Medical Xpress

COVID-19 vaccine effectiveness in adolescents

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The Clalit Research Institute, in collaboration with researchers from Harvard University, analyzed one of the world's largest integrated health record databases to examine the effectiveness of the Pfizer/BioNTech

BNT162B2 vaccine against the Delta variant of SARS-CoV-2 among adolescents. The study provides the largest peer-reviewed evaluation of the effectiveness of a COVID-19 vaccine among adolescents in a nationwide mass-vaccination setting, and the first such study where the Delta variant was dominant. The study was conducted in Israel, an early global leader in COVID-19 vaccination rates.

The results of this study validate and complement the previously reported findings of a Pfizer/BioNTech Phase-III randomized clinical trial, which focused on symptomatic infections in the face of non-Delta variants, and which, with 1,983 vaccinated adolescents between the ages of 12 and 15 years, could not precisely assess vaccine effectiveness. The present study's large size allows a more precise assessment of the vaccine's effectiveness across different time periods.

The study took place from June 8, 2021 through September 14, 2021. It coincided with Israel's fourth wave of coronavirus infection and illness, during which the Delta (B.1.617.2) variant was the dominant strain in the country for new infections.

Researchers reviewed data from 94,354 vaccinated adolescents aged 12 to 18. These adolescents were carefully matched with 94,354 unvaccinated adolescents based on an extensive set of demographic, geographic and health-related attributes associated with risk of infection, risk of severe disease, health status and health seeking behavior. Individuals were assigned to each group dynamically based on their changing vaccination status (13,423 individuals moved from the unvaccinated cohort into the vaccinated cohort during the study). Multiple sensitivity analyses were conducted to ensure that the estimated vaccine effectiveness was robust to potential biases.

The results show that in fully vaccinated adolescents (7 to 21 days after the second dose), the risk of symptomatic COVID-19 decreased by 93%

compared with the unvaccinated, while the risk of documented infection decreased by 90%. In the period immediately preceding the second dose (days 14-20 after the first dose), vaccine effectiveness was lower, but still substantial—the risk of symptomatic COVID-19 decreased by 57% in vaccinated individuals, and the risk of documented infection by 59%. There was insufficient data to provide an estimate on the reduction in the incidence of severe disease, hospitalization and mortality, as these outcomes are rare among adolescents.

The research was conducted by Dr. Noam Barda, Dr. Noa Dagan, Michael Leshchinsky, Dr. Eldad Kepten, and Prof. Ran Balicer from the Clalit Research Institute, as well as Prof. Miguel Hernán and Prof. Marc Lipsitch of the Harvard T.H. Chan School of Public Health, and Prof. Ben Reis of Boston Children's Hospital and Harvard Medical School.

"The extensive nationwide rollout of Israel's COVID-19 vaccination campaign to adolescents at the very beginning of the delta variant wave, provided the Clalit Research Institute with a unique opportunity to assess, through its rich and comprehensive digital datasets, the effectiveness of the vaccine for adolescents against delta in a real-world setting," said Prof. Ran Balicer, senior author of the study, Director of the Clalit Research Institute and Chief Innovation Officer for Clalit. "These results show convincingly that one week after the second dose, this vaccine is highly effective in adolescents against symptomatic COVID-19 and against all documented infections. These data should facilitate informed individual risk-benefit decision-making, and, in our view, make a strong argument in favor of opting-in to get vaccinated, especially in countries where the virus is currently widespread," added Prof. Balicer, who also serves as Chairman of Israel's National Expert Advisory Team on COVID-19 response.

Prof. Ben Reis, Director of the Predictive Medicine Group at the Boston Children's Hospital Computational Health Informatics Program and

Harvard Medical School, said, "To date, one of the main drivers of vaccine hesitancy has been a lack of information regarding the effectiveness of the vaccine. This careful epidemiological study provides reliable information on vaccine effectiveness, which we hope will be helpful to those who have not yet decided about vaccination."

Prof. Miguel Hernán, Director of the CAUSALab and Professor at the Harvard T.H. Chan School of Public Health, said, "This research is a perfect example of how randomized trials and observational healthcare databases complement each other. The adolescent-focused trial of the Pfizer/BioNTech vaccine provided compelling evidence of its effectiveness to prevent symptomatic infection, but the estimates for severe disease and specific age groups were too imprecise. This analysis of Clalit's high-quality database emulates the design of the original trial, uses its findings as a benchmark, and expands upon them to confirm the vaccine's effectiveness in adolescents. This combination of evidence from randomized trials and observational studies is a model for efficient medical research, something which is especially important in COVID times."

Prof. Marc Lipsitch, Director of the Center for Communicable Disease Dynamics and Professor at the Harvard T.H. Chan School of Public Health, said, "In all studies of vaccine effectiveness, a major challenge is to ensure that those we are comparing to identify the vaccine's effect are similar in the other characteristics that may predict whether they get infected or ill. This is especially hard in the context of a rapidly growing, age-targeted vaccine campaign. Clalit's extraordinary database made it possible to design a study that addressed these challenges in a way that provides tremendous confidence in the inferences that come out of the study."

The research is published in *New England Journal of Medicine*.

More information: Effectiveness of the BNT162b2 COVID-19 Vaccine against the B.1.617.2 (Delta) Variant in Adolescents, *New England Journal of Medicine*, 2021.

Provided by Clalit Research Institute