Factors associated with COVID-19 non-vaccination in adolescents hospitalized without COVID-19

Leila C. Sahni, PhD, MPH1 Ashley M. Price, MPH2; Samantha M. Olson, MPH2; Margaret M. Newhams, MPH3; Pia S. Pannaraj, MD, MPH4; Aline B. Maddux, MD, MScS5; Natasha B. Halasa, MD6; Katherine E. Bline, MD7; Melissa A. Cameron, MD8; Stephanie P. Schwartz, MD9; Tracie C. Walker, MD10; Katherine Irby, MD10; Kathleen Chiotos, MD, MSCE11; Ryan A. Nofziger, MD12; Elizabeth H. Mack, MD13; Laura Smallcomb, MD14; Tamara T. Bradford, MD15; Satoshi Kamiyama, MD16; Keiko M. Tarquinio, MD17; Natalie Z. Cevjanovic, MD18; Jennifer E. Schuster, MD19; Samina S. Bhumba, MD20; Emily R. Levy, MD21; Charlotte V. Hobbs, MD22; Melissa L. Cullimore, MD23; Bria M. Coates, MD24; Sabrina M. Heidemann, MD25; Shira J. Gertz, MD26; Michele Kong, MD27; Heidi R. Flori, MD28; Mary A. Staat, MD29; Matt S. Zinter, MD30; Janet R. Hume, MD31; Brandon M. Chatani, MD32; Mary G. Gaspers, MD33; Mia Maamari, MD34; Adrienne G. Randolph, MD, MSc35; Manish P. Patel, MD36; Julie A. Boom, MD1

1 Department of Pediatrics, Baylor College of Medicine, Immunization Project, Texas Children’s Hospital, Houston, TX 77030, USA
2 CDC COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA
3 Department of Anesthesiology, Critical Care, and Pain Medicine, Boston Children’s Hospital, Boston, MA 02115, USA
4 Division of Infectious Diseases, Children’s Hospital Los Angeles and Departments of Pediatrics and Molecular Microbiology and Immunology, University of Southern California, Los Angeles, CA 90027, USA
5 Department of Pediatrics, Section of Critical Care Medicine, University of Colorado School of Medicine and Children’s Hospital Colorado, Aurora, CO 80045, USA
6 Division of Pediatric Infectious Diseases, Department of Pediatrics, Vanderbilt University Medical Center, Nashville, TN 37232, USA
7 Division of Pediatric Critical Care Medicine, Nationwide Children’s Hospital Columbus, OH 43205, USA
8 Division of Pediatric Hospital Medicine, UC San Diego-Rady Children’s Hospital, San Diego, CA 92123, USA
9 Department of Pediatrics, University of North Carolina at Chapel Hill Children’s Hospital, Chapel Hill, NC 27514, USA
10 Section of Pediatric Critical Care, Department of Pediatrics, Arkansas Children’s Hospital, Little Rock, AR 72202, USA
11 Division of Critical Care Medicine, Department of Anesthesiology and Critical Care, Children’s Hospital of Philadelphia, Philadelphia, PA 19104, USA
12 Division of Critical Care Medicine, Department of Pediatrics, Akron Children’s Hospital, Akron, OH 44308, USA
13 Division of Pediatric Critical Care Medicine, Medical University of South Carolina, Charleston, SC 29425, USA
14 Department of Pediatrics, Medical University of South Carolina, Charleston, SC 29425, USA
15 Department of Pediatrics, Division of Cardiology, Louisiana State University Health Sciences Center and Children’s Hospital of New Orleans, New Orleans, LA 70118, USA
16 The Center for Childhood Infections and Vaccines of Children’s Healthcare of Atlanta and the Department of Pediatrics, Emory University School of Medicine, Atlanta, GA 30322, USA
17 Division of Critical Care Medicine, Department of Pediatrics, Emory University School of Medicine, Children’s Healthcare of Atlanta, Atlanta, GA 30322, USA
18 Division of Critical Care Medicine, UCSF Benioff Children’s Hospital Oakland, CA 94609, USA
19 Division of Pediatric Infectious Diseases, Department of Pediatrics, Children’s Mercy Kansas City, Kansas City, MO 64108, USA
20 The Ryan White Center for Pediatric Infectious Disease and Global Health, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN 46202, USA
21 Divisions of Pediatric Infectious Diseases and Pediatric Critical Care Medicine, Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN 55905, USA

© The Author(s) 2022. Published by Oxford University Press on behalf of The Journal of the Pediatric Infectious Diseases Society. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.
Corresponding author: Leila C. Sahni, PhD, MPH. Texas Children's Hospital, 1102 Bates Ave Ste 1550, Houston, TX 77030. Telephone: (832) 824-2057; email: lcsahni@texaschildrens.org

Alternate corresponding author: Julie A. Boom, MD, Texas Children's Hospital, 1102 Bates Ave Ste 1550, Houston, TX 77030. Telephone: (832) 822-3433; email: jaboom@texaschildrens.org

Conflicts of interest and source of funding: This work was supported by the Centers for Disease Control and Prevention, via subcontract through Boston Children's Hospital coordinating center. Some authors have disclosures of interest relevant to this work. ICMJE disclosure of interest forms will be completed for all authors upon acceptance.
Abstract

Background: Pfizer-BioNTech COVID-19 vaccine received emergency use authorization for persons ≥16 years in December 2020 and for adolescents 12-15 years in May 2021. Despite the clear benefits and favorable safety profile, vaccine uptake in adolescents has been suboptimal. We sought to assess factors associated with COVID-19 non-vaccination in adolescents 12-18 years of age.

Methods: Between June 1, 2021 and April 29, 2022, we assessed factors associated with COVID-19 non-vaccination in hospitalized adolescents ages 12-18 years enrolled in the Overcoming COVID-19 vaccine effectiveness network. Demographic characteristics and clinical information were captured through parent interview and/or electronic medical record abstraction; COVID-19 vaccination was assessed through documented sources. We assessed associations between receipt of COVID-19 vaccine and demographic and clinical factors using univariate and multivariable logistic regression and estimated adjusted odds ratios (aOR) for each factor associated with non-vaccination.

Results: Among 1,665 hospitalized adolescents without COVID-19, 56% were unvaccinated. Unvaccinated adolescents were younger (median age 15.1 years vs. 15.4 years, p<0.01) and resided in areas with higher social vulnerability index (SVI) scores (median 0.6 vs 0.5, p<0.001) than vaccinated adolescents. Residence in the Midwest [aOR 2.60 (95% CI: 1.80, 3.79)] or South [aOR 2.49 (95% CI: 1.77, 3.54)] US census regions, rarely or never receiving influenza vaccine [aOR 5.31 (95% CI: 3.81, 7.47)], and rarely or never taking precautions against COVID-19 [aOR 3.17 (95% CI: 1.94, 5.31)] were associated with non-vaccination against COVID-19.

Conclusions: Efforts to increase COVID-19 vaccination of adolescents should focus on persons with geographic, socioeconomic, and medical risk factors associated with non-vaccination.

Keywords: COVID-19 vaccine, risk factors, adolescent
Background

Throughout the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, pediatric coronavirus disease 2019 (COVID-19) has been largely overshadowed by adult illness. Despite being generally characterized as mild, pediatric COVID-19 has resulted in >15 million infections, >150,000 hospitalizations, and >1,700 child and adolescent deaths in the US.1,2 Racial and ethnic minority children and those with underlying medical conditions such as obesity, lung disease, and immunosuppression are at increased risk for hospitalization and death.3,4 Among US children and adolescents, adolescents ages 12-17 years experienced the highest proportion of cases during the first three waves of the COVID-19 pandemic.5 Pfizer-BioNTech COVID-19 (BNT162b2) vaccine received initial emergency use authorization (EUA) from the Food and Drug Administration for persons ≥16 years in December 2020, and this was expanded in May 2021 to include adolescents 12-15 years of age.6 These EUAs were quickly followed by interim recommendations for administration from the Advisory Committee on Immunization Practices (ACIP).7 Real-world observational vaccine effectiveness studies have demonstrated the Pfizer-BioNTech vaccine to be highly effective against hospitalization and ICU admission for adolescents.8 Although rare cases of myocarditis/pericarditis have been linked to vaccination, especially in adolescent and young adult males, Pfizer-BioNTech COVID-19 vaccine is safe and well-tolerated.9,10 Despite the clear benefits and favorable safety profile, vaccine uptake in adolescents has been suboptimal, and hospitalizations due to COVID-19 are ten times higher in unvaccinated adolescents.11,12 As of April 30, 2022, only 59% of US adolescents have received ≥2 doses of Pfizer-BioNTech COVID-19 vaccine.13 We sought to assess factors associated with COVID-19 non-vaccination in adolescents 12-18 years of age, using persons hospitalized for non-COVID-19 illness, who are anticipated to be generally representative of the population of adolescents in each institution’s catchment area, as a proxy for the source population.
Methods

We analyzed data from the Overcoming COVID-19 pediatric vaccine effectiveness (VE) network, a network of 31 children’s hospitals in 23 states conducting active surveillance for pediatric hospitalizations. Details of the Overcoming COVID-19 VE investigation have been previously published; in brief, adolescents 12-18 years of age hospitalized with acute COVID-19 as the primary admission diagnosis or a clinical syndrome consistent with COVID-19 or multi-system inflammatory syndrome in children (MIS-C) were identified and enrolled as case-patients.\textsuperscript{14,15} Due to potential biases related to the selection of controls initially, two groups of control-patients were enrolled: children hospitalized with COVID-19-like illness with a negative SARS-CoV-2 RT-PCR or antigen test (“test-negative” control-patients) and children with no COVID-19 symptoms who may or may not have been tested for SARS-CoV-2 (“syndrome-negative” control-patients).\textsuperscript{8} Sites attempted to enroll all patients hospitalized with COVID-19; control-patients without COVID-19 were identified after case enrollment, and were matched by age, hospital, and calendar week (within 3 weeks) of case-patient hospitalization. Prior analyses demonstrated that vaccine effectiveness results did not vary by type of control-patient, so enrollment of syndrome-negative control-patients was halted in December 2021, only traditional test-negative control-patients were enrolled for the remainder of the study, and both control types were combined in subsequent analyses.\textsuperscript{8,16} As our primary interest was to identify factors associated with COVID-19 non-vaccination in the source population for hospitals in the Overcoming COVID-19 network, we restricted analyses to hospital-based controls without COVID-19 enrolled between June 1, 2021 and April 29, 2022. Cases with COVID-19 were excluded because vaccines are highly effective against preventing hospitalization with COVID-19 and thus cases were less likely to be vaccinated.\textsuperscript{8}

Demographic characteristics, clinical information, SARS-CoV-2 testing history, influenza vaccination history (parent reported receipt of influenza vaccine in the preceding 12 months and frequency of receipt; every year, most years, some years, rarely, never), and frequency of precautions taken to protect against COVID-19 in the 14 days prior to
hospitalization (e.g., social distancing, mask wearing, hand washing; precautions not taken, rarely taken, often taken, always taken) were captured through parent interview and/or electronic medical record abstraction by trained study personnel. All case- and control-patients were enrolled irrespective of their COVID-19 vaccination status, which was not assessed until after completion of the parent/guardian interview and/or medical record abstraction. COVID-19 vaccination status was determined through documented sources only, including searches of state immunization information systems (IIS), electronic medical records, or documentation from patient immunization cards. We categorized participants as unvaccinated if they had received no doses of COVID-19 vaccine prior to hospitalization and vaccinated if they had received 2 doses. We excluded patients with 1 dose of vaccine and those without documented vaccination history. This activity was reviewed by CDC and participating institutions and was conducted consistent with applicable federal law and CDC policy (45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq).

We calculated unweighted estimates of COVID-19 vaccination coverage by age group (12-15 years vs. 16-18 years) and by study month. We compared characteristics of vaccinated and unvaccinated controls using chi-squared, Kruskal-Wallis, and Wilcoxon rank sum tests. We assessed associations between non-receipt of COVID-19 vaccine and demographic and clinical factors using univariate and multivariable logistic regression. We estimated adjusted odds ratios (aOR) for each predictor associated with non-vaccination. We assessed two adjusted models: 1) adjusting for a priori variables of age, sex, race/ethnicity and census region, and 2) adjusting for a priori variables and additional variables associated with COVID-19 non-vaccination in bivariate analysis with p<0.20 (Table 1). Since the adjusted model including a priori and additional variables associated with COVID-19 non-vaccination reduced the sample size by 45%, the a priori model was selected as the final model.
Results

A total of 1,665 SARS-CoV-2-negative control-patients were enrolled from 31 pediatric hospitals during June 2021 through April 2022, including 1,072 (64%) test-negative and 593 (36%) syndrome-negative control-patients. The two control types enrolled before December 2021 did not differ by age, race/ethnicity, sex, or region but differed by social vulnerability index and underlying conditions (Supplemental Table 1). Among all control-patients, 56% (n=933) were unvaccinated, 50% (n=831) were female, 43% (n=715) were non-Hispanic white, and 68% (n=1,135) had ≥1 underlying medical conditions (Table 1). The plurality (40%, n=669) were enrolled from the South US census region, reflecting matching of control-patients with COVID-19 case-patient enrollment.

COVID-19 vaccine uptake increased in early months in the study period (June through October 2021), but plateaued in later months (November 2021 through April 2022, Figure 1). Unvaccinated adolescents were younger (median age 15.1 years vs. 15.4 years, p<0.01) and resided in areas with higher social vulnerability index (SVI) scores (median 0.6 vs 0.5, p<0.001) compared to vaccinated adolescents. No differences were observed between unvaccinated and vaccinated patients by sex, presence of underlying medical conditions, or prior hospitalization in the preceding 12 months (Figure 2, Table 1). Although race/ethnicity was independently associated with non-vaccination in univariate analyses, no association was observed in adjusted analyses. In adjusted analyses, residence in the Midwest [aOR 2.60 (95% CI: 1.80, 3.79)] or South [aOR 2.49 (95% CI: 1.77, 3.54)] census regions was associated with non-receipt of COVID-19 vaccine, compared to residence in the Northeast.

Parental report of prior season influenza vaccination of adolescents was most strongly associated with COVID-19 vaccination. The odds of COVID-19 non-vaccination were 5 times higher [aOR 5.31 (95% CI: 3.81, 7.47)] among adolescents who rarely or never were vaccinated against influenza compared to adolescents who were vaccinated every year. Similarly, parental report of non-receipt of current season influenza vaccination of their adolescents was associated with greater odds of COVID-19 non-vaccination [aOR 3.21
Adolescents whose parents reported they rarely or never took precautions to protect themselves against COVID-19 had greater odds of non-vaccination compared to adolescents who always took precautions [aOR 3.17 (95% CI: 1.94, 5.31)]. Finally, compared to in-person school attendance, adolescents who attended school virtually had greater odds of non-receipt of COVID-19 vaccine [aOR 1.68 (95% CI: 1.27, 2.22)].

Discussion

In this multi-state assessment of factors associated with COVID-19 non-vaccination in adolescents, the majority of adolescents (56%) were unvaccinated, which is higher than national estimates (38%). Multiple factors have hindered COVID-19 vaccine uptake in adolescents, including widespread misinformation about vaccine safety, parental vaccine hesitancy, and lack of perceived need for COVID-19 vaccination in this population. Our study population was composed of hospitalized adolescents without COVID-19, one-fifth of whom reported ≥1 hospitalization in the prior 12 months and two-thirds of whom reported ≥1 underlying medical condition. We did not specifically assess reasons for non-vaccination in this population, but suspect that the low vaccine uptake observed in our assessment might be due to lack of routine well-child care and vaccine hesitancy triggered by perception of medical fragility, concerns about vaccine side effects, and low perception of risk among some parents of adolescents with complex medical needs. In a pre-vaccine assessment of parental intent, Goldman et al found that parents of children with chronic illness were less willing to vaccinate their children against COVID-19 compared with parents of healthy children. This is unfortunate as adolescents with chronic illness face increased risk of severe COVID-19 disease, hospitalization, and death. Conversely, parents of adolescents with complex medical needs with high health literacy who closely follow evidence-based recommendations may be more likely to vaccinate their adolescents. We also noted that unvaccinated adolescents were slightly younger than vaccinated adolescents. This is not surprising as the EUA for older adolescents ≥16 years predated authorization for younger adolescents 12-15 years by 5 months. Thus, parents of older adolescents have had more
time to weigh the risks and benefits of vaccination and opt-in to COVID-19 vaccine for their teens. As observed with other adolescent vaccines, vaccine coverage increases slowly over time following vaccine introduction. In addition, other assessments of COVID-19 vaccine have demonstrated that parents of older adolescents have expressed greater intent to vaccinate than parents of younger adolescents.

Early assessments of COVID-19 vaccine uptake suggested that non-Hispanic Black and Hispanic/Latino individuals were less likely to be vaccinated than non-Hispanic white individuals. In our adolescent population, race/ethnicity did not predict COVID-19 non-vaccination. This is consistent with more recent analyses suggesting that racial and ethnic disparities in vaccine uptake have narrowed. Instead of racial and ethnic differences, we found that geographic location (living in the South or Midwest US census regions) was associated with lower COVID-19 vaccine uptake. Our findings are similar to other assessments, which noted low COVID-19 vaccination in adults residing in Southern states. Furthermore, unvaccinated adolescents resided in areas with higher SVI, which has been previously associated with low COVID-19 vaccine uptake.

In our population of adolescents, parental report of influenza vaccination, both current and past season, was strongly associated with COVID-19 vaccine uptake. Other adult and pediatric assessments examining history of influenza vaccine and COVID-19 vaccine acceptance had similar findings. Studies of influenza vaccine acceptance have shown that absence of a strong provider recommendation, low perceived risk of disease, lack of perceived benefit of vaccination, and low perceived vaccine effectiveness are associated with non-receipt of influenza vaccine. We believe that many of these factors likely apply to COVID-19 vaccine acceptance for adolescents. Beyond this, children and adolescents who are regularly vaccinated against influenza are more likely to receive routine preventive care, and, therefore, have increased opportunities to receive a recommendation for vaccines, including COVID-19 vaccine.

Finally, consistent with other studies of COVID-19 vaccine acceptance, we noted that adolescents who less frequently adopted COVID-19 precautionary measures were less
likely to be vaccinated against COVID-19 than adolescents who frequently or always used these measures. Adolescent acceptance of COVID-19 precautions is heavily influenced by parental attitudes and behaviors and parental norms play a key role in COVID-19 vaccine uptake. Although we did not measure parent vaccination status, we believe the contribution of parental influence should not be overlooked when considering factors that contribute to adolescent COVID-19 vaccination. In addition, some adolescents may hold strong beliefs regarding COVID-19 vaccination and might seek vaccination without parental guidance, as permitted in some states. Efforts to promote acceptance of adolescent COVID-19 vaccination should focus on strategies previously demonstrated to be successful in improving uptake of other vaccines, such as strong provider recommendations for vaccination, convenient access, and coordinated and consistent messaging dispelling myths and combatting misinformation.

Our findings are subject to several limitations. First, our assessment contains a relatively small number of participants and is confined to adolescents only, thus we were unable to assess factors associated with COVID-19 vaccination in younger children. Additionally, because control-patients were identified only after enrollment of an eligible case-patient, sites with large numbers of COVID-19 hospitalizations in geographic regions where the burden of COVID-19 was high are over-represented in our analyses. In some cases, these areas may have had lower COVID-19 vaccination rates than corresponding areas with fewer pediatric COVID-19 hospitalizations. Furthermore, because control-patients were matched by age and week of admission to case-patients with COVID-19, the adolescent population included in this assessment and the factors identified as being associated with COVID-19 non-vaccination may differ from the true source population; the relatively high prevalence of underlying medical conditions among case-patients and control-patients suggests this might be the case. The primary objective of the Overcoming COVID-19 network is to evaluate severe pediatric COVID-19; therefore, this assessment includes only hospitalized adolescents and our findings may not be generalizable across the full spectrum of pediatric COVID-19 if adolescents with milder disease differed in vaccination
behavior. Additionally, because each of the participating institutions are tertiary care facilities and care for patients from large geographic areas, location of care might not represent true geographic location of residence. However, this difference is unlikely to be large enough to result in misclassification of census region of residence. Minimal collection of information not directly related to risk for and treatment of COVID-19 facilitated rapid and large patient enrollment but precluded the examination of risk factors known to be associated with acceptability and uptake of COVID-19 vaccines and other vaccines (e.g., parental COVID-19 vaccination status and sociodemographic factors). Finally, some information was self-reported (e.g., influenza vaccination status) and available for only a subset of participants.

In conclusion, factors negatively impacting COVID-19 vaccine uptake are multifactorial and have resulted in suboptimal vaccination of adolescents. Our assessment identifies potential persons for intervention, including adolescents residing in specific geographic regions of the U.S., those with higher SVI scores, those with underlying medical conditions, and those less likely to adhere to evidence-based recommendations.
**Acknowledgments:** This work was supported by the Centers for Disease Control and Prevention, via subcontract through Boston Children's Hospital coordinating center.
References

1. Centers for Disease Control and Prevention. COVID Data Tracker. Demographic trends of COVID-19 cases and deaths in the US reported to CDC. Accessed September 28, 2022. Available at: https://covid.cdc.gov/covid-data-tracker/#demographics

2. Centers for Disease Control and Prevention. COVID Data Tracker. New admissions of patients with confirmed COVID-19 per 100,000 population by age group, United States August 1, 2020—February 13, 2022. Accessed September 28, 2022. Available at: https://covid.cdc.gov/covid-data-tracker/#new-hospital-admissions

3. Woodruff RC, Campbell AP, Taylor CA, et al. Risk factors for severe COVID-19 in children. Pediatrics. 2022;149(1):e2021053418.

4. Oliver S. EtR Framework: Pfizer-BioNTech COVID-19 vaccine in adolescents aged 12-15 years. Accessed February 11, 2022. Available at: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-05-12/04-COVID-Oliver-508.pdf

5. Centers for Disease Control and Prevention. COVID Data Tracker. Centers for Disease Control and Prevention. Published March 28, 2020. Accessed February 6, 2022. https://covid.cdc.gov/covid-data-tracker

6. Food and Drug Administration. Coronavirus (COVID-19) Update: FDA Authorizes Pfizer-BioNTech COVID-19 Vaccine for Emergency Use in Adolescents in Another Important Action in Fight Against Pandemic. FDA. Published May 13, 2021. Accessed February 6, 2022. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-pfizer-biontech-covid-19-vaccine-emergency-use
7. Wallace M, Woodworth KR, Gargano JW, et al. The Advisory Committee on Immunization Practices’ Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine in Adolescents Aged 12–15 Years — United States, May 2021. MMWR Morb Mortal Wkly Rep. 2021;70(20):749-752.

8. Olson SM, Newhams MM, Halasa NB, et al. Effectiveness of BNT162b2 Vaccine against Critical Covid-19 in Adolescents. N Engl J Med. doi:10.1056/NEJMoa2117995.

9. Oster ME, Shay DK, Su JR, et al. Myocarditis Cases Reported After mRNA-Based COVID-19 Vaccination in the US From December 2020 to August 2021. JAMA. 2022;327(4):331-340. doi:10.1001/jama.2021.24110.

10. Rosenblum HG, Gee J, Liu R, et al. Safety of mRNA vaccines administered during the initial 6 months of the US COVID-19 vaccination programme: An observational study of reports to the Vaccine Adverse Event Reporting System and v-safe. Lancet Infect Dis. 2022. doi: 10.1016/S1473-3099(22)00054-8.

11. Delahoy MJ, Ujamaa D, Whitaker M, et al. Hospitalizations Associated with COVID-19 Among Children and Adolescents — COVID-NET, 14 States, March 1, 2020–August 14, 2021. MMWR Morb Mortal Wkly Rep. 2021;70(36):1255-1260.

12. Frenck RW, Klein NP, Kitchin N, et al. Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents. N Engl J Med. 2021;385(3):239-250. doi:10.1056/NEJMo0a2107456

13. Centers for Disease Control and Prevention. COVID-19 Vaccination Coverage and Vaccine Confidence Among Children. Published November 30, 2021. Accessed
14. Son MBF, Murray N, Friedman K, et al. Multisystem Inflammatory Syndrome in Children - Initial Therapy and Outcomes. *N Engl J Med*. 2021;385(1):23-34.

15. Feldstein LR, Rose EB, Horwitz SM, et al. Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. *N Engl J Med*. 2020;383(4):334-346.

16. Olson SM, Newhams MM, Halasa NB, et al. Effectiveness of Pfizer-BioNTech mRNA vaccination against COVID-19 hospitalization among persons aged 12-18 years—United States, June-September 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70(42):1483-1488.

17. Lail J, Fields E, Paolella A, et al. Primary care quality improvement metrics and National Committee on Quality Assurance medical home recognition for children with medical complexity. *Pediatr Qual Saf*. 2019;4(6):e231.

18. Samad L, Tate AR, Dezateux C, Peckham C, Butler N, Bedfor H. Differences in risk factors for partial and no immunization in the first year of life: prospective cohort study. *BMJ*. 2006;332(7553):1312-1313.

19. Gamliel A, Ziv-Baron T, Siegel RM, et al. Using weight-for-age percentiles to screen for overweight and obese children and adolescents. *Prev Med*. 2015;81:174-179.

20. Goldman RD, Yan TD, Seiler M, et al. Caregiver willingness to vaccinate their children against COVID-19: Cross sectional survey. *Vaccine*. 2020(38):7668-7673.
21. Martin B, DeWitt PE, Russell S, et al. Characteristics, outcomes, and severity risk factors associated with SARS-CoV-2 infection among children in the US National COVID Cohort Collaborative. *JAMA Netw Open*. 2022;5(2):e2143151.

22. Lawrence PR, Feinberg I, Spratling R. The relationship of parental health literacy to health outcomes of children with medical complexity. *J Pediatr Nurs*. 2021;60:65-70.

23. Kuehn BM. HPV Vaccination Coverage Has Increased Among Adolescents. *JAMA*. 2021;326(14):1366.

24. Rogers AM, Cook RE, Button JA. Parent and peer norms are unique correlates of COVID-19 vaccine intentions in a diverse sample of US adolescents. *J Adol Health*. 2021;69:910-916.

25. María Nápoles A, Stewart AL, Strassle PD, et al. Racial/ethnic disparities in intent to obtain a COVID-19 vaccine: A nationally representative United States survey. *Prev Med Rep*. 2021;24:101653.

26. Nguyen KH, Nguyen K, Geddes M, Allen JD, Corlin L. Trends in COVID-19 vaccination receipt and intention to vaccinate, United States, April to August, 2021. *Am J Infect Control*. 2021. doi: 10.1016/j.ajic.2021.12.022.

27. Szilagyi PG, Thomas K, Shah MD, et al. Likelihood of COVID-19 vaccination by subgroups across the US: post-election trends and disparities. *Hum Vaccines Immunother*. 2020;17(10):3262-3267.
28. Nguyen KH, Nguyen K, Corlen L, Allen JD, Chung M. Changes in COVID-19 vaccination receipt and intention to vaccinate by socioeconomic characteristics and geographic area, United States, January 6—March 29, 2021. *Ann Med.* 2021;53(1):1419-1428.

29. Caban-Martinez AJ, Silvera CA, Santiago KM, Louzado-Feliciano P, Burgess JL, Smith DL, Jahnke S, Horn GP, Graber JM. COVID-19 Vaccine Acceptability Among US Firefighters and Emergency Medical Services Workers: A Cross-Sectional Study. *J Occup Environ Med.* 2021;63(5):369-373.

30. Mirpuri P, Rovin RA. COVID-19 and Historic Influenza Vaccinations in the United States: A Comparative Analysis. *Vaccines* (Basel). 2021;9(11):1284.

31. Shekhar R, Sheikh AB, Upadhyay S, Singh M, Kottewar S, Mir H, Barrett E, Pal S. COVID-19 Vaccine Acceptance among Health Care Workers in the United States. *Vaccines* (Basel). 2021;9(2):119.

32. Fisher KA, Bloomstone SJ, Walder J, et al. Attitudes toward a potential SARS-CoV-2 vaccine: A survey of US adults. *Ann. Intern. Med.* 2020;173(12):964-973.

33. Hughes MM, Wang A, Grossman MK, et al. County-level COVID-19 vaccination coverage and social vulnerability—United States, December 14, 2020-March 1, 2021. *MMWR Morb Mortal Wkly Rep.* 2021;70(12):431-436.

34. Schmid P, Rauber D, Betsch C, et al. Barriers of influenza vaccination intention and behavior – A systematic review of influenza vaccine hesitancy, 2005-2016. *PLoS One.* 2017;12(1):e0170550.
35. Wang Y, Liu U. Multilevel determinants of COVID-19 vaccination hesitancy in the United States: A rapid systematic review. *Prev. Med. Rep.* 2022;25:101673. doi: 10.1016/j.pmedr.2021.101673.

36. Hill AV, Moehling Geffel K, Lavage DR, et al. Parent-reported intention to vaccinate children against COVID-19: Influences of COVID-19 and seasonal influenza vaccination. *Clin Pediatr.* 2022;61(2):107-111.

37. Poehling KA, Fairbrother G, Zhu Y, et al. Practice and child characteristics associated with influenza vaccine uptake in young children. *Pediatrics.* 2010;126(4):665-673.

38. Imburgia TM, Hendrix KS, Donahue KL, Sturm LA, Zimet GD. Predictors of influenza vaccination in the U.S. among children 9-13 years of age. *Vaccine.* 2017;35(18):2338-2342.

39. Latkin CA, Dayton L, Yi G, Colon B, Kong X. Mask usage, social distancing, racial, and gender correlates of COVID-19 vaccine intentions among adults in the US. *PLoS One.* 2021;16(2):e0246970. doi: 10.1371/journal.pone.0246970.

40. Wagner AL, Porth JM, Wu Z, Boulton ML, Finlay JM, Kobayashi LC. Vaccine Hesitancy during the COVID-19 pandemic: A latent class analysis of middle-aged and older US Adults. *J Community Health.* 2022. doi: 10.1007/s10900-022-01064-w.

41. Lam CN, Kaplan C, Saluja S. Relationship between mask wearing, testing, and vaccine willingness among Los Angeles County adults during the peak of the COVID-19 pandemic. *Transl Behav Med.* 2021. doi: 10.1093/tbm/ibab150.
42. Ryan G, Askelson NM, Miotto MB, et al. Lessons learned from human papillomavirus vaccination to increase uptake of adolescent COVID-19 vaccination. J Adolesc Health. 2022;70(3):359-360.
Table 1. Risk factors associated with non-vaccination among control patients aged 12-18 years 31 pediatric hospitals in 23 states, June 2021 – April 2022, United States

Figure 1. COVID-19 vaccine coverage among control patients by age group (12-15 years vs. 16-18 years) and month of enrollment

Figure 2. Demographic factors and COVID-19 vaccination status among control patients aged 12-18 years 31 pediatric hospitals in 23 states, June 2021 – April 2022, United States
| Characteristic                              | Unvaccinated (N=933) | Vaccinated (N=732) | p-value | OR     | 95% CI  | aOR     | 95% CI  |
|--------------------------------------------|----------------------|--------------------|---------|--------|---------|---------|---------|
| Age in Years, Median (IQR)                 | 15.1 (13.7, 16.8)    | 15.4 (13.9, 16.8)  | <0.01   |        |         |         |         |
| Age Category, No. (%)                      |                      |                    |         |        |         |         |         |
| 12-15 years                                | 591 (63.3)           | 443 (60.5)         | 0.24    | 1.13   | 0.92 - 1.38 | 1.18 | 0.96 - 1.45 |
| 16-18 years                                | 342 (36.7)           | 289 (39.5)         |         | REF    | REF     | REF     | REF     |
| Sex, No. (%)                               |                      |                    |         |        |         |         |         |
| Female                                     | 464 (49.7)           | 367 (50.1)         | 0.87    |        |         |         |         |
| Male                                       | 468 (50.2)           | 365 (49.9)         |         | 1.01   | 0.84 - 1.23 | 0.99 | 0.82 - 1.21 |
| Race/Ethnicity, No. (%)                    |                      |                    |         |        |         |         |         |
| White, non-Hispanic                        | 423 (45.3)           | 292 (39.9)         | <0.01   | 1.52   | 1.18 - 1.95 | 1.32 | 1.01 - 1.72 |
| Black, non-Hispanic                        | 219 (23.5)           | 146 (19.9)         |         | 1.57   | 1.18 - 2.10 | 1.31 | 0.96 - 1.79 |
| Hispanic, any race                         | 188 (20.2)           | 197 (26.9)         |         | <0.01  | REF     | REF     | REF     |
| Other, non-Hispanic                        | 61 (6.5)             | 67 (9.2)           | 0.05    | 0.95   | 0.64 - 1.42 | 0.92 | 0.61 - 1.38 |
| Unknown                                    | 42 (4.5)             | 30 (4.1)           | 0.14    | 1.47   | 0.88 - 2.46 | 1.42 | 0.84 - 2.41 |
| Social Vulnerability Index\(^x\), Median (IQR) | 0.6 (0.3, 0.8)     | 0.5 (0.2, 0.8)    | <0.01   |        |         |         |         |
| U.S. Census Region, No. (%)                |                      |                    |         |        |         |         |         |
| Northeast                                  | 67 (7.2)             | 103 (14.1)         | <0.01   | 2.71   | 1.88 - 3.93 | 2.60 | 1.80 - 3.79 |
| Midwest                                    | 257 (27.5)           | 146 (19.9)         |         | 2.48   | 1.76 - 3.51 | 2.49 | 1.77 - 3.54 |
| South                                      | 413 (44.3)           | 256 (35.0)         |         | 1.33   | 0.93 - 1.91 | 1.45 | 1.00 - 2.10 |
| West                                       | 196 (21.0)           | 227 (31.0)         |         |        |         |         |         |
| Underlying Health Conditions - no./total no. (%) |          |                    |         |        |         |         |         |
| No underlying conditions                   | 307/931 (33.0)       | 219/730 (30.0)     | 0.20    | 1.15   | 0.93 - 1.42 | 1.21 | 0.97 - 1.50 |
| At least one underlying condition          | 624/931 (67.0)       | 511/730 (70.0)     |         |        |         |         |         |
| Respiratory, including asthma              | 251/928 (27.0)       | 195/728 (26.8)     | 0.91    |        |         |         |         |
| Cardiovascular                             | 72/929 (7.8)         | 67/726 (9.2)       | 0.28    |        |         |         |         |
| Condition                               | No. (% 1) | Total No. (% 2) | p-value  |
|-----------------------------------------|-----------|-----------------|----------|
| Neurologic/Neuromuscular                | 173/928 (18.6) | 157/728 (21.6)  | 0.14     |
| Immunosuppression or autoimmune         | 101/931 (10.8) | 81/729 (11.1)   | 0.87     |
| Endocrine, including diabetes           | 97/930 (10.4)  | 77/728 (10.6)   | 0.92     |
| Obesity ‡                               | 264/929 (36.2) | 190/728 (26.0)  | 0.14     |
| Other chronic conditions ¶              | 361/929 (38.9) | 314/729 (43.2)  | 0.08     |

**Other Characteristics – No./Total No. (%)**

| Prior Hospitalizations in past year ¶¶ | Yes | No | p-value |
|----------------------------------------|-----|----|---------|
|                                        | 191/553 (34.5) | 362/533 (65.5) | 0.89     |
|                                        | 168/492 (34.1)  | 324/492 (65.9)  |          |

| History of influenza vaccine ¶¶       | Every Year | Most Years | Some Years | Rarely or Never |
|---------------------------------------|------------|------------|------------|-----------------|
| Yes                                   | 159/550 (28.9) | 290/504 (57.5) | 35/504 (7.0) | 81/504 (16.1) |
|                                       | 10/2       | 1.9        | 3.0        | 4.8             |
|                                       | <0.01      | <0.01      | <0.01      | <0.01           |

| Receipt of current season influenza vaccine ¶¶ | Yes | No | p-value |
|------------------------------------------------|-----|----|---------|
|                                               | 201/571 (35.2) | 322/505 (63.8) | 0.0 < 0.1 |
|                                               | 32/4      | 3.2        | <0.01     |
|                                               | <0.01     | <0.01      | <0.01     |

| Adoption of COVID-19 precautions ¶¶         | Always | Often | Rarely or Never |
|---------------------------------------------|--------|-------|-----------------|
|                                             | 271/483 (56.1) | 142/483 (29.4) | 70/483 (14.5) |
|                                             | 334/459 (72.8) | 99/459 (21.6)  | 26/459 (5.7)  |
|                                             | 0.0 < 0.1 | 0.0 < 0.1      | 0.0 < 0.1     |

| School Attendance ¶¶                        | In-person school attendance | No in-person school attendance |
|---------------------------------------------|-----------------------------|-------------------------------|
|                                             | 337/526 (64.1) | 189/526 (35.9) |
|                                             | 358/486 (73.7) | 128/486 (26.3) |
|                                             | 0.0 < 0.1       | 0.0 < 0.1                   |

**Abbreviations:** IQR = Interquartile Range, SVI = Social Vulnerability Index

* COVID-19 vaccination status included the following two categories: 1) unvaccinated, defined as no receipt of any SARS-CoV-2 vaccine before hospitalization and 2) fully vaccinated, defined as receipt of 2 doses of mRNA vaccine before hospitalization.
† Models adjusted for age (continuous), sex, race/ethnicity, and census region.

¥ Scores on the Social Vulnerability Index range from 0 to 1.0, with higher scores indicating greater social vulnerability. Details regarding this index are available on the website of the Agency for Toxic Substances and Disease Registry of the Centers for Disease Control and Prevention at https://www.atsdr.cdc.gov/placeandhealth/svi/index.html. The median scores on the Social Vulnerability Index for case patients and controls are based on 2018 data.

‡ Obesity is defined as clinician documented obesity in the medical record or BMI >= 95th percentile for those with height and weight available (for those without height available weight-for-age percentile >= 90th percentile identified obese children.⁹

¶ Other chronic conditions included, but not limited to, obesity, rheumatologic/autoimmune disorder, hematologic disorder, renal or urologic dysfunction, gastrointestinal/hepatic disorder, metabolic or confirmed or suspected genetic disorder, or atopic or allergic condition.

¶¶ In-person school attendance, prior hospitalization, history of influenza vaccine, and COVID-19 precautions in the past year were based on self-reported data from parent or guardian.
Figure 2