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In 2018, governments at the UN High Level Meeting on Tuberculosis (UNHLM) made bold commitments to end TB.

Foremost among these actions was to scale up tuberculosis (TB) preventive treatment (TPT) rapidly to at least 30 million people by 2022, including 24 million household contacts of TB patients and 6 million people living with HIV (PLHIV). In 2018, countries reported achieving TPT coverage in 1.8 million PLHIV, in about 350,000 contacts < 5 years and in 79,000 older contacts.

Less than three years are now left until the end of 2022. At the current rate of recruitment, the target for TPT in PLHIV should be reached, but the targets for household contacts will not. The current COVID-19 emergency presents an additional challenge for TB programmes worldwide. Nonetheless, this should not stop TB programmes from planning and launching a systematic and invigorated drive to boost contact investigation, TPT and treatment for TB.

Reaching the UNHLM targets requires collective efforts and more investment. A comprehensive strategy that includes TPT is an excellent investment.

To overcome the main barriers standing in the way of global scale-up in TPT, countries, partners, donors and communities should work together to:

- ensure that all TB programmes aiming to end or eliminate TB include TPT as an integral part of a comprehensive strategy
- advocate strongly and communicate widely for TPT scaleup
- strengthen contact investigation in the community and in households of people with active TB especially in the current context of the COVID-19 pandemic
- initiate contacts of all ages on TPT after TB disease is ruled out
- expand TPT in HIV services and in facilities caring for other people eligible for TPT
- develop capacity to test for TB infection and to exclude TB disease
- provide better tolerated and shorter TPT options on a large scale
- ensure adherence and completion of the full course of TPT
- collect data on contact investigation, and the initiation and completion of TPT to monitor programme performance

Overcoming key barriers to scale up tuberculosis preventive treatment (TPT)

A Call to Action

Tuberculosis (TB) preventive treatment (TPT) is an essential intervention towards achieving the goals of the End TB Strategy. Its effectiveness in reducing progression from TB infection to disease ranges from 60% to 90% and protection can last many years. Despite this, global action to expand TPT has been very slow and urgent steps should now be taken to accelerate the programmatic uptake of TPT.

The current COVID-19 emergency will challenge TB prevention and care worldwide, including the roll-out of TPT. Nonetheless, TB programmes should continue to scale up TB services and seek synergies when measures to combat COVID-19 are implemented. People who are confined at home due to COVID-19 may be more exposed to TB in their household, making it more important for contact investigation to target both conditions and to expand massively the TPT coverage among contacts.

This call to action highlights the main considerations that countries need to take when integrating TPT into their TB preventive measures, aligned to other recent guidance on the subject^{i,ii}. It addresses primarily programme managers and technical agencies helping them to revise their strategies and prepare funding proposals. This call stresses the specific need to strengthen contact investigation, a key activity that is underdeveloped in many countries and where a huge unmet need exists for TB preventive action. This does not diminish the importance of ensuring good coverage among people living with HIV (PLHIV) and others who could benefit from TPT¹.

TPT must be framed as an indispensable component of a comprehensive TB strategy. This is more critical without the prospect of an immunizing vaccine in a near future. National TB strategic plans and funding proposals should include TPT activities, with ambitious targets and proper budgets.

Programmatic considerations for contact investigation and TB preventive treatment

- People who are exposed to active TB are at increased risk for TB infection and disease. TB disease may be as high as 5% or more among household contacts, particularly children. PLHIV exposed to active TB have a higher risk for rapid progression to TB disease. Contact investigation aims to identify these people and evaluate if they need treatment for TB disease or TPT. These activities can arrest the progression of infection and treat disease early on in its course, reducing its severity, lethality and transmission.
- Contact investigation can also identify people exposed to drug-resistant TB. This requires different approaches to TPT and follow up, but they can still benefit from TPT. This is particularly common in eastern European and central Asian countries as well as other settings elsewhere with a high prevalence of resistance to the rifamycins and isoniazid, the mainstay components of TPT regimens in use today.
- TPT for contacts who are also in HIV care may be integrated in differentiated HIV service delivery (DSD) as these are scaled up for ARV services and for intensified TB case finding, particularly in high HIV burden settings. Provision of TPT for PLHIV should not however be delayed until DSD is firmly in place.
- In addition to households, contact investigation and active TB case finding are also important in congregate settings and healthcare facilities.

¹ These include people initiating anti-TNF treatment, or receiving dialysis, or preparing for an organ or haematological transplant, or who have silicosis, as well as prisoners, health care workers, migrants, homeless people and people who use drugs.

Governments and donors should commit adequate funding and human resources to undertake effective
household contact investigation and management by enrolling enough staff, mobilizing communities,
providing transport support, providing access to appropriate diagnostics, supplying medication and
treatment adherence support and modernizing record keeping and funding operational research into the
best models of care to scale up TPT activities.

Testing for TB infection

- Testing for TB infection using tuberculin skin testing (TST) or interferon-gamma release assays (IGRAs)
 helps direct TPT to people who may benefit most from it and avert unnecessary TPT and related harms. A
 positive test could also motivate better people to take TPT. However, national programmes currently have
 limited capacity for testing. Quality-assured TST is in limited supply and IGRAs are more expensive and
 require blood samples to be taken and transported to well-equipped laboratories.
- Overcoming the infrastructural and supply barriers to the provision of TST/IGRA is desirable and the longerterm goal should be to build the health system capacity needed for this, in terms of human resources, logistics and supply chain and monitoring and evaluation. This will also lay the foundation for the swift rollout in future of new improved point-of-care tests for TB infection.
- However, in the short term, any unavailability of TST/IGRA should not be a barrier to giving TPT to those
 groups most at risk of developing TB disease. In children under five years who are in contact with active TB
 and in PLHIV, TB infection testing is **not** required given the urgency to treat exposure in these subpopulations.
- In addition to testing for TB infection, exclusion of TB disease is important before starting TPT. Chest radiography can play an important role in ruling out TB disease and increase confidence in TPT. Counselling is another important component of people-centred care, to help individuals make an informed choice when offered TPT, based on a clear understanding of the potential benefits and harms of treatment.
- Governments and donors should factor in the human and infrastructural resources necessary to bring testing of TB infection and chest radiography within reach of more people

TB preventive treatment options and support

- The 2020 update of the WHO TPT guidelines recommends multiple treatment options that may be better suited to certain target populations, including children and PLHIV in high or low TB burden settingsⁱⁱⁱ.
- Transition to shorter, better tolerated rifamycin-based TPT regimens, with better prospects for adherence should be one of the goals of programmes.
 - Rifapentine-containing regimens lasting 4 or 12 weeks (3HP and 1HP) are now recommended for many people in need of TPT;
 - These regimens may also be used in children but 3 months of isoniazid-rifampicin (3HR) is currently preferred due to availability of child-friendly dispersible fixed-dose combinations;
 - The triple combination of isoniazid+cotrimoxazole+B6 may be a preferred option for TPT among PLHIV, including pregnant and postpartum women;
 - o TPT to protect people exposed to MDR-TB under programmatic settings should also be considered
- While shorter rifamycin-based regimens and other TPT are generally safe, ancillary medicines (e.g. pyridoxine) and tests (e.g. liver function tests) should be available if needed. They are not routinely required and should therefore not be a barrier to the scale-up of TPT.
- Until supplies to optimize TPT with newer regimens are secured countries should not withhold older approaches like 6 months isoniazid from adults and children who need it.

- People on TPT should be actively supported to complete their treatment and maximize the benefit of treatment. For this purpose, programmes may organise in-person encounters and use communication technologies for medication adherence support, no different from what is employed to treat active TB.
- Governments and donors should provide for the uninterrupted supply of TPT medicines and promote transition to optimal TPT approaches for both drug-susceptible and drug resistant TB. They should strive for person centred approaches, upholding privacy and protection from stigma.

Monitoring and evaluation of TB preventive treatment

- Monitoring and evaluation (M&E) of programmatic performance should focus on three indicators
 - 1. Coverage of contact investigation
 - 2. TPT coverage (initiation)
 - 3. TPT completion
- M&E activities should be integrated into the existing national Health Management Information Systems.
 Governments and donors should promote the use of electronic data capture to generate the top indicators for strategic information and to help collect other data useful for individual care, such as patient-level reporting on adverse events while on treatment and any corrective actions put in place.

Key references

https://www.who.int/activities/preventing-tb/

[&]quot; https://www.theglobalfund.org/media/6349/core tbhumanrightsgenderequality technicalbrief en.pdf; https://www.theglobalfund.org/media/4765/core hiv infonote en.pdf

These treatments are available from the Global Drug Facility of the Stop TB Partnership http://www.stoptb.org/assets/documents/gdf/drugsupply/GDFMedicinesCatalog.pdf