Shifting Perspectives on Vaccination:
COVID-19 Vaccine Hesitancy and Impacts on Childhood Immunizations

A DISSERTATION

SUBMITTED TO THE FACULTY OF THE UNIVERSITY OF MINNESOTA

BY

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IN PARTIAL FULFILLMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

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July 2025

ACKNOWLEDGMENTS

This dissertation would not have been possible without the support of many people. First, I am grateful to my advisor, Dr. Ruby Nguyen, for your support and encouragement, which has spanned every stage of my academic career. Thank you for continuously pushing me to pursue challenging opportunities and for believing in my potential. I am also sincerely thankful to the members of my committee, Dr. Caitlin Ward, Dr. Alicen Spaulding, Dr. Nancy Sherwood, and Dr. Michael Osterholm, who so generously shared their time and thoughtful feedback. Your perspectives have greatly enriched my work, and your mentorship has been invaluable. To Dr. Ward, thank you for your willingness to engage in in-depth discussions about analyses, modeling choices, and interpretation. I am especially grateful for your guidance, which has enabled me to work through complex decisions and arrive at thoughtful solutions. To Dr. Spaulding, thank you for sharing both your expertise in infectious disease epidemiology and your approach to graduate training and career development; your mentorship helped me approach this process with focus and perspective. I am indebted to many students, staff, and faculty within the Division of Epidemiology and Community Health who helped me along the way. In particular, I would like to thank the staff and faculty who helped ensure I had funding during these uncertain times. A special thank you to my friends Allison Lind and Daokun Sun. I am so grateful to have shared a classroom with such incredibly smart, talented, and kind individuals. Your camaraderie made even the most challenging parts of the past few years so much more manageable.

To my family, thank you for your constant love and support. To my sisters, Margaret and Kate, and my brother-in-law, Marcos, thank you for bringing humor to the past few years. To my nieces Irene and Marian, thank you for your joyful presence in my life. To my partner, Nick, thank you for being a steady source of understanding and support through it all. Thank you for always letting me tag along during your fieldwork; it was a gift to spend time in nature with you whenever I needed a break. And to my parents, Megan and Larry, thank you for everything; you truly kept me going. Mom, you've always been ready to celebrate both the small and big wins. Dad, I credit you with my ability to write (without which this dissertation would not exist). Thank you for reading everything from my elementary school essays to manuscripts included here.

Manuscript 1 was supported by the J.B. Hawley Student Research Award from the Division of Epidemiology & Community Health, University of Minnesota School of Public Health.

The data used in Manuscript 2 was supported by the Environmental influences on Child Health Outcomes (ECHO) program, Office of the Director, National Institutes of Health, under the following awards: U24OD023382 [Data Analysis Center, Jacobson, Catellier]; U2COD023375 [Coordinating Center, Newby, Smith]; U24OD023319 [Participant Reported Outcomes (PRO) Core, Gershon, Cella]; UH3OD023251 (Alshawabkeh), UH3OD023320 (Aschner, Stroustrup, Teitelbaum), UH3OD023332 (Trasande, Kopp, Swingler), UH3OD023287 (Breton), UH3OD023253 (Camargo), UH3OD023248 (Dabelea, Starling), UH3OD023313 (Deoni), UH3OD023328 (Duarte), UH3OD023318 (Dunlop), UH3OD023279 (Elliott), UH3OD023289 (Ferrara, Croen), UH3OD023282 (Gern), UH3OD023290 (Herbstman), UH3OD023365 (Hertz-

Picciotto), UH3OD023244 (Hipwell), UH3OD023275 (Karagas), UH3OD023271 (Karr), UH3OD023285 (Kerver), UH3OD023347 (Lester), UH3OD023389 (Leve), UH3OD023344 (MacKenzie), UH3OD023342 (Lyall), UH3OD023288 (McEvoy), UH3OD023349 (O'Connor), UH3OD023286 (Oken), UH3OD023348 (O'Shea, Fry), UH3OD023272 (Schantz, Woodruff), UH3OD023249 (Stanford, Giardino, Porucznik), UH3OD023305 (Trasande), UH3OD023268 (Litonjua, Weiss), UH3OD023337 (Wright, Wright), Human Health Exposure Analysis Resource DataCenter [U2CES026544 (Fennell), U2CES030857 (Fennell, Sumner, Du), U2CES026542 (Parsons, Kannan), U2CES026533 (Peterson), U2CES026561 (Wright)], U24ES026539 (HHEAR Coordinator Center, O'Brien), U2CES026555 (Human Health Exposure Analysis Resource Data Center, Teitelbaum). These data are from the first public release from this ongoing study. The content of this report is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the ECHO Cohort investigators.

ABSTRACT

The COVID-19 pandemic disrupted vaccine delivery, public trust in vaccines, and long-standing immunization norms, raising concerns about sustained declines in vaccine uptake. These disruptions occurred alongside increased skepticism towards public health institutions and politicization of vaccine discourse, creating conditions in which hesitancy toward the COVID-19 vaccine may have extended to other immunizations. This dissertation examined the individual, familial, and community-level impacts of the pandemic on vaccine intentions and behaviors, focusing on adult COVID-19 booster acceptance, caregiver-child vaccine decision-making, and trends in routine childhood vaccination coverage.

Manuscript 1 presents findings from a cross-sectional survey conducted at the 2023 Minnesota State Fair to identify predictors of intention to receive the updated 2023–2024 COVID-19 vaccine. Perceived vaccine safety emerged as the strongest predictor of intention, with associations also observed for COVID-19 risk perception, public health knowledge, and political affiliation.

Manuscript 2 analyzed data from families in the Environmental influences on Child Health Outcomes (ECHO) Cohort to examine caregiver-child alignment in COVID-19 vaccine hesitancy. Caregiver vaccination status was strongly associated with child vaccination status. The reasons for hesitancy, particularly regarding safety, trust in healthcare providers, and vaccine testing, were highly concordant across the reasons caregivers reported for themselves and the reasons they reported for their children. COVID-19 vaccine hesitancy among caregivers for themselves and their children was also associated with intentional delay or refusal of routine childhood vaccinations.

Manuscript 3 evaluated changes in routine childhood vaccination rates in Minnesota from 2015 to 2023 using county-level data and examined whether there was an impact of political composition and COVID-19 vaccination coverage on changes in vaccination rates. Results indicated significant and sustained declines in vaccine coverage following the onset of the pandemic. Counties with a higher Republican vote share exhibited lower vaccination rates when combined with low COVID-19 vaccine uptake, suggesting a politicized spillover effect of COVID-19 vaccine skepticism on routine immunizations.

Together, these studies demonstrate the enduring impact of the COVID-19 pandemic on vaccine attitudes and behaviors, particularly for childhood vaccinations. The findings underscore the influence of vaccine safety perceptions, institutional trust, and sociopolitical context on vaccine uptake, providing essential insights to guide public health efforts to rebuild trust and address low vaccination coverage in a post-pandemic public health landscape.

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LIST OF ABBREVIATIONS

ACIP: Advisory Committee on Immunization Practices
ADO: Adolescent Life Stage
CAR: Conditional Autoregressive Model
CDC: Centers for Disease Control and Prevention
COVID-19: Coronavirus Disease 2019
DASH: NIH Data and Specimen Hub
DTaP: Diphtheria, Tetanus, and Pertussis
D2D: Driven to Discover Research Building
EC: Early Childhood Life Stage
ECHO: Environmental influences on Child Health Outcomes Cohort
EWCP: ECHO-Wide Cohort Data Collection Protocol
FDA: US Food and Drug Administration
GEE: Generalized Estimating Equations
Hep A: Hepatitis A Vaccine
Hep B: Hepatitis B Vaccine
Hib: Haemophilus Influenzae Type B Vaccine
IPV: Polio Vaccine
INLA: Integrated Nested Laplace Approximation
Inf: Infancy Life Stage
MC: Middle Childhood Life Stage
MMR: Measles, Mumps, and Rubella Vaccine
NIH: National Institute of Health
PASC: Post-acute sequelae of SARS-CoV-2 infection
PCA: Principal Component Analysis
PCV: Pneumococcus Vaccine
RV: Rotavirus Vaccine
SAGE: WHO Strategic Advisory Group of Experts on Immunization Working Group
SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus
SES: Socioeconomic Status
SVI: Social Vulnerability Index
Tdap: Tetanus, Diphtheria, and Pertussis
US: United States
WHO: World Health Organization

CHAPTER 1. OVERVIEW AND SPECIFIC AIMS

OVERVIEW AND SPECIFIC AIMS

Since its emergence in 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused over 103 million cases of Coronavirus disease 2019 (COVID-19) and more than 1 million deaths in the United States (US).[1,2] The pandemic has had an impact on all age groups, including children who, while in general, experience milder symptoms than adults, have still been greatly impacted by the effects of the virus. Beyond the direct health impacts of the pandemic, the rollout of COVID-19 vaccines marked a pivotal moment in public health and, for some, may have reshaped perceptions of vaccination and exacerbated pre-existing vaccine skepticism. A recent study published in Nature Medicine estimates that as many as 29% of US adults may have become less willing to accept routine immunizations, including influenza, measles, and hepatitis B vaccines, following the COVID-19 pandemic.[3] Therefore, the COVID-19 pandemic has profoundly impacted vaccine attitudes and behaviors across the US.

The COVID-19 vaccines have been critical tools in mitigating the spread and severity of the virus. COVID-19 vaccines were developed and deployed at an unprecedented speed, effectively reducing the incidence of severe illness.[4] However, COVID-19 vaccine uptake levels remain below the recommended levels in the US. As of May 2024, 81% of US adults had received at least one dose of a COVID-19 vaccine, but just 21% had received the updated 2023–2024 COVID-19 vaccine as recommended.[5] Additionally, vaccine coverage is even lower in children than in adults, with only 14% of children under the age of 17 up to date with the 2023–2024 COVID-19 vaccine.[5] The pandemic brought unprecedented disruptions to healthcare access,

delaying routine childhood vaccinations and sparking debates about vaccine safety and necessity. There is growing concern that negative attitudes towards COVID-19 vaccines may spill over into hesitancy or refusal of other recommended vaccines, including routine childhood vaccines. The COVID-19 pandemic offers a unique opportunity for a natural experiment to explore changes in vaccine attitudes and behaviors towards all types of vaccines.

The potential erosion in vaccine confidence could have significant public health implications. Childhood vaccination remains one of the most powerful public health tools for reducing illness and death among children, dramatically diminishing the global burden of once-common diseases. In the US alone, the CDC estimates that between 1994 and 2023, routine childhood vaccinations have prevented tens of millions of hospitalizations and more than 1 million deaths.[6] A major contributor to this public health success is the role of vaccinations in establishing herd immunity, which is the indirect protection provided against an infectious disease when a significant proportion of a population is immune to infection.[7] The threshold for achieving herd immunity is often high. For highly contagious diseases such as measles and pertussis, an estimated 90–95% of the population must be vaccinated to maintain herd immunity.[8,9] Consequently, understanding shifting attitudes towards routine vaccines is crucial, as even modest declines in vaccination coverage can leave communities vulnerable to outbreaks of preventable diseases.

Dissertation Aims

This dissertation research investigated the impact of the COVID-19 pandemic on vaccine hesitancy and acceptance, focusing on three key areas: continued COVID-19 vaccine acceptance among adults, the interplay between caregiver and child vaccine attitudes, with an emphasis on

the spillover effects on routine childhood vaccines, and changes in routine childhood vaccination rates after the onset of the pandemic. In a series of three manuscripts, I pursued the following aims:

Manuscript 1: Predictors of willingness to receive updated 2023–2024 COVID-19 booster vaccines among a convenience sample of adults in Minnesota

Aim 1A: Describe the characteristics of adults who are likely to receive a COVID-19 booster vaccine in the coming year and identify determinants of intention to receive an updated 2023–2024 COVID-19 booster vaccine among adults, including perceptions of COVID-19 risk, vaccine safety, public health knowledge, political affiliation, and fear of pandemics.

> **Hypothesis 1A:** I hypothesized that greater knowledge of key principles of public health, higher levels of fear of pandemics, higher perception of COVID-19 risk, and vaccine safety would be associated with a greater likelihood of intention to receive an updated COVID-19 booster vaccine in the coming year.

Aim 1B: Investigate determinants of vaccine intention specifically among adults who are in the middle of the vaccine acceptance continuum (i.e., those who are more neutral or undecided about their intention to receive an updated COVID-19 vaccine in the coming year).

> **Hypothesis 1B:** I hypothesized that among individuals who are more neutral, compared to those with strong opinions, about receiving the 2023–2024 updated COVID-19 vaccine, factors strongly associated with polarized vaccine opinions and intentions, such as beliefs about perceived safety of vaccines, will be less influential.

Manuscript 2: Association between caregiver and child COVID-19 vaccine hesitancy and refusal of routine childhood vaccinations among children in the ECHO Cohort

Aim 2A: Assess the relationship between adult caregivers' COVID-19 vaccination status and their children's vaccination status and examine demographic, socio-economic, and medical determinants of COVID-19 vaccination among families in the ECHO cohort.

Hypothesis 2A: I hypothesized that the vaccination status of adult caregivers of children would be associated with the vaccination status or intentions to vaccinate their children. I also hypothesized that children with lower socio-economic status would be less likely to be vaccinated for COVID-19 compared to their counterparts of higher socio-economic status. Demographic factors such as age, race, and ethnicity will also be associated with vaccination uptake or intention. I hypothesized that younger children would be less likely to have received a COVID-19 vaccine and that children from racial and ethnic minorities would be less likely to have been vaccinated for COVID-19 compared to non-Hispanic white children.

Aim 2B: Investigate whether the reasons for COVID-19 vaccine hesitancy of adult caregivers to accept the COVID-19 vaccine for themselves correspond with the reasons for hesitancy to vaccinate their children. Additionally, to explore the reasons given by caregivers who accepted the COVID-19 vaccine for themselves but did not accept the vaccine for their children.

Hypothesis 2B: I hypothesized that the reasons adult caregivers are hesitant to accept the COVID-19 vaccine for themselves will correspond to the reasons they are hesitant to have their children vaccinated. I hypothesized that the most common reasons for vaccine hesitancy among caregivers and children would be related to vaccine safety, including perceived side effects and long-term effects of the vaccine, as well as perceptions about

the risk of COVID-19, specifically that the risk of contracting COVID-19 is low. Furthermore, among caregivers who have been vaccinated, I hypothesized that their hesitancy to vaccinate their children would be child-specific, including higher odds of reporting concerns about whether the vaccine had been adequately tested in children and beliefs that children are at a lower risk of severe illness from COVID-19.

Aim 2C: Examine whether COVID-19 vaccine hesitancy among caregivers and children is associated with intentional delay or refusal of other pediatric vaccines, including Diphtheria/Tetanus/Pertussis (DTaP), Hepatitis A (Hep A), Hepatitis B (Hep B), Haemophilus Influenzae Type B (Hib), Polio (IPV), Meningococcal, Measles/Mumps/Rubella (MMR), Pneumococcus (PCV), Rotavirus (RV), Varicella (Chickenpox), Tetanus/Diphtheria/Pertussis (Tdap), and Human papillomavirus (HPV).

Hypothesis 2C: I hypothesized that caregivers who are hesitant to accept the COVID-19 vaccine for themselves or their children would be more likely to refuse or intentionally delay other childhood vaccines.

Manuscript 3: Childhood vaccination rates and COVID-19 vaccination coverage by county voting patterns

Aim 3A: Investigate whether rates of routine childhood vaccinations of children aged 24 to 35 months old in Minnesota changed after the onset of the COVID-19 pandemic, after adjusting for county-level socioeconomic status.

Hypothesis 3A: I hypothesized that rates of routine childhood vaccinations in Minnesota significantly decreased after the onset of the COVID-19 pandemic in 2020 compared to

pre-pandemic rates (2015–2019). Additionally, I hypothesized that rates of decline were more pronounced for vaccines with a history of vaccine skepticism (e.g., MMR) or where pediatric COVID-19 hesitancy may be more readily applicable (e.g., Varicella). I hypothesized that lower levels of county-level socioeconomic status, as measured by the CDC's Social Vulnerability Index, would be associated with declines in vaccination.

Aim 3B: Assess whether Minnesota county-level changes in childhood vaccination rates of children aged 24 to 35 months after the onset of the pandemic differ by COVID-19 vaccine primary series non-completion rates and whether this association is modified by county political composition after adjusting for county-level socioeconomic status.

Hypothesis 3B: I hypothesized that counties in Minnesota with higher COVID-19 primary vaccine series non-completion rates and higher proportions of Republican voters have lower overall routine childhood vaccination rates following the availability of COVID-19 vaccines (2021–2023). Furthermore, I hypothesized that the association between COVID-19 primary series vaccine non-completion and childhood vaccination rates is modified by county political composition, such that counties with both high COVID-19 vaccine non-completion and strong Republican majorities would have low childhood vaccination rates after adjusting for county-level socioeconomic status.

This dissertation advances our understanding of vaccine hesitancy during a critical period in public health. By exploring the interplay between COVID-19 vaccine attitudes, routine childhood vaccination patterns, and sociopolitical factors, this work highlights opportunities for targeted interventions to promote vaccine uptake and resilience in an uncertain public health landscape.

CHAPTER 2. BACKGROUND AND RATIONALE

BACKGROUND

Coronavirus disease 2019 (COVID-19)

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is among the greatest, if not the greatest, infectious disease challenges of the 21st century. Since emerging in December 2019, the World Health Organization (WHO) has reported over 103 million cases of COVID-19 in the United States (US).[10] The clinical presentation of COVID-19 can range from asymptomatic or mild illness to severe or critical illness. Since 2019, COVID-19 has resulted in more than 1 million deaths in the US. As of 2022, it represented the fourth leading cause of death after heart disease, cancer, and unintentional injuries.[1,2,11]

The disease burden of COVID-19 remains significant, continuing to result in serious health consequences. Hospitalization rates for COVID-19 remain higher than for other seasonal respiratory illnesses.[5,12] Additionally, a substantial number of COVID-19 cases remain. In the US alone, the year 2023 concluded with approximately 35,000 weekly hospitalizations and 1,500 deaths per week due to COVID-19.[5] The impact is particularly severe for immunocompromised individuals and those with other underlying medical conditions, who shoulder a disproportionate burden of the disease.[13] Those at greatest risk of developing severe disease are individuals aged 60 years or older and those with underlying medical comorbidities. Underlying medical conditions that predispose individuals to more severe COVID-19 illness include, but are not limited to, obesity, heart disease, immunodeficiency, kidney disease, anxiety, depressive

disorders, and asthma.[14] Additionally, those with more than one underlying medical condition have an even greater risk of severe outcomes from COVID-19.[14]

While individuals aged 60 and older are at greatest risk of developing severe disease from COVID-19, it is still a significant health problem for children. It is estimated that children account for 2 to 5% of reported COVID-19 cases. However, this is likely an underestimation because many cases in children are mild or asymptomatic.[15] Studies estimate the rate of asymptomatic infection in children ranges from 16% to 35%.[16–18] However, this is also likely an underestimation, as asymptomatic children are less likely to seek testing.[19] Serologic studies indicate that around half of the children who test positive for COVID-19 reported no symptoms.[20,21] A review of 89 articles on COVID-19 in children published through March 2021 found that children with COVID-19 can experience a wide spectrum of clinical manifestations.[19] Fever is the most common initial symptom, followed by cough, rhinorrhea, and sore throat. Other common symptoms include headache, diarrhea, vomiting, fatigue, myalgia, tachypnea, tachycardia, and rash.[19] Anosmia (loss of smell) and ageusia (loss of taste) are less frequent in children than in adults.[19] Similar to adults, children with medical conditions may also be at greater risk of severe illness from COVID-19. A cross-sectional study of 43,465 children with COVID-19 from a large healthcare database found that almost 30% had at least one underlying medical condition.[22] Medical conditions, including obesity, cardiac and circulatory anomalies, and asthma, were associated with more severe disease in children.[22]

COVID-19 vaccines

A year after the first identification of COVID-19, the US Food and Drug Administration (FDA) granted Emergency Use Authorization to Pfizer-BioNTech, Moderna, and J&J/Janssen to produce and manufacture COVID-19 vaccines.[4] By August 2021 and January 2022, the Pfizer-BioNTech and Moderna COVID-19 vaccines, respectively, had received full FDA approval.[23,24] In September 2022, the CDC endorsed updated bivalent vaccines from both manufacturers. In April 2022, the CDC simplified the COVID-19 vaccination guidelines by discontinuing the original monovalent COVID-19 vaccine series and recommending that individuals aged six years and older receive one updated (bivalent) mRNA COVID-19 vaccine, regardless of whether they previously completed their (monovalent) primary series.[25] For the 2023–2024 and 2024–2025 seasons, updated booster vaccines from Pfizer-BioNTech, Moderna, and Novavax were available and recommended for everyone 6 months and older.[26]

Despite the availability of licensed and thoroughly tested vaccines, uptake remains at less than target levels in the US. As of May 2024, 81% of US adults had received at least one dose of a COVID-19 vaccine, but just 21% had received the updated 2023–2024 COVID-19 vaccine as recommended.[5] Additionally, vaccine coverage is worse in children than in adults. The CDC estimates that only 53% of children between the ages of 6 months and 17 years had received at least one dose of a COVID-19 vaccine, and only 14% had received the 2023–2024 COVID-19 vaccine.[5,27] Numerous factors have been identified as influential in determining an individual's willingness to receive COVID-19 vaccines. Sociodemographic characteristics, including age, educational attainment, socioeconomic status, and political affiliation, are well-established determinants of COVID-19 vaccine acceptance.[28] Other factors such as perceptions of vaccine

safety and disease risk, mental and physical status, and social media use have also been found to influence willingness to receive COVID-19 vaccines.[29,30] Additionally, there is some evidence that knowledge of herd immunity, or community protection, and altruistic motives are associated with motivation to receive vaccines, including the COVID-19 vaccine.[30–33]

Routine childhood vaccines

The US Advisory Committee for Immunization Practices (ACIP) recommends a seven-vaccine series for early childhood (Table 2.1).[34,35] These vaccines include: Diphtheria, Tetanus, and Pertussis (DTaP); Hepatitis B (Hep B); Haemophilus influenzae type b (Hib); Measles, Mumps, and Rubella (MMR); Pneumococcal Conjugate Vaccine (PCV); Polio; and Varicella. The series is typically completed by age two and is critical for preventing potentially life-threatening illnesses during early childhood. The US Healthy People 2020 public health goals aimed to increase and maintain high vaccination coverage among children. Specifically, the goal was to raise the overall percentage of children receiving the seven-vaccine series from a 2012 baseline level of 68.4% to 80%. Additional targets included increasing Hep B coverage to 85%, and PCV, Hib, and DTaP coverage to 90%.[36] The US has largely fallen short of those goals. National Immunization Survey data estimates that children born in 2019–2020 had only 69.1% coverage for the seven-vaccine series, and DTaP, PCV, and Hib all fell short of their targets.[37(p24)]

Table 2.1 Summary of the childhood seven-vaccine series and the number of recommended doses for children aged 24 months

Vaccine	Number of doses recommended for children 24 months
Hepatitis B (Hep B)	3
Diphtheria, tetanus, and acellular pertussis (DTaP)	4
Haemophilus influenzae type b (Hib)	3 or 4
Pneumococcal conjugate vaccine (PCV)	4
Inactivated poliovirus vaccine (IPV)	3
Measles, mumps, and rubella (MMR)	1
Varicella	1

Childhood vaccination remains one of the most effective interventions for reducing childhood morbidity and mortality, dramatically lowering the global burden of once-common diseases. In the US alone, the CDC estimates that between 1994 and 2023, routine childhood vaccinations have prevented 508 million cases of illness, 32 million hospitalizations, and more than 1 million deaths.[6] A key factor in the success of routine childhood vaccinations in preventing disease is their ability to establish herd immunity. Herd immunity refers to indirect protection from an infectious disease that occurs when a significant proportion of a population becomes immune to infection through vaccination or prior infections.[7] This concept is crucial because it reduces the likelihood of disease transmission within a community, particularly protecting individuals who are not immune. Herd immunity thresholds depend on the infectious agent and the effectiveness of the vaccine. Achieving these thresholds can prevent disease outbreaks or, in some rare cases, aid efforts to eradicate diseases, as seen with smallpox and polio in certain regions. The estimated level of immunization required to achieve herd immunity for measles, pertussis, and mumps is between 90% and 95%.[7] As such, even small declines in vaccination coverage can lead to outbreaks, posing significant risks to vulnerable populations. There are multiple examples of

measles outbreaks in the US because of under-vaccinated communities, including in Minnesota.[8,9]

Recent evidence highlights the significant public health risks associated with declining childhood vaccination rates in the US. A modeling study projected that a 10% reduction from current MMR coverage could result in more than 11 million measles cases, over 1 million hospitalizations, and more than 10,000 deaths over the next 25 years.[38] The consequences are even more severe with greater declines in coverage. For instance, a 25% drop in coverage is projected to result in over 26.9 million measles cases and more than 50,000 pediatric deaths within 25 years. Diseases that have been rare for the past several decades could re-emerge as endemic in the decades to come.[38] However, the implications of declining immunization are already apparent. During the 2023–2024 influenza season, the US recorded 226 pediatric flu deaths, the highest number since the 2009 H1N1 pandemic. This is amid a sharp decline in childhood flu vaccination rates, from approximately 64% in 2019 to just 48% in 2024.[39,40] Similarly, pockets of low MMR vaccination coverage have contributed to a resurgence of measles outbreaks nationwide. Between January and June 2025, there have been 21 measles outbreaks, with at least 1,197 confirmed cases and three deaths.[41] Of these cases, 95% were unvaccinated or had unknown vaccination status, and 12% required hospitalization. Notably, a major outbreak in Texas, which has been ongoing for six months, accounts for 744 confirmed cases.[42] However, infectious disease experts caution that the true number of cases is likely higher, as many cases in communities with low trust in healthcare and vaccines are likely going unreported.[43]

Vaccine hesitancy

Vaccine hesitancy, as defined by the WHO Strategic Advisory Group of Experts (SAGE) on Immunization Working Group is the delay in acceptance or refusal of vaccines despite the availability of services. [44,45] It exists on a continuum, as illustrated in Figure 2.1. This continuum ranges from anti-vaccine to vaccine-hesitant to pro-vaccine beliefs.[44,45] Vaccine hesitancy is complex and context-specific. In 2011, SAGE proposed a 3C model of vaccine hesitancy, including complacency, constraints, and confidence.[44,45] In 2018, Betsch et al. expanded the 3C *model* to include two additional factors influencing hesitancy: calculation and collective responsibility.[46] This 5C model is illustrated in Figure 2.2 and outlines five psychological antecedents of vaccination: confidence (trust in the safety and effectiveness of vaccines and the health systems that deliver them), complacency (perception of disease risk), constraints (structural and psychological barriers to access), calculation (engagement in information searching), and collective responsibility (willingness to protect others through vaccination).[46] This framework highlights the multifaceted nature of vaccine hesitancy, suggesting that tailored interventions are needed to address the specific contextual barriers to vaccine acceptance in a given community. Understanding these dynamics is critical for designing effective public health strategies to improve vaccination rates.

Figure 2.1 Vaccine hesitancy continuum adapted from the WHO SAGE Immunization working group

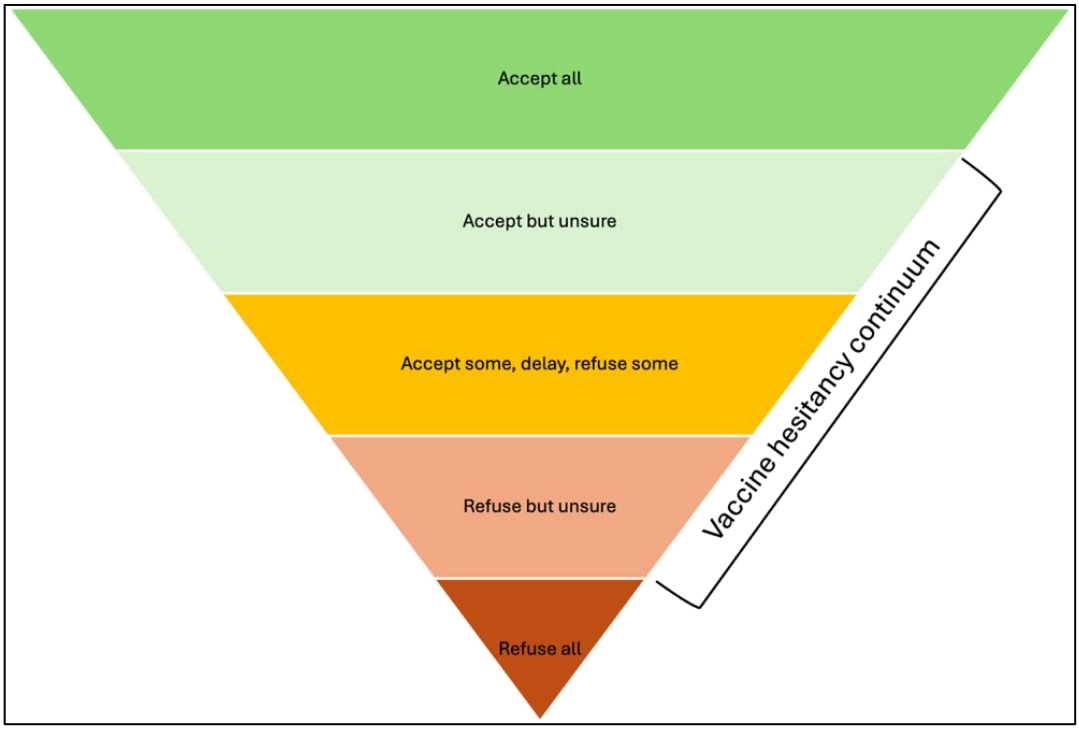
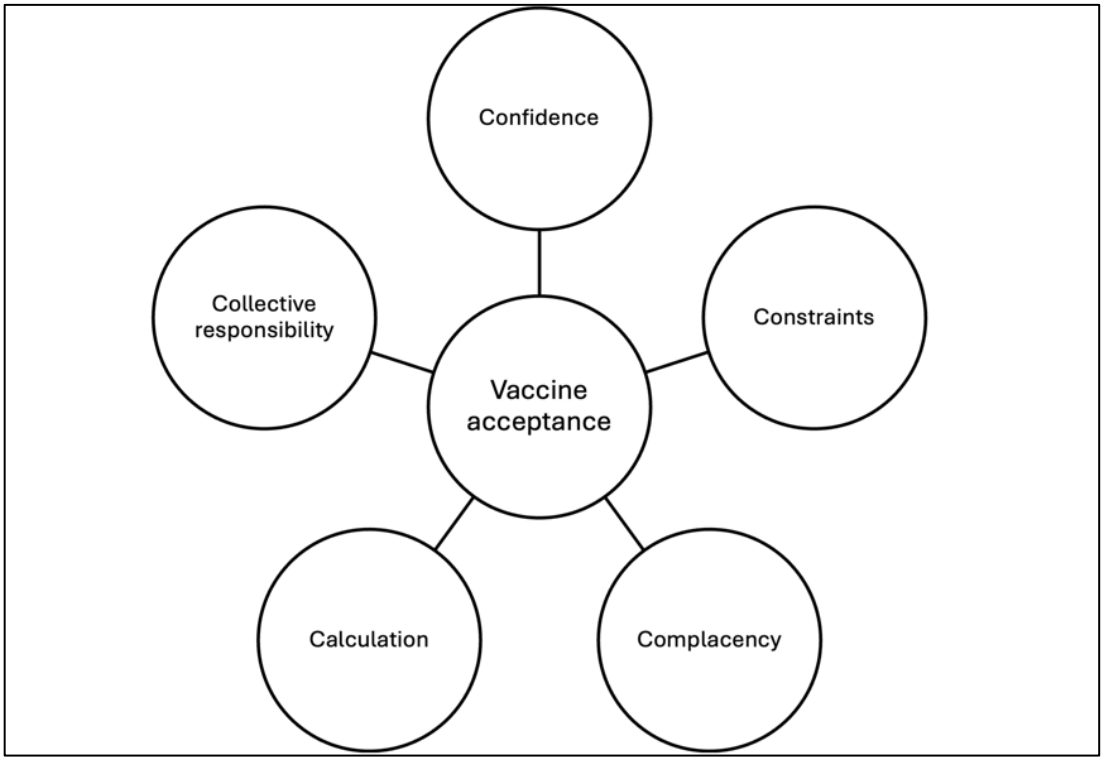


Figure 2.2 Psychological antecedents of vaccination adapted from 5C scale (Betsch *et al.*)



Parental hesitancy to vaccinate children against COVID-19

Parental hesitancy to vaccinate their children against COVID-19 is influenced by a variety of factors, both objective and subjective. Studies have shown that parents with lower levels of education and income, and lower trust in vaccine development and approval processes, are less likely to vaccinate their children against COVID-19.[47] Additionally, parents who are unvaccinated for COVID-19 are significantly more likely not to vaccinate their children.[47–50] Many of the predictors for the hesitancy of adults to accept COVID-19 vaccines for themselves are the same as those for children.[47] Concerns about the safety and side effects of the vaccine are common reasons for hesitancy for both adults and children.[51] Broader societal factors, including political affiliation and exposure to misinformation, also significantly influence vaccination decisions. Parents at the extremes of the political spectrum, particularly those aligned with far-right (or highly conservative) ideologies, are less likely to vaccinate their children, even if they themselves are vaccinated.[51] This finding underscores the importance of addressing vaccine skepticism in politically polarized populations to improve vaccine uptake.

COVID-19 pandemic impact on hesitancy toward other recommended childhood vaccinations

The COVID-19 pandemic had a profound impact on daily life, public health, and healthcare, including significant disruptions to routine healthcare services.[52,53] One immediate consequence was a decline in childhood vaccination rates, particularly during the early stages of the pandemic when widespread lockdowns, overwhelmed healthcare systems, and fears of virus exposure led to reduced access to routine medical care.[37,54,55] In the US, the first pandemic-related restrictions and stay-at-home orders began in March 2020, and their duration varied by jurisdiction,

generally lasting until April or May 2020.[56] Many families faced challenges in scheduling and attending vaccination appointments, which resulted in missed doses of critical vaccines for children.[57,58] While some studies indicate that childhood vaccination rates began to recover as healthcare access improved, evidence suggests that this recovery has not been enough to catch up to pre-pandemic levels. Declines in vaccine uptake may have persisted beyond the acute phase of the pandemic.[58] This raises concerns about whether shifts in attitudes toward vaccines, particularly negative opinions fueled by COVID-19 vaccine skepticism, have spilled over to affect acceptance of other routine childhood immunizations.[59,60] Understanding the factors that contribute to this ongoing hesitancy, including the influence of misinformation and politicization of vaccines, is critical.

DISSERTATION OVERVIEW AND RATIONALE

Overview

To address the gaps in knowledge about changes to vaccination patterns around the COVID-19 pandemic, Manuscript 1 investigated factors associated with adults' intention to receive the 2023-2024 updated COVID-19 vaccine after the end of the US COVID-19 public health emergency among adults and has been published.[61] Manuscript 2 examined determinants of COVID-19 vaccination among 6,395 families with children in the NIH Environmental influences on Child Health Outcomes (ECHO) Cohort and the relationship between caregiver COVID-19 vaccination status and their children's vaccination status, the alignment between caregiver and child reasons for vaccine hesitancy, as well as sociodemographic determinants of childhood COVID-19 vaccination. Additionally, Manuscript 2 examined the relationship between COVID-

19 vaccination status and intentional delay or refusal of routine childhood vaccines. Finally, Manuscript 3 evaluated changes in routine childhood vaccination rates in Minnesota from 2015 to 2023, investigating how these trends vary by county-level COVID-19 vaccine acceptance and political composition.

Data sources

Driven to Discover Minnesota State Fair for Manuscript 1

Data used for Manuscript #1 were obtained from a convenience sample at the 2023 Minnesota State Fair. Participants were recruited at the University of Minnesota Driven to Discover Research Building (D2D), a dedicated research facility at the Minnesota State Fair and select Minnesota county fairs. The D2D Facility at the Minnesota State Fair provides the opportunity to efficiently recruit and collect data from participants quickly. The Minnesota State Fair is the second-largest state fair in the US in terms of gross attendance and has the highest daily attendance. An estimated 20% of Minnesota's population attends the State Fair each year. Additionally, the D2D building has been successful at recruiting a large proportion of participants from outside the 11-county metro area.[62] Additionally, we recruited participants from rural county fairs, further increasing the ability to study geographically diverse participants.

The Environmental influences on Child Health Outcomes (ECHO) Cohort for Manuscript 2

Data used for Manuscript #2 are from the Environmental influences of Child Health Outcomes (ECHO) Cohort, a comprehensive research initiative launched by the National Institutes of Health (NIH) in 2016.[63] The ECHO Cohort was designed to study the effects of a broad range of early environmental exposures on child health. ECHO leverages data from over 69 existing and

newly established pediatric cohort studies across the US, encompassing more than 57,000 children and their caregivers.[63] The ECHO pediatric cohorts represent a diverse population of children from various racial, ethnic, and socioeconomic backgrounds. Data collection is guided by the ECHO-Wide Cohort Data Collection Protocol (EWCP), which ensures standardized and harmonized data collection across participating cohorts. The EWCP facilitates the collection of a broad array of information on early-life exposures and targeted child health outcomes, including upper and lower airway conditions, obesity, and neurodevelopment.[63]

In response to the COVID-19 pandemic, the ECHO Cohort promptly adapted its data collection efforts to include COVID-19-related exposures and outcomes. This adaptation included developing and administering novel COVID-19-specific questionnaires in April 2020.[64] These questionnaires, available in both English and Spanish, assessed COVID-19 infection status, access to healthcare services, and later COVID-19 vaccination status.[65] De-identified data from the ECHO Program is publicly available upon approval through the NIH Data and Specimen Hub (DASH).[64,66] This de-identified COVID-19-related data includes participants who completed COVID-19 surveys from April 2020 through August 2023. COVID-19-related surveys were a required component of both remote and in-person study visits for participants in the ECHO Cohort. This dataset was designed to enable analyses that characterize the risk factors and disparities in COVID-19 infection among children and to follow COVID-infected children to determine the effects of COVID-19 infection, making it an ideal dataset to accomplish the aims of this proposal.[64]

The ECHO Cohort provides a unique and valuable dataset that will allow for the examination of COVID-19's impact on children across a diverse population. This dataset provides the opportunity to address key gaps in our understanding of COVID-19 and the impact of COVID-19 vaccinations, including the correlation between caregiver and child vaccine hesitancy and reasons for vaccine hesitancy in both groups.

Minnesota Vaccination and Political Data by County for Manuscript 3

Data used for the analysis in Manuscript 3 were drawn from multiple publicly available and reliable sources. This included the Minnesota Public Health Data Access portal[67], the CDC's COVID-19 vaccination tracker[5], the social vulnerability index[68], and the MIT Election Data and Science Lab.[69]

Childhood immunization data were obtained from the Minnesota Public Health Data Access portal.[67] This dataset is a county-level aggregated dataset summarizing Minnesota Immunization Information Connection data.[70] This dataset provides annual county-level vaccination rates for select vaccinations administered to children in Minnesota. For children in our target age group, aged 24 to 35 months, data were available from 2015 to 2023.

Data on COVID-19 vaccine acceptance at the county level were obtained from the CDC.[5] The CDC dataset provided cumulative counts and proportions of county populations who received at least one dose of a COVID-19 vaccine, completed the primary vaccine series, and received booster doses. The data spanned from December 13, 2020, to May 12, 2023.

The CDC Social Vulnerability Index (SVI) was used to provide measures of the relative social vulnerability of US communities.[68] It assigns rankings on 16 social factors grouped into four themes: socioeconomic status, household characteristics, racial and ethnic minority status, and housing type and transportation. SVI is updated biannually and was available for 2014, 2016, 2018, 2020, and 2022.

County-level returns for US presidential elections served as a proxy for a county's political composition. This data was sourced from the MIT Election Data and Science Lab.[69] This dataset included county-level returns for US presidential elections from 2012 to 2020.

Rationale

COVID-19 remains a persistent and evolving public health challenge. Hospitalization rates remain significantly higher for COVID-19 than for other seasonal respiratory illnesses. During the 2023–2024 respiratory illness season, the overall rate of COVID-19-associated hospitalizations was 139.5 per 100,000 people, compared to a flu-associated hospitalization rate of 82.3 per 100,000 for the same period.[5,12] Surges in rates of infections driven by new variants, including the FLiRT variants (descendants of the Omicron variant named for their spike protein mutations) during the summer of 2024, and the NB.1.8.1 variant in 2025, further underscore the ongoing threat of COVID-19.[5,71] Alongside its clinical burden, the COVID-19 pandemic has posed unprecedented challenges to public trust and vaccine acceptance, both of which are critical elements of effective public health strategies.

Vaccination remains a crucial yet underutilized strategy for mitigating the spread of COVID-19. Additionally, uptake has waned for each subsequent recommended COVID-19 vaccine dose. There is particularly low uptake among children, potentially due to a lack of trust in the safety of the vaccine and misconceptions that COVID-19 infection is not severe and, thus, not a threat to children. Yet, many children have a medical condition that puts them at greater risk for more severe COVID-19, and even mild or asymptomatic cases can lead to post-acute sequelae of SARS-CoV-2 infection (PASC), or long COVID.[22,72] PASC significantly increases the burden of COVID-19, leading to long-term health issues that can profoundly impact children's development, education, and quality of life.[73,74] Furthermore, emerging evidence suggests that the COVID-19 pandemic has affected the uptake of other routine and recommended vaccinations.[59,60]

The COVID-19 pandemic represents a natural experiment, offering unique opportunities to study vaccine hesitancy. The rapid development and deployment of COVID-19 vaccines occurred alongside heightened politicization of public health measures. These dynamics created the opportunity for shifts in attitudes toward vaccines, potentially extending beyond COVID-19 to include broader hesitancy toward long-established immunizations. Even small declines in vaccination coverage can have profound public health consequences, particularly for diseases such as measles and pertussis, which require particularly high levels of community immunity to ensure herd immunity and prevent outbreaks.

Caregivers play a pivotal role in shaping pediatric health outcomes. Their beliefs and decisions significantly influence children's access to preventative care, including vaccines. Understanding

adults' attitudes and beliefs about vaccines, as well as examining the alignment between caregivers and children's vaccine acceptance, provides critical insights into family-level health beliefs and behaviors. Additionally, understanding the demographic, socio-economic, and medical determinants of vaccination highlights disparities that may influence vaccine decision-making and identifies opportunities for targeted interventions.

By exploring individual, family, and community-level dynamics, this research addresses critical gaps in understanding the impact of the COVID-19 pandemic on vaccine hesitancy. It highlights the intersections of public health, societal changes, and individual decision-making, providing a foundation for developing resilient strategies to mitigate vaccine-preventable disease risks in an uncertain public health landscape.

CHAPTER 3. MANUSCRIPT 1

Manuscript 1: Predictors of willingness to receive updated 2023–2024 COVID-19 booster vaccines among a convenience sample of adults in Minnesota

BACKGROUND AND AIMS

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, had a significant global impact, leading to unprecedented efforts in vaccine development.[2,75,76] For the 2023–2024 season, several updated booster vaccines are available and recommended for everyone aged six months and older.[26] While the future of COVID-19 vaccine recommendations remains somewhat uncertain, there are indications that suggest the vaccine will be updated and recommended annually, mirroring the approach taken with the seasonal influenza vaccine.[77]

Despite the availability of licensed and thoroughly tested vaccines, uptake remains less than ideal in the US. As of May 2023, when US vaccine uptake was last updated, 81% of the population had received at least one dose of a COVID-19 vaccine; however, only 17% of the US population had received a bivalent booster dose, as recommended at the time. Of particular concern is uptake among those age 65 and older, some of the most vulnerable to severe disease outcomes, only 43% had received a bivalent booster dose.[5] Addressing this challenge goes beyond providing access to vaccines and requires a concerted effort to enhance vaccine acceptance and trust.

The World Health Organization Strategic Advisory Group of Experts on Immunization working group describes vaccine acceptance as a continuum of beliefs from anti-vaccine to vaccine-hesitant to pro-vaccine.[44] Numerous factors have been identified as influential in determining an

individual's willingness to receive COVID-19 vaccines. Sociodemographic characteristics such as age, educational attainment, socioeconomic status, and political affiliation have a well-established relationship with COVID-19 vaccine acceptance.[28] Other factors such as perception of vaccine safety and disease risk, mental and physical status, and social media use have also been found to influence willingness to receive COVID-19 vaccines.[29,30] Additionally, there is some evidence that knowledge of herd immunity, or community protection, and altruistic motives are associated with motivation to receive influenza and COVID-19 vaccines.[30–33] Understanding which factors continue to be important as COVID-19 vaccines move from pandemic response to routine annual vaccines is crucial to tailoring effective public health strategies to increase COVID-19 booster vaccine uptake.[78]

Historically, vaccination rates in Minnesota have been slightly higher than national estimates. However, despite these higher vaccination rates, Minnesota also has some of the most stark disparities in COVID-19 vaccine uptake, making it an ideal state to study determinants of vaccination.[79] The Minnesota State Fair is attended by as many as two million individuals each year. In addition to state and county fairs, it presents an opportunity to survey a large number of individuals in a short period of time.[62] The primary objective of this study was to identify determinants of intention to receive COVID-19 booster vaccines in 2023, the first year after the COVID-19 Public Health Emergency was ended. We were particularly interested in examining what factors were most influential in vaccine intention in those who are neutral or on the fence about getting vaccinated. In this manuscript, we pursued the following specific aims:

Aim 1A: Describe the characteristics of adults who are likely to receive a COVID-19 booster vaccine in the coming year and identify determinants of intention to receive an updated 2023–2024 COVID-19 booster vaccine among adults, including perceptions of COVID-19 risk, vaccine safety, public health knowledge, political affiliation and fear of pandemics.

> **Hypothesis 1A:** I hypothesized that greater knowledge of key principles of public health, higher levels of fear of pandemics, higher perception of COVID-19 risk and vaccine safety would be associated with increased intention to plan to receive an updated COVID-19 booster vaccine in the coming year.

Aim 1B: Investigate determinants of vaccine intention specifically among adults who are in the middle of the vaccine acceptance continuum, those who are more neutral or undecided about their intention to receive an updated COVID-19 vaccine in the coming year.

> **Hypothesis 1B:** I hypothesized that among individuals who are more neutral, compared to those with strong opinions, about receiving the 2023–2024 updated COVID-19 vaccine factors strongly associated with polarized vaccine opinions and intentions, such as beliefs about perceived safety of vaccines, will be less influential.

METHODS

Study design and survey

The study conducted was a cross-sectional survey at the University of Minnesota Driven to Discover Research Facilities at two Minnesota county fairs, Stevens County Fair (August 9th–11th, 2023) and Beltrami County Fair (August 12th–13th, 2023) and at the 2023 Minnesota State Fair (August 24th–September 5th, 2023). Fair attendees were eligible for the study if they were 18 years or older and could read English. Eligible participants completed a self-administered online

survey using the university-supported Qualtrics online survey platform[80]. The survey consisted of a maximum of 41 questions grouped into six sections: health characteristics, public health knowledge, fear of future pandemics, COVID-19 and COVID-19 vaccines, flu and flu vaccines, and demographics (Supplementary Table 3.1). The survey took approximately 10 minutes to complete. Participants received a tote bag, or incentive of equivalent value, upon completion of the survey. The University of Minnesota Institutional Review Board (IRB) provided approval for this study.

Overall, 1,256 participants enrolled in the study. Twenty participants did not complete the survey question related to the primary outcome, and another 361 participants who did not complete at least one of the questions related to exposures of interest or relevant demographics were excluded from the analysis. This resulted in an analytic dataset that consisted of 895 participants.

Measures

Outcome

Our primary outcome was the participant's intention to receive a recommended COVID-19 booster vaccine in the coming year if offered. Participants were asked, "How likely are you to get a COVID-19 booster vaccine if it is recommended for you this coming year?". Response options were on a 5-point Likert scale ranging from "extremely unlikely" to "extremely likely."

Predictors

Key predictors for this study included perceived COVID-19 vaccine safety, perceived risk of COVID-19 infection, public health knowledge, fear of future pandemics, and political affiliation.

Perceived COVID-19 risk and perceived COVID-19 vaccine safety were assessed through 5-point Likert-style survey questions adapted from the Vaccine Confidence Survey Question Bank.[81] For analysis, perceived risk was dichotomized as "Not at all concerned" versus any level of concern, and perceived vaccine safety was dichotomized as "Extremely safe" versus any other selection.

Public health knowledge was assessed through four survey questions that aimed to gauge participants' understanding of key public health concepts, which included primary prevention, pandemic, endemic, and herd immunity. Participants were asked to select the correct definition for each of these terms from five options presented. Participants who selected the correct answer were categorized as knowledgeable about that term. Those who selected the correct answer for each of the four public health terms were categorized as knowledgeable about public health; all others were categorized as not knowledgeable. This method has previously been used to assess herd immunity and vaccine acceptance; the survey question assessing herd immunity was taken from a previous study conducted at the Minnesota State Fair.[31] Other key concepts regarding public health knowledge were selected based on proposed conceptual foundations for public health literacy and key public health concepts identified by the CDC.[82,83] This categorization approach was chosen because each term, as well as overall knowledge of all terms, demonstrated a significant association with vaccine intention in bivariate analysis. By consolidating these

terms into a single composite measure, we aimed to maintain model parsimony and minimize the risk of convergence issues during analysis.

Participants were asked four 7-point Likert-style questions adapted from the Fear of COVID-19 Scale to determine fear of future pandemics.[84] Responses were numerically coded and summed. For analysis, this variable was dichotomized at the median.

Participants were also asked to select their political affiliation from the following list: "Democrat," "Republican," "Independent," "Other," or "Prefer not to answer." For analysis, political affiliation was dichotomized as "Democrat" versus all other selections because Democrats were distinctively more likely to report vaccination intention compared to Republicans, Independents, and others, making them a meaningful comparison group. Additionally, Democrats also represented the largest group of survey respondents, pooling the other political groups who represented fewer participants allowed us to avoid model convergence issues in the ordinal logistic regression.

Control variables

To address potential confounding of the associations between COVID-19 booster vaccine intention and our determinants of vaccination of interest, we identified potential confounders a priori in the literature and through a conceptual diagram. We selected the minimal sufficient adjustment variables to include in the analysis to estimate the total effect of perceived COVID-19 vaccine safety, perceived COVID-19 risk, public health knowledge, fear of future pandemics, and political affiliation on vaccine intention. These included age, income, educational attainment,

medical conditions, work in public health or healthcare, sources of vaccine information, and anxiety.

Age was dichotomized as 65 or older or not for analysis. This dichotomization was chosen based on the CDC's communication regarding the risk of severe illness and differing COVID-19 booster recommendations for those 65 and older. This threshold aligns with public health messaging and vaccine eligibility criteria, ensuring the analysis reflects differences in vaccine intention influenced by risk perceptions and targeted recommendations for this age group. Per the National Academies of Sciences, Engineering, and Medicine, sex and gender were assessed through two questions.[85] Participants were also asked to self-report their race and ethnicity, annual household income, and educational attainment. For analysis, income was dichotomized at $50,000 or above, and education was dichotomized as a college degree or more versus less than a college degree. Participants were also asked to report whether they had a medical condition that would put them at risk for severe illness from COVID-19. Anxiety was identified as an important confounder of the relationship between fear of pandemics and intention to receive COVID-19 vaccines; as such, it was assessed with the GAD-2.[86,87]

Additionally, participants were asked about their previous COVID-19 vaccination status with a series of three questions, "Have you received a COVID-19 vaccine?", "How many COVID-19 vaccine doses have you received (including primary series and booster vaccines)?" and "Have you received a COVID-19 booster vaccine dose since September of 2022 (otherwise known as an updated or bivalent booster)?". If participants indicated they had not received a COVID-19

vaccine or they had not received a bivalent booster vaccine, they were asked for the primary reason they had not. The responses to these questions are included in a descriptive analysis.

To assess sources of vaccine information, participants were asked, "Where do you most often hear about vaccines?". For analysis, responses were dichotomized into a variable assessing if participants receive the majority of their vaccine information from social media ("Social media" or "Websites written by individuals or blogs" versus any other response). This decision was based on evidence that social media platforms, including blogging websites, are significant sources of vaccine misinformation, which have been shown to contribute to increased vaccine hesitancy and decreased vaccine uptake.[88–90]

Statistical analysis

R version 4.1.3 was used for all analyses.[91] The primary outcome of our analysis was the level of intention to receive a COVID-19 booster vaccine in the coming year if it was recommended.

Descriptive statistics

We tabulated counts and proportions of study participants for each demographic and health characteristic by COVID-19 booster intention level. We used bivariate statistical tests, including the Kruskal-Wallis rank sum test for continuous variables, Fisher's exact test for categorical variables, Fisher's exact test simulated for categorical variables with small cell counts, and Pearson's chi-squared test for binary predictors. Missing and unknown data were excluded during bivariate analysis.

Associations between predictors of vaccine willingness and COVID-19 booster vaccine intention

To assess factors associated with intention to receive a COVID-19 booster vaccine in the coming year, if it was recommended, we used ordinal logistic regression. Our dependent variable was categorical COVID-19 booster vaccine intention. Our independent variables included public health knowledge, fear of future pandemics, perceived COVID-19 risk, perceived COVID-19 vaccine safety, and political affiliation. We ran both unadjusted and adjusted models. Adjusted models controlled for the following potential confounders: age, income, educational attainment, medical conditions that put individuals at greater risk for severe COVID-19 illness, work in public health or healthcare, sources of vaccine information, and anxiety. Confounders were identified via a conceptual model (Supplemental Figure 3.1).

To examine what factors influence booster vaccine intention among those who are in the middle of the vaccine intention continuum, we conducted the same analysis as outlined above with a subset of our participants who reported being neither extremely likely nor extremely unlikely to receive a COVID-19 booster vaccine in the coming year.

RESULTS

Descriptive statistics

A total of 1,256 individuals enrolled in this cross-sectional study. All participant demographics are described in Table 3.1 but in brief, the mean age of our participants was 48 years, ranging from 18 to 93 years and the majority of participants identified as women (61%). Most participants were white (83%) and non-Hispanic (91%). Participants reported being in good health, with only 20% of participants indicating they had a medical condition that would put

them at greater risk for severe COVID-19 illness. Participants had high levels of educational attainment, more than 60% possessed a college degree. A quarter of participants reported working in healthcare and 16% reported working in public health (Supplemental Table 3.1). Most participants were Democrats (54%), while only 13% reported Republican affiliation, 13% reported being independent, 6% reported some other political affiliation, and 13% of participants preferred not to report their political affiliation (Supplemental Table 3.1).

Vaccine intention and key predictors of vaccine intention

Intention to receive the COVID-19 booster vaccine in the coming year if it was recommended was high; 56% of participants reported they were extremely likely to receive the vaccine this year, another 15% reported being likely, 8% were undecided, 7% reported being unlikely, and 12% reported being extremely unlikely to receive the vaccine (Table 3.1).

Supplemental Table 3.2 describes participants' intention to receive a COVID-19 booster vaccine in relation to key predictors of interest. Overall, public health knowledge was low; only 31% of participants correctly identified all four key public health concepts. While 92% of participants could correctly define the term "pandemic," only 70% correctly defined "endemic," and only 45% selected the correct definition of "primary prevention." Higher proportions of individuals with high vaccine intention correctly identified each of the public health terms. For example, 94% of those who reported they were extremely likely to receive a COVID-19 vaccine in the coming year correctly defined herd immunity, whereas only 71% of those who reported being extremely unlikely to receive a COVID-19 vaccine the coming year correctly identified the term. Knowledge of public health terms individually and overall, were both associated with higher

levels of COVID-19 booster vaccine intention in bivariate analysis ($p<0.001$). Fear of future pandemics was also low among participants. The mean combined score for the pandemic fear measures was 14.7 (sd: 5.5) on a 28-point scale. This combined measure was also associated with higher levels of intention to receive the COVID-19 booster vaccine in bivariate analysis ($p<0.001$). Those who reported they were extremely likely to receive a COVID vaccine in the coming year had a mean pandemic fear score of 16.1 (sd: 4.8), whereas those who reported being extremely unlikely to receive a COVID vaccine had a mean score of 8.4 (sd: 4.8). Perceived risk of COVID-19 varied greatly among participants, and roughly one-quarter were not at all concerned about COVID-19 infection. Additionally, most participants believed the COVID-19 vaccine to be extremely safe (55%). Higher levels of both perceived COVID-19 risk and perceived COVID-19 vaccine safety were more commonly reported in participants with greater intention to receive a COVID-19 vaccine in the coming year ($p<0.001$).

Almost all participants (92%) had received at least one COVID-19 vaccine in the past (Supplemental Table 1.2). The most common reasons provided for not receiving any COVID-19 vaccine were related to concerns about vaccine side effects (n=35; 35%) and concerns about vaccine efficacy (n=26; 26%) (Table 3.2). Sixty-five percent of participants reported receipt of the bivalent/updated COVID-19 booster vaccine (Supplemental Table 3.2). The most common reasons provided for not receiving an updated bivalent COVID-19 vaccine among those who had previously been vaccinated for COVID-19 were related to lack of concern about getting sick (n=79; 21%); 104 participants (27%) had some other reason for not being vaccinated that was not listed in our survey (Table 3.2). In bivariate analysis, perceived vaccine safety, perceived

COVID-19 infection risk, and COVID-19 vaccine history were all associated with the intention to receive the COVID-19 vaccine in the coming year (Supplemental Table 3.2).

Associations between predictors of vaccine willingness and COVID-19 booster vaccine intention by ordinal logistic regression

There was a strong positive association between perceived vaccine safety, perceived COVID-19 risk, public health knowledge, fear of future pandemics, and political affiliation and COVID-19 booster vaccine intention in the coming year in both unadjusted and adjusted models (Table 3.3). Odds were slightly attenuated for each of the predictors in the adjusted model. After adjusting age, income, education, medical conditions, work in public health or healthcare, sources of vaccine information, anxiety, as well as the other key predictors (perceived risk of COVID-19 infection, public health knowledge, fear of future pandemics and political affiliation), the odds of being in any higher level of booster intention (vs any lower level of intention) among participants who perceived the COVID-19 vaccine as extremely safe was 15.3-times the odds of those who did not perceive it as extremely safe (aOR: 15.3, 95% CI: 10.6–22.2). After adjusting for all other variables in the model, for participants who had any concern about COVID-19 infection, the odds of being more likely to intend to receive a booster vaccine in the coming year was 3.5-times the odds of those who had no concerns related to COVID-19 infection (aOR: 3.5, 95% CI: 2.4–5.1). After adjusting for all other variables in the model, public health knowledge (aOR: 1.3; 95%CI: 0.9–1.8), pandemic fear (aOR: 3.4; 95%CI: 2.4–4.8), and Democratic political affiliation (aOR: 2.8, 95% CI: 1.8–4.4) were also positively associated with higher intention to receive the COVID-19 booster vaccine.

When excluding participants who reported they were extremely unlikely or extremely likely to receive a COVID-19 booster vaccine from the analysis to examine those in the middle/neutral portion of the vaccine acceptance continuum, perceived vaccine safety and perceived COVID-19 risk continued to be highly influential predictors of intent to receive booster vaccine (Table 3.3). However, the odds were greatly attenuated compared to the full analytic dataset (perceived vaccine safety [aOR: 4.1, 95% CI: 2.2–7.5]; perceived COVID-19 risk [aOR: 2.8, 95% CI: 1.6–4.7]). Pandemic fear (aOR: 2.1; 95% CI: 1.2–3.6) and Democratic political affiliation (aOR: 2.5, 95% CI: 1.4–4.4) also continued to be positively associated with higher vaccine intention.

DISCUSSION

We found that perception of vaccine safety was the most influential factor related to intention to receive the COVID-19 booster vaccine in our full outcome analysis and sensitivity analyses. Most participants believed the vaccine to be extremely or moderately safe, and those who viewed the vaccine as extremely safe had higher booster vaccine intention compared to those who did not. This strong association underscores the pivotal role that confidence in vaccine safety plays in an individual's vaccine decision-making. Several other studies have highlighted the importance of vaccine safety in relation to vaccine intention.[30,92–94] A 2021 study of Finnish adults found that vaccine safety was the strongest predictor of intentions to accept COVID-19 vaccine[30]. In their sample, perceived vaccine safety explained 52% of the variance in intentions to vaccinate. A 2021 study of US adults found similar results; perceived vaccine safety was the factor with the highest magnitude of impact on vaccine willingness. Those who perceived the vaccine to be safe had substantially higher odds of receiving or planning to receive the COVID-19 vaccine (aOR: 40.0, 95% CI: 19.0–84.2).[92]

Beyond vaccine safety, we also found several other factors were related to participants' decisions regarding the COVID-19 booster. Concern about COVID-19 infection varied greatly among study participants. However, in our study, those who had any level of concern about COVID-19 infection had about 3 to 5 times the odds of higher COVID-19 booster vaccine intention in the coming year than those who were not at all concerned. This is consistent with other studies which have also found that perceived risk of COVID-19 increases vaccine intention, although to a lesser magnitude than vaccine safety.[30] Although less influential, key public health concepts were associated with higher levels of vaccine intention. This is consistent with other studies that have found that knowledge of herd immunity and altruistic characteristics are associated with increased willingness to receive COVID-19 and influenza vaccines.[31–33] Additionally, those who reported they were extremely likely to receive a booster vaccine in the coming year were less likely to get their vaccine information from social media, more likely to report Democratic political affiliation, and reported higher levels of income and education. These results align with other studies of sociodemographic characteristics associated with COVID-19 vaccine intention, which report that booster-hesitant individuals are more likely to identify as conservative and report lower levels of income and education.[92,93,95,96]

This study has some limitations worth noting. First, this study drew from a convenience sample which was not fully representative of the general population as our participants were more likely to be non-Hispanic White and had higher levels of income and educational attainment than the general Minnesota population. However, the demographics of our study population did approximate those of State Fair attendees, as in 2019 approximately 52% of attendees were

female, 48% were aged 18-45 years, most reported incomes over $75,000 per year (58%), and at least some college education (40% had a college degree or more, and 34% reported some college).[97] Vaccine coverage was also much higher among our participants than nationally with 92% of our participants reporting at least one COVID-19 vaccine (compared to 81% nationally) and 65% of our participants reporting receiving a bivalent booster vaccine (compared to 17% nationally).[5] An additional limitation is our inability to understand the role of perceived vaccine effectiveness because we did not assess related questions in our survey. We learned that this factor was the second most common reason for choosing not to receive a COVID-19 vaccine in the past. Those who are distrustful of scientific studies or vaccination may have chosen not to participate, and individuals who were most concerned about COVID-19 may not have attended a crowded event such as the State Fair. Additionally, the vast majority of our participants intended to receive a COVID-19 booster vaccine in the coming year which limited our ability to include non-binary predictors in our models due to issues with model convergence.

This study also presents several strengths. First, it is an extensive and detailed survey of a large sample of adults conducted during a pivotal point in time, before the CDC's Advisory Committee on Immunization Practices released their COVID-19 booster vaccine recommendations for 2023. As a result, we were able to capture the opinions of individuals in the lead-up to this season's vaccination campaign. This allowed us to examine what is important to people as they decide if they will accept vaccines in the coming year. Second, we were able to examine a large number of factors that may be associated with vaccine intention and highlight areas for future study and educational campaigns.

As we move further away from the pandemic and anticipate the need for annual updates to the COVID-19 vaccine, understanding the factors that sway individuals towards accepting vaccination will become increasingly crucial. Our research underscores the importance of vaccine safety in influencing intentions to get vaccinated, a finding echoed in other vaccine studies.

TABLES

Table 3.1 Demographic and health characteristics of participants in relation to intention to receive COVID-19 booster vaccine in the coming year if it is recommended (N=1,236)

Characteristic	Overall, N = 1,236	Extremely likely, N = 702	Likely, N = 189	Undecided, N = 106	Unlikely, N = 85	Extremely unlikely, N = 154	p-value
Age							<0.001[+]
Mean (sd)	48 (19)	51 (19)	43 (18)	42 (19)	42 (17)	46 (18)	
Unknown	6	4	2	0	0	0	
Sex and gender							0.1[*]
Cisgender women	762	457 (60%)	112 (15%)	60 (7.9%)	52 (6.8%)	81 (11%)	
Cisgender men	437	222 (51%)	73 (17%)	40 (9.2%)	31 (7.1%)	71 (16%)	
Transgender women	3	2 (67%)	1 (33%)	0 (0%)	0 (0%)	0 (0%)	
Transgender men	9	6 (67%)	1 (11%)	2 (22%)	0 (0%)	0 (0%)	
Other	13	8 (62%)	1 (7.7%)	3 (23%)	0 (0%)	1 (7.7%)	
Unknown	12	7	1	1	2	1	
Race							<0.001[*]
White	1,031	607 (59%)	146 (14%)	79 (7.7%)	69 (6.7%)	130 (13%)	
American Indian, Alaskan Native	17	7 (41%)	6 (35%)	4 (24%)	0 (0%)	0 (0%)	
Black, African American	27	12 (44%)	4 (15%)	6 (22%)	3 (11%)	2 (7.4%)	
Asian	66	31 (47%)	21 (32%)	7 (11%)	4 (6.1%)	3 (4.5%)	
Other	29	13 (45%)	2 (6.9%)	5 (17%)	3 (10%)	6 (21%)	
Multiple races	32	15 (47%)	7 (22%)	0 (0%)	2 (6.2%)	8 (25%)	
Unknown	34	17	3	5	4	5	
Hispanic ethnicity							0.6[±]

Hispanic or Latino	44	23 (52%)	8 (18%)	4 (9.1%)	5 (11%)	4 (9.1%)	
Not Hispanic or Latino	1,118	639 (57%)	174 (16%)	96 (8.6%)	72 (6.4%)	137 (12%)	
Unknown	74	40	7	6	8	13	
Education							<0.001*
Less than high school	3	1 (33%)	1 (33%)	1 (33%)	0 (0%)	0 (0%)	
High school graduate or equivalent (e.g., GED)	124	38 (31%)	26 (21%)	23 (19%)	17 (14%)	20 (16%)	
Some college, including associate degree or trade school	308	148 (48%)	48 (16%)	28 (9.1%)	25 (8.1%)	59 (19%)	
Bachelor's degree	403	237 (59%)	58 (14%)	31 (7.7%)	27 (6.7%)	50 (12%)	
Graduate degree	396	277 (70%)	56 (14%)	23 (5.8%)	16 (4.0%)	24 (6.1%)	
Unknown	2	1	0	0	0	1	
Annual household income							<0.001*
Less than $20,000	66	31 (47%)	12 (18%)	12 (18%)	7 (11%)	4 (6.1%)	
$20,000- 49,999	175	85 (49%)	22 (13%)	22 (13%)	19 (11%)	27 (15%)	
$50,000- 99,999	362	208 (57%)	57 (16%)	26 (7.2%)	22 (6.1%)	49 (14%)	
Over $100,000	487	303 (62%)	76 (16%)	29 (6.0%)	27 (5.5%)	52 (11%)	
Unknown	146	75	22	17	10	22	

+Kruskal-Wallis rank sum test

‡Fisher's exact test

*Fisher's exact test for count data with simulated p-value (based on 2000 replicates)

Table 3.2 Primary reason for declining COVID-19 vaccine in the past among participants (N=481)

Characteristic	Primary reason for never receiving any COVID-19 vaccine, N=99	Primary reason for not receiving COVID-19 bivalent booster, N= 382
I'm concerned about potential side effects	35 (35%)	61 (16%)
I don't think the COVID-19 vaccine is effective	26 (26%)	24 (6.3%)
I am not worried about getting sick	9 (9.1%)	79 (21%)
Vaccines are against my religious or personal beliefs	7 (7.1%)	1 (0.3%)
I did not know about this vaccine	3 (3.0%)	51 (13%)
I have a medical condition and cannot get vaccinated	2 (2.0%)	3 (0.8%)
I did not know where to get one or could not find one	1 (1.0%)	11 (2.9%)
Getting vaccinated is too time consuming or expensive	0	11 (2.9%)
Other	12 (12%)	104 (27%)
I don't know	0	29 (7.6%)
Prefer not to answer	4 (4.0%)	8 (2.1%)

Table 3.3 Adjusted and unadjusted odds ratios (95% CI) of booster vaccine intention from ordinal logistic regression

	Full outcome dataset (booster intention from extremely unlikely to extremely likely)				Subset of outcome dataset, middle of vaccine intention continuum (unlikely to likely)			
	Unadjusted (N=1,045)		Adjusted* (N=873)		Unadjusted (N=289)		Adjusted* (N=246)	
Predictor	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Perceived COVID-19 vaccine safety (ref: not extremely safe)	16.2	(11.6–22.6)	15.3	(10.6–22.2)	3.8	(2.1–6.6)	3.7	(2.0–7.0)
Perceived COVID-19 risk (ref: no concern)	4.3	(3.1–5.9)	3.5	(2.4–5.1)	2.4	(1.4–4.0)	2.6	(1.5–4.8)
Public health knowledge (ref: not knowledgeable)	1.3	(0.9–1.8)	1.3	(0.9–1.8)	1.2	(0.7–2.1)	0.9	(0.5–1.7)
Pandemic fear > median (ref: below median)	2	(1.5–2.7)	3.4	(2.4–4.8)	1.4	(0.9–2.3)	2.1	(1.2–3.6)
Democrat (ref: not Democrat)	3.4	(2.5–4.6)	2.8	(1.8–4.4)	1.9	(1.2–3.1)	2.5	(1.4–4.4)

* Adjusted for age, income, education, work in public health or healthcare, sources of vaccine information, medical conditions, and anxiety

CHAPTER 4. MANUSCRIPT 2

Manuscript 2: Association between caregiver and child COVID-19 vaccine hesitancy in the ECHO Cohort

BACKGROUND AND AIMS

COVID-19 has had a significant impact on global health, including among children. The Centers for Disease Control and Prevention (CDC) estimates that 96.3% of children in the United States (US) have had at least one COVID-19 infection, representing more than 65 million children.[5] Although children generally experience milder forms of the disease than adults, they are not immune to the risks and burdens associated with COVID-19 infection.[98] Children can experience severe illness, and as many as 10–20% may develop post-acute sequelae of SARS-CoV-2 infection (PASC), commonly known as long COVID.[5,99] Additionally, the potential for transmission within households and communities also underscores the importance of vaccinating children to control the spread of the virus and protect vulnerable populations. A study of over 160,000 households with both adults and children found that 70% of the reported 38,000 COVID-19 cases had a pediatric index case, suggesting that children are important viral vectors, particularly when school is in session.[100] This emphasizes the importance of COVID-19 vaccinations as a critical tool in mitigating the spread of the virus and reducing severe outcomes, including in pediatric populations.

Vaccines were made available to children aged five and older in mid-2021, with approval for children six months and older in 2022.[101] Clinical trials and observational studies have demonstrated the vaccines' safety and effectiveness in reducing the risk of severe illness and hospitalization in children. A systematic review of 51 studies in children aged 5–11 years found

that COVID-19 mRNA vaccines were moderately effective against infections and provided good protection against hospitalization.[102] Additionally, evidence suggests that vaccines are even more effective in children aged 12–17 years.[103] However, vaccine uptake among children has lagged that of adults, partly due to parental concerns and hesitancy. The CDC estimates that 48% of US children between the ages of 6 months and 17 years have not received at least one COVID-19 vaccine; additionally, only 7.5% received the 2023–2024 updated COVID-19 vaccine, compared to 81% and 21%, respectively, among adults.[27]

The World Health Organization (WHO) refers to vaccine hesitancy as the "delay in acceptance or refusal of safe vaccines despite the availability of vaccine services."[44] Several studies have examined parental hesitancy to vaccinate their children against COVID-19, identifying various factors influencing vaccine hesitancy. Common determinants include sociodemographic factors such as younger parental age, lower levels of education and income, as well as psychological antecedents, including a lack of confidence (perceiving vaccines as unsafe and ineffective) and complacency (perceiving the disease as low risk).[104] A systematic review of 27 articles on parental COVID-19 vaccine acceptance found that the most common reasons for hesitancy to vaccinate children were related to the perceived safety and efficacy of the COVID-19 vaccine.[104] However, these studies were often limited by specific geographic focus, cross-sectional designs, small sample sizes, and data collection periods predating the widespread availability of vaccines for children. Additionally, many of the observational studies included in the review were performed outside the US, presenting a challenge as acceptance rates and reasons for vaccine hesitancy may vary greatly across different populations globally.[104] Moreover, prior studies have typically examined parental willingness to vaccinate themselves and their children as separate

phenomena without directly comparing the reasons for vaccine hesitancy between these two decisions. As a result, there is a limited understanding of whether the factors influencing parents' decisions to accept the vaccine for themselves align with the reasons they might hesitate to vaccinate their children. Consequently, there is a need for more comprehensive research that considers a broader, more diverse population, includes variations across different waves of the pandemic, and examines the similarities and differences in vaccine hesitancy between parents and their children, especially in the US, which has a unique vaccine hesitancy landscape.

The COVID-19 pandemic also negatively impacted the uptake of other routine childhood vaccinations. Disruptions to healthcare access, school closures, and fear of exposure to COVID-19 contributed to delays and declines in routine immunization coverage worldwide during the pandemic.[37,54,55] In addition to the logistical disruptions, the pandemic introduced new challenges related to vaccine attitudes. We do not yet fully understand the extent to which COVID-19 vaccine refusal is associated with refusal or delay of other routine childhood vaccines. Understanding this dynamic is crucial for public health, as even slight declines in routine vaccination coverage can erode herd immunity. Before the pandemic, reaching and maintaining the vaccination coverage necessary for herd immunity was already tenuous in some communities.[105] The added burden of COVID-19-related disruptions and the potential for further skepticism and reduced vaccine uptake present a significant public health challenge, as they risk exacerbating these vulnerabilities.

This manuscript addresses gaps in our understanding of the impact of the COVID-19 pandemic on vaccine hesitancy in children by examining the association between the self-reported

vaccination status of caregivers and their children within the NIH ECHO Cohort, a geographically, ethnically, and socially diverse sample of families.[63,106] In addition to exploring the association between caregiver and child vaccination status, the present study also investigates the reasons behind vaccine hesitancy among adult caregivers, both for themselves and for their children, assessing whether these reasons align or differ. This approach offers a more nuanced understanding of vaccine acceptance within families. Furthermore, this research assesses the association between COVID-19 and routine vaccine hesitancy, which previous studies have not thoroughly investigated. This manuscript addresses important gaps in the literature on parental willingness and hesitancy to vaccinate themselves and their children through the following aims:

Aim 2A: Assess the relationship between adult caregivers' COVID-19 vaccination status and their children's vaccination status and examine demographic, socio-economic, and medical determinants of COVID-19 vaccination among families in the ECHO cohort.

> **Hypothesis 2A:** I hypothesized that the vaccination status of adult caregivers of children would be associated with the vaccination status or intentions to vaccinate their children. I also hypothesized that children with lower socio-economic status would be less likely to be vaccinated for COVID-19 compared to their counterparts of higher socio-economic status. Demographic factors such as age, race, and ethnicity will also be associated with vaccination uptake or intention. I hypothesized that younger children would be less likely to have received a COVID-19 vaccine and that children from racial and ethnic minorities would be less likely to have been vaccinated for COVID-19 compared to non-Hispanic white children.

Aim 2B: Investigate whether the reasons for COVID-19 vaccine hesitancy of adult caregivers to accept the COVID-19 vaccine for themselves correspond with the reasons for hesitancy to vaccinate their children. Additionally, to explore the reasons given by caregivers who accepted the COVID-19 vaccine for themselves but did not accept the vaccine for their children.

Hypothesis 2B: I hypothesized that the reasons adult caregivers are hesitant to accept the COVID-19 vaccine for themselves will correspond to the reasons they are hesitant to have their children vaccinated. I hypothesized that the most common reasons for vaccine hesitancy among caregivers and children would be related to vaccine safety, including perceived side effects and long-term effects of the vaccine, as well as perceptions about the risk of COVID-19, specifically that the risk of contracting COVID-19 is low. Furthermore, among caregivers who have been vaccinated, I hypothesized that their hesitancy to vaccinate their children would be child-specific, including higher odds of reporting concerns about whether the vaccine had been adequately tested in children and beliefs that children are at a lower risk of severe illness from COVID-19.

Aim 2C: Examine whether COVID-19 vaccine hesitancy among caregivers and children is associated with intentional delay or refusal of other pediatric vaccines, including Diphtheria/Tetanus/Pertussis (DTaP), Hepatitis A (Hep A), Hepatitis B (Hep B), Haemophilus Influenzae Type B (Hib), Polio (IPV), Meningococcal, Measles/Mumps/Rubella (MMR), Pneumococcus (PCV), Rotavirus (RV), Varicella (Chickenpox), Tetanus/Diphtheria/Pertussis (Tdap), and Human papillomavirus (HPV).

Hypothesis 2C: I hypothesized that caregivers who are hesitant to accept the COVID-19 vaccine for themselves or their children would be more likely to refuse or intentionally delay other childhood vaccines.

METHODS

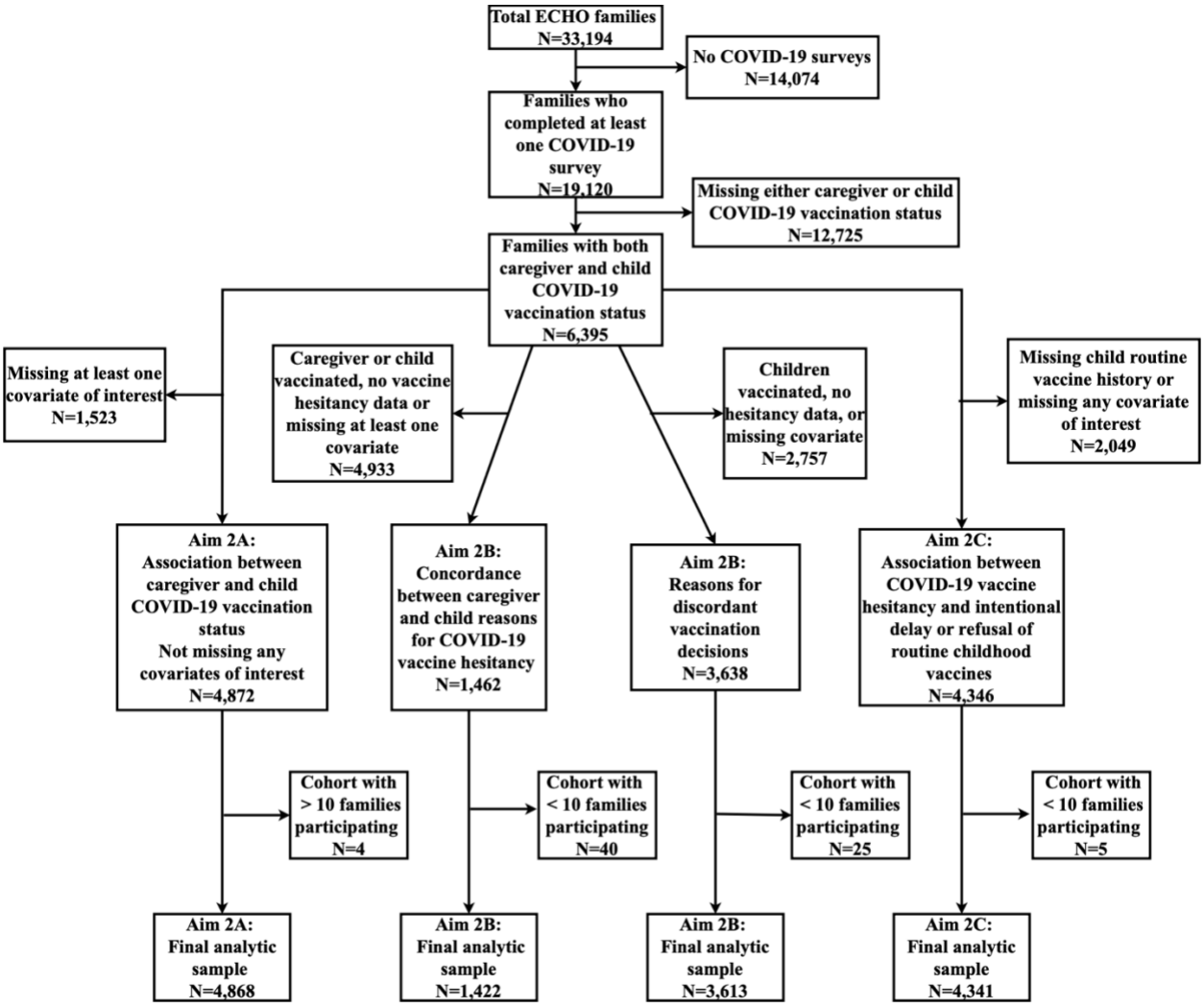
Study Population

The ECHO-wide cohort has enrolled more than 57,000 children and 61,000 pregnant participants since its launch in 2016. ECHO continues to collect data on these participants and newly enrolled participants. By collecting data from existing and new cohorts across the US, ECHO aims to represent diverse racial, sociodemographic, and geographic backgrounds. The local and central ECHO Institutional Review Board approved the ECHO study protocol. Written informed consent and parental/guardian permission were obtained, along with child assent as appropriate, for participation in the ECHO-wide Cohort Data Collection Protocol and specific cohorts. De-identified data from the ECHO Program is available through the NIH Data and Specimen Hub (DASH).[64,66,107] In response to the COVID-19 pandemic, the ECHO Cohort promptly adapted its data collection efforts to include COVID-19-related exposures and outcomes. This adaptation included developing and administering novel COVID-19-specific questionnaires starting in April 2020.[64] This effort was led by the NIH ECHO COVID-19 Task Force, co-chaired by Dr. Tracy Bastain and Dr. Carrie Breton. The team included 21 cohort investigators and representatives for the ECHO NIH Program Office, Coordinating Center, and Data Analysis Center.[65] The questionnaires were tailored for pregnant women, caregivers, and children (via parent-report) and adolescents (via self-report), combining original items with modified content from existing surveys to capture information on COVID-19 infection, vaccine attitudes, and the psychosocial and economic impacts of the pandemic.[65] The de-identified COVID-19-related data included participants who completed COVID-19 surveys from April 2020 through August 2023. While

these surveys continued to be collected following August 2023, this is the last date available in the public dataset.

Participants were only included in this analysis if the child and caregiver completed at least one COVID-19 survey with reported COVID-19 vaccination status. As of August 31, 2023, a total of 33,194 families had agreed to participate in the new ECHO-wide Cohort data collection. A total of 19,120 families completed at least one COVID-19 survey. Data from 6,395 families, including both the child's and caregiver's vaccination status, were available for this analysis. Cohorts with fewer than 10 participating families were excluded from the analysis to reduce outcome homogeneity and ensure model stability. Excluding cohorts with very small sample sizes is a common approach in studies using ECHO Cohort data, as small cell counts can lead to challenges with model convergence. Additionally, each aim required slightly different inclusion criteria, as outlined in Figure 4.1. All participants in this analysis completed the COVID-19-related surveys after December 2021. While most families only had one participating child, 517 families had multiple children participating. 497 families had two children participating, 19 had three children participating, and one family had four children participating. Additionally, while most families only completed one COVID-19 survey during the relevant data collection period, some completed up to four surveys. Six hundred eighty-six families completed two surveys during the relevant period, 212 completed three surveys, and 68 families completed four surveys.

Figure 4.1 Criteria for inclusion of ECHO Cohort families in each analytic sample by specific aim for Manuscript 2



Evaluation of selection bias

To assess potential differences between participants included in the analysis and those excluded, we generated descriptive summary tables comparing key family characteristics from a random sample of three cohort sites. Within each cohort, families were grouped based on whether they were included in the analyses for Aims 2A, 2B, and 2C or excluded from all three analytic aims.

For each group, demographic, socioeconomic, and health-related variables were summarized. All variables were summarized descriptively, without statistical testing, and reported with means and standard deviations or frequency and percentage as appropriate. These comparisons enabled the identification of any systematic differences between included and excluded participants across cohort sites.

Across the sampled cohorts, participants included in the analytic aims did not differ substantially from those excluded regarding key sociodemographic and health-related characteristics (Supplemental Table 4.1). The distribution of child age groups, race and ethnicity, caregiver vaccination history, and maternal socioeconomic status were generally similar between included and excluded families, suggesting minimal selection bias due to analytic inclusion criteria.

Repeat observations and sibling participants

To account for potential correlations between sibling participants and to simplify the analytic framework, this study employed a family-level analysis by pooling data from families with multiple participating children or multiple surveys into a single family-level record rather than incorporating multiple levels of correlation due to repeated observations and sibling participation. This approach allowed for the use of Generalized Estimating Equations (GEE), which are robust to clustering at the cohort level and provide population-average effects. GEE was preferred over multilevel modeling to address concerns about model convergence and to align with the study's objective of obtaining population-level interpretations.

The limited number of children with multiple surveys and families with multiple children further justified this decision. It is assumed that caregivers who accept the vaccine for one child are

unlikely to decline for another, supporting the appropriateness of pooling repeated measures for the same family. Moreover, this study does not aim to examine temporal changes in vaccine acceptance using longitudinal data, reinforcing the decision to treat repeated measures in a pooled fashion.

Measures

The ECHO Cohort employs a data collection protocol that mandates each cohort to gather specific measures during defined life stages of participants. Essential measures must be collected at least once during each relevant life stage, but may be collected multiple times, especially during periods of rapid developmental change or prolonged duration, such as the prenatal period or adolescence. In addition to essential measures, the ECHO Cohort also identifies recommended measures that, while not required, are strongly encouraged to be collected as frequently as feasible within each life stage. Caregivers completed all relevant surveys for children under the age of 13 years. Table 4.1 outlines the ECHO data elements, the surveys from which each element was taken, whether the data element was essential or recommended, and the life stage at which the data element was measured.

Table 4.1 Summary of relevant measures from the ECHO-Wide Cohort Data Collection Protocol included in analysis for Manuscript 2

Data element	Relevant survey(s)	Essential or recommended	Life stages measured
Child COVID-19 vaccination status	Child COVID-19 Parent Report Questionnaire, Child COVID-19 Vaccination Parent Report Questionnaire	Essential	Infant, Early Childhood, Middle Childhood, Adolescent

Child routine/recommended vaccination status	Child Medical History	Essential	Infant, Early Childhood, Middle Childhood, Adolescent
Caregiver COVID-19 vaccination status	Adult COVID-19 Questionnaire, Caregiver COVID-19 Vaccination Survey	Essential, Recommended	Infant, Early Childhood, Middle Childhood, Adolescent
Child and caregiver reasons for COVID-19 vaccine hesitancy	Child COVID-19 Parent Report Questionnaire, Adult COVID-19 Questionnaire	Essential	Infant, Early Childhood, Middle Childhood, Adolescent
Child race	Demographics of Child Survey	Essential	Infant
Child age	Demographics of Child Survey	Essential	Infant
Mother age	Participant Registration	Essential	Prenatal
Caregiver education and income	Child Derived Demographics Socioeconomic Status	Essential	Infant, Early Childhood, Middle Childhood, Adolescent
Child chronic illness history	Child Medical History	Essential	Infant, Early Childhood, Middle Childhood, Adolescent
Child pandemic distress	Child COVID-19 Parent Report Questionnaire	Essential	Infant, Early Childhood, Middle Childhood, Adolescent
Caregiver pandemic distress	Adult COVID-19 Questionnaire	Essential	Infant, Early Childhood, Middle Childhood, Adolescent

Child concern about contracting COVID-19	Child COVID-19 Parent Report Questionnaire	Essential	Infant, Early Childhood, Middle Childhood, Adolescent

Outcomes

Child COVID-19 vaccination status

Caregivers reported child COVID-19 vaccination status. Parents were asked whether their child received any COVID-19 vaccine, along with the vaccination date (de-identified to the month and year of the dose) and the vaccine product name/manufacturer. For the family-level analysis, the vaccination status of all children within a family was aggregated to create a single family-level variable indicating whether any child in the family had ever received a COVID-19 vaccine.

Child routine/recommended vaccination status

Routine and recommended vaccination data were also collected via caregiver-report. Caregivers were asked whether any immunizations for the child had ever been intentionally delayed or not given due to a decision by the caregiver. Caregivers reported intentional delay or refusal for the following vaccines: Diphtheria, Tetanus, and Pertussis (DTaP); Hepatitis A (Hep A); Hepatitis B (Hep B); Haemophilus Influenzae Type B (Hib); Polio (IPV), Meningococcal; Measles, Mumps and Rubella (MMR); Pneumococcus (PCV); Rotavirus (RV); and Varicella (Chickenpox). At the family level, a caregiver was classified as having delayed or refused a routine/recommended childhood vaccine if they reported intentional delay or refusal for any vaccine for at least one of their children.

Predictors

Caregiver COVID-19 vaccination status

Caregivers were asked to report whether they had received a COVID-19 vaccine, the dates of vaccination, and the name and manufacturer of the vaccine product. Participants were categorized as having received the vaccine as long as they self-reported vaccination, regardless of whether they could recall the exact date of vaccination.

Child and caregiver reasons for COVID-19 vaccine hesitancy

The WHO refers to vaccine hesitancy as the "delay in acceptance or refusal of safe vaccines despite the availability of vaccine services."[44] In the ECHO Cohort, reasons for vaccine hesitancy were assessed in both the children and caregivers. Parents who reported they had not, did not plan to, or were unsure about vaccinating themselves or their children for COVID-19 were asked to select the reasons for hesitancy. They could select from a list of 13 options and were asked to mark all options that applied (Table 4.2). For analysis, these responses were aggregated to reflect all reasons caregivers had ever selected for themselves or their children. If a caregiver selected a reason for hesitancy for one child, it was included at the family level regardless of whether it was selected for all children in the family. If a caregiver selected a reason for hesitancy for themselves on any completed survey, it was included as a reason for caregiver hesitancy.

Table 4.2 Response options for the reason caregiver and child have not received or do not plan to receive the COVID-19 vaccine from ECHO COVID-19 Questionnaire for participating families in the ECHO Cohort, December 2021–August 2023

Response option
I am at low risk and do not need it
I already had COVID-19
I am worried about the side effects
My friends and family do not recommend it
My doctor/healthcare provider does not recommend it
I have read information that suggests the vaccine is unsafe
The vaccine was not well tested in racially and ethnically diverse people
Not enough is known about the long-term effects of the vaccine
I do not trust the doctor/healthcare provider's recommendation to get it
I do not have time to get vaccinated
I do not have transportation to get vaccinated
I might have to pay an out-of-pocket cost to get vaccinated
Other (please specify): _____
The vaccine was not well tested among children*

*Child response option only

Sociodemographic variables

The child's demographics were captured through a required questionnaire administered once after birth. These included the child's age, derived from the date of birth, and sex. Race and ethnicity were also self-reported. Caregivers could select from the following racial categories, including "White," "Black or African American," "American Indian or Alaska Native," "Asian," "Some other race," "Prefer not to answer," or "Don't know." They also reported Hispanic, Latino, or Spanish origin. For family-level analysis, indicator variables were created to identify whether at least one child in the family was in a demographic category. Because of small numbers in some groups by race and ethnicity, for this analysis, race and ethnicity were included as a binary indicator variable defined as "racial or ethnic minority", whether at least one child in

the family was of a race other than non-Hispanic white. Additionally, indicator variables were created to identify whether at least one child in the family was in any of the following age group categories: 0–6 months, 6 months–5 years, 6–11 years, and 12–17 years. These categorizations were chosen to match the differing vaccine approval timelines for children.[108]

Caregiver education and family income were assessed as part of the child socioeconomic status measures. Education was measured as the highest level of education completed by the caregiver and was categorized into four groups: less than high school, high school degree (GED or equivalent), some college without a degree (including associate's degree or trade school), and bachelor's degree or higher. Income was also assessed and categorized according to the percentage of the total combined household income during the last calendar year compared to the federal poverty level (FPL), based on the number of total household members and the number of children under 18 years old. The categories included $\leq$130% of the FPL, <130% to 350% of the FPL, and >350% of the FPL.

To address substantial missingness in caregiver education and income data and maintain a larger sample size for analysis, a combination socioeconomic status (SES) variable was created. This approach reduced the impact of missing data, which would otherwise have limited the analytic sample to 560 families if only those with complete data for both variables were included. The combined SES variable included the following categories: high SES- participants who met criteria for high income (>350%) FPL or high education (bachelor's degree or higher) or both; low SES- participants who responded to either income or education, or both, but did not meet

criteria for high SES; missing/did not respond- participants who were missing data for both income and education variables.

Child medical history

The child's medical history was collected through parent-report. Parents provided information on diagnosis with chronic medical conditions and the age of diagnosis via the medical history questionnaire, a measure collected at least once during each ECHO life stage. For this study, attention was given to conditions identified by the CDC as risk factors for severe COVID-19 illness. These conditions included asthma, anxiety, depression, attention-deficit hyperactivity disorder, cystic fibrosis, trisomy 21, sickle cell disease, heart conditions, and cerebral palsy. For analysis, this variable was defined as a binary indicator of whether any child in the family reported having one or more of these chronic medical conditions.

COVID-19-related variables

COVID-19-related variables were captured through the Child and Caregiver COVID-19 questionnaires. These variables included distress caused by the COVID-19 pandemic and concern about contracting COVID-19 at school or daycare. The distress caused by the pandemic was assessed for both the child and caregiver and was rated on a scale from 1 (no distress) to 10 (extreme distress). A child's concern about getting COVID-19 was also assessed; the potential levels of concern were "Not at all," "A little bit," "Somewhat," "Quite a bit," and "Very much." For the family-level analysis, the maximum pandemic-related distress and concern about contracting COVID-19 score reported by any child in the family was used to represent the household's distress/concern.

Statistical analysis

Descriptive statistics

Descriptive statistics were calculated to summarize the characteristics of the study population, including child and caregiver demographics, socioeconomic status, and health-related variables. The characteristics of the children were stratified by their COVID-19 vaccination status. Frequencies and percentages were computed for categorical variables. Continuous variables were summarized using means and standard deviations. Bivariate analyses were conducted to compare the characteristics between vaccinated and unvaccinated children using the appropriate statistical tests, including Pearson's chi-square or Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables.

Generalized Estimating Equations (GEE) modeling strategy

R version 4.1.3 was used for all analyses.[91] GEE models were implemented using the `gee` package in R for each analytical aim.[109] The outcome variables for each aim were coded as binary variables. As such, we specified a binomial family with a logistic link function. GEE was chosen to account for the correlation by Cohort/Study site, as participants were recruited from diverse ECHO cohorts across the US, using an exchangeable working correlation structure. Robust standard errors were calculated to account for the correlation within Cohort sites, and odds ratios (ORs) with 95% confidence intervals (CIs) were reported for all predictors. Statistical significance was set at an alpha of 0.05.

Analysis for Aim 2A

The outcome variable, child vaccination status, was coded as a binary variable: vaccinated for COVID-19 versus not vaccinated for COVID-19. Predictors in the model included child demographic characteristics (race, ethnicity, age, and mother's age at survey completion), binary presence of medical conditions that place a child at higher risk of severe COVID-19, socioeconomic status (mother's highest level of education and household income relative to the FPL), and COVID-19 pandemic related factors (caregiver vaccination status, child concern about contracting COVID-19 and child and caregiver pandemic related distress).

Analysis for Aim 2B

A series of models were used to examine the association between the reasons for vaccine hesitancy among adult caregivers and the reasons for vaccine hesitancy for their children. Each model used a distinct child hesitancy reason as the outcome variable. The main predictors in each model were the caregivers' reasons for vaccine hesitancy. Reasons for child and caregiver hesitancy are shown in Table 4.2. Only the eight most common reasons were included in each model. Too few participants selected time, transportation, or cost of vaccines as reasons for hesitancy to include them in the model.

An additional model was constructed to examine the reasons for caregiver-reported COVID-19 vaccine hesitancy for their children among caregivers who had received the COVID-19 vaccine themselves. The predictors in this analysis were the specific reasons for child vaccine hesitancy (Table 4.2). The outcome was a discordant vaccination status within the caregiver-children dyad, defined as the caregiver accepting the COVID-19 vaccine for themselves but not for their child.

Sensitivity analysis for Aim 2B

Principal component analysis (PCA) was used as a sensitivity analysis to account for potentially high correlation in the reasons for caregiver vaccine hesitancy. PCA was used to reduce the dimensionality of the caregiver hesitancy variables and identify principal components that explain the most variance in the reasons for hesitancy. The eight most common reasons for caregiver hesitancy were included as binary variables in the PCA. These reasons include those listed in Table 4.2.

Principal components were extracted based on eigenvalues greater than one, and visual inspection of plots of the cumulative variance explained was used to determine the optimal number of components. Retained components were chosen to represent latent patterns or clusters of reasons for caregiver vaccine hesitancy. Each retained component was interpreted based on the loading values of the individual caregiver hesitancy variables. The PCA was conducted using the `prcomp` function in base R, and results were visualized using the `factoextra` package.[110]

The scores for the retained caregiver principal components were then included as predictors in a series of GEE models. The outcome for each model was the reason for child vaccine hesitancy as the outcome variable. This allowed for the assessment of how patterns of caregiver vaccine hesitancy influence specific reasons for child hesitancy.

Analysis for Aim 2C

Refusal or intentional delay of each vaccine was summarized descriptively to provide an overview of vaccine-specific hesitancy patterns. However, due to low frequencies of delay or

refusal reported for individual vaccines, the analytic model aggregated these responses into a single variable indicating whether the caregiver ever intentionally delayed or refused any routine or recommended childhood vaccine for any of their children.

The outcome variable, refusal or intentional delay of at least one routine or recommended childhood vaccine, was coded as a binary variable: self-report of intentional delay or refusal of at least one routine or recommended childhood vaccine unrelated to pandemic-related disruptions in routine medical care compared to no delays or refusals. Predictors in the model included caregiver and child COVID-19 vaccination status, child demographic characteristics (race, ethnicity, age, and mother's age at survey completion), binary presence of medical conditions that place a child at higher risk of severe COVID-19, and socioeconomic status (mother's highest level of education and household income relative to the FPL).

RESULTS

Table 4.3 describes the characteristics of families included in the analyses stratified by COVID-19 vaccination status. Of the 6,395 families, 25% of caregivers had not accepted the COVID-19 vaccine for themselves, and 59% had not accepted the vaccine for any of their children. The number of children in the families included in the analysis ranged from one to four, with a mean of one. Approximately 4% of families had a child between 0 and 6 months old, 39% had a child between 6 months and 5 years old, 52% had a child between 6 and 11 years old, and 9% had a child between 12 and 17 years old. About half of the families were non-Hispanic white (51%). The mean age of mothers at the time of the first completed survey was 37 years (sd: 7).

Approximately 20% of families had at least one child with a high-risk medical condition that could increase the risk of severe COVID-19. Most families were categorized as having a high socioeconomic status (44%), 16% were categorized as having a low socioeconomic status, and 40% did not answer either of the survey questions relevant to socioeconomic status.

In the bivariate analysis, families with children who had received at least one dose of the COVID-19 vaccine (41% of the sample) were more likely to have older mothers (mean age 40 vs. 35 years, $p < 0.001$), more likely to come from households with higher socioeconomic status (64% high SES vs. 30% low SES, $p < 0.001$), and more likely to have a child with a medical condition (27% vs 15%, $p < 0.001$). Additionally, non-Hispanic white families had a higher proportion of vaccination (50% vaccinated) compared to families with at least one child in a racial or ethnic minority (39% vaccinated).

Aim 2A

Table 4.4 presents the results of modeling the odds of COVID-19 vaccine refusal among children in 4,868 families from the ECHO cohort. Children of caregivers with lower levels of SES had significantly higher odds of being unvaccinated. Compared to children whose caregivers had high SES, those with low SES had 2.41 times the odds of vaccine hesitancy (OR: 2.41, 95% CI: 2.01–2.88), and those whose caregivers did not respond to SES survey questions had 1.71 times the odds of being unvaccinated (OR: 1.71, 95% CI: 1.40–2.09).

Children whose parents rated their pandemic-related distress at or above the mean had significantly lower odds of being unvaccinated compared to those with ratings below the mean

(OR: 0.65, 95% CI: 0.55–0.78). Children whose parents reported they were a little bit or somewhat concerned about contracting COVID-19 were also less likely to be unvaccinated (OR: 0.67, 95% CI: 0.57–0.79). This association was also observed among those who were quite a bit or very concerned about contracting COVID-19 (OR: 0.61, 95% CI: 0.45–0.84). Caregiver vaccination status was most strongly associated with child vaccination status. Children of caregivers unvaccinated for COVID-19 were significantly more likely to be unvaccinated themselves (OR: 13.20, 95% CI: 10.30–16.93).

Aim 2B

Among 1,588 unvaccinated caregivers and 3,788 unvaccinated children in the ECHO Cohort, concerns about the long-term effects of the COVID-19 vaccine were common, with 48% of caregivers reporting this reason for themselves and 44% endorsing this reason for their children (Table 4.5). Hesitancy due to worry about side effects was reported by 38% of caregivers and 43% of children. Caregiver cited concerns that the vaccine was not well tested in racial and ethnic minorities more often as a reason for hesitancy for their children (25%) than for themselves (11%). Moreover, 22% of caregivers indicated that they hesitated to vaccinate their children because the vaccine had not been well-tested in children (data not available for caregivers).

Table 4.6 outlines the results of an analysis of 1,422 caregiver-child pairs that did not receive the COVID-19 vaccine. Odds ratios were used to examine the concordance between caregivers' reasons for hesitancy to vaccinate themselves and their hesitancy to vaccinate their children. This analysis showed strong concordance between all caregiver and child reasons for hesitancy. For

instance, caregivers who reported that "not enough is known about the long-term effects of the vaccine had ~17 times the odds of citing this concern for vaccinating their children (OR: 17.17, 95% CI: 12.72–23.17). This concordance was observed for each possible reason for hesitancy to varying degrees. Similarly, concerns about side effects (OR: 14.77, 95% CI: 24.99–59.35), mistrust in healthcare provider recommendations (OR: 38.51, 95% CI: 16.28–35.79), and having read information vaccine was unsafe (OR: 24.14, 95% CI: 16.28–35.79) all showed similarly strong associations. Additionally, caregivers who reported reading information suggesting the vaccine was unsafe demonstrated elevated odds of endorsing multiple reasons for child vaccine hesitancy. Specifically, caregivers who reported vaccine hesitancy for this reason were more likely to report concerns about vaccine side effects in their children (OR: 1.54, 95% CI: 1.03–2.30), that the vaccine was not adequately test in racially and ethnically diverse populations (OR: 1.89, 95% CI: 1.33–2.68), and mistrust of healthcare provider recommendations. Furthermore, prior COVID-19 infection among caregivers was associated with specific child-directed concerns, including low risk perception for children (OR: 2.06, 95% CI: 1.45–2.92) and the belief that the vaccine was not adequately tested in diverse populations (OR: 1.55, 95% CI: 1.14–2.12).

Among the 3,167 caregivers of unvaccinated children, analyses revealed that vaccinated caregivers had significantly lower odds of reporting certain reasons for hesitancy to vaccinate their children (Table 4.7). For example, vaccinated caregivers were less likely to report concerns about long-term effects (OR: 0.67, 95% CI: 0.57–0.80), that the vaccine was unsafe (OR: 0.41, 95% CI: 0.32–0.52), or distrust of the healthcare provider's recommendation (OR: 0.44, 95% CI: 0.34–0.58). In contrast, hesitancy to vaccinate one's children despite accepting the vaccine for

themselves was associated with increased odds of reporting the vaccine was not well tested among children (OR: 3.71, 95% CI: 2.31–5.96).

Aim 2B sensitivity analysis

Principal component analysis (PCA) was conducted as a sensitivity analysis for Aim B to identify underlying patterns in caregiver vaccine hesitancy. Supplemental Figure 4.1 presents a scree plot, which shows that the first two principal components explained 51% of the total variance (PC1= 35%, PC2= 16%), both had eigenvalues greater than 1 (Supplemental Table 4.2), indicating they each explained more variance than an average single item. Given this and visual examination of the scree plot, PC1 and PC2 were retained for further analysis. PC1 was characterized by positive loading values for all components, and in particular, strong loading values related to concerns about vaccine safety, side effects, and long-term effects (Supplemental Table 4.3). This suggests that caregivers scoring high on this component were hesitant due to broad vaccine concerns. PC2 had positive loadings on mistrust in healthcare provider recommendations and concerns about vaccine testing, and negative loading values related to risk perception and prior infection. This suggests that caregivers scoring high on this component were individuals without prior infection who may be at high risk but have vaccine-related skepticism of medical providers and research, but not necessarily long-term effects or side effects of the vaccine.

Two additional components, PC3 and PC4, explained smaller portions of variance (12% and 10%, respectively) but still revealed interesting patterns. PC3 was characterized by strong negative loadings on low-risk perception and mistrust in healthcare provider recommendations,

as well as higher positive loadings related to concerns about long-term effects and side effects. This suggests that this component may capture high perceptions of COVID-19 risk and concerns about side effects. PC4 exhibited high positive loading values for concerns about equitable vaccine testing and low risk perception, as well as negative loading values for concerns about side effects and mistrust in provider recommendations. This pattern suggests a dimension we term as skepticism of testing equity, where individuals may generally trust providers but remain concerned about equity in vaccine research and safety assessments. While PCs 3 and 4 offered additional nuance, only PCs 1 and 2 were included in regression models due to their stronger explanatory power (eigenvalues > 1) and model convergence concerns; inclusion of these additional components led to model instability. The loadings for PC3 and PC4 are presented (Supplemental Table 4.3) as they provide insight into how individual items cluster together and contribute to broader dimensions of vaccine hesitancy.

A series of GEE models included the principal component scores to assess the relationship between caregiver vaccine hesitancy and hesitancy in vaccinating their children (Table 4.8). Broad vaccine concerns (PC1) among caregivers had odds ratios of greater than one for all caregiver-reported reasons for child vaccine hesitancy (ranging from 1.49 to 5.71), indicating that higher levels of broad vaccine concerns among caregivers were associated with higher odds of endorsing any reason for their child's vaccine hesitancy. For the perceived high risk with the medical skepticism component (PC2), the association varied by child vaccine hesitancy reason. Some higher PC2 scores were positively associated with caregiver-reported reasons for child vaccine hesitancy, such as distrust in healthcare provider recommendations (OR: 5.41, 95% CI: 4.01–7.56), belief that the vaccine was unsafe (OR: 1.54, 95% CI: 1.33–1.78), and belief the

vaccine was not well tested in racially and ethnically diverse people (OR: 1.32, 95% CI: 1.18–1.48). Additionally, those who scored high on PC2 had significantly lower odds of reporting some reasons for hesitancy to vaccinate their children including, low risk perception (OR: 0.40, 95% CI: 0.35–0.46), prior COVID-19 infection (OR: 0.48, 95% CI: 0.42–0.55), and concern about side effects (OR: 0.76, 95% CI: 0.68–0.85). The direction of the PC2 effects corresponds with the direction of the loadings on PC2, indicating high similarity between caregiver vaccine hesitancy reasons and caregiver-reported reasons for child vaccine hesitancy, as was found in the primary analysis.

Aim 2C

Table 4.9 illustrates the results of the GEE modeling of the association between child and caregiver COVID-19 vaccine status and intentional delay or refusal of other routine or recommended childhood vaccinations. After adjusting for mother and child age, race/ethnicity, child medical conditions, and socioeconomic status, caregiver and children's COVID-19 vaccination status were significantly associated with intentional delay or refusal of any recommended childhood vaccine. Families with children who were unvaccinated for COVID-19 had 2.76 times (OR: 2.76, 95% CI: 2.22–3.44) the odds of having delayed or refused a recommended childhood vaccine compared to families with children vaccinated for COVID-19. Additionally, children of caregivers who were unvaccinated for COVID-19 had 1.75 times (OR: 1.75, 95% CI: 1.44–2.13) the odds of at least one childhood vaccine being intentionally delayed or refused, regardless of the child's COVID-19 vaccination status.

Table 4.10 further examines the childhood vaccines that were delayed or refused and the associated reasons for delay or refusal among families in the ECHO Cohort. Notably, few caregivers indicated that COVID-19 pandemic-related reasons were responsible for the delay or refusal of these vaccines (10%). A total of 745 families reported delay or refusal of any vaccine. The most common reasons for delay or refusal were safety concerns (49%), the belief that the child was receiving too many vaccines (34%), and personal beliefs (34%).

DISCUSSION

Our findings demonstrate that caregiver COVID-19 vaccination status is one of the most important factors associated with child COVID-19 vaccine acceptance or hesitancy. In the ECHO Cohort, families whose caregivers had not received at least one COVID-19 vaccine dose were significantly more likely to have not vaccinated any of their children than caregivers who had received at least one COVID-19 vaccine dose. This finding is consistent with previous studies, which have demonstrated a strong association between a caregiver's COVID-19 vaccination status and their willingness to vaccinate their child.[111,112] In a 2023 Texas survey of nearly 5,000 parents, those who remained unvaccinated themselves had 28 times the odds of having an unvaccinated child compared to parents who had received a COVID-19 vaccine.[113] Similarly, a national US study found child vaccination intent was significantly greater among parents who had already received the vaccine or intended to receive it.[111] This trend appears worldwide, as a multinational meta-analysis of 44 studies has shown that parent COVID-19 vaccine uptake is a key predictor of intending to vaccinate one's child.[112] Despite this strong association, nuances exist. Some caregivers who choose to get vaccinated themselves still

hesitate to vaccinate their children. Surveys conducted in late 2021 revealed that even many vaccinated parents were more cautious about having their children receive the COVID-19 vaccine, often citing unknown long-term effects or the need for further research in children.[114] This was consistent with our analysis, which indicated that perceptions that the vaccine had not been well tested in children were most strongly associated with hesitancy to vaccinate one's child, even if they had accepted the COVID-19 vaccine for themselves.

We also observed strong concordance between caregiver and child reasons for hesitancy among unvaccinated caregiver-child pairs. Overall, a larger proportion of caregivers identified perceived insufficient vaccine testing as a concern for pediatric vaccine acceptance compared to adult vaccine hesitancy. When examining matched caregiver-child responses, mistrust in healthcare provider vaccine recommendations, exposure to vaccine-critical information (reporting that they have read information suggesting the vaccine is unsafe), and concern about side effects showed strong concordance. The results indicate that caregiver vaccine hesitancy is not only consistent across self- and child-directed concerns but also influenced by prior infection, safety perceptions, and broader skepticism toward vaccine-related information. Certain caregiver concerns, such as exposure to vaccine-critical information, were associated with higher odds of several different reasons for hesitancy to vaccinate their children. This suggests that the consumption of vaccine-critical information may generalize to broader hesitancy beliefs, including concerns about safety, equity in testing, and institutional trust. To our knowledge, no other studies have directly examined the alignment in reasons for hesitancy between caregivers and their children. However, our findings are consistent with previous research, which has identified common adult-reported concerns about pediatric COVID-19 vaccination, including concerns regarding side effects and

safety, perceived vaccine novelty, institutional mistrust, and broader vaccine skepticism.[115,116] Understanding the common overlapping reasons for vaccine hesitancy among caregivers and children is important, as public health or educational campaigns can be designed to target shared beliefs and improve vaccine uptake across all age groups. Notably, reasons for vaccine hesitancy in our study differed between vaccinated and unvaccinated caregivers. Among vaccinated caregivers who chose not to vaccinate their children, concerns centered around the perceived lack of testing and safety data specific to children. This highlights the need for tailored messaging strategies: efforts should focus on providing transparent, age-specific safety data for vaccinated caregivers and addressing perceived gaps in pediatric vaccine research. In contrast, interventions targeting unvaccinated caregivers may need to address broader distrust in vaccines and health institutions.

Finally, our analysis revealed an association between COVID-19 vaccination status and the delay or refusal of other routine childhood immunizations. Although the temporality of this relationship is unclear, these findings suggest a potential spillover effect of COVID-19 vaccine hesitancy that warrants further investigation. Public health experts have been closely monitoring the potential spillover effects of COVID-19 vaccine hesitancy on other routine immunizations. There is evidence that the pandemic era's attitudes and disruptions have, at least in part, negatively impacted routine childhood immunization rates. A 2023 study found that 11–13% of US parents now view routine childhood vaccines as less safe, less effective, or less important than they did before the COVID-19 pandemic.[117] Empiric vaccination data during the pandemic support some of these worries. The CDC reported declines in routine vaccine coverage for children born in 2020–2021 compared to those born in the previous year. By 24 months of age,

children born in 2020–2021 had vaccination rates that were 1.3 to 7.8 percentage points lower across nearly all required immunizations compared to the pre-pandemic cohort.[37] It is unclear how much of this drop is related to pandemic-related disruptions versus changes in vaccine hesitancy and misinformation. However, our study found that few parents reported delayed or refused routine vaccines due to COVID-19-related disruptions. Parents were more likely to report safety concerns, beliefs that their children were receiving too many vaccines, and personal beliefs as reasons for delay or refusal. It is essential to recognize that COVID-19 vaccine hesitancy and its associated effects are heterogeneous. A recent analysis of the National Immunization Survey revealed that, nationally, parental hesitancy rates for routine childhood vaccines have remained relatively stable at around 20% from 2019 to 2022.[118] However, within that overall steady state, there have been divergent trends. Of note, vaccine hesitancy has increased in certain subgroups, including those living below the poverty line. There are likely other subgroup differences in pandemic-related vaccine hesitancy spillover that remain underexplored.

This study has several important limitations. While the ECHO Cohort first deployed COVID-19-related surveys in April 2020, questions assessing reasons for vaccine hesitancy were not introduced until December 2021. As a result, we may have missed early attitudes and hesitancies that could have changed over time, and the changes in survey questions limited the sample available for analysis. Additionally, there were missing data for some key variables due to updates in the survey design, as well as missing demographic, socioeconomic status, and medical history information, including routine vaccine history. Before the implementation of the ECHO-wide protocol, such data had not been collected by all cohorts. These gaps in the data

necessitated the creation of a composite variable for socioeconomic status to preserve sample size, which reduced the number of participants available for generalized estimating equation modeling of routine vaccine refusal and delay, ultimately reducing our sample from 6,395 to 4,341. However, when comparing the characteristics of included and excluded participants in a sample of cohort sites in our study, we found little evidence of selection bias resulting from missing data.

This study also has several key strengths. First, it includes a large and diverse sample of children and their caregivers across the US, providing generalizable data; roughly half of the families included in this analysis identified as a racial or ethnic minority. Second, while other studies have compared the vaccination status of caregivers and their children, this study is unique in that it also assessed the concordance between the reasons for vaccine hesitancy among caregivers and their children. To our knowledge, no previous studies have explored these reasons in such depth, offering new insights into the dynamics of vaccine hesitancy within families.

This study highlights the central role of caregivers' COVID-19 vaccination status in shaping pediatric vaccine decisions and underscores the strong alignment in reasons for hesitancy between caregivers and their children. While most unvaccinated caregivers chose not to vaccinate their children, even some vaccinated caregivers expressed reluctance, primarily due to concerns about insufficient testing and safety in children. This distinction highlights the need for nuanced public health messaging that addresses both generalized vaccine skepticism and concerns specific to children. Furthermore, we found that caregiver exposure to vaccine-critical information was linked to a broad array of other reasons for hesitancy, suggesting that

misinformation may have a compounding effect on vaccine attitudes. Notably, our findings also suggest a potential spillover of COVID-19 vaccine hesitancy into routine childhood immunization decisions, although the direction and mechanisms of this association require further study. By identifying shared concerns among caregiver-child dyads and differences based on caregiver vaccination status, this research provides insights for developing more tailored strategies to improve vaccine uptake across various age groups.

TABLES

Table 4.3 Characteristics of 6,395 families from the ECHO Cohort with available caregiver and child COVID-19 by receipt of the COVID-19 vaccine for any child within a family, December 2021–August 2023

Characteristic	Overall, N = 6,395	Any child in family received at least 1 COVID-19 vaccine, N = 2,607	No children in family have received any COVID-19 vaccine, N = 3,788	p-value
Male children in family				0.8
Yes	3,422 (54%)	1,390 (53%)	2,032 (54%)	
No	2,973 (46%)	1,217 (47%)	1,756 (46%)	
Female children in family				0.038
Yes	3,236 (51%)	1,360 (52%)	1,876 (50%)	
No	3,159 (49%)	1,247 (48%)	1,912 (50%)	
At least one child in family racial or ethnic minority				<0.001
Yes	3,129 (49%)	1,013 (39%)	2,116 (57%)	
No	3,203 (51%)	1,587 (61%)	1,616 (43%)	
Unknown	63	7	56	
Mother age at first completed COVID-19 survey				<0.001
Mean (SD)	37 (7)	40 (6)	35 (6)	
Minimum, Maximum	19,65	20,61	19,65	
Unknown	59	33	26	
At least one child in family age between 0–6 months				<0.001
Yes	245 (3.8%)	7 (0.3%)	238 (6.3%)	
No	6,150 (96%)	2,600 (100%)	3,550 (94%)	
At least one child in family age between 6 months–5 years				<0.001
Yes	2,505 (39%)	491 (19%)	2,014 (53%)	
No	3,890 (61%)	2,116 (81%)	1,774 (47%)	
At least one child in family age between 6–11 years				<0.001
Yes	3,314 (52%)	1,862 (71%)	1,452 (38%)	
No	3,081 (48%)	745 (29%)	2,336 (62%)	

At least one child in family age between 12–17 years				<0.001
Yes	563 (8.8%)	367 (14%)	196 (5.2%)	
No	5,832 (91%)	2,240 (86%)	3,592 (95%)	
Number children in family				<0.001
Mean (SD)	1 (0)	1 (0)	1 (0)	
Minimum, Maximum	1,4	1,4	1,3	
Mother's socioeconomic status (combination education and income)				<0.001
High SES	2,807 (44%)	1,679 (64%)	1,128 (30%)	
Low SES	1,017 (16%)	342 (13%)	675 (18%)	
Missing, No Response	2,571 (40%)	586 (22%)	1,985 (52%)	
Any child in family has medical condition that puts them at high risk from COVID infection				<0.001
Yes	1,284 (20%)	704 (27%)	580 (15%)	
No	5,111 (80%)	1,903 (73%)	3,208 (85%)	
Caregiver received at least one dose of COVID-19 vaccine				<0.001
Yes	4,807 (75%)	2,495 (96%)	2,312 (61%)	
No	1,588 (25%)	112 (4.3%)	1,476 (39%)	
Ever intentionally delayed or refused at least one routine or recommended childhood immunization				<0.001
Yes	745 (17%)	212 (11%)	533 (22%)	
No	3,683 (83%)	1,796 (89%)	1,887 (78%)	
Unknown	1,967	599	1,368	

Table 4.4 Odds ratios and 95% confidence intervals for COVID-19 vaccine hesitancy for 4,868 families with children in the ECHO Cohort who completed surveys between December 2021 and August 2023

	OR (95% CI)
Racial or ethnic minority (ref: Non-Hispanic white)	1.11 (0.95, 1.29)
Child in household age 0–6 months	4.34 (1.40, 13.42)
Child in household age 6 months–5 years	1.58 (1.01, 2.47)
Child in household age 6–11 years	0.49 (0.32, 0.76)
Child in household age 12–17 years	0.45 (0.28, 0.71)
Mother age (continuous, years)	0.92 (0.90, 0.93)
Any medical condition (ref: no medical condition)	0.87 (0.72, 1.04)
Mother's SES (ref: High SES)	
Low SES	2.41 (2.01, 2.88)
No response for SES survey questions	1.71 (1.40, 2.09)
Child rating of pandemic distress at or above mean (ref: below mean)	0.65 (0.55, 0.78)
Child concern about contracting COVID (ref: none)	
A little bit or somewhat concerned	0.67 (0.57, 0.79)
Quite a bit or very concerned	0.61 (0.45, 0.84)
Caregiver unvaccinated for COVID-19 (ref: vaccinated)	13.20 (10.30, 16.93)
Caregiver rating of pandemic distress at or above mean (ref: below mean)	0.92 (0.78, 1.08)

Table 4.5 Comparison of reasons for hesitancy to receive COVID-19 vaccine for 1,588 unvaccinated caregivers and 3,788 unvaccinated children in the ECHO Cohort who completed surveys between December 2021 and August 2023

Reason for hesitancy	Caregivers N= 1,588	Children N= 3,788
Not enough is known about the long-term effects of the vaccine		
Yes	759 (48%)	1,600 (44%)
No	829 (52%)	2,038 (56%)
Unknown		150
I am worried about the side effects		
Yes	606 (38%)	1,566 (43%)
No	982 (62%)	2,072 (57%)
Unknown		150
I am at low risk and do not need it		
Yes	351 (22%)	963 (26%)
No	1,237 (78%)	2,675 (74%)
Unknown		
The vaccine was not well tested in racially and ethnically diverse people		
Yes	182 (11%)	923 (25%)
No	1,406 (89%)	2,715 (75%)
Unknown		150
The vaccine was not well tested among children		
Yes	-	798 (22%)
No	-	2,840 (78%)
Unknown	-	150
I already had COVID-19		
Yes	380 (24%)	589 (16%)
No	1,208 (76%)	3,049 (84%)
Unknown		150
I have read information that suggests the vaccine is unsafe		
Yes	280 (18%)	440 (12%)
No	1,308 (82%)	3,198 (88%)
Unknown		150
I do not trust the doctor/healthcare provider's recommendation to get it		
Yes	203 (13%)	308 (8.5%)
No	1,385 (87%)	3,330 (92%)
Unknown		150

My friends and family do not recommend it		
Yes	111 (7.0%)	236 (6.5%)
No	1,477 (93%)	3,402 (94%)
Unknown		150
My doctor does not recommend it		
Yes	59 (3.7%)	115 (3.2%)
No	1,529 (96%)	3,523 (97%)
Unknown		150
I do not have enough time to get vaccinated		
Yes	28 (1.8%)	23 (0.6%)
No	1,560 (98%)	3,615 (99%)
Unknown		150
I do not have transportation to get vaccinated		
Yes	4 (0.3%)	12 (0.3%)
No	1,584 (100%)	3,626 (100%)
Unknown		150
I might have to pay out-of-pocket costs to get vaccinated		
Yes	7 (0.4%)	8 (0.2%)
No	1,581 (100%)	3,630 (100%)
Unknown		150
Other		
Yes	168 (11%)	329 (9.0%)
No	1,420 (89%)	3,309 (91%)
Unknown		150

Table 4.6 Odds ratios and 95% confidence intervals of the association between caregiver reason for hesitancy to vaccinate dependent children for COVID-19 and caregiver reasons for hesitancy to vaccinate themselves against COVID-19 (N= 1,422)

	Reasons for hesitancy for caregiver to vaccinate their children (OR, 95% CI)						
Reasons for hesitancy for caregiver to accept vaccine for themselves	Not enough is known about the long-term effects of the vaccine	I am worried about the side effects	I am at low risk and do not need it	The vaccine was not well tested in racially and ethnically diverse people	I already had COVID-19	I have read information that suggests the vaccine is unsafe	I do not trust the doctor/healthcare provider's recommendation to get it
Not enough is known about the long-term effects of the vaccine	17.17 (12.72, 23.17)	1.31 (0.98, 1.75)	1.05 (0.74, 1.51)	1.63 (1.22, 2.18)	1.15 (0.77, 1.72)	1.27 (0.83, 1.95)	0.82 (0.50, 1.33)
I am worried about the side effects	1.81 (1.34, 2.44)	14.77 (10.98, 19.88)	1.28 (0.89, 1.84)	1.35 (1.01, 1.82)	1.56 (1.07, 2.28)	1.68 (1.13, 2.49)	1.05 (0.65, 1.69)
I am at low risk and do not need it	1.19 (0.86, 1.66)	1.16 (0.85, 1.60)	31.81 (22.43, 45.12)	0.91 (0.67, 1.25)	1.46 (1.04, 2.04)	1.37 (0.89, 2.09)	1.03 (0.65, 1.63)
The vaccine was not well tested in racially and ethnically diverse people	0.67 (0.42, 1.07)	1.14 (0.73, 1.78)	0.74 (0.46, 1.18)	7.61 (4.94, 11.73)	1.05 (0.64, 1.74)	2.02 (1.25, 3.28)	1.48 (0.82, 2.67)
I already had COVID-19	1.18 (0.83, 1.66)	1.36 (0.97, 1.91)	2.06 (1.45, 2.92)	1.55 (1.14, 2.12)	11.06 (7.70, 15.89)	0.99 (0.65, 1.48)	1.16 (0.71, 1.89)
I have read information that suggests the vaccine is unsafe	1.39 (0.91, 2.11)	1.54 (1.03, 2.30)	1.23 (0.78, 1.91)	1.89 (1.33, 2.68)	0.93 (0.61, 1.44)	24.14 (16.28, 35.79)	2.58 (1.58, 4.23)
I do not trust the doctor/healthcare provider's recommendation to get it	0.91 (0.58, 1.43)	0.75 (0.52, 1.08)	0.77 (0.48, 1.23)	1.49 (1.00, 2.21)	0.91 (0.58, 1.45)	1.84 (1.19, 2.85)	38.51 (24.99, 59.35)

Table 4.7 Odds ratios and 95% confidence intervals for the association between parental COVID-19 vaccine acceptance and child COVID-19 vaccine hesitancy and reason for hesitancy to vaccinate dependent children for COVID-19 among 3,613 caregiver-children pairs in the ECHO Cohort.

Reasons for hesitancy for caregiver to vaccinate their children	OR (95% CI)
Not enough is known about the long-term effects of the vaccine	0.67 (0.57, 0.80)
Worried about the side effects	1.16 (0.98, 1.36)
Low risk and do not need it	1.04 (0.88, 1.23)
The vaccine was not well tested in racially and ethnically diverse people	0.32 (0.20, 0.51)
The vaccine was not well tested among children	3.71 (2.31, 5.96)
Already had COVID-19	1.26 (1.03, 1.55)
I have read information that suggests the vaccine is unsafe	0.41 (0.32, 0.52)
I do not trust the doctor/healthcare provider's recommendation to get it	0.44 (0.34, 0.58)

Table 4.8 Odds ratios and 95% confidence intervals of the association between caregiver reason for hesitancy to vaccinate dependent children for COVID-19 and caregiver reasons for hesitancy to vaccinate themselves against COVID-19 from PCA (N= 1,422)

	Reasons for hesitancy for caregiver to vaccinate their children (OR, 95% CI)							
Reasons for hesitancy for caregiver to accept vaccine for themselves from PCA	Not enough is known about the long-term effects of the vaccine	I am worried about the side effects	I am at low risk and do not need it	The vaccine was not well tested in racially and ethnically diverse people	I already had COVID-19	I have read information that suggests the vaccine is unsafe	I do not trust the doctor/healthcare provider's recommendation to get it	The vaccine was not well tested among children
PC1	2.30 (2.06, 2.57)	2.14 (1.95, 2.36)	1.68 (1.53, 1.83)	1.83 (1.69, 1.99)	1.66 (1.49, 1.84)	5.71 (4.69, 6.95)	2.18 (1.92, 2.47)	1.49 (1.37, 1.61)
PC2	0.90 (0.80, 1.02)	0.76 (0.68, 0.85)	0.40 (0.35, 0.46)	1.32 (1.18, 1.48)	0.48 (0.42, 0.55)	1.54 (1.33, 1.78)	5.51 (4.01, 7.56)	1.01 (0.91, 1.12)

Table 4.9 Odds ratios and 95% confidence intervals for delay or refusal of recommended childhood vaccines delay or refusal for 4,341 children in the ECHO Cohort

Characteristic	OR (95% CI)
Racial or ethnic minority (ref: Non-Hispanic white)	0.79 (0.66, 0.95)
Child in household age 0–6 months	1.21 (0.63, 2.33)
Child in household age 6 months–5 years	1.07 (0.70, 1.63)
Child in household age 6–11 years	1.39 (0.94, 2.06)
Child in household age 12–17 years	2.30 (1.57, 3.36)
Mother age (continuous, years)	1.01 (0.99, 1.02)
Any medical condition (ref: no medical condition)	1.31 (1.08, 1.58)
Mother's SES (ref: High SES)	
Low SES	0.76 (0.61, 0.94)
No response for SES survey questions	0.73 (0.48, 1.09)
Children unvaccinated for COVID-19 (ref: vaccinated)	2.76 (2.22, 3.44)
Caregiver unvaccinated for COVID-19 (ref: vaccinated)	1.75 (1.44, 2.13)

Table 4.10 ECHO Cohort families reporting refusal or intentional delay of vaccination by vaccine and associated reason for hesitancy, 2021–2023 (N=745)

		Reason for refusal (N, %)									
Vaccine	**Number of families who delayed or refused**	**Religious beliefs**	**Personal beliefs**	**Safety concerns**	**Need more information about vaccines**	**Child receiving too many vaccines**	**Child has already had the disease/ condition**	**Other**	**COVID-19 resulted in delay**	**Child's doctor not offering visits due to COVID outbreak**	**Not comfortable going to provider out of concern for child getting COVID-19**
Any vaccine	745	80 (11%)	253 (34%)	367 (49%)	183 (25%)	256 (34%)	52 (7%)	107 (14%)	74 (10%)	14 (2%)	26 (3%)
DTaP	90	15 (17%)	39 (43%)	51 (57%)	22 (24%)	29 (32%)	9 (10%)	12 (13%)	14 (16%)	5 (6%)	6 (7%)
Hep A	92	13 (14%)	43 (47%)	53 (58%)	21 (23%)	36 (39%)	10 (11%)	10 (11%)	15 (16%)	5 (5%)	6 (7%)
Hep B	91	13 (14%)	41 (45%)	49 (54%)	18 (20%)	36 (40%)	10 (11%)	9 (10%)	16 (18%)	5 (5%)	6 (7%)
Hib	79	11 (14%)	37 (47%)	44 (56%)	15 (19%)	23 (29%)	9 (11%)	10 (13%)	11 (14%)	5 (6%)	4 (5%)
Meningococcal	83	10 (14%)	32 (46%)	40 (57%)	14 (20%)	20 (29%)	6 (9%)	8 (11%)	11 (16%)	4 (6%)	5 (7%)
MMR	70	16 (17%)	44 (47%)	58 (62%)	24 (26%)	34 (37%)	11 (12%)	11 (12%)	16 (17%)	5 (5%)	6 (6%)
PCV	93	10 (7%)	68 (45%)	97 (64%)	65 (43%)	15 (10%)	27 (18%)	17 (11%)	25 (16%)	4 (3%)	6 (4%)
Polio	65	11 (17%)	27 (42%)	36 (55%)	12 (18%)	17 (26%)	6 (9%)	10 (15%)	12 (18%)	4 (6%)	4 (6%)
Rotavirus	84	12 (14%)	40 (48%)	52 (62%)	20 (24%)	29 (35%)	11 (13%)	10 (12%)	12 (14%)	4 (5%)	4 (5%)
TDaP	86	5 (10%)	22 (46%)	30 (63%)	14 (29%)	18 (38%)	7 (15%)	7 (15%)	7 (15%)	1 (2%)	3 (6%)
Varicella	48	12 (14%)	36 (42%)	48 (56%)	16 (19%)	31 (36%)	10 (12%)	11 (13%)	10 (12%)	3 (3%)	4 (5%)

*Percents add up to more than 100 because some families delayed or refused more than one vaccine and selected more than one reason for refusal

CHAPTER 5. MANUSCRIPT 3

Manuscript 3: Childhood vaccination rates and COVID-19 vaccination coverage by county voting patterns

BACKGROUND AND AIMS

The COVID-19 pandemic represents one of the most significant public health crises in recent history, fundamentally altering healthcare delivery, access, and trust in medical information.[119–121] Public health recommendations evolved rapidly as scientific understanding of COVID-19 changed. This environment of evolving information proved challenging for many in the public, potentially undermining trust in public health authorities. During the early phases of the pandemic, restrictions on in-person interactions and limited healthcare access created substantial barriers to routine preventative care services, including routine childhood immunizations.[52,53] There is evidence that rates of some recommended childhood vaccinations declined due to these disruptions by as much as seven percentage points.[37] Although some studies suggest a partial rebound in vaccination rates following the initial pandemic disruptions, it remains unclear whether coverage has fully returned to pre-pandemic levels or compensated for the initial deficit.[58,122] This may be leaving lingering gaps in childhood protection against vaccine-preventable diseases.

These disruptions to routine care underscore the importance of reinforcing the value of childhood vaccination more broadly. Childhood vaccination remains one of the most effective interventions for reducing childhood morbidity and mortality, dramatically lowering the global burden of once-common diseases. In the US alone, the CDC estimates that between 1994 and 2023, routine childhood vaccinations have prevented 508 million cases of illness, 32 million hospitalizations,

and more than 1 million deaths.[6] The concept of herd immunity is integral to this prevention. Herd immunity refers to the indirect protection from an infectious disease that occurs when a significant proportion of a population becomes immune to infection through vaccination or prior infections.[7] This concept is crucial because it reduces the likelihood of disease transmission within a community, particularly protecting individuals who are not immune. Herd immunity thresholds depend on the infectious agent and the vaccine's effectiveness, and achieving these thresholds can prevent disease outbreaks. High vaccine coverage must be sustained across communities to maintain herd immunity and prevent outbreaks. Even minor declines in vaccination rates can create clusters of susceptibility, leaving populations vulnerable to preventable illness. For instance, the herd immunity thresholds for measles, pertussis, and mumps are between 90% and 95%, and outbreaks may occur when vaccination rates drop below these thresholds.[8,9]

A recent simulation study suggests that even maintaining current vaccination rates may be inadequate to prevent a resurgence of measles.[38] Without improvements in vaccination coverage, the US could experience hundreds of thousands of measles cases over the next 25 years, with a high likelihood of measles re-establishing endemicity within two decades.[38] Further declines in vaccination could exacerbate this burden, potentially resulting in millions of preventable hospitalizations and hundreds of thousands of preventable deaths. The study additionally suggests that other rare diseases, such as rubella and polio, may become endemic under scenarios of substantial vaccination decline. Specifically, rubella could reach endemic levels if vaccination coverage decreases by 35%, and polio has an estimated 50% likelihood of becoming endemic should vaccination coverage drop by 40%.[38]

These projections underscore the serious consequences of declining vaccine coverage, consequences that may be exacerbated by the spillover of COVID-19 vaccine skepticism that emerged during the pandemic.[59,60] Before the pandemic, vaccine hesitancy was recognized as a complex social phenomenon influenced by various factors, including confidence, constraints, complacency, risk calculation, and collective responsibility.[46] The pandemic and the COVID-19 vaccine rollout have further complicated our understanding of vaccine acceptance and hesitancy, adding another layer of nuance in the form of highly politicized public discourse. Misinformation and disinformation circulated widely during the pandemic, and resistance to public health recommendations often mapped onto broader political divides.[123–125] While it is well-documented that acceptance of COVID-19 vaccines exhibited strong associations with political affiliation[61,124,126], it remains uncertain whether this polarization has extended to routine childhood vaccinations. An additional challenge is the growing distrust of governmental health agencies. Kaiser Family Foundation polling data from January of 2025 reflect this erosion in trust.[127,128] In 2025, only 61% of United States (US) adults reported they trust the Centers for Disease Control and Prevention (CDC) "a great deal" or "a fair amount," down from 66% in 2023 and 67% in 2020. This decline is primarily driven by a nine-percentage-point decline in trust among Republicans, from 48% to 39%, between 2023 and 2025, compared to a two-percentage-point decline among Democrats, from 87% to 85%.[128] Similar declines are seen for other health agencies. This is important as other research has shown political trust plays an important role in individuals' views toward the government's handling of vaccine safety and, ultimately, whether they choose to accept vaccines.[129]

These trends raise concern that politicized mistrust and misinformation about the COVID-19 vaccine may not remain isolated but instead influence broader vaccine attitudes. A recent qualitative study, based on interviews of US pediatricians in two states, provided evidence of such a spillover effect.[130] Clinicians reported that public scrutiny of the COVID-19 vaccines, including media coverage and misinformation, broadly influenced parental trust in vaccines, either amplifying hesitancy or bolstering trust depending on pre-existing attitudes.[130] Many parents generalized their concerns about the risks of the COVID-19 vaccine to other vaccines. This furthers the concern that negative beliefs about COVID-19 vaccines could be generalized to childhood vaccines, particularly those with a history of controversy.

Certain vaccines, such as Measles, Mumps, and Rubella (MMR), and Varicella (chickenpox), may be disproportionately affected by declining public trust. MMR has long been targeted by misinformation campaigns, particularly related to the debunked claim linking it to autism, making it especially vulnerable to renewed skepticism.[131] Varicella may be similarly impacted, as common reasons for pediatric COVID-19 vaccine hesitancy, such as the belief the illness is mild, can be more easily extrapolated to chickenpox, a disease many adults remember having in their youth. Given these existing narratives, heightened vaccine distrust may have more readily spilled over to these specific vaccines, further reducing uptake compared to others without this history or perception.

Despite the urgency of understanding these issues, significant gaps remain in our understanding of the sustained impact of the COVID-19 pandemic on routine childhood vaccination rates and the interplay between political affiliation and acceptance of the COVID-19 vaccine. These gaps

limit our ability to design targeted interventions to restore and maintain high levels of pediatric vaccine coverage. Minnesota provides an ideal setting for investigating these questions. Although the state is perceived as liberal-leaning, and a Republican presidential candidate has not won in Minnesota since 1972, there is notable political polarization across its 87 counties.[132] Additionally, despite generally high overall health rankings, Minnesota faces significant health disparities, including those related to vaccine uptake.[79,133] Finally, Minnesota collects and disseminates county-level childhood vaccination rates, which are more granular than those publicly available from national datasets or many state databases.

To address gaps in our understanding of how the pandemic and political-related changes may affect childhood vaccination rates, we examined rates of routine vaccination in children aged 24 to 35 months in Minnesota before and after onset of the COVID-19 pandemic, assessing the extent to which these changes were associated with local levels of COVID-19 vaccine coverage and political composition, through the following aims:

Aim 3A: Investigate whether rates of routine childhood vaccinations of children aged 24 to 35 months old in Minnesota changed after the onset of the COVID-19 pandemic, after adjusting for county-level socioeconomic status.

> **Hypothesis 3A**: I hypothesized that rates of routine childhood vaccinations in Minnesota significantly decreased after the onset of the COVID-19 pandemic in 2020 compared to pre-pandemic rates (2015–2019). Additionally, I hypothesized that rates of decline were more pronounced for vaccines with a history of vaccine skepticism (e.g., MMR) or where pediatric COVID-19 hesitancy may be more readily applicable (e.g., Varicella). I

hypothesized that lower levels of county-level socioeconomic status, as measured by the CDC's Social Vulnerability Index, would be associated with declines in vaccination.

Aim 3B: Assess whether Minnesota county-level changes in childhood vaccination rates of children aged 24 to 35 months after the onset of the pandemic differ by COVID-19 vaccine primary series non-completion rates and whether this association is modified by county political composition after adjusting for county-level socioeconomic status.

Hypothesis 3B: I hypothesized that counties in Minnesota with higher COVID-19 primary vaccine series non-completion rates and higher proportions of Republican voters have lower overall routine childhood vaccination rates following the availability of COVID-19 vaccines (2021–2023). Furthermore, I hypothesized that the association between COVID-19 primary series vaccine non-completion and childhood vaccination rates is modified by county political composition, such that counties with both high COVID-19 vaccine non-completion and strong Republican majorities would have low childhood vaccination rates after adjusting for county-level socioeconomic status.

METHODS

Study design

This study employed a retrospective analysis utilizing four publicly available data sources to investigate changes in childhood vaccination rates in Minnesota and their associations with county-level COVID-19 vaccine acceptance and political composition. The data sources included: (1) County-level COVID-19 vaccine acceptance data from the CDC[5], (2) county-level returns for US presidential elections from the MIT Election Data and Science Lab[69], (3) county-

level social vulnerability indicators from the CDC[68], (4) Childhood immunization data from the Minnesota Public Health Data Access Portal.[67]

Measures

Predictors

County-level COVID-19 vaccine uptake

Data on COVID-19 vaccine coverage at the county level were obtained from the CDC.[5] The CDC dataset provided cumulative counts and proportions of county populations who received at least one dose of a COVID-19 vaccine, completed the primary vaccine series, and received booster doses. The data spanned from December 13, 2020, to May 12, 2023. The cumulative proportion of the county population that had not completed the COVID-19 primary vaccine series by the end of each calendar year was used for analysis. For 2023, the proportion vaccinated by May was used, as this was when the CDC discontinued reporting COVID-19 vaccination rates.

County-level political composition

County-level returns for US presidential elections served as a proxy for a county's political composition. This data was sourced from the MIT Election Data and Science Lab.[69] This dataset included county-level returns for US presidential elections from 2012 to 2020. For this analysis, data from the 2020 presidential election were utilized to represent county political composition during the study period for Aim 3B. The total number of votes for each presidential candidate was collected, and the proportion of votes for the Democratic and Republican candidates was determined. To categorize counties by political leaning, the national average Republican vote

share across all counties in the 2020 election was calculated at 65%. Although this figure exceeds the overall national proportion of votes for the Republican candidate in 2020 (46.9%), it reflects the unweighted average of county-level proportions rather than the population-weighted national average. It is important to note that this average is influenced by the significant variation in county population sizes. As a result, the average of county-level proportions does not equate to a population-weighted national average. This 65% threshold was employed to define counties with a strong majority Republican vote share.

Social vulnerability index

The CDC Social Vulnerability Index (SVI) was used to provide measures of the relative social vulnerability of US communities.[68] It assigns rankings from 0 to 1 based on 16 social factors grouped into four themes: socioeconomic status (poverty levels, unemployment rates, housing cost, and education levels), household characteristics (percentage of elderly and children, individuals with disabilities, single-parent household and those with limited English proficiency), racial and ethnic minority status (racial and ethnic minority representation), and housing type and transportation (evaluates factors such as multi-unit housing, crowding, mobile homes, lack of vehicle access and group quarters). Scores closer to 1 indicate greater social vulnerability. SVI is updated biannually and was available for 2014, 2016, 2018, 2020, and 2022. For analysis, data from each release year were used for that year and carried forward to represent the nearest subsequent year. For example, the 2022 SVI values were used for 2022 and 2023. In preliminary bivariate analysis (not shown), only the socioeconomic status theme was associated with the outcome and other predictors. Therefore, only the socioeconomic theme was retained in the final models to promote model parsimony, and it was included as a continuous variable. Although SVI

data were available for 2014, changes in the measurement methodology in 2016 made the 2014 data incompatible with later years. Therefore, we used the 2016 SVI as a proxy for 2015.

Outcome

Childhood immunization data were obtained from the Minnesota Public Health Data Access portal.[67] This dataset is a county-level aggregated dataset summarizing Minnesota Immunization Information Connection data.[70] This dataset provides annual county-level vaccination rates for select vaccinations administered to children in Minnesota. For children in our age group of interest, aged 24 to 35 months old, data were available from 2015 to 2023. We chose to focus on the routine seven vaccine series, including: Diphtheria, Tetanus, and Pertussis (DTaP); Hepatitis B (Hep B); Haemophilus influenzae type b (Hib); Measles, Mumps, and Rubella (MMR); Pneumococcal Conjugate Vaccine (PCV); Polio; and Varicella. Annual vaccination rates for each vaccine were calculated as the proportion of the eligible population in each county that received the vaccine yearly.

Data integration and variable construction

All datasets were merged using county identifiers (county FIPS code) to create a comprehensive dataset for analysis.

Descriptive analysis

Descriptive maps illustrating political composition, county-level COVID-19 vaccine coverage, and the SVI socioeconomic status metric were developed to visualize the geographic distribution of covariates. Additionally, maps of vaccination rates across Minnesota counties for each childhood vaccine were created to contextualize the analysis. These maps depict temporal and

spatial variations in vaccination coverage before and after the onset of the pandemic. Maps depicting the county-level total population of Minnesota and the population aged 24-25 months were also generated.

County-level characteristics, including the average county-level political composition, COVID-19 vaccination coverage, and rates of coverage with the seven-vaccine childhood series, were also summarized in tabular format. Childhood vaccination coverage increased steadily from 2015 through 2019, and began to decline in 2021, with rates remaining lower through 2023. In addition, average county-level childhood vaccination coverage was plotted annually from 2015 to 2023, stratified by political composition, defined as counties with Republican vote share above or below 65% in the most recent preceding US presidential election, to visually assess differences in temporal trends.

Statistical analyses

To investigate changes in childhood vaccination rates in Minnesota following the COVID-19 pandemic, we conducted a retrospective spatiotemporal analysis using hierarchical Bayesian spatial modeling implemented through Integrated Nested Laplace Approximation (INLA), using the package `R-INLA`.[134] To account for spatial autocorrelation between counties, an adjacency matrix was constructed using county shapefiles and queen contiguity (i.e., counties were considered neighbors if they shared at least one point). This spatial structure was implemented using the `spdep` package in R, and the resulting neighbor list was converted into a binary adjacency matrix, which was then converted into a sparse matrix suitable for INLA modeling. This graph was incorporated as a spatial random effect using a Conditional Autoregression

(CAR) prior. All analyses were adjusted for county-level measures of socioeconomic status. Given the continuous distribution of county-level vaccination rates, all models assumed a Gaussian family for the outcome. Fixed effects were specified with uninformative priors, a mean at the null (zero), and a large variance (precision of $1x10^{-6}$ or variance of 1,000,000).

Aim 3A: Post-pandemic changes in vaccination rates

To assess whether routine childhood vaccination rates changed after the onset of the COVID-19 pandemic, we modeled annual county-level vaccination rates as the outcome for each vaccine among the age group of children aged 24 to 35 months. The year was included as a categorical variable, with 2019 as the reference year to facilitate comparison with the pre-pandemic period (2015–2018) and the post-pandemic period (2020–2023). The primary focus was to estimate the difference in annual vaccination rates relative to 2019, the last full year before the pandemic began. The output of this analysis consisted of percent differences in county-level vaccination rates relative to 2019, along with corresponding 95% credible intervals.

Aim 3B: Association between changes in post-pandemic childhood vaccination rates and COVID-19 vaccination rates, and political composition

For our second aim, the outcomes in the spatial models were county-level childhood vaccination rates among children 24 to 35 months from 2021 to 2023. The predictors included county-level COVID-19 vaccine hesitancy, as proxied by primary series non-completion rate, county political composition, and the interaction between political composition and COVID-19 vaccination rates. To account for repeated annual measurements within counties during the study period, a second unstructured random effect was included using an independent and identically distributed normal

prior. This effect captured residual within-county correlation over time that was not explained by fixed effects. This analysis produced beta estimates and 95% credible intervals, presenting the differences in mean childhood vaccination rates associated with the relevant predictors.

RESULTS

Descriptive analysis

Figures 5.1–5.4 present four map panels illustrating key spatial and temporal trends across Minnesota relevant to childhood vaccination. Based on presidential election results, Figure 5.1 displays county-level political composition from 2012 to 2024. While Minnesota counties have remained consistent in their partisan alignment, the state as a whole has trended more Republican in recent elections, particularly in rural areas. In contrast, Democratic support has remained concentrated in the urban core counties, especially in and around the Twin Cities. Figure 5.2 shows the percentage of county populations completing the COVID-19 primary vaccine series from 2021 to 2023, revealing persistently lower uptake in many of the same Republican-leaning and rural counties. Figure 5.3 presents county-level maps of the CDC Social Vulnerability Index socioeconomic status measure from 2016 to 2022. Overall, social vulnerability remained relatively stable across the study period. Figure 5.4 displays county-level trends in vaccination coverage for each vaccine in the routine childhood series from 2015 to 2023 in Minnesota. Across most vaccines, coverage was relatively high and increasing until 2020. However, a noticeable decline began in 2021 and persisted through 2023. There were pronounced geographic disparities, with several counties in southwestern, central, and northern Minnesota consistently

demonstrating lower coverage. The total population and population aged 24–35 months by county in Minnesota are presented in Supplemental Figures 5.1 and 5.2.

Table 5.1 summarizes the population covered in this analysis, along with a summary of county-level characteristics, including political composition, COVID-19 vaccination coverage, and rates of childhood seven-vaccine series coverage. Childhood vaccination coverage increased steadily from 2015 through 2019, and began to decline in 2021, with rates remaining lower through 2023. Supplemental Figure 5.3 illustrates that, across most vaccines, counties with a strong majority Republican vote share consistently had lower average childhood vaccination rates than counties without a strong majority Republican vote share.

Aim 3A: Post-pandemic changes in vaccination rates

Across all routine childhood vaccines analyzed, county-level vaccination rates among children aged 24 to 35 months showed a general upward trend from 2015 to 2019, followed by a decline from 2021 to 2023, after adjusting for county-level socioeconomic status (Table 5.2). For all routine childhood vaccines, rates were significantly lower in 2015 and 2016 compared to 2019. For example, DTaP coverage was 3.55 percentage points lower in 2015 ($\hat{\beta}$: -3.55, 95% CI: -5.04 to -2.06) and 3.18 points lower in 2016 ($\hat{\beta}$: -3.18, 95% CI: -4.67 to -1.69) compared to 2019. Similar early-period deficits were observed for all vaccines. Gradual increases in coverage were observed from 2016 to 2018, with several vaccines reaching peak levels in 2018. Notably, the Hib vaccination rate increased significantly between 2017 and 2018 ($\hat{\beta}$: 5.89, 95% CI: 4.06 to 7.72). In 2020, vaccination rates remained relatively stable or slightly increased for many

vaccines compared to 2019. Two examples are DTaP ($\hat{\beta}$: 0.84, 95% CI: -0.65 to 2.33) and MMR ($\hat{\beta}$: 0.60, 95% CI: -0.55 to 1.74), although these were not statistically significant.

However, by 2021, coverage began to decline sharply across most vaccines. DTaP coverage dropped by 3.91% ($\hat{\beta}$: -3.91, 95% CI: -5.40 to -2.42) and remained similarly low in 2022 ($\hat{\beta}$: -4.00, 95% CI: -5.49 to -2.51) and 2023 ($\hat{\beta}$: -4.85, 95% CI: -6.34 to -3.36). Consistent declines were also observed for Hep B, Hib, MMR, PCV, Polio, and Varicella (Table 5.2). These reductions remained statistically significant through 2023. The Varicella and MMR vaccines experienced some of the largest and most persistent declines in coverage. For Varicella, vaccination rates were 5.12% lower in 2021 compared to 2019 ($\hat{\beta}$: 5.12, 95% CI: -6.27 to -3.96) and remained reduced in 2022 ($\hat{\beta}$: -4.49, 95% CI: -5.64 to -3.34) and 2023 ($\hat{\beta}$: -6.55, 95% CI: -7.70 to -5.40). Similarly, MMR coverage declined by 3.78% in 2021 ($\hat{\beta}$: 3.78, 95% CI: -4.92, to -2.63), 3.17% in 2022 ($\hat{\beta}$: 3.17, 95% CI: -4.32 to -2.03), and 5.11% in 2023 ($\hat{\beta}$: 5.11, 95% CI: -6.26 to -3.97) compared to 2019.

High SVI scores (indicating lower socioeconomic status) were associated with lower vaccination rates, with rates ranging from 4.61% lower ($\hat{\beta}$: -4.61, 95% CI: -7.39 to -1.81) for DTaP to 2% lower for Hep B ($\hat{\beta}$: -2.00, 95% CI: -4.32 to 0.32).

Aim 3B: Association between changes in post-pandemic childhood vaccination rates, COVID-19 vaccination rates, and political composition

In models restricted to the post-COVID-19 vaccine availability period (2021–2023), significant interactions were observed between county-level political composition (Republican vote share >

65%) and COVID-19 vaccination rates for five vaccines (Hep B, Hib, MMR, Polio, and Varicella). These interactions suggest that county political leanings influence the relationship between changes in childhood vaccination rates and COVID-19 vaccination coverage (Table 5.3, Figure 5.5).

The statistically significant negative interaction effects indicate that in counties with a strong majority Republican vote share, decreases in COVID-19 vaccination coverage were associated with greater declines in routine childhood vaccination rates compared to counties without a strong majority Republican vote share. This pattern was observed across several vaccines, including Hep B ($\hat{\beta}$: -0.30, 95% CI: -0.57 to -0.02), Hib ($\hat{\beta}$:-0.51, 95% CI: -0.75 to -0.28), MMR ($\hat{\beta}$: -0.34, 95% CI: -0.61 to-0.06), Polio ($\hat{\beta}$: -0.28, 95% CI: -0.54 to-0.03), and Varicella ($\hat{\beta}$: -0.31, 95% CI: -0.58 to -0.03). For DTaP ($\hat{\beta}$: -0.26, 95% CI: -0.59 to 0.09) and PCV ($\hat{\beta}$: -0.25, 95% CI: -0.53 to 0.03) the interaction effects were similar in magnitude and direction to the statistically significant interactions, indicating that decreasing COVID-19 primary series coverage was associated with greater declines in childhood vaccination coverage in strongly Republican counties. However, these effects did not reach the threshold for statistical significance.

For example, for the MMR vaccine, each one percentage-point decrease in COVID-19 coverage was associated with an additional 0.34% reduction in MMR vaccination coverage in strong Republican-majority counties compared to non-strong Republican-majority counties. Thus, if COVID-19 vaccination coverage decreased by 10%, counties with a strong Republican majority

would experience an estimated additional 3.4% reduction in MMR coverage compared to counties without a strong Republican majority.

Figure 5.5 illustrates these interaction effects. In the figure, we plot estimated rates of childhood vaccination against COVID-19 vaccine acceptance, stratified by whether counties had a high Republican vote share (> 65% in the 2020 US presidential election). The lines represent the posterior mean slopes of the association between COVID-19 vaccine uptake and childhood vaccination rates within each political group. In Democrat-leaning counties, the slope is approximately flat, indicating that increases in COVID-19 vaccination rates were not associated with changes in routine childhood vaccination rates. In contrast, in Republican-leaning counties, we observe a negative slope. Lower COVID-19 vaccine coverage was associated with lower rates of routine vaccination.

DISCUSSION

Routine childhood vaccination rates for children aged 24–35 months in Minnesota declined significantly in 2021 compared to pre-pandemic levels in 2019. Alarmingly, these declines have persisted through 2022 and 2023, with rates for many vaccines worsening over time. This pattern has also been observed across the United States, where kindergarten vaccination coverage with state-required vaccines declined from 95% in 2019–2020 to 93% in 2022–2023[136], and birth cohorts from 2020 and 2021 have lower coverage with nearly all vaccines compared to children born pre-pandemic.[37] These sustained drops in vaccination raise serious concerns about long-term vaccine coverage and herd immunity for preventable childhood diseases. Our analysis indicated a decline of approximately 3 to 5% in childhood vaccination rates across Minnesota

following the pandemic, which would represent 1,994 to 3,323 fewer children being vaccinated annually compared to pre-pandemic levels.

While much of the focus has been on pandemic-related declines, it is also important to highlight notable improvements observed before 2020. For instance, Hib vaccination coverage increased by almost six percentage points in Minnesota between 2017 and 2018. One possible explanation for this rise is the introduction of Vaxelis®, a hexavalent combination vaccine (DTaP-IPV-Hib-Hep B) approved in the US in 2018.[137] Combination vaccines, such as Vaxelis®, can improve vaccination rates by reducing the number of injections required.[138]

Our findings indicate that county-level political composition modifies the relationship between COVID-19 vaccination coverage and routine childhood vaccination rates. In counties with a strong Republican majority, decreases in COVID-19 vaccination coverage were associated with larger declines in routine childhood vaccination rates. While our adjusted models did not support a consistent main effect of political composition, descriptive patterns suggested that average childhood vaccination coverage was lower in counties with a Republican majority. These findings align with broader national trends in politicized attitudes toward vaccines. Recent Gallup polling showed a sharp decline in the share of Americans considering childhood vaccination "extremely important," falling from 58% in 2019 to 40% in 2023.[139] Notably, this decline was primarily driven by Republicans and Republican-leaning independents. Only 26% of this group now say childhood vaccination is "extremely important," down from 52% in 2019. Further supporting this trend are recently analyzed adverse event reports submitted to the Vaccine Adverse Event Reporting System, which showed a sharp spike in MMR side effect

reports following the COVID-19 vaccine rollout, disproportionately concentrated in Republican-leaning states.[59] Taken together, these data suggest that pandemic-era skepticism toward COVID-19 vaccination may have spilled over into public perceptions of childhood vaccines.

These findings that suggest a politicized spillover effect largely align with a recent multi-state analysis using local-level vaccination data from 11 states among kindergarten-aged children.[140] The study found that COVID-19 vaccine hesitancy, as measured by non-vaccination rates, was modestly associated with declines in MMR and DTaP vaccination rates between 2019 and 2022 in counties with a strong Republican lean.[140] The authors estimated that a 1% decrease in COVID-19 vaccination was associated with a 0.06% decrease in MMR vaccination and a 0.1% decrease in DTaP vaccination in these counties.[140] While their estimates did not meet conventional thresholds for statistical significance, the direction of the associations was consistent with our findings. A few factors may explain why our study identified a stronger and statistically significant association. First, we examined the complete routine childhood vaccine series rather than only MMR and DTaP, allowing for a broader assessment of vaccine behavior. Second, our focus on children aged 24–35 months may have captured an age group more vulnerable to parental shifts in vaccine confidence during the COVID-19 pandemic. In the US, children receive most of their routine immunizations before their second birthday.[34] Furthermore, pediatric COVID-19 vaccine hesitancy has been notably higher among parents of younger children, as reflected in some of the lowest uptake rates for the COVID-19 vaccine.[5,27] This heightened skepticism during a key period for routine immunization may have led to the refusal or delay of routine vaccines.

Among the vaccines we assessed, declines in coverage were particularly pronounced for MMR and Varicella. These vaccines also demonstrated strong negative associations with a high Republican vote share and strong interactions between Republican vote share and COVID-19 vaccination coverage. The pronounced decline in MMR vaccination is concerning, although unsurprising, given the vaccine's history as a frequent target of misinformation. Recent measles outbreaks, including the outbreak in Texas that began in January 2025[42], highlight the urgent need to maintain high levels of MMR coverage. Minnesota has also experienced previous measles outbreaks[141,142], and similar events have occurred in other parts of the country when vaccination rates have dropped below the herd immunity threshold.[143,144] In 2023, while the overall MMR coverage in Minnesota for 24–35-month-olds was 78%, county-level vaccination coverage ranged from 57% to 95%, highlighting substantial geographic disparities in protection and risk of outbreaks in under-vaccinated areas. The decline in varicella vaccination may reflect reasons for hesitancy that can be easily extrapolated from pediatric COVID-19 vaccine hesitancy. These include perceptions that chickenpox is not a severe illness, concerns about vaccine efficacy, and beliefs that natural immunity is preferable to vaccine-acquired immunity.[145] For parents who view the risk of the disease as minimal, concerns, however unfounded, about vaccine safety may outweigh the perceived benefits, leading to lower uptake.

While we anticipated declines in vaccines like MMR and Varicella, we were surprised by the extent of decline across nearly all routine vaccines and the consistent pattern of association with county-level political composition. These trends are evident in Minnesota, a more liberal-leaning state with a strong public health infrastructure. This raises concerns about the potential for even more pronounced effects in states with less supportive social and political environments for

vaccination. The findings highlight broad issues of vaccine confidence and uptake that require urgent public health attention.

This study has several limitations that must be acknowledged. First, aggregate county-level data may mask underlying heterogeneity within counties. For instance, larger or more demographically diverse counties may exhibit significant differences in vaccination rates across neighborhoods that cannot be captured in county-level analyses. In areas with high heterogeneity within counties, future research incorporating more granular data, such as that at the census tract-level, might offer more insights, but it is not publicly available. Another limitation arises from potential unmeasured confounding factors. Although our analysis adjusts for socioeconomic status measure through the SVI, other determinants, such as cultural attitudes toward healthcare or local outreach programs, are not captured by publicly available data. Finally, the ecological design of this study limits the ability to infer individual-level causal relationships, as aggregated relationships at the county level do not necessarily reflect the behaviors or experiences of individual residents within those counties.

This study also has several notable strengths. One of the primary strengths of this study is the vaccination data used in this analysis. The data is from the Minnesota Immunization Information Connection (MIIC). MIIC stores and compiles individuals' immunization records, which are reported directly from pharmacies, healthcare providers, and schools. Every major healthcare system in Minnesota takes part in MIIC, ensuring high reporting accuracy and reliability. Another distinct advantage is that Minnesota's data is more granular than that of other available sources; many states report only statewide vaccine uptake. This is particularly important for

states such as Minnesota, which have distinct geopolitical distributions. Finally, this is a timely contribution to an under-researched area. To our knowledge, only one other study has specifically examined the relationship between COVID-19 vaccine hesitancy and the uptake of routine childhood vaccinations. The previous study assessed a limited set of vaccines and focused only on the kindergarten age group. By contrast, our study evaluates the full routine vaccine series among children aged 24–35 months, providing a more comprehensive and earlier investigation of how emerging vaccine attitudes may be shaping pediatric immunization rates. This work adds a critical dimension to ongoing discussions on vaccine confidence, underscoring the importance of understanding political and social influences on public health.

In the wake of the COVID-19 pandemic, routine childhood vaccinations have declined and, alarmingly, have remained low well beyond the initial period of pandemic disruption. Our findings suggest that this sustained decline may be a lingering consequence of the pandemic and reflect a broader politicization of vaccine attitudes, with evidence of spillover from COVID-19 vaccine hesitancy into routine pediatric immunizations. This trend poses a serious public health threat as under-vaccination increases the risk of outbreaks of vaccine-preventable diseases. To prevent further erosion of herd immunity, public health agencies must deliver clear, evidence-based messaging about the safety and effectiveness of childhood vaccines and prioritize outreach to communities where vaccination coverage is the lowest and hesitancy is most entrenched.

TABLES

Table 5.1 Summary of Minnesota county-level characteristics, 2015–2023

Characteristics	2015	2016	2017	2018	2019	2020	2021	2022	2023
Total Minnesota Population	5,485,238	5,528,630	5,577,487	5,629,416	5,680,337	5,706,494	5,742,036	5,801,769	5,800,386
Minnesota Population Age 24–35 Months	73,691	74,776	74,406	74,717	72,494	70,871	70,508	67,912	66,478
County-level Republican vote share (%)									
Mean (sd)	-	57.9 (9.1)	-	-	-	60.2 (10.0)	-	-	-
Median (IQR)	-	60 (11.1)	-	-	-	63.3 (11.5)	-	-	-
Range	-	26.0–73.4	-	-	-	26.1–75.8	-	-	-
County-level COVID-19 vaccine coverage (%)									
Mean (sd)	-	-	-	-	-	-	55.3 (7.4)	60.2 (8.1)	60.5 (8.2)
Median (IQR)	-	-	-	-	-	-	54.8 (7.4)	59.5 (8.2)	59.8 (8.4)
Range	-	-	-	-	-	-	40.2–78.0	43.1–83.2	43.3–83.8
County-level childhood seven vaccine series coverage (%)									
Mean (sd)	62.8 (9.7)	65.6 (9.1)	67.0 (8.0)	70.7 (6.4)	70.3 (6.1)	71.2 (7.0)	65.9 (7.8)	66.0 (7.8)	64.4 (7.9)
Median (IQR)	62.5 (11.6)	65.0 (12.2)	66.2 (11.0)	71.4 (9.6)	70.3 (8.6)	72.0 (8.8)	67.0 (11.4)	67.0 (9.9)	65.4(10.4)
Range	35.6–83.4	43.3–87.3	49.7–89.5	53.4–83.2	55.8–82.3	51.7–85.5	47.8–83.9	40.6–80.0	35.6–78.9

Table 5.2 Percent changes in routine childhood vaccination rates and corresponding 95% credible intervals (CI) among children aged 24–35 months in Minnesota adjusted for county-level socioeconomic status, 2015–2023

Vaccine	2015	2016	2017	2018	2019	2020	2021	2022	2023	Social vulnerability, low socioeconomic status (continuous 0 to 1)
Diphtheria, Tetanus, and Pertussis (DTaP) $\hat{\beta}$, 95% CI	-3.55 (-5.04, -2.06)	-3.18 (-4.67, -1.69)	-1.66 (-3.15, -0.17)	0.87 (-0.62, 2.36)	ref	0.84 (-0.65, 2.33)	-3.91 (-5.4, -2.42)	-4.00 (-5.49, -2.51)	-4.85 (-6.34, -3.36)	-4.61 (-7.39, -1.81)
Hepatitis B (Hep B) $\hat{\beta}$, 95% CI	-3.59 (-4.83, -2.35)	-2.93 (-4.16, -1.69)	-1.68 (-2.91, -0.44)	-4.27 (-5.51, -3.04)	ref	0.37 (-0.87, 1.60)	-1.84 (-3.07, -0.60)	-1.94 (-3.18, -0.71)	-3.78 (-5.01, -2.54)	-2.00 (-4.32, 0.32)
Haemophilus influenzae type b (Hib) $\hat{\beta}$, 95% CI	-3.00 (-4.3, -1.71)	-2.45 (-3.75, -1.16)	-0.22 (-1.51, 1.08)	5.67 (4.38, 6.96)	ref	0.57 (-0.72, 1.86)	-4.66 (-5.95, -3.37)	-2.66 (-3.95, -1.36)	-4.73 (-6.02, -3.43)	-3.69 (-6.04, -1.34)
Measles, Mumps, and Rubella (MMR) $\hat{\beta}$, 95% CI	-2.46 (-3.6, -1.31)	-2.37 (-3.52, -1.23)	-0.14 (-1.29, 1.00)	1.87 (0.72, 3.01)	ref	0.60 (-0.55, 1.74)	-3.78 (-4.92, -2.63)	-3.17 (-4.32, -2.03)	-5.11 (-6.26, -3.97)	-3.23 (-5.42, -1.03)
Pneumococcal Conjugate Vaccine (PCV) $\hat{\beta}$, 95% CI	-2.78 (-4.06, -1.50)	-2.38 (-3.65, -1.1)	-0.39 (-1.67, 0.88)	1.33 (0.05, 2.61)	ref	0.72 (-0.56, 2.00)	-3.02 (-4.30, -1.75)	-2.37 (-3.65, -1.09)	-4.8 (-6.08, -3.52)	-3.62 (-6.03, -1.19)
Polio $\hat{\beta}$, 95% CI	-1.91 (-3.05, -0.77)	-2.45 (-3.59, -1.31)	-0.84 (-1.98, 0.30)	0.34 (-0.80, 1.48)	ref	0.12 (-1.02, 1.26)	-1.87 (-3.01, -0.72)	-2.62 (-3.76, -1.48)	-3.69 (-4.83, -2.55)	-2.96 (-5.14, -0.78)
Varicella $\hat{\beta}$, 95% CI	-2.25 (-3.40, -1.10)	-2.83 (-3.98, -1.68)	-0.15 (-1.30, 1.00)	0.43 (-0.72, 1.58)	ref	-0.02 (-1.18, 1.13)	-5.12 (-6.27, -3.96)	-4.49 (-5.65, -3.34)	-6.55 (-7.7, -5.4)	-3.13 (-5.38, -0.88)

Table 5.3 Association and 95% credible intervals between county-level COVID-19 coverage, Republican vote share, and coverage for routine childhood vaccines in children aged 24–35 months in Minnesota, 2021–2023

Vaccine	Intercept	2022 (ref: 2021)	2023 (ref: 2021)	COVID-19 primary series percent non-completion (continuous)	Republican vote share >65% (ref: Republican vote share < 65%)	Social vulnerability, low socioeconomic status (continuous 0 to 1)	COVID-19 primary series percent non-completion x Republican vote share >65%
Diphtheria, Tetanus, and Pertussis (DTaP) $\hat{\beta}$, 95% CI	73.6 (66.18, 81.17)	-0.09 (-1.77, 1.59)	-0.94 (-2.64, 0.76)	0.07 (-0.11, 0.26)	9.05 (-6.71, 24.33)	-10.32 (-14.15, -6.47)	-0.26 (-0.59, 0.09)
Hepatitis B (Hep B) $\hat{\beta}$, 95% CI	84.83 (78.21, 91.58)	-0.15 (-1.43, 1.13)	-1.99 (-3.3, -0.68)	0.08 (-0.09, 0.24)	11.48 (-1.38, 24.18)	-4.34 (-7.74, -0.95)	-0.30 (-0.57, -0.02)
Haemophilus influenzae type b (Hib) $\hat{\beta}$, 95% CI	77.29 (72.36, 82.22)	1.76 (-0.04, 3.56)	-0.32 (-2.13, 1.49)	0.1 (-0.02, 0.22)	21.16 (10.41, 31.92)	-7.12 (-9.63, -4.61)	-0.51 (-0.75, -0.28)
Measles, Mumps, and Rubella (MMR) $\hat{\beta}$, 95% CI	82.68 (76.54, 88.96)	0.43 (-0.93, 1.78)	-1.52 (-2.9, -0.14)	0.06 (-0.09, 0.21)	14.69 (1.88, 27.21)	-6.07 (-9.24, -2.86)	-0.34 (-0.61, -0.06)
Pneumococcal Conjugate Vaccine (PCV) $\hat{\beta}$, 95% CI	82.02 (75.66, 88.45)	0.52 (-0.85, 1.9)	-1.91 (-3.31, -0.51)	0.05 (-0.11, 0.2)	9.78 (-3.13, 22.52)	-8.11 (-11.39, -4.77)	-0.25 (-0.53, 0.03)
Polio $\hat{\beta}$, 95% CI	87.3 (81.4, 93.32)	-0.91 (-2.12, 0.3)	-1.99 (-3.23, -0.75)	0.05 (-0.1, 0.2)	11.69 (-0.2, 23.37)	-5.96 (-8.99, -2.91)	-0.28 (-0.54, -0.03)
Varicella $\hat{\beta}$, 95% CI	85.67 (79.59, 91.89)	0.19 (-1.17, 1.55)	-1.9 (-3.28, -0.51)	0 (-0.15, 0.15)	12.66 (-0.15, 25.14)	-6.34 (-9.47, -3.17)	-0.31 (-0.58, -0.03)

FIGURES

Figure 5.1 Republican vote share in US presidential elections by Minnesota county, 2012–2024

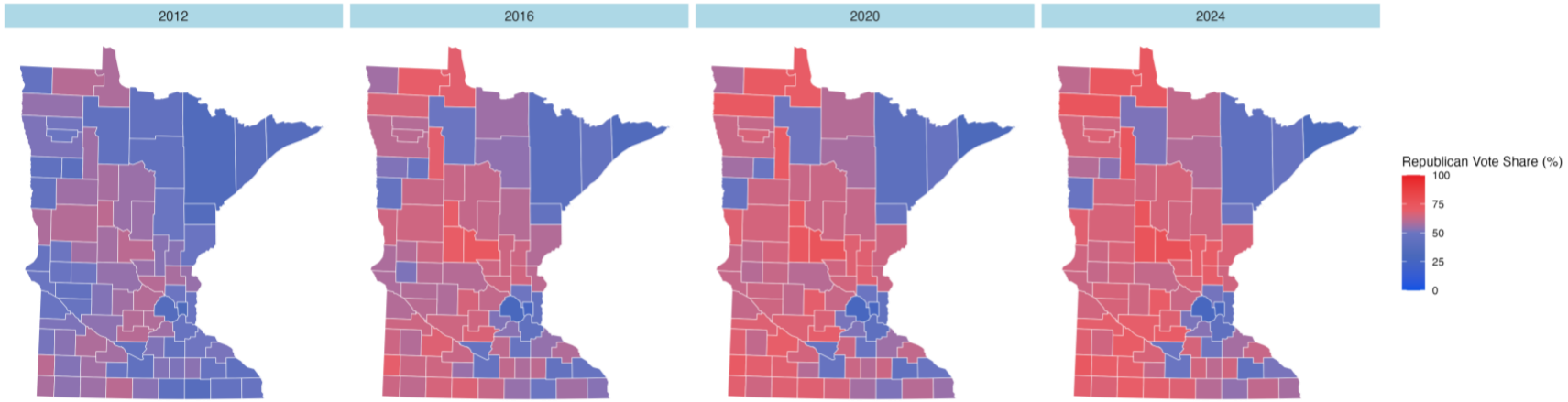


Figure 5.2 Rates of COVID-19 vaccine primary series completion by year in Minnesota counties, 2021–2023

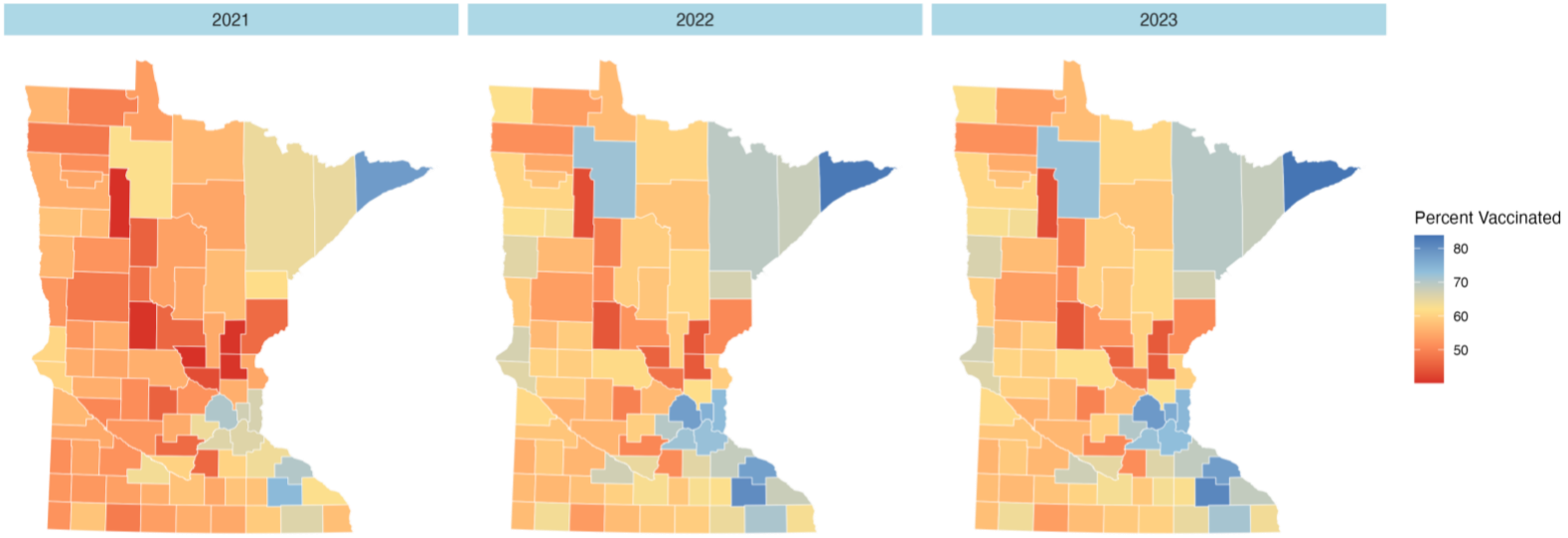


Figure 5.3 Social Vulnerability Index socioeconomic status metric in Minnesota counties, 2016–2022

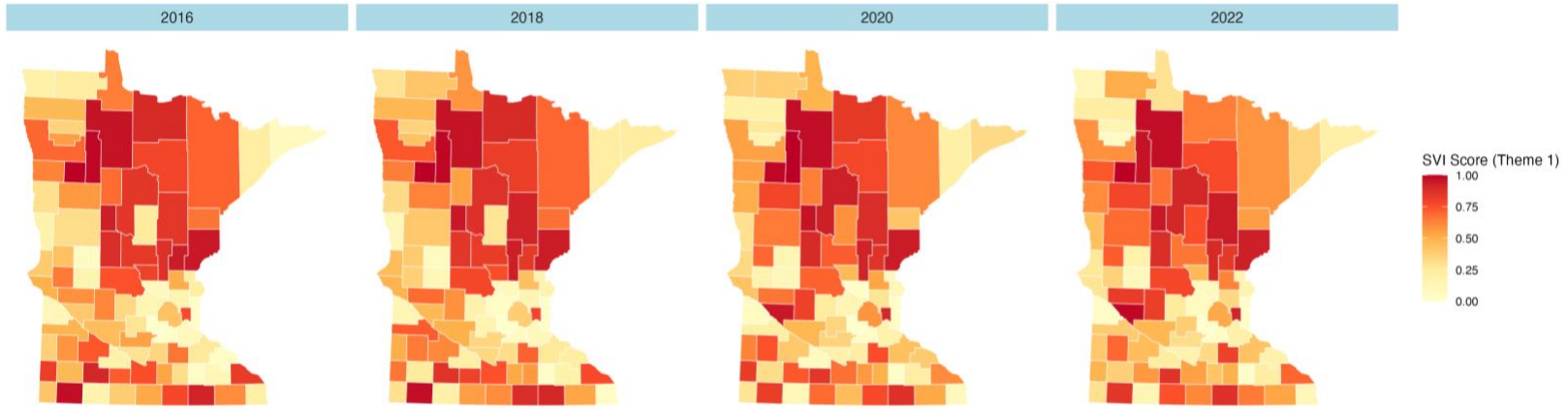


Figure 5.4 Rates of routine vaccination in children aged 24–35 months by year in Minnesota counties, 2015–2023

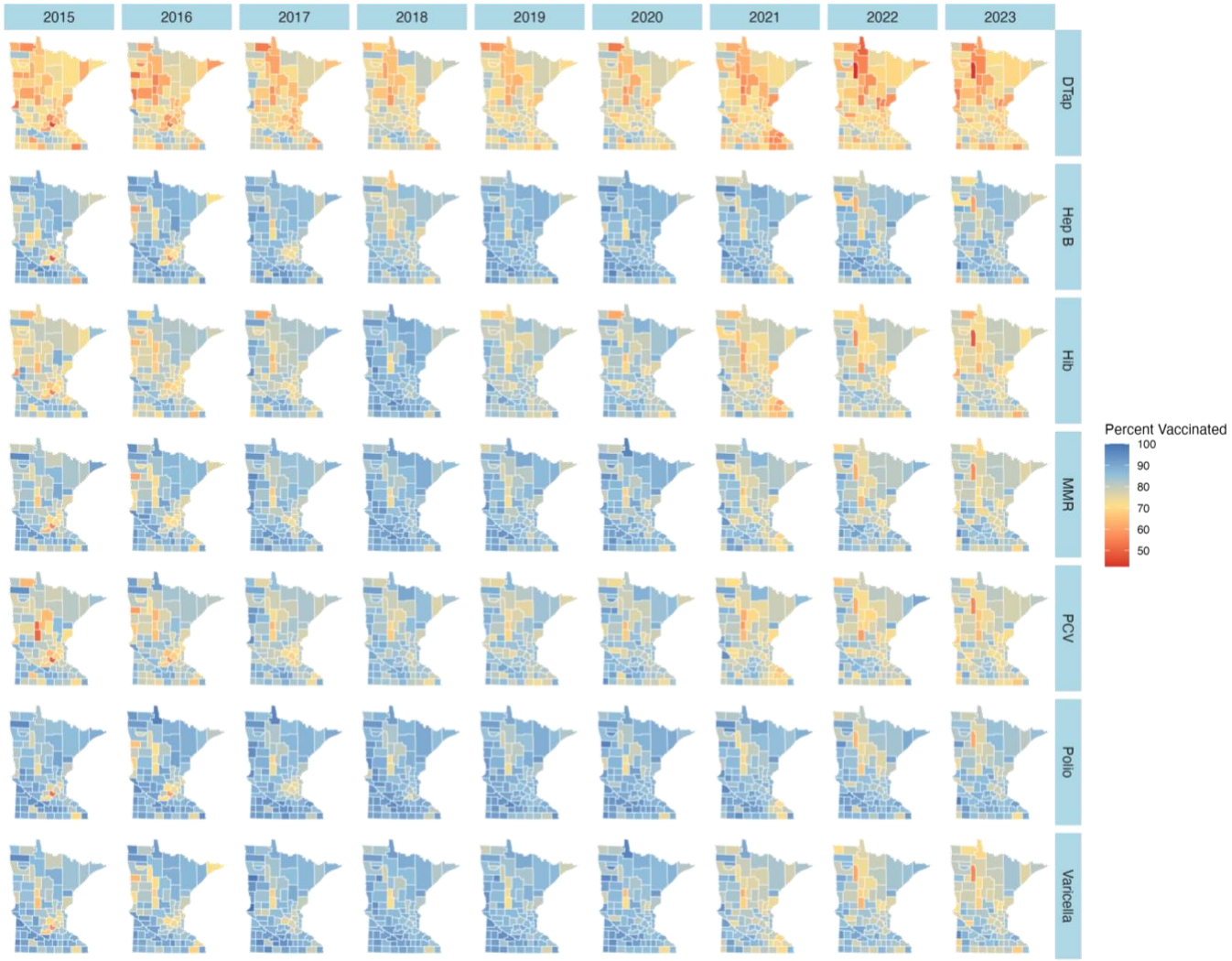
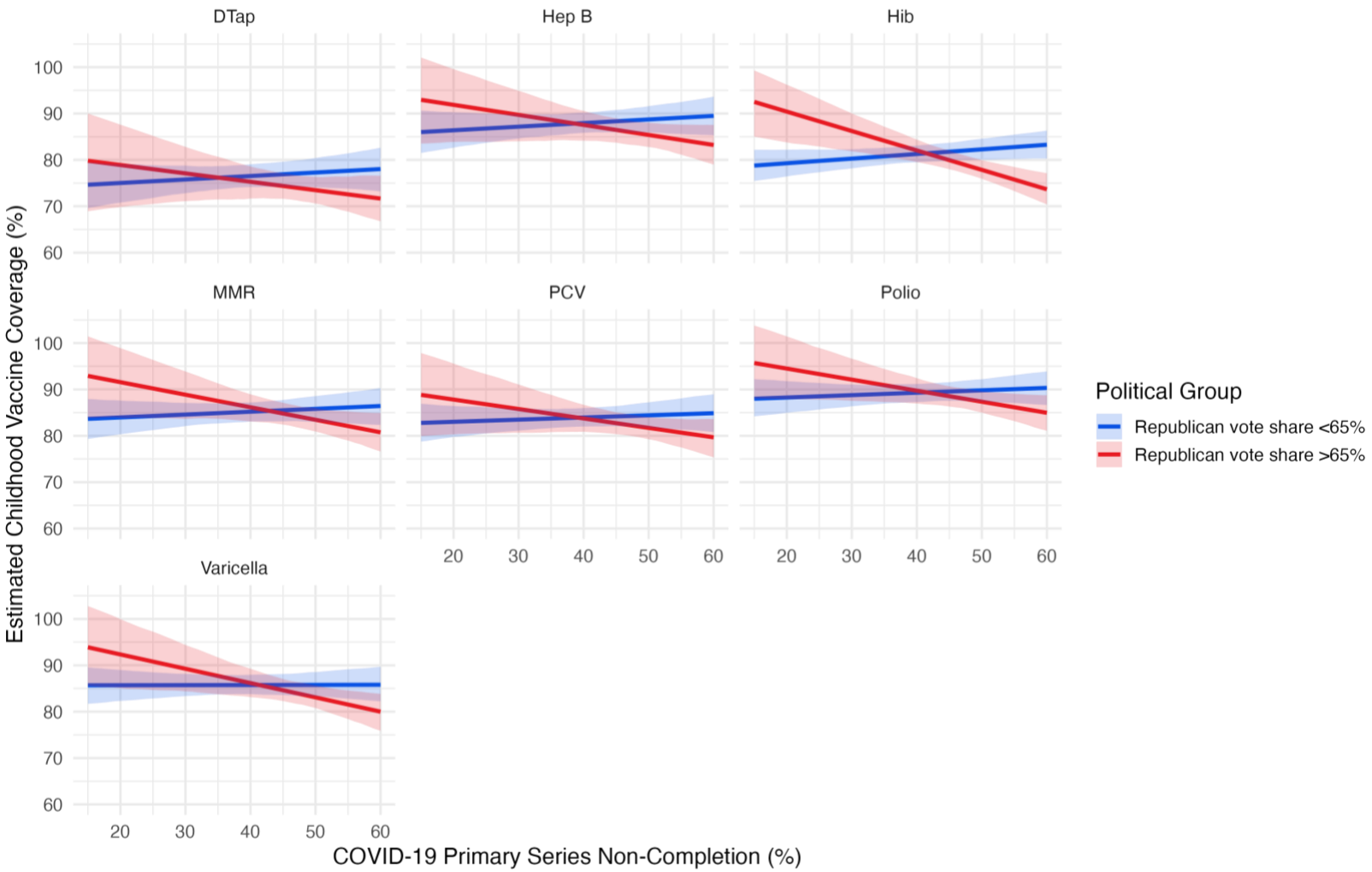


Figure 5.5 Estimated rates of routine vaccine coverage for children aged 24–35 months by county-level COVID-19 primary vaccine series non-completion rate and political composition



CHAPTER 6. SUMMARY AND CONCLUSIONS

The COVID-19 pandemic represents a critical inflection point for public health, particularly in its impact on vaccine acceptance and hesitancy. While the pandemic has underscored the importance of vaccines as a cornerstone of public health, it has also amplified vaccine hesitancy and skepticism toward public health recommendations. These trends raise urgent questions about willingness to accept COVID-19 vaccines following the end of the public health emergency, caregiver decision-making around COVID-19 vaccine acceptance for their children, political polarization of vaccine acceptance, and changes in the acceptance of routine childhood vaccines in the wake of the pandemic. This dissertation investigated these interconnected issues, focusing on the pandemic's potential to impact the uptake of vital routine vaccines, thereby undermining herd immunity and increasing the risk of outbreaks of preventable diseases.

This dissertation found a clear association between political affiliation and COVID-19 vaccine acceptance. Republican-identifying adults were significantly less likely than their Democratic counterparts to report intentions to continue receiving COVID-19 vaccines after the end of the US public health emergency. Furthermore, we found that parents who declined COVID-19 vaccines for themselves or their children were more likely to have delayed or refused other routine childhood vaccines. Finally, ecological analyses demonstrated that low county-level COVID-19 vaccination uptake was associated with lower routine childhood vaccination coverage in Republican-leaning Minnesota counties. Taken together, these findings suggest that COVID-19 vaccine hesitancy may have extended into broader resistance toward routine vaccines, with this spillover effect being especially pronounced among individuals and communities aligned with conservative political ideologies.

Understanding the factors influencing COVID-19 vaccine acceptance in adults and children, the broader consequences of the COVID-19 pandemic on children, and the social, political, and demographic determinants of vaccine hesitancy is critical to informing public health policies and improving health outcomes. Findings from this dissertation could inform public health strategies aimed at rebuilding trust in vaccines and countering the long-term impacts of the pandemic on vaccine hesitancy, particularly for children. Public health must adapt to an increasingly uncertain landscape where vaccine hesitancy could be amplified by influential skeptics in positions of authority. Efforts to improve vaccine uptake must address underlying distrust and politicization of science that has taken root in many communities. By establishing evidence of interconnected attitudes related to vaccine hesitancy, this dissertation can help inform adaptive public health messaging that anticipates and addresses vaccine skepticism across evolving political and social climates.

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SUPPLEMENTAL TABLES

Supplemental Table 3.1 Additional demographic and health characteristics of participants in relation to intention to receive COVID-19 booster vaccine in the coming year if it is recommended (N=1,236)

Characteristic	Overall, N = 1,236	Extremely likely, N = 702	Likely, N = 189	Undecided, N = 106	Unlikely, N = 85	Extremely unlikely, N = 154	p-value
Medical condition							<0.001^
Yes	245	169 (69%)	35 (14%)	9 (3.7%)	11 (4.5%)	21 (8.6%)	
No	907	489 (54%)	145 (16%)	90 (9.9%)	65 (7.2%)	118 (13%)	
Unknown	84	44	9	7	9	15	
Anxiety (GAD-2)							0.029^
Yes	212	105 (50%)	40 (19%)	25 (12%)	20 (9.4%)	22 (10%)	
No	1,019	593 (58%)	148 (15%)	81 (7.9%)	65 (6.4%)	132 (13%)	
Unknown	5	4	1	0	0	0	
Worked in healthcare							0.7^
Yes	319	180 (56%)	44 (14%)	27 (8.5%)	27 (8.5%)	41 (13%)	
No	904	515 (57%)	144 (16%)	76 (8.4%)	57 (6.3%)	112 (12%)	
Unknown	13	7	1	3	1	1	
Worked in public health							>0.9^
Yes	197	111 (56%)	34 (17%)	15 (7.6%)	14 (7.1%)	23 (12%)	
No	1,011	575 (57%)	152 (15%)	90 (8.9%)	68 (6.7%)	126 (12%)	
Unknown	28	16	3	1	3	5	
Political affiliation							<0.001*
Democratic	671	514 (77%)	94 (14%)	36 (5.4%)	18 (2.7%)	9 (1.3%)	
Republican	166	29 (17%)	22 (13%)	19 (11%)	31 (19%)	65 (39%)	
Independent	163	77 (47%)	26 (16%)	19 (12%)	8 (4.9%)	33 (20%)	
Other	80	27 (34%)	13 (16%)	10 (12%)	8 (10%)	22 (28%)	
Unknown	156	55	34	22	20	25	

+Kruskal-Wallis rank sum test
^Pearson's chi-squared test
‡Fisher's exact test
*Fisher's exact test for count data with simulated p-value (based on 2000 replicates)

Supplemental Table 3.2 Factors associated with participants' intention to receive COVID-19 booster vaccine in the coming year if it is recommended (N=1,236)

Characteristic	Overall, N = 1,236	Extremely unlikely, N = 154	Unlikely, N = 85	Undecided, N = 106	Likely, N = 189	Extremely likely, N = 702	p-value
Correctly defined all public health terms							<0.001^
Yes	371 (31%)	18 (12%)	7 (8.4%)	23 (23%)	46 (26%)	277 (40%)	
No	831 (69%)	132 (88%)	76 (92%)	79 (77%)	134 (74%)	410 (60%)	
Unknown	34	4	2	4	9	15	
Vaccine information from social media							0.002^
Yes	105 (8.7%)	9 (6.3%)	9 (11%)	16 (15%)	25 (14%)	46 (6.7%)	
No	1,098 (91%)	134 (94%)	72 (89%)	88 (85%)	160 (86%)	644 (93%)	
Unknown	33	11	4	2	4	12	
Sum of pandemic fear measures							<0.001+
Mean (sd)	14.7 (5.5)	8.4 (4.8)	12.6 (5.5)	14.7 (5.2)	15.8 (5.0)	16.1 (4.8)	
Unknown	19	3	2	1	2	11	
Believes COVID-19 vaccine is extremely safe							<0.001^
Yes	685 (56%)	2 (1.4%)	6 (7.3%)	21 (21%)	73 (39%)	583 (83%)	
No	536 (44%)	146 (99%)	76 (93%)	81 (79%)	116 (61%)	117 (17%)	
Unknown	15	6	3	4	0	2	
Is concerned about contracting COVID-19							<0.001^
Yes	909 (74%)	34 (22%)	43 (51%)	70 (67%)	150 (80%)	612 (88%)	
No	318 (26%)	119 (78%)	42 (49%)	34 (33%)	38 (20%)	85 (12%)	
Unknown	9	1	0	2	1	5	
Received at least one COVID-19 vaccine							<0.001^
Yes	1,131 (92%)	78 (51%)	65 (78%)	99 (96%)	188 (99%)	701 (100%)	

No	98 (8.0%)	74 (49%)	18 (22%)	4 (3.9%)	1 (0.5%)	1 (0.1%)	
Unknown	7	2	2	3	0	0	
Received a COVID-19 bivalent booster vaccine							<0.001^
Yes	693 (65%)	10 (13%)	16 (26%)	34 (35%)	95 (56%)	538 (80%)	
No	381 (35%)	66 (87%)	46 (74%)	62 (65%)	76 (44%)	131 (20%)	
Unknown	162	78	23	10	18	33	
Number of COVID-19 vaccine doses received							<0.001+
Mean (sd)	3.09 (1.33)	1.11 (1.27)	1.96 (1.33)	2.59 (1.05)	3.12 (0.87)	3.73 (0.86)	
Minimum, Maximum	0, 6	0, 5	0, 5	0, 5	0, 5	0, 6	
Unknown	13	2	2	3	0	6	

^Pearson's Chi-squared test;
+Kruskal-Wallis rank sum test

Supplemental Table 4.1 Comparison of characteristics of families included and excluded from analysis from a random sample of three ECHO cohort sites from analytic samples, 2021–2023

	Sample Cohort 1				Sample Cohort 2				Sample Cohort 3			
	Included in analysis Aim 1 N= 322	**Included in analysis Aim 2** N= 73	**Included in analysis Aim 3** N= 331	**Excluded from analysis** N= 164	**Included in analysis Aim 1** N= 266	**Included in analysis Aim 2** N= 302	**Included in analysis Aim 3** N= 299	**Excluded from analysis** N= 348	**Included in analysis Aim 1** N= 227	**Included in analysis Aim 2** N= 131	**Included in analysis Aim 3** N= 235	**Excluded from analysis** N= 164
At least one child in family racial or ethnic minority												
Yes	119 (37%)	35 (48%)	127 (38%)	72 (44%)	209 (79%)	242 (95%)	242 (81%)	281 (87%)	136 (60%)	74 (56%)	144 (61%)	98 (60%)
No	203 (63%)	38 (52%)	204 (62%)	92 (56%)	57 (21%)	14 (5.5%)	57 (19%)	41 (13%)	91 (40%)	57 (44%)	91 (39%)	66 (40%)
Unknown						46		26				
Mother age at first completed COVID-19 survey												
Mean (SD)	41.0 (5.3)	36.0 (5.2)	40.9 (5.5)	39.9 (5.8)	36 (7)	31.9 (6.0)	35 (7)	33 (7)	35 (6)	33.9 (5.8)	35 (6)	35 (7)
Minimum, Maximum	27.6, 53.5	27.6, 50.6	27.6, 53.5	27.4, 55.3	19, 54	19.3, 47.8	19, 54	20, 52	24, 56	23.9, 48.5	24, 56	23, 54
Unknown				1								7
At least one child in family age between 0-6 months												

Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	68 (26%)	151 (50%)	80 (27%)	63 (18%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
No	322 (100%)	73 (100%)	331 (100%)	164 (100%)	198 (74%)	151 (50%)	219 (73%)	285 (82%)	227 (100%)	131 (100%)	235 (100%)	164 (100%)
At least one child in family age between 6 months - 5 years												
Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	122 (46%)	201 (67%)	151 (51%)	177 (51%)	5 (2.2%)	3 (2.3%)	5 (2.1%)	2 (1.2%)
No	322 (100%)	73 (100%)	331 (100%)	164 (100%)	144 (54%)	101 (33%)	148 (49%)	171 (49%)	222 (98%)	128 (98%)	230 (98%)	162 (99%)
At least one child in family age between 6 - 11 years												
Yes	322 (100%)	73 (100%)	331 (100%)	164 (100%)	171 (64%)	75 (25%)	185 (62%)	146 (42%)	227 (100%)	131 (100%)	235 (100%)	162 (99%)
No	0 (0%)	0 (0%)	0 (0%)	0 (0%)	95 (36%)	227 (75%)	114 (38%)	202 (58%)	0 (0%)	0 (0%)	0 (0%)	2 (1.2%)
At least one child in family age between 12 -17 years												
Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.8%)	1 (0.3%)	2 (0.7%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
No	322 (100%)	73 (100%)	331 (100%)	164 (100%)	264 (99%)	301 (100%)	297 (99%)	347 (100%)	227 (100%)	131 (100%)	235 (100%)	164 (100%)
Number children in family												
1	321 (100%)	73 (100%)	331 (100%)	164 (100%)	247 (93%)	279 (92%)	275 (92%)	327 (94%)	202 (89%)	117 (89%)	207 (88%)	145 (88%)

2	1 (0.3%)				11 (4.1%)	15 (5.0%)	16 (5.4%)	19 (5.5%)	23 (10%)	13 (9.9%)	26 (11%)	18 (11%)
3					7 (2.6%)	6 (2.0%)	7 (2.3%)	2 (0.6%)	2 (0.9%)	1 (0.8%)	2 (0.9%)	1 (0.6%)
4					1 (0.4%)	2 (0.7%)	1 (0.3%)					
Mother's socioeconomic status (combination education and income)												
High SES	257 (80%)	33 (45%)	263 (79%)	111 (68%)	108 (41%)	65 (22%)	113 (38%)	113 (32%)	83 (37%)	35 (27%)	85 (36%)	59 (36%)
Low SES	1 (0.3%)	0 (0%)	0 (0%)	1 (0.6%)	12 (4.5%)	28 (9.3%)	12 (4.0%)	17 (4.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Missing, No Response	64 (20%)	40 (55%)	68 (21%)	52 (32%)	146 (55%)	209 (69%)	174 (58%)	218 (63%)	144 (63%)	96 (73%)	150 (64%)	105 (64%)
Any child in family has medical condition that puts them at high risk from COVID infection												
Yes	98 (30%)	27 (37%)	98 (30%)	46 (28%)	84 (32%)	48 (16%)	96 (32%)	88 (25%)	134 (59%)	73 (56%)	136 (58%)	98 (60%)
No	224 (70%)	46 (63%)	233 (70%)	118 (72%)	182 (68%)	254 (84%)	203 (68%)	260 (75%)	93 (41%)	58 (44%)	99 (42%)	66 (40%)
Unknown												
Caregiver vaccinated for COVID-19												
Yes	283 (88%)	44 (60%)	290 (88%)	3 (100%)	203 (76%)	203 (67%)	238 (80%)	13 (93%)	155 (68%)	65 (50%)	159 (68%)	2 (50%)

No	39 (12%)	29 (40%)	41 (12%)	0 (0%)	63 (24%)	99 (33%)	61 (20%)	1 (7.1%)	72 (32%)	66 (50%)	76 (32%)	2 (50%)
Unknown				161				334				160
Any children vaccinated for COVID-19												
Yes	257 (80%)	0 (0%)	262 (79%)	1 (100%)	122 (46%)	0 (0%)	132 (44%)	10 (63%)	83 (37%)	0 (0%)	86 (37%)	2 (33%)
No	65 (20%)	73 (100%)	69 (21%)	0 (0%)	144 (54%)	302 (100%)	167 (56%)	6 (38%)	144 (63%)	131 (100%)	149 (63%)	4 (67%)
Unknown				163				332				158

Supplemental Table 4.2 Eigenvalues and cumulative variance associated with principal components of caregiver hesitancy to accept the COVID-19 vaccine for themselves among 1,422 caregivers in the ECHO Cohort

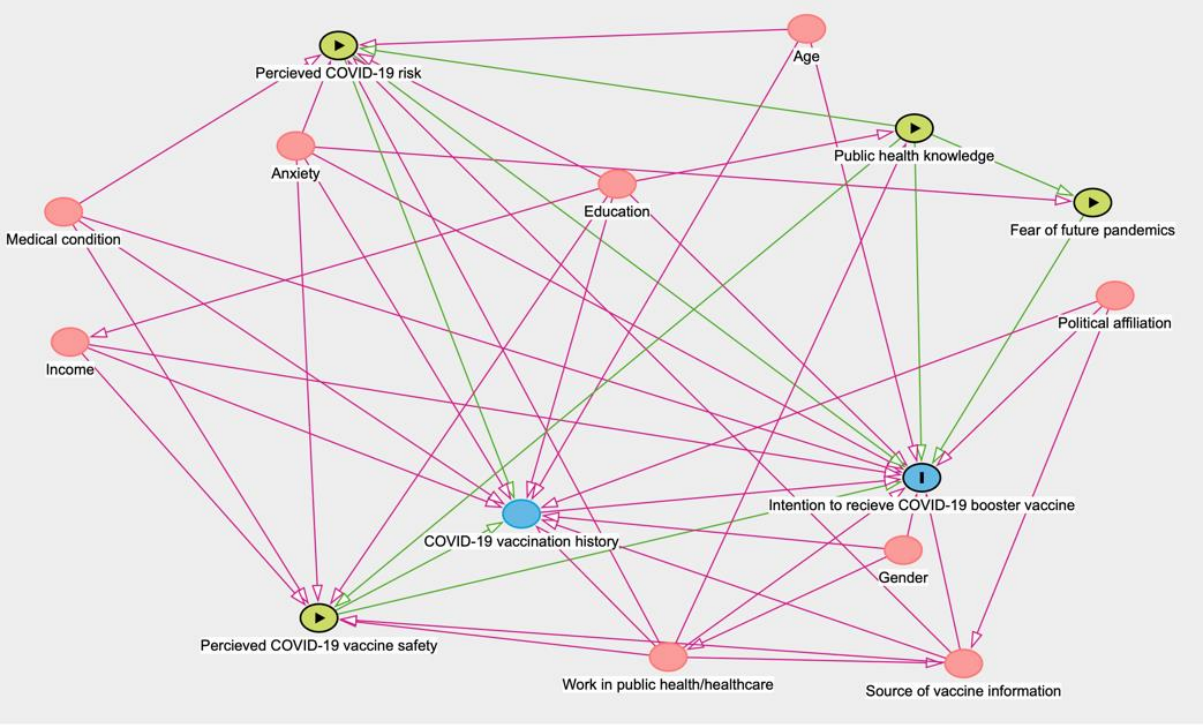
Component	Eigenvalue	Cumulative Variance
PC1	2.43	0.35
PC2	1.17	0.51
PC3	0.86	0.64
PC4	0.71	0.74
PC5	0.66	0.83
PC6	0.63	0.92
PC7	0.55	1.00

Supplemental Table 4.3 Loading values associated with the first four principal components of caregiver hesitancy to accept the COVID-19 vaccine for themselves among 1,422 caregivers in the ECHO Cohort

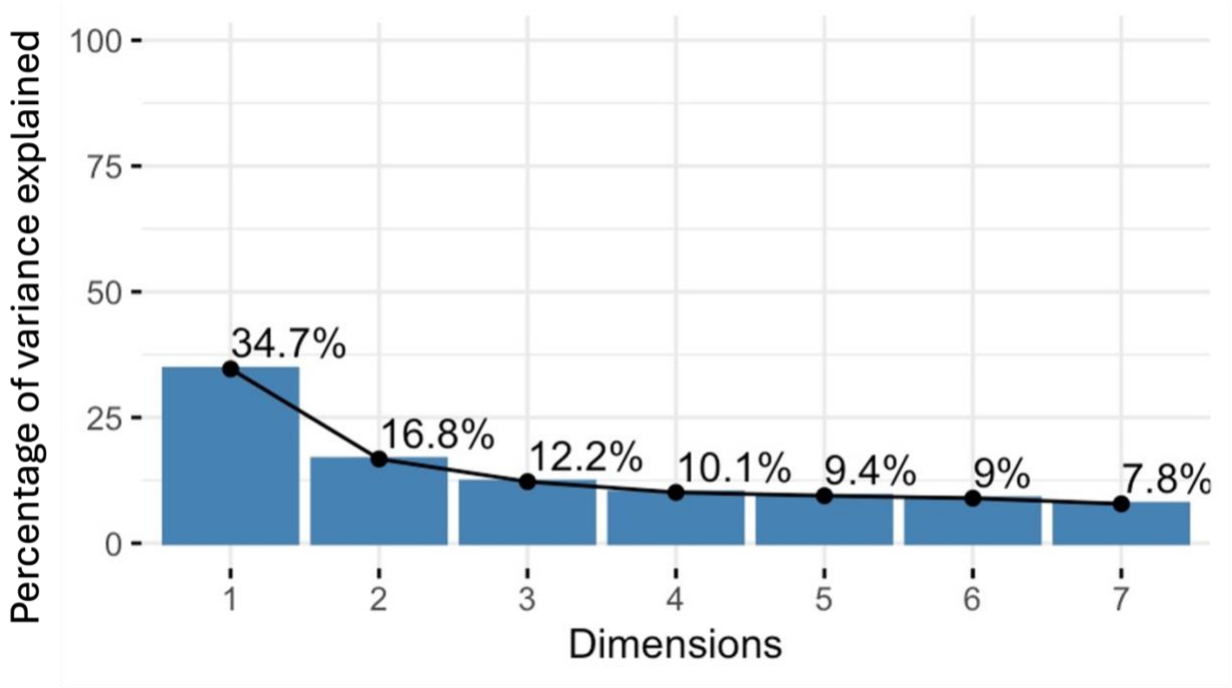
Loading Variables	PC1	PC2	PC3	PC4
Not enough is known about the long-term effects of the vaccine	0.43	-0.02	0.26	0.06
I am worried about the side effects	0.44	-0.15	0.29	-0.48
I am at low risk and do not need it	0.27	-0.47	-0.70	0.35
The vaccine was not well tested in racially and ethnically diverse people	0.37	0.44	0.17	0.58
I already had COVID-19	0.33	-0.56	0.17	-0.10
I have read information that suggests the vaccine is unsafe	0.46	0.19	0.00	0.13
I do not trust the doctor/healthcare provider's recommendation to get it	0.30	0.46	-0.55	-0.52

SUPPLEMENTAL FIGURES

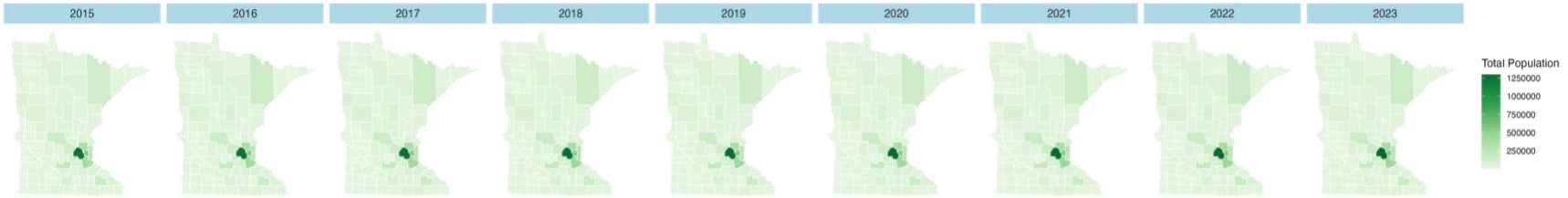
Supplemental Figure 3.1 Conceptual model of the relationship between intention to receive COVID-19 booster vaccines and perceived vaccine safety, perceived COVID-19 risk, public health knowledge, and fear of pandemics



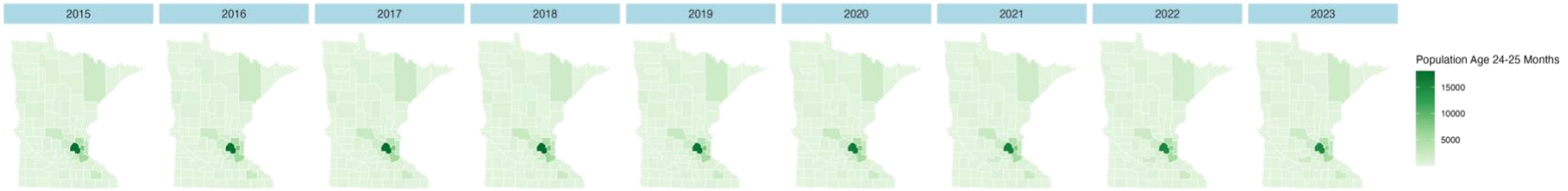
Supplemental Figure 4.1 Scree plot for principal component analysis of reasons for caregiver hesitancy to accept the COVID-19 vaccine for themselves among 1,422 caregivers in the ECHO Cohort



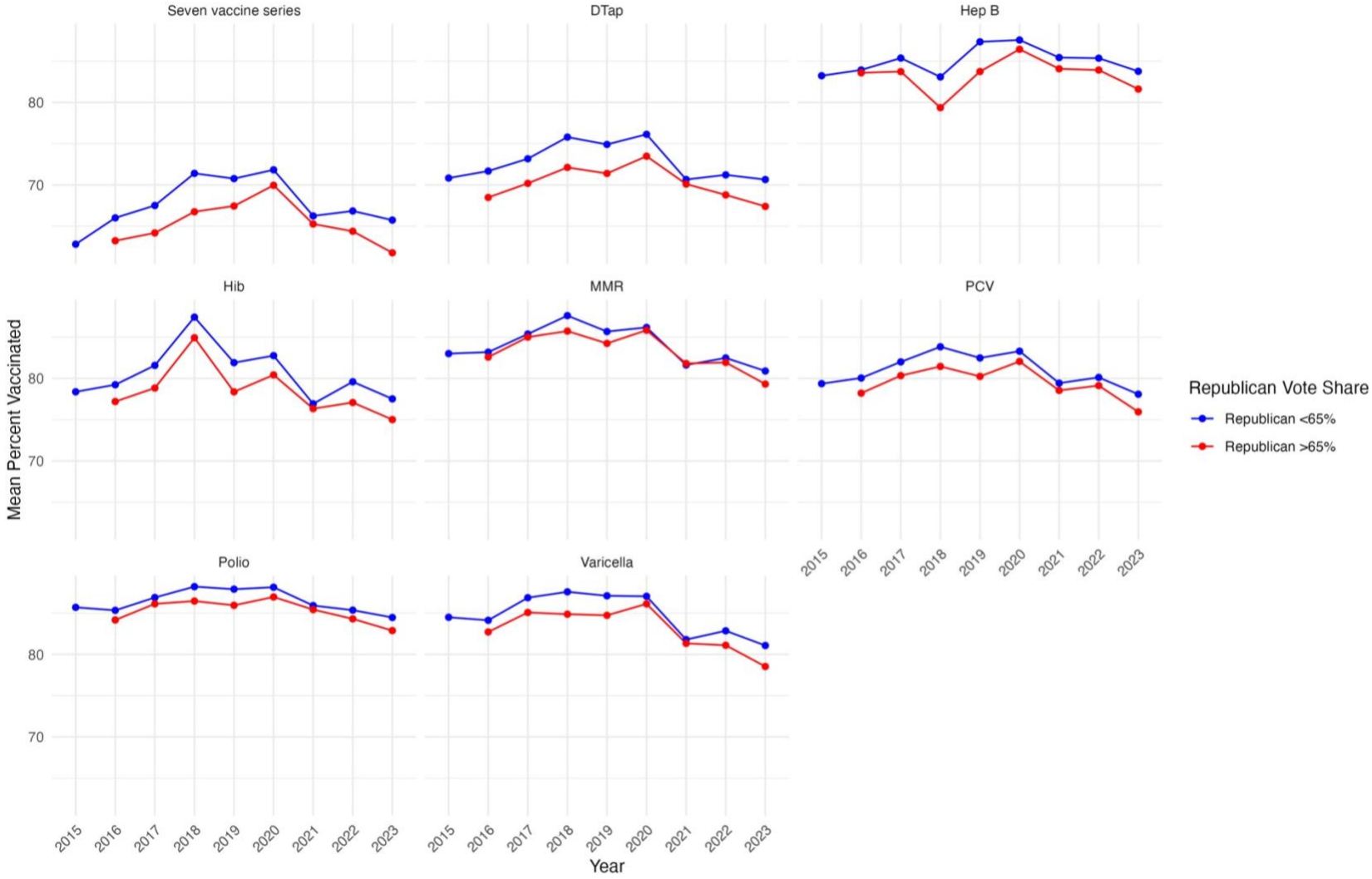
Supplemental Figure 5.1Minnesota total population by county, 2015–2023



Supplemental Figure 5.2 Minnesota population aged 24–35 months by county, 2015–2023



Supplemental Figure 5.3 Trends in average county-level childhood vaccination rates by year (2015–2023), stratified by political composition (Republican vote share above or below 65%)



*Note: No counties met the ≥65% Republican vote share threshold in 2015; no data were plotted for this group in that year