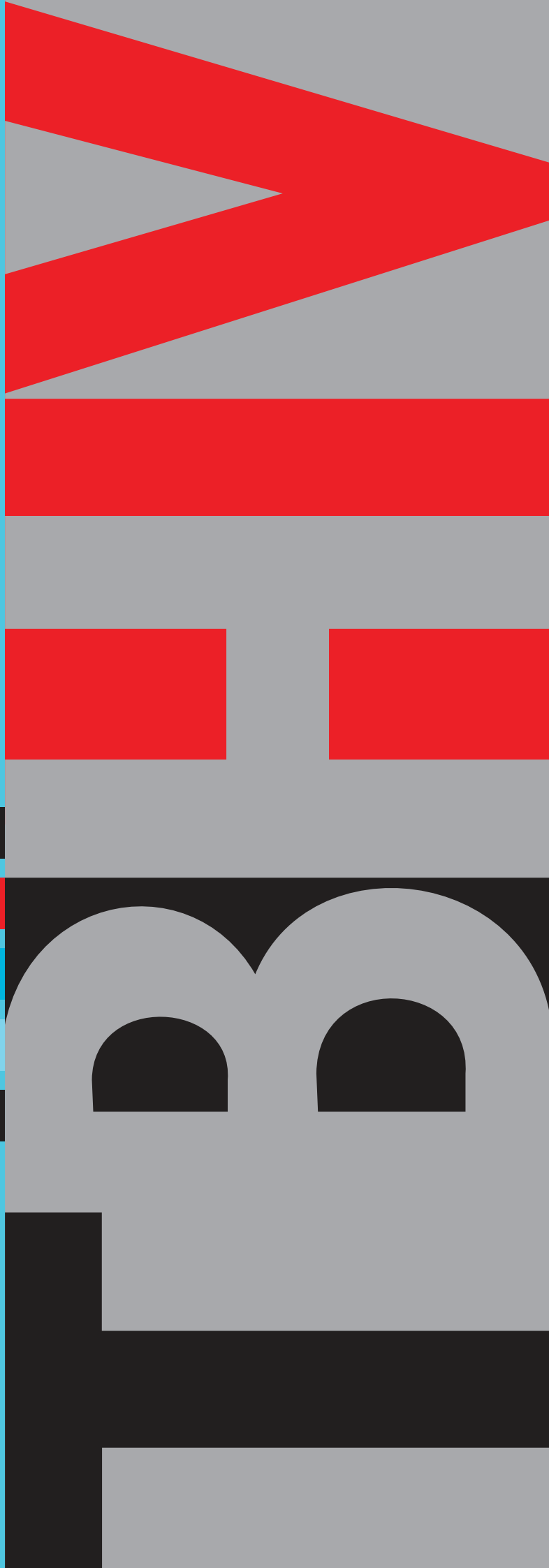
WHO policy on collaborative TB/HIV activities

Guidelines for national programmes and other stakeholders



World Health Organization

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Summary of declaration of interests

All members of the Policy Updating Group were asked to complete a World Health Organization (WHO) *Declaration of interests for WHO consultants* form. Five members of the group declared a conflict of interest. Constance Benson declared consulting, scientific and technical advisory work on antiretroviral therapy new drug development with Merck, GlaxoSmithKline and ViiV for less than US$ 5000 each. Pedro Cahn declared ongoing research support and consulting work with Abbott for an amount of US$ 3000. He declared receiving US$ 2000 from Bristol-Myers Squibb and US$ 2000 from Tibotec for serving on a speakers' bureau. He also declared scientific advisory work for Merck, Pfizer, GlaxoSmithKline and Avexa for an amount of US$ 2000 each. Mark Harrington declared giving testimony to the Institute of Medicine of the United States National Academies in panels on multidrug-resistant TB in 2008 and 2009. Charles Holmes declared employment by Gilead up to January 2008 in the clinical research unit focusing on phase I studies of experimental antiretroviral drugs. He declared no financial or other interest in Gilead. Salim S. Abdool Karim declared receiving US$ 2500 from Merck to attend the advisory panel meeting on microbicides in March 2011.

The declared conflicts of interest were discussed within the WHO Steering Group and with the Policy Updating Group before deliberations on the policy document, and it was concluded that these conflicts would not prohibit any of the members from participating in the process. Declarations of interest were collected from all non-WHO reviewers. Four peer reviewers declared potential conflicts of interest. Helen Ayles declared an ongoing research grant for her research unit with Delft Diagnostic Systems of € 100 000 to develop a computer-aided diagnostic for reading digital chest X-rays as well as having received a digital chest X-ray unit for an amount of US$ 250 000. François Boillot declared being the owner, director of and employed by a consulting company providing services in international health including in TB/HIV issues. Susan Swindells declared consulting services (advisory board) with Pfizer in 2008 (US$ 1800) and 2009 (US$ 1750), with Merck in 2009 (US$ 3500), with Tibotec in 2009 (US$ 1500) and with Abbott Molecular in 2010 (US$ 1000). She also declared previous research support to her institution from Bristol Myers Squibb that ended in 2010 (US$ 14929), from Pfizer that ended in 2011 (US$ 28125) and ongoing research support from GlaxoSmithKline for an amount of US$ 104034 and US$ 60676. Jay K. Varma declared non-monetary support (supplies and equipment) in 2010 valued at approximately US$ 10 000 from Cellestis to the government research unit of China and collaborators in Inner Mongolia to examine the prevalence of TB in health-care workers in collaboration with the United States Centers for Disease Control and Prevention. The WHO Steering Group discussed these declarations and concluded that they would not exclude the reviewers from the process. All declarations of conflict of interests are retained on electronic file by the WHO Stop TB Department.

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Contents

Abbreviations

AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
ARV	antiretroviral
BCG	Bacille Calmette–Guérin (vaccine)
CBO	community-based organization
CPT	cotrimoxazole preventive therapy
DOT	directly-observed treatment
DOTS	the basic package that underpins the Stop TB Strategy
GRADE	grading of recommendations assessment, development and evaluation
GRC	guidelines review committee
HCW	health-care worker
HIV	human immunodeficiency virus
IPT	isoniazid preventive therapy
MCH	maternal and child health
MDG	Millennium Development Goal
NGO	nongovernmental organization
PMTCT	prevention of mother-to-child transmission
PICO	population, intervention, comparison, outcome
TB	tuberculosis
TB/HIV	the intersecting epidemics of TB and HIV
TST	tuberculin skin test
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization

Executive summary

In 2004, the World Health Organization (WHO) published an interim policy on collaborative TB/HIV activities in response to demand from countries for immediate guidance on actions to decrease the dual burden of tuberculosis (TB) and human immunodeficiency virus (HIV). The term interim was used because the evidence was incomplete at that time. Since then, additional evidence has been generated from randomized controlled trials, observational studies, operational research and best practices from programmatic implementation of the collaborative TB/HIV activities recommended by the policy. Furthermore, a number of TB and HIV guidelines and policy recommendations have been developed by WHO's Stop TB and HIV/AIDS departments. Updated policy guidelines were therefore warranted to consolidate the latest available evidence and WHO recommendations on the management of HIV-related TB for national programme managers, implementers and other stakeholders.

The process of updating the policy was overseen by a WHO Steering Group and advised by a Policy Updating Group that followed WHO recommendations for developing guidelines. The Policy Updating Group comprised policy-makers, programme managers, experts in TB and HIV, donor agencies, civil society organizations including people living with HIV, and a grading of recommendations assessment, development and evaluation (GRADE) methodologist. The WHO Steering Group prepared the initial draft, which was circulated to the Policy Updating Group and discussed via e-mail and a conference call. The refined draft policy was reviewed again by the members of the Policy Updating Group and sent to a wide range of peer reviewers before finalization.

These policy guidelines on collaborative TB/HIV activities are a compilation of existing WHO recommendations on HIV-related TB. They follow the same framework as the 2004 interim policy document, structuring the activities under three distinct objectives: establishing and strengthening mechanisms for integrated delivery of TB and HIV services; reducing the burden of TB among people living with HIV and initiating early antiretroviral therapy; and reducing the burden of HIV among people with presumptive TB (that is, people with signs and symptoms of TB or with suspected TB) and diagnosed TB.

Unlike the 2004 document, the updated policy emphasizes the need to establish mechanisms for delivering integrated TB and HIV services, preferably at the same time and location. Those working to integrate the services should consider the epidemiology of HIV and TB, the health-system factors that are specific to individual countries, the management of HIV programmes and TB-control programmes and evidence-based models of service delivery. In addition, mechanisms for delivering the integrated services should be established as part of other health programmes such as maternal and child health, harm reduction services and prison health services. Monitoring and evaluation of collaborative TB/HIV activities should be done within one national system using standardized indicators and reporting and recording formats. TB prevalence surveys should include HIV testing, and HIV surveillance systems should incorporate TB screening as routine practice. The updated policy recommends setting national and local targets for collaborative TB/HIV activities through a participatory process (for example, through the national TB/HIV coordinating body and national consultations) to facilitate implementation and mobilize political commitment. Long-term and medium-term national strategic plans aligned with the health system of individual countries should be developed to scale up activities nationwide. National HIV programmes and TB-control programmes should establish linkage and partnerships with other line ministries and civil society organizations – including nongovernmental and community organizations – for programme development, implementation and monitoring of collaborative TB/HIV activities.

Interventions to reduce the burden of TB among people living with HIV include the early provision of antiretroviral therapy (ART) for people living with HIV in line with WHO guidelines and the *Three I's for HIV/TB*: intensified TB case-finding followed by high-quality antituberculosis treatment, isoniazid preventive therapy (IPT) and infection control for TB. The policy recommends the use of a simplified clinical algorithm for TB screening that relies on the absence or presence of four clinical symptoms (current cough, weight loss, fever and night sweats) to identify people eligible for IPT or for further diagnostic work-up of TB. Managerial direction at national and sub-national levels is needed to implement administrative, environmental and personal protective measures against TB infection in health-care facilities and congregate settings. These measures should include surveillance of HIV and TB among health-care workers and relocation of health workers living with HIV from areas with high TB exposure, in addition to providing ART and IPT.

The updated policy, in contrast to the 2004 policy, recommends offering routine HIV testing to patients with presumptive or diagnosed TB as well as to their partners and family members as a means of reducing the burden of HIV. TB patients who are found to be HIV-positive should be provided with co-trimoxazole preventive therapy (CPT). Antiretroviral treatment should be given to all HIV-positive TB patients as soon as possible within the first 8 weeks of commencing antituberculosis treatment, regardless of their CD4 cell-counts. Those HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells cells/mm^3) should receive ART immediately within the first 2 weeks of initiating TB treatment. TB patients, their family and community members should be provided with HIV prevention services.

HIV programmes and TB-control programmes should collaborate with other programmes to ensure access to integrated and quality-assured services for women, children, prisoners and for people who use drugs; this population should also receive harm-reduction services including drug dependence treatment in in-patient and out-patient settings.

WHO-recommended collaborative TB/HIV activities

A. Establish and strengthen the mechanisms for delivering integrated TB and HIV services
A.1. Set up and strengthen a coordinating body for collaborative TB/HIV activities functional at all levels
A.2. Determine HIV prevalence among TB patients and TB prevalence among people living with HIV
A.3. Carry out joint TB/HIV planning to integrate the delivery of TB and HIV services
A.4. Monitor and evaluate collaborative TB/HIV activities
B. Reduce the burden of TB in people living with HIV and initiate early antiretroviral therapy (the *Three I's for HIV/TB*)
B.1. Intensify TB case-finding and ensure high quality antituberculosis treatment
B.2. Initiate TB prevention with Isoniazid preventive therapy and early antiretroviral therapy
B.3. Ensure control of TB Infection in health-care facilities and congregate settings
C. Reduce the burden of HIV in patients with presumptive and diagnosed TB
C.1. Provide HIV testing and counselling to patients with presumptive and diagnosed TB
C.2. Provide HIV prevention interventions for patients with presumptive and diagnosed TB
C.3. Provide co-trimoxazole preventive therapy for TB patients living with HIV
C.4. Ensure HIV prevention interventions, treatment and care for TB patients living with HIV
C.5. Provide antiretroviral therapy for TB patients living with HIV

1. Background and process

1.1. Introduction

The human immunodeficiency virus (HIV) pandemic presents a significant challenge to global tuberculosis (TB) control. TB is a leading preventable cause of death among people living with HIV. To mitigate the dual burden of TB/HIV in populations at risk of or affected by both diseases, the Stop TB Department and the Department of HIV/AIDS of the World Health Organization (WHO) published an *Interim policy on collaborative TB/HIV activities* in 2004 (*1*). The policy, which provided guidance for Member States and other partners on how to address the HIV-related TB burden, has been one of the most widely accepted policies issued by both departments. Many countries have implemented the policy in a relatively short time; more than 170 countries had reported implementing its components by the end of 2010.

As the evidence base for all the recommendations was not complete at the time the policy was developed in 2003–2004, the term "interim" was applied. In addition to scaling up implementation of the recommended collaborative TB/HIV activities, rapid generation of evidence was emphasized to inform and update the policy. Since then, additional evidence in the field of TB and HIV has been generated from randomized controlled trials, observational studies and operational research. Furthermore, WHO has developed a number of guidelines and policy recommendations to improve the management of TB and HIV. This document updates the 2004 interim policy to reflect current evidence and experience in implementing collaborative TB/HIV activities.

1. 2. Scope of the policy

The purpose of the policy is to provide national programmes and stakeholders with guidelines on how to implement and scale-up collaborative TB/HIV activities. It is complementary to and in synergy with the established core activities of TB and HIV prevention, diagnosis, treatment and care programmes. Implementing the interventions recommended in the Stop TB strategy is the core function of national TB control programmes or their equivalents (*2*). Similarly, the delivery of priority interventions – to provide knowledge of HIV status, prevent transmission of HIV and other sexually-transmitted infections, and provide diagnosis, treatment and care for HIV – forms the basis of the health-sector HIV response and is the core function of national HIV programmes or their equivalents (*3*). The policy emphasizes the provision of quality-assured, comprehensive and integrated services to prevent, diagnose and treat TB and HIV and provide care for people living with or at risk of HIV and/or TB, their families and communities. It is also aligned with *Treatment 2.0*, an initiative coordinated by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and WHO, which aims to achieve and sustain universal access to HIV treatment and maximize its preventive benefits through a five-point agenda towards simplification and improved effectiveness and efficiency: optimizing drug regimens, advancing point-of-care and other simplified platforms for diagnosis and monitoring, reducing costs, adapting delivery systems and mobilizing communities (*4*).

Although the policy promotes strengthened collaboration between national TB-control programmes and HIV programmes or their equivalents, defining effective and pragmatic mechanisms to jointly manage such programmes and deliver integrated services should depend on the epidemiology of TB and HIV as well as context-specific and evidence-based considerations of the health system issues in the country. The policy will be reviewed and updated in five years (2017), in compliance with WHO procedure.

1.3. Target audience

These policy guidelines are intended for decision-makers in the field of health and for managers of TB-control programmes and HIV programmes working at all levels in the health sector, including the private-for-profit sector, as well as donors, development agencies, nongovernmental organizations and other civil society organizations supporting such programmes, and people living with, at risk of or affected by HIV and TB. The recommendations contained in these guidelines also have important implications for the strategic directions and activities of other line ministries working on TB, HIV or harm reduction services, such as ministries responsible for prisons, mining and workplace health services, youth in education facilities, and other stakeholders in maternal and child health programmes.

1.4. Process of updating the policy

The process of updating the policy followed that recommended by the WHO Guidelines Review Committee (GRC). A WHO Steering Group and a Policy Updating Group comprising policy-makers, programme managers, TB and HIV experts, donor agencies, civil society organizations including people living with HIV, and a methodologist in Grading of Recommendations Assessment, Development and Evaluation (GRADE) were established to oversee the process and develop recommendations. The policy guidelines build on the basic framework of the interim policy document that structured collaborative TB/HIV activities under three distinct objectives (establishing and strengthening the mechanisms for delivering integrated TB and HIV services, reducing the burden of TB among people living with HIV, and reducing the burden of HIV among people diagnosed with or presumed to have TB).

Recommendations from the following documents that have been approved by the GRC were used to update the policy:

- *Guidelines for intensified case-finding for tuberculosis and isoniazid preventive therapy for people living with HIV in resource-constrained settings, 2010*
- *Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: towards universal access, recommendations for a public health approach, 2010 version*
- *Antiretroviral therapy for HIV infection in adults and adolescents, recommendations for a public health approach, 2010 revision*
- *Treatment of tuberculosis guidelines, fourth edition, 2009*
- *WHO policy on TB infection control in health-care facilities, congregate settings and households, 2009*
- *Policy guidelines for collaborative TB and HIV services for injecting and other drug users: an integrated approach, 2009*
- *A guide to monitoring and evaluation for collaborative TB/HIV activities, 2009 (adjudicated by GRC as a non-guideline)*
- *Guidelines for surveillance of drug resistance in tuberculosis, fourth edition, 2009 (adjudicated by GRC as a non-guideline)*
- *Delivering HIV test results and messages for re-testing and counselling in adults, 2010*
- *Joint WHO/ILO policy guidelines on improving health worker access to prevention, treatment and care services for HIV and TB, 2010*
- *Guidelines for couples HIV testing and counselling [in press], 2012.*

In addition, the following four questions (three clinical and one programmatic) that were not covered by the aforementioned documents were identified by the Steering Group and a comprehensive systematic review of the available scientific evidence was conducted to formulate the related recommendations.

1. *What are the benefits of HIV testing and counselling among patients with presumptive TB (that is, patients with signs and symptoms of TB or suspected TB) and diagnosed TB, and the partners and family members of those found to be HIV-positive?*
2. *Does the administration of routine co-trimoxazole preventive therapy, as compared with no co-trimoxazole preventive therapy, reduce the number of illness episodes and deaths in TB patients living with HIV?*
3. *Can earlier initiation of antiretroviral therapy at higher CD4 counts (more than 350 cells/mm^3) be used to prevent active TB in people living with HIV?*
4. *What models are available to deliver integrated TB and HIV services for people living with HIV?*

Systematic literature reviews of studies related to these four questions were conducted using PubMed, MEDLINE, EMBASE and various other databases using combinations of different keywords to search for studies related to each question. A search was also conducted for abstracts presented at conferences on TB and lung diseases organized by the International Union Against Tuberculosis and Lung Disease (The Union) and the International AIDS Society. Investigators of large-scale HIV clinical trials were also asked for information, especially about the role of earlier initiation of ART to prevent TB. All retrieved titles and abstracts were reviewed for their relevance to the topic in question. The reference lists of the retrieved studies were also reviewed to identify further studies that met the eligibility criteria. In addition, recognized experts in the field were contacted to identify any unpublished studies that did not appear in the initial electronic search for each question. Details on evidence retrieval and quality assessment for the three clinical questions are described in the annexes, which are available online. Details of the other recommendations can be found in the guidelines listed above and in the references section.

1.5. Quality of evidence and strength of recommendation

The quality of evidence and the strength of each recommendation were assessed using the GRADE methodology for the three clinical questions (1–3 above). In the GRADE assessment process, the quality of a body of evidence is defined as the extent to which one can be confident that the reported estimates of effect (desirable or undesirable) available from the evidence are close to the actual effects of interest. The usefulness of an estimate of the effect (of the intervention) depends on the level of confidence in that estimate. The higher the quality of evidence, the more likely a strong recommendation can be made; however, the decision regarding the strength of the evidence also depends on other factors. Although the GRADE evidence assessment process was used for the clinical questions, it was not always possible to complete GRADE profiles for all the questions because there was a lack of data and information to calculate the necessary risk ratios.

In the GRADE profiles, the following levels of assessment of the evidence were used:

Evidence level	Rationale
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the effect
Low	Further research is very likely to have an estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

The strength of evidence and recommendation is presented for the three clinical questions that were specifically reviewed for the development of this policy. The strength of evidence and recommendation from the other documents approved by the GRC are also presented when possible. However, given the lack of the data necessary to calculate risk ratios, and as they largely represent programmatic processes, the strength of evidence for the activities included in section A of the collaborative TB/HIV activities and for the programmatic question (4 above) is not presented.

The rationale for strong and conditional recommendations is presented in the table below.

Strength of recommendation	Rationale
Strong	The panel is confident that the desirable effects of adherence to the recommendation outweigh the undesirable effects.
Conditional (weak)	The panel concludes that the desirable effects of adherence to the recommendation probably outweigh the undesirable effects. However: • data to support the recommendation are scant; or • the recommendation is only applicable to a specific group, population or setting; or • new evidence may result in changing the balance of risk to benefit; or • the benefits may not warrant the cost or resource requirements in all settings.

The draft document, including the population/intervention/comparison/outcome (PICO) questions, was prepared by a WHO Steering Group, representing the WHO HIV/AIDS and Stop TB departments, and then circulated to the members of the Policy Updating Group for feedback. The group discussed the overall structure of the policy through email-based discussion, assessed the evidence along with the risks and benefits of the three clinical questions, and determined the recommendations and their strengths. A telephone conference call was organized among members of the Policy Updating Group to further discuss issues that were not clarified during the email-based discussions. The policy was revised based on feedback obtained from emails and telephone conference discussion and reviewed again by the Policy Updating Group before consensus was reached. The policy was then circulated to 34 internal and external peer reviewers. Comments from internal and external peer reviewers were discussed among the WHO Steering Group, and the document was finalized by the coordinators of the process.

1.6. Adaptation of the policy

The interim policy on collaborative TB/HIV activities has been widely implemented since its publication in 2004. National programmes and other stakeholders should use the experiences garnered over the years to adapt their policies with the update to best suit their local circumstances. Factors should include the epidemiology of TB and HIV and the health-care delivery system specific to individual countries. The adaptation process should include national-level policy and programmatic decisions to determine the best country-specific programme management mechanism for providing integrated TB and HIV services. The ultimate goal of the adaptation should be scaled up nationwide coverage of collaborative TB/HIV activities to reduce HIV-associated TB mortality and morbidity depending on the epidemiology of TB and HIV.

2. Goal and objectives of collaborative TB/HIV activities

The goal of collaborative TB/HIV activities is to decrease the burden of TB and HIV in people at risk of or affected by both diseases. The objectives are:

(1) To establish and strengthen the mechanisms of collaboration and joint management between HIV programmes and TB-control programmes for delivering integrated TB and HIV services preferably at the same time and location;

(2) To reduce the burden of TB in people living with HIV, their families and communities by ensuring the delivery of the *Three I's for HIV/TB* and the early initiation of ART in line with WHO guidelines;

(3) To reduce the burden of HIV in patients with presumptive and diagnosed TB, their families and communities by providing HIV prevention, diagnosis and treatment.

3. Recommended collaborative TB/HIV activities

This section builds on the structure of the 2004 policy as it provides a well established framework for many countries in their response to HIV-related TB. It focuses on collaborative activities that address the interface of the TB and HIV epidemics and that should be carried out as part of the health sector response to HIV/AIDS (Table 1).

Table 1 Recommended collaborative TB/HIV activities

A. Establish and strengthen the mechanisms for delivering integrated TB and HIV services
A.1. Set up and strengthen a coordinating body for collaborative TB/HIV activities functional at all levels
A.2. Determine HIV prevalence among TB patients and TB prevalence among people living with HIV
A.3. Carry out joint TB/HIV planning to integrate the delivery of TB and HIV services
A.4. Monitor and evaluate collaborative TB/HIV activities
B. Reduce the burden of TB in people living with HIV and initiate early antiretroviral therapy (the *Three I's for HIV/TB*)
B.1. Intensify TB case-finding and ensure high quality antituberculosis treatment
B.2. Initiate TB prevention with Isoniazid preventive therapy and early antiretroviral therapy
B.3. Ensure control of TB Infection in health-care facilities and congregate settings
C. Reduce the burden of HIV in patients with presumptive and diagnosed TB
C.1. Provide HIV testing and counselling to patients with presumptive and diagnosed TB
C.2. Provide HIV prevention interventions for patients with presumptive and diagnosed TB
C.3. Provide co-trimoxazole preventive therapy for TB patients living with HIV
C.4. Ensure HIV prevention interventions, treatment and care for TB patients living with HIV
C.5. Provide antiretroviral therapy for TB patients living with HIV

Collaborative TB/HIV activities will be more successful where national control strategies based on international evidence-based guidelines are effectively implemented. The recommended activities can be implemented by a broad base of stakeholders and implementers including TB-control programmes and HIV programmes or their equivalents, nongovernmental organizations, other civil society organizations including communities and faith-based organizations, and the private-for-profit or corporate sector.

A. Establish and strengthen the mechanisms for delivering integrated TB and HIV services

A.1. Set up and strengthen a coordinating body for collaborative TB/HIV activities functional at all levels

Recommendations

1. **HIV programmes and TB-control programmes or their equivalents should create and strengthen a joint national TB/HIV coordinating body, functional at regional, district, local and facility levels (sensitive to country-specific factors), with equal or reasonable representation of the two programmes including of people at risk of or affected by both diseases, and other line ministries (e.g. working on harm reduction and prison or mining health services).**
2. **The TB/HIV coordination bodies should be responsible for the governance, planning, coordination and implementation of collaborative TB/HIV activities as well as mobilization of financial resources.**

HIV programmes and TB-control programmes, including their partners in other line ministries (for example, in ministries responsible for prison or mining health services), the private-for-profit sector and civil society organizations should work together to provide access to integrated services, preferably at the same time and location, for the prevention, diagnosis, treatment and care of TB/HIV. National coordinating bodies are needed at all levels of the health system to ensure strong and effective collaboration between HIV programmes and TB-control programmes and to offer a platform for coordination and synergy among stakeholders. Representation of people at risk of or affected by both diseases is essential to ensure effective implementation of integrated services and programme success. National AIDS commissions, which coordinate the multisectoral response to HIV, should also be included in national TB/HIV coordination efforts.

A national coordinating body for collaborative TB /HIV activities should have clear and consensus-based terms of reference. The important areas of responsibility are:

- *governance and coordination at national and sub-national levels*
- *resource mobilization*
- *provision of general policy and programme direction for the management of activities*
- *capacity-building including training*
- *ensuring coherence of communications about TB and HIV*
- *ensuring the involvement of civil society, nongovernmental and community organizations, and individuals*

In countries where coordinating bodies already exist (such as country coordinating mechanisms for the Global Fund to Fight AIDS, Tuberculosis and Malaria), strengthening their role through revised terms of reference and its expansion based on performance and achievements may be needed to deliver integrated TB and HIV services, preferably at the same time and location.

Evidence from operational research and descriptive studies has shown that effective coordinating bodies that operate at all levels and which include the participation of all stakeholders – from HIV programmes and TB-control programmes, civil society organizations, patients and communities – are feasible and ensure broad commitment and ownership (*5, 6*). A national coordinating body should also address governance issues, including the division of labour and resources for implementing joint plans.

A.2. Determine HIV prevalence among TB patients and TB prevalence among people living with HIV

Recommendations

1. Surveillance of HIV should be conducted among TB patients and surveillance of active TB disease among people living with HIV in all countries, irrespective of national adult HIV and TB prevalence rates, in order to inform programme planning and implementation.
2. Countries with unknown HIV prevalence rates among TB patients should conduct a seroprevalence (periodic or sentinel) survey to assess the situation.
3. In countries with a generalized epidemic state,[1] HIV testing and counselling of all patients with presumptive or diagnosed TB should form the basis of surveillance. Where this is not yet in place, periodic surveys or sentinel surveys are suitable alternatives.
4. In countries with a concentrated epidemic state[2] where groups at high risk of HIV infection are localized in certain administrative areas, HIV testing and counselling of all patients with presumptive or diagnosed TB in those administrative areas should form the basis of surveillance. Where this is not yet in place, periodic (special) or sentinel surveys every 2–3 years are suitable alternatives.
5. In countries with a low-level epidemic state,[3] periodic (special) or sentinel surveys are recommended every 2–3 years.
6. HIV testing should be an integral part of TB prevalence surveys and antituberculosis drug resistance surveillance.

Surveillance is essential to inform programme planning and implementation. There are three key methods for surveillance of HIV among TB patients: periodic surveys (cross-sectional HIV seroprevalence surveys among a small representative group of TB patients within a country); sentinel surveys (using TB patients as a sentinel group within the general HIV sentinel surveillance system); and data from the routine HIV testing and counselling of patients with presumptive or diagnosed TB. The surveillance method chosen will depend on the underlying HIV epidemic state (for definitions see footnotes[1,2,3]), the overall TB situation, and the availability of resources and experience. Incorporating HIV testing with TB prevalence surveys and antituberculosis drug resistance surveillance offers an opportunity to expand HIV testing and improve knowledge among national TB control programmes on the relationship between HIV and drug-resistant TB at the population level (*7, 8*). It also provides critically important individual benefits to people living with HIV, including better access to testing, early case detection and rapid initiation of treatment. With the increasing availability of HIV treatment, unlinked anonymous testing for HIV is not recommended because results cannot be traced back to individuals who need HIV care and treatment (*8*).

Surveys should follow nationally recommended guidelines. TB patients or people newly diagnosed with HIV identified during the surveillance should immediately be provided with TB and HIV treatment and services based on national guidelines. The surveillance of active TB disease among people living with HIV, whenever feasible, will be useful to inform programmes. Rates of TB among people newly enrolled in HIV care and/or among those initiating ART could be monitored based on analysis of routine programme data.

Evidence from descriptive studies has shown HIV surveillance among TB patients to be a critical activity in understanding the trends of the epidemic and in the development of sound strategies to address the dual TB/HIV epidemic.

1 Generalized epidemic state: HIV prevalence is consistently >1% in pregnant women.

2 Concentrated epidemic state: HIV prevalence is consistently >5% in at least one defined subpopulation and is <1% in pregnant women in urban areas.

3 Low-level epidemic state: HIV prevalence has not consistently exceeded 5% in any defined subpopulation.

A.3. Carry out joint TB/HIV planning to integrate the delivery of TB and HIV services

Recommendations

1. Joint planning should clearly define the roles and responsibilities of HIV and TB control programmes in implementing, scaling-up and monitoring and evaluating collaborative TB/HIV activities at all levels of the health system.
2. HIV programmes and TB-control programmes should describe models to deliver client and family-centred integrated TB and HIV services at facility and community levels compatible with national and local contexts.
3. HIV programmes and TB-control programmes should ensure resource mobilization and adequate deployment of qualified human resources to implement and scale-up collaborative TB/HIV activities in accordance with country-specific situations.
4. HIV programmes and TB-control programmes should formulate a joint training plan to provide pre-service and in-service training, and continuing competency-based education on collaborative TB/HIV activities for all categories of health-care workers. Job descriptions of health workers should be developed and/or adapted to include collaborative TB/HIV activities.
5. HIV programmes and TB-control programmes should ensure that there is sufficient capacity to deliver health care (e.g. adequate laboratories, supplies of medicines, referral capacity, private sector involvement, focus on key populations such as women, children, people who use drugs and prisoners) and effectively implement and scale up collaborative TB/HIV activities.
6. HIV programmes and TB-control programmes should develop specific strategies to enhance the involvement of nongovernmental and other civil society organizations and individuals affected by or at risk of both diseases in developing and implementing policy and programmes, and the monitoring and evaluation of collaborative TB/HIV activities at all levels.
7. Well designed TB/HIV advocacy activities that are jointly planned to ensure coherence between their messages and targeted at key stakeholders and decision-makers, should be carried out at global, national, regional and local levels.
8. The joint communication strategies should ensure the mainstreaming of HIV components in TB communication and of TB components in HIV communication.
9. All stakeholders of collaborative TB/HIV activities, including HIV programmes and TB-control programmes, should support and encourage operational research on country-specific issues to develop the evidence base for efficient and effective implementation of collaborative TB/HIV activities.

Medium and long-term joint strategic planning to successfully and systematically scale up collaborative TB/HIV activities nationwide and deliver integrated TB and HIV services, preferably at the same time and location with due consideration to prevention of TB transmission should be developed. HIV programmes and TB-control programmes should either devise a joint TB/HIV plan, or introduce TB/HIV components in their national plans for prevention, diagnosis, treatment and care. The roles and responsibilities of each programme in implementing specific TB/HIV activities at all levels must be clearly defined. Joint planning should be harmonized with the country's national health strategic plans and health-system strengthening agenda. Key areas to be covered include quality-assured health services; a well-performing health workforce; well-functioning information systems; equitable access to essential medicinal products, vaccines and technologies; good health financing; and leadership and governance (*9*). Crucial elements for joint TB/HIV planning include the activities detailed in objectives A, B and C of this document, as well as resource mobilization, capacity-building and training, TB/HIV advocacy, programme communication, the involvement of civil society organizations including nongovernmental organizations, people living with HIV, people who have been diagnosed with TB (including people who have completed antituberculosis treatment) and communities, engagement of private for profit and operational research. HIV programmes and TB-

control programmes should also plan and coordinate reviews of joint programmes as well as routine monitoring and evaluation of integrated services.

A. 3.1. Models of integrated TB and HIV service delivery

The systematic review conducted for the preparation of these policy guidelines identified five models for delivering integrated TB and HIV services (*10*). Few studies from this review reported on patient-relevant impacts such as outcomes of treatment or on programme outcomes such as early diagnosis of HIV and TB, early initiation of ART, prompt TB diagnosis and treatment, and retention into care, hindering a direct comparison of the various models. The selection of models for delivering quality-assured integrated TB and HIV services should consider local and national health system issues. The models described below are therefore not exhaustive or prescriptive. National HIV programmes and TB-control programmes need to define the best model for delivering integrated services that enables the provision of quality-assured comprehensive services as soon as and as close as possible to where people living with HIV and TB and their families reside. Such efforts should include integrating services for the prevention, diagnosis, treatment and care of TB and HIV into maternal and child health services, including the prevention of vertical (mother to child) transmission of HIV, and treatment centres for drug dependency where applicable.

The models identified in the systematic review include:

Entry via TB service and referral for HIV testing and care: In this model TB services refer patients to services providing HIV testing, with or without subsequent HIV care. It requires minimal additional logistic and financial input and can be achieved through joint training of health care workers from both programmes, modification of existing record keeping systems and referral forms, and regular meetings of staff from both services to strengthen referral linkages. Strengths of this model include the simplicity of introducing the required measures and the low cost. The key weakness is loss of patients if referral fails (e.g. due to lack or cost of transportation). This model may not be the best option in high HIV prevalent settings where both services should be provided as close and as integrated as possible.

Entry via TB service and referral for HIV care after HIV testing: In this model, TB clinics offer HIV testing on site and refer people found to be HIV positive for HIV care. Depending on the HIV testing policy of the country this model may require additional HIV testing counselling space and also additional staff members depending on the burden in the clinic. Whatever the HIV test results, people should be provided with HIV prevention information. If referral for HIV care fails, consequences may include additional HIV transmission to partners and children and delays in initiating life-saving HIV care and treatment.

Entry via HIV service and referral for screening, diagnosis and treatment of TB: In this model HIV services refer people living with HIV for TB screening, diagnosis and treatment. Few reports described how patients were selected for referral. Appropriate referral criteria and system are essential to the effective functioning of this model. Failure of the referral process can lead to ongoing TB transmission and progression of TB disease.

Entry via HIV service and referral for TB diagnosis and treatment after TB screening: In this model people living with HIV are screened for TB and referred for TB diagnosis and treatment based on the outcome of the screening. The infrastructure needed for this model varied considerably, depending on whether additional interventions such as isoniazid preventive therapy (IPT) are offered by the HIV clinic or sputum sample collection on site that requires heightened infection control measures. The WHO recommended symptom based screening algorithm should be used and people living with HIV who are unlikely to have active TB should be provided with IPT (*11*).

TB and HIV services provided at a single facility (at the same time and location): This model includes a spectrum of activities to provide patient centred care by the same trained health care provider at the same visit, a "one-stop service". It includes: TB clinic provides HIV treatment; HIV clinic provides TB treatment; primary health centre provides integrated diagnosis and treatment for TB and HIV either in one or separate rooms; hospital provides integrated diagnosis and treatment for TB and HIV either in one or separate rooms. This model could be particularly efficient in settings with high HIV prevalence where most TB patients have HIV and in settings where

availability of human resources is an issue, avoiding the need for referral and offering better coordinated care for patients. A concern with this model is the risk of nosocomial spread of TB. It should be noted however that the risk of TB transmission is not unique to this model, as it exists in general waiting areas of all health facilities in high burden settings (wherever coughing patients with undiagnosed pulmonary TB are regularly presenting). Thus, implementation of proper infection control measures is crucial throughout health facilities in high burden settings in order to minimize the risk of nosocomial spread of TB to immunosuppressed people living with HIV. However, integrated care supports early detection and treatment of undiagnosed infectious tuberculosis, and may result in a reduction of TB risk compared with separate services. Increase in notification of smear-negative pulmonary and extrapulmonary TB and of treatment success rates in integrated TB/HIV was also observed in Lesotho and South Africa (*12, 13*). This model also supports timely initiation of ART in TB patients living with HIV without the necessity to refer them as shown in South Africa (*13*).

A.3.2. Resource mobilization and capacity building

Collaborative TB/HIV activities, which build on well-resourced strategies, may not require much additional financial input. If either or both programmes are under-resourced in funds or human capacity, additional resources should first be mobilized to strengthen each programme. Joint proposals to solicit resources for implementing collaborative activities should be prepared, within the framework of the joint coordinating body, building on the comparative strengths of both programmes and the specific needs of the country. Alternatively, both HIV and TB funding proposals (for example to the Global Fund to fight AIDS, TB and Malaria, to the United States President's Emergency Plan for AIDS Relief, or any other funding streams) should include resources to address collaborative TB/HIV activities in each proposal with clear division of labour to avoid duplication of efforts.

Joint capacity-building for collaborative activities should include training of TB, HIV and primary health-care workers in TB/HIV issues. Ensuring continued competency-based education of health-care workers through clinical mentoring, regular supportive supervision and the availability of standard operating procedures and job aids, reference materials and up-to-date national guidelines is important. Capacity should also be enhanced in the health-care system, for example in the laboratory, supply management, health information, referral and integrated service delivery systems, to enable them to cope better with the increasing demands of collaborative TB/HIV activities (*14*).

A.3.3 Involving nongovernmental and other civil society organizations and communities

Expanding collaborative TB/HIV activities beyond the health sector through meaningful involvement with communities, nongovernmental and civil society organizations and individuals in the planning, implementation and monitoring of TB/HIV activities at all levels is crucially important. People at risk of or affected by TB and HIV as well as community-based organizations working on advocacy, treatment literacy and community mobilization are key actors in generating the required demand for integrated services at all levels of care. Their recognition and support, including financial support, is therefore critical. Advocacy targeted at influencing policy and sustaining political commitment, programme implementation and resource mobilization is very important to accelerate the implementation of collaborative TB/HIV activities.

Services for TB prevention, diagnosis, treatment and care can be integrated with those for HIV, and vice versa, through community-based organizations such as community-based TB care or HIV home-based care. Trained home-based care and community health-care workers as well as nongovernmental organizations have been successful in providing TB and HIV services in various countries (*15–19*). Community-based TB (*20, 21*) and HIV care services (*22*) are cost effective. While implementing collaborative TB/HIV activities, it is imperative that civil society organizations including nongovernmental and community-based organizations advocate, promote and follow national TB and HIV guidelines, including monitoring and evaluation of TB/HIV activities using nationally recommended indicators.

A.3.4. Engaging the private-for-profit sector

The engagement of the private-for-profit sector in implementing collaborative TB/HIV activities requires coordination and collaboration among HIV programmes and TB-control programmes as well as private service providers and their professional associations. This collaboration can be either at national, state, regional, provincial or district level, depending on the local context. Private-for-profit sector representation should be included in TB/HIV coordinating bodies at all levels and should be encouraged to initiate and implement collaborative activities in accordance with national norms and guidelines (*23*).

A.3.5. Addressing the needs of key populations: women, children and people who use drugs

Active TB has been diagnosed at rates up to 10 times higher in pregnant women living with HIV than in women without HIV infection (*24*); maternal TB is associated with a 2.5-fold increased risk of vertical transmission of HIV infection to the unborn child (*25*). Similarly, HIV infection is a risk factor for active TB disease in infants or children. More severe forms of TB disease and higher mortality rates are reported in children living with HIV (*26*). Bacille Calmette–Guérin (BCG) is a live vaccine and should not be given to infants and children with known HIV infection (*27*). However, HIV infection cannot reliably be determined at birth, and the majority of infants born to HIV-infected mothers will be HIV-uninfected. BCG should therefore be administered to infants born to HIV-infected mothers in HIV-prevalent settings unless the infant is confirmed as HIV-infected. National HIV programmes and TB-control programmes should ensure that TB prevention, screening, diagnosis and treatment as well as HIV prevention, diagnosis, treatment and care services are integrated with those for maternal and child health (MCH) (*28*) and prevention of HIV vertical transmission.

People living with HIV in congregate settings, such as prisons and centres for refugees or internally displaced persons, and people who use drugs have a higher risk of and incidence of TB and HIV infection (*29*). People who inject drugs and use alcohol hazardously have a higher risk of coinfection with HIV, TB and hepatitis. The joint plans – especially in settings where injecting drug use is fuelling the HIV epidemic – should therefore ensure that services for prevention, diagnosis, treatment and care of TB are combined with harm reduction measures, including the provision of testing for hepatitis B and C infection, and referral for treatment of people found to have infectious hepatitis. Prisons should ensure that integrated services are available to deliver effective prevention, including TB infection control measures, diagnosis and treatment of HIV, TB and hepatitis as well as harm reduction services.

A.3.6. Advocacy and communication

Advocacy targeted at influencing policy, programme implementation, and resource and community mobilization is important to accelerate the implementation of collaborative TB/HIV activities at all levels. Two-way communication between the programmes and the general public and with affected populations can inform and create awareness about both diseases and is crucial for ensuring that patients actively seek out and demand services. Effective communication measures focused on communities rather than individuals that combine a series of elements from the use of data, science, research, policy and advocacy can inform the public, shape perceptions and attitudes, mitigate stigma, enhance the protection of human rights, create demand for services, form stronger links with health services and systems, improve provider client relationships, and monitor and evaluate TB/HIV activities. Joint TB/HIV communication strategies should ensure the mainstreaming of HIV components in TB communication and of TB components in HIV communication.

A.3.7. Operational research to scale up collaborative TB/HIV activities

Cultural and system-wide differences between HIV and TB care providers and operational difficulties for providing effective and appropriate interventions have contributed to a lack of progress in expanding collaborative TB/HIV activities. Operational research is needed to define how best to provide high-quality integrated TB and HIV interventions at facility and community levels in order to inform global and national policy and strategy development (*30*). Priority research questions for TB/HIV in HIV-prevalent and resource-limited settings, including for operational research, have been identified and need to be urgently answered (*31*).

A.4 Monitor and evaluate collaborative TB/HIV activities

Recommendations

1. **HIV programme and TB-control programmes should establish harmonized indicators and standard reporting and recording templates to collect data for monitoring and evaluation of collaborative TB/HIV activities.**
2. **Organizations implementing collaborative TB/HIV activities should embrace harmonized indicators and establish a reporting mechanism to ensure that their data are captured by the national monitoring and evaluation system of the country.**
3. **The WHO guide to monitoring and evaluation of collaborative TB/HIV activities and the three interlinked patient monitoring systems for HIV care/ART, MCH/PMTCT and TB/HIV should be used as a basis to standardize country-specific monitoring and evaluation activities.**

Monitoring and evaluation provides the means to assess the quality, effectiveness, coverage and delivery of collaborative TB/HIV activities. It promotes a learning culture within and across the programmes and ensures continuous improvement of individual and joint programme performance. Monitoring and evaluation involves collaboration between the programmes and the general health system, the development of referral linkages between different services and organizations, and joint supervision. These activities should be integrated with existing monitoring and evaluation systems. Establishing and identifying harmonized indicators that should be captured by each programme are essential to avoid duplication of effort (*32*); and national reporting and recording formats should be standardized. Using the three interlinked patient monitoring systems for HIV care/ART, MCH/PMTCT, and TB/HIV (*33*) will facilitate the cross-checking and reconciliation of data between HIV programmes and TB-control programmes at local and country levels and will strengthen country ownership of data. Evidence from operational research (*34, 35*) has shown the importance of standardized monitoring and evaluation of collaborative TB/HIV activities to determine the impact of the activities and to ensure implementation and effective programme management.

B. Reduce the burden of TB among people living with HIV and initiate early antiretroviral therapy (the *Three I's for HIV/TB*)

B.1 Intensify TB case-finding and ensure high-quality antituberculosis treatment

Recommendations

1. **Adults and adolescents living with HIV should be screened for TB with a clinical algorithm; those who report any one of the symptoms of current cough, fever, weight loss or night sweats may have active TB and should be evaluated for TB and other diseases (*strong recommendation, moderate quality of evidence*).**
2. **Children living with HIV who have any of the following symptoms – poor weight gain, fever or current cough or contact history with a TB case – may have TB and should be evaluated for TB and other conditions. If the evaluation shows no TB, children should be offered IPT regardless of their age (*strong recommendation, low quality of evidence*).**
3. **TB patients with known positive HIV status and TB patients living in HIV-prevalent settings should receive at least 6 months of rifampicin treatment regimen (*strong recommendation, high quality of evidence*). The optimal dosing frequency is daily during the intensive and continuation phases (*strong recommendation, high quality of evidence*).**

Community-based studies have reported high rates of undiagnosed TB both among people living with HIV and HIV-negative individuals (*36, 37*). Early identification of signs and symptoms of TB followed by diagnosis and prompt initiation of treatment in people living with HIV, their household contacts, groups at high risk for HIV and people living in congregate settings (e.g. prisons, workers' hostels, police and military barracks) increases the chances of survival, improves quality of life and reduces transmission of TB in the clinic and the community. Prompt diagnosis and treatment of TB among HIV-negative people is also crucial to reduce TB transmission to people living with HIV.

All people living with HIV should be regularly screened for TB using a clinical symptom-based algorithm consisting of current cough, fever, weight loss or night sweats at the time of initial presentation for HIV care and at every visit to a health facility or contact with a health-care worker afterwards (*11, 38*). Adults and adolescents living with HIV who report any one of the symptoms of current cough, fever, weight loss or night sweats may have active TB and should be evaluated for TB and other diseases. Screening for TB is important regardless of whether they have received or are receiving IPT or ART. Similarly, children living with HIV who have any one of the following symptoms – poor weight gain, fever or current cough or contact history with a TB case – may have TB and should be evaluated for TB and other conditions.

In people with a positive screen, the diagnostic workup for TB should be done in accordance with national guidelines and principles of sound clinical practice to identify either active TB or an alternative diagnosis. Smear-negative pulmonary and extrapulmonary TB is common among people living with HIV and associated with poor treatment outcomes and excessive early mortality. If smear-negative pulmonary TB or extrapulmonary TB is suspected, diagnostic processes should be expedited using all available and appropriate investigations, including mycobacterial culture (*39*). In high-HIV prevalence settings, where WHO approved molecular tests (e.g. Xpert MTB/RIF) are available, they should be the primary diagnostic test for TB in people living with HIV (*40*). Among seriously ill patients in HIV-prevalent settings, empirical antituberculosis treatment should be initiated in case of negative investigations and no improvement to parenteral antibiotics (*39*). Patients should be referred to the next level of care to confirm diagnosis. If referral is impossible, antituberculosis treatment should be completed.

New TB patients living with HIV should receive a TB regimen containing 6 months of rifampicin (2 months of isoniazid, rifampicin, pyrazinamide and ethambutol followed by 4 months of rifampicin and isoniazid, 2HRZE/4RH) on a daily schedule (*41*); and should be started on ART regardless of CD4 count as soon as possible within the first 8 weeks of antituberculosis treatment (*42*).

B.2 Initiate TB prevention with Isoniazid preventive therapy and early antiretroviral therapy

Recommendations

1. Adults and adolescents living with HIV should be screened with a clinical algorithm; those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT (*strong recommendation, moderate quality of evidence*).
2. Adults and adolescents who are living with HIV, have unknown or positive tuberculin skin test (TST) status and are unlikely to have active TB should receive at least 6 months of IPT as part of a comprehensive package of HIV care. IPT should be given to such individuals irrespective of the degree of immunosuppression, and also to those on ART, those who have previously been treated for TB and pregnant women (*strong recommendation, high quality of evidence*).
3. Adults and adolescents living with HIV who have an unknown or positive TST status and who are unlikely to have active TB should receive at least 36 months of IPT. IPT should be given to such individuals irrespective of the degree of immunosuppression, and also those on ART, those who have previously been treated for TB and pregnant women (*conditional recommendation, moderate quality of evidence*).
4. Tuberculin skin test (TST) is not a requirement for initiating IPT in people living with HIV (*strong recommendation, moderate quality of evidence*). People living with HIV who have a positive TST benefit more from IPT; TST can be used where feasible to identify such individuals (*strong recommendation, high quality of evidence*).
5. Providing IPT to people living with HIV does not increase the risk of developing isoniazid-resistant TB. Therefore, concerns regarding the development of INH resistance should not be a barrier to providing IPT (*strong recommendation, moderate quality of evidence*).
6. Children living with HIV who do not have poor weight gain, fever or current cough are unlikely to have active TB (*strong recommendation, low quality of evidence*).
7. Children living with HIV who are more than 12 months of age and who are unlikely to have active TB on symptom-based screening and have no contact with a TB case should receive six months of IPT (10mg/kg/day) as part of a comprehensive package of HIV prevention and care services (*strong recommendation, moderate quality of evidence*).
8. In children living with HIV who are less than 12 months of age, only those who have contact with a TB case and who are evaluated for TB (using investigations) should receive six months IPT if the evaluation shows no TB disease (*strong recommendation, low quality of evidence*).
9. All children living with HIV after successful completion of treatment for TB disease should receive isoniazid for an additional 6 months (*conditional recommendation, low quality of evidence*).
10. All people living with HIV with CD4 counts of ≤350 cells/mm^3 irrespective of the WHO clinical stage should start ART (*Strong recommendation, moderate quality of evidence*).

Isoniazid is given to individuals with latent infection with *Mycobacterium tuberculosis* in order to prevent progression to active disease. Exclusion of active TB is critically important before IPT is started. The absence of all of current cough, night sweats, fever, or weight loss can identify a subset of adolescents and adults living with HIV who have a very low probability of having TB disease that can reliably be initiated on IPT. This screening rule has a negative predictive value of 97.7% (95% CI [confidence interval] 97.4–98.0) at 5% TB prevalence among people living with HIV. In children, the absence of poor weight gain, fever and current cough can identify children who are unlikely to have TB. Isoniazid is given daily as self-administered therapy for at least 6 months as part of a comprehensive

package of HIV care for all eligible people living with HIV irrespective of degree of immunosuppression, ART use, previous TB treatment and pregnancy. Information about IPT should be made available to all people living with HIV. Providing IPT as a core component of HIV preventive care should be the responsibility of national HIV programmes and HIV service providers.

Evidence has shown that IPT is as efficacious but safer than rifampicin and pyrazinamide containing regimens used for prevention of latent TB infection (*43*). IPT was also found to be effective in reducing the incidence of TB and death from TB in HIV-infected patients with a positive tuberculin skin test (TST) (*44, 45*). Evidence from Botswana and South Africa suggests an increased benefit with 36 months or longer duration of IPT, particularly in people who are TST-positive in settings with higher TB prevalence and transmission (*46, 47*). However, operational challenges for TST represent significant impediments to accessing IPT in resource-limited settings, and TST should therefore not be a requirement for initiating IPT among people living with HIV.

ART is a powerful strategy to reduce TB incidence among people living with HIV across a broad range of CD4 cell-counts. ART reduces the individual risk of TB by 54% to 92% (*48*) and the population-based risk by 27% to 80% (*49, 50*) among people living with HIV. Studies conducted in Brazil and South Africa showed up to 90% reduction in TB risk among HIV-infected patients with a positive TST who received both ART and IPT (*51, 52*). ART also reduces TB recurrence rates by 50% (*53*). Modelling exercise from nine sub-Saharan African countries indicated that the most profound reduction in incidence of HIV-related TB is seen when ART is initiated as soon as people test HIV positive (*54*).

WHO recommends that all adolescents and adults, including pregnant women with HIV infection, and CD4 counts ≤350 cells/mm^3 should be started on ART regardless of symptoms (*42*). As part of the TB/HIV policy updating process, a systematic review including data from randomized controlled trials and large multicentre cohorts was conducted and analysed using the GRADE system to explore the role of earlier initiation of ART (at CD4 counts >350 cells/mm^3) for preventing TB in people living with HIV. The review showed that the risk of TB is reduced by half among people living with HIV when ART is initiated at CD4 counts >350 cells/mm^3 (see Annex 1 for evidence retrieval and quality assessment).

Therefore, based on these observations and the systematic review conducted, the Policy Updating Group unanimously agreed on the role of earlier access to and initiation of ART (e.g. CD4 counts >350 cells/mm^3) for the prevention of TB and other clinical conditions for people living with HIV. The inclusion of a separate recommendation on earlier initiation of ART at CD4 counts >350 cells/mm^3 solely as a means of TB prevention was debated and it was agreed to be beyond the scope of the TB/HIV Policy Updating Group and this policy document. The paucity of data around issues of feasibility, equity, costs and patient-related factors preclude the inclusion of a specific recommendation in this policy document. While addressing those areas that need further research, the Group recommends that the next revision of the WHO guidelines on ART should address this issue specifically in light of its implication on TB risk reduction and other clinical conditions.

B.3 Ensure control of TB Infection in health-care facilities and congregate settings

Recommendations

1. **HIV programmes and TB-control programmes should provide managerial direction at national and subnational levels for the implementation of TB infection control in health-care facilities and congregate settings.**
2. **Each health-care and congregate setting should have a TB infection control plan of the facility, preferably included into a general infection control plan, supported by all stakeholders, which includes administrative, environmental and personal protection measures to reduce transmission of TB in health-care and congregate settings, and surveillance of TB disease among workers.**
3. **Health-care workers, community health workers and care providers living with HIV should be provided with ART and IPT if eligible. Furthermore, they should be offered an opportunity for transfer to work in clinical sites that have the least risk of TB transmission.**

In health-care facilities and congregate settings where people with TB and HIV are frequently crowded together, infection with TB is increased. HIV promotes progression to active TB both in people with recently acquired infection or with latent *Mycobacterium tuberculosis* infection. Evidence has shown an increased risk of TB exacerbated by the HIV epidemic among health-care workers, medical and nursing students with patient contact (*55*), prisoners (*29*) and people in police and military barracks (*56*). Improving access to HIV and TB prevention, treatment, care and support services for health-care workers, as well as of workers in congregate settings, is therefore crucial (*57*).

Implementation of TB infection control measures requires managerial activities at national, sub-national and facility levels, which include establishing coordinating bodies at all levels; developing a plan preferably incorporated into a broader infection control plan; appropriate health facility design and use; surveillance of TB disease among health-care workers; an advocacy and communication strategy; monitoring and evaluation; and operational research (*58*).

At facility level, measures to reduce TB transmission include administrative, environmental and personal protection controls, which are aimed at generally reducing exposure to M. tuberculosis of health-care workers, prison staff, police and any other persons living or working in the congregate settings. Administrative controls consist of triage to identify people with TB symptoms, separation of infectious cases, control of the spread of pathogens (cough etiquette and respiratory hygiene), rapid diagnosis and prompt initiation of TB treatment, and reduced hospitalization. Environmental controls include maximizing ventilation systems (natural or mechanical) and using upper-room ultraviolet germicidal irradiation (if applicable). Personal protective interventions include use of respirators and prevention, treatment and care packages for health-care workers including HIV prevention interventions, and ART and IPT for workers who are living with HIV. Health-care workers should have access to acceptable, confidential and quality-assured HIV testing. Health-care workers living with HIV should be provided with ART, but even with adequate response to treatment they will remain at higher risk of TB. Transfer of their clinical responsibilities into sites that have the least risk of TB transmission and regular TB screening should be considered to mitigate this risk. Similarly, health-care workers with active TB should be relocated from HIV care facilities. Patients and their communities should be trained on TB transmission, infection control and cough etiquette to reduce the risk of TB transmission in health-care facilities and congregate settings.

C. Reduce the burden of HIV in patients with presumptive and diagnosed TB

C.1 Provide HIV testing and counselling to patients with presumptive and diagnosed TB

Recommendations

1. **Routine HIV testing should be offered to all patients with presumptive and diagnosed TB (*strong recommendation, low quality of evidence*)**
2. **Partners of known HIV-positive TB patients should be offered voluntary HIV testing and counselling with mutual disclosure (*strong recommendation for all people with HIV in all general HIV epidemic settings*)**
3. **TB-control programmes should mainstream provision of HIV testing and counselling in their operations and routine services.**

The vast majority of people living with HIV do not know their HIV status and seek health care from general service providers. HIV testing and counselling for people with diagnosed or presumptive TB offers an entry point for a continuum of prevention, care, support and treatment for HIV and for TB. Evidence from observational studies shows that testing patients with presumptive and diagnosed TB and their contacts for HIV yields a high number of new diagnoses of HIV infection, as prevalence of HIV is higher than among the general adult population (see Annex 2 for evidence retrieval, quality assessment and strength of recommendation). The yield of HIV-positive testing in TB patients varies significantly (from 6.3% to 77%). Studies in sub-Saharan Africa have shown that HIV testing of presumptive TB cases who turn out not to have active TB disease also yields high HIV-positive results (*59, 60*). One study in Thailand showed 74% acceptance rate of HIV testing among contacts of TB patients and a higher (13.8%) HIV prevalence rate among contacts of HIV-positive TB cases as compared with contacts of HIV-negative TB cases (2.5%) (*61*). Voluntary HIV testing and counselling for sexual or needle-sharing partners, with shared disclosure and mutual support, may also improve the uptake of and adherence to ART, benefiting both the index individual and their partners regardless of HIV status (*62*).

Despite the low quality of evidence, the Policy Updating Group strongly recommended routine HIV testing and counselling to all patients with presumptive and diagnosed TB as benefits of testing accrue to the patient, their partner, the family and the community at large. The testing should be readily available and voluntary, informed consent should be obtained and confidentiality should be protected. Moreover, TB patients with a new potential HIV exposure or who are at higher risk of HIV exposure and with an HIV-negative test result should be re-tested after 4 weeks from the time of initial testing (*63*). Age-appropriate algorithms should be in place for undertaking HIV testing in young children, and HIV testing should be family- and child-focused (*64*). All people diagnosed with HIV infection should be offered HIV prevention, diagnosis, treatment and care services, including ART. These services should be offered by TB-control programmes or through effective referral to HIV services.

C.2 Introduce HIV prevention interventions for patients with presumptive and diagnosed TB

Recommendations

1. TB-control programmes should implement comprehensive HIV prevention strategies for their patients and their partners, targeting sexual, parenteral or vertical transmission or should establish a referral linkage with HIV programmes to do so.
2. HIV programmes and TB-control programmes should implement procedures for voluntary, acceptable and confidential HIV counselling and testing for health-care providers and for reduction of occupational and nosocomial exposure to HIV infection in their services.
3. All personnel working with presumptive and confirmed TB cases, people living with HIV and people who use drugs should be able to assess risk factors for HIV infection and transmission and should provide comprehensive information and services to their clients to minimize their risks.
4. HIV programmes and TB-control programmes should collaborate with harm reduction services to ensure universal access to comprehensive TB and HIV prevention, diagnosis, treatment and care as well as drug treatment services, including opioid substitution therapy, for people who use drugs in a holistic person-centred approach to maximize access and adherence within one setting as much as possible.
5. TB-control programmes should ensure that vertical transmission of HIV is prevented by referring all HIV-positive pregnant women attending TB services to providers of services for prevention of vertical transmission of HIV for antiretroviral therapy or prophylaxis as needed.

Prevention of HIV includes interventions to (i) prevent sexual transmission such as male and female condoms, male circumcision, HIV testing and counselling including couples counselling and testing, early ART as per WHO guidelines; (ii) prevent transmission through sharing contaminated injecting equipment among injecting drug users; combined with (iii) behavioural interventions and brief interventions to prevent hazardous alcohol use and use of other psychostimulants (*3*).

HIV prevention services also include prevention of vertical transmission of HIV, which comprises two key approaches (*65*). HIV-infected women, including during pregnancy, with CD4 counts ≤350 cells/mm^3 irrespective of WHO clinical staging or in clinical stage 3 or 4 irrespective of the CD4 cell-count, should start lifelong ART for their own health, which is also safe and effective in reducing vertical transmission. For HIV-infected pregnant women who do not need ART for their own health, prophylaxis with triple ARV medicines or with zidovudine plus lamivudine to prevent HIV transmission is needed and should be continued until one week after all infant exposure to breast milk has ended (*65*).

In sub-Saharan African countries with very high HIV prevalence and low male circumcision rates, medical male circumcision in HIV-negative men is also recommended, combined with HIV testing and counselling and promotion of consistent condom use (*3*).

In health-care settings, transmission of HIV can be prevented through primary prevention measures such as standard precautions, injection safety, blood safety and safe waste disposal, as well as secondary prevention measures such as occupational post-exposure prophylaxis.

Among people who inject drugs, comprehensive harm reduction programming such as wide access to sterile injecting equipment, opioid substitution therapy and outreach services to reduce the risk of HIV transmission and other negative health effects of injecting drug use should be implemented (*66*).

Review of the evidence has shown that HIV prevention methods such as voluntary counselling and testing, prevention of vertical transmission of HIV and condom distribution are cost effective (*22, 67*). The provision of

HIV preventive interventions by TB-control programmes or effective referral of patients to HIV programmes has been successfully implemented in many countries (*68, 69*). Improved treatment of sexually transmitted infections has been shown to reduce HIV incidence in an environment characterized by an emerging HIV epidemic (*70*). Randomized trials in areas of high HIV prevalence have shown that male circumcision reduces the risk of heterosexually acquired HIV in men up to 60% (*71*). Systematic reviews have shown that behavioural interventions targeting HIV-positive individuals in resource-limited settings are effective, especially among HIV-serodiscordant couples (*72*). Meta-analysis randomized controlled trials and community-based studies support the use of ART for HIV prevention in HIV-serodiscordant heterosexual couple (*73, 74*).

C.3 Provide co-trimoxazole preventive therapy for TB patients living with HIV

Recommendation

Routine co-trimoxazole preventive therapy should be administered in all HIV-infected patients with active TB disease regardless of CD4 counts (*strong recommendation, high quality of evidence*)

Co-trimoxazole preventive therapy (CPT) is a broad spectrum antimicrobial agent that prevents a range of secondary bacterial and parasitic infections in eligible adults and children living with HIV. TB patients living with HIV should receive CPT and it should be implemented as an integral component of the HIV chronic care package. CPT is a simple, well-tolerated and cost-effective intervention for people living with HIV and can be administered concomitantly to ART. Evidence from randomized controlled trials, including areas of high levels of antibiotic resistance, has shown reduced mortality, morbidity and hospitalization with no significant increase in adverse events among smear-positive TB patients with HIV regardless of their CD4 counts (*75, 76*) (see Annex 3 for evidence retrieval, quality assessment and strength of recommendation). Other non-randomized and operational studies showed that CPT is feasible (*77, 78*), safe and reduces mortality rates in TB patients (*77, 79*). Moreover, CPT did not select for sulfadoxine–pyrimethamine-resistant malaria parasites among HIV-uninfected household members of people living with HIV receiving the medicine, and reduces the number of malaria episodes among household members (*80*).

Therefore, the Policy Updating Group strongly recommended that routine CPT should be administered in all HIV-infected patients with active TB disease regardless of their CD4 cell count. Moreover, HIV programmes and TB-control programmes should establish a system to provide CPT to all eligible people living with HIV who have active TB.

C.4 Ensure HIV prevention interventions, treatment and care for TB patients living with HIV

Recommendations

1. **All people living with HIV who are diagnosed with TB should receive integrated services for prevention, diagnosis, treatment and care of TB and HIV.**
2. **HIV programmes and TB-control programmes should ensure access to a continuum of comprehensive and integrated prevention, care and treatment for people living with HIV who are receiving or who have completed their antituberculosis treatment.**

A comprehensive package of prevention, diagnosis, treatment and care interventions (continuum of care) should be provided to all people living with HIV, ideally starting well before the need for ART. Pre-ART care includes regular assessment of the clinical and immunological stages of infection, prevention of illness, care for opportunistic infections, preparation for adherence to ART, nutritional support, provision of safe water, sanitation and hygiene, psychosocial support, and prevention and management of mental health disorders, including alcohol and other

substance use. It is also essential to provide HIV prevention methods for people already living with HIV to prevent inadvertent HIV transmission ("positive prevention" or "prevention for positives").

A continuum of care should also be provided to people living with HIV who are receiving or who have completed their antituberculosis treatment through integrated services or strengthened referral systems. Evidence has shown that linking TB and HIV prevention, diagnosis, treatment and care services may generate synergies, strengthen both programmes and scale-up the delivery of these interventions to HIV-infected TB patients (*10*).

Particular attention should be paid to seriously ill patients (e.g. patients with multidrug-resistant and extensively drug-resistant TB). Palliative care, both chronic and terminal as needed, should be offered to ensure that patients and their families live out their lives with minimal suffering and loss of dignity, even when all available curative treatments have been exhausted (*81*).

C.5 Provide antiretroviral therapy for TB patients living with HIV

Recommendations

1. **ART should be started in all TB patients living with HIV irrespective of their CD4 counts (*strong recommendation, low quality of evidence*).**
2. **Antituberculosis treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment (*strong recommendation, moderate quality of evidence*). Those HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells cells/mm^3) should receive ART immediately within the first 2 weeks of initiating TB treatment.**
3. **Efavirenz should be used as the preferred non-nucleoside reverse transcriptase inhibitor in patients starting ART while on antituberculosis treatment (*strong recommendation, high quality of evidence*).**

Antiretroviral therapy greatly improves the survival and the quality of life of TB patients living with HIV, prevents HIV transmission and should be considered part of HIV and TB treatment and prevention. The availability of ART can also encourage people to be tested for HIV. HIV programmes and TB-control programmes should ensure that TB patients diagnosed with HIV infection are offered ART as early as possible, preferably within integrated services or within TB health facilities. Effective referral to HIV services remains an alternative but relies on sound referral systems and patients' ability to afford other costs such as transport and lost wages. HIV programmes and TB-control programmes should work together to guarantee ART to all TB patients living with HIV in as decentralized a manner as possible.

Observational studies conducted in both resource-limited and high-income settings have shown that ART is associated with significant reductions in mortality risk (between 54% and 95%) (*48*). Evidence from randomized controlled trials shows that early initiation of ART during antituberculosis treatment is associated with reduced mortality rates, especially in patients with profound immunosuppression (e.g. CD4 less than 50 cells cells/mm^3). The CAMELIA trial conducted in Cambodia which enrolled 661 HIV-infected TB patients with a median CD4 count of 25 cells/mm^3 showed that mortality was reduced by 34% when ART was initiated 2 weeks vs 8 weeks after onset of antituberculosis treatment (*82*). The STRIDE and SAPIT trials found similar results of reduced deaths and AIDS-related events with combined and earlier ART and antituberculosis treatment, by 42% and 68% respectively, especially among people with a CD4 count less than 50 cells/mm^3 (*83, 84*). Based on these three trials, ART should be started as a matter of emergency (within 2 weeks after the onset of antituberculosis treatment) in TB patients with a CD4 count less than 50 cells/mm^3 and as early as possible in the remaining cases. Caution is needed in people living with HIV with TB meningitis as immediate ART was significantly associated with more severe adverse events when compared with initiation of ART 2 months after the start of antituberculosis treatment (*85*).

Patients should be closely followed-up to assess the occurrence of side-effects related to co-treatment and of TB-associated immune reconstitution inflammatory syndrome (IRIS), which is common in patients with TB started on

ART but usually self-limited. HIV stakeholders and service providers should establish a mechanism to ensure that people living with HIV receive antituberculosis treatment with ART, emphasizing integrated and patient-centred care. Early use of ART is also recommended for TB patients living with HIV who also receive medication with second-line antituberculosis regimens for drug-resistant TB.

Rifampicin reduces drug levels of both nonnucleoside reverse transcriptase inhibitors and protease inhibitors through induction of the cytochrome P450 liver enzyme system. A randomized controlled trial in Thailand comparing efavirenz and nevirapine-based ART in HIV-infected TB patients receiving rifampicin showed that both standard doses of efavirenz and nevirapine were effective in achieving viral load suppression (*86*). However, reports of efficacy, safety and tolerability of efavirenz and nevirapine administered with rifampicin varied across observational studies (*87, 88*). When rifampicin is given with protease inhibitors, highly variable and mainly subtherapeutic plasma concentrations of the protease inhibitor are observed, even in the presence of boosted doses of ritonavir (*89*). Rifabutin, listed in the WHO Model List of Essential Medicines, is a less potent inducer of the cytochrome P450 system which can be used in patients on ART regimens that include a protease inhibitor.

4. National targets for scaling up collaborative TB/HIV activities

Recommendation

Countries implementing collaborative TB/HIV activities should set their own country-specific process and impact targets for scaling up collaborative TB/HIV activities towards achieving the Millennium Development Goals.

Nationwide scale-up of collaborative TB/HIV activities is needed to achieve the targets set in the Global Plan to Stop TB (*90*) and the Universal Access goals established by the HIV community (*91*). These targets are in line with the Millennium Development Goals, to reduce mortality of people living with HIV from TB and to achieve universal access to treatment for HIV for all who need it.

Experience and best practices from countries that have pioneered nationwide expansion of collaborative TB/HIV activities have allowed identifying enablers of scaling-up (*92*). Setting time-bound targets for collaborative TB/HIV activities at national, regional, district and facility levels in a participatory manner (e.g. through the TB/HIV coordinating bodies) is essential. It facilitates timely implementation and monitoring, and helps to mobilize political commitment from HIV programmes and TB-control programmes and other stakeholders. Creating an environment conducive to the development of appropriate policy, operational guidelines, training manuals and protocols in line with international guidelines is essential. Expanding HIV testing in facilities by supporting TB health-care workers to test patients with presumptive and diagnosed TB and in communities is important to scaling up activities in HIV-prevalent settings. Similarly, as part of the public health approach of ART scale up, every effort should be exerted to expand the scale up of ART including using the highly decentralized TB service outlets. Ensuring an uninterrupted supply of HIV rapid tests, antituberculosis and antiretroviral medicines, and other HIV and TB commodities is crucial. Implementing recording and reporting formats that capture collaborative TB/HIV activities with inclusion of TB components in HIV registers and HIV components in TB registers is another enabler. Finally, it is of utmost importance to document the progress of implementation and performance of programmes as well as best practices in countries to inform and guide national and international policy recommendations.

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