)	Total number of patients patient with confirmed or suspected COVID-19 in ICU beds (per day)	County level	Centered on its mean and standardized by standard deviation
Time	Continuous variable for time		Centered on its mean and standardized by standard deviation

Appendix Table 2. Logistic regression results for odds ratio of testing sero-positive for SARS-CoV2 in Orange County. This regression differs from Table 4 (<https://wwwnc.cdc.gov/EID/article/27/10/21-0103-T4.htm>) in that it excludes zip code level covariates other than the cumulative incidence.

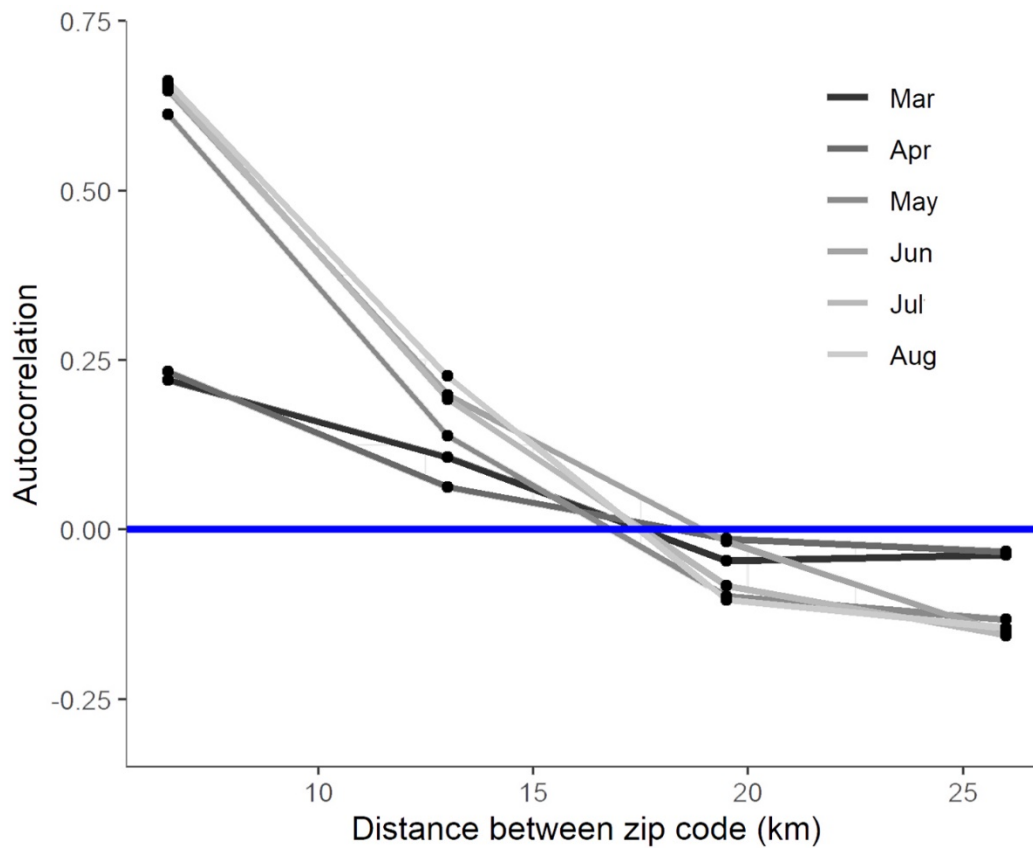
Characteristic	Counts		Adjusted Odds Ratio* with (95% CI)†
	SARS-CoV2+	Total	
Age			
18–24	19 (5.43%)	158 (5.35%)	Reference
25–29	31 (8.86%)	234 (7.92%)	1.113 (0.59, 2.08)
30–34	33 (9.43%)	275 (9.31%)	0.98 (0.53, 1.82)
35–39	35 (10%)	328 (11.1%)	0.836 (0.45, 1.54)
40–49	83 (23.71%)	651 (22.04%)	1.066 (0.62, 1.84)
50–59	82 (23.43%)	659 (22.31%)	1.071 (0.62, 1.86)
60–69	46 (13.14%)	418 (14.15%)	0.99 (0.55, 1.8)
70–79	18 (5.14%)	188 (6.36%)	0.931 (0.46, 1.9)
80+	3 (0.86%)	43 (1.46%)	0.676 (0.19, 2.42)
Sex			
Female	222 (63.43%)	1668 (56.47%)	Reference
Male	128 (36.57%)	1286 (43.53%)	0.731 (0.58, 0.92)
Race‡			
White	108 (30.86%)	1228 (41.57%)	Reference
Asian	47 (13.43%)	435 (14.73%)	1.286 (0.89, 1.87)
Black	5 (1.43%)	42 (1.42%)	1.309 (0.5, 3.43)
Hispanic	162 (46.29%)	1010 (34.19%)	1.578 (1.2, 2.08)
Pacific Islander	3 (0.86%)	12 (0.41%)	3.62 (1, 13.16)
Unknown	25 (7.14%)	227 (7.68%)	1.254 (0.78, 2.01)
% Zip Code SARS-CoV2+§			1.473 (1.24, 1.74)

*Model intercept represents odds of testing sero-positive for SARS-CoV2 for a white female diagnosed with SARS-CoV2 in the 18–24 age group in a zip code in the first quartile of college degree and insured with the average population density, and average percent of SARS-CoV2 positive individuals in Orange County. The odds of this individual testing sero-positive is estimated to be 0.074 (0.031,0.178)

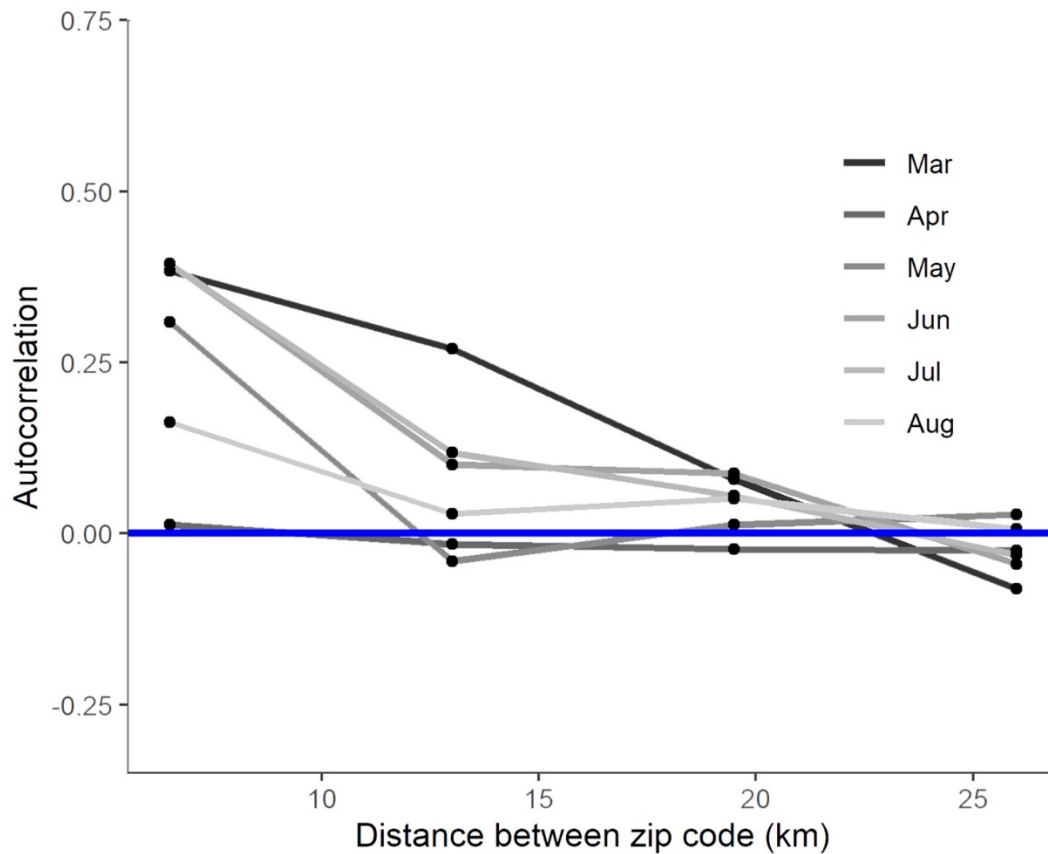
†95% confidence interval computed with robust standard errors

‡Native American/Native Alaskan race group not included in analysis due to lack of data, no individual of this race group tested seropositive

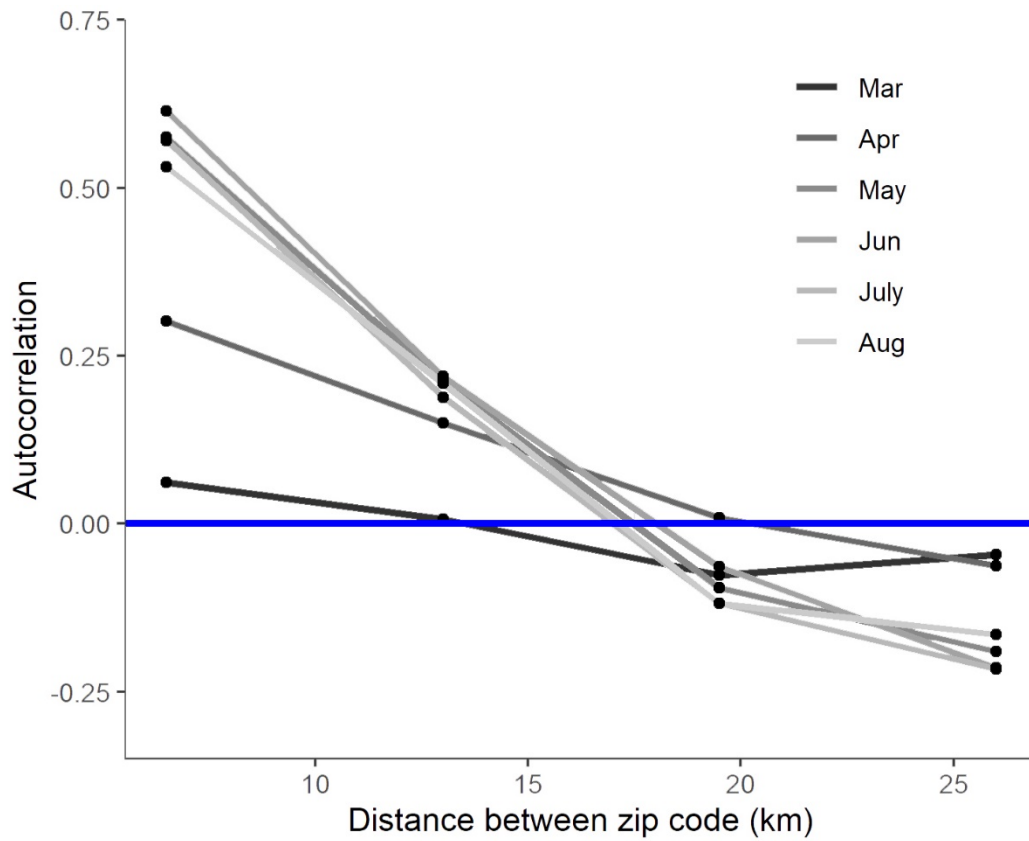
§Number of individuals who tested positive in individual's zip code reported to OC Public Health Department from March 1st to August 16th, divided by estimated population of zip code



Appendix Figure 1. Spatial correlogram indicating degree of clustering (along y-axis) in reported COVID-19 case incidence by distance (km) away from neighboring zip codes in Orange County, California. Clustering in March is indicated by the black line and subsequent months are indicated by progressively lighter colors. Clustering has been present since the first month (March) but since May the pattern has been stronger and has remained consistent.



Appendix Figure 2. Spatial correlogram indicating degree of clustering (along y-axis) in COVID-19 testing intensity by distance (km) away from neighboring zip codes in Orange County, California. Clustering in March is indicated by the black line and subsequent months are indicated by progressively lighter colors. Clustering in March was strong and by May was almost non-existent at any spatial extent (May's correlogram falls along the horizontal blue line, with an autocorrelation coefficient near zero). Clustering in testing intensity was again strong in June and July.



Appendix Figure 3. Spatial correlogram indicating degree of clustering (along y-axis) in COVID-19 test positivity by distance (km) away from neighboring zip codes in Orange County. There was almost no clustering in test positivity in March, at the beginning of the epidemic (the line for March falls near the zero point). Clustering in test positivity was apparent in April, increased in May, and has remained at approximately the same level since.