Supplemental Online Content

Dorabawila V, Hoefer D, Bauer U, et al. Effectiveness of the BNT162b2 vaccine among children aged 5 to 11 and 12 to 17 years in New York after the emergence of the Omicron variant. *JAMA*. Published online May 13, 2022. doi:10.1001/jama.2022.7319

eMethods

eFigure. New Cases among Children Newly Vaccinated from December 13, 2021 to January 2, 2022

eReferences

This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods

Data Sources

Four NYS databases were linked to examine COVID-19 outcomes among children 5-17 years. The Citywide Immunization Registry (CIR) and the NYS Immunization Information System (NYSIIS) collect COVID-19 provider vaccination data for residents of New York City and the rest of NYS, respectively. The Electronic Clinical Laboratory Reporting System (ECLRS) collects all reportable COVID-19 test results. The Health Electronic Response Data System (HERDS) includes a statewide, daily electronic survey of inpatient facilities, including all new admissions with laboratory-confirmed COVID-19 and the primary reason for admission.

Dataset construction

Vaccination registry (NYSIIS/CIR) COVID-19 data were combined and deduplicated based on first name, last name, date of birth (DOB), and ZIP code then matched to laboratory data (ECLRS) using a deterministic algorithm based on first name, last name, and DOB, and to hospital admissions (HERDS) based on initials, sex, DOB, and ZIP code. Partially and fully-vaccinated children in each age group were subtracted from the census population in the applicable age groups to arrive at the unvaccinated children count. Partially-vaccinated children in each weekly period were excluded from the analyses. Children vaccinated during a weekly period and those with one dose were considered partially-vaccinated.

COVID-19 cases include all laboratory confirmed positive nucleic acid amplification test (NAAT) or antigen results reported to ECLRS based on the most recent specimen collection date[1]. While some antigen tests have lower sensitivity compared to NAAT[2,3,4], these are all laboratory confirmed positive tests. In NYS, about 25% of laboratory confirmed results are antigen and thus are included in all reporting and analysis. COVID-19 hospitalizations were admissions reported to HERDS. Fully-vaccinated is defined as series completion plus 14 days.

US Food and Drug Administration emergency use authorization for children 16-17 years was given on December 11, 2020, for 12-15 years on May 10, 2021 and for 5-11 years on October 29, 2021. With Advisory Committee on Immunization Practices (ACIP) approval on November 2, 2021 for children 5-11 years, the earliest period with sufficient children aged 5-11 fully-vaccinated (4.7%) was the week of December 13-19. Thus, this is the first week possible for open cohort comparisons between the two age groups.

Unvaccinated populations were estimated as census population minus partially and fully-vaccinated populations. Partially-vaccinated children were excluded from analysis -both numerators and denominators. Data management and summarization was conducted in SAS (version 9.4; SAS Institute).

Weekly cohort analysis – *statistical methods*

Confidence intervals for incidence rate ratios (IRR) comparing vaccinated vs. unvaccinated children for the cases outcome were estimated using standard approximate Normal distribution methods.[5] For the outcome of hospitalizations, which were more sparse, we used the exact mid-P Fisher method[6]. OpenEpi was used to estimate these confidence intervals[7].

Time since vaccination analysis

This analysis included three weekly cohorts of children who completed the primary series from December 13, 2021 to January 2, 2022. The follow-up period from January 3-30 allowed observation of outcomes for a minimum of 4 weeks for each group and during period when Omicron prevalence was high. The number of children aged 5-11 years included in this analysis was higher compared to those 12-17 years, largely due to a function of when the vaccine was authorized for these age groups.

Outcomes among the three weekly cohorts were arranged into time-since-vaccination categories during the four January 3-30, 2022 follow-up weeks by combining cohorts as illustrated via colored diagonal cells in eFigure. For example, cases within ≤13 days of full-vaccination (grey shading) are children that were vaccinated between December 27-January 2 with an outcome window between January 3-9, 2022. Similarly, cases 28-34 days after full-vaccination (light-blue shading) represented the sum of the following 3 groups: (1) persons vaccinated between December 12-19 and with cases between January 10-16;(2) persons vaccinated between December 20-26 and with cases between January 17-; and (3) persons vaccinated between December 27-January 2 and with cases between January 24-30.

Incident case rates among the vaccinated, by time-since-vaccination interval, were constructed. The numerator, cases, was the sum in each time-since-vaccination group. If we consider cases between 28-34 days, there were 3 vaccination groups (light blue) that were combined, per the colored diagonals in eFigure. The denominator is the person days of children observed fully-vaccinated during the time-since-vaccination interval and contributing to the numerator (pink shading). In the example of 28-34 days, all three weekly cohorts were vaccinated for that interval, thus total person days from the 3 weeks for children 5-11 years contributed to the denominator. Thus incidence rates for those vaccinated (R_V) were $R_V = \frac{\sum_{i=1}^{k} C_{V,i}}{\sum_{i=1}^{k} N_{V,i}}$, with $var(R_V) = \frac{\sum_{i=1}^{k} C_{V,i}}{\left(\sum_{i=1}^{k} N_{V,i}\right)^2}$, where i is the cohort, k is the number of cohorts combined, $C_{V,i}$ is the number of cases among vaccinated cohort members, and $N_{V,i}$ is the number of vaccinated person days observed in the cohort for the interval.[5]

Rates among an unvaccinated comparison group were constructed from unvaccinated rates in the same weeks contributing to a given time-since-vaccination interval, directly standardized to the person-time of those vaccinated, as follows. The directly-standardized rate for the unvaccinated (DSR_U), was estimated as $DSR_U = \frac{\sum_{i=1}^{k} N_{V,i} R_{U,i}}{\sum_{i=1}^{k} N_{V,i}}$, with $var(DSR_U) = \frac{\sum_{i=1}^{k} \frac{(N_{V,i})^2 R_{U,i}}{N_{U,i}}}{\left(\sum_{i=1}^{k} N_{V,i}\right)^2}$, where $R_{U,i}$ is the unvaccinated case rate ($\frac{C_{U,i}}{N_{U,i}}$, cases among unvaccinated / unvaccinated persons, as calculated for the open-cohort method) and $N_{U,i}$ is number of unvaccinated persons in a given week contributing to the interval .[8,9]

The incidence rate ratio (IRR) for each time-since-vaccination interval was estimated as $IRR = \frac{DSR_U}{R_V}$, with $var(ln[IRR]) = \frac{var(R_V)}{R_V^2} + \frac{var(DSR_U)}{DSR_U^2}$, and $95\%\ CI = e^{\ln(IRR) \pm 1.96\sqrt{var(\ln(IRR))}}$.[6,7.] The computations were implemented in Excel.

eFigure: New Cases among Children Newly Vaccinated from December 13, 2021 to January 2, 2022[a]

Cohort	Person Days Newly Vaccinated	Follow Up Week: Jan 3 – 9	Jan 10-16	Jan 17-23	Jan 24-30
5-11 Years					
Dec 13-19	$N_{V,i}$	$C_{V,i}$	$C_{V,i}$	$C_{V,i}$	$C_{V,i}$
Dec 20-26	$N_{V,i}$	$C_{V,i}$	$C_{V,i}$	$C_{V,i}$	$C_{V,i}$
Dec 27-Jan 2	$N_{V,i}$	$C_{V,i}$	$C_{V,i}$	$C_{V,i}$	$C_{V,i}$
12-17 Years					
Dec 13-19	$N_{V,i}$	$C_{V,i}$	$C_{V,i}$	$C_{V,i}$	$C_{V,i}$
Dec 20-26	$N_{V,i}$	$C_{V,i}$	$C_{V,i}$	$C_{V,i}$	$C_{V,i}$
Dec 27-Jan 2	$N_{V,i}$	$C_{V,i}$	$C_{V,i}$	$C_{V,i}$	$C_{V,i}$

[a] Days since full vaccination are indicated in background color: Grey: <=13 days, Orange: 14-20 days, Yellow: 21-27 days, Light-blue: 28-34 days, Green: 35-41 days, Dark-blue: 42-48 days. Person days is shaded in pink.

eReferences

1. Rosenberg ES, Holtgrave DR, Dorabawila V, et al. New COVID-19 Cases and Hospitalizations Among Adults, by Vaccination Status—New York, May 3–July 25, 2021. MMWR Morb Mortal Wkly Rep 2021;70:1306–11. doi: https://doi.org/10.15585/mmwr.mm7037a7external icon PMID:34529645

2. US Food and Drug Administration. Omicron Variant: Impact on Antigen Diagnostic Tests (As of 12/28/2021). SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests. https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests#omicronvariantimpact.

3. Soni A, Herbert C, Filippaios A, Broach J at al. Comparison of Rapid Antigen Tests' Performance between Delta (B.1.61.7; AY.X) and Omicron (B.1.1.529; BA1) Variants of SARS-CoV-2: Secondary Analysis from a Serial Home Self-Testing Study. medRxiv. 2022 Mar 2:2022.02.27.22271090. doi: 10.1101/2022.02.27.22271090.

4. Osterman A, Badell I, Basara E, et al. Impaired detection of omicron by SARS-CoV-2 rapid antigen tests. Med Microbiol Immunol. 2022 Feb 20:1-13. doi: 10.1007/s00430-022-00730-z

5. Lash TL, VanderWeele TJ, Haneuse S, Rothman KJ. *Modern Epidemiology* (4th ed.). Philadelphia, PA: Wolters Kluwer; 2021

6. Martin DO, Austin H. Exact estimates for a rate ratio. Epidemiology. 1996 Jan;7(1):29-33. doi: 10.1097/00001648-199601000-00006. PMID: 8664397.

7. Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for Public Health, Version. www.OpenEpi.com, updated 2013/04/06, accessed 2022/04/11.

8. Direct Standardization. https://www.statsdirect.com/help/rates/standardize_compare_two_rates.htm.. Accessed on February 9, 2022.

9. Chiang CL. Standard error of the age-adjusted death rate. US Department of Health, Education and Welfare: Vital Statistics Special Reports 1961;47:271-285.