Covid-19 Vaccine Protection among Children and Adolescents in Qatar

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ABSTRACT

BACKGROUND

The BNT162b2 vaccine against coronavirus disease 2019 (Covid-19) has been authorized for use in children 5 to 11 years of age and adolescents 12 to 17 years of age but in different antigen doses.

METHODS

We assessed the real-world effectiveness of the BNT162b2 vaccine against infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) among children and adolescents in Qatar. To compare the incidence of SARS-CoV-2 infection in the national cohort of vaccinated participants with the incidence in the national cohort of unvaccinated participants, we conducted three matched, retrospective, target-trial, cohort studies — one assessing data obtained from children 5 to 11 years of age after the B.1.1.529 (omicron) variant became prevalent and two assessing data from adolescents 12 to 17 years of age before the emergence of the omicron variant (pre-omicron study) and after the omicron variant became prevalent. Associations were estimated with the use of Cox proportional-hazards regression models.

RESULTS

Among children, the overall effectiveness of the 10-μg primary vaccine series against infection with the omicron variant was 25.7% (95% confidence interval [CI], 10.0 to 38.6). Effectiveness was highest (49.6%; 95% CI, 28.5 to 64.5) right after receipt of the second dose but waned rapidly thereafter and was negligible after 3 months. Effectiveness was 46.3% (95% CI, 21.5 to 63.3) among children 5 to 7 years of age and 16.6% (95% CI, −4.2 to 33.2) among those 8 to 11 years of age. Among adolescents, the overall effectiveness of the 30-μg primary vaccine series against infection with the omicron variant was 30.6% (95% CI, 26.9 to 34.1), but many adolescents had been vaccinated months earlier. Effectiveness waned over time since receipt of the second dose. Effectiveness was 35.6% (95% CI, 31.2 to 39.6) among adolescents 12 to 14 years of age and 20.9% (95% CI, 13.8 to 27.4) among those 15 to 17 years of age. In the pre-omicron study, the overall effectiveness of the 30-μg primary vaccine series against SARS-CoV-2 infection among adolescents was 87.6% (95% CI, 84.0 to 90.4) and waned relatively slowly after receipt of the second dose.

CONCLUSIONS

Vaccination in children was associated with modest, rapidly waning protection against omicron infection. Vaccination in adolescents was associated with stronger, more durable protection, perhaps because of the larger antigen dose. (Funded by Weill Cornell Medicine–Qatar and others.)
The messenger RNA (mRNA) vaccine BNT162b2 (Pfizer–BioNTech) against coronavirus disease 2019 (Covid-19) has been authorized for use in adolescents 12 to 17 years of age and in children 5 to 11 years of age but in antigen doses of 30 μg and 10 μg, respectively.1,2 Qatar launched mass Covid-19 immunization campaigns using these vaccines, first involving adolescents in several phases starting in February 2021 and then involving children 5 to 11 years of age starting in February 2022 (Section S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org).

We assessed the real-world effectiveness of the two-dose primary vaccine series against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection for the 10-μg dose of BNT162b2 vaccine among children and the 30-μg dose of BNT162b2 vaccine among adolescents. Assessment was part of a national study in Qatar, a country that has experienced five SARS-CoV-2 waves, dominated sequentially by the index virus,3 the B.1.1.7 (alpha) variant,4 the B.1.351 (beta) variant,5 the B.1.1.529 (omicron) subvariants BA.1 and BA.2,6 and the omicron subvariants BA.4 and BA.5,7 in addition to a prolonged low-incidence phase dominated by the B.1.617.2 (delta) variant.8

Methods

Study Population and Data Sources

We conducted this study in Qatar and analyzed data from the national, federated databases for Covid-19 laboratory testing, vaccination, hospitalization, and death, retrieved from the integrated, nationwide, digital-health information platform. These databases include all SARS-CoV-2–related data, such as results from all polymerase-chain-reaction (PCR) tests, and associated demographic information, with no missing information since the onset of the pandemic. The databases also include results from rapid antigen tests that were conducted at health care facilities starting from January 5, 2022. Rapid antigen test kits are available for purchase in pharmacies in Qatar, but outcomes of home-based testing are not reported in the national databases and thus were not factored in our study, including in the estimations of cumulative incidence or incidence rate. Detailed descriptions of the population of Qatar and of the national databases have been reported previously.3,5,6,9,10

Study Design and Cohorts

Three matched, retrospective cohort studies emulating randomized target trials10,11 were conducted to investigate the effectiveness of the BNT162b2 vaccine among children 5 to 11 years of age and among adolescents 12 to 17 years of age at least 14 days after the receipt of the second vaccine dose. The target of estimation was the effect of being vaccinated among persons who received the vaccine; the average treatment effect among treated persons quantifies vaccine effectiveness among the subpopulation that was vaccinated.

In each study, the incidence of infection or of severe,12 critical,12 or fatal13 Covid-19 was compared between the national cohort of previously uninfected persons who had completed the two-dose BNT162b2 primary series (designated as the vaccinated cohort) and the national control cohort of persons who were previously uninfected and were unvaccinated (designated as the control cohort). The focus of the studies was on vaccine-related immunity and not on a hybrid immunity of previous infection and vaccination. Persons with a record of previous infection were excluded.

Documentation of infection was based on positive PCR or rapid antigen testing. Laboratory methods are presented in Section S2. To inform the national Covid-19 response in Qatar, 5% of positive cases are targeted for viral-genome sequencing, and a larger proportion is targeted for genotyping with the use of multiplex real-time reverse-transcriptase PCR variant screening. The classification of Covid-19 cases as being severe (acute care hospitalization),12 critical (hospitalization in the intensive care unit),12 or fatal13 followed World Health Organization guidelines (Section S3).

Cohort Matching and Follow-up

Vaccinated persons were matched one to one with unvaccinated persons in the control cohort according to sex, age, nationality, and number of coexisting conditions (none, one, or two or more) in order to account for differences in SARS-CoV-2 exposure risk in Qatar.3,14-17 Matching according to these factors was previously shown to provide adequate control of differences in exposure risk in Qatar.3,18-21

Matching was also done according to the calendar month of receipt of the second vaccine dose for the vaccinated cohort and the calendar month of receipt of a SARS-CoV-2–negative test for the
control cohort. That is, persons who received their second vaccine dose in a specific month were matched with unvaccinated persons who had a record of a SARS-CoV-2–negative test in that same calendar month, to ensure that these persons were in Qatar at the same time. Matching was performed iteratively such that persons in the control cohort were alive, infection-free, and unvaccinated at the start of follow-up.

Each matched pair was followed from the calendar day on which the vaccinated person had completed 14 days after receiving the second dose. To ensure exchangeability, data on both members of each matched pair were censored when the vaccinated participant received a third (booster) dose or when a control participant received a first dose of vaccine. Participants were followed until the first of any of the following events: documented SARS-CoV-2 infection (defined as the first positive PCR or rapid antigen test after the start of follow-up, regardless of the presence of symptoms), booster vaccination in participants who had received the primary vaccine series (with matched-pair censoring), receipt of the first dose of vaccine in control participants (with matched-pair censoring), death, or the end of the study. Many participants contributed follow-up time first as unvaccinated persons (before receipt of the first dose), while being matched with vaccinated persons, and subsequently contributed follow-up time as vaccinated persons (after receipt of the second dose) while being matched with unvaccinated persons. Allowing such crossover in the study design may reduce potential differences arising from unmeasured risk behaviors related to vaccination or infection status.

**Omicron 10-μg BNT162b2 Study Involving Children**

In the omicron study involving children, we estimated the effectiveness of the pediatric 10-μg dose of the BNT162b2 vaccine against omicron infection among children 5 to 11 years of age. Virtually all cases of SARS-CoV-2 infection since the onset of the omicron wave have been due to omicron subvariants. Any child who had received two doses of vaccine between February 3, 2022 (earliest record of two-dose vaccination in children), and July 12, 2022 (end of study), was eligible for inclusion in the vaccinated cohort on day 14 after receipt of the second dose, provided that the child had no record of SARS-CoV-2 infection before the start of follow-up. Any child with a SARS-CoV-2–negative test during the study was eligible for inclusion in the control cohort, provided that the child had no record of infection or vaccination before the start of follow-up.

**Pre-Omicron 30-μg BNT162b2 Study Involving Adolescents**

In the pre-omicron study, we estimated the effectiveness of the 30-μg dose of the BNT162b2 vaccine against SARS-CoV-2 infection before the emergence of the omicron variant (pre-omicron period) among adolescents 12 to 17 years of age. Any adolescent who had received two doses of the BNT162b2 vaccine between February 1, 2021 (earliest record of two-dose vaccination in adolescents), and November 30, 2021 (end of study), was eligible for inclusion in the vaccinated cohort, provided that the adolescent had no record of infection before the start of follow-up. Follow-up was from day 14 after receipt of the second dose until November 30, 2021 (first evidence of the omicron variant in Qatar), to ensure that incidence was due to a pre-omicron variant. Any adolescent with a SARS-CoV-2–negative test during the study was eligible for inclusion in the control cohort, provided that the adolescent had no record of infection or vaccination before the start of follow-up.

**Omicron 30-μg BNT162b2 Study Involving Adolescents**

In the omicron study involving adolescents 12 to 17 years of age, we estimated the effectiveness of the 30-μg dose of the BNT162b2 vaccine against infection with the omicron variant. Any adolescent who had received two doses of the BNT162b2 vaccine between February 1, 2021, and July 12, 2022 (end of study), was eligible for inclusion in the vaccinated cohort, provided that the adolescent had no record of infection or receipt of a third dose of vaccine before the start of follow-up. Follow-up was from December 19, 2021 (onset of the omicron wave in Qatar), if the second dose of vaccine had been received at least 14 days before this date (i.e., before the omicron wave) and from day 14 after receipt of the second dose otherwise. Any adolescent with a SARS-CoV-2–negative test between February 1, 2021, and July 12, 2022, was eligible for inclusion in the control cohort, provided that the adolescent had no record of infection or vaccination before the start of follow-up.
before the start of follow-up. The study was replicated to estimate the effectiveness of a third (booster) 30-μg dose of the BNT162b2 vaccine against omicron infection among adolescents 12 to 17 years of age.

OVERSIGHT
The institutional review boards at Hamad Medical Corporation and Weill Cornell Medicine–Qatar approved this retrospective study with a waiver of informed consent. The study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Table S1). The authors vouch for the accuracy and completeness of the data and for the fidelity of the study to the protocol. The data set used in this study is the property of the Ministry of Public Health of Qatar and was provided to the researchers through a restricted-access agreement for the preservation of confidentiality of patient data. The funders had no role in the study design; the collection, analysis, or interpretation of the data; or the writing of the manuscript.

STATISTICAL ANALYSIS
The eligible and matched cohorts were described with the use of frequency distributions and measures of central tendency; the study groups within the cohorts were compared with the use of standardized mean differences. A standardized mean difference of 0.1 or less indicated adequate matching. The Kaplan–Meier estimator method was used to estimate the cumulative incidence of infection, which was defined as the proportion of persons who became infected, out of those who were at risk; the primary end point during follow-up was a breakthrough infection in the vaccinated cohort or an infection in the control cohort. The incidence rate of infection in each cohort, defined as the number of identified infections divided by the number of person-weeks contributed by all persons in the cohort, was estimated, with a corresponding 95% confidence interval, with the use of a Poisson log-likelihood regression model with the stptime command in Stata software, version 17.0. The number of averted infections was estimated from the difference in the cumulative incidence curves. The number of averted infections was estimated from the cumulative incidence curves. The incidence of vaccine-preventable infection was estimated as the vaccine effectiveness multiplied by the incidence rate among control participants.23

Sensitivity analyses with adjustment for the effectiveness estimates for differences in testing frequency between cohorts were conducted. Statistical analyses were conducted with the use of Stata/SE software, version 17.0 (StataCorp).

RESULTS
OMICRON 10-μg BNT162B2 STUDY INVOLVING CHILDREN
Figure S1 shows the process of selection of the study population. Table 1 describes the characteristics of the participants in the full study population and the matched cohorts. Each matched cohort included 18,728 children. The study was conducted in the total pediatric population of Qatar; thus, the study population is broadly representative of the pediatric population of Qatar (Table S2).
The median follow-up was 69 days (interquartile range, 31 to 97) in the vaccinated cohort and 69 days (interquartile range, 30 to 97) in the control cohort (Fig. 1A). During follow-up, there were 184 infections in the vaccinated cohort and 248 infections in the control cohort. None of the infections progressed to severe, critical, or fatal Covid-19. The incidence of infection coincided...
The cumulative incidence of infection at 110 days after the start of follow-up was 2.1% (95% confidence interval [CI], 1.7 to 2.4) in the vaccinated cohort and 2.4% (95% CI, 2.0 to 2.7) in the control cohort (Fig. 1A).

The overall hazard ratio for infection, which was adjusted for sex, age, nationality group, number of coexisting conditions, and calendar month of the second vaccine dose or the SARS-CoV-2-negative test, was 0.74 (95% CI, 0.61 to 0.90) (Table 2). The overall vaccine effectiveness against omicron infection was 25.7% (95% CI, 10.0 to 38.6). Effectiveness decreased with time after receipt of the second vaccine dose (Fig. 1B). Effectiveness was highest (49.6%; 95% CI, 28.5 to 64.5) right after receipt of the second dose but waned rapidly thereafter and was 11.0% (95% CI, −26.8 to 37.5) by the third month after receipt of the second dose.

Vaccine effectiveness was 46.3% (95% CI, 21.5 to 63.3) among children 5 to 7 years of age and 16.6% (95% CI, −4.2 to 33.2) among those 8 to 11 years of age. The median date of the second vaccine dose was April 14, 2022, among children 5 to 7 years of age and April 10, 2022, among those 8 to 11 years of age. Overall, effectiveness according to year of age showed a declining trend (Fig. S2A). Effectiveness against symptomatic infection was 36.9% (95% CI, −29.9 to 69.4). The number needed to vaccinate to prevent one infection was 333.3. The incidence rate of vaccine-preventable infection was 3.7 cases per 10,000 person-weeks.

**PREOMICRON 30-μG BNT162B2 STUDY INVOLVING ADOLESCENTS**

Figure S3 shows the process of selection of the study population. Table 3 describes the characteristics of the participants in the full study population and the matched cohorts. Each matched cohort included 23,317 adolescents.

The median follow-up was 45 days (interquartile range, 16 to 88) in the vaccinated cohort and 43 days (interquartile range, 15 to 85) in the control cohort (Fig. 2A). During follow-up, there were 67 infections in the vaccinated cohort and 523 infections in the control cohort. None of the infections progressed to severe, critical, or fatal Covid-19. Infections coincided with the time that the alpha, beta, and especially delta variants were predominant.\(^8\)\(^9\)\(^24\) The cumulative incidence of infection at 135 days after the start of follow-up was 2.5% in the vaccinated cohort and 2.0% in the control cohort (Fig. 2B). The overall vaccine effectiveness against symptomatic infection was 23.0% (95% CI, 10.5 to 35.4). The number needed to vaccinate to prevent one infection was 431.8. The incidence rate of vaccine-preventable infection was 3.4 cases per 10,000 person-weeks.
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was 0.8% (95% CI, 0.6 to 1.0) in the vaccinated cohort and 4.1% (95% CI, 3.7 to 4.6) in the control cohort (Fig. 2A).

The overall adjusted hazard ratio for infection was 0.12 (95% CI, 0.10 to 0.16) (Table 2). The overall vaccine effectiveness against pre-omicron infection was 87.6% (95% CI, 84.0 to 90.4). Effectiveness decreased with time after receipt of the second vaccine dose (Fig. 3A). Effectiveness was highest (95.3%; 95% CI, 92.0 to 97.2) right after the second dose but waned slowly thereafter.

Vaccine effectiveness was 89.4% (95% CI, 84.5 to 92.7) among adolescents 12 to 14 years of age and 85.7% (95% CI, 79.7 to 89.8) among those 15 to 17 years of age. The median date of the second vaccine dose was August 23, 2021, among adolescents 12 to 14 years of age and July 14, 2021, among those 15 to 17 years of age. Effectiveness according to year of age was stable (Fig. S2B).

Effectiveness against symptomatic infection was 91.2% (95% CI, 84.8 to 94.9). The number needed to vaccinate to prevent one infection was 30.3. The incidence rate of vaccine-preventable infection was 24.7 cases per 10,000 person-weeks.

**Table 2. Effectiveness of the BNT162b2 Vaccine against SARS-CoV-2 Infection among Children and Adolescents in Qatar.**

| Epidemiologic Measure | Vaccinated Cohort | Control Cohort | Effectiveness (95% CI) |
|-----------------------|-------------------|----------------|------------------------|
| **Children 5–11 yr of age, omicron study** | | | |
| Total follow-up — no. of person-wk | 173,451 | 173,082 | |
| Incidence rate of infection per 10,000 person-wk (95% CI) | 10.6 (9.2–12.3) | 14.3 (12.7–16.2) | |
| Hazard ratio for infection with an omicron subvariant (95% CI) | 0.74 (0.61–0.90) | — | 25.7 (10.0–38.6) |
| Unadjusted analysis | 0.74 (0.61–0.90) | — | 25.7 (10.0–38.6) |
| Adjusted analysis* | | | |

| **Adolescents 12–17 yr of age, pre-omicron study** | | | |
| Total follow-up — no. of person-wk | 192,309 | 185,751 | |
| Incidence rate of infection per 10,000 person-wk (95% CI) | 3.5 (2.7–4.4) | 28.2 (25.8–30.7) | |
| Hazard ratio for infection with a pre-omicron subvariant (95% CI) | 0.13 (0.10–0.16) | — | 87.5 (83.8–90.3) |
| Unadjusted analysis | 0.12 (0.10–0.16) | — | 87.6 (84.0–90.4) |
| Adjusted analysis* | | | |

| **Adolescents 12–17 yr of age, omicron study** | | | |
| Total follow-up — no. of person-wk | 338,838 | 319,291 | |
| Incidence rate of infection per 10,000 person-wk (95% CI) | 74.4 (71.5–77.3) | 104.5 (101.0–108.1) | |
| Hazard ratio for infection with an omicron subvariant (95% CI) | 0.72 (0.69–0.76) | — | 27.7 (23.8–31.3) |
| Unadjusted analysis | 0.69 (0.66–0.73) | — | 30.6 (26.9–34.1) |
| Adjusted analysis* | | | |

* The Cox regression analysis was adjusted for sex, age, nationality, number of coexisting conditions, and calendar month of receipt of the second vaccine dose for the vaccinated participant or the SARS-CoV-2–negative test for the control participant.
Table 3. Baseline Characteristics of Adolescents 12 to 17 Years of Age in Two Studies of Effectiveness of the 30-μg Dose of the BNT162b2 Vaccine.*

| Characteristic | Pre-Omicron Study | Omicron Study |
|---------------|-------------------|---------------|
|               | Vaccinated Cohort | Control Cohort | Matched Cohorts† | Vaccinated Cohort | Control Cohort | Matched Cohorts† |
|               | (N = 81,647)      | (N = 66,006)  | SMD‡              | (N = 89,505)      | (N = 86,280)  | SMD‡              |

**Age**

| Distribution — no. (%) | Pre-Omicron Study | Omicron Study |
|------------------------|-------------------|---------------|
| 12 yr                  | 3,174 (3.9)       | 2,767 (11.9)  |
| 13 yr                  | 16,581 (20.3)     | 17,713 (19.8) |
| 14 yr                  | 16,427 (20.1)     | 17,218 (19.2) |
| 15 yr                  | 15,675 (19.2)     | 16,259 (18.2) |
| 16 yr                  | 14,998 (18.4)     | 15,447 (17.3) |
| 17 yr                  | 14,792 (18.1)     | 15,003 (16.8) |

**Sex — no. (%)**

| Male                  | 41,191 (51.3)     | 45,936 (51.3)  |
| Female                | 39,728 (48.7)     | 43,569 (48.7)  |

**Nationality — no. (%)¶**

| Nationality          | Pre-Omicron Study | Omicron Study |
|----------------------|-------------------|---------------|
| Bangladeshi          | 1,054 (1.3)       | 414 (2.3)     |
| Egyptian             | 8,894 (10.9)      | 2,051 (11.5)  |
| Filipino             | 3,029 (3.7)       | 345 (1.9)     |
| Indian               | 12,943 (15.9)     | 2,735 (15.3)  |
| Nepalese             | 102 (0.1)         | 7 (<0.1)      |
| Pakistani            | 5,089 (6.2)       | 1,051 (5.9)   |
| Qatari               | 22,927 (28.1)     | 5,024 (28.1)  |
| Sri Lankan           | 603 (0.7)         | 100 (0.6)     |
| Sudanese             | 3,130 (3.8)       | 616 (3.4)     |
| Other‖               | 23,876 (29.2)     | 5,560 (31.1)  |

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*Shown are the baseline characteristics of the eligible and matched cohorts in the studies of the effectiveness of the 30-μg dose of the BNT162b2 vaccine among adolescents 12 to 17 years of age against infection with a pre-omicron variant of SARS-CoV-2 and against infection with an omicron subvariant.

† Vaccinated and control cohorts were matched in a 1:1 ratio according to sex, age, nationality, number of coexisting conditions, and calendar month of receipt of the second vaccine dose for the vaccinated participant or the SARS-CoV-2–negative test for the control participant.

‡ The SMD is the difference in the mean of a covariate between groups divided by the pooled standard deviation. An SMD of 0.1 or less indicates adequate matching.

§ The SMD is for the mean difference between groups, divided by the pooled standard deviation.

¶ Nationalities were chosen to represent the most populous groups in Qatar.

‖ In the pre-omicron study, this group included up to 135 other nationalities in the unmatched cohorts and 75 other nationalities in the matched cohorts. In the omicron study, this group included up to 143 other nationalities in the unmatched cohorts and 73 other nationalities in the matched cohorts.
The median follow-up was 162 days (interquartile range, 48 to 205) in the vaccinated cohort and 149 days (interquartile range, 34 to 205) in the control cohort (Fig. 2B). During follow-up, there were 2520 infections in the vaccinated cohort, of which 1 progressed to critical Covid-19, and 3337 infections in the control cohort, of which 1 progressed to severe Covid-19 and another to critical Covid-19. The incidence of infection coincided initially with the major wave of infections caused by the omicron BA.1 and BA.2 subvariants in January 2022 (Fig. 2B).$^6,10$ Subsequently, the incidence of infection was due to the omicron BA.1, BA.2, BA.4, or BA.5 subvariants.$^6,7,10$ The cumulative incidence of infection at 195 days after the start of follow-up was 15.9% (95% CI, 15.3 to 16.4) in the vaccinated cohort and 20.7% (95% CI, 20.1 to 21.3) in the control cohort (Fig. 2B).

The overall adjusted hazard ratio for infection was 0.69 (95% CI, 0.66 to 0.73) (Table 2). The overall vaccine effectiveness against omicron infection was 30.6% (95% CI, 26.9 to 34.1). Effectiveness decreased with time after receipt of the second dose (Fig. 3B). It was highest (51.3%; 95% CI, 34.9 to 63.6) among participants who had received their second dose most recently (between January 1, 2022, and July 12, 2022) but was negligible (−1.7%; 95% CI, −16.9 to 11.5) among those who had completed their primary series between February 1, 2021, and June 30, 2021. The overall vaccine effectiveness was 35.5% (95% CI, 5.2 to 56.1) among adolescents who had been vaccinated between February 3, 2022, and July 12, 2022, which is the same time period during which vaccination was rolled out for children 5 to 11 years of age.

Vaccine effectiveness was 35.6% (95% CI, 31.2 to 39.6) among adolescents 12 to 14 years of age and 20.9% (95% CI, 13.8 to 27.4) among those 15 to 17 years of age. The median date of the second vaccine dose was November 11, 2021, among adolescents 12 to 14 years of age and September 19, 2021, among those 15 to 17 years of age. Effectiveness according to year of age showed a declining trend (Fig. S2C). Effectiveness against symptomatic infection was 43.6% (95% CI, 35.1 to 50.9). The number needed to vaccinate to prevent one infection was 20.8. The incidence rate of vaccine-preventable infection was 32.0 cases per 10,000 person-weeks. Despite the lower vaccine effectiveness against omicron infection than against infection with a pre-omicron variant, many infections were averted by vaccination owing to

| No. of coexisting conditions | — no. (%). |
|-----------------------------|-----------|
| 0                           | 64,614 (79.1) | 52,741 (79.9) | 71,144 (79.5) | 60,464 (81.9) |
| 1 or 2                      | 13,478 (16.5) | 10,344 (15.7) | 15,522 (16.9) | 12,394 (16.2) |
| ≥3                          | 3,555 (4.4) | 2,921 (4.4) | 3,309 (4.2) | 2,857 (3.9) |

Shown are the baseline characteristics of the eligible and matched cohorts in the studies of the effectiveness of the 30-μg dose of the BNT162b2 vaccine among adolescents 12 to 17 years of age against infection with a pre-omicron variant of SARS-CoV-2 and against infection with an omicron subvariant. An SMD of 0.1 or less indicates adequate matching. An SMD is the difference in the mean of a covariate between groups divided by the pooled standard deviation. The SMD is for the mean difference between groups, divided by the pooled standard deviation.
The very high incidence of infection during the omicron BA.1 and BA.2 wave.

Figure S5 shows the process for selecting the study population for the additional analysis to estimate booster effectiveness. Table S3 describes the characteristics of the participants in the full study population and the matched cohorts. In this additional analysis, the overall vaccine effectiveness against omicron infection was 36.7% (95% CI, 24.6 to 46.9). The cumulative-incidence curves suggested a rapid waning of effectiveness 4 months after receipt of the booster dose (Fig. S6).

SENSITIVITY ANALYSES AND CROSSOVER DESIGN

Sensitivity analyses with adjustment for differences in testing frequency between study groups in the three cohort studies yielded results that were similar to those of primary analyses (Table S4). Across the three studies, the percentage of participants in the vaccinated cohorts who contributed follow-up time as also unvaccinated ranged between 7.0% and 11.3%.

DISCUSSION

The 10-μg dose of the BNT162b2 vaccine in children was associated with only modest protection against omicron infection, with a vaccine effectiveness of approximately 25%. This protection was also short-lived, decreasing from approximately 50% right after receipt of the second dose to negligible levels after 3 months. However, the 30-μg dose of the BNT162b2 vaccine in adolescents was associated with stronger protection against omicron infection and with slower waning. The protection that was associated with this dose was approximately 30%, but some of the adolescents had been vaccinated months earlier. The vaccine effectiveness would have been higher in closer proximity to the second dose. Among adolescents who had been vaccinated concurrently with children, protection was approximately 35%. These findings suggest that the antigen dose is a determinant in the effectiveness of the vaccine. This effect remains to be investigated directly by comparison of the dose effects in same-age children or in same-age adolescents. The effectiveness of the booster dose among adolescents showed a similar level and pattern to that of the primary vaccine series.

Protection with the 30-μg dose of BNT162b2 among adolescents was stronger against pre-omicron infection than against omicron infection and waned slowly. Protection was approximately 95% right after receipt of the second dose and remained strong at more than 50% for at least 5 months. Overall, the protection and waning patterns that were associated with the 30-μg dose among adolescents paralleled those among adults, although protection seemed to be slightly stronger among adolescents than among adults.
Protection against omicron infection was higher among younger participants than among older participants. Protection was approximately 45% among children 5 to 7 years of age but was only approximately 15% among those 8 to 11 years of age, although the median vaccination date was similar in the two cohorts. Protection was approximately 35% among adolescents 12 to 14 years of age but was only approximately 20% among those 15 to 17 years of age, with the caveat that the cohort of those 15 to 17 years of age had a median vaccination date that was 2 months earlier than that for the cohort of those 12 to 14 years of age. The study findings are consistent with evidence about vaccine protection among children and adolescents in other countries.2,26-30

Our study has limitations. With the lower severity of SARS-CoV-2 infection among children than among adults29,31 and the lower severity of omicron infections than infections with pre-omicron variants,2,23 too few severe,12 critical,12 or fatal13 cases of Covid-19 were observed for us to estimate the vaccine effectiveness against severe Covid-19. Other studies have shown high vaccine effectiveness against severe Covid-19 among children and adolescents.30,34-36

We investigated the incidence of documented infections and defined our cohorts as being previously uninfected on the basis of an absence of a record of previous infection, but other infections may have occurred and gone undocumented. Some members of the cohorts may have had a previous infection that was never documented. Testing frequency differed between the cohorts, mainly owing to different testing guidelines for travel for vaccinated persons as compared with unvaccinated persons, but sensitivity analyses that were conducted with adjustment for these differences showed overall findings that were similar to those of the primary analyses (Table S4). Home-based rapid antigen testing is not documented and thus was not factored in our analyses. However, it is unlikely that home-based testing would have had a differential effect on the followed cohorts. Matching was done to control for confounders that are known to affect infection exposure in Qatar,1,14-17 and this procedure may have also controlled for or reduced any differences in home-based testing between the cohorts, given that matching was performed on the basis of key
sociodemographic factors of the population of Qatar. Because the studies were observational, the participants in the investigated cohorts were not unaware of their status, nor was there randomization; therefore, unmeasured or uncontrolled confounding cannot be ruled out. In the studies involving adolescents, the size of the matched cohorts was substantially smaller than the size of the eligible cohorts, largely because of the rapid scale-up of vaccination, a situation that perhaps reduced the representativeness of the cohorts relative to the total population.

Although the cohorts were matched according to sex, age, nationality, and number of coexisting conditions, such matching was not possible for other factors (e.g., geographic region) because such data were unavailable. Matching was done to control for measured confounders that are known to affect infection exposure in Qatar.14-17 Differences due to unmeasured confounders are possible. However, we had estimated that a relaxing of the matching criteria in additional analyses would have increased the size of the adolescent cohorts by approximately 15% but would have led to similar effectiveness estimates. This outcome suggests that there was insensitivity of the matching method to the observed confounders.

Moreover, the matching prescription had already been investigated in previous studies with different epidemiologic designs and designs that included control groups to test for null effects.18-21 These control groups included unvaccinated cohorts that were compared with vaccinated cohorts within 2 weeks after receipt of the first dose,9,18-20 when vaccine protection is negligible,1 and cohorts that received the mRNA-1273 vaccine (Moderna) that were compared with those that received the BNT162b2 vaccine, also in the first 2 weeks after receipt of the first dose.21 These studies have shown repeatedly and at different times during the pandemic that this matching prescription provides adequate control of the differences in infection exposure,9,18-21 a finding that suggests that the matching method may also control for differences in infection exposure in the present studies.

In this observational study, we found that the 10-μg dose of the BNT162b2 vaccine in children was associated with modest and rapidly waning protection against omicron infection. However, the 30-μg dose in adolescents was associated with stronger and more durable protection, a finding that suggests a role for the antigen dose in determining protection. Protection with the 30-μg dose was strong against pre-omicron infection and waned relatively slowly. Age appeared to influence vaccine protection. Our findings suggest the need to reconsider the value and strategies of vaccinating healthy children in the omicron era with the use of currently available vaccines.

The contents of this article are solely the responsibility of the authors.

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APPENDIX

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