

## Impact of BCG vaccination against *Mycobacterium tuberculosis* infection in adult healthcare workers: A nested clinical trial

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**Background:** The effectiveness of the Bacille Calmette-Guérin (BCG) vaccine for adult pulmonary tuberculosis (TB) remains uncertain. This study aimed to evaluate the effect of BCG-Denmark vaccination in preventing initial and sustained interferon- $\gamma$  release assay conversion in Brazilian health-care workers.

**Methods:** This nested randomized controlled trial within the BRACE trial (NCT04327206) enrolled Brazilian adult healthcare workers from three sites in Brazil: Manaus, Campo Grande, and Rio de Janeiro, irrespective of previous BCG vaccination. Exclusions included contraindications to BCG, over 1 month of TB treatment, previous adverse BCG reactions, recent BCG vaccination, or non-compliance with interventions. Eligible participants were randomly assigned (1:1) to either the BCG group (0.1 mL intradermal injection of BCG-Denmark [Danish strain 1331; AJ Vaccines, Copenhagen]) or the placebo group (intradermal injection of 0.9% saline) via web-based randomization in blocks (2, 4, or 6), stratified by study site, age, and comorbidity. The QuantiFERON-TB Gold (QFT) Plus test (Qiagen; Hilden, Germany) assessed TB infection at baseline and 12 months. The primary efficacy outcome was QFT Plus conversion ( $\geq 0.35$  IU/mL) by 12 months in participants with a negative baseline result ( $< 0.35$  IU/mL).

**Results:** Between Oct 07, 2020, and April 12, 2021, 1985 (77.3%) of 2568 participants were eligible for QFT Plus assessment at 12 months: 996 (50.2%) in the BCG group and 989 (49.8%) in the placebo group. Among them, 1475 (74.3%) were women, 510 (25.7%) were men, and the median age was 39 years (IQR 32–47). QFT Plus conversion occurred in 66 (3.3%) of 1985 participants: 34 (3.4%) in the BCG group and 32 (3.2%) in the placebo group (risk ratio 1.09 [95% CI 0.67–1.77];  $p=0.791$ ).

**Conclusion:** BCG-Denmark vaccination did not reduce Brazilian health-care workers' initial QFT Plus conversion risk. This highlights the need for further research into TB prevention in high-risk populations.

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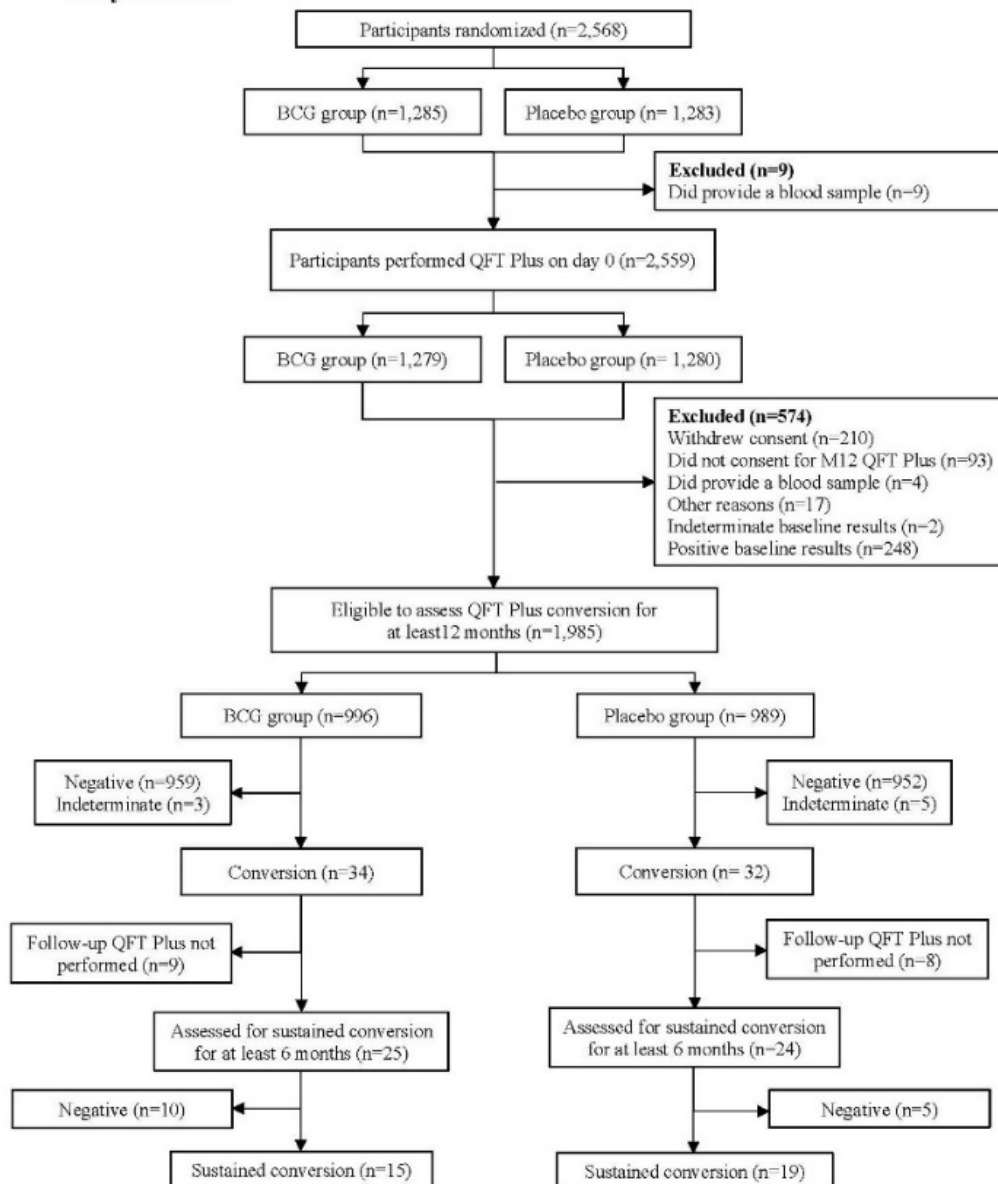


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**Conflicts of Interest**

None

**Study flowchart.**



BCG: Bacille Calmette–Guérin, QFT Plus: QuantiFERON TB Gold Plus.

