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Characterization of Post-Vaccination COVID-19 Cases Among School-Aged Children in Georgia: An Exploration by Urbanicity

By

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Master of Public Health

Epidemiology

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B.S., Louisiana State University, 2021

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An abstract of

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of

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Abstract

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Background

The vulnerability of pediatric populations to COVID-19 infections and geographic trends of COVID-19 infections in the United States shifted after the emergence of new variants and emergency-use authorization of mRNA COVID-19 vaccines. Nationally, and in Georgia, children became more susceptible to severe infections, and the burden of disease shifted from urban counties towards rural counties. The purpose of this thesis is to characterize breakthrough infection burden among school-aged children in Georgia and examine the relationship between urbanicity and breakthrough infections during major variant periods of the COVID-19 pandemic between June 1, 2021, and December 31, 2022.

Methods

Surveillance data on vaccinated COVID-19 cases between the ages of 5-17 years in Georgia were used in this analysis. Cases were classified as residing in a rural or urban county, and as residing in Metropolitan Atlanta or Non-Metropolitan Atlanta using the 2013 National Center for Health Statistics Urban-Rural Classification Scheme for Counties. Poisson regression was used to determine associations between residence classification and breakthrough infections by school age group during the entire study period and for each variant period, stratified by race, ethnicity, and political affiliation of the counties.

Results

The risk of breakthrough infection among children who lived in urban or Metropolitan Atlanta counties was significantly higher than that of children who lived in rural or Non-Metropolitan Atlanta counties. While urbanicity analyses had limited significant differences, the Metropolitan Atlanta analyses indicated significant differences across each stratification of race, ethnicity, and political affiliation for each age group. The incidence density ratios of the urbanicity and metropolitan variant analyses peaked during the Omicron BA.2 period, with more dramatic increases in the metropolitan analyses. Results demonstrated a stepwise inverse relationship between breakthrough risk and age group, with the oldest age group (14-17 years) having the smallest risk, and the youngest age group (5-10 years) having the highest risk.

Conclusion

Promoting primary vaccination series will raise the herd immunity of the pediatric population and lower the risk of infection among each age group. Booster vaccinations must be promoted among highly vaccinated populations to prevent mass waning immunity events that increase the risk of breakthrough infections during prolonged pandemic events.

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Introduction

The COVID-19 pandemic created many unique and shifting challenges within the United States. In the early phases of the pandemic, children presented with relatively fewer and less severe symptoms compared to adults, and few were hospitalized.[1,2] If infected, many children were asymptomatic cases; if symptomatic, the most common symptoms included fever and upper respiratory infection symptoms.[1,3] Pediatric cases also had mortality rates of less than 1% in the United States.[3] Early assessments conducted during February 2021 suggested that 9% of all United States' COVID-19 cases were comprised of pediatric cases, and it was suspected that children were a primary driver of asymptomatic transmission within communities.[3]

As the pandemic progressed and different variants of the SARS-CoV-2 virus emerged, vulnerability profiles also changed across the United States. Clinical presentations in children shifted as new variants of SARS-CoV-2 began circulating, specifically after the emergence of the Delta and Omicron BA.1 variants.[4] Children started to comprise a larger proportion of COVID-19 cases, with concomitant increases in severity that potentially required hospitalization.[2] Hospitalization rates among children peaked nationally during the weeks of September 11, 2021 (Delta variant dominance) and January 8, 2022 (Omicron BA.1 variant dominance).[2] Pediatric ICU admission rates during the Omicron surge were found to be 1.4 times higher than those reported during the Delta wave of the pandemic.[2] Consistent throughout every phase of the pandemic, however, was that minority populations of all ages were more heavily impacted by the pandemic and were more likely to be hospitalized.[2,3]

Effectiveness of COVID-19 mRNA vaccines in children and adolescents were also impacted by the emergence and circulation of new variants. Among children and adolescents who completed the primary Pfizer vaccine series, protection against symptomatic and severe infection was stronger when the Delta variant was the dominant circulating strain compared to when the Omicron BA.1 variant predominated.[5] Furthermore, vaccine effectiveness generally decreased over time across all pediatric ages.[5–7]

National trends in geographic burden of COVID-19 cases also shifted throughout the pandemic and with the emergence of new variants, especially after the emergency use approval of the COVID-19 vaccines. During the beginning of the pandemic, most incident cases were concentrated in urban counties and the Northeast and Mid-Atlantic regions of the United States; as time passed, the burden shifted towards the South and West regions of the United States and rural counties.[8,9] As vaccines were released to the general public, areas with lower vaccination rates experienced higher burden of incident cases per population. Specifically, between July 2021 and August 2021, rural counties in the US accounted for 82.2% of the lowest vaccination rates among all counties, and had 2.4 more new cases per 100,000 people than highly vaccinated, urban areas.[9] Despite national increases in case incidence due to the Delta and Omicron BA.1 waves, it was hypothesized that rural regions experienced more cases relative to urban areas during this time because of lower availability of healthcare resources for treatment and vaccination, and heightened vaccine hesitancy.[9,10]

The State of Georgia experienced similar epidemiologic trends and vaccination rates to those described on the national scale. Since February 15, 2023, Georgia has identified 2,341,378 confirmed COVID-19 cases, with notable spikes occurring during the Alpha, Delta, Omicron BA.1, and Omicron BA.5 variant surges.[11] Compared to adults, children aged 5-17 years comprised a lower proportion of cases during the first year of the pandemic until the Delta and Omicron BA.1 waves. Pediatric case burden then receded after the Omicron BA.1 wave.[11] As of February 15, 2023, Georgia's overall vaccination coverage was 59% of its total population, with

24.8% of children aged 5-9 years, 44% of children aged 10-14 years, and 57.1% of adolescents aged 15-19 years having received at least one COVID-19 vaccine dose.[12]

Throughout the COVID-19 pandemic, Georgia had observed variable rates of COVID-19 infections and vaccine uptake between its urban and rural regions. Across the state's population, vaccination counts are highest in Metropolitan Atlanta counties, while vaccinations per population are concentrated in the central region of the state.[12] With respect to case burden by county, the majority of counties, rural and urban, had high cumulative case rates by the end of 2022, but the case rates varied between surges during different variant periods.[11] Previous literature has investigated geographic trends of COVID-19 infections based on the percentage of all vaccinated citizens within each county in the United States.[9] However, these analyses excluded all data from Georgia, included data only during a short period in 2021, and were not specific to children.

The objective of this thesis is to characterize post-vaccination COVID-19 case (i.e., "breakthrough infection") burden among school-aged children in Georgia and examine the relationship between urbanicity and breakthrough infections during the COVID-19 pandemic between June 1, 2021, and December 31, 2022. This will be assessed through Poisson regression analyses of comparisons between urban versus rural and Metropolitan Atlanta versus Non-Metropolitan Atlanta pediatric vaccination breakthrough infection risks over the full study period and during each period of dominant variant circulation, stratifying on race, ethnicity, and county-level political affiliation.

The results from this thesis will contribute to the limited knowledge of trends in COVID-19 vaccine breakthrough infections among school-aged children, specifically in Georgia. These analyses also allow breakthrough infections to serve as a proxy for examining vaccine effectiveness among children in Georgia over the latter half of the pandemic and across each major

COVID-19 variant wave. By examining breakthrough infections by urbanicity and metropolitan status, the impacts of complex regional differences on vaccine effectiveness among school-aged children can be explored. Characterizing regional differences in breakthrough infections can also assist state leaders to determine where to prioritize primary series and booster vaccination promotions for children.

Methods

Study Design

A retrospective cohort study was conducted to characterize the burden of pediatric post-vaccination COVID-19 infections (i.e., "breakthrough infections") in Georgia. Breakthrough infections were defined using the Georgia Department of Public Health's definition: any laboratory-confirmed SARS-CoV-2 infection occurring at least 14 days after completing a primary vaccination series, and no positive SARS-CoV-2 laboratory test within 90 days prior to the current test.[13] For children aged 5-17 years who received both their primary series and a booster dose, breakthrough infections were defined as any Georgia resident between the ages of 5-17 years who had a laboratory-confirmed SARS-CoV-2 infection at least 14 days after receiving their booster dose on or after August 13, 2021, and no positive SARS-CoV-2 laboratory test within 90 days prior to the current test.[13]

Vaccination information for each case was obtained from the Georgia Registry of Immunization Transactions (GRITS) and was matched to each case as of February 7, 2023. The vaccination status of each case was classified as one of the following: (1) unvaccinated if they had not received any vaccination, (2) partially vaccinated if they received one dose of any age-approved vaccine, (3) fully vaccinated if they completed their primary vaccination series of any vaccine according to age-appropriate guidelines, or (4) fully vaccinated plus booster if they completed their primary vaccine series and obtained an additional vaccine dose from any manufacturer on or after August 13, 2021 according to age-appropriate guidelines. If a case was reported ill within 14 days of their first vaccination dose, they were considered unvaccinated at time of infection. Likewise, if a case was reported ill within 14 days of their second vaccination, they were considered partially vaccinated at time of infection, and considered fully vaccinated at time of infection if infected within 14 days of receiving their booster dose.

Cases were stratified into age groups to reflect primary, middle, and high school enrollment, respectively: 5-10 years old, 11-13 years old, and 14-17 years old. Dividing cases into these smaller categories based on typical school-based age ranges provides a more nuanced and relatable interpretation of breakthrough infections by attempting to account for the different social and environmental factors affecting children of different life stages. This includes, but is not limited to, different social mixing patterns, contact rates and extracurricular activities among children of different ages.

The urbanicity assignment of cases was determined by the classification of their county of residence per the 2013 National Center for Health Statistics (NCHS) Urban-Rural Classification Scheme for Counties.[14] The Metropolitan-Atlanta region classification follows the 2013 NCHS Atlanta-Sandy Springs-Roswell Metropolitan Statistical Area definition, which includes Fulton, Barrow, Bartow, Butts, Carroll, Cherokee, Clayton, Cobb, Coweta, Dawson, DeKalb, Douglas, Fayette, Forsyth, Gwinnett, Haralson, Heard, Henry, Jasper, Lamar, Meriwether, Morgan, Newton, Paulding, Pickens, Pike, Rockdale, Spalding, and Walton counties.[14] As of the time of this analysis, the 2013 Urban-Rural Classification Scheme for Counties was the most up-to-date version of this classification scheme developed by the NCHS.

Periods of variant predominance were determined based upon when at least 70% of sequenced cases nationwide during a particular week resulted positive for the same variant.[15]

Using an approximation of the Centers for Disease Control and Prevention Museum COVID-19 Timeline, the major variants and their periods of dominance being evaluated in this study were outlined as follows: Delta (June 1, 2021 – November 30, 2021), Omicron BA.1 (December 1, 2021 – April 12, 2022), Omicron BA.2 (April 13, 2022 – July 5, 2022), Omicron BA.5 (July 6, 2022 – October 31, 2022), and Omicron BQ.1/BQ.11 (November 1, 2022 – December 31, 2022).[16] Although the Alpha variant predominance period (January 1, 2021 – May 31, 2021) meets the criteria for inclusion, too few children were vaccinated before or during that timeframe to produce reliable results for analysis, and the period was therefore excluded. The periods for Beta, Gamma, and Omicron BA.4 variants were excluded from the analysis because they did not independently meet the aforementioned predominance criteria.

Source Population, Study Population, and Ethical Considerations

Children and adolescents who were aged 5-17 years old, residents of Georgia, and reported to the Georgia State Electronic Notifiable Disease Surveillance System (SendSS) as having a laboratory-confirmed positive SARS-CoV-2 test (PCR or antigen) between June 1, 2021, to December 31, 2022, were included in the source population. For these analyses, individuals who completed their primary vaccination series or their primary vaccination series plus a booster were considered fully vaccinated and retained in the cohort, and individuals who partially completed their vaccination series or did not receive any vaccine were considered unvaccinated and were dropped from the cohort. The timeframe of the study was determined by the availability of pediatric vaccines through emergency use authorization and full approval granted by the US Food and Drug Administration (FDA) (Supplement 1).[17] Because these data were collected as part of Georgia Department of Public Health COVID-19 surveillance, all individual-level information of cases was deidentified for this thesis. Case matching to vaccination records in GRITS was done by Georgia Department of Public Health staff before the dataset was shared with study personnel.

The study methods were reviewed and approved by the Georgia Department of Public Health Institutional Review Board.

Data Sources

Surveillance data of each pediatric COVID-19 case for the State of Georgia was provided by the Georgia Department of Public Health. Weekly and cumulative vaccination counts and rates for each county, by school age group, were obtained from the publicly available Georgia Institute of Technology School Aged COVID-19 Dashboard.[18]

Data Analysis

Rates of breakthrough infections were calculated and plotted by age group for the full study period. Poisson regression models were used to compare total breakthrough infections among urban versus rural counties of residence and Metropolitan Atlanta versus Non-Metropolitan Atlanta counties of residence during the entire timeframe and for each variant period, stratified on race, ethnicity, and political party affiliation of the county based on the results of the 2020 Presidential Election.[19] These stratifications were chosen because of their potential effect on vaccine receipt within each county classification.

Results

Descriptive Results

Over 80% of all pediatric COVID-19 cases included in the source population lived in an urban county, and approximately 55% lived in Metropolitan Atlanta. The majority (80%) were unvaccinated for COVID-19 at the time of their reported infection (Table 1). High school students (22.0%, 14–17 years age group) had the highest proportion having completed their primary vaccination series, followed by middle school students (15.0%, 11–13 years age group) and primary school students (7.3%, 5–10 years age group) (Table 1). This same stepwise pattern in primary series completion by the age group was also observed for booster vaccine receipt (Table 1).

Among 291,785 pediatric COVID-19 cases reported in Georgia between June 1, 2021, and December 31, 2022, 46,593 (16.0%) were instances of post-vaccination infections (i.e., breakthrough infections). The highest breakthrough infection rates were among high school students during the entire study period except during the Omicron BA.2 wave, when breakthrough rates among primary school students surpassed those observed among high school students (Figure 1).

Table 1. Demographic characteristics of COVID-19 cases from surveillance data collected between June 1, 2021, and December 31, 2022, stratified by age group (n=291,785). Each column corresponds to the number of individuals within each demographic category and the percentage within each age group (5 – 10 Years Old, 11 – 13 Years Old, and 14 – 17 Years Old).

	Age Group		
Variable	**5 – 10 Years Old N = 115,987**	**11 – 13 Years Old N = 71,359**	**14 – 17 Years Old N = 104,439**
County Residency			
Rural	18,786 (16%)	12,236 (17%)	18,600 (18%)
Urban	97,201 (84%)	59,123 (83%)	85,839 (82%)
Metropolitan-Atlanta Residency			
Yes	64,606 (56%)	38,613 (54%)	56,271 (54%)
No	51,381 (44%)	32,746 (46%)	48,168 (46%)
County Political Affiliation			
Democratic	63,189 (54%)	36,700 (51%)	52,558 (50%)
Republican	52,798 (46%)	34,659 (49%)	51,881 (50%)
Sex			
Female	57,286 (49%)	35,570 (50%)	55,946 (54%)
Male	58,020 (50%)	35,403 (50%)	48,009 (46%)
Unknown	681 (0.6%)	386 (0.5%)	484 (0.5%)
Race			
American Indian / Alaskan Native	114 (<0.1%)	62 (<0.1%)	130 (0.1%)
Asian	4,567 (3.9%)	2,282 (3.2%)	2,964 (2.8%)
Black	38,276 (33%)	22,739 (32%)	32,577 (31%)
Native Hawaiian / Pacific Islander	119 (0.1%)	95 (0.1%)	123 (0.1%)
Other	9,125 (7.9%)	5,345 (7.5%)	7,139 (6.8%)
Unknown	19,993 (17%)	12,679 (18%)	18,126 (17%)
White	43,793 (38%)	28,157 (39%)	43,380 (42%)
Ethnicity			
Hispanic / Latino	12,655 (11%)	8,075 (11%)	12,058 (12%)
Non-Hispanic / Latino	79,135 (68%)	48,293 (68%)	70,732(68%)
Not Specified	24,197 (21%)	14,991 (21%)	21,649 (21%)
Vaccination Status			
Fully Vaccinated with Booster	467 (0.4%)	852 (1.2%)	3,264 (3.1%)
Fully Vaccinated	8,430 (7.3%)	10,413 (15%)	23,167 (22%)
Partially Vaccinated	4,200 (3.6%)	2,804 (3.9%)	4,121 (3.9%)
Unvaccinated	102,890 (89%)	57,290 (80%)	73,887 (71%)

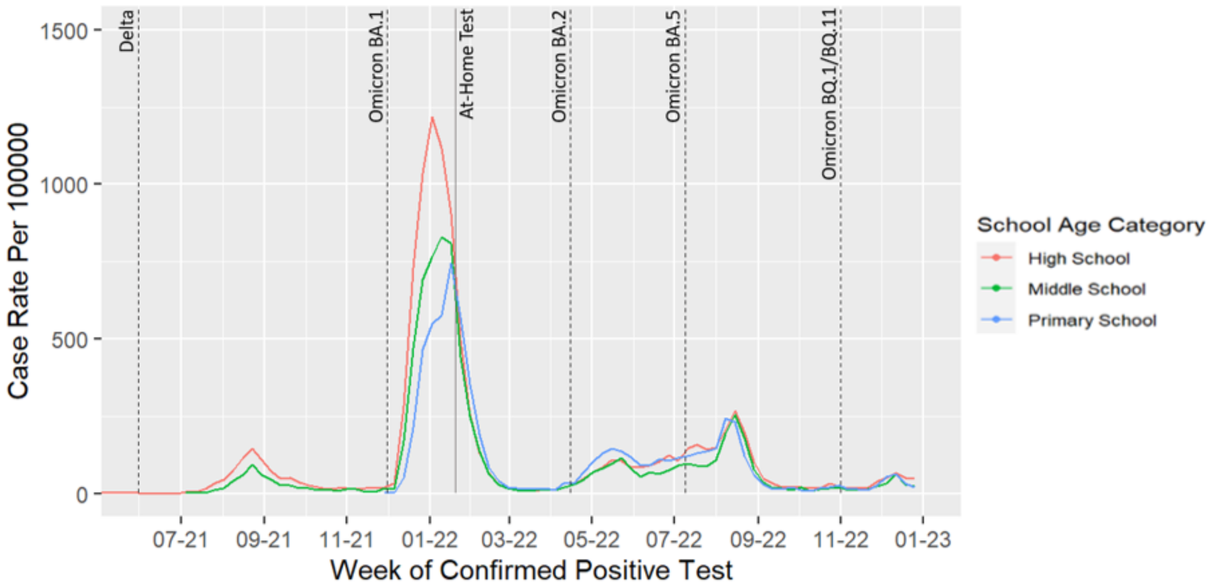


Figure 1. Breakthrough infection rates among school-aged children from June 1, 2021, through December 31, 2022, stratified by age group. Dotted vertical lines represent the beginning of a new variant predominance period and are labelled with their corresponding variant. The first mass distribution of government-supplied at-home testing kits on January 19, 2022, is indicated with a solid line.

Overall Breakthrough Analyses

Children who resided in either an urban county or a metropolitan county and identified as either Black or White were significantly more likely to experience a breakthrough COVID-19 infection than their Black or White counterparts residing in rural or Non-Metropolitan Atlanta counties. ($IDR_{Urban, Black}$ = 7.5 p-value 0.0037; $IDR_{Urban, White}$ = 8.1 p-value 0.0007; $IDR_{Metro, Black}$ = 6.5 p-value <0.0001; $IDR_{Metro, White}$ = 7.1 p-value <0.0001). Children who identified as non-Hispanic or Latino and resided in an urban county were 7.9 times more likely to experience a breakthrough infection compared to all non-Hispanic or Latino children who lived in rural counties (p-value < 0.0001), and all children who identified as non-Hispanic or Latino and lived in Metropolitan Atlanta were 7.6 times more likely to have a breakthrough infection compared to the equivalent population in Non-Metropolitan Atlanta (p-value < 0.0001). Significant associations were also observed between breakthrough infection rates among all children who resided in either urban counties or metropolitan counties regardless of the political affiliation of the county; however, higher ratios of breakthrough infections were observed among urban and metropolitan counties that were affiliated with the Democratic Party ($IDR_{Urban, Democratic} = 14.1$ p-value 0.014; $IDR_{Metro, Democratic} = 6.2$ p-value < 0.0001) (Table 2).

Urban students enrolled in each level of education who also identified as either White, Black, non-Hispanic or Latino, or lived in a Democratic Party-affiliated county had a significantly elevated risk of infection compared to rural students enrolled in the same level of education and identical demographic classifications (Table 2). Urban high school students who lived in Republican Party-affiliated counties were also 3.06 times more likely to have a breakthrough infection compared to rural high school students who lived in Republican Party-affiliated counties (p-value 0.032). Aside from the aforementioned observations, there was no significant difference between urban and rural students in each age group who identified as any of the other race, ethnic, and political affiliation categories (Table 2).

While the other race and ethnicity categories were not significant under the urban versus rural analysis, all stratification categories in every age group and among overall cases demonstrated that Metropolitan Atlanta children were significantly more likely to have a breakthrough infection than the corresponding population in Non-Metropolitan Atlanta Counties (Table 2). Notably, those who identified as Asian and resided in a metropolitan county were between 18 and 33 times more likely to experience a breakthrough infection compared to children who identified as Asian and resided in a non-metropolitan county ($\text{p-value}_{\text{all children}}$ 0.0063; $\text{p-value}_{\text{high school}}$ 0.0057; $\text{p-value}_{\text{middle school}}$ 0.0066; $\text{p-value}_{\text{primary school}}$ 0.0025) (Table 2).

When comparing the risk of breakthrough infection between the three school-age groups, a significant stepwise, inverse relationship between breakthrough infection ratios and age group was identified across all stratification categories for both urbanicity and metropolitan analyses. For example, among the race stratification for Black students in the urbanicity analysis, high school students exhibited the lowest ratios (IDR = 7.1 p-value 0.0069), followed by middle school students (IDR = 7.7 p-value 0.038), then primary school students (IDR = 12.5 p-value 0.047) (Table 2).

Table 2. Incidence density ratios of breakthrough infections with 95% confidence intervals comparing urban county of residence against rural county of residence, and Metropolitan Atlanta residence against Non-Metropolitan Atlanta residence, stratified by demographics and school-age group from June 1, 2021, through December 31, 2022 (α = 0.05)**.**

	Urban vs. Rural		**Metropolitan Atlanta vs. Non-Metropolitan Atlanta**	
	Incidence Density Ratio (95% CI)	**P-Value**	**Incidence Density Ratio (95% CI)**	**P-Value**
Combined Ages				
Race				
Asian	24.7 (0.169, 3622)	0.21	20.3 (2.34, 177)	0.0063
Black	7.5 (1.92, 29.1)	0.0037	6.5 (3.00, 14.0)	< 0.0001
Other	7.6 (0.353, 165)	0.19	7.1 (1.39, 36.6)	0.019
Not Specified	6.8 (0.45, 103)	0.17	5.4 (1.77, 16.7)	0.0031
White	8.1 (2.42, 27.3)	0.0007	7.1 (3.54, 14.2)	< 0.0001
Ethnicity				
Hispanic or Latino	9.7 (0.58, 162)	0.11	6.4 (1.68, 24.3)	0.0065
Not specified	10.0 (0.74, 135)	0.084	6.2 (2.09, 18.1)	0.001
Non-Hispanic or Latino	7.9 (3.07, 20.5)	< 0.0001	7.6 (4.4, 13.1)	< 0.0001
Political Affiliation				
Democratic	14.1 (1.70, 117)	0.014	6.2 (3.20, 12.1)	< 0.0001
Republican	3.27 (1.34, 7.99)	0.0094	2.97 (1.48, 6.0)	0.0021
High School (14-17 Years)				
Race				
Asian	23.5 (0.192, 2872)	0.20	18.8 (2.35, 150)	0.0057
Black	7.1 (1.71, 29.1)	0.0069	5.9 (2.64, 13.2)	< 0.0001
Other	7.2 (0.360, 143)	0.20	6.5 (1.34, 31.9)	0.021
Not Specified	5.8 (0.398, 85.1)	0.20	4.8 (1.58, 14.8)	0.0059

White	7.4 (2.01, 27.4)	0.0026	6.3 (2.99, 13.2)	< 0.0001
Ethnicity				
Hispanic or Latino	9.1 (0.56, 147)	0.12	5.9 (1.56, 22.3)	0.0088
Not specified	9.7 (0.74, 128)	0.083	5.6 (1.88, 16.7)	0.002
Non-Hispanic or Latino	7.0 (2.30, 21.3)	0.0006	6.7 (3.52, 12.8)	< 0.0001
Political Affiliation				
Democratic	14.4 (1.81, 114)	0.012	5.8 (2.84, 12.0)	< 0.0001
Republican	3.06 (1.10, 8.5)	0.032	2.74 (1.31, 5.8)	0.0077
Middle School (11-13 Years)				
Race				
Asian	25.7 (0.173, 3808)	0.20	20.9 (2.33, 188)	0.0066
Black	7.7 (1.13, 53.2)	0.038	6.6 (2.32, 18.6)	0.0004
Other	7.9 (0.297, 208)	0.22	7.3 (1.29, 40.7)	0.024
Not Specified	6.4 (0.331, 123)	0.22	5.4 (1.47, 19.6)	0.011
White	8.1 (1.33, 49.7)	0.023	7.0 (2.61, 18.7)	0.0001
Ethnicity				
Hispanic or Latino	10.3 (0.46, 234)	0.14	6.6 (1.46, 29.8)	0.014
Not specified	11.0 (0.57, 212)	0.11	6.3 (1.69, 23.2)	0.006
Non-Hispanic or Latino	7.9 (1.40, 45.0)	0.019	7.5 (2.92, 19.3)	< 0.0001
Political Affiliation				
Democratic	14.8 (1.23, 179)	0.034	6.1 (2.30, 16.1)	0.0003
Republican	3.15 (0.65, 15.3)	0.15	2.9 (1.06, 7.7)	0.039
Primary School (5-10 Years)				
Race				
Asian	41.5 (0.223, 7752)	0.16	33.4 (3.42, 325)	0.0025
Black	12.5 (1.03, 152)	0.047	10.5 (3.06, 36.0)	0.0002
Other	12.7 (0.332, 488)	0.17	11.6 (1.82, 74)	0.0095
Not Specified	10.3 (0.376, 282)	0.17	8.6 (2.02, 36.4)	0.0036
White	13.2 (1.19, 146)	0.036	11.2 (3.41, 36.5)	< 0.0001
Ethnicity				
Hispanic or Latino	17.0 (0.49, 592)	0.12	10.5 (1.98, 56)	0.0057
Not specified	18.2 (0.60, 547)	0.095	10.0 (2.26, 44)	0.0024
Non-Hispanic or Latino	13.1 (1.19, 144)	0.036	12.0 (3.69, 38.7)	< 0.0001
Political Affiliation				
Democratic	23.8 (1.37, 414)	0.030	9.7 (3.00, 31.2)	0.0001
Republican	5.1 (0.57, 45)	0.15	4.5 (1.38, 25.0)	0.013

COVID-19 Variant Impact Analysis

Delta Period

When examining data from all combined ages, children who lived in urban counties and identified as either White or non-Hispanic were significantly more likely to report a breakthrough infection than the corresponding age and demographic group that lived in rural counties (Table 3). The same pattern of significant differences between urban and rural counties was observed among high school students. None of the other stratifications by race, ethnicity, and county political affiliation demonstrated significant differences between urban and rural counties overall or within each age group (Table 3).

During the Delta wave, Metropolitan Atlanta students were significantly more at risk for breakthrough infections compared to Non-Metropolitan Atlanta students across several categories. Students who identified as Asian, White, Black, and non-Hispanic or Latino across each age group in metropolitan counties had significantly elevated risk compared to students in the same demographics in non-metropolitan counties (Table 3). In addition, metropolitan-area high school students had significantly higher breakthrough infection rates within each ethnicity category (p-value$_{\text{Hispanic/Latino}}$ 0.05; p-value$_{\text{not specified}}$ 0.0271; p-value$_{\text{non-Hispanic/Latino}} < 0.0001$). Among children residing in Democratic counties, the elevated breakthrough risk among Metropolitan-Atlanta area children as compared to Non-Metropolitan Atlanta children was consistent within and across all school-age strata (Table 3). This was not observed among children residing in Republican counties, where the increased metropolitan-associated risk was driven largely by the high school-aged children ($IDR_{\text{High School}} = 3.30$ p-value 0.0076). All other demographic and political stratifications showed no significant differences in breakthrough infection risk between Metropolitan and Non-Metropolitan Atlanta counties during the Delta variant period (Table 3).

Omicron BA.1 Period

Among urban students during the Omicron BA.1 period, significantly increased risk of breakthrough infection occurred among students who identified as either Black, White, or non-Hispanic or Latino in the overall, high school, and middle school age groups (Table 4). County-level political affiliation with either party was associated with an increased risk among all urban students collectively, and among urban high school students individually, with the Democratic Party affiliation holding a higher risk than the Republican Party affiliation (Table 4). Urban county associations with the Democratic Party also had an increased risk of breakthrough infection among middle school students (p-value 0.0471). No significant differences were observed between urban and rural primary school students. All stratifications by race, ethnicity, and county political party affiliation were significantly different between metropolitan and non-metropolitan counties, with the exception of middle school students stratified on county affiliation with the Republican Party (Table 4).

Omicron BA.2 Period

The urbanicity analyses for the Omicron BA.2 period demonstrated limited significant differences between students in urban and rural counties. All students who identified as Black, White, or non-Hispanic or Latino and resided in an urban county were more at risk for a breakthrough infection than all the students who identified as Black, White, or non-Hispanic or Latino, and resided in a rural county (IDR_{Black} = 15.7 p-value 0.0354; IDR_{White} = 15.0 p-value 0.0232; $IDR_{non\text{-}Hispanic}$ = 13.1 p-value 0.005). In contrast, every race, ethnicity, and political affiliation stratification for the overall and individual age group metropolitan analyses yielded significant differences between metropolitan and non-metropolitan students (Table 5). In most instances, the incidence density ratios of the metropolitan analyses were at least doubled their value from the Omicron BA.1 period.

Omicron BA.5 Period

Urban versus rural analyses for the Omicron BA.5 period found identical patterns of significant differences among all students combined. During the Omicron BA.5 period, however, significant differences were also identified among the high, middle, and primary school students independently when stratified on White, Black, and non-Hispanic or Latino categories (Table 6). Similar to Omicron BA.2, all stratifications within the metropolitan analysis yielded significant differences between metropolitan and non-metropolitan students overall and within each age group (Table 6).

Omicron BQ.1/BQ.11

Overall, urban children who identified as White, Black, or non-Hispanic or Latino during the Omicron BQ.1/BQ.11 period had significantly higher breakthrough infection rates than rural children who identified as each corresponding demographic (Table 7). When the age groups were examined independently, a significant increase in risk occurred between urban and rural high school students who identified as either White or non-Hispanic or Latino (Table 7). All stratifications in the metropolitan analyses yielded significant results (Table 7).

All other stratifications on race, ethnicity, and political party affiliation during these periods did not identify significant differences between urban and rural students. Importantly, when significant differences did occur within age groups in both urban and metropolitan comparisons, there was a stepwise inverse increase in risk, from the oldest age group (high school students) having the lowest risk, to the youngest age group (primary school students) having the highest risk.

Table 3. Incidence density ratios of breakthrough infections with 95% confidence intervals comparing urban county of residence against rural county of residence, and Metropolitan Atlanta residence against Non-Metropolitan Atlanta residence, stratified by race, ethnicity, and county political affiliation during the Delta COVID-19 variant period (June 1, 2021 – November 30, 2021) ($\alpha = 0.05$). Incidence density ratios were not calculated for primary school students because the population size was too small.

	Urban vs. Rural		**Metropolitan Atlanta vs. Non-Metropolitan Atlanta**	
	Incidence Density Ratio (95% CI)	**P-Value**	**Incidence Density Ratio (95% CI)**	**P-Value**
Combined Ages				
Race				
Asian	13.7 (0.103, 1825)	0.294	12.4 (1.17, 131)	0.0365
Black	8.1 (0.83, 79)	0.0715	7.6 (2.48, 23.2)	0.0004
Other	7.4 (0.0186, 2944)	0.51	5.7 (0.60, 54)	0.130
Not Specified	3.71 (0.0924, 149)	0.49	3.61 (0.73, 18.0)	0.117
White	7.3 (1.75, 30.6)	0.0064	6.7 (2.99, 15.0)	< 0.0001
Ethnicity				
Hispanic or Latino	5.3 (0.116, 239)	0.393	5.9 (0.90, 38.2)	0.0651
Not specified	6.5 (0.201, 212)	0.291	4.5 (0.98, 20.8)	0.0535
Non-Hispanic or Latino	6.8 (1.86, 24.9)	0.0038	7.1 (3.49, 14.5)	< 0.0001
Political Affiliation				
Democratic	8.4 (0.190, 374)	0.271	5.1 (1.92, 13.8)	0.0011
Republican	3.06 (0.89, 10.6)	0.077	3.32 (1.35, 8.2)	0.0089
High School (14-17 Years)				
Race				
Asian	13.2 (0.136, 1283)	0.269	11.6 (1.31, 102)	0.0277
Black	7.9 (0.92, 68)	0.060	8.0 (2.80, 22.8)	0.0001
Other	10.7 (0.040, 2838)	0.41	5.8 (0.73, 47)	0.0973
Not Specified	3.80 (0.118, 122)	0.45	3.39 (0.76, 15.2)	0.1097
White	7.1 (1.70, 29.8)	0.0073	6.4 (2.92, 14.2)	< 0.0001
Ethnicity				
Hispanic or Latino	6.0 (0.164, 223)	0.328	5.9 (1.00, 34.6)	0.050
Not specified	8.0 (0.298, 213)	0.216	5.1 (1.20, 21.4)	0.0271
Non-Hispanic or Latino	7.7 (2.05, 29.3)	0.0025	6.8 (3.29, 14.1)	< 0.0001
Political Affiliation				
Democratic	10.8 (0.301, 386)	0.193	5.3 (2.04, 13.9)	0.0006
Republican	3.50 (1.00, 12.3)	0.051	3.30 (1.37, 7.9)	0.0076
Middle School (11-13 Years)				
Race				
Asian	16.1 (0.093, 2779)	0.291	13.7 (1.19, 159)	0.0359
Black	9.6 (0.386, 241)	0.168	9.5 (2.03, 44)	0.0043

Other	13.0 (0.026, 6527)	0.42	7.0 (0.66, 73)	0.107
Not Specified	4.6 (0.071, 300)	0.47	4.0 (0.64, 25.4)	0.137
White	8.7 (0.63, 119)	0.107	7.7 (2.08, 28.3)	0.0022
Ethnicity				
Hispanic or Latino	5.0 (0.059, 414)	0.48	6.9 (0.81, 59)	0.078
Not specified	6.5 (0.095, 448)	0.384	6.0 (0.86, 41)	0.072
Non-Hispanic or Latino	6.4 (0.42, 97)	0.183	8.0 (2.04, 31.3)	0.0029
Political Affiliation				
Democratic	8.0 (0.102, 622)	0.351	5.6 (1.24, 25.2)	0.0251
Republican	2.58 (0.184, 36.2)	0.48	3.46 (0.79, 15.1)	0.099

Table 4. Incidence density ratios of breakthrough infections with 95% confidence intervals comparing urban county of residence against rural county of residence, and Metropolitan Atlanta residence against Non-Metropolitan Atlanta residence, stratified by race, ethnicity, and county political affiliation during the Omicron BA.1 COVID-19 variant period (December 1, 2021 – April 12, 2022) (α = 0.05).

	Urban vs. Rural		**Metropolitan Atlanta vs. Non-Metropolitan Atlanta**	
	Incidence Density Ratio (95% CI)	**P-Value**	**Incidence Density Ratio (95% CI)**	**P-Value**
Combined Ages				
Race				
Asian	23.0 (0.138, 3832)	0.229	17.7 (2.13, 146)	0.0078
Black	7.0 (1.68, 29.0)	0.0075	5.6 (2.56, 12.3)	< 0.0001
Other	6.0 (0.272, 134)	0.255	5.4 (1.05, 28.1)	0.044
Not Specified	5.6 (0.354, 89)	0.221	5.0 (1.63, 15.3)	0.0048
White	7.9 (2.32, 26.8)	0.0009	6.5 (3.29, 12.9)	< 0.0001
Ethnicity				
Hispanic or Latino	8.1 (0.47, 142)	0.150	5.3 (1.35, 21.0)	0.0169
Not specified	8.7 (0.59, 128)	0.114	5.6 (1.92, 16.5)	0.0017
Non-Hispanic or Latino	7.5 (2.85, 19.8)	< 0.0001	6.7 (3.88, 11.6)	< 0.0001
Political Affiliation				
Democratic	12.9 (1.23, 134)	0.0328	5.4 (2.78, 10.4)	< 0.0001
Republican	3.11 (1.24, 7.8)	0.0159	2.74 (1.35, 5.6)	0.0053
High School (14-17 Years)				
Race				
Asian	22.5 (0.178, 2835)	0.207	17.1 (2.33, 125)	0.0052
Black	6.6 (1.54, 27.8)	0.0108	5.2 (2.37, 11.6)	< 0.0001
Other	5.9 (0.309, 114)	0.237	5.2 (1.08, 24.6)	0.0392
Not Specified	5.1 (0.357, 73)	0.229	4.6 (1.55, 13.8)	0.0059
White	7.3 (2.03, 26.3)	0.0024	6.0 (2.94, 12.2)	< 0.0001

Ethnicity				
Hispanic or Latino	7.7 (0.48, 123)	0.149	5.1 (1.35, 19.4)	0.0165
Not specified	9.4 (0.70, 127)	0.090	5.4 (1.86, 15.7)	0.0019
Non-Hispanic or Latino	6.8 (2.25, 20.4)	0.0007	6.1 (3.31, 11.5)	< 0.0001
Political Affiliation				
Democratic	14.2 (1.51, 134)	0.0205	5.3 (2.61, 10.6)	< 0.0001
Republican	2.97 (1.07, 8.3)	0.0374	2.62 (1.26, 5.5)	0.0103
Middle School (11-13 Years)				
Race				
Asian	25.0 (0.163, 3832)	0.21	18.1 (2.20, 148)	0.007
Black	7.3 (1.05, 51)	0.045	5.6 (2.01, 15.3)	0.0009
Other	6.6 (0.257, 170)	0.254	5.5 (1.01, 29.6)	0.049
Not Specified	5.7 (0.301, 108)	0.246	4.9 (1.40, 17.2)	0.0131
White	8.1 (1.35, 49)	0.0223	6.4 (2.47, 16.4)	0.0001
Ethnicity				
Hispanic or Latino	8.8 (0.391, 196)	0.171	5.4 (1.20, 24.2)	0.0278
Not specified	10.7 (0.54, 214)	0.120	5.7 (1.59, 20.4)	0.0075
Non-Hispanic or Latino	7.7 (1.37, 43)	0.0204	6.5 (2.62, 16.1)	< 0.0001
Political Affiliation				
Democratic	14.8 (1.04, 210)	0.0471	5.2 (2.00, 13.3)	0.0007
Republican	3.09 (0.63, 15.2)	0.166	2.57 (0.97, 6.8)	0.059
Primary School (5-10 Years)				
Race				
Asian	43 (0.185, 10337)	0.175	30.4 (3.18, 291)	0.003
Black	12.8 (0.70, 231)	0.085	9.3 (2.47, 35.3)	0.001
Other	11.6 (0.228, 587)	0.222	9.2 (1.38, 62)	0.0221
Not Specified	10.0 (0.260, 383)	0.216	8.2 (1.81, 37.4)	0.0063
White	14.2 (0.86, 235)	0.064	10.7 (2.99, 38.2)	0.0003
Ethnicity				
Hispanic or Latino	15.3 (0.321, 732)	0.166	9.2 (1.57, 53)	0.0138
Not specified	18.8 (0.42, 847)	0.131	9.7 (2.01, 46)	0.0046
Non-Hispanic or Latino	13.5 (0.78, 233)	0.074	11.0 (3.05, 39.9)	0.0003
Political Affiliation				
Democratic	24.6 (0.85, 708)	0.062	8.7 (2.42, 31.4)	0.0009
Republican	5.1 (0.370, 71)	0.223	4.3 (1.17, 16.1)	0.0279

Table 5. Incidence density ratios of breakthrough infections with 95% confidence intervals comparing urban county of residence against rural county of residence, and Metropolitan Atlanta residence against Non-Metropolitan Atlanta residence, stratified by race, ethnicity, and county political affiliation during the Omicron BA.2 COVID-19 variant period (April 13, 2022 – July 5, 2022) (α = 0.05).

	Urban vs. Rural		**Metropolitan Atlanta vs. Non-Metropolitan Atlanta**	
	Incidence Density Ratio (95% CI)	**P-Value**	**Incidence Density Ratio (95% CI)**	**P-Value**
Combined Ages				
Race				
Asian	24.2 (0.0035, 168000)	0.48	41 (2.01, 832)	0.0158
Black	15.7 (1.21, 203)	0.0354	14.8 (5.1, 43)	< 0.0001
Other	31.2 (0.0006, 1560000)	0.53	30.2 (1.86, 489)	0.0165
Not Specified	8.3 (0.0303, 2270)	0.46	8.2 (1.63, 41)	0.0107
White	15.0 (1.45, 155)	0.0232	17.7 (6.3, 49)	< 0.0001
Ethnicity				
Hispanic or Latino	28.7 (0.0107, 76700)	0.40	22.5 (2.26, 224)	0.0079
Not specified	12.0 (0.090, 1590)	0.320	12.8 (2.81, 58)	0.001
Non-Hispanic or Latino	13.1 (2.17, 79)	0.005	16.7 (7.6, 36.5)	< 0.0001
Political Affiliation				
Democratic	14.1 (0.58, 342)	0.104	9.7 (4.3, 22.0)	< 0.0001
Republican	3.61 (0.77, 16.8)	0.103	6.1 (2.38, 15.4)	0.0002
High School (14-17 Years)				
Race				
Asian	25.3 (0.0033, 193000)	0.48	32.7 (1.51, 710)	0.0263
Black	10.5 (0.58, 193)	0.1126	11.8 (3.57, 39.1)	< 0.0001
Other	26.5 (0.0005, 1530000)	0.56	25.0 (1.45, 431)	0.0266
Not Specified	7.3 (0.0237, 2250)	0.50	6.4 (1.13, 36.3)	0.0361
White	10.3 (0.69, 153)	0.0904	13.7 (4.1, 46)	< 0.0001
Ethnicity				
Hispanic or Latino	26.0 (0.0089, 75900)	0.42	19.5 (1.87, 205)	0.0131
Not specified	10.1 (0.067, 1520)	0.365	10.5 (2.07, 54)	0.0045
Non-Hispanic or Latino	9.0 (0.97, 83)	0.0534	13.4 (4.9, 36.6)	< 0.0001
Political Affiliation				
Democratic	10.2 (0.313, 331)	0.192	8.8 (3.34, 23.1)	< 0.0001
Republican	2.99 (0.50, 17.8)	0.228	5.3 (1.82, 15.5)	0.0022
Middle School (11-13 Years)				
Race				
Asian	51 (0.0026, 983000)	0.44	49 (1.84, 1300)	0.0201
Black	21.0 (0.232, 1900)	0.186	17.7 (3.30, 95)	0.0008
Other	53 (0.0005, 5180000)	0.50	37.4 (1.78, 788)	0.0198
Not Specified	14.6 (0.0119, 17900)	0.46	9.6 (1.23, 75)	0.0311

White	20.5 (0.361, 1170)	0.143	20.6 (4.2, 102)	0.0002
Ethnicity				
Hispanic or Latino	57 (0.0077, 419000)	0.374	28.5 (2.00, 407)	0.0135
Not specified	22.2 (0.0371, 13200)	0.342	15.4 (2.02, 117)	0.0082
Non-Hispanic or Latino	19.7 (0.375, 1040)	0.140	19.5 (4.3, 89)	0.0001
Political Affiliation				
Democratic	17.4 (0.257, 1170)	0.184	11.0 (2.70, 45)	0.0008
Republican	5.1 (0.189, 138)	0.332	6.7 (1.55, 28.8)	0.011
Primary School (5-10 Years)				
Race				
Asian	64 (0.0031, 1330000)	0.41	57 (2.28, 1420)	0.0138
Black	26.8 (0.3624, 1980)	0.134	20.5 (4.3, 97)	0.0001
Other	67 (0.0005, 8870000)	0.48	43 (2.06, 919)	0.0154
Not Specified	18.6 (0.0210, 16500)	0.3985	11.1 (1.59, 78)	0.0153
White	26.2 (0.274, 2500)	0.1605	23.9 (5.3, 108)	< 0.0001
Ethnicity				
Hispanic or Latino	57 (0.0065, 495000)	0.383	32.3 (2.28, 459)	0.0102
Not specified	22.1 (0.044, 11200)	0.329	17.4 (2.59, 117)	0.0033
Non-Hispanic or Latino	19.7 (0.304, 1280)	0.162	22.1 (5.5, 89)	< 0.0001
Political Affiliation				
Democratic	17.6 (0.272, 1150)	0.178	12.1 (3.33, 44)	0.0002
Republican	5.2 (0.158, 171)	0.356	7.3 (1.86, 28.9)	0.0045

Table 6. Incidence density ratios of breakthrough infections with 95% confidence intervals comparing urban county of residence against rural county of residence, and Metropolitan Atlanta residence against Non-Metropolitan Atlanta residence, stratified by race, ethnicity, and county political affiliation during the Omicron BA.5 COVID-19 variant period (July 6, 2022 – October 31, 2022) (α = 0.05).

	Urban vs. Rural		**Metropolitan Atlanta vs. Non-Metropolitan Atlanta**	
	Incidence Density Ratio (95% CI)	**P-Value**	**Incidence Density Ratio (95% CI)**	**P-Value**
Combined Ages				
Race				
Asian	17.7 (0.215, 1450)	0.202	19.9 (2.26, 176)	0.0071
Black	6.0 (1.97, 18.1)	0.0016	6.4 (3.27, 12.5)	< 0.0001
Other	5.3 (0.46, 61)	0.182	7.2 (1.68, 31.1)	0.0079
Not Specified	5.2 (0.49, 55)	0.170	4.9 (1.84, 13.3)	0.0015
White	6.0 (1.96, 18.3)	0.0017	5.6 (2.84, 11.1)	< 0.0001
Ethnicity				
Hispanic or Latino	8.8 (0.79, 98)	0.077	5.6 (1.77, 17.9)	0.0035

Not specified	6.9 (0.68, 70)	0.101	5.5 (2.00, 15.1)	0.0009
Non-Hispanic or Latino	5.8 (2.46, 13.9)	< 0.0001	6.9 (4.0, 11.8)	< 0.0001
Political Affiliation				
Democratic	6.8 (1.23, 38.1)	0.0279	5.8 (2.99, 11.1)	< 0.0001
Republican	2.95 (1.31, 6.7)	0.0092	2.97 (1.56, 5.7)	0.001
High School (14-17 Years)				
Race				
Asian	17.2 (0.21, 1410)	0.205	18.3 (2.08, 161)	0.0088
Black	5.8 (1.66, 20.3)	0.006	5.9 (2.77, 12.4)	< 0.0001
Other	5.3 (0.43, 64)	0.192	6.6 (1.50, 28.9)	0.0125
Not Specified	5.1 (0.45, 58)	0.186	4.5 (1.57, 12.8)	0.0051
White	5.7 (1.56, 21.2)	0.0086	5.1 (2.33, 11.0)	< 0.0001
Ethnicity				
Hispanic or Latino	8.5 (0.71, 102)	0.091	5.1 (1.53, 17.3)	0.0081
Not specified	7.0 (0.65, 76)	0.109	5.0 (1.69, 14.5)	0.0035
Non-Hispanic or Latino	5.6 (1.81, 17.2)	0.0028	6.2 (3.11, 12.3)	< 0.0001
Political Affiliation				
Democratic	6.9 (1.13, 42)	0.0364	5.5 (2.56, 11.7)	< 0.0001
Republican	2.96 (1.06, 8.2)	0.0381	2.75 (1.31, 5.8)	0.0075
Middle School (11-13 Years)				
Race				
Asian	17.2 (0.187, 1590)	0.217	20.2 (2.12, 193)	0.0089
Black	5.8 (1.10, 30.8)	0.0378	6.5 (2.44, 17.2)	0.0002
Other	5.3 (0.351, 79)	0.229	7.3 (1.48, 35.8)	0.0147
Not Specified	5.1 (0.377, 70)	0.220	4.9 (1.51, 16.2)	0.0083
White	5.7 (1.15, 28.6)	0.0329	5.60 (2.15, 14.6)	0.0004
Ethnicity				
Hispanic or Latino	8.7 (0.55, 137)	0.124		
Not specified	7.2 (0.50, 102)	0.146	5.8 (1.45, 23.5)	0.0129
Non-Hispanic or Latino	5.7 (1.19, 27.2)	0.0296	5.6 (1.57, 20.1)	0.0078
Political Affiliation			7.0 (2.76, 17.8)	< 0.0001
Democratic	6.4 (0.77, 53)	0.086	5.7 (2.16, 15.0)	0.0004
Republican	2.72 (0.65, 11.4)	0.169	2.86 (1.09, 7.5)	0.0334
Primary School (5-10 Years)				
Race				
Asian	20.7 (0.218, 1972)	0.191	25.3 (2.64, 241)	0.005
Black	7.0 (1.27, 38.8)	0.0258	8.1 (3.07, 21.4)	< 0.0001
Other	6.3 (0.389, 103)	0.195	9.1 (1.81, 45)	0.0074
Not Specified	6.2 (0.42, 91)	0.187	6.2 (1.86, 20.5)	0.0029
White	6.9 (1.25, 38.3)	0.027	7.0 (2.63, 18.7)	0.0001
Ethnicity				
Hispanic or Latino	10.4 (0.63, 172)	0.101	7.2 (1.79, 29.1)	0.0055
Not specified	8.6 (0.53, 139)	0.129	6.9 (1.92, 25.1)	0.0031
Non-Hispanic or Latino	6.8 (1.29, 36.2)	0.0241	8.7 (3.36, 22.4)	< 0.0001

Political Affiliation				
Democratic	7.9 (0.97, 64)	0.054	7.1 (2.68, 19.0)	< 0.0001
Republican	3.36 (0.71, 15.8)	0.125	3.59 (1.34, 9.6)	0.0108

Table 7. Incidence density ratios of breakthrough infections with 95% confidence intervals comparing urban county of residence against rural county of residence, and Metropolitan Atlanta residence against Non-Metropolitan Atlanta residence, stratified by race, ethnicity, and county political affiliation during the Omicron BQ.1/BQ.11 COVID-19 variant period (November 1, 2022 – December 31, 2022) (α = 0.05).

	Urban vs. Rural		**Metropolitan Atlanta vs. Non-Metropolitan Atlanta**	
	Incidence Density Ratio (95% CI)	**P-Value**	**Incidence Density Ratio (95% CI)**	**P-Value**
Combined Ages				
Race[1]				
Asian	-	-	20.8 (1.22, 355)	0.0359
Black	5.2 (1.27, 21.2)	0.0216	8.3 (3.70, 18.7)	< 0.0001
Other	10.6 (0.188, 597)	0.251	7.9 (1.23, 51)	0.0298
Not Specified	3.58 (0.165, 78)	0.42	5.6 (1.46, 21.3)	0.0118
White	5.2 (1.14, 23.9)	0.0332	7.7 (3.33, 17.6)	< 0.0001
Ethnicity				
Hispanic or Latino	7.4 (0.154, 355)	0.311	6.5 (1.45, 29.0)	0.0143
Not specified	5.0 (0.236, 108)	0.301	7.4 (2.06, 26.6)	0.0021
Non-Hispanic or Latino	4.8 (1.58, 14.6)	0.0057	8.2 (4.3, 15.4)	< 0.0001
Political Affiliation				
Democratic	3.93 (0.59, 26.3)	0.158	5.5 (2.53, 12.1)	< 0.0001
Republican	2.12 (0.72, 6.2)	0.172	3.50 (1.58, 7.7)	0.002
High School (14-17 Years)				
Race[1]				
Asian	-	-	18.2 (1.08, 304)	0.044
Black	4.8 (0.98, 23.7)	0.053	7.4 (3.01, 18.1)	< 0.0001
Other	11.1 (0.185, 662)	0.250	7.0 (1.06, 45)	0.043
Not Specified	3.03 (0.122, 75)	0.50	4.8 (1.21, 19.1)	0.0254
White	5.4 (1.05, 28.0)	0.044	6.4 (2.51, 16.3)	0.0001
Ethnicity				
Hispanic or Latino	8.0 (0.164, 392)	0.294	5.6 (1.19, 26.2)	0.0293
Not specified	5.1 (0.229, 115)	0.302	6.5 (1.68, 25.0)	0.0067
Non-Hispanic or Latino	4.4 (1.12, 17.4)	0.034	6.9 (3.19, 15.2)	< 0.0001
Political Affiliation				
Democratic	4.8 (0.68, 33.4)	0.115	4.7 (1.92, 11.3)	0.0007

Republican	2.26 (0.62, 8.3)	0.219	3.04 (1.26, 7.3)	0.013
Middle School (11-13 Years)				
Race[1]				
Asian	-	-	21.7 (1.09, 433)	0.044
Black	4.7 (0.48, 47)	0.182	8.8 (2.55, 30.5)	0.0006
Other	10.9 (0.139, 850)	0.283	8.3 (1.07, 65)	0.043
Not Specified	2.98 (0.084, 105)	0.55	5.8 (1.14, 29)	0.0345
White	5.3 (0.48, 59)	0.172	7.6 (2.23, 26.2)	0.0012
Ethnicity				
Hispanic or Latino	9.6 (0.118, 790)	0.314	7.5 (1.24, 46)	0.0285
Not specified	6.2 (0.151, 253)	0.336	8.8 (1.73, 44)	0.0086
Non-Hispanic or Latino	5.3 (0.59, 48)	0.136	9.4 (2.85, 31.0)	0.0002
Political Affiliation				
Democratic	4.4 (0.289, 67)	0.286	5.7 (1.69, 19.2)	0.005
Republican	2.08 (0.288, 15.0)	0.47	3.72 (1.09, 12.7)	0.0364
Primary School (5-10 Years)				
Race[1]				
Asian	-	-	34.4 (1.79, 661)	0.019
Black	8.3 (0.53, 128)	0.131	14.0 (3.79, 52)	< 0.0001
Other	19.0 (0.148, 2420)	0.235	13.2 (1.56, 111)	0.0179
Not Specified	5.2 (0.122, 222)	0.390	9.1 (1.69, 49)	0.0102
White	9.3 (0.50, 172)	0.135	12.1 (3.31, 44)	0.0002
Ethnicity				
Hispanic or Latino	12.0 (0.97, 1506)	0.312	9.3 (1.46, 59)	0.0183
Not specified	7.7 (0.140, 428)	0.318	10.8 (2.01, 58)	0.0055
Non-Hispanic or Latino	6.6 (0.42, 104)	0.177	11.6 (3.24, 42)	0.0002
Political Affiliation				
Democratic	4.8 (0.235, 97)	0.309	8.4 (2.36, 29.6)	0.001
Republican	2.26 (0.190, 26.9)	0.52	5.4 (1.47, 20.2)	0.0113

[1] The "Asian" race category was combined with the "Other" race category for urban versus rural analyses because the sample size was too small to assess the "Asian" race category independently.

Discussion

In this analysis of nearly 300,000 reported pediatric COVID-19 infections between June 1, 2021, and December 31, 2022, in Georgia, approximately 16.0% occurred after vaccination. Because COVID-19 vaccinations were developed to prevent severe disease, not to prevent all infections, post-vaccination infections events (i.e., breakthrough infections) were always likely to occur. When considering the burden of infections during a long-lasting pandemic, such as the

COVID-19 pandemic, breakthrough infections are both expected and preferable to instances of natural infection that would be more likely to cause severe illness. As a result, breakthrough infections are an important vaccine-related outcome worthy of nuanced examination, and this study aimed to contribute new knowledge about COVID-19 breakthrough case epidemiology in school-aged children for future vaccination education and promotion purposes.

Overall, there is evidence that there are significant differences in breakthrough infection risk between urban and rural counties, and Metropolitan Atlanta and Non-Metropolitan Atlanta counties, modified by race, ethnicity, and political affiliation. Specifically, children of all ages who reside in urban or Metropolitan Atlanta counties are more at risk for a breakthrough infection compared to rural or Non-Metropolitan Atlanta children of all ages. This is likely due to higher vaccination rates in urban and Metropolitan Atlanta counties than in rural and Non-Metropolitan Atlanta counties, which therefore contributes a higher proportion of the population that is susceptible to a breakthrough infection.

With respect to overall trends in breakthrough infections by school-age group, breakthroughs occurred more frequently among high school students than any other age group for most variant periods. This is most likely attributable to the fact that vaccinations were available to high school students first, and therefore for the longest period of time. More high schoolers were able to get vaccinated, which increase the likelihood of “achieving” a breakthrough infection as the pandemic progressed. Upon a more nuanced regional examination, high school-aged urban and Metropolitan Atlanta students had the lowest stratified risks for experiencing a breakthrough infection across the full time period and all analyzed variant waves compared to middle school and primary school students. This may be due to a potentially higher herd immunity level that high school populations had reached compared to the other age groups from their higher vaccination rates coupled with natural immunity from unvaccinated infections. The observed higher ratio of infections identified among Asian children in Metropolitan Atlanta compared to Non-Metropolitan Atlanta may be explained by the population densities of where children who identify in that race category tend to live within Georgia.

Trends in the urbanicity analyses indicate that the risk of breakthrough infections associated with residing in an urban county as compared to a rural county generally increased from the Delta period through the Omicron BA.2 period, then decreased through the rest of the study period. In contrast, trends in the metropolitan analyses showed a general decrease in incidence density ratios from the Delta to Omicron BA.1 period, a substantial increase during the Omicron BA.2 period in which ratios are nearly doubled their value from the Omicron BA.1 period, then decrease sharply during the Omicron BA.5 wave and become relatively stable through the end of the study period.

Across all variant analyses, the most dramatic increase in breakthrough infection risk was observed between Metropolitan Atlanta and Non-Metropolitan Atlanta during the Omicron BA.2 period. These increases were observed across all demographic and age group strata. For example, Black high school students who lived in Metropolitan Atlanta were 11.8 times more likely to experience a breakthrough infection during the Omicron BA.2 period, compared to being 5.2 times more likely during the Omicron BA.1 period ($p\text{-value}_{BA.2} < 0.0001$; $p\text{-value}_{BA.1} < 0.0001$). We hypothesize that this profound increase in risk during this particular variant wave may reflect a substantial vaccine-variant mismatch, a mass waning immunity event, or some combination of those two phenomena within the vaccinated pediatric population. The original COVID-19 vaccine was not developed against the more recent SARS-CoV-2 variants and decreased vaccine-derived protection against the Delta and Omicron BA.1 variants has been documented.[5–7] Additionally, parents in Georgia exhibited diverging opinions over whether to vaccinate their children due to safety concerns and political beliefs. Metropolitan Atlanta is comprised predominantly of Democratic Party-affiliated counties and had the highest vaccination rates of children in Georgia. If, compared to Non-Metropolitan Atlanta areas, more parents in the Atlanta region opted to vaccinate their children as soon as pediatric vaccines became available, this behavior could have set up a dramatic geo-political "vaccine differential" leading in a mass waning immunity event among pediatric populations when Omicron BA.2 emerged. In addition, having a large population of children vaccinated with the original vaccine that was documented to be less effective against later variants could have substantially reduced population immunity level to the Omicron BA.2 variant and could have also contributed to the observed spike in breakthrough infection risk.

Strengths

Overall strengths of the study include the sample size of the source and study population, which allow for increased reliability of results interpretations. Due to mandated reporting of COVID-19 vaccinations, it is likely that most, if not all, vaccinations among children have been captured in the surveillance data and incorporated into the study.

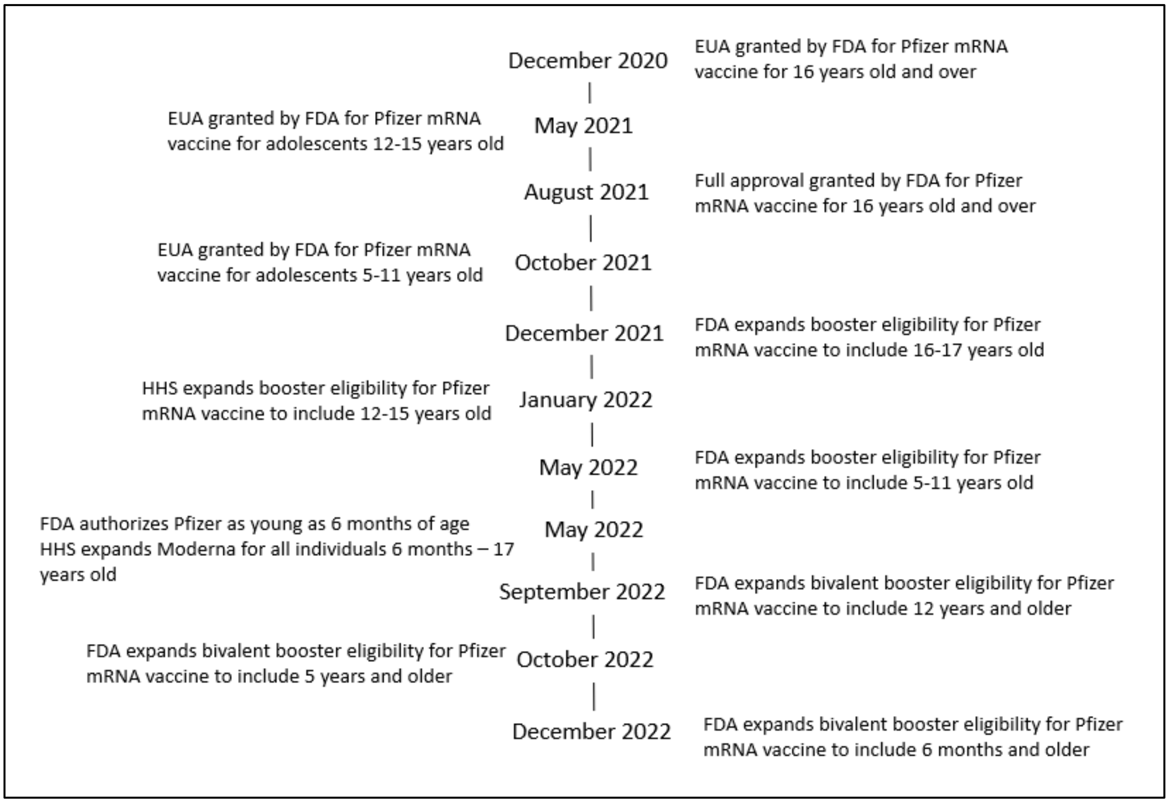
Limitations

Limitations of this study includes the potential underestimation of incidence density ratio estimates due to the use of surveillance data to calculate cases of COVID-19 infections among all children by county of residence. Mass at-home testing kit distributions that began in late January 2022 contributed to the restricted ability of health officials to identify all cases occurring in Georgia if an infected person used this testing method. Additionally, information was unavailable at the time of analysis to stratify vaccination rates in each county by sex.

Conclusion

It would be beneficial to continue to promote primary vaccination series among children, especially among under-vaccinated pediatric populations, to reduce the severity and risk of experiencing breakthrough infections by raising the herd immunity of the population. Prioritization of booster vaccines among all children who received a primary vaccination series, especially among regions with high primary series vaccination rates, could prevent spikes in SARS-CoV-2 cases during future variants. To truly understand the relationships described in this study, future research should examine the interplay of the timing of when children receive their primary vaccination series, the duration of vaccinated immunity and natural immunity within children, and when peaks in breakthrough infections occur by county urbanicity status.

Supplement



Supplement 1. Timeline of COVID-19 vaccination emergency use authorizations, full approvals, and booster approvals for children in the United States.

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