



World Health
Organization

TDR For research on
diseases of poverty
UNICEF • UNDP • World Bank • WHO

Short, all-Oral Regimens For Rifampicin-resistant Tuberculosis: The ShORRT Research Package

Background

Tuberculosis (TB) is the leading cause of death from a single infectious agent, ranking above HIV/AIDS and malaria. Annually, an estimated 10 million people develop TB disease.

Resistance to anti-TB drugs is a major obstacle to effective TB care and prevention globally. Drug-resistant TB (DR-TB) is multi-factorial and is fuelled by sub-optimal treatment of patients, airborne transmission of the TB bacilli. Nearly half a million people were estimated to have developed multidrug-resistant or rifampicin-resistant TB (MDR/RR-TB) in 2018.

MDR/RR-TB cannot be treated with the standard 6-month course of first-line medication which is effective in most TB patients, and it requires longer and less tolerable treatment with generally poor outcomes.

Attempts to reduce the length of conventional MDR/RR-TB regimens and to use a combination of drugs which is tolerable have been ongoing for several years through various studies. Based on recent evidence, in 2019 the World Health Organization (WHO) released updated guidelines that are expected to lead to major improvements in

treatment outcomes and quality of life of MDR/RR-TB patients, including reduced socioeconomic impact. In these guidelines, the adoption of modified all-oral shorter regimens is recommended under operational research conditions.

In order to facilitate the conduct of operational research by countries, and to generate data that are harmonised across different implementation settings, a standardised methodology is required at least for two of the key elements under investigation, namely the effectiveness and safety of the all-oral shorter treatment regimens.

Evidence from this research can inform programmatic implementation at the country level, and also provide important data to the global TB community to strengthen the evidence base and inform treatment guidance.

Integral components related to the implementation and uptake of the new treatment regimens should be considered by National Tuberculosis Programmes as they bear programmatic implications. These include the feasibility and acceptability of the new regimens, and their impact on quality of life of patients, and associated costs to the patients and the health system.

The ShORRT research package

TDR, in close collaboration with the Global TB Programme at WHO, and technical partners, is leading the development of ShORRT, an implementation/operational research (IR/OR) package, including data collection tools and key procedures, to assess the effectiveness, safety, feasibility, acceptability, cost and impact (including on the Quality of Life) of the use of all-oral shorter drug regimens for MDR/RR-TB patients.

The ShORRT research package is aligned with the 2019 WHO [*Consolidated guidelines on drug-resistant tuberculosis treatment*](#), and the [*Companion Handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis*](#).

Objective of the study

To determine the effectiveness, safety, feasibility, cost and impact on the quality of life of all-oral shorter MDR/RR-TB treatment regimens under programmatic conditions.



Study design

Longitudinal study design with one single cohort of MDR/RR-TB patients receiving the all-oral shorter drug regimens for MDR/RR-TB patients.

Alternatively, a stepped-wedge design comparing the all oral shorter MDR/RR-TB regimen to the standard MDR-TB treatment in use in the country.

Outcomes of interest

1. Effectiveness:

Primary outcome: the proportion of MDR-TB patients who have a favourable treatment outcome, defined as “cured” or “treatment completed” without recurrence during 12 months after successful treatment.

2. Safety:

Primary outcome: the proportion of MDR/RR-TB patients with serious adverse events, occurring event during treatment and up to 6 months after the end of the treatment.

3. Complementary research outcomes:

- Health related Quality of Life of MDR/RR-TB patients
- Level of stigma experienced by MDR/RR-TB patients and health care providers
- Feasibility of the implementation of all-oral shorter MDR/RR-TB treatment regimens
- Acceptability of all-oral shorter MDR/RR-TB treatment regimens
- Cost and cost-effectiveness from a societal and/or health care perspective, socioeconomic impact for MDR/RR-TB patients

The ShORRT research package: how does it work?

The ShORRT research package consists of two main components. The first component (Part A) provides a template protocol and data collection tools for studies investigating the [effectiveness](#) and [safety](#) of all-oral shorter MDR/RR-TB regimens.

The second component (Part B) describes protocols and offers data collection tools for recommended complementary research into assessing health-related quality of life of MDR/RR-TB patients, to measure stigma experienced by MDR/RR-TB patients and health care providers, to ascertain the feasibility of the implementation of all-oral shorter MDR/RR-TB regimens, and the acceptability of patient support services and model of care to patients and health care providers, and for conducting cost and cost-effectiveness analysis.

During country adaptation, investigators can integrate relevant sections of the above recommended complementary research into the main protocol or develop stand-alone protocols for sub-studies of interest.

Investigators who have developed their own study protocol(s) can choose to only adopt and adapt the data collection tools, study procedures, and training materials.

TDR/GTB support to country study teams

The team at TDR and GTB, and technical partners are available to provide in-country and remote support to study teams during the adaptation of the study protocol and implementation of the IR/OR.

For any query, investigators can e-mail ShORRT@who.int

Available resources

The generic protocol, key study procedures, data collection tools and training materials are available at https://www.who.int/tdr/research/tb_hiv/en/

- [WHO Consolidated Guidelines on drug-resistant tuberculosis treatment](#)
- [Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis](#)