CORRESPONDENCE

Effectiveness of BNT162b2 Vaccine against Delta Variant in Adolescents

TO THE EDITOR: The B.1.617.2 (delta) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has emerged as the dominant strain circulating in many regions worldwide. The BNT162b2 mRNA vaccine against coronavirus disease 2019 (Covid-19) was found to be effective in preventing infection with the delta variant in a recent observational study,[1] but other reports have suggested reduced vaccine effectiveness against this variant.[2,3] On May 10, 2021, the U.S. Food and Drug Administration approved the emergency use of BNT162b2 in adolescents 12 years of age or older on the basis of a clinical trial that had been conducted before the delta variant had become prevalent in the United States.[4] Additional evidence was needed regarding the effectiveness of the BNT162b2 vaccine among adolescents, particularly against the delta variant.

We sought to estimate the vaccine effectiveness of BNT162b2 against the delta variant among vaccinated adolescents for whom an unvaccinated match was found. We used data from Clalit Health Services, the largest health care organization in Israel, to conduct an observational cohort study involving adolescents between the ages of 12 and 18 years who had no prior SARS-CoV-2 infection noted in their electronic medical record and who had been vaccinated between June 8 and September 14, 2021. According to the sequencing of samples obtained from infected persons that was performed by the Israeli Ministry of Health during this period, the delta variant was responsible for more than 95% of new infections in the general population in Israel.

We used the same methods that were used in our previous studies of vaccine effectiveness, which were conducted in the same health care organization using the same database.[5] (See the Methods section in the Supplementary Appendix, available with the full text of this letter at NEJM.org.) Vaccine effectiveness was defined as 1 minus the risk ratio, which was estimated over several follow-up periods for documented SARS-CoV-2 infection and symptomatic Covid-19. More severe outcomes related to Covid-19 are rare in this age group.

Of 184,905 vaccinated adolescents, 130,464 met the eligibility requirements, and 94,354 of these vaccine recipients were successfully matched with 94,354 unvaccinated controls (Fig. S1 and the Methods section in the Supplementary Appendix). The eligible population was similar to the matched population with respect to several demographic and clinical characteristics (Tables S1 and S2). The frequency of polymerase-chain-reaction testing for SARS-CoV-2 was similar in the vaccinated and unvaccinated populations (9.4 and 9.9 tests per 100 persons per week, respectively). The median follow-up was 27 days after baseline, which was defined as the administration of the first dose among the vaccine recipients. Kaplan–Meier curves for SARS-CoV-2 infection in both the vaccinated and unvaccinated groups were similar during the initial days, after which the incidence began to rise more slowly in the vaccinated group (Table 1 and Fig. S2).

The estimated vaccine effectiveness against documented SARS-CoV-2 infection was 59% (95% confidence interval [CI], 52 to 65) on days 14 through 20 after the first dose, 66% (95% CI, 59 to 72) on days 21 to 27 after the first dose, and 90% (95% CI, 88 to 92) on days 7 to 21 after the second dose. The estimated vaccine effectiveness against symptomatic Covid-19 was 57% (95% CI, 39 to 71) on days 14 to 20 after the first dose, 82% (95% CI, 73 to 91) on days 21 to 27 after the first dose, and 93% (95% CI, 88 to 97) on days 7 to 21 after the second dose.

In a recent randomized trial involving 1983 vaccinated adolescents between the ages of 12 and 15 years with no history of SARS-CoV-2 infection, investigators estimated that the vaccine effectiveness of two doses of BNT162b2 was 100% (95% CI, 75 to 100) against symptomatic infection by non-delta variants.[4] The present observational study provides substantially more precise

Table 1. Effectiveness of BNT162b2 Vaccine among Adolescents.*

Time Period	Documented SARS-CoV-2 Infection				Symptomatic Covid-19			
	Unvaccinated Group	Vaccinated Group	Vaccine Effectiveness (95% CI)	Risk Difference (95% CI)	Unvaccinated Group	Vaccinated Group	Vaccine Effectiveness (95% CI)	Risk Difference (95% CI)
	events (no. at risk)		%	*no. of events/ 100,000 persons*	*events (no. at risk)*		%	*no. of events/ 100,000 persons*
Days 14–20 after first dose	463 (69,408)	192 (69,609)	59 (52–65)	436.5 (363.1–510.2)	95 (70,203)	41 (70,227)	57 (39–71)	86.1 (49.0–123.7)
Days 21–27 after first dose	400 (56,997)	137 (57,358)	66 (59–72)	514.7 (423.1–590.6)	84 (57,803)	15 (57,878)	82 (73–91)	133.0 (101.1–169.4)
Days 7–21 after second dose	818 (46,384)	79 (46,815)	90 (88–92)	2032.7 (1866.3–2184.6)	151 (47,194)	11 (47,303)	93 (88–97)	379.6 (317.0–451.3)

* Data are for adolescents between the ages of 12 and 18 years who were members of Clalit Health Services from June 8 to September 14, 2021. The study population included 94,354 adolescents in both the unvaccinated and vaccinated groups.

estimates of vaccine effectiveness among adolescents between the ages of 12 and 18 years for both documented infection and symptomatic disease in a setting in which the delta variant was predominant. Our estimates of the effectiveness of two doses of the BNT162b2 vaccine against the delta variant among adolescents are similar to estimates of effectiveness against the alpha variant in the general population with the use of the same study design[5] and are similar to the estimate of 88% (95% CI, 85 to 90) against the delta variant in the general population in an observational study that used a different design.[1]

Our results show that the BNT162b2 mRNA vaccine was highly effective in the first few weeks after vaccination against both documented infection and symptomatic Covid-19 with the delta variant among adolescents between the ages of 12 and 18 years.

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