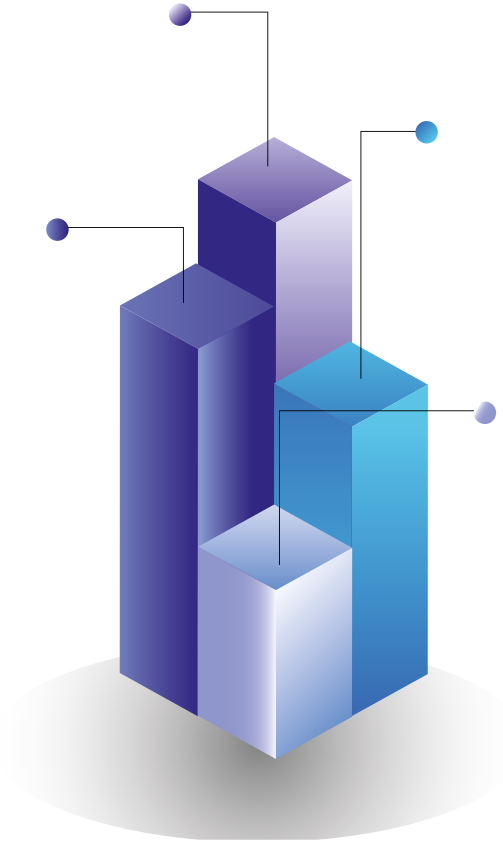
Meeting report of the WHO expert consultation on drug-resistant tuberculosis treatment outcome definitions

17-19 November 2020



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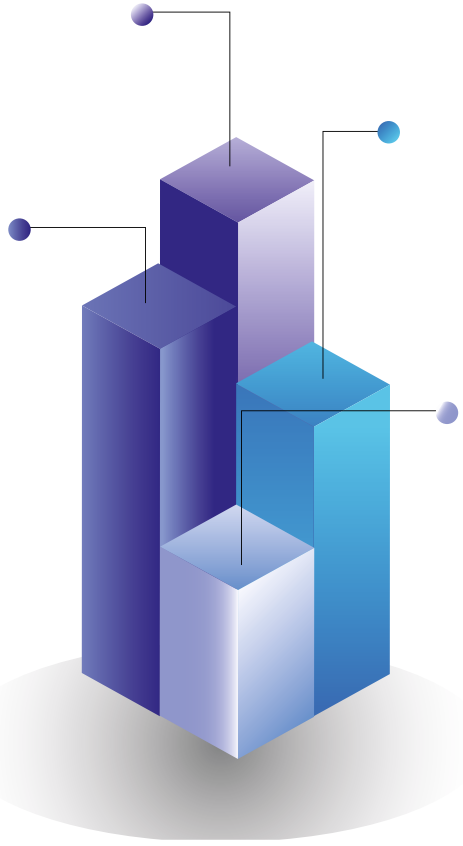

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Contents

Abbreviations

ADR	adverse drug reaction
AIDS	acquired immunodeficiency syndrome
BPaL	bedaquiline, pretomanid and linezolid
DNA	deoxyribonucleic acid
DR-TB	drug-resistant tuberculosis
DST	drug-susceptibility testing
DS-TB	drug-susceptible tuberculosis
HIV	human immunodeficiency virus
MDR/RR-TB	multidrug-resistant or rifampicin-resistant tuberculosis
MDR-TB	multidrug-resistant tuberculosis
NTP	national tuberculosis programme
RNA	ribonucleic acid
RR-TB	rifampicin-resistant tuberculosis
TB	tuberculosis
WHO	World Health Organization
XDR-TB	extensively drug-resistant tuberculosis

Executive summary

The World Health Organization (WHO) held an online consultation on the definitions of drug-resistant tuberculosis (DR-TB) treatment outcomes, on 17–19 November 2020. Organized by the WHO Global TB Programme, Geneva, Switzerland, the consultation was attended by 66 participants, representing countries, bilateral and multilateral agencies, international organizations, nongovernmental organizations, civil society and academia.

The consultation discussed recent and potential future developments in treatment regimens for both DR-TB and drug-susceptible TB (DS-TB) and considered possible changes to the treatment outcome definitions needed for programmatic monitoring. The specific objectives of the consultation were to discuss:

- recent developments in treatment regimens and in diagnostics for monitoring treatment of DR-TB, and to determine how these developments affect the current definitions of treatment outcomes; and
- options for changing the treatment outcome definitions, including the pros and cons of these options from various perspectives (e.g. clinical, programmatic and surveillance).

The online consultation ran for a total of 9 hours, with a 3-hour session on 3 consecutive days. Most of the time was devoted to discussion of four topics:

- recent developments in tuberculosis (TB) treatment and diagnostics for treatment monitoring;
- principles and strategic issues that will underlie the new definitions of treatment outcomes;
- operational issues related to the definitions of treatment outcomes; and
- an outline of the new definitions of treatment outcomes, including next steps.

Before the meeting, the WHO Global TB Programme shared a concept note with participants for review and feedback. The note provided overviews of the history of definitions of treatment outcomes and of recent developments in TB treatment and diagnostics for treatment monitoring. It also provided a rationale for potential changes in the definitions of treatment outcomes, with the main reasons for changes being that:

- recent DR-TB treatment regimens are shorter, whereas the current definitions are mainly applicable to longer regimens;
- the all-oral nature of recommended regimens departs from the traditional intensive and continuation phases, whereas the current definitions include timing of culture conversion;
- expected treatment response thresholds occur earlier with new combinations of medicines, whereas the current definitions link assessment to bacteriological conversion; and
- there is still no reliable, suitable and universally applicable biomarker for treatment follow-up and monitoring; thus, a clear definition of bacteriological conversion and reversion is needed to inform the treatment regimen (i.e. whether to continue, halt or modify it).

The difference in treatment outcome definitions for DR-TB and DS-TB is also considered a challenge for implementation. Hence, it would be ideal to have a simplified set of treatment outcome definitions, applicable to both DR-TB and DS-TB.

The concept note proposed three options for outcome definitions to be discussed at the consultation. Options 1 and 2 related to DR-TB treatment outcomes only, whereas option 3 was applicable to both DR-TB and DS-TB.

During the consultation, participants identified general principles that are important and relevant to the revision of treatment outcome definitions, and suggested that the revised definitions will need to:

- be simple and, if possible, applicable to treatment of both DS-TB and DR-TB;
- be applicable to treatment regimens of different lengths;
- de-emphasize the traditional division between intensive and continuation phases;
- identify the appropriate threshold for bacteriological conversion (or reversion) in relation to the definitions of “treatment failed”, “cured” and “treatment completed”;
- consider the use of appropriate diagnostics for treatment monitoring;
- have clear parameters for defining treatment failure, based on a decision to change or stop treatment, or reliable evidence for non-response; and
- be practical for clinical and programmatic monitoring, and feasible for national TB programmes (NTPs) to implement.

The consultation highlighted the following strategic issues, which should guide the development of new treatment outcome definitions:

- Harmonization of treatment outcomes for DS-TB and DR-TB is needed, although some peculiarities and specifics should remain (e.g. treatment monitoring by sputum culture for DR-TB and by sputum microscopy for DS-TB).
- Despite some distinct phases remaining in current regimens, the overall trend is towards monotonous regimens. Thus, linking definitions to treatment phases should be avoided, which means that the time threshold to declare cure or treatment failure should be revised.
- While considering new treatment monitoring tools, we will continue to rely on the available tools (i.e. sputum culture for DR-TB and sputum microscopy for DS-TB), despite their drawbacks.
- At the end of treatment, it is important and feasible for programmes to ascertain cure. The idea of sustained cure may have value, but perhaps only in operational research, depending on needs and the resources available.

Participants spent some time discussing proposed definitions of the treatment outcome categories: “treatment failed”, “cured”, “treatment completed”, “died”, “lost to follow-up” and “not evalu-