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Risk Predictors of SARS-CoV-2 of Orange County, CA Children

THESIS

submitted in partial satisfaction of the requirements
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MASTER OF SCIENCE

in Epidemiology

by

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Abstract of the Thesis:

Risk Predictors of SARS-CoV-2 of Orange County, CA Children

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Master of Science in Epidemiology

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Associate Professor Andrew Odegaard, Chair

This study examines the association between demographic and zip code related factors and SARS-CoV-2 testing positivity among children ages 0-11 in Orange County, California to determine potential risk predictors. We used a retrospective analysis and the OCHCA database to calculate these effects. Our study found that children who identified as Hispanic or Latine, or were categorized as "Other" were most at risk for testing positive for SARS-CoV-2, even after adjusting for age, sex, race, and taking into account zip code-related factors. In addition, zip code related average income and population densities exhibited protective and increased odds, respectively. However, our study also acknowledges the limitations present, including the use of zip code level information in place of individual level information that was not present, and the probable biases involved in passive collection methods. Despite these limitations, the study provides important insight into potential predictors that may be contributing to disparities in SARS-CoV-2 testing rates among Orange County children and highlights the need for community-based efforts to reduce the burden on the most at risk.

Introduction:

In Orange County, California, minority populations, particularly children in cities like Santa Ana, Orange, and Anaheim, have been disproportionately affected by SARS-CoV-2, the virus responsible for COVID-19. COVID-19 is a contagious respiratory infection caused by the SARS-CoV-2 virus, which was first identified in Wuhan, China, in December 2019. Minority communities, particularly those with low-income Hispanic and Latine populations, have experienced higher rates of infection[1]. Previous studies have shown that preexisting conditions and social determinants of health contribute to severe COVID-19, defined as severe respiratory distress requiring ICU admission, mechanical ventilation, or even death[3]. Although children are less likely than adults to present severe COVID-19, contraction of the virus may lead to prolonged effects known as long COVID[4,5].

To determine the burden of SARS-CoV-2 on children in Orange County, it is necessary to analyze data on all cases of SARS-CoV-2 among children aged 0 to 11 years between March 2020 and October 21, 2021, prior to vaccine approval[6]. By limiting the time period to prior to vaccine rollout, we eliminate many of the potential confounders that could present themselves in relation to test positivity, such as a reduction in testing due to lessened symptomatic disease prevalence. This information will provide a better understanding of the predictive factors for SARS-CoV-2 without the influence of the vaccine. Additionally, age, sex, race, and zip code descriptive data will be analyzed to determine odds ratios per association of the outcome of a positive SARS-CoV-2 test. This analysis will guide the allocation of resources for further longitudinal studies on the long-term effects of SARS-CoV-2 and preventive measures.

Methods:

Study Design and Setting: This retrospective cohort study used data from the Orange County Health Care Agency SARS-CoV-2 database to investigate potential predictors of SARS-CoV-2 between March 2020 and October 21, 2021, among children aged 0-11 in Orange County, California.

Exclusion Criteria: Participants were excluded if they were over the age of 11, were not from a valid residential Orange County zip code, had incomplete demographic data, or had collection occur after the date of October 21, 2021. If the participant had repeat positive test results within a 3-week period based on the incident ID number and date, then the additional positive tests were excluded. The exclusion criteria yielded a final sample size of 112,502. Positive SARS-CoV-2 test results were ascertained via PCR tests at county testing facilities with FDA Emergency Use Authorized tests. Preliminary demographic data were acquired by the facilities either via survey or direct questioning, which allowed for missingness of data and the lack of standardization of information acquisition across facilities.

Zip Code Level Sociodemographic Data: Zip code-level predictors included population density, average household size, and average income. These predictors were also used during the exclusionary process to reduce the amount of missing zip code data in the analysis. All data were obtained from the United States Census Bureau and the California Department of Housing and Community Development[7-9]. A total of 84 unique zip codes were included.

Race Data: A single categorical variable for race/ethnicity was created for the purposes of individual-level predictors. Individuals who identified their race as White, Asian, African American, or Native American were assigned to those respective categories. Those who did not identify as any of the above and did not identify themselves as Hispanic or Latine were placed into an "Other" category. However, if the participant identified as Hispanic or Latine, they were categorized as such.

Statistical Analysis: We utilized binomial logistic regressions and binomial mixed effects logistic regressions with random intercepts to investigate the odds of testing positive for SARS-CoV-2 based on demographic, socioeconomic, and population density predictors. The predictors within our models were sex, age, time, race, zip code income quartiles, and population density quartiles.

Software: Analyses were conducted by utilizing SAS 9.4. Test Positivity graphs were created with Microsoft Excel Version 16.72.

Ethics Considerations: The data used in the analysis consisted of anonymized SARS-CoV-2 test outcome record. Therefore, no ethnical approval was sought.

Results:

A total of 264,290 PCR SARS-CoV-2 tests were conducted by OCHCA for individuals aged 0-11 prior to October 21, 2021. After exclusion criteria, 112,502 distinct PCR tests were conducted in two age groups: 0-4 and 5-11. Approximately 36% of all tests were conducted on the 0-4 age group, while the remainder (64%) were conducted on the older age group of 5-11.

Test Positivity: Test positivity, as defined as the percentage of individuals who test positive for the SARS-CoV-2 virus among all those who are tested, was determined based on age group and further stratified by individual age or race. Figures 1 and 2 demonstrate test positivity over time for the respective strata. Both age groups depicted overall trends of greater test positivity at the inception of the study period, with declines as time proceeded. Overall trends depicted increases in test positivity as individual age increased, with the exception of age 0, which exhibited higher positivity than the other ages within its subset. Figure 2, which depicted test positivity over time per race, displayed similar time trends as figure 1. In addition, the White and Hispanic population exhibited the highest test positivity rates within both age ranges.

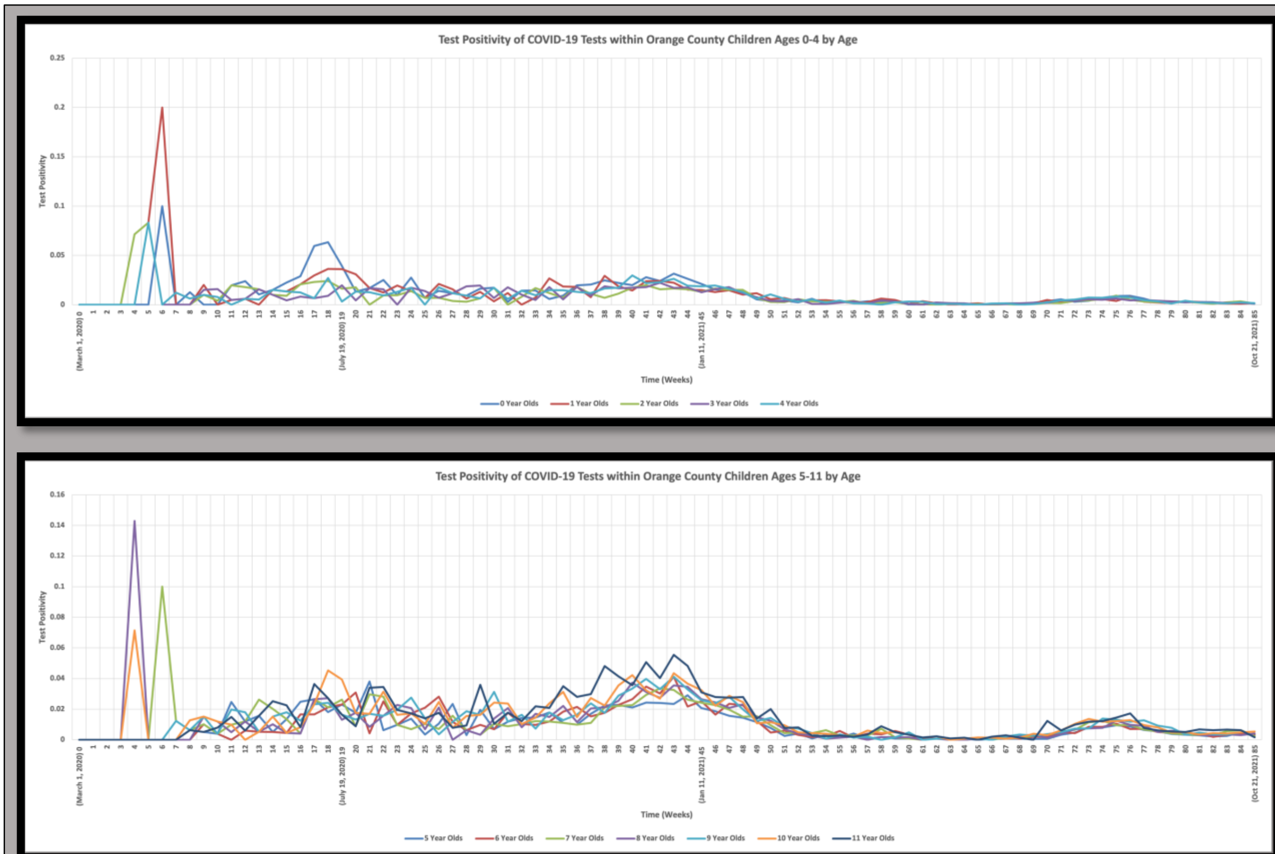

Figure 1:
SARS-CoV-2 Test Positivity of Orange County Children by Age

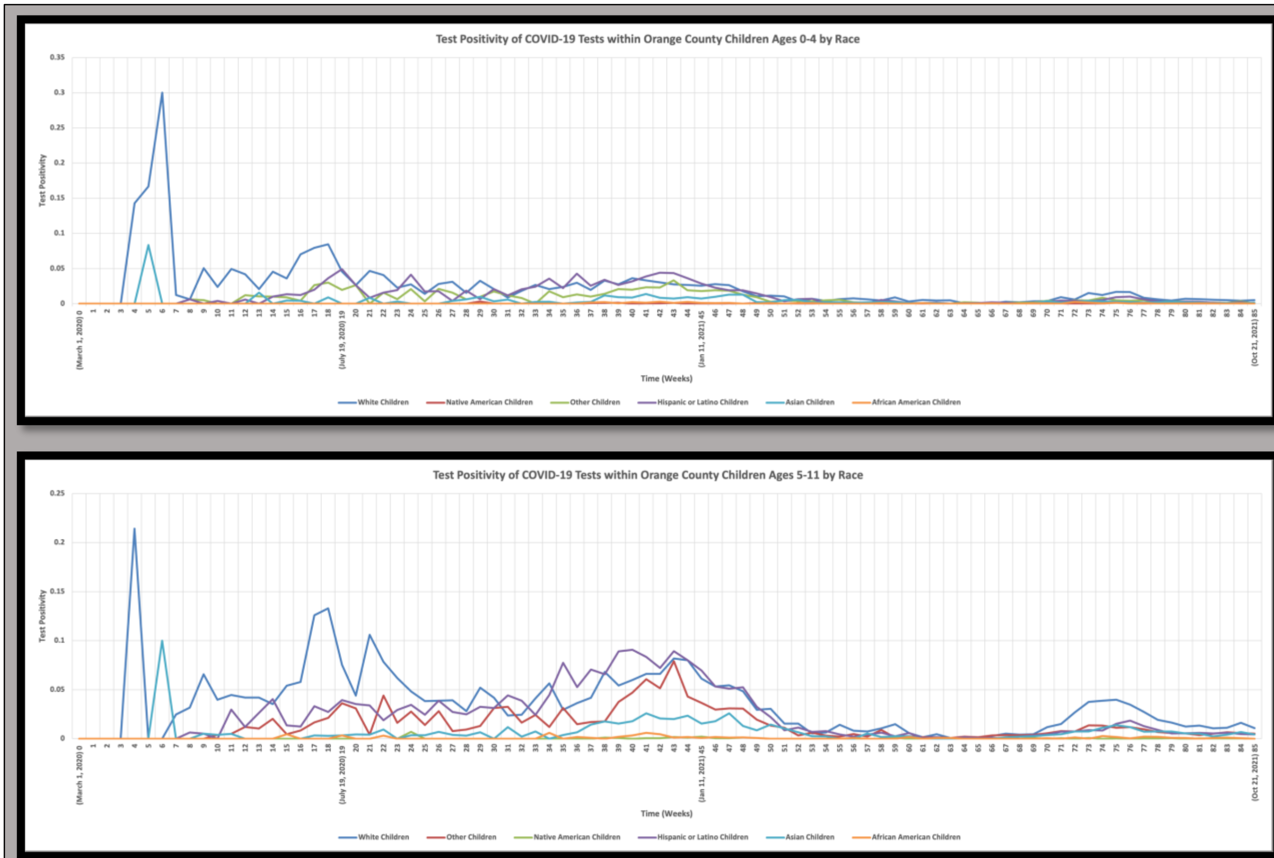

Figure 2:
SARS-CoV-2 Test Positivity of Orange County Children by Race

Results from Binomial Mixed Effects Logistic Regression with Random Intercept: The binomial mixed effects logistic regression with random intercept model, shown in Table 1, showed similar trends to the binomial logistic regression model, but with a better fit, indicated by a lower AIC value. For the 0-4-year-old age group, being male had a protective effect against positive SARS-CoV-2 test results, with an odds ratio of 0.908 (95% CI 0.848–0.972). However, those who identified as Hispanic or Latine or Other had an increased odds of 1.981 (95% CI 1.815–2.162) and 1.338 (95% CI 1.219–1.469), respectively, while those who identified as Asian had a decreased odds of 0.843 (95% CI 0.748–0.951). In addition, statistically significant odds ratios were found for the highest quartile zip code population density (aOR 1.303; 95% CI 1.024–1.659), time in weeks (aOR 0.971; 95% CI 0.969–0.972), and age of the participant (aOR 1.095; 95% CI 1.070–1.120).

For the older age group of 5-11, statistically significant odds ratios were found for all racial groups: African American (aOR 0.748; 95% CI 0.610–0.916), Asian (aOR 0.670; 95% CI 0.618–0.727), Hispanic or Latine (aOR 1.758; 95% CI 1.652–1.872), Native American (aOR 0.689; 95% CI 0.496–0.957), Other (aOR 1.099; 95% CI 1.029–1.174). Additionally, 3rd quartile zip code incomes (aOR 0.815; 95% CI 0.671–0.990), 4th quartile zip code population densities (aOR 1.276; 95% CI 1.013–1.606), time (aOR 0.964; 95% CI 0.963–0.965), and age (aOR 1.072; 95% CI 1.060–1.085) were significantly associated with SARS-CoV-2 test results.

Table 1: Odds Ratios via Binomial Mixed Effects Logistic Regression with Random Intercept (Accounting Zip Code) *

Group	0–4-Year-Old			5–11-Year-Old		
	No. (%)			No. (%)		
	SARS-CoV-2 Positive	Total Tests	Adjusted odds ratio† (95% CI)	SARS-CoV-2 Positive	Total Tests	Adjusted odds ratio† (95% CI)
Adjusted Model 2 – Binomial GLMM Logistic Regression with Random intercept (Accounting Zip Code)						
Female	1881 (48.40)	18724 (46.10)	REF	4026 (48.26)	34491 (47.98)	REF
Male	2005 (51.60)	21895 (53.90)	**0.908 (0.848, 0.972)**	4317 (51.74)	37392 (52.02)	0.976 (0.930, 1.024)
White	1474 (37.93)	18166 (44.72)	REF	3187 (38.20)	29895 (41.59)	REF
African American	72 (1.85)	823 (2.03)	1.234 (0.957, 1.590)	111 (1.33)	1430 (1.99)	**0.748 (0.610, 0.916)**
Asian	388 (9.98)	6431 (15.83)	**0.843 (0.748, 0.951)**	908 (10.88)	14575 (20.28)	**0.670 (0.618, 0.727)**
Hispanic or Latine	1144 (29.44)	6892 (16.97)	**1.981 (1.815, 2.162)**	2483 (29.76)	11312 (15.74)	**1.758 (1.652, 1.872)**
Native	18 (0.46)	360 (0.89)	0.774 (0.479, 1.253)	40 (0.48)	611 (0.85)	**0.689 (0.496, 0.957)**
Other	790 (20.33)	7947 (19.56)	**1.338 (1.219, 1.469)**	1614 (19.35)	14060 (19.56)	**1.099 (1.029, 1.174)**
Zip Code Income Level Quartiles						
1st Quartile	1229 (31.63)	10406 (25.62)	REF	3086 (36.99)	19804 (27.55)	REF
2nd Quartile	1101 (28.33)	9992 (24.60)	0.973 (0.826, 1.146)	2066 (24.76)	16614 (23.11)	0.945 (0.797, 1.121)
3rd Quartile	881 (22.67)	10446 (25.72)	0.918 (0.756, 1.115)	1696 (20.33)	17957 (24.98)	**0.815 (0.671, 0.990)**
4th Quartile	675 (17.37)	9775 (24.07)	0.823 (0.644, 1.051)	1495 (17.92)	17508 (24.36)	0.810 (0.646, 1.015)
Zip Code Population Density Quartiles						
1st Quartile	770 (19.81)	10703 (26.35)	REF	1521 (18.23)	18639 (25.93)	REF
2nd Quartile	841 (21.64)	10060 (24.77)	1.020 (0.842, 1.235)	1926 (23.09)	18256 (25.40)	1.074 (0.930, 1.240)
3rd Quartile	1029 (26.48)	10359 (25.50)	1.091 (0.880, 1.353)	2052 (24.60)	17461 (24.29)	1.107 (0.925, 1.325)
4th Quartile	1246 (32.06)	9497 (23.38)	**1.303 (1.024, 1.659)**	2844 (34.09)	17527 (24.38)	**1.276 (1.013, 1.606)**
Time	3886 (100)	40619 (100)	**0.971 (0.969, 0.972)**	8343 (100)	71883 (100)	**0.964 (0.963, 0.965)**
Age	3886 (100)	40619 (100)	**1.095 (1.070, 1.120)**	8343 (100)	71883 (100)	**1.072 (1.060, 1.085)**

*Values are no. (%) except where indicated. A random intercept was included for ZIP Code. The period covered in this analysis is March 1, 2020–October 21, 2021. 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 first quartile of ZIP code income and in the first quartile of ZIP code population density. 95% CIs computed with robust SEs. Bolded Figures signify statistical significance.

Discussion:

In our analysis of SARS-CoV-2 test data from Orange County, we observed abnormally high-test positivity rates during the initial weeks of the pandemic in March 2020, which corresponded to the lockdown in the United States. The high level of test positivity was likely due to the lack of availability of tests and the available ones being utilized for symptomatic individuals. As the availability of tests increased, the positivity rates decreased and stabilized to levels typically below 5%, as expected[10]. However, as time progressed, we observed further elevations in the magnitude of test positivity corresponding to observed case increases during the reopening and closing of businesses in the summer of 2020 and the winter case surge of 2020.

Consistent with other research that has been released, those who identify as Hispanic or Latine experience higher odds of testing positive for SARS-CoV-2 in comparison to their white counterparts[11-13]. The association was observed in both age groups and with higher magnitude in the younger cohort, despite controlling for multiple zip-code related factors. Children placed into the catchall race coined as "other" also exhibited higher odds of testing positive despite the category being fairly wide in definition and skewing the results closer to the null. As time progressed, the odds of testing positive decreased for both age groups; however, it increased with respect to every year increase in age.

Interestingly, male children of the youngest cohort exhibited protective effects against testing positive for SARS-CoV-2. This association was not seen in the 5-11-year-old group and has not been seen in other research conducted[12,14,15]. Children, especially those as young as the cohort depicted, typically do not present themselves with sex differences for infectious diseases or if present, the outcomes are typically worse for males[16,17]. Similarly, contrary results from other research were exhibited in African American individuals. Research indicates that this demographic should experience higher odds of positivity; however, the demographics of the study populations were older individuals, which draws into question the exchangeability between the two[11,18,19]. Our results demonstrated protective effects for both Asian and African American populations; however, the effect was exclusive to the older cohort for African Americans. Although protective effects were also seen in Native American children ages 5-11, the sample size was very small.

Zip code factors, such as population density and average income level, are known to be under the guise of social determinants of health, which dictate the conditions of an individual's upbringing and environment. These factors are traditionally known to affect the risk of contracting infectious diseases as well as the severity of disease[20,21]. While not all quartiles of the zip code related factors exhibited significant effects, a general trend where income level decreased the odds of positivity and increased population density resulted in higher odds being observed. Minority populations are typically known to represent the lowest quartile of income and highest quartile of population density due to systemic racism, which would contribute to the results observed here[21,22].

Study limitations include the lack of individual-level information for those tested. Zip code average income levels and population density were utilized for the analysis, which could alter the magnitude of the association for each individual. For example, a child could actually come from an affluent family but live in an area deemed lower income based on zip code information. This possibility could skew the level of association viewed. Additionally, the passive case detection records used in this study could be biased in multiple ways, such as unequal access to testing or over-selection of cases due to symptomatic disease[23,24]. Overrepresentation of affluent and white individuals was seen early in the testing as access to care faltered for others. In addition, there is a general lack of consensus on race of individuals. While the majority depicted a race that is colloquially known, many had ambiguous terms such as “American” or “Other,” which were grouped together. Furthermore, groupings of Hispanic or Asian, etc., do not have specific level information on ethnicity, which is a major limitation of the data.

Study strengths include the overall demographic composition of Orange County, California. Whereas other states and counties may have a vast majority of individuals that represent one race, California, specifically Orange County, is very diverse in its ethnic and racial composition. In addition, the population sample sizes are large, which assists the power of the study.

In conclusion, our analysis of SARS-CoV-2 test data in Orange County children revealed abnormally high-test positivity during the initial weeks of the pandemic likely due to the lack of test availability and their utilization primarily for symptomatic individuals. As time progressed, test positivity levels decreased, but with periodic increases corresponding to observed case surges. Our results confirmed previous research indicating higher odds of testing positive for SARS-CoV-2 among Hispanic or Latine individuals as well as those categorized as "other" race. The association seen between test positivity and zip code factors such as income level and population density demonstrated the impact of social determinants of health on the risk of contracting infectious diseases. While there were some limitations in our study, including the lack of individual-level information and ambiguous race categorization, the overall demographic composition of Orange County and large population sample sizes strengthened our findings. Our results highlight the importance of considering social determinants of health in developing public health interventions to prevent and control infectious diseases, particularly community-based measures to assist minority groups.

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Appendix - Logistic Models

Binomial Logistic Model

- Logit: Positive Tests = Sex + Ethnicity + Zip Code Income Levels + Population Density Levels + Time (Weeks) + Age
- ŷ (Ages 0-4) = -0.8389 - 0.0438(Sex) + 0.0818(African) - 0.2995(Asian) + 0.5653(Hispanic) - 0.3831(Native) + 0.1634(Other) + 0.0495(Zip Quartile 2) - 0.00346(Zip Quartile 3) - 0.1180(Zip Quartile 4) - 0.0718(Population Quartile 2) - 0.00263(Population Quartile 3) + 0.1697(Population Quartile 4) - 0.0296(Time) + 0.0899(Age)
- ŷ (Ages 5-11) = -0.6191 - 0.0109(Sex) - 0.2276(African) - 0.3442(Asian) + 0.6573(Hispanic) - 0.3083(Native) + 0.1585(Other) + 0.0594(Zip Quartile 2) - 0.0831(Zip Quartile 3) - 0.0897(Zip Quartile 4) - 0.0323(Population Quartile 2) + 0.00139(Population Quartile 3) + 0.1350(Population Quartile 4) - 0.0366(Time) + 0.0706(Age)

Binomial Mixed Effects Logistic Regression with Random Intercept (Accounting Zip Code)

- Logit: Positive Tests = Sex + Ethnicity + Zip Code Income Levels + Population Density Levels + Time (Weeks) + Age + Random Intercept (Zip Code)
- ŷ (Ages 0-4) = -0.9574 - 0.09636(Sex) + 0.2099(African) -0.1708(Asian) + 0.6837(Hispanic) -0.2557(Native) + 0.2912(Other) -0.02723(Zip Quartile 2) - 0.08524(Zip Quartile 3) - 0.1946(Zip Quartile 4) + 0.01964(Population Quartile 2) + 0.08729(Population Quartile 3) + 0.2650(Population Quartile 4) -0.02962(Time) + 0.09034(Age)

- $\hat{y}$ (Ages 5-11) = -0.5423 - 0.02429(Sex) - 0.2909(African) - 0.4002(Asian) + 0.5645(Hispanic) - 0.3726(Native) + 0.09455(Other) - 0.05651(Zip Quartile 2) - 0.2040(Zip Quartile 3) - 0.2110(Zip Quartile 4) + 0.07116(Population Quartile 2) + 0.1017(Population Quartile 3) + 0.2436(Population Quartile 4) - 0.03665(Time) + 0.06979(Age)
- Results from Binomial Logistic Regression: As a result, the binomial logistic regression model has multiple strong predictors for test positivity and multiple protective factors. In the 0-4 age group males exhibited an 8.4% (95% CI 0.856–0.981) reduction in odds of testing positive for SARS-CoV-2. Those who identify as Hispanic or Latine had 2.000 (95% CI 1.834–2.182) times the odds of testing positive than non-Hispanic Whites, whereas Asian (aOR 0.842; 95% CI 0.749–0.948) persons had lower odds of testing positive than did non-Hispanic Whites. Those identified as Other had 1.338 (95% CI 1.219–1.468) times odds of testing positive than non-Hispanic Whites. Children living in the highest population density and zip code income percentile exhibited 1.303 (95% CI 0.700–0.977) times and 0.827 (95% CI 0.700–0.977) times the odds of testing positive, respectively. As the study period progressed, time in weeks was associated with 0.971 (95% CI 0.969–0.972) times decrease in odds of testing positive, while every year increase in age was associated with 1.094 (95% CI 1.069–1.120) times increase in odds of testing positive for SARS-CoV-2. The older 5-11 age group exhibited increased odds of testing positive for SARS-CoV-2 if the individual was Hispanic or Latine, Other, of the 3rd or 4th Quartile of Zip Code Population Density, and as they increased in age with odds ratios of 1.809 (95% CI 1.701–1.925), 1.099 (95% CI 1.029–1.174), 1.111 (95% CI 1.001–1.234), 1.270 (95% CI 1.122–1.437), and 1.073 (95% CI 1.060–1.086),

respectively. In addition, the older 5-11 age group demonstrated protective effects against a positive SARS-CoV-2 test if the individual was African American, Asian, Native American, of the 3rd and 4th Quartile of Zip Code Income, and as time increased with odds ratios of 0.747 (95% CI 0.610–0.914), 0.665 (95% CI 0.614–0.719), 0.689 (95% CI 0.496–0.956), 0.822 (95% CI 0.744–0.907), 0.816 (95% CI 0.721–0.924), and 0.964 (95% CI 0.963–0.965), respectively.

Table 1: Odds Ratios via Binomial Logistic Regression*

Group	0–4-Year-Old			5–11-Year-Old		
	No. (%)		Adjusted odds ratio† (95% CI)	No. (%)		Adjusted odds ratio† (95% CI)
	SARS-CoV-2 Positive	Total Tests		SARS-CoV-2 Positive	Total Tests	
Adjusted Model 1 – Binomial Logistic Regression						
Female	1881 (48.40)	18724 (46.10)	REF	4026 (48.26)	34491 (47.98)	REF
Male	2005 (51.60)	21895 (53.90)	**0.916 (0.856, 0.981)**	4317 (51.74)	37392 (52.02)	0.979 (0.933, 1.026)
White	1474 (37.93)	18166 (44.72)	REF	3187 (38.20)	29895 (41.59)	REF
African American	72 (1.85)	823 (2.03)	1.233 (0.958, 1.588)	111 (1.33)	1430 (1.99)	**0.747 (0.610, 0.914)**
Asian	388 (9.98)	6431 (15.83)	**0.842 (0.749, 0.948)**	908 (10.88)	14575 (20.28)	**0.665 (0.614, 0.719)**
Hispanic or Latine	1144 (29.44)	6892 (16.97)	**2.000 (1.834, 2.182)**	2483 (29.76)	11312 (15.74)	**1.809 (1.701, 1.925)**
Native	18 (0.46)	360 (0.89)	0.775 (0.479, 1.253)	40 (0.48)	611 (0.85)	**0.689 (0.496, 0.956)**
Other	790 (20.33)	7947 (19.56)	**1.338 (1.219, 1.468)**	1614 (19.35)	14060 (19.56)	**1.099 (1.029, 1.174)**
Zip Code Income Level Quartiles						
1st Quartile	1229 (31.63)	10406 (25.62)	REF	3086 (36.99)	19804 (27.55)	REF
2nd Quartile	1101 (28.33)	9992 (24.60)	0.978 (0.891, 1.073)	2066 (24.76)	16614 (23.11)	0.947 (0.874, 1.027)
3rd Quartile	881 (22.67)	10446 (25.72)	0.927 (0.820, 1.049)	1696 (20.33)	17957 (24.98)	**0.822 (0.744, 0.907)**
4th Quartile	675 (17.37)	9775 (24.07)	**0.827 (0.700, 0.977)**	1495 (17.92)	17508 (24.36)	**0.816 (0.721, 0.924)**
Zip Code Population Density Quartiles						
1st Quartile	770 (19.81)	10703 (26.35)	REF	1521 (18.23)	18639 (25.93)	REF
2nd Quartile	841 (21.64)	10060 (24.77)	1.024 (0.891, 1.176)	1926 (23.09)	18256 (25.40)	1.074 (0.983, 1.174)
3rd Quartile	1029 (26.48)	10359 (25.50)	1.097 (0.945, 1.274)	2052 (24.60)	17461 (24.29)	**1.111 (1.001, 1.234)**
4th Quartile	1246 (32.06)	9497 (23.38)	**1.303 (1.114, 1.525)**	2844 (34.09)	17527 (24.38)	**1.270 (1.122, 1.437)**
Time	3886 (100)	40619 (100)	**0.971 (0.969, 0.972)**	8343 (100)	71883 (100)	**0.964 (0.963, 0.965)**
Age	3886 (100)	40619 (100)	**1.094 (1.069, 1.120)**	8343 (100)	71883 (100)	**1.073 (1.060, 1.086)**

- *Values are no. (%) except where indicated. The period covered in this analysis is March 1, 2020–October 21, 2021. 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 first quartile of ZIP code income and in the first quartile of ZIP code population density. 95% CIs computed with robust SEs. Bolded Figures signify statistical significance.