Tuberculosis vaccine may enable elimination of the disease in cattle by reducing its spread

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Bovine tuberculosis is an infectious disease of cattle that results in large economic costs and health impacts across the world. Credit: Jacqueline Garget

Vaccination not only reduces the severity of TB in infected cattle, but reduces its spread in dairy herds by 89%, research finds. The research, led by the University of Cambridge and Penn State University, improves prospects for the elimination and control of bovine tuberculosis (TB), an infectious disease of cattle that results in large economic costs and health impacts across the world. The study is published in the journal *Science*.

This is the first study to show that BCG-vaccinated cattle infected with TB are substantially less infectious to other cattle. This remarkable indirect effect of the vaccine beyond its direct protective effect has not been measured before.

The spillover of infection from livestock has been estimated to account for about 10% of human tuberculosis cases. While such zoonotic TB (zTB) infections are most commonly associated with gastrointestinal infections related to drinking contaminated milk, zTB can also cause chronic lung infections in humans. Lung disease caused by zTB can be indistinguishable from regular tuberculosis, but is more difficult to treat due to natural antibiotic resistance in the cattle bacteria.

TB remains endemic in many countries around the world, including in Europe and the Americas, where its control costs farmers and taxpayers hundreds of millions of dollars each year.

The new study found that vaccination not only reduces the severity of TB in infected cattle, but reduces its spread in dairy herds by almost 90%. Credit: Jacqueline Garget

In the study, carried out in Ethiopia, researchers examined the ability of the vaccine, Bacillus Calmette-Guérin (BCG), to directly protect cattle that receive it, as well as to indirectly protect both vaccinated and unvaccinated cattle by reducing TB transmission. Vaccinated and unvaccinated animals were put into enclosures with naturally infected animals, in a novel crossover design performed over two years.

"Our study found that BCG vaccination reduces TB transmission in cattle by almost 90%. Vaccinated cows also developed significantly fewer visible signs of TB than unvaccinated ones. This suggests that the

vaccination not only reduces the progression of the disease, but that if vaccinated animals become infected, they are substantially less infectious to others," said Andrew Conlan, Associate Professor of Epidemiology at the University of Cambridge's Department of Veterinary Medicine and a corresponding author of the study.

Using livestock census and movement data from Ethiopia, the team developed a transmission model to explore the potential for routine vaccination to control bovine tuberculosis.

"Results of the model suggest that vaccinating calves within the dairy sector of Ethiopia could reduce the reproduction number of the bacterium—the R_0—to below 1, arresting the projected increase in the burden of disease and putting herds on a pathway towards elimination of TB," Conlan said.

The study showed that vaccinating dairy calves could put herds on a pathway towards elimination of TB. Credit: Jacqueline Garget

The team focused their studies in Ethiopia, a country with the largest cattle herd in Africa and a rapidly growing dairy sector that has a growing burden of bovine tuberculosis and no current control program, as a representative of similarly situated transitional economies.

"Bovine tuberculosis is largely uncontrolled in low- and middle-income countries, including Ethiopia," said Abebe Fromsa, associate professor of agriculture and veterinary medicine at Addis Ababa University in Ethiopia and the study's co-lead author. "Vaccination of cattle has the potential to provide significant benefits in these regions."

"For over a hundred years, programs to eliminate bovine tuberculosis have relied on intensive testing and slaughtering of infected animals," said Vivek Kapur, professor of microbiology and infectious diseases and Huck Distinguished Chair in Global Health at Penn State and a corresponding author of the study.

He added, "This approach is unimplementable in many parts of the world for economic and social reasons, resulting in considerable animal suffering and economic losses from lost productivity, alongside an increased risk of spillover of infection to humans. By vaccinating cattle, we hope to be able to protect both cattle and humans from the consequences of this devastating disease."

Professor James Wood, Alborada Professor of Equine and Farm Animal Science in the University of Cambridge's Department of Veterinary

Medicine, noted that despite TB being more prevalent in lower-income countries, the United Kingdom, Ireland and New Zealand also experience considerable economic pressures from the disease which continues to persist despite intensive and costly control programs.

Wood said, "For over 20 years the UK government has pinned hopes on cattle vaccination for bovine tuberculosis as a solution to reduce the disease and the consequent costs of the controls. These results provide important support for the epidemiological benefit that cattle vaccination could have to reduce rates of transmission to and within herds."

More information: Abebe Fromsa et al, BCG vaccination reduces bovine tuberculosis transmission, improving prospects for elimination, *Science* (2024). DOI: 10.1126/science.adl3962. www.science.org/doi/10.1126/science.adl3962

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