World Health Organization

Rapid Communication

on forthcoming changes to the programmatic management of tuberculosis preventive treatment

February 2020

WHO/UCN/TB/2020.4

Suggested citation. Rapid Communication on forthcoming changes to the programmatic management of tuberculosis preventive treatment. Geneva: World Health Organization; 2020 (WHO/UCN/TB/2020.4). Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.

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Background & rationale

Tuberculosis (TB) remains a threat to global public health and is the top infectious cause of death globally. Each year about 10 million people develop TB and 1.5 million die from it. An estimated one fourth of the world's population is infected with the TB bacterium, of whom 5–10% advance to active TB disease in their lifetime. The risk of developing active TB after infection depends on several factors, the most important being the person's immunological status. TB preventive treatment (TPT), given to people at the highest risk of progressing from TB infection to disease, remains a critical intervention to achieve the global targets of the End TB Strategy, as reiterated by the UN High Level Meeting on TB in 2018. TPT fits within a larger framework of preventive actions envisaged by Pillars 1 and 2 of the End TB Strategy, ranging from screening for active TB, infection control, prevention and care of HIV and other co-morbidities and health risks, access to universal health care, social protection and poverty alleviation.

Delivering TPT effectively and safely requires programmatic coordination at several key steps in the cascade of preventive care: identifying individuals at highest risk, testing them for infection, excluding active TB disease, choosing the treatment option that is best suited to an individual, managing adverse drug reactions, supporting medication adherence and monitoring programmatic performance.

In support of efforts to coordinate these activities successfully, the Global TB Programme of the World Health Organization (WHO/GTB) has developed guidelines on TPT, intended primarily for national policy-makers and practitioners working on TB, HIV and infectious diseases in public and private sectors and in the community. The latest WHO guidance on TPT was released in 2018. Since then, two important trials of shorter rifamycin-containing regimens were published. In addition, results from other studies on the safety of isoniazid in pregnancy were reported. More evidence also became available about the co-administration of rifamycins and dolutegravir in people living with HIV (PLHIV). Finally, user feedback pointed to areas that could benefit from additional clarification and operational advice to enhance the implementation of the guidance.

In July 2019 WHO convened a Guideline Development Group (GDG) to assess the implications of the new findings on the programmatic management of TB preventive treatment. The evidence summaries, decisions, and resulting policy changes were documented using the GRADE approach (Grading of Recommendations, Assessment, Development and Evaluation) to assess the evidence systematically. The full recommendations will be published by WHO/GTB on World TB Day 2020.

This Rapid Communication is being published to prepare stakeholders for the forthcoming changes in the 2020 update of the TPT guidelines, which is particularly important at this juncture as many countries develop new project proposals for the Global Fund.

WHO gratefully acknowledges the work of the GDG members and other experts involved in the development of the guidelines, the evidence reviewers, the data contributors and the study participants for the successful update in 2020.

Main updates

The key updates of the 2020 guidelines will feature the following:

- The GDG for the 2020 guidelines broadened the applicability of five of the previous recommendations across all burden settings while highlighting the implications of implementation in areas with low and high TB incidence. In this context the importance of appropriate resource mobilization is stressed.
- A regimen of one month of daily rifapentine plus isoniazid ("1HP") and another regimen of four months of daily rifampicin ("4R") are now proposed as TPT options for both high- and low- TB incidence settings.
- Based upon the latest study results the GDG considered that a systematic deferral of isoniazid preventive treatment (IPT) to the postpartum period in pregnant women living with HIV would deprive them of significant protection when they are highly vulnerable to TB. While acknowledging a need for more research, pregnancy does not disqualify women living with HIV from receiving preventive treatment with the TB medicines isoniazid and rifampicin.
- There are no grounds to support dose changes when rifapentine and dolutegravir are used together (however the dose of dolutegravir needs to be increased when it is given with rifampicin).
- Overall, the guidelines document has also been extensively revised, with a reorganization of the content of the different sections; additional commentary accompanying the recommendations; an updating of references to the most recent citations and evidence; aligning the durations of certain regimens to the ones most often used; and merging the four previous algorithms into one. The research gaps have also been updated to reflect the latest status of the evidence.

Next steps

The new guidelines, along with the GRADE evidence tables, will be the first to be released under the rubric of the new *WHO consolidated TB guidelines,* which will gradually group all recommendations on TB. This guidelines series will be complemented by matching modules of a consolidated operational handbook that will provide practical advice on how to put in place the recommendations at the scale needed to achieve national and global impact. The first handbook module in this series will also be on the programmatic management of TPT and will accompany the release of the TPT guidelines in March 2020 for World TB Day.

WHO will work with countries and technical and funding agencies to maximize the uptake of the new guidelines and support associated measures, such as access to rifapentine and access to diagnostics for TB infection and disease.

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