



Potential for New BCG Revaccination Strategies, Hope For Subunit Vaccines

Results from the Phase 2 clinical trial of the H4 vaccine candidate and BCG revaccination



An innovative trial in adolescents with two TB vaccines

This was the first randomized, controlled, prospective Prevention of Infection (POI) trial ever conducted to study whether vaccination can prevent *Mycobacterium tuberculosis* (Mtb) infection in high-risk, healthy adolescents. Conducted in the Western Cape Province of South Africa, the trial tested the ability of **Bacille Calmette-Guérin (BCG)** and new vaccine candidate **H4:IC31** to help prevent an initial or a sustained TB infection.

Why BCG?

The BCG vaccine is nearly 100 years old. A single dose given at birth is moderately effective in preventing severe TB in infants and young children, but does not adequately protect teens and adults, who are most at risk for developing and spreading TB. This study wanted to investigate if a second dose of BCG (revaccination) for adolescents might provide protection against Mtb infection.

What were the results?

- **BCG showed a significant ability to help people control or clear a TB infection.** BCG showed efficacy in preventing sustained TB infections—meaning participants who initially tested positive for TB infection were more likely to have cleared or controlled the infection within six months. H4 also showed a trend towards being able to prevent sustained TB infections, although not at statistically significant levels.
- In this study, TB infection was determined by a commercially available blood test called the QuantiFERON®-TB Gold in Tube test (QFT-GIT)
- **Neither vaccine showed any significant ability to prevent people from getting an initial TB infection**

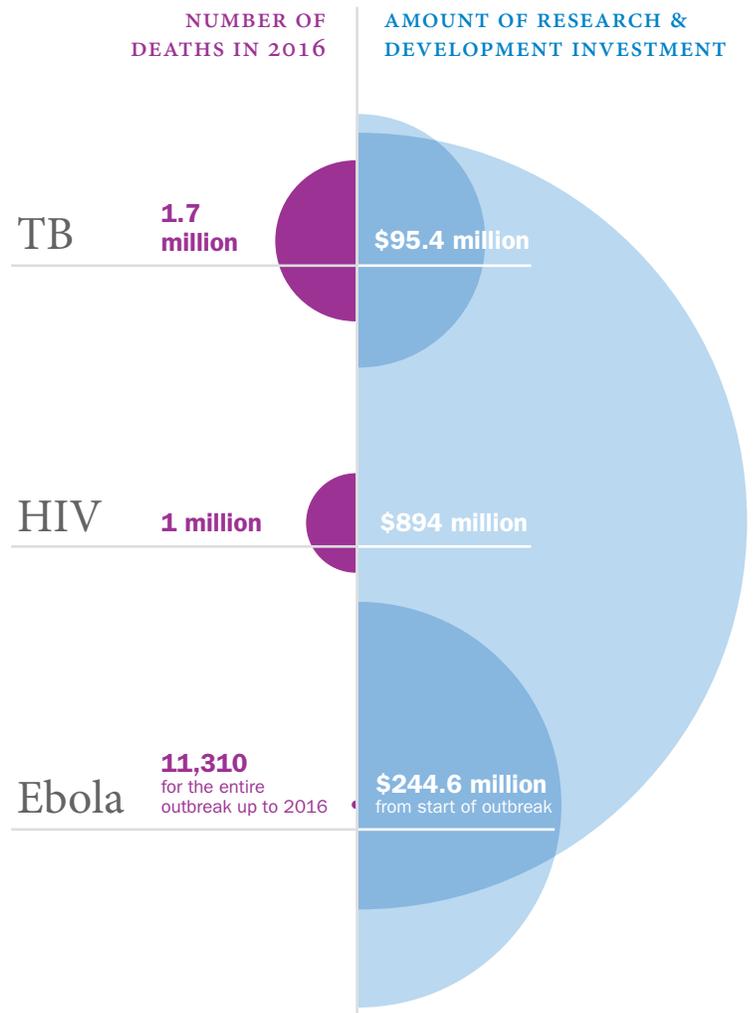
What this means for the field

- **The H4 results, while not robust enough to move forward with the candidate, are very encouraging for other subunit vaccines in the pipeline.** This was the first efficacy signal ever demonstrated by a subunit TB vaccine candidate.
- **The BCG results warrant further evaluation of BCG revaccination as a potential strategy to help prevent TB in not yet infected people in high-incidence countries until a better vaccine is developed.**

We will not end the TB epidemic without new vaccines and vaccination strategies. Success depends on innovation and more investment.

Fast Facts

- 1/3 of the world is infected with *Mycobacterium tuberculosis* (Mtb). That's more than 2 billion people.
- Some people will clear the infection on their own, but around 10% will progress to TB disease.
- With 10.4 million new cases and 1.7 million deaths in 2016, TB was deadlier than Ebola, malaria, or even HIV.



Glossary

H4:IC31 – a new subunit vaccine being developed by Aeras and Sanofi Pasteur. Previously tested for safety and immune response in animals and humans.

Subunit vaccine – a type of vaccine that contains just a fragment of the bacteria to elicit an appropriate immune response.

Bacille Calmette-Guérin (BCG) – the only currently licensed TB vaccine in the world.

TB infection – When a person is infected with Mtb, but does not have symptoms or feel ill. In this study, TB infection was determined by a commercially available blood test called the QuantiFERON®-TB Gold in Tube test (QFT-GIT).

TB disease – When a TB infection has progressed to a more serious state. People with TB disease have active symptoms and can infect others. About 10% of people who are infected with TB will go on to get TB disease.

Sustained Infection – In this study, sustained infection was defined as someone having positive QFT-GIT tests for 6 months.

POI – Prevention of Infection. A new study design that can be used to evaluate the biologic effect of a vaccine candidate before advancing to larger, longer and more costly prevention of disease (POD) studies.