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Effectiveness of BNT162b2 vaccine against SARS-CoV-2 infection and severe COVID-19 in children aged 5–11 years in Italy: a retrospective analysis of January–April, 2022

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Summary

Background

By April 13, 2022, more than 4 months after the approval of BNT162b2 (Pfizer–BioNTech) for children, less than 40% of 5–11-year-olds in Italy had been vaccinated against COVID-19. Estimating how effective vaccination is in 5–11-year-olds in the current epidemiological context dominated by the omicron variant (B.1.1.529) is important to inform public health bodies in defining vaccination policies and strategies.

Methods

In this retrospective population analysis, we assessed vaccine effectiveness against SARS-CoV-2 infection and severe COVID-19, defined as an infection leading to hospitalisation or death, by linking the national COVID-19 surveillance system and the national vaccination registry. All Italian children aged 5–11 years without a previous diagnosis of infection were eligible for inclusion and were followed up from Jan 17 to April 13, 2022. All children with inconsistent vaccination data, diagnosed with SARS-CoV-2 infection before the start date of the study or without information on the municipality of residence were excluded from the

s. With unvaccinated children as the reference group, we estimated vaccine effectiver th

ere partly vaccinated (one dose) and those who were fully vaccinated (two doses).

Findings

By April 13, 2022, 1 063 035 (35·8%) of the 2 965 918 children aged 5–11 years included in the study had received two doses of the vaccine, 134 386 (4·5%) children had received one dose only, and 1 768 497 (59·6%) were unvaccinated. During the study period, 766 756 cases of SARS-CoV-2 infection and 644 cases of severe COVID-19 (627 hospitalisations, 15 admissions to intensive care units, and two deaths) were notified. Overall, vaccine effectiveness in the fully vaccinated group was 29·4% (95% CI 28·5–30·2) against SARS-CoV-2 infection and 41·1% (22·2–55·4) against severe COVID-19, whereas vaccine effectiveness in the partly vaccinated group was 27·4% (26·4–28·4) against SARS-CoV-2 infection and 38·1% (20·9–51·5) against severe COVID-19. Vaccine effectiveness against infection peaked at 38·7% (37·7–39·7) at 0–14 days after full vaccination and decreased to 21·2% (19·7–22·7) at 43–84 days after full vaccination.

Interpretation

Vaccination against COVID-19 in children aged 5–11 years in Italy showed a lower effectiveness in preventing SARS-CoV-2 infection and severe COVID-19 than in individuals aged 12 years and older. Effectiveness against infection appears to decrease after completion of the current primary vaccination cycle.

Funding

None.

Translation

For the Italian translation of the summary see Supplementary Materials section.

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Introduction

The global COVID-19 pandemic that started in 2019 continues to be an important public health threat worldwide in 2022. Although SARS-CoV-2 infection usually has a milder course in children than in adults it still has the potential to cause severe disease,[1] especially in those with underlying health conditions.[2] Children are also at risk of developing paediatric inflammatory multisystem syndrome.[3] In Italy, COVID-19

has caused more than 10 000 hospitalisations and almost 200 admissions to intensive care units (ICUs) in children aged 11 years or younger since the start of the pandemic.[4]

COVID-19 vaccination in young children could have three benefits: (1) a direct benefit by preventing severe and persistent COVID-19; (2) an indirect benefit by preventing SARS-CoV-2 infection, which could lead to social, psychological, and physical benefits by reducing school absenteeism and allowing a higher degree of social interaction between children; and (3) a benefit to the general population by reducing SARS-CoV-2 onward transmission to other age groups.

After the recommendation from the European Medicines Agency,[5] on Dec 7, 2021, the Italian Ministry of Health extended the use of the BNT162b2 (Pfizer–BioNtech) vaccine to children aged 5–11 years with a two dose regimen, (two 10 µg doses) to be given 21 days apart.[6] According to the Italian COVID-19 vaccines report, by April 13, 2022, more than 1·2 million (38%) of about 3·6 million eligible 5–11-year-olds had received at least one dose of the vaccine and more than 1·1 million (34%) had completed the primary cycle of two doses. The randomised trial that led to the approval of the vaccine in 5–11-year-olds found that BNT162b2 was efficacious[7] and post-approval studies have confirmed its safety in this age group.[8] However, very few studies estimating real-world effectiveness are available, and the published studies have all been done in the USA.[9, 10, 11, 12] Furthermore, the effectiveness of the vaccine against the current dominant variant in Europe, omicron (B.1.1.529), might have changed compared with the context in which the previous randomised trials were done. Estimating the degree of protection in young children against infection and severe disease could inform authorities in the implementation and planning of public health interventions targeting both children and the community at large.

Research in context

Evidence before this study

We aimed to identify all the available evidence around vaccine effectiveness of COVID-19 vaccines in children aged 5–11 years. With no restrictions on date or language, we searched PubMed for papers published from the inception of the database to April 4, 2022, with the search terms (“Comirnaty” OR “BNT162b2” OR “Pfizer”) AND (“vaccine*”) AND (“children” OR “adolescent*” OR “young”) AND (“effective*” OR “risk” OR “efficac*”) AND (“SARS-CoV-2” OR “COVID-19” OR “severe acute respiratory syndrome coronavirus 2” OR “coronavirus disease 19”) AND (“severity” OR “hospitalisation” OR “hospitalization” OR “hospital” OR “em

care" OR "mortality" OR "lethality" OR "death"). We also searched medRxiv and SSRN and websites of national institutes of public health in Europe (Germany, Spain, the UK, and France) and the USA for unpublished estimates of vaccine effectiveness using the same search terms. We identified three published studies and one preprint estimating vaccine effectiveness in children aged 5–11 years, all of them in omicron (B.1.1.529) prevalent contexts. All four studies were done in the USA, and they all estimated vaccine effectiveness with two doses using unvaccinated children as the control group. Only one published cohort study and the preprint cohort study estimated vaccine effectiveness against symptomatic or asymptomatic infection. The published cohort study estimated vaccine effectiveness to be 31% 14–82 days after the second dose; the preprint study reported an effectiveness of 65% at 0–13 days after the second dose, declining to 12% 28–34 days after the second dose. A test negative case-control trial estimated a vaccine effectiveness of 46% against urgent care and emergency department encounters; a second test negative case-control study estimated a vaccine effectiveness of 68% against hospitalisation with a median time of follow-up of 34 days. In both cases, the precision of the estimates was low due to the small number of severe events observed.

Added value of this study

Our study is the largest to date to estimate vaccine effectiveness in children aged 5–11 years and the only one done outside the USA. We estimated vaccine effectiveness against infection and severe COVID-19 with a higher precision than previous studies. By using individual-level data, we were able to adjust for several individual and contextual factors. To assess the presence of possible bias due to uncontrolled confounders, we did several sensitivity analyses based on different assumptions and control groups. Given the longitudinal nature of our data sources, we were also able to assess how vaccine effectiveness against infection evolved through time since vaccination during a longer period of follow-up than any previous study.

Implications of all the available evidence

Many countries in Europe and elsewhere have relatively low levels of vaccine coverage in children aged 5–11-years. Our results suggest that BNT162b2 vaccine is moderately effective in preventing infection and severe disease in this age group. However, effectiveness is lower than in her age groups and, at least against infection, it seems to wane. These results should b

interpreted by public health authorities alongside data around vaccine safety and the probability of mortality and morbidity from COVID-19 in this age group.

The aim of this study was to estimate the effectiveness of the paediatric BNT162b2 vaccine in preventing SARS-CoV-2 infections and severe COVID-19 (hospitalisation or death) in children using routinely collected data in Italy.

Methods

Study design and population

This was a nationwide retrospective analysis of 5–11-year-olds in Italy. All 5–11-year-olds for whom records could be linked were screened for inclusion. All children with incongruent vaccination data (ie, more than two doses or at least one non-BNT162b2 dose), diagnosed with SARS-CoV-2 infection before the start date of the study (Jan 17, 2022), or without information on the municipality of residence were excluded from the analysis. Dissemination of COVID-19 surveillance data was authorised by Decree Law number 24 on March 24, 2022 (article 13).

Procedures

We used deterministic record linkage by individual tax code to combine data from the national vaccination registry, which was held by the Ministry of Health and collected individual information on COVID-19 vaccinations administered in Italy, with data on SARS-CoV-2 notified infections (confirmed by antigen or PCR positive tests, or both, from either public or private laboratories and pharmacies) from the Italian National COVID-19 Integrated Surveillance System, coordinated by the National Institute of Health.[4] Data were extracted on April 13, 2022, from both sources. The number of people in the non-vaccinated population, and without a SARS-CoV-2 notified infection, was obtained by subtracting the number of people who were vaccinated or with a previous SARS-CoV-2 diagnosis from the Italian resident population stratified by sex, age, and municipality of residence, as of Jan 1, 2021. The Italian resident population was derived from census data updated yearly by the National Institute of Statistics using the demographic balance from the population registry of each Italian municipality.[13]

Outcomes

asured two outcomes: the incidence of notified SARS-CoV-2 infection (asymptomatic mmatic) and the incidence of severe COVID-19, defined as a SARS-CoV-2 infection resul ho

admission or death within 28 days. Only deaths for which COVID-19 was the most likely cause are recorded in the national surveillance system, as per Italian guidelines based on indications from WHO.[14] Equally, the surveillance system foresees that cases are recorded as hospitalised only if the hospitalisation is directly attributable to SARS-CoV-2 infection and not due to other causes.

The timeline for each event are reported in figure 1. The study start date was Jan 17, 2022, 14 days after the first children received the second dose of BNT162b2 mRNA vaccine. Participants were followed up until the date of diagnosis or the end of the follow-up period, whichever occurred first. We used different dates of end-to-follow-up to account for time from diagnosis to disease progression. The end date for the outcome of severe COVID-19 was March 13, 2022, and the end date for the analysis of SARS-CoV-2 infection was April 10, 2022. The two end dates made it possible to consider all notified cases of confirmed infection with a follow-up period of at least 28 days after diagnosis to document possible worsening of clinical symptoms, and to account for 3 days of possible delay in notification. The study period was characterised by the predominance of the omicron variant.

Figure 1 Timeline of periods of selection and events in the study population

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Statistical analysis

Individual time of exposure was divided according to vaccination status and into weekly time intervals. Vaccination status was defined in three categories: unvaccinated, partly vaccinated (one dose), and fully vaccinated (two doses). On the basis of previous studies,[15, 16] we allowed 14 days from the time of vaccine inoculation to its immunological effect. Thus, children were classified as unvaccinated for the first 14 days after the first dose and as partly vaccinated for the first 14 days after the second dose. Incidence rate ratios (IRRs) of SARS-CoV-2 infections and severe COVID-19 for partly and fully vaccinated children compared with unvaccinated children were estimated using the negative binomial generalised linear mixed model, ng geographical region of residence as the random effect and exposure measured in (; of uded two individual variables, sex and age (as categorical variables), as fixed effects. ed

contextual variables: (1) vaccination coverage at the municipal level in the population aged 30–50 years, split into two categories low (≤75%) and high (>75%); (2) level of urbanisation of the municipality of residence (urban, semi-urban, and rural) from the 2011 census, as reported by the National Institute of Statistics using the European Degree of Urbanisation classification;[17] and (3) the weekly regional incidence of COVID-19 in the general population. Vaccine effectiveness was calculated as (1 minus the IRR) multiplied by 100.

Using the same multivariable regression model, we assessed the possible loss of immunity provided by the paediatric vaccination against SARS-CoV-2 infection at 14-day intervals from full vaccination (0–14 days, 15–28 days, 29–42 days, and 43–84 days).

A sensitivity analysis was done to assess the robustness of our results with respect to the exclusion criteria used to define the study population. We estimated IRRs of SARS-CoV-2 infections and severe COVID-19; all 599 169 notified infections that preceded vaccination were included in the analysis (appendix 2 p 2). We then estimated vaccine effectiveness excluding people with SARS-CoV-2 infection diagnosed in the previous 90 days (appendix 2 p 2). The rationale was that in Italy, and other European countries, reinfections are only considered as such 90 days after the primary infection. Both models included previous diagnosis as a fixed effect covariate.

To avoid possible confounding factors arising from differences between the vaccinated and the unvaccinated populations, we did another sensitivity analysis estimating vaccine effectiveness on the vaccinated population alone. In this analysis, we used the exposure interval of 4–10 days from the first dose of vaccine as a reference (appendix 2 p 2). We did not consider the time intervals of 11–14 days and 0–3 days after first dose because some protection might be evident 10 days after the first dose of vaccine, and, from days 0 to 3, a deferral bias could affect the incidence in the first few days after the first dose (eg, people with symptoms probably postponed vaccination).[18] Adjusted vaccine effectiveness was estimated using the same model, including the frailty status (healthy, immunocompromised, or affected by a chronic pathology) as an additional covariate (information available only for people who were vaccinated through the national vaccination registry and obtained at the time of vaccination; appendix 2 p 3).

All the analyses were done using R (version 4.1.2).[19] The negative binomial generalised linear mixed model was estimated using the R package glmmTMB.[20] We described the methods and presented findings according to the reporting guidelines for observational studies that are based on routinely collected health data (appendix 2 p 4).

Role of the funding source

vas no funding source for this study.

Results

In Italy, the vaccination campaign against COVID-19 in 5–11-year-olds started on Dec 16, 2021. The beginning of the study period (Jan 17, 2022) coincides with the date when the first children completed the primary cycle (ie, had received two doses of BNT162b2). 2 965 918 children were included in the study with a median follow-up of 71 days (figure 2); the population characteristics and demographics at the end of the study (April 13, 2022) are reported in table 1. On April 13, 2022, 1 063 035 (35·8%) children had completed the primary cycle of two doses, 134 386 (4·5%) had received one dose, and 1 768 497 (59·6%) were unvaccinated. Vaccination coverage increased with age and was lower in areas where uptake in 30–50-year-olds was low. We also observed that children in rural and semi-urban areas were more frequently unvaccinated than those living in urban municipalities. We did not observe differences in vaccination status according to sex (table 1).

Figure 2 Study profile

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Table 1 Population characteristics at the end of the study (April 13, 2022)

	Not vaccinated group (n=1 768 497)	Partly vaccinated group (n=134 386)	Fully vaccinated group (n=1 063 035)
Sex			
Male	911 202 (51·5%)	69 830 (52·0%)	543 720 (51·1%)
Female	857 295 (48·5%)	64 556 (48·0%)	519 315 (48·9%)
Age			
5 years	301 157 (17·0%)	14 060 (10·5%)	95 788 (9·0%)
6 years	270 983 (15·3%)	16 081 (12·0%)	126 147 (11·9%)
7 years	262 018 (14·8%)	18 063 (13·4%)	139 516 (13·1%)
8 years	251 694 (14·2%)	19 023 (14·2%)	150 768 (14·2%)
9 years	248 813 (14·1%)	20 495 (15·3%)	164 652 (15·5%)
10 years	232 431 (13·1%)	22 769 (16·9%)	179 765 (16·9%)

Data are n (%).

*** Level of urbanisation of the municipality of residence as reported by the National Institute of Statistics using the European Degree of Urbanisation.**

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766 756 cases of SARS-CoV-2 infection were notified to the National COVID-19 Integrated Surveillance System. The highest incidence rate was observed in the unvaccinated group (426·9 per 100 000 person-days [95% CI 425·8–428·1]) and the lowest in the fully vaccinated group (234·5 per 100 000 person-days [233·2–

table 2). Overall, 644 children had severe COVID-19 and required hospitalisation (15 of whom were

ed to an ICU; two died; all were unvaccinated). Of the two children who died, one had

ole

congenital and chronic comorbidities, but the other child was not known to have any health conditions (appendix 2 p 9). The highest rate of severe COVID-19 was observed in the unvaccinated group (0·6 per 100 000 person-days) and the lowest in the fully vaccinated group (0·3 per 100 000 person-days; table 2). We did not observe an age gradient in the incidence rate of severe COVID-19, with children aged 5 years having a similar rate (0·40 per 100 000 person-days) to those aged 11 years (0·41 per 100 000 person-days; appendix 2 p 9).

Table 2 BNT162b2 vaccine effectiveness against laboratory-confirmed SARS-CoV-2 infection and severe disease in children aged 5–11 years

	Number of infections	Person-days	Rate per 100 000 person-days	Crude IRR (95% CI)	Vaccine effectiveness (95% CI)	Adjuste vaccine effective (95% CI
Infection						
Unvaccinated group	562 083	131 656 589	426·9	1	NA	NA
Partly vaccinated group	83 441	25 860 465	322·7	0·76 (0·75-0·76)	24·4 (23·9-24·9)	27·4 (26 28·4)
Fully vaccinated group	121 232	51 699 305	234·5	0·55 (0·55-0·55)	45·1 (44·8-45·4)	29·4 (28 30·2)
Severe disease						
Unvaccinated group	510	89 464 006	0·57	1	NA	NA
Partly						

:idence rate ratio. NA=not applicable.

*** Vaccine effectiveness adjusted by sex, age, vaccination coverage at the municipal level in 30–50-year-olds, level of urbanisation of the municipality of residence, and regional weekly incidence in the general population, and region of residence was included in the model as a random effect.**

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Adjusted vaccine effectiveness against SARS-CoV-2 infection was higher in the fully vaccinated group (29·4% [95% CI 28·5–30·2]) than in those in the partly vaccinated group (27·4% [26·4–28·4]; table 2). The adjusted vaccine effectiveness against severe COVID-19 was 38·1% (95% CI 20·9–51·5) in the partly vaccinated group and 41·1% (22·2–55·4) in the fully vaccinated group (table 2). Vaccine effectiveness against SARS-CoV-2 infection peaked at 0–14 days after full vaccination (38·7% [95% CI 37·7–39·7]); vaccine effectiveness then declined to 21·2% (19·7–22·7) at 43–84 days after the second dose (figure 3; appendix 2 p 10).

Figure 3 Effectiveness of BNT162b2 vaccine against laboratory-confirmed SARS-CoV-2 infection

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Similar estimates for vaccine effectiveness against SARS-CoV-2 infection and severe COVID-19 were obtained in the sensitivity analyses assessing the robustness of our results with respect to the exclusion criteria used to define the study population. Using the first 4–10 days after the first dose in the vaccinated population as the reference exposure and additionally adjusting for clinical vulnerability, vaccine effectiveness against infection was 24·3% (95% CI 20·6–27·8) in the partly vaccinated group and 21·8% (16·1–27·2) in the fully vaccinated group (appendix 2 p 2). Vaccine effectiveness against severe COVID-19 was 39·4 (95% CI 3·8–61·9) in the partly vaccinated group and 44·1% (9·0–65·7) in the fully vaccinated group (appendix 2 p 2).

Discussion

By April 13, 2022, less than 40% of 5–11-year-olds had completed the COVID-19 vaccination cycle in Italy. Our results, based on data from the whole Italian population in this age group, suggest that vacci

was moderately effective in preventing asymptomatic or symptomatic infection and severe disease.

Our estimates of the effectiveness of full vaccination against SARS-CoV-2 infection are significantly lower than those reported in the clinical trial that led to the approval of BNT162b2 in children (90·7% in the approval trial *vs* 29·4% in our study).[7] However, differences in the results between randomised trials and effectiveness studies have been previously reported for COVID-19 vaccination in other age groups. One of the several factors that could explain the differences observed is that the trial was done during a period of delta variant (B.1.617.2) dominance which was less transmissible and less able to evade immunity conferred by vaccination than the omicron variant, which accounted for more than 80% of infections in Italy during our study.[21] However, our estimates of vaccine effectiveness against infection coincide with the estimate reported in the USA in a previous study.[9] This prospective cohort study found a vaccine effectiveness against infection of 31% (95% CI 9–48) at 14–82 days after completion of the primary cycle in a sample of 1364 children aged 5–11 years, very similar to our estimate of 29·4% after a similar interval of 0–84 days after full vaccination. We found that vaccine effectiveness against infection peaked 0–14 days after full vaccination at 38%, declining to approximately 20% after 42 days. A similar pace in the decline of effectiveness against infection has been reported in an unpublished study.[12] This decline could be due to immunity waning, as described in the adult population vaccinated with mRNA vaccines,[22] but the decline in effectiveness appears to occur faster in 5–11-year-olds compared with 12–15-year-olds[9] and adults older than 18 years.[23]

Our results are also consistent with findings from the two published studies measuring vaccine effectiveness against severe COVID-19 in 5–11-year-olds.[10, 11] The first study, based on a sample of 9181 cases, found a vaccine effectiveness against emergency department and urgent care encounters of 46%,[10] slightly higher than our 41% estimate against severe disease. The second study reports a higher vaccine effectiveness against hospitalisations (68%) than that reported in our study, but a substantially shorter interval after vaccination (median 34 days) was used in this study,[11] compared with our investigation (median 71 days). However, results from these two studies[10, 11] and our study overlap at the 95% CI level because of the low precision of estimates derived from the small number of severe events in this age group. In our study, most severe adverse events were non-ICU hospital admissions in surviving patients. Very few patients were admitted to an ICU or died, all of whom were unvaccinated.

Our estimates of vaccine effectiveness against infection and against severe COVID-19 in 5–11-year-olds were significantly lower than estimates in older age groups,[9, 23, 24] including estimates derived from the same data sources such as the weekly analysis provided by the Italian National Institute of Health that shows a vaccine effectiveness during a period of omicron dominance in people aged 12 years and older of

ainst infection and around 71% against severe disease.[4] The reasons why vaccine eff ies

e lower in 5–11-year-olds than in older age groups are still unclear. One explanation c ɔe t

the lower vaccine dose (10 µg) used in 5–11-year-olds induces a lower immune response compared with the full 30 µg dose used in children older than 12 years, adolescents, and adults.[12] An alternative explanation could be that the differences observed in severe disease are an artifact induced by a differential threshold of hospital admission associated with age.[25, 26] However, we did not observe differences in the rates of hospital admission between children aged 5 years and those aged 11 years. The lower effectiveness observed in this age group should be interpreted alongside safety data in Italy from the existing pharmacovigilance systems,[27] as well as data from elsewhere, suggesting that adverse serious events caused by vaccination with paediatric BNT162b2 are extremely rare.[28, 29]

Although our analysis includes all 5–11-year-old children in Italy, it refers to a specific period when omicron, particularly the lineage BA.1, was dominant.[21] During this period, the high viral circulation characterised by a higher probability of asymptomatic infection in children could contribute to a larger proportion of hidden infections, with a subsequent increase in the rate of protective immune response also in unvaccinated children possibly contributing to an underestimation of vaccine effectiveness. Moreover, in a fast-evolving pandemic it is possible that these results are not generalisable to other contexts (eg, levels of viral circulation and emergence of new variants). More studies to evaluate vaccine efficacy in different contexts or with different dosage or administration timing could contribute to the evaluation of effective vaccination strategies in children.

Our study has several limitations. Information on the unvaccinated population was obtained using population estimates from the National Institute of Statistics. Although these estimates are considered robust, there might be small differences between the estimated and the real number of people residing in Italy over the study period, due to population dynamics; however, population predictions are expected to be relatively stable in children. Moreover, because we had limited information on the unvaccinated children, we could not adjust our estimates for some individual characteristics that could affect the probability of vaccination and the risk of developing COVID-19 outcomes, such as clinical vulnerability or risky behaviours (eg, adherence to physical distancing rules and non-pharmaceutical interventions). Another possible confounding factor that could affect the main analysis is a potential differential degree of under ascertainment of cases according to vaccination status. To test the extent to which clinical vulnerability or under ascertainment could have biased our estimates, we did a sensitivity analysis using the first few days after vaccination (before immunity is developed) as the reference exposure period and adjusted for frailty conditions (immunocompromised and chronic diseases). The consistency of the findings between our main and sensitivity analysis, and between our results and estimates from other studies, suggests that any effect of such limitations was small. Due to the low number of severe events observed, our estimates of effectiveness against severe COVID-19 have poor precision. This limitation also that we could not measure whether the estimate changed over time. Furthermore, al ı lc

and regional authorities are required to report only hospitalisations directly attributable to COVID-19 to the surveillance system, a small percentage of such events could be misclassified. Compared with already published data, vaccination of 5–11-year-olds against COVID-19 with paediatric BNT162b2 in Italy is less effective at preventing SARS-CoV-2 infection and severe COVID-19 than in people aged 12 years and older. Effectiveness against infection appears to decline after completion of the primary cycle. These findings underline the need for more studies and could support public health authorities in choosing the most appropriate vaccination strategy in this age group for their context.

Contributors

CS, MDM, AM-U, and MF designed the study. CS, DP, and MF extracted and linked the data. CS did the analysis supported by AM-U and MF. SBa and VP ensured quality of vaccination data. AB, DP, and FR ensured quality of COVID-19 surveillance. CS, MDM, and AM-U wrote the manuscript. MCR, AS, FMI, PPo, ATP, SBr, GR, and PPe reviewed and edited the manuscript. All authors reviewed and approved the final version and authorised the submission of the manuscript. All authors had access to the data. CS, AM-U, MDM, PPe, and MF verified the underlying data reported in the manuscript.

Data sharing

Individual-level data reported in this study are not publicly available for ethical and legal reasons. However, data are available from the Istituto Superiore di Sanità (https://www.iss.it/richiesta-dati-covid19) upon reasonable request.

Declaration of interests

We declare no competing interests.

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ɔlementary Materials

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Supplementary appendix 2

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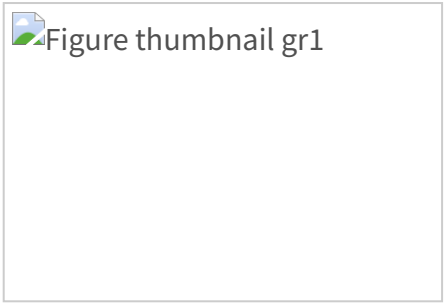

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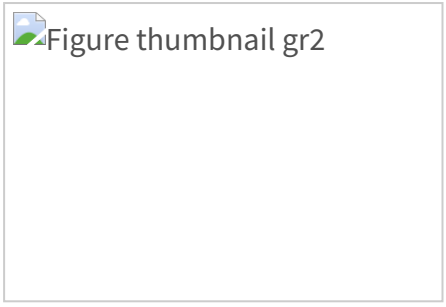

Figure 2 Study profile

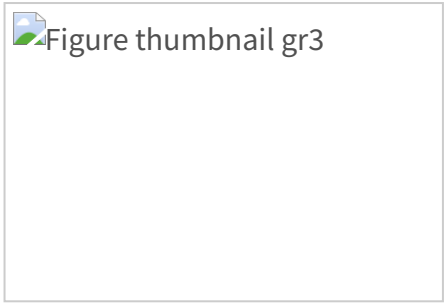

Figure 3 Effectiveness

16

Tables

Table 1: Population characteristics at the end of the study (April 13, 2022)

Table 2: BNT162b2 vaccine effectiveness against laboratory-confirmed SARS-CoV-2 infection and severe disease in children aged 5–11 years

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