United States of America

SMART4TB Consortium

PRISM-TB Trial

Program for Rifampicin-resistant disease with Stratified Medicine for TB

BACKGROUND

The U.S. government invests in and promotes American health innovation globally, with TB treatment research a vital component of these efforts. Drug-resistant TB—a dangerous strain of TB that can't be cured by standard first-line antibiotics—is more difficult and expensive to treat. According to the Global TB Report 2025, 390,000 people a year fall ill with drug- resistant TB and while recent advances have improved treatment using a combination of more powerful, safer medicines: bedaquiline, pretomanid, linezolid, and moxifloxacin, the current recommended regimen still takes six months of treatment. People receive the same length of treatment, regardless of their individual risk factors, PRISM-TB is exploring shorter, more personalized strategies that could help improve treatment and save lives around the world while decreasing the risk of more drug-resistant strains in the U.S.

STUDY GOAL

To evaluate whether shorter treatment, three or four months, depending on individual risk factors (stratification) for treatment failure or relapse, is effective at curing drug-resistant TB in adults and adolescents.

STUDY LEADERS

Gustavo Velásquez at the University of California, San Francisco (UCSF) in partnership with Johns Hopkins University and **William Worodria** at the World Alliance for Lung and Intensive Care Medicine in Uganda, **Rosa Infante Castro** at Policlínico SES in Peru and **Olivia Peña Vasquez** at Hospital Nacional Sergio E. Bernales in Peru, and **Bazarragchaa Tsogt** at the Mongolian Anti-Tuberculosis Coalition

STUDY POPULATION

Adults and adolescents, including pregnant and lactating women, aged ≥14 years with confirmed TB of the lungs that is resistant to the first-line antibiotic rifampicin.

STUDY LOCATIONS

Mongolia
Peru
Uganda

STUDY DESIGN (ClinicalTrials.gov NCT06441006)

PRISM-TB is a Phase 2c/3 **multi-arm multi-stage**, **randomized**, **controlled**, **noninferiority** trial enrolling 200 participants. The main objectives are to find out:

- Whether shorter treatment strategies are as effective as standard treatment—as measured by TB-related unfavorable outcomes (death, **relapse**, or **treatment failure**) at 18 months after treatment. The treatment strategies being tested are:
  - Four months for all participants and
  - Three months or six months depending on individual factors noted in the box on the following page
- Whether shorter treatment strategies are as safe as the control, by looking at the proportion of participants who experience adverse events that are serious or of special interest.
- A risk-benefit analysis with a desirability of outcome ranking (DOOR) to select optimal treatment for Stage 2.

Multi-arm multi-stage (MAMS) trials allow comparing several regimens, with prespecified decision-making for which regimen(s) can advance to the next stage and are more efficient than multiple separate studies.

A **randomized controlled** trial assigns participants to the study intervention (in this case, the three- or four-month regimens) or the control (the standard of care), to balance participant characteristics with a goal of minimizing bias.

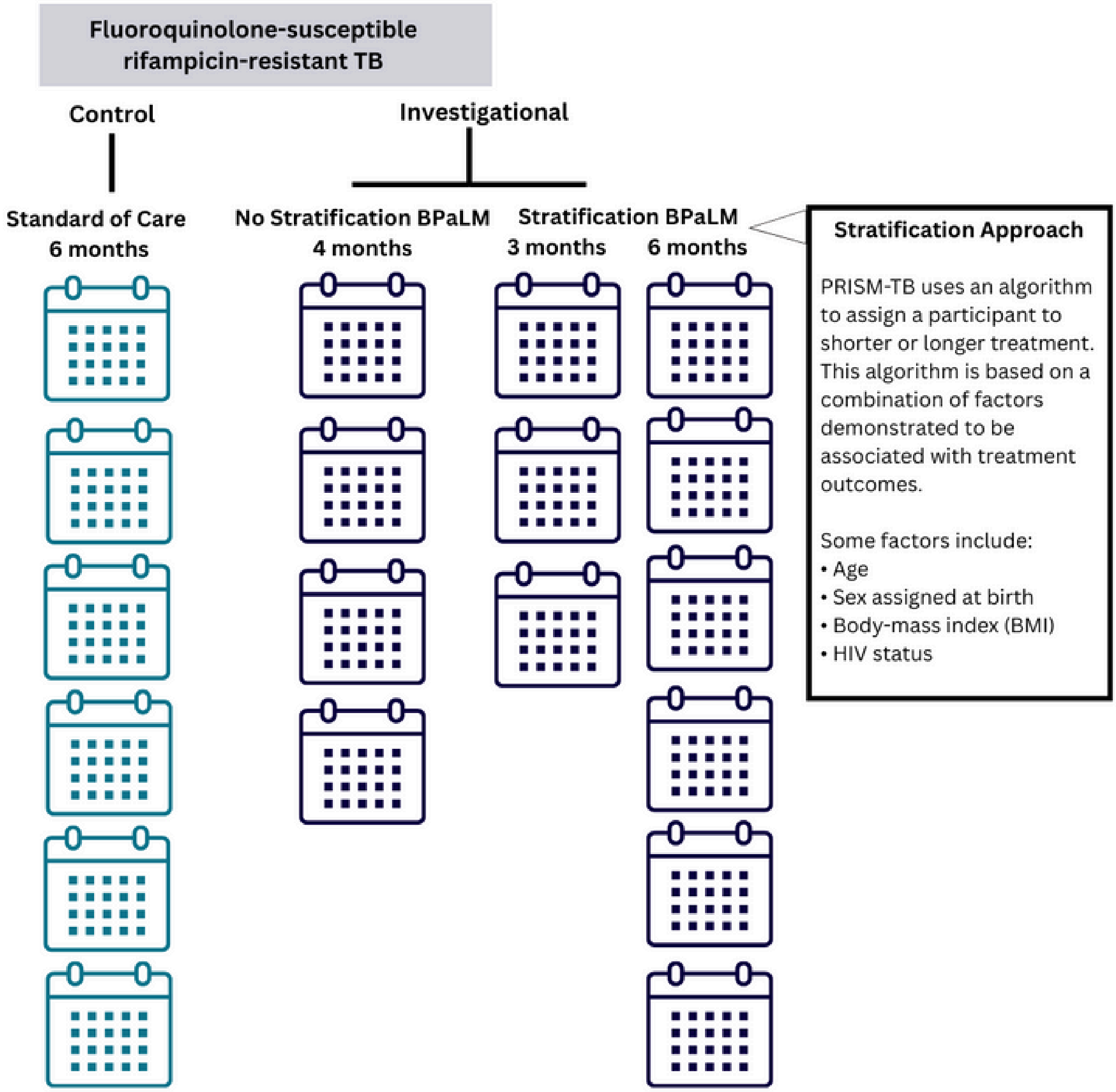
Noninferiority trials test that the treatment being studied is not worse than standard treatment.

Relapse is a return of TB disease following a period of partial improvement.

Treatment failure is when the treatment fails to cure TB.

Adverse event is any unfavorable and unintended sign (including laboratory test results), symptom or diagnosis that occurs in a study participant during the study.

STUDY DESIGN, CONTINUED



B=bedaquiline, Pa=pretomanid, L=linezolid, M=moxifloxacin

If you have any questions, please contact prism.central@ucsf.edu

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