

BCG vaccine prevents tuberculosis in young children, but not adults: study

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Amid longstanding debate on the effectiveness of the tuberculosis vaccine, a new study suggests that the vaccine is protective against TB in children under 5, but adolescents and adults in high-burden countries



may need additional protection to maintain immunity beyond childhood.

The <u>tuberculosis</u> (TB) vaccine, bacille Calmette-Guérin (BCG), is one of the most widely administered vaccines across the globe. Nearly 100 years old, it is the only vaccine ever administered to treat TB, which afflicts more than 10 million people each year.

Despite the age and widespread use of the BCG vaccine, there is still considerable debate on its effectiveness in preventing TB, and how long immunity may last after it is administered in infancy. And as experts study and propose new TB vaccines to supplement the BCG vaccine, an important consideration is the age at which these new vaccines should be administered to high-risk populations.

Now, a new study led by a Boston University School of Public Health (BUSPH) researcher provides new insight and clarity on these issues.

Published in *The Lancet Global Health*, the study found that BCG vaccination at birth does provide significant protection against TB disease—but only among children under 5 years old. The vaccine provided no protection among adolescents or adults in this study.

These results suggest that protectiveness from the BCG vaccine may begin to wane as children get older and, thus, children over 10 years old and adults should receive a booster BCG vaccine—and eventually a new, supplemental vaccine, as the researchers note that the BCG booster may also have limited efficacy—for immunity against TB beyond childhood. Unfortunately, a BCG booster has limited efficacy, so new vaccines are needed.

"Unlike many of the mRNA COVID-19 vaccines, which we know are highly effective, there is widespread debate on the BCG vaccine's effectiveness and duration of protection, as well as whether the vaccine



only works in selective settings," says study lead author Dr. Leonardo Martinez, assistant professor of epidemiology at BUSPH. "Our findings indicate that BCG vaccination is effective at preventing tuberculosis in young children. Since tuberculosis in children is a highly debilitating and severe disease, BCG vaccination should continue to be used."

However, since the results show that the vaccine was ineffective in adolescents and adults, "boosting immunoprotection is needed for older populations," Martinez says. "Novel vaccines are urgently needed to supplement BCG vaccination in high-burden settings."

These findings provide up-to-date assessments on TB vaccine effectiveness, as the majority of previously published studies on this subject were conducted more than 50 years ago, with varying results, and primarily in settings with a relatively low burden of the disease. This new analysis presents data over the past 10 years, from high-burden settings in 17 countries, including South Africa, China, Vietnam, Indonesia, Uganda, The Gambia, and Brazil.

For the study, Martinez and colleagues analyzed individual-level data from 26 <u>longitudinal studies</u> that included nearly 70,000 participants exposed to TB from 1998 to 2018. The researchers examined the impact of BCG vaccination for all TB disease, as well as specifically for pulmonary and extrapulmonary TB. The analysis examined variability across the studies, including the use of skin and blood TB infection tests, and accounted for potentially confounding factors such as HIV, exposure status, and history of prior TB, amongst others.

Among all children under 5 years old, BCG vaccination was 37 percent effective. The researchers did not find conclusive evidence that the vaccine was protective among children over 10 or among adults. When focusing only on pulmonary TB, BCG vaccination was 19 percent effective, however this effect was also only among young <u>children</u>.



Although the BCG vaccine is not widely administered in the United States, Martinez says that this new information lends important implications for the US and other wealthy countries.

"The vast majority of tuberculosis in the US and other high-income countries occurs in immigrants who recently traveled to the US from settings with a high burden of tuberculosis," he says. "Several costeffectiveness and mathematical modeling studies have found that devoting resources to countries with a high burden of tuberculosis outside the US is amongst the most effective intervention to control tuberculosis inside the US. So although our results are mostly in settings with a high burden of tuberculosis, they are also relevant to low-burden settings."

The researchers stress that substantial investment in TB vaccine development is critical to controlling global TB.

"We urgently need vaccines that are effective against TB in adults," says study coauthor Dr. C. Robert Horsburgh, professor of epidemiology. "There are a number of promising TB <u>vaccine</u> candidates under study and we hope that one or more of them will prove effective."

Click here to read the <u>full study</u>, and <u>here to read the accompanying</u> <u>commentary</u> by Mark Hatherill of the South African Tuberculosis Vaccine Initiative at the University of Cape Town's Institute of Infectious Disease and Molecular Medicine, and Frank Cobelens in the Department of Global Health at Amsterdam University Medical Centers, University of Amsterdam.

More information: Leonardo Martinez et al, Infant BCG vaccination and risk of pulmonary and extrapulmonary tuberculosis throughout the life course: a systematic review and individual participant data metaanalysis, *The Lancet Global Health* (2022). <u>DOI:</u>



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