Association of Severe Acute Respiratory Syndrome Coronavirus 2 Vaccination or a Prior Positive Test Result in Adolescents during the Delta Variant Surge in Kentucky

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In a cross-sectional study of 89 736 adolescents in Kentucky, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination provided an estimated protection against infection of 81% when the highly transmissible Delta variant was predominant. Vaccination provided added benefit to those with a history of prior infection. These findings support the recommendation that all adolescents receive SARS-CoV-2 vaccination. *(J Pediatr 2022;248:119-21)*.

Coronavirus disease 2019 (COVID-19) messenger RNA (mRNA) vaccines are effective in preventing severe illness and death caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Delta variant,[1,2] although protection against asymptomatic and mild disease may be reduced compared with previous variants.[3,4] Data for adolescents are limited.[5,6] We evaluated the association of SARS-CoV-2 vaccination or a prior positive test result with subsequent infection (as indicated by a positive test result for SARS-CoV-2) in adolescents during a period when the Delta variant was predominant in Kentucky.

Methods

All antigen and nucleic acid amplification test (eg, reverse-transcription polymerase chain reaction) results in Kentucky are required to be reported to the Kentucky Department for Public Health and are captured in the Kentucky Electronic Disease Surveillance System (EDSS). Adolescents (aged 12-17 years) who underwent SARS-CoV-2 testing during August-September 2021 and had no prior positive result within 90 days were identified using the Kentucky EDSS.

Data for vaccines administered in Kentucky are maintained in the Kentucky Immunization Registry. Vaccination status was determined from review of the Registry for those adolescents who had test results in the EDSS for August and September 2021. Only adolescents vaccinated with an mRNA vaccine (Pfizer-BioNTech or Moderna) were included in the vaccinated group; adolescents who received the Janssen vaccine or a vaccine with unspecified manufacturer prior to the testing date were excluded.

In this analysis, "vaccination" is defined as completion of primary vaccination series ≥14 days prior to the date of testing during the study period (August 1-September 30, 2021); "no vaccination" is defined as no vaccine received prior to the date of testing; and "prior positive test result" is defined as a positive test >90 days prior to a test result during the study period. Those who received only 1 dose of vaccine or completed the primary vaccine series within 14 days of testing were excluded from the analysis. The first test was used for adolescents with multiple tests during the study period with concordant results. Adolescents with both negative and positive test results during the study period were included based on the positive test result.

Prevalence ratios (PRs) and 95% CIs were calculated comparing vaccination and no prior positive test result, no vaccination but a prior positive test result, and vaccination plus a prior positive test result with no vaccination and no prior positive test result. PRs and 95% CIs were calculated for those with prior positive test results in the vaccinated and nonvaccinated groups. PRs also were calculated after adjustment for age and sex. Inclusion of age and sex in the PR calculations changed estimates by <5%; consequently, unadjusted results are reported. Statistical analyses were performed using R version 4.1.0 (R Foundation for Statistical Computing).

This activity was reviewed by the Centers for Disease Control and Prevention and was conducted consistent with applicable federal law and Centers for Disease Control

COVID-19	Coronavirus disease 2019
EDSS	Electronic Disease Surveillance System
mRNA	Messenger RNA
PR	Prevalence ratio
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2

Table I. Selected demographic and test characteristics of adolescents aged 12-17 years tested for SARS-CoV-2 in Kentucky, August-September, 2021

Characteristics	Unvaccinated, no prior infection	Fully vaccinated, no prior infection	Unvaccinated, prior infection	Fully vaccinated, prior infection
Number tested	70 034	15 540	3307	855
Age, y, mean (SD)	14.5 (1.8)	14.8 (1.8)	14.9 (1.7)	15.2 (1.7)
Sex, n (%)				
Female	33 810 (48.3)	7285 (46.9)	1776 (53.7)	496 (58.0)
Male	32 919 (47.0)	6440 (41.4)	1525 (46.1)	356 (41.6)
Unknown	3305 (4.7)	1815 (11.7)	6 (0.2)	3 (0.4)
Race, n (%)				
White	41 444 (59.2)	8885 (57.2)	2566 (77.6)	643 (75.2)
Black	4600 (6.6)	799 (5.1)	225 (6.8)	67 (7.8)
Other	3654 (5.2)	854 (5.5)	146 (4.4)	54 (6.3)
Unknown	20 336 (29.0)	5002 (32.2)	370 (11.2)	91 (10.6)
Ethnicity, n (%)				
Hispanic	2404 (3.4)	504 (3.2)	125 (3.8)	42 (4.9)
Non-Hispanic	45 290 (64.7)	9472 (61.0)	2832 (85.6)	728 (85.1)
Unknown	11 340 (31.9)	5564 (35.8)	350 (10.6)	85 (9.9)
Days since second vaccine dose, median (IQR)	N/A	78 (53-99)	N/A	75 (45-96)
Days from prior positive, median (IQR)	N/A	N/A	240 (200-289)	252 (212-298)

N/A, not applicable.

and Prevention policy (eg, 45 C.F.R. part 46.102(l) (2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.). The data used were collected as part of routine public health surveillance and case investigation, and consequently, this project was determined to be a non-research activity.

Results

Of the 97 690 unique adolescents tested, 16 395 (16.8%) were fully vaccinated, 73 341 (75.1%) were unvaccinated, and 7954 (8.1%) were excluded from the analysis. Excluded individuals were those who received only 1 dose of an mRNA vaccine, completed the primary mRNA vaccine series within 14 days of testing, or received a non-mRNA vaccine (ie, Janssen) outside of authorization. Of the 89 736 adolescents included in the analysis, 4162 (4.6%) had a prior positive test result. Selected demographic and test characteristics are provided in Table I. Race and ethnicity were unknown for nearly 32% of those tested and so were not included in the analyses.

The prevalence of positive test results was 30.4% for adolescents with no vaccination and no prior positive test result, 5.8% for those with vaccination and no prior positive test result, 10.3% for those with no vaccination but a prior positive test result, and 2.3% for those with vaccination plus a prior positive test result (Table II). The estimated protection against infection during the study period illustrated in Table II shows that adolescents who were fully vaccinated and had a history of prior infection had the highest estimated protection (92.3%; 95% CI, 88.0%-95.1%). Among adolescents with a prior positive test result, those who were unvaccinated had a greater likelihood of reinfection compared with those who were vaccinated (PR, 4.4; 95% CI, 2.8%-7.0%). Adjusting for age, sex, and days since prior infection did not substantially change the PR (4.6; 95% CI, 3.0-7.4). Even in the context of a prior positive test result, vaccination provided an estimated protection of 77.4% (95% CI, 64.3%-85.7%).

Discussion

During a time of predominant circulation of the SARS-CoV-2 Delta variant, vaccination provided protection against infection, as indicated by a positive test result, with estimated protection of 81% during a period of substantial to high community transmission (ie, >10 new cases per day per 100 000 persons in the local county). Our results are

Table 2. SARS-CoV-2 prevalence, prevalence ratio, and estimated protection by vaccination status and history of a prior infection among adolescents aged 12-17 years tested in Kentucky, August-September, 2021

Group*	Number tested	Positive (prevalence), n (%)	Prevalence ratio[†] (95% CI)	Estimated protection[‡] (95% CI)
Unvaccinated, prior infection	3307	342 (10.3)	0.340 (0.304-0.380)	66.0% (62.0-69.6)
Fully vaccinated, no prior infection	15 540	898 (5.8)	0.190 (0.177-0.203)	81.0% (79.7-82.3)
Fully vaccinated, prior infection	855	20 (2.3)	0.077 (0.049-0.120)	92.3% (88.0-95.1)

*Referent was 'unvaccinated, no prior infection' (n = 70 034; positive 21 308 [30.4%]).
†Prevalence ratio (PR) equals prevalence in group of interest divided by prevalence in referent group, with 95% CI.
‡Estimated protection calculated as (1-PR) × 100%, with associated 95% CI.

compatible with those of Reis et al, who reported vaccine effectiveness of 90% among adolescents aged 12-18 years at 7-21 days after completion of the Pfizer-BioNTech 2-dose series during a time when the Delta variant was predominant in Israel.[6] Vaccine effectiveness against COVID-19 hospitalization was estimated as 93% in a recent study including 19 US pediatric hospitals.[7]

Adolescents with history of infection can be reinfected, and the likelihood of reinfection may be influenced by various factors, including the characteristics of the initial infection, underlying immune status of the individual, time since initial infection, and specifics of an exposure. In the current study, a prior positive test result provided an estimated protection against reinfection of 66% during the study period. Additional data on protection from reinfection after initial SARS-CoV-2 infection in adolescents are lacking, but the estimated protection in the current study is lower than that obtained for adults aged 20-39 years in a 2020 study of cases in Kentucky. Estimated protection against reinfection in that study was 81%, but the study was performed in the pre-Delta era and used a different study design.[8] In an adult population, the positive benefit of vaccination in those with history of a positive test result was reported from Kentucky (pre-Delta), where reinfected adults had more than twice the odds of being unvaccinated compared with controls without reinfection.[9]

The findings in this report are subject to some limitations. Inconsistencies between data sources may have led to incorrect vaccination classification; a positive result in an individual with prior infection might have reflected persistence of virus; reasons for testing were unknown and might not have been consistent across subpopulations (eg, vaccinated vs unvaccinated); and individuals with vaccination or prior infection may have been more likely to be tested only when symptomatic, potentially underestimating protection against infection. False-positive and false-negative results could have resulted in case misclassification. Vaccination was within 6 months for most of those vaccinated, so the duration of protection and waning of vaccine-derived immunity could not be addressed. Prior infection could have occurred up to 16 months earlier, precluding direct comparisons of the protection provided by prior infection and by vaccination. Any potential impact of race and ethnicity could not be evaluated owing to missing data; unmeasured confounders also may have played a role. This primarily laboratory-based study did not allow for evaluation of clinical outcomes. Finally, data were from a single state and time, and thus our findings might not be generalizable.

Fully vaccinated adolescents were well protected from infection when community transmission was substantial to high and the Delta variant was predominant in Kentucky. Among adolescents with a prior positive test result but no vaccination who were tested during the study period, the unvaccinated were 4 times more likely than the vaccinated to have a positive result. Unless otherwise contraindicated, vaccination is recommended for all adolescents, regardless of infection history.[10] ∎

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