

Effectiveness of the BNT162b2 mRNA COVID-19 vaccine in children under 5 years

To the Editor: Despite approval of the BNT162b2 mRNA vaccine (Pfizer/BioNTech vaccine Comirnaty) for children aged 6 months to 4 years by the European Medicines Agency (EMA) and the Federal Drug Administration (FDA) in 2022, little data on BNT162b2 vaccine effectiveness (VE) are available for this age group. We have retrospectively described the safety of BNT162b2 administered off-label in children younger than 5 years in Germany (1). Using data from this authentication-based retrospective survey obtained between April 14, 2022, and May 9, 2022 (1), we here report VE of BNT162b2 during an Omicron BA.1-2-dominant period.

We analyzed 4,615 children, aged 2.8 ± 1.2 years (mean \pm SD), who received their first dose of BNT162b2 on January 1, 2022, or thereafter (Supplemental Table 1 and Supplemental Figure 1; supplemental material available online with this article; <https://doi.org/10.1172/JCI173329DS1>). We used Cox regression to estimate relative VE of 2 BNT162b2 doses, as indicated in the Supplemental Methods. We used the period between the first and second vaccine dose as the reference period (24.8 ± 0.6 days) and the period ≥ 7 days after dose 2 to before dose 3 as the postvaccination period (59.5 ± 23.6 days). By this approach, the relative HR of SARS-CoV-2 infections was calculated after administration of 2 versus 1 dose of BNT162b2, and this was transformed to VE by the calculation $VE = 100 \times (1 - HR)$.

Table 1 shows that VE was substantial for SARS-CoV-2 infections, symptomatic SARS-CoV-2 infections, and SARS-CoV-2 infections leading to medication use. Differences in dosage of BNT162b2 yielded no change in VE. A sensitivity analysis assessed the geographic and potential sex differences in VE by stratification (Supplemental Table 2). The HR of each model parameter is shown in Supplemental Table 3.

The present analysis showed that, in comparison with 1 dose of BNT162b2 alone, children receiving a second dose of BNT162b2 had a substantially lower risk for being diagnosed with a SARS-CoV-2 infection or experiencing a SARS-CoV-2 infection leading to symptoms or medication use. The present data are well in line with those from an emerging report on the US population, where a VE of 54.2% (95% CI, 45.8–61.2) was reported for previously uninfected children receiving 2 doses of BNT162b2 compared with unvaccinated children (2). The current data have some limitations. First, children are rarely tested for SARS-CoV-2, and medical attention is not often sought for their SARS-CoV-2 symptoms. However, this study coincided with (a) a time when mandatory school/institution testing for SARS-CoV-2 was common in Germany, (b) substantial vaccination efforts and campaigns, and (c) the Omicron BA.1 and BA.2 waves, allowing an unusual window of opportunity for study of many recently vaccinated and previously uninfected individuals in this sensitive age group, experiencing symptomatic or asymptomatic infections. Next, the assessed vaccination strategy of BNT162b2 was not the one approved by EMA and FDA; our strategy consisted of 2, instead of 3, administrations of BNT162b2, at dosages higher than $3 \mu\text{g}$ in most participants. Furthermore, the reported VE does not necessarily correspond to the currently circulating SARS-CoV-2 variants. Finally, the present data are retrospective and await confirmation by prospective and randomized studies. In conclusion, this study offers early, industry-independent insight into the potential VE of the BNT162b2 vaccine in children aged below 5 years, at a time when few immunogenicity or VE data are available (2, 3).

Christoph Strumann,¹ Otavio Ranzani,^{2,3} Jeanne Moor,^{4,5}
Reinhard Berner,⁶ Nicole Töpfner,⁶ Cho-Ming Chao,^{7,8,9}
and Matthias B. Moor^{10,11,12}

Table 1. Vaccine effectiveness of 2 doses of BNT162b2 COVID-19 vaccine during the Omicron BA.1 and BA.2 phase, compared with 1 dose

Postvaccination period	All SARS-CoV-2 infections	Symptomatic SARS-CoV-2 infectionst	SARS-CoV-2 infections leading to medication use
≥ 7 Days after dose 2 to before dose 3 (P value) [95% CI]	53.1 (<0.001) [36.3–69.9]	57.5 (<0.001) [40.8–74.2]	66.2 (<0.001) [43.7–88.7]
3 μg	47.1 (<0.001) [20.7–73.6]	61.4 (<0.001) [40.0–82.7]	70.2 (<0.001) [44.6–95.7]
5 μg	54.5 (<0.001) [36.6–72.5]	56.8 (<0.001) [37.9–75.6]	66.9 (<0.001) [43.3–90.5]
10 μg	54.3 (<0.001) [34.9–73.6]	56.9 (<0.001) [36.7–77.1]	62.9 (<0.001) [32.6–93.2]
Infections, n (%)	779 (16.9)	621 (13.3)	261 (5.7)
Children, n	4,615	4,615	4,615

The vaccine effectiveness in percentage was estimated by $\widehat{VE} = 100 \times (1 - \exp\{\hat{\beta}_{pvp}\})$, where $\hat{\beta}_{pvp}$ represents the estimated coefficient for the postvaccination period of a Cox model stratified by region-specific (north, west, east, south, and abroad) calendar day. Medication use, prior chronic diseases, age, sex, weight, and dosage information for the first vaccination are included as control variables. A comparison of estimates for the different outcomes showed no significant difference ($P > 0.05$).

¹Institute of Family Medicine, University Hospital Schleswig-Holstein, Campus Luebeck, Luebeck, Germany. ²Barcelona Institute for Global Health, ISGlobal, Universitat Pompeu Fabra, Barcelona, Spain. ³Pulmonary Division, Heart Institute (InCor), Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil. ⁴Department of General Internal Medicine, Inselspital University Hospital Bern, Bern, Switzerland. ⁵Institute of Primary Health Care, University of Bern, Bern, Switzerland. ⁶Department of Pediatrics, University Hospital and Medical Faculty Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany. ⁷University Children's Hospital, University Medical Center Rostock, University of Rostock, Rostock, Germany. ⁸Department of Pediatrics, Helios University Medical Center, Witten/Herdecke University, Heusnerstr, Wuppertal, Germany. ⁹Cardio-Pulmonary Institute, Universities of Giessen and Marburg Lung Center, German Center for Lung Research, Justus-Liebig University Giessen, Giessen, Germany. ¹⁰Division of Renal Medicine, Department of Clinical Science, Intervention and Technology and ¹¹Division of Pathology, Department of Laboratory Medicine, Karolinska Institutet, Stockholm, Sweden. ¹²Department of Nephrology and Hypertension, Inselspital University Hospital Bern, Bern, Switzerland.

1. Toepfner N, et al. Comparative safety of the BNT162b2 Messenger RNA COVID-19 vaccine vs other approved vaccines in children younger than 5 years. *JAMA Netw Open*. 2022;5(10):e2237140.
2. Lin DY, et al. Effects of COVID-19 vaccination and previous SARS-CoV-2

infection on Omicron infection and severe outcomes in children under 12 years of age in the USA: an observational cohort study [published online June 16, 2023]. *Lancet Infect Dis*. [https://doi.org/10.1016/S1473-3099\(23\)00272-4](https://doi.org/10.1016/S1473-3099(23)00272-4).

3. FDA. Vaccines and related biological products advisory committee meeting. FDA; 2022. Accessed September 5, 2023. <https://www.fda.gov/media/159195/download>.

Address correspondence to: Cho-Ming Chao, Zentrum für Kinder- und Jugendmedizin, HELIOS Universitätsklinikum Wuppertal, Universität Witten/Herdecke, Heusnerstraße 40 – 42283 Wuppertal, Germany. Phone: 49.0.202.896.3840; Email: cho-ming.chao@helios-gesundheit.de.

Authorship note: CMC and MBM are co-senior authors.

Conflict of interest: The authors have declared that no conflict of interest exists.

Copyright: © 2023, Strumann et al. This is an open access article published under the terms of the Creative Commons Attribution 4.0 International License.

Submitted: June 26, 2023; **Accepted:** August 29, 2023; **Published:** November 1, 2023.

Reference information: *J Clin Invest*. 2023;133(21):e173329. <https://doi.org/10.1172/JCI173329>.