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Effectiveness of BNT162b2 against COVID-19 in adolescents



In the UK, COVID-19 vaccination for adults began in December, 2020.¹ Because children and adolescents have a low risk of severe COVID-19 and due to concerns about rare but potentially severe myocarditis after mRNA vaccination—mainly after the second dose in young adult males—the UK Joint Committee on Vaccination and Immunisation (JCVI) initially recommended one dose for 16–17-year-olds from Aug 4, 2021,² and recommended against vaccinating 12–15-year-olds because of marginal benefits versus risk. UK ministers subsequently recommended vaccinating this group with BNT162b2 (Comirnaty, Pfizer-BioNTech) or mRNA-1273 (Spikevax, Moderna) from Sept 13, 2021, to prevent education disruption.³ Contrary to the authorised 3-week interval, the UK recommends 8–12 weeks between doses, because of the high protection provided by the first dose and higher antibody responses after a later second dose.⁴ The UK strategy provided a unique opportunity to assess single-dose mRNA vaccine effectiveness in adolescents during a period of high community infection with the highly transmissible delta (B.1.617.2) variant and subsequently with the more transmissible, and now dominant, omicron (B.1.1.529) variant.

We used a test-negative, case-control design to estimate vaccine effectiveness after one BNT162b2 dose against PCR-confirmed symptomatic infection with the delta and omicron variants of SARS-CoV-2 in England, as described previously.⁵ Vaccination status in symptomatic 12–15-year-olds and 16–17-year-olds with PCR-confirmed SARS-CoV-2 infection was compared with vaccination status in symptomatic adolescents in the same age groups who had a negative SARS-CoV-2 PCR test (appendix pp 1–3).

From Sept 13, 2021, onwards, there were 617 259 eligible tests for 12–15-year-olds and 225 670 for 16–17-year-olds with a test date within 10 days of symptom onset date that could be linked to the National Immunisation Management system (match rate 92.5%; appendix pp 4–6). Vaccine uptake and confirmed infections by age group and over time are summarised in the appendix (p 9).

After one vaccine dose in 12–15-year-olds, vaccine effectiveness against symptomatic disease caused by

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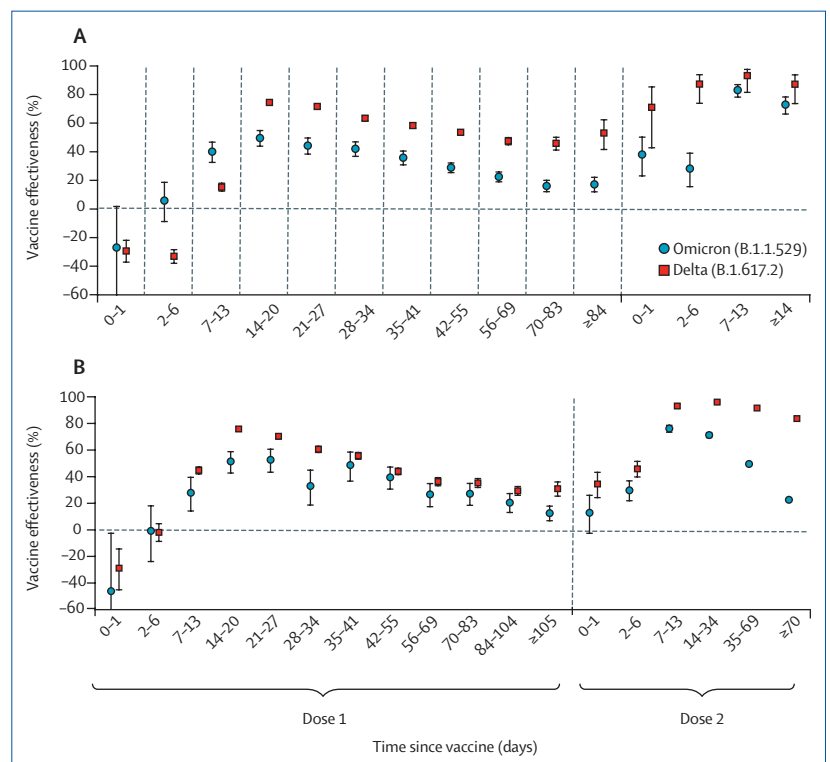


Figure: Vaccine effectiveness in 12–15-year-olds (A) and 16–17-year-olds (B) with symptomatic, PCR-confirmed COVID-19. Error bars are 95% CI.

the delta variant peaked at days 14–20 after vaccination (74.5% [95% CI 73.2–75.6]) and then declined gradually, reaching 45.9% (41.2–50.1) at days 70–83 (figure A; appendix p 10). For the omicron variant, vaccine effectiveness was significantly lower at these timepoints, peaking at 49.6% (95% CI 43.9–54.8) at days 14–20 after the first dose before dropping to 16.1% (12.1–20.0) at days 70–83. After two doses, vaccine effectiveness increased and peaked 7–13 days later at 93.2% (81.5–97.5) for the delta variant and at 83.1% (78.2–86.9) for the omicron variant (appendix p 10).

For 16–17-year-olds, vaccine effectiveness after dose one against symptomatic disease with the delta variant peaked at days 14–20 (75.9% [95% CI 74.3–77.3]) and declined gradually to 29.3% (25.9–32.6; figure B; appendix p 10) at days 84–104. For omicron, the vaccine effectiveness peak was significantly lower at 52.7% (43.3–60.5) between days 21–27 and fell to 12.5% (6.9–17.8) from day 105 onwards. After dose two, vaccine effectiveness peaked at 14–34 days (96.1% [95.2–96.8]) for the delta variant and at 7–13 days (76.1% [73.4–78.6]) for the omicron variant. Effectiveness fell rapidly for omicron after day 34, reaching 22.6% (14.5–29.9) 70 days after dose two, compared with 83.7% (72.0–90.5) for the delta variant (appendix p 10).

For the delta variant, vaccine effectiveness against hospitalisation at 28 days after dose one was 83.4% (95% CI 54.0–94.0; appendix p 11) for 12–15-year-olds and 76.3% (61.1–85.6; appendix p 11) for 16–17-year-olds. There was insufficient follow-up time for assessing hospitalisation after two doses and for the omicron variant in both age groups.

Vaccination with BNT162b2 in both adolescent age groups was associated with lower vaccine effectiveness against symptomatic COVID-19 caused by the omicron variant compared with the delta variant. By 84 days after dose one, vaccine effectiveness against symptomatic disease with the omicron variant dropped to 20.5% for day 84–104 in 16–17-year-olds, highlighting the need for a second dose in both age groups. A second dose was associated with a rapid increase in vaccine effectiveness within 2 weeks of vaccination, with higher protection against the delta variant compared with the omicron variant. 16–17-year-olds were vaccinated earlier than 12–15-year-olds; therefore, they had longer follow-up. In 16–17-year-olds, vaccine effectiveness

against the omicron variant dropped rapidly compared with the delta variant, consistent with observed trends in UK adults receiving a similar two-dose extended BNT162b2 schedule.⁵ Similar trends will probably occur in 12–15-year-olds over time. Reassuringly, very high protection was reported against hospitalisations due to the delta variant, even after a single vaccine dose. More follow-up is needed to assess protection against hospitalisation due to the omicron variant, any additional protection offered by the second dose, and duration of protection against hospitalisation for both variants.

Preliminary trials reported 93% (mRNA-1273) to 100% (BNT162b2) efficacy in preventing COVID-19 in 12–15-year-olds from 7 days (BNT162b2) or 14 days (mRNA-1273) after two doses given 3–4 weeks apart,^{6,7} but the short interval between doses prevents comparison with our cohort. Real-world vaccine effectiveness data after two BNT162b2 doses include a US study using a similar test-negative case-control design as this study, which estimated 93% (95% CI 83–97) vaccine effectiveness against hospitalisation from June 30, to Sept 30, 2021,⁸ early Israeli data estimated 91.5% (88.2–93.9) vaccine effectiveness against delta variant infection in 12–15-year-olds.⁹

To date, this study is the only vaccine effectiveness evaluation against the omicron variant in adolescents after one and two mRNA vaccine doses. In adults from the UK, a similar high vaccine effectiveness against symptomatic disease was observed for both the delta (91%) and omicron (66%) variants 2–4 weeks after two BNT162b2 doses given 8–12 weeks apart,⁵ which was similar to data from South Africa reporting vaccine effectiveness of 70% against the omicron variant 2 weeks or more after the second vaccine dose.¹⁰

The rapid waning of protection after the first and second BNT162b2 dose against symptomatic disease with the omicron variant, the now dominant variant in the UK and worldwide, indicates that the current adolescent immunisation programme as a stand-alone intervention is unlikely to sustain suppression of infections in the medium-to-long term. If the aim of the programme is to reduce infections, then regular boosters will likely be needed.

We declare no competing interests. NA and SNL contributed equally. UKHSA has legal permission, provided by Regulation 3 of The Health Service (Control of Patient Information) Regulations 2002, to process patient confidential information for national surveillance of communicable diseases and as such, individual patient consent is not required to access records.

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To our friend, John

Didier had the privilege of getting to know John McConnell as an editor of *The Lancet* when John handled his paper on hand hygiene promotion in 2000.¹ It was, for Didier, an honour to work with such a unique person. Subsequently, John and Didier had the great pleasure of working side by side along the journey to create *The Lancet Infectious Diseases* (TLID): it took several years to convince different people and entities but, in the end, TLID was born. John was strong, patient, unfailingly nice to everyone, and very open to suggestions. The first issue of TLID was published in August, 2001, more than 20 years ago. TLID published only reviews at that time, but soon and thanks to John's efforts, dedication, and convincing arguments, TLID opened up to accept original research papers with the undoubted success we all recognise today. This success is John's success, supported by a team who grew up year after year and continuously worked in John's spirit, and made TLID what it is today. Defending the values and ethics of the best peer-reviewed journals was certainly among John's top qualities; these are critical to the *Lancet* family of journals. So many thanks must be given to John for the huge service he made to the scientific community. Long live TLID—John's baby.

John was unknown to Tim when we wrote the first NDM-1 paper in TLID.² While writing that Article, it was clear it would create some political fallout and within

2 days (Aug 10–12, 2010) it had registered 4·7 million internet hits.² John, the TLID editorial team, and Tim's international team found themselves in a political maelstrom being accused of many falsehoods. But, from that moment, Tim and John became brothers-in-arms and good friends. The following paper in April, 2011, on the spread of NDM-1 in the New Delhi environment also provided a negative response and, again, Tim and John were both embroiled in international politics.³ Didier kindly put on a special NDM-1 session at the 2011 International Conference on Prevention and Infection Control (ICPIC), which gave John and Tim the opportunity to explain the background to the NDM-1 story. The support from John and his team during this period was one of the key reasons why antimicrobial resistance (AMR) suddenly became topical and of international importance. His support during this period, when under immense international pressure, was unyielding, unremitting, and unapologetic.

In 2015, when Tim and his Chinese colleagues approached TLID regarding the first report of mobile colistin resistance (MCR-1), John and his team, aware of the international ramifications, entered into a healthy dialogue with them to ensure that the science supported the paper's conclusions.⁴ John and his team were very supportive, not only of the way the story should be told,



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