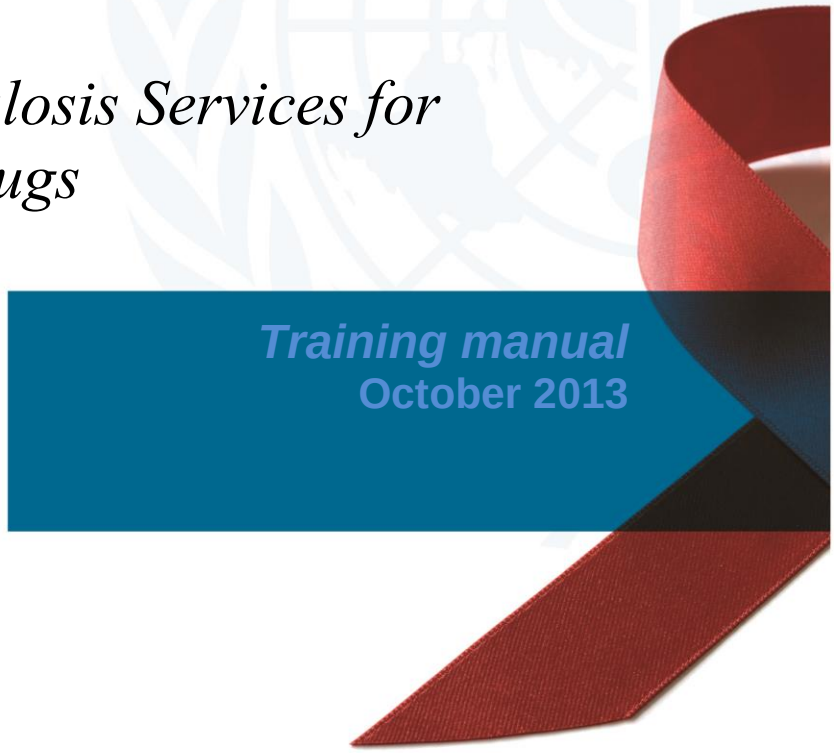
Developing Tuberculosis Services for People Who Use Drugs



Training manual

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EURASIAN HARM REDUCTION NETWORK
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Eurasian Harm Reduction Network
The Eurasian Harm Reduction Network (EHRN) is a regional network of harm reduction programs, groups of people who use drugs (PUD) and their allies from across 29 countries of Central and Eastern Europe and Central Asia (CEECA) who work to advocate for the universal human rights of people who use drugs in order to protect their lives and health. EHRN's mission it is to promote humane, evidence-based harm reduction approaches to drug use, with the aim of improving health and wellbeing, whilst protecting human rights at the individual, community and societal level.

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ABBREVIATIONS AND ACRONYMS

AFB	Acid fast bacilli
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral therapy
CBO	Community-based organization
CPT	Co-trimoxazole preventive therapy
CSO	Civil society organization
CTC	Combined Therapy Centre
DOT	Directly Observed Treatment
DOTS	The basic package that underpins the Stop TB Strategy
DST	Drug susceptibility testing
EECA	Eastern Europe and Central Asia
EHRN	Eurasian Harm Reduction Network
EPTB	Extrapulmonary tuberculosis
HAART	Highly active antiretroviral therapy
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
ICF	Intensified TB case-finding
IGRA	Interferon-gamma release assays
IPT	Isoniazid preventive therapy
LPA	Line probe assay
MDR-TB	Multidrug-resistant tuberculosis (defined as TB caused by strains of M. tuberculosis that are resistant to at least isoniazid and rifampicin)
NGO	Non-governmental organization
OSF	Open Society Foundations
OST	Opioid substitution treatment
PLHIV	People living with HIV
PDC	Pulmonary Diagnostic Centre
PPD	Purified protein derivative
PWID	People who inject drugs
PWUD	People who use drugs
TB	Tuberculosis
TB-IC	Tuberculosis infection control
TST	**T**uberculin skin test
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization
XDR-TB	Extensively drug-resistant tuberculosis (defined as MDR-TB plus resistance to a fluoroquinolone and at least one second-line injectable agent: amikacin, kanamycon and/or capreomycin)

Introduction

There were around 8.7 million new cases of tuberculosis (TB) and about 1.4 million people died from TB in 2011. There is no established link between the risk of TB disease and any particular drug, however people who use drugs (PWUD) are often among the most vulnerable and socially excluded people and are, therefore, exposed to many other risk factors for TB such as poverty, homelessness, overcrowding and imprisonment. HIV infection further increases the risk of developing TB disease among PWUD. TB is a leading cause of mortality among PWUD living with HIV – both all-cause and TB-associated mortality rates are several times higher among PWUD living with HIV than among other people living with HIV. TB incidence has fallen or stabilized among PWUD in many industrialized countries but not in Eastern Europe and Central Asia.

This manual aims to contribute to the comprehensive response to HIV, TB and drug use and support linkages between HIV prevention, TB control and harm reduction strategies and services in Eastern Europe and Central Asia. It compiles clinical and programmatic information about TB, HIV and drug use aligned with the most up to date normative guidance issued by WHO.

The manual has been written for people who are responsible for delivering services for PWUD, including those working in harm reduction, drug treatment or other health and social care services to increase their capacity in proving TB related services for PWUD. This manual may also be of use to civil society and drug user community advocates in better understanding TB and its links with drug use and HIV.

Although the training manual might be useful for all stakeholders involved in harm reduction and TB as a resource of information, it is primarily designed for trainers developing and delivering trainings to civil society, community and health care workers in the field of harm reduction, TB and HIV.

The manual will be revised when the new evidence and guidance for addressing tuberculosis infection is released.

Training guide

The manual is structured around a three-day learning programme with modules that introduce TB, diagnostic tests and procedures, general principles of treatment and care and provides supporting evidence and analyses TB prevention and infection control issues.

Although the manual is designed for three days, the programme is modular and intended to be easily adapted according to specific people's needs, the local situation and the opportunities and resources available. The training could be delivered over three consecutive days or as a single module at a time, which might reduce the disruption to the organization's work. The content can also be used selectively, using only those modules which are the most relevant for the specific audience.

The training can be adapted for delivery to people who are completely new to working with PWUD and/or TB and can also be used as a refresher course for people who already have experience in the field. It uses a participatory, interactive approach which provides many opportunities for participants to share their questions, uncertainties and expertise in ways that are suited to their own group.

The manual provides guidance on preparing and delivering training and also contains supporting content for facilitators and background information on the topics. The trainer should bear in mind that TB services vary substantially across countries. In some countries PWUD have access to a wide variety of the latest treatment options; in others there are still a lot of obstacles for people to receive treatment and keep receiving it. Having local knowledge on TB prevalence, treatment and care options will help the trainer to adapt the programme to their audience's specific needs.

Using the manual

People using this manual to support the delivery of the training need to be familiar with its content and have skills in delivering training. The manual outlines basic principles required for the training. The course is structured around a three-day training programme, with each day being seven to eight hours including two coffee breaks and lunch. Each module has its approximate duration indicated, although this will depend on the participants' knowledge, experience and specific needs. The authors suggest completing exercises in the order presented and according to the indicated time.

The training programme is structured to allow flexibility of use appropriate to local learning objectives and participants' abilities and needs. It is designed to help you to select the most relevant modules and presentation slides for the audience. The training structure allows facilitators to look for illustrations and figures from participants' own experiences and best practices and encourages them to make any adjustments in accordance with the specific context. Trainers are encouraged to follow the guidelines and refer to the recommended readings. However, the manual is advisory and can be constantly updated. Particular attention should be paid to the practical and learning needs of PWUD invited to the training.

The training manual is designed for a group of up to 20 participants – ideally, 14–16 persons. Much smaller or larger groups may require specific preparation and modification of the curriculum, timing, learning activities and participants' contributions.

Preparing the training

Make sure to familiarize yourself with the training manual before delivering the training. Read the modules and their corresponding presentations and handouts. Ensure that your knowledge is up to date by familiarizing yourselves with the accompanying resources, guidelines and recommended reading materials.

Check for local examples, illustrations and statistics to update slides and expand on the materials provided.

Venue

The venue for the training should provide opportunities for a fluent learning process without distraction. Make sure it is suitable to accommodate a group of up to 20 people. Bear in mind that the training incorporates both whole-group and small-group activities. The location should be easily accessible for the participants. Specific consideration should be paid to the needs of participants with disabilities or special needs. You may need to give specific instructions relating to travel, parking and public transport.

Participants

Ensure that all participants have received the training outline and are aware of the learning objectives before the training. You may provide them with the references to the resources and additional reading materials to help them to prepare for the training.

Since PWUD may attend the training, either as trainers or participants, it is particularly important to check for the availability of opioid substitution therapy (OST) support for those who need it. If necessary,

any special request needed for the inclusion of foreign clients in the programme should be made beforehand.

Since some participants may have specific dietary requirements, either because they are on a certain treatment or simply for their personal beliefs, you should make sure that a specific diet is available and requirements for food related to certain treatments are met. It is recommended to address the needs of vegetarians and vegans.

The participants' invitations may include arranging travel and/or offering travel costs and an attendance fee. Consider what arrangements are needed for those receiving or requiring OST to support their attendance and participation, and consider how the programme timing can be adjusted to meet the needs of PWUD.

Facilitators

For smaller groups, a single facilitator can usually administer the training effectively. This training initially intended for a group size of up to 20 people and requires at least two facilitators to enhance and maintain the quality of the training and manage the various group activities. If you are planning to have a bigger group – more facilitators should be involved. Make sure that your co-facilitators are familiarized with the training materials and feel comfortable running a training.

Co-facilitation may include other professionals, advocates or experienced PWUD. Consider whether there are opportunities to establish relationships with local TB medical experts or PWUD or others affected by TB who can support your training and increase your knowledge and confidence in the subject area.

Have a facilitators' meeting before the training to agree on the agenda, roles and responsibilities in running the training. During delivery facilitators should confer with each other after each module to address any issues that arise (such as engaging participants who have been less involved than others). Delivering training with co-facilitators allows for note-taking to record important discussions and questions as they arise and can serve as a record for subsequent follow-up.

Material checklist

This manual contains training materials that can be used during various training sessions. However, you should also feel free to think creatively about ways in which these can be incorporated into exercises or other training methods. There are other resources on the topic, many of which have been developed for the specific situation in certain countries. When you are preparing training materials for the training, feel free to contact local institutions (such as ministries that deal with health, the police, narcotics, justice, public security, youth affairs), WHO/United Nations organizations and international and local NGOs to see whether any relevant materials are available. These materials may include training guidelines, case studies, checklists, videos, brochures or reading materials.

Handouts – copy sufficient course handouts and relevant materials for the number of training participants and have these ready for distribution at the start of the training.

Module completion certificate – should be supported by the agency responsible for the training and confirm attendance on completion. This may be useful for people who have to demonstrate ongoing professional development. For some people this also boosts participation and motivation during the training and enhances the way it is used subsequently.

Training delivery

Before the training starts – think about the time and space in which the group will be working. Arrange the chairs so that everyone can see all the other group members. Make sure you know the agenda and timings of the session, so you can present it for the participants. Think of any equipment you will be using in the session and check that it works (computer, projector, markers etc.). Make catering arrangements for coffee breaks and lunch. Arrive in plenty of time on the day so that you can feel in control of all of the above.

Starting the training – once participants have arrived and gathered prior to the training, start at the agreed time. Open the training by welcoming the participants, introducing yourself and any co-facilitator. The training should always start with a round of introductions: usually, everyone in the group takes turns to state their name, where they work, and – if they wish – something about their background. This should be non-demanding and allow the individual to offer something about themselves to the group.

Initiating the first module – after the introductory exercise summarize the outline of the day, timings and how the training will proceed. Ensure that you are familiar with all practical arrangements at the training venue, such as the location of coffee breaks and lunches, toilets, expected fire drills, gathering points and so on, and convey these to the training group.

Group rules – define the training rules and attendance and state the behaviour you expect from participants. It will be easier to deal with unhelpful behaviour if it occurs. This is best done as an extension of the introduction and expectations section. Ask the group members to suggest 'ways of working' they would find helpful. Put the rules up on a flipchart as they are stated and keep the sheet in a visible place so that the rules can be referred to if necessary.

Depending on the cultural background and specific characteristics of the training participants, you may wish to consider rules such as:

- Arrive on time for the beginning of each module and after each break
- State opinions honestly so that we can benefit from frank discussions
- Questions may be asked freely at any time
- One person speaks at a time (particularly vital with translation)
- Comments should be made to the whole group: no side conversations
- Listen to a person's full opinions or ideas and do not react immediately: in this way we can consider what we really think of a new or opposing idea, instead of just reacting to it
- Work towards resolving conflicts rather than taking up inflexible positions
- Discuss ideas or opinions, not the person expressing them
- Agree to switch off mobile phones and laptops while in the training room
- No violence (verbal/physical): people must feel free to express opinions that may not be popular so that we can learn from these opinions
- No smoking in the training room, and no alcohol or drug consumption during the training modules.

Confidentiality within the training should be discussed and agreed. Participants should not share any sensitive information disclosed during the training with others (e.g. challenging or compromising practice issues, current or former drug use or similar disclosures). It should be emphasized that participants are responsible for their own judgments about what they may contribute within the training. It should be made clear that confidentiality is not absolute – child protection concerns, violence or suicidal intentions are not bound to confidentiality.

Training expectations can be useful to gain an understanding of individual and collective expectations. Be clear that all participants should have the opportunity to express what they are hoping to achieve. Generally, expectations should be written on flipchart paper, as they will be presented to the whole group. If anyone's expectations are very different from the training's learning objectives, this needs to be addressed clearly from the outset.

Ending modules – at the end of each module, let the group know that they are reaching the end of the available time. This will also help you to bring the discussion to a close and draw conclusions. Offer a summary at the end of each module and a more comprehensive one at the end of the training.

Methodology

This training has been designed to include a range of formats and styles to help address diverse learning styles. Before beginning the training, it is sometimes useful to employ an exercise known as an 'ice-breaker' to help participants become comfortable with each other and with the facilitators. In some groups, simple introductions may be sufficient. Ice-breaking exercises can also be used if tension has risen to a high level among participants, if facilitators sense that frustration is rising, or to begin each day of a multi-day training.

Group discussion – when discussions are going on among the whole group, seat yourself and co-facilitators as part of the circle; this gives a non-verbal message that you are giving up your position of authority for a while to allow a very frank discussion.

Lecture/didactic presentation – when you are lecturing, you may want to stand, since this draws attention to you. It may also give you a certain level of authority, although this is a matter of personal preference and teaching style. Lectures can be a less engaging form of training delivery but are important for communicating key information. There are many ways to perform a lecture, such as combining it with questions to the audience and interactive communication.

Use questions and feedback to break up the lecturing process, especially if the participants are becoming bored. Ask questions to clarify whether everyone has a similar level of basic knowledge, before moving on to new topic. Ask what participants know or feel about a particular topic. It can be helpful to clarify whether they have had any experience of the subjects being discussed.

Small group work/exercises – irrespective of the length of the small-group task, the main objectives for the small group need to be established and clear before it is formed. Everyone needs to be aiming to achieve the same thing from the group work – otherwise, it is unlikely that the group will be able to work as a unit. Facilitators should assure that all members of the group actively participate in the exercise. After the work in a small group there should be reflection among the whole group. Before the group starts its task, nominate one person who will be reporting back. Allow sufficient time for the small-group reports.

Role-playing, exercises and games are often valued elements of training. Often, participants remember the sensation of being in a particular role or playing a game more strongly than they remember other information. These techniques are particularly useful for developing skills. While other training techniques can increase knowledge, skills are normally enhanced through practice. Role plays could help participants to feel what it might be like to be, say, a PWUD concerned and anxious about the significance of their HCV status and treatment options. They can help participants to think about their attitudes towards people who inject and other drug users. Activities that involve physical movement can be especially useful after lunch, when energy levels are often lower.

Brainstorming is a method used to collect opinions and information rapidly, generate ideas and develop solutions to problems creatively. Brainstorming can help you choose a topic, develop an approach to a topic, or deepen your understanding of the topic's potential. Basic rules for brainstorming:

- The question should be clear
- Allow participants a few moments to contemplate the question before being given the chance to offer answers, comments or ideas
- Everyone should participate
- There should be no immediate criticism or discussion of the ideas presented
- Ideas are recorded on a flipchart (usually by a facilitator while the co-facilitator fields key words or phrases called out by participants)
- The process should move quickly
- A time limit should be set.

Case studies can be defined as training methods where participants examine a story that involves real situations and people. These methods are among the most powerful tools in training. 'Real-life' situations, especially when these can be personalized by participants, tend to have a very strong impact on learning. Make sure you prepare several case studies and make enough copies to hand them out to all participants.

Evaluating the training

Evaluation is an important part of the training process because trainings develop organically over time as knowledge and understanding changes. The training evaluation process is designed to help you to assess participants' reactions to the training and to determine its effectiveness. It is often useful to prepare a summary report based on the results of the evaluation to help either you or other trainers to offer similar trainings or courses in the future. Such a report should include:

- the name of the training, dates and venue;
- the organizers and commissioners of the training;
- the facilitators' names (and organizations they represent);
- participants' names and brief information about them (e.g. their workplace, locality, contact email addresses);
- trainers' comments on major issues that arose during the training;
- the results of the training/course evaluations, highlighting those that are significant;
- recommendations for changes to course materials, methods and participant selection.

BACKGROUND

According to WHO, in 2011, there were an estimated 8.7 million new cases of TB (13% co-infected with HIV) and 1.4 million people died from TB, including almost one million deaths among HIV-negative individuals and 430 000 among people who were HIV-positive[1,2]. WHO, UNAIDS and the Stop TB Partnership have set a target that, by 2015, TB mortality rates among people who are HIV-positive should be reduced by 50%.[3]

In 2008 WHO issued *Policy Guidelines for Collaborative TB and HIV Services for Injecting and Other Drug Users: an Integrated Approach*[4], and, in 2012, a new *Policy on Collaborative TB/HIV Activities: Guidelines for National Programmes and Other Stakeholders*.[5] The latest *Clinical protocol Management of tuberculosis and HIV coinfection among adults and adolescents*, developed by Regional WHO office in Europe was released in 2013. These and a few other documents are the main sources of reference for TB and HIV treatment and prevention among PWUD.

This trainer's manual compiles existing clinical and programmatic information about TB, HIV and drug use. It aims to present information in a way that is suitable for the community service providers and people without special clinical training, and guide them to a better TB response.

Basic information about TB

TB is an infectious disease caused by the *Mycobacterium tuberculosis (M. tuberculosis).* The mycobacteria multiply at a very slow rate, but survive for weeks in a dry state and need a host organism to grow. *M. tuberculosis* primarily affects the lungs. If people with active TB disease affecting the lungs or larynx have not been diagnosed and treated or have not received enough treatment they may infect others. Infectious particles are produced through coughing, sneezing, talking or singing. Left untreated, each person with pulmonary TB will infect on average between 10 and 15 people per year.[6] The risk of transmission depends on the length of exposure and the bacterial load – or the infectiousness – of a patient. People who are exposed to *M.tuberculosis* may become infected, and are regarded as having latent TB infection (LTBI). One third of the global population in the world have LTBI;[1] only 10% of the persons latently infected by *M.tuberculosis* will develop active TB disease in his/her life-time.[7] The risk is highest in the first two to five years after the infection or in persons who have dysfunctions of the immune system. For example, people living with HIV (PLHIV) who have LTBI are about 21–34 times more likely to develop TB disease than those who are HIV-negative.[4]

TB among people who use drugs

People who inject drugs may have an increased risk of acquiring tuberculosis (TB) disease independent of their HIV status. There is no established link between the risk of TB disease and any particular drug; however, PWUD are often among the most vulnerable and socially excluded people and are, therefore, exposed to many other risk factors for TB such as poverty, homelessness, overcrowding and imprisonment.[4] PWID may be more likely to transmit *M.tuberculosis* because of advanced TB, unattended disease and higher rates of treatment failure.

HIV infection further increases the risk of developing TB disease among PWUD.[8] Untreated LTBI and untreated HIV infection among PWUD are associated with a risk of TB disease of about 7% to 10% per year.[9]

TB incidence has fallen or stabilized among PWID in many industrialized countries but not in Eastern Europe and central Asia.[10] This might be partially attributed to the fact that the HIV epidemic is also mounting in this area driven by injecting drug use, and resulting from high prevalence of unsafe practices

(using shared injecting equipment).[11,12] The routes of HIV transmission among non-injecting PWUD are much less clear than among PWID, [13] although patterns of HIV transmission have been identified among people who smoke stimulant drugs, though not to the same extent as PWID.[13]

TB is a leading cause of mortality among PWID living with HIV.[14] Both all-cause and TB-associated mortality rates are several times higher among PWUD living with HIV than among other people living with HIV.

Drug-resistant TB

Drug resistance is a man-made phenomenon caused by the improper use of medications for the treatment of drug-susceptible *M.tuberculosis* strains, whether due to incorrect prescription of drugs or to their improper intake.[15]

Multidrug-resistant (MDR) TB identifies a disease due to *M.tuberculosis* which is resistant to at least isoniazid and rifampin, the two most important first line TB drugs. MDR-TB can be successfully treated by appropriate combinations of 'second-line' drugs, which include fluorquinolones and injectable agents[16]. Second-line drugs are more expensive, have more side effects than the first-line drugs and are not readily available in many countries of the world. MDR-TB requires a longer course of treatment of 20 months or more.

Extensively drug-resistant tuberculosis (XDR) TB refers to MDR-TB sustained by an *M.tuberculosis* strain which is also resistant to the most important second line drugs, specifically a fluoroquinolone and at least one injectable agent: amikacin, kanamycin and/or capreomycin.

Diagnosis and appropriate treatment of MDR-TB and XDR-TB are recognized as the major challenges to TB control: these forms of TB are more difficult to diagnose, more difficult to treat, and generate enormous costs for the health system.[2]

MDR and XDR TB bacteria can be transmitted from one individual to another, and a newly infected person can have drug-resistant TB from the beginning, without previous exposure to TB medications.

PWID have an increased risk of developing MDR-TB.[17,18,19] The WHO European Region has the highest prevalence of MDR-TB in the world,[20] together with large populations of PWID.

To address the problem of drug-resistant TB, the 'Consolidated Action Plan to Prevent and Combat Multidrug- and Extensively Drug-Resistant Tuberculosis in the WHO European Region 2011–2015'[21] was launched in 2011. The plan emphasizes rapid diagnosis, equitable access to treatment and care, a systems approach, involvement of civil society organizations (CSOs), social determinants, partnership, strong monitoring and reporting and new drug and diagnostics development.

HIV testing and counseling

The right to know one's HIV status is fundamental to accessing life-saving prevention, care and treatment services. Provider-initiated HIV testing and counseling should be a routine procedure in all health care settings. In addition, non–health care settings dealing with PWUD should have the capacity to offer an HIV test and counsel for HIV.

HIV testing should be conditional to an informed consent of the person being tested and right to refuse it, with adequate pre-test and post-test counseling, protection of confidentiality and effective access to services for treatment and care. Decisions on whether to use HIV rapid tests or traditional assays should take into account all advantages and disadvantages, including cost and availability of the HIV test kits,

reagents and equipment, staff, resources, infrastructure, laboratory expertise and personnel, as well as considerations on the number of samples to be tested, sample collection and transport methods, testing setting, convenience and patients' ability to return for results.

Knowing the HIV status of a PWUD has very important implications in terms of TB preventive interventions, particularly to decide about diagnosis and treatment of latent tuberculosis infection.

TB case-finding among PWUD

The most efficient method for preventing transmission of TB is early identification and appropriate treatment of infectious TB patients.

Considering their high risk of TB, all PWUD, wherever they receive care, should be regularly screened for TB at every visit to a health facility or contact with a health worker. Contacts of smear-positive TB patients are at high risk of being infected and of developing TB disease, justifying active case detection in these individuals.

The screening for TB should first start from investigating the presence of all the following four symptoms:

- Current cough
- Fever
- Weight loss
- Night sweats

The presence of one or more of these symptoms prompts the application of a diagnostic procedure for TB as the person has a presumptive TB condition.

Diagnostic procedures for TB in PWUD with presumptive TB

Persons who have presumptive TB (i.e. with the presence of any one of the above symptoms) requires the physician to further explore the possibility of active TB disease. The following next steps should be taken:

- Medical examination to look for the presence of signs of pulmonary or extrapulmonary TB.
- Sputum smear microscopy of two sputum samples taken even on the same day, was, since recently, the recommended and the most common diagnostic tool worldwide. However, the sensitivity of this method is suboptimal and depends also on the human factor.
- Sputum culture, which involves growing live TB bacteria in laboratory conditions, is more sensitive that microscopy for the identification of mycobacteria in both pulmonary and extrapulmonary specimens, and it is essential for drug susceptibility testing (DST). DST from a bacteriological culture should be performed in all TB patients because it is a valuable diagnostic support for selecting the most appropriate TB treatment regimen based on the drug resistance pattern. This is particularly important in the European region, which faces the highest level of MDR-TB. In specific circumstances when DST of all newly diagnosed TB patients is unfeasible, at least all previously treated TB patients and all those with a suspicion of drug resistant TB should have DST.[22] Previously treated patients are defined as those who have received at least 1 month of anti-TB drugs in the past, may have positive or negative bacteriology and may have disease at any anatomic site. They may be the result of a relapse from previous TB episode successfully treated (cure or treatment as documented outcomes), a treatment failure or the return after treatment defaulting (defaulting

treatment for more than 2 months)[23]. Culture is expensive, time consuming and requires technologically advanced laboratory facilities.

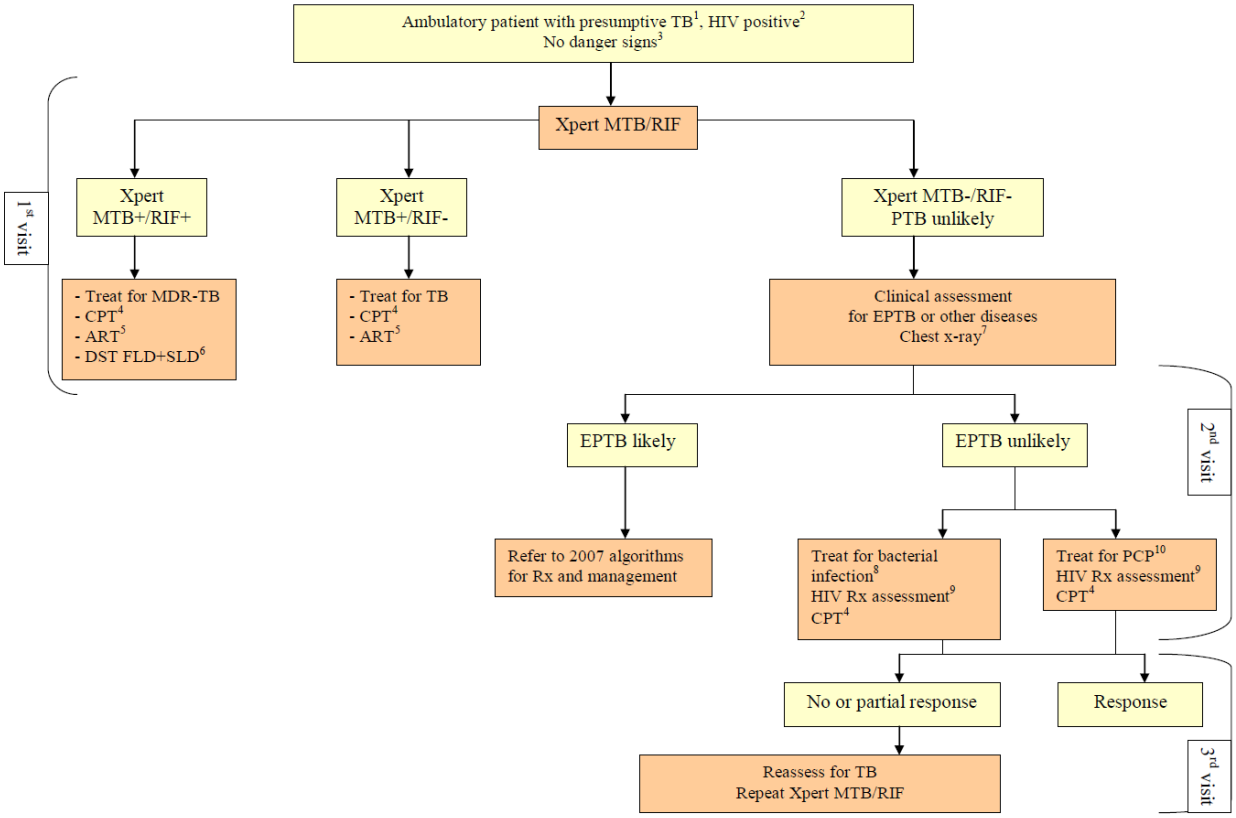
- The Xpert MTB/RIF assay, of one sputum sample, is the nucleic acid amplification test (NAAT) currently available and endorsed by WHO as the currently recommended diagnostic tool[24] because it combines high sensitivity and rapidity (takes 3 hours), and it offers combined diagnosis of TB and MDR-TB (through the surrogate identification of rifampicin resistance). The Xpert MTB/RIF is particularly helpful in HIV infected persons and in high HIV prevalence settings where highly sensitive diagnostic methods are essential. WHO promotes the use of diagnostic algorithms which use the Xpert MTB/RIF assay as the entry diagnostic procedure among HIV infected persons with presumptive TB (both ambulatory and critically ill)[25] (Figure 1 and 2). For patients with signs of extrapulmonary TB, microbiological investigations (using Xpert MTB/RIF or culture) on samples obtained by needle aspiration or tissue biopsy should be performed.
- Chest radiography is useful in patients with negative sputum smears because it is sensitive in identifying the presence of pneumonia. However, radiography has very low specificity for TB, i.e. no radiographic pattern is specific to TB (the classical hallmarks of the disease, cavitation, apical distribution, pulmonary fibrosis, shrinkage and calcification, are inconsistent, especially in HIV infected individuals).
- In case of presumptive extrapulmonary TB, any additional appropriate investigation, including computed tomography and other recommended technologies (if affordable).
- When pulmonary TB diagnosis is still uncertain, a full course of broad-spectrum antibiotics could be useful to rule out non-specific bacterial infections. First-line anti-TB drugs and fluoroquinolones (second-line anti-TB drugs) should not be used for antibacterial empirical treatment under these circumstances.

A summary of the different tests can be found in Table 1.

Table 1. Tests for tuberculosis[26,27]

Test name	Advantages	Disadvantages/Limitations
TST	Indicative of LTBI	Has poor specificity because of cross-reactivity with the antigens of the Bacille Calmette Guerin (BCG) vaccine, as well as many of the nontuberculous mycobacteria. False-negative results may occur in PLHIV with low CD4 count. Requires a second visit.
IGRA test	Indicative of LTBI, can be accomplished after a single patient visit	Potential for false-positive tests due to cross-reactivity is significantly lower with IGRAs than with the TST. Is more likely than traditional TST to diagnose LTBI in PWID; more expensive than TST.
Chest x-ray	Important adjunct to the diagnosis of smear-negative pulmonary TB	No radiological pattern is specific for TB.
Sputum smear microscopy	In nearly all clinical circumstances in settings of high TB prevalence, identification of AFB[1] by microscopic examination is highly specific for the *M. tuberculosis.*	Direct smear microscopy is relatively insensitive as at least 5000 bacilli per millilitre of sputum are required for direct microscopy to be positive. Smear sensitivity is reduced in patients with extrapulmonary TB and those with HIV co-infection. Microscopy for AFB cannot distinguish *M. tuberculosis* from other AFB, nor viable from non-viable organisms, nor drug-susceptible from drug-resistant strains.
Sputum culture	Provides a definitive diagnosis of TB; can detect cases earlier. Culture also provides the necessary isolates for DST.	More complex and expensive than microscopy to perform. Requires 4 – 6 weeks to get results.
DST	Provides a definitive diagnosis of drug-resistant TB and the list of drugs whicxh are effective against a specific strain	Requires appropriate laboratory infrastructure,adequate training of staff, and good quality control systems
Molecular testing: line probe assay (LPA)	Rapidly identifies MDR-TB or HIV-associated TB; standardized testing, potential for high throughput, and reduced biosafety needs	Does not eliminate the need for conventional culture and DST capability; currently available LPAs are registered for use only on smear-positive sputum specimens *M. tuberculosis* isolates grown from smear-negative specimens by conventional culture methods. LPAs are suitable for implementation at central/national reference laboratory level, with potential for decentralization to regional level if appropriate infrastructure can be ensured.
Molecular testing: Xpert MTB/RIF assay	Detects both TB and rifampicin resistance in a single test. Rifampicin resistance is a good and reliable proxy for MDR-TB in high-burden settings. Doesn't require much time.	Does not eliminate the need for conventional culture and DST capability; requires uninterrupted and stable electrical power supply and yearly calibration of the cartridge modules. The positive predictive value of Xpert MTB/RIF is low in settings where rifampicin resistance is rare, and results need to be confirmed by DST or LPA. Costly to conduct.

Figure 1: Algorithm for ambulatory management of PLHIV with presumptive TB[25]



1 Among adults and adolescents living with HIV, a patient with presumptive TB is defined as a person who reports any one of current cough, fever, weight loss or night sweats. Among children living with HIV, a TB suspect is defined as a person who reports one of poor weight gain, fever, current cough, or history of contact with a TB case.

2 In all persons with unknown HIV status, HIV testing should be performed according to national guidelines. In patients who are HIV negative or remain HIV unknown (e.g. declined testing), a patient with presumptive TB is defined according to national case definitions. A person with unknown HIV status can still be classified as HIV-positive if there is strong clinical evidence of HIV infection.

3 The danger signs include any one of the following: respiratory rate> 30/min, temperature>39°C, heart rate>120/min and unable to walk unaided.

4 CPT = cotrimoxazole preventive therapy

5 ART = antiretroviral therapy. All TB patients living with HIV are eligible for ART irrespective of CD4 count. Start TB treatment first, followed by ART as soon as possible within the first 8 weeks of TB treatment. See WHO Policy on collaborative TB/HIV activities.

6 In low MDR-TB prevalence settings, a confirmatory test for rifampicin resistance should be performed. See MDR-TB Xpert MTB/RIF algorithm.

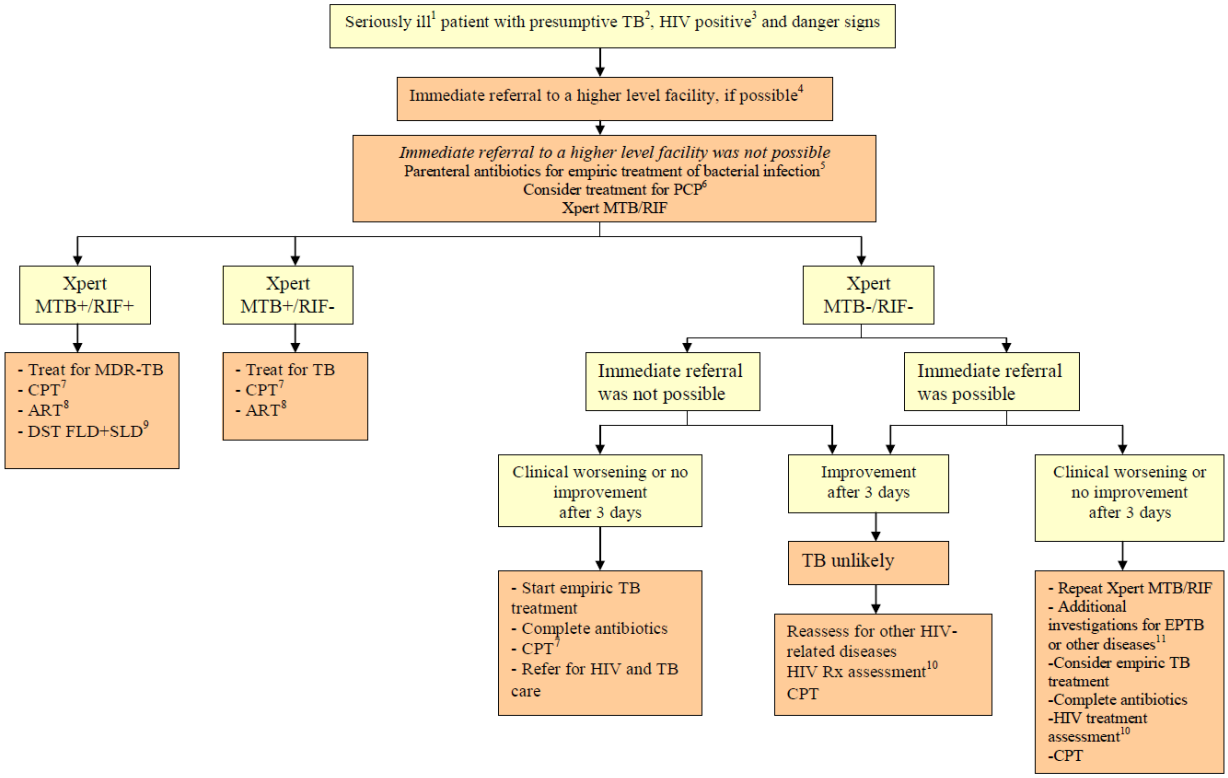
7 A chest x-ray can assist with the diagnosis of extra-pulmonary TB (e.g., pleural, pericardial) and help assess for other etiologies of respiratory illness. It should only be performed in those settings where the quality of the film and its interpretation are assured.

8 Antibiotics (except fluoroquinolones) to cover both typical and atypical bacteria should be considered.

9 An HIV treatment assessment includes WHO clinical staging and/or CD4 count to assess eligibility for antiretroviral therapy. See ART guidelines.

10 PCP= Pneumocystis jirovecii pneumonia

Figure 2: Algorithm for management of PLHIV who are presumed to have TB and are seriously ill



1 Seriously ill refers to the presence of danger signs, including: respiratory rate> 30/min, temperature>39°C, heart rate>120/min and unable to walk unaided.

2 Among adults and adolescents living with HIV, a patient with presumptive TB is defined as a personwho reports any one of the following: current cough, fever, weight loss or night sweats. Among children living with HIV, a patient with presumptive TB is defined as a person who reports one of poor weight gain, fever, current cough, or history of contact with a TB case.

3 In all persons with unknown HIV status, HIV testing should be performed according to national guidelines. In high HIV prevalent settings, seriously ill patients should be tested using Xpert MTB/RIF as the primary diagnostic test regardless of HIV status.

4 The highest priority should be to provide the patient with life - sustaining supportive therapy, such as oxygen and parenteral antibiotics. If life - sustaining therapy is not available at the initial point of care, the patient should be transferred immediately to a higher level facility before further diagnostic testing.

5 Antibiotics (except fluoroquinolones) to cover both typical and atypical bacteria should be considered.

6 PCP= Pneumocystis jirovecii pneumonia

7 CPT = cotrimoxazole preventive therapy

8 ART = antiretroviral therapy. All TB patients living with HIV are eligible for ART irrespective of CD4 count. Start TB treatment first, followed by ART as soon as possible within the first 8 weeks of TB treatment. See WHO Policy on collaborative TB/HIV activities.

9 In low MDR - TB prevalence setting, a confirmatory test for Rifampicin resistance should be performed. See MDR-TB algorithm.

10 An HIV treatment assessment includes WHO clinical staging and/or CD4 count to assess eligibility for antiretroviral therapy. See ART guidelines.

11 Additional investigations for TB may include chest x-ray, liquid culture of sputum, lymph node aspiration for acid - fast bacilli microscopy and culture, abdominal ultrasound. Non-tuberculosis mycobacterial infection should be considered in the differential diagnosis of patients who have a negative Xpert but a sputum or extra-pulmonary specimen with acid - fast bacilli.

TB treatment

The aim of health services is to cure all patients in whom TB has been diagnosed, either on the basis of microbiological demonstration or following the judgment of a clinician.

TB treatment requires full adherence, preferably under direct observation and patient support, and should follow internationally recommended standards. Every newly diagnosed TB patient should receive a TB regimen which consists of a two-month intensive phase of four first-line drugs given daily: rifampicin, isoniazid, ethambutol, and pyrazinamide (HRZE). The intensive phase is followed by a continuation phase based on rifampicin and isoniazid (HR) given daily for four months. Three times weekly dosing of HR during the continuation phase is an acceptable alternative where it is not possible to adopt the daily dosing.

A summary of the recommended standard regimens for the treatment of TB is presented in the Table 2.

Table 2. A summary of the recommended standard regimens for the treatment of TB

Treatment regimen	Comments
2 H + R + Z + E 4 (H + R)	Standard treatment for new TB patients
2 H + Rfb + Z + E 4 H + Rfb	Alternative standard treatment for new TB patients
2 H + R + Z + E 4 H3 + R3	Alternative standard treatment for new TB patients when daily dosing is difficult to arrange
2 H + R + Z + E 4 (H + R) + E	Alternative standard treatment for new TB patients in settings with high levels of isoniazid resistance and awaiting the results of drug susceptibility testing
2 H + R + Z + E + S 1 (H + R) + Z + E 5 (H + R) + E	Preferred standard treatment for people lost to follow-up or relapsing from previous TB treatment in settings with low or medium levels of isoniazid resistance
Empirical multidrug-resistant TB regimen	Empirical treatment based on the country's drug resistance susceptibility profile for people for whom previous TB treatment had failed in settings with low or medium levels of isoniazid resistance or all previously treated people with TB in settings with high levels of isoniazid resistance and awaiting the results of drug susceptibility testing

Adherence to TB treatment

Adherence is crucial for the success of TB treatment. Patients with poor adherence are at very high risk for developing drug-resistant strains of *M.tuberculosis*. Drug-resistant TB is difficult to treat, can be transmitted to others and generates high costs.

Direct observation of drug intake (DOT) is strongly recommended to reinforce adherence to TB treatment, combined with context-specific and patient-centered support. Although being very demanding for health services, implementation of appropriate DOT strategies should receive the utmost priority and should specifically target most at risk populations and MDR TB patients.

Adherence may be particularly challenging in special population groups, such as PWUD. Barriers to adherence vary between settings, so services should consult with users and their representatives first to find the most effective ways to overcome them and the best local solutions. In general, abstaining from treating PWID due to adherence issues is not justified. Drug users, with adequate support, stable care and experienced personnel can adhere to long term treatment and can have clinical outcomes comparable to those of people who do not use drugs. Evidence indicates effectiveness of adherence reminders, adherence counselling, contingency management, supervised therapy and ancillary services. Special role in adherence support has the provision of anti-TB treatment in services providing opioid substitution therapy (OST) with methadone or buprenorphine. Co-location of multiple services has been shown to result in improved health outcomes. Social support has been associated with improved outcomes in DOT programmes for treating TB.

Adverse treatment and their management

Adverse events to TB treatment may occur and may be a determinant of reduced adherence from the patient side.

TB treatment can have hepatotoxic side effects, particularly in individuals co-infected with hepatitis B or C (HBV/HCV) or with heavy alcohol use. Isoniazid, rifampicin and pyrazinamide are all associated with drug-induced hepatitis. It is recommended that, during the initial 2-4 weeks of TB treatment, a complete clinical evaluation should be done at least weekly. Serum glutamic pyruvate transaminase (SGPT) must be assessed at least once at the end of the first month. If there are signs of significant liver injury (SGPT levels 5 times higher than the upper normal value for the test) all TB drugs should be stopped until liver function tests improve and clinical symptoms (nausea, abdominal pain) resolve before reintroducing the anti-TB drugs. Once drug-induced hepatitis has resolved, the drugs are reintroduced one at a time. If symptoms recur or liver function tests become abnormal as the drugs are reintroduced, the last drug added should be stopped. Rifampicin is less likely than isoniazid or pyrazinamide to cause hepatotoxicity, it is the most effective agent and should be preserved in the treatment management as far as possible. If the patient is severely ill with TB and it is considered unsafe to stop TB treatment, a non-hepatotoxic regimen consisting of streptomycin, ethambutol and a fluoroquinolone should be started.

Second-line TB drugs have many more adverse effects than the first-line anti-TB drugs, but management of these adverse effects is possible even in resource-poor settings. Timely and intensive monitoring for, and management of, adverse effects caused by second-line drugs are essential for MDR-TB treatment. It is essential for patients to be aware of possible side-effects, to know their nature and to have access to clinical and laboratory services to help detect side-effects, and medications to treat adverse effects when they occur. Details on side effects management for second line TB drugs are available elsewhere[28].

Drug interactions

Drug interactions may complicate TB treatment: the following factors require special approaches in the clinical management of PWUD who receive TB medications:

- Interaction of illicit drugs and OST with anti-TB drugs results into increased hepatotoxicity[29]. This requires a careful selection and dosage of anti-TB drugs and closer monitoring of the liver function. Cycloserine causes high incidence of adverse effects, including seizures, in patients dependent on alcohol or other substances and should be possibly not included in the MDR-TB treatment.
- Rifampicin substantially reduces the concentration and effect of methadone: dose adjustment (increased dosing) of methadone is required in order to maintain the substitution effect.[22] As an

alternative, rifampicin could be replaced by rifabutin, as there is no reported interaction between rifabutin and methadone.

- Antiretroviral and anti-TB medications have drug–drug interactions that affect the clinical management of people living with HIV and TB. This is especially true for rifampicin, which reduces the levels of both NNRTIs (nonnucleoside reverse transcriptase inhibitors) and PIs (Protease inhibitors).

Clinical protocol *Management of tuberculosis and HIV coinfection among adults and adolescents*, published by WHO Regional Office for Europe in 2013, summarizes the major drug-drug interactions that may occur in people who use drugs, having HIV and TB, and provides recommendations for their clinical management.

Treatment of MDR-TB

TB is a curable disease - in favourable conditions drug-susceptible TB has very high cure rates, close to 100%, however, for MDR-TB this figure declines to 70-90% in the best health systems, and drop to 30% for XDR-TB patients who are HIV-negative.[30]

A MDR-TB patient requires an anti-TB treatment with an intensive phase of at least 8 months and a continuation phase of at least 12 months. More details on the treatment can be found in widely available WHO guidelines.[22,28] Patients who are likely to have MDR-TB, while awaiting DST results, can start an empirical MDR-TB regimen based on an anti-TB drug resistance profile identified from a country-representative anti-TB drug resistance survey/surveillance (DRS). Candidates to an empirical MDR-TB treatment regimen include patients to whom the standard treatment regimen did not work and those exposed to a MDR-TB patient especially if they present with severe disease. More details on the TB treatment can be found in widely available WHO guidelines.

Whenever the results of DST become available, patients can have an individually-tailored MDR-TB regimen still based on few important principles: at least four effective second-line anti-TB drugs to be given daily and under direct observation (DOT) and including a fluoroquinolone, a parenteral agent, ethionamide (or prothionamide), and either cycloserine or PAS if cycloserine cannot be used. A later-generation fluoroquinolone should be preferred to an earlier-generation fluoroquinolone. The first-line anti-TB drug pyrazinamide should also be included. Some experts recommend using high-dose isoniazid (defined as 16–20 mg/kg/day) in the presence of resistance to low concentrations of isoniazid (>1% of bacilli resistant to 0.2 µg/ml but susceptible to 1 µg/ml of isoniazid), whereas isoniazid is not recommended for high dose resistance (>1% of bacilli resistant to 1 µg/ml of isoniazid).

Much more data are needed to better understand dosing for the drugs used for drug-resistant TB, their safety and toxicity, and drug-to-drug interactions; there is little to no data regarding these drugs and OST.

Special populations: PWUD who have TB/HIV co-infection

PWUD have a high burden of HIV in addition to the higher risk of TB[31]. WHO has produced specific guidelines on collaborative HIV and TB service provision for people who inject drugs (PWID)[4]. The consideration that alcohol dependence, active drug use and mental health problems should not be used as reasons to withhold TB and HIV treatment is a pivotal recommendation.

Active TB in PLHIV is an indication for the need to initiate antiretroviral treatment (ART) as soon as possible and regardless of CD4 cell count or HIV viral load. In general, treatment of TB in PLHIV should be

considered as a priority and start as soon as possible after TB diagnosis. ART should be added within the first eight weeks of commencing anti-TB treatment. Those HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts of less than 50 cells/mm3) should receive ART immediately within the first two weeks of initiating TB treatment.

ART should be considered part of HIV and TB treatment and prevention, which prolongs and enhances quality of life, preserves and improves immune function and reduces the risk of HIV transmission in PLHIV. Because HIV is a chronic lifelong infection which currently cannot be cured, PLHIV have to be followed medically for the rest of their lives, and ART is a core component of their treatment and care.

Recommendations on combined management of TB and HIV co-infection have been recently issued[32].

Specific factors which require special approaches in the clinical management of PWUD with TB/HIV co-infection include the following:

- Interactions between ARV and methadone may commonly occur. These may diminish the effectiveness of either or both therapies by causing opioid withdrawal or overdose, increased methadone toxicity, and/or decreased ARV efficacy. Efavirenz (EFV), nevirapine (NVP), and lopinavir/ritonavir (LPV/r) have been associated with significant decreases in methadone levels. Patients and drug dependence treatment facilities should be informed of the likelihood of this interaction. The clinical effect is usually seen after 7 days of co-administration and may be managed by increasing the methadone dosage, usually in 5-mg to 10-mg increments daily until the desired effect is achieved.[33] See also *Clinical Protocol Management of tuberculosis and HIV coinfection among adults and adolescents*, WHO Regional Office for Europe, 2013.
- Limited information is currently available about interactions between buprenorphine and ARV agents. Findings from available studies show that the drug interaction profile of buprenorphine is more favorable than that of methadone.[34]
- Naltrexone is not metabolized via the CYP450 enzyme system and is not expected to interact with NNRTIs (nonnucleoside reverse transcriptase inhibitors) and PIs (Protease inhibitors).[35]
- Frequent co-infection with HCV and/or HBV and the interactions with drugs used for the treatment of hepatitis.[36,37,38] Viral hepatitis infections should not be contraindication for HIV or TB treatment, but require closer monitoring of the liver function. Treatment of HIV/HBV co-infection should include the antitretroviral drugs TDF and FTC (3TC). In general, PegIFN and ribavirin treatment of HCV infection should be deferred until the completion of TB treatment; however, in the presence of severe liver fibrosis or cirrhosis decision on treatment should be taken individually.
- Poor treatment adherence that calls for additional patient support.[39, 40] OST supports the adherence to TB and HIV treatment.[41,42] OST has to be integrated into provision of TB and HIV in-patient and outpatient treatment services.
- Poor access to the health care system. Collaboration with harm-reduction programmes may be essential in organizing effective outreach services such as education, HIV testing, TB screening and preventive treatment, DOT and tracing those who didn't complete TB treatment.[43,44]

Identification of latent tuberculosis infection

There is no current demonstration that PWUD who do not have HIV infection may benefit from the treatment of LTBI. Therefore, tests to diagnose LTBI (including TST and/or IGRAs) are not recommended in these individuals.

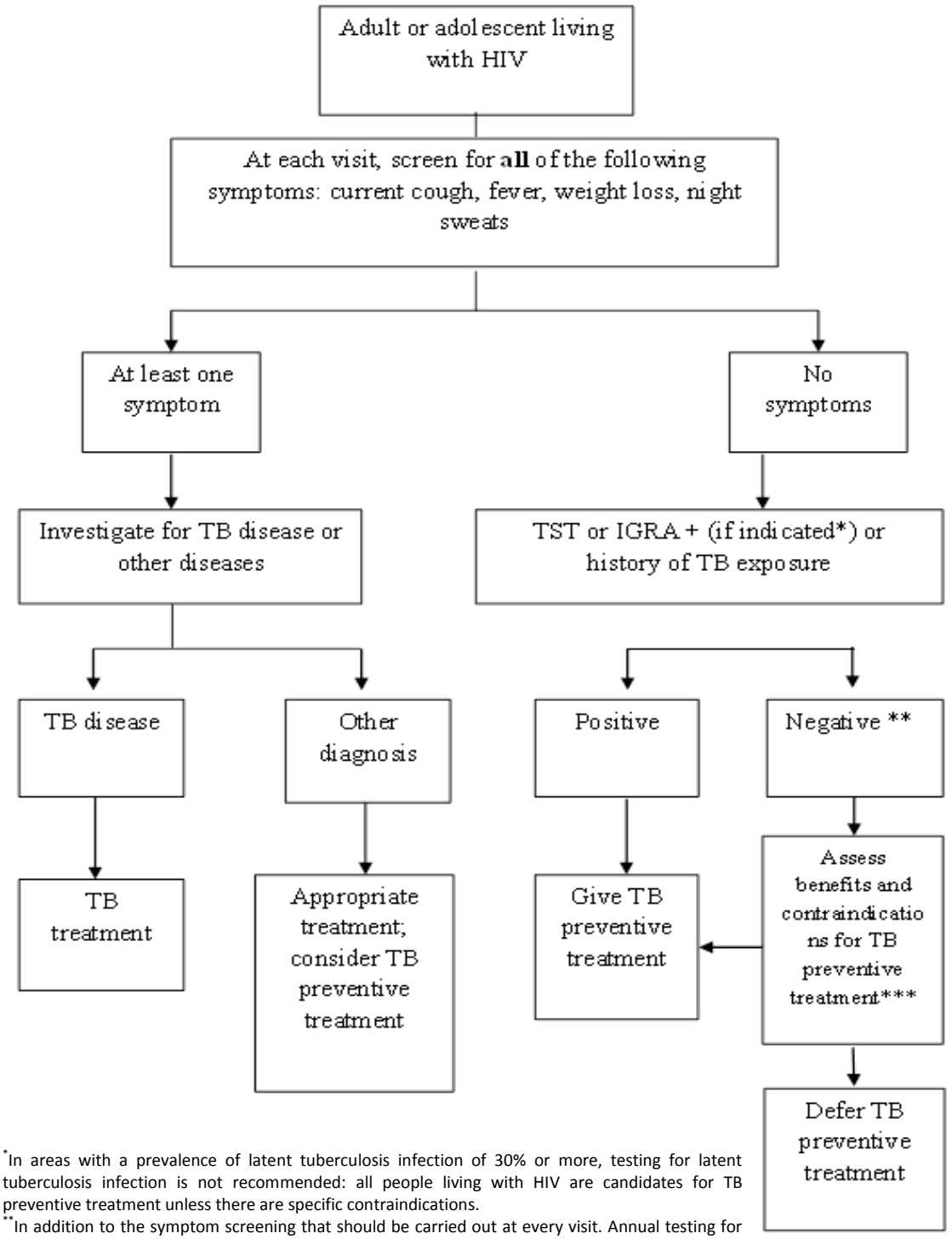
In PWUD who are also living with HIV, once active TB is reasonably ruled out, the health care provider should proceed further by investigating a status of latent tuberculosis infection (LTBI) (Figure 3). In settings where the prevalence of LTBI in the general population is high (above 30%) all PLHIV are candidate to preventive therapy of LTBI irrespective of any further diagnostic investigation. The same applies to PLHIV who are exposed to infectious TB patients, independently from the background prevalence of LTBI.

In settings where the prevalence of LTBI in the general population is low (below the threshold of 30%) and with enough resources and capacity, a diagnostic test should be used to detect LTBI.

The standard test for detecting LTBI is the tuberculin skin test (TST), which is based on the exposure to purified protein derivatives of M. tuberculosis (Mendel– Mantoux technique). Information on how to perform a TST are described elsewhere. A positive TST, defined in PLHIV as >5 mm of skin induration, is indicative of a past or recent TB infection. For TST results to be read, patients must return to a medical care setting 48–72 hours after its placement. This requirement may serve as a barrier to test completion, particularly for people whose lives may be complicated by active drug use. Furthermore, TST is not an ideal test due to its low sensitivity (especially in PLHIV and other immunocompromised persons) and low specificity (especially in BCG vaccinated persons).

A new technique based on testing a blood sample using an interferon gamma release assay (IGRA) has become available to investigate LTBI. Details on implementation and performance og IGRA are available elsewhere. Some studies may suggest increased sensitivity of IGRAs among drug users. However, in general terms, given comparable performance but increased cost, replacing the TST by IGRAs as a public health intervention in resource-constrained settings is not recommended. In the European region setting, the selection of the most suitable test for the detection of LTBI should take into consideration: a) the context for testing (the likeliness that the patient returns for reading the skin reaction after 48-72 hours); BCG vaccination or exposure to non-tuberculosis environmental mycobacteria); b) capacity/training of the healthcare personnel to use the test; c) test availability and the overall cost of testing.

Figure 3. Algorithm for assessing TB risk and disease in an HIV-positive person. Source: Management of Tuberculosis and HIV co-infection. Clinical Protocol for the WHO European Region[32].



*In areas with a prevalence of latent tuberculosis infection of 30% or more, testing for latent tuberculosis infection is not recommended: all people living with HIV are candidates for TB preventive treatment unless there are specific contraindications.

**In addition to the symptom screening that should be carried out at every visit. Annual testing for latent tuberculosis infection is recommended for people living with HIV who are in a high-risk category, such as people who inject drugs and prisoners.

***In countries in which prevalence of latent tuberculosis infection among people living with HIV is less than 30%, people living with HIV without documented latent tuberculosis infection or history of TB exposure can benefit from TB preventive treatment when highly exposed to TB, such as in high-risk populations such as prisons.

Treatment of latent tuberculosis infection

Tuberculosis preventive treatment should be initiated in all PWUD who are living with HIV, are free of TB disease, and who have presumptive or confirmed LTBI based on tests results and/or history of TB exposure. Treatment consists of isoniazid preventive therapy (IPT). The existing evidence demonstrates that IPT reduces the risk of active TB among PLHIV by 33% overall and by 64% when targeted to PLHIV who had a positive TST.[45]

The concern that IPT could further amplify an existing isoniazid resistance is disputed by the fact that the number of bacilli in LTBI is very low, preventing selection of pre-existent genetic mutations which confer drug resistance. Evidence demonstrates that the administration of IPT does not increase the development of drug resistance to isoniazid.[46,47,48,49] In countries with high level of resistance to isoniazid, while IPT does not amplify drug resistance, its efficacy in preventing TB is reduced proportionally to the extent of background isoniazid resistance. Even considering this shortfall, the delivery of IPT to PLHIV will still be beneficial for a significant proportion of PLHIV living in areas with high prevalence of isoniazid resistance and should be recommended.

The recommended dose of isoniazid for TB preventive treatment is 5 mg/kg (300 mg maximum dose) once daily. Isoniazid does not have clinically significant interactions with HIV drugs.

IPT should be given at least for 6 months. This duration of treatment is consistent with evidence from low TB incidence areas that extending duration to 12 months (or 9 months) increases protection but it does it only marginally.[45] In settings with a high incidence of TB, isoniazid preventive therapy among people living with HIV appears to have a short-lasting effect (1–2.5 years) because the drug cannot protect against reinfection[32].

The risk of adverse effects of IPT is low.[50] Isoniazid may cause drug induced hepatitis, which is mostly of mild to moderate intensity, and peripheral neuropathy. Routine monitoring of liver function is not generally necessary, except in PLHIV who have concomitant risk factors for liver injury (i.e. concomitant viral hepatitis, addition to alcohol and drugs, etc.). However, all individuals assuming isoniazid should be instructed on how to recognize and immediately report clinical symptoms of liver injury (nausea, vomiting, jaundice, etc.).

IPT for PWUD who are also HIV infected should be dispensed with other treatments, such as OST, in settings where this is implemented and with assistance of social workers and peer- supporters.[13] Lack of adherence to IPT does not promote drug resistance, thus IPT does not strictly require DOT. However, adherence to IPT is important for its effectiveness and could be promoted by integrating services such as, for example, staff of HIV and drug dependence services counseling patients and delivering IPT, ensuring coordinated clinical management of side effects, etc. The role of outreach and other harm reduction activities, such as needle and syringe programs, usually run by NGOs, should be explored in effective delivery of IPT. In general, concerns regarding adherence should not be a barrier to implementing IPT.

Infection control

In terms of infection control for tuberculosis, 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 outreach workers and social workers living with HIV from areas with high TB exposure, in addition to providing ART and IPT.

Access to treatment

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 OST, for PWUDs in a holistic person-centred approach to maximize access and adherence within one setting.[3]

The basic treatment and care case-management should be provided by a multi-disciplinary team comprised of a physician/s (in many countries being one specialist on infectious diseases and HIV and one specialist on pulmonology and TB), a nurse and a social worker or non-medical service provider. Each of the team members has a distinct role in providing treatment and care, and their services should be complementary. It is essential that team members collaborate on regular basis in planning, implementation and monitoring of all activities related to the case management. A network of other specialists and self-help groups should be available to support people with TB/HIV coinfection, including the provision of opioid substitution therapy for people who inject drugs.

Hospitalization is essential for patients severely ill or with associated conditions requiring closer clinical monitoring. However, in all cases of hospitalization, it is an imperative to ensure non-disruption of other medical services the patient is receiving, by providing them in the same place where the patient is hospitalized (e.g. providing HIV treatment and OST in TB facilities for PWID).

The decision on how TB and HIV treatment should be delivered after hospital discharge and during TB treatment continuation phase should be taken by considering what is the most convenient option for the patient in order to ensure adherence to treatment. Inclusion of lay workers, such as social workers and non-governmental actors and communities can effectively provide patient support and directly-observed TB treatment (DOT) which enhance the completion of treatment so important for a successful outcome and in preventing the development of drug resistant TB.

Finally, collaboration between TB, HIV and harm reduction programmes is essential in organizing effective outreach services such as education, screening, TB preventive treatment, DOT for TB and the tracing of those who didn't complete the TB treatment to improve preventive measures and treatment outcomes of PWUD, thereby saving lives, protecting communities and contributing positively to public health.[32]

A special approach for people who use drugs

Although PWUD need special approaches in terms of screening and identification of active TB disease or LTBI, assistance with treatment adherence and prevention of TB infection, these issues are rarely addressed in Eastern Europe and Central Asia (EECA countries).

- Access to diagnostic services is more difficult for PWUD because of stigmatization and a lack of patient-centred services. Diagnostic and treatment approaches commonly-used in EECA are not always suitable for PWUD.
- Staff at health care facilities is not always trained in terms of communication skills and clinical knowledge to work with PWUD.
- TB treatment, HIV treatment and substitution therapy are usually not available in one physical location.
- Sometimes, in some countries, clients have to pay to be diagnosed and/or treated.

A number of activities can be implemented by the affected communities, including but not limited to PWUD, their families and CBOs/NGOs, with the aim of improving the current situation. These activities can include:

- participation in situation assessment, project and program implementation, monitoring and evaluation;
- peer counselling;
- community mobilization, information campaigns and advocacy. National advocacy efforts should focus on addressing local challenges and using the appropriate advocacy strategies, which can be identified during the situation assessment. National and regional advocacy can target the level of policymakers, service providers and/or the community. The focus of regional advocacy in EECA is usually on regional policy and legislation and improving networking and collaboration with regional stakeholders (the European Parliament, WHO, United Nations agencies and international NGOs). The present training covers subjects related to situation assessment, advocacy planning, effective advocacy campaigns and partnership building.

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Annex 1

The principles of harm reduction (website of EHRN)

http://www.harm-reduction.org/harm-reduction.html

- **Some level of drug use in society is inevitable** and varies according to culture, drug supply, as well as social, economic and other factors.
- Drug use encompasses a continuum of behaviors from severe problematic drug use to total abstinence, and acknowledges that **some ways of using are more dangerous than others**
- Does not attempt to minimize or ignore the **harm and danger associated with drug use**
- The largest costs and harms for society and individuals are related to **problem drug use** (PDU) defined by EMCDDA as "injecting drug use or long duration/regular use of opioids, cocaine and /or amphetamines" which describes a small proportion of all drug users and should be a priority for harm reduction efforts.
- **Based on human rights** (such as access to health care for all) drug users as an integral part of the society
- **Interventions should be pragmatic** (based on achievable short-term goals rather than idealistic ones like a drug free world)
- Interventions should be **evidence-based**
- **Individual and community well-being** are the criteria for successful interventions and policies rather than only cessation of drug use.
- Interventions should be **comprehensive** recognizing that various drug-related harms merit various responses
- Interventions should be **cost-effective** to maximize the benefit from scarce resources.
- Interventions should be **client-oriented**, attractive for clients and addressing their needs and preferences.
- **Drug users should be involved meaningfully in the planning**, implementation and evaluation of harm reduction programs and policy.
- Harm reduction affirms **drugs users themselves as the primary agents of reducing the harms of their drug use**, and seeks to empower users to share information and support each other in strategies which meet their actual conditions of use.
- Calls for the **non-judgmental, non-coercive** provision of services
- Recognizes that the realities of poverty, class, racism, social isolation, past trauma, sex-based discrimination and other **social inequalities affect both people's vulnerability to and capacity for effectively dealing with drug-related harm**.

Annex 2

DOTS and STOP TB Strategies

Components of the Stop TB strategy

1. Pursue high-quality DOTS expansion and enhancement

- Secure political commitment, with adequate and sustained financing
- Ensure early case detection, and diagnosis through quality-assured bacteriology
- Provide standardized treatment with supervision, and patient support
- Ensure effective drug supply and management
- Monitor and evaluate performance and impact

2. Address TB-HIV, MDR-TB, and the needs of poor and vulnerable populations

- Scale-up collaborative TB/HIV activities
- Scale-up prevention and management of multidrug-resistant TB (MDR-TB)
- Address the needs of TB contacts, and of poor and vulnerable populations

3. Contribute to health system strengthening based on primary health care

- Help improve health policies, human resource development, financing, supplies, service delivery and information
- Strengthen infection control in health services, other congregate settings and households
- Upgrade laboratory networks, and implement the Practical Approach to Lung Health (PAL)
- Adapt successful approaches from other fields and sectors, and foster action on the social determinants of health

4. Engage all care providers

- Involve all public, voluntary, corporate and private providers through Public-Private Mix (PPM) approaches
- Promote use of the International Standards for Tuberculosis Care (ISTC)

5. Empower people with TB, and communities through partnership

- Pursue advocacy, communication and social mobilization
- Foster community participation in TB care, prevention and health promotion
- Promote use of the Patients' Charter for Tuberculosis Care

6. Enable and promote research

- Conduct programme-based operational research
- Advocate for and participate in research to develop new diagnostics, drugs and vaccines

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DOTS strategy components

1. Political commitments needed to foster national and international partnerships, which should be linked to long-term strategic action plans prepared by National TB Programs. Strategic action plans should address technical and financial requirements and promote accountability for results at all levels of the health system; they should include TB-related and other relevant indicators, and – where appropriate – political commitment should be backed up by national legislation. Local partnerships with many potential contributors will help improve TB care in terms of access, equity and quality

2. Diagnosis by quality ensured sputum spear microscopy -bacteriology remains the recommended method of TB case detection, first using sputum smear microscopy and then culture and drug susceptibility testing (DST). A wide network of properly equipped laboratories with trained personnel is necessary to ensure access to quality-assured sputum smear microscopy. This is likely to require additional investments in the laboratory network in many countries. In addition, every country should have a well-resourced and fully functioning national reference laboratory.

3. Standardized short-course anti-TB treatment under direct observation - the mainstay of TB control is organizing and administering standardized treatment across the country for all adult and paediatric TB cases – sputum smear-positive, smear-negative, and extrapulmonary. Services for TB care should identify and address factors that may make patients interrupt or stop treatment. Supervised treatment, which may have to include direct observation of therapy (DOT), helps patients to take their drugs regularly and complete treatment, thus achieving cure and preventing the development of drug resistance. Supervision must be carried out in a context-specific and patient-sensitive manner, and is meant to ensure adherence on the part both of providers (in giving proper care and support) and of patients (in taking regular treatment). Patient and peer support groups can help to promote adherence to treatment. Locally appropriate measures should be undertaken to identify and address physical, financial, social and cultural barriers – as well as health system – barriers to accessing TB treatment services.

4. Uninterrupted supply of quality assured anti-TB drugs - an effective drug supply and management system is essential. A reliable system of procurement and distribution of all essential anti-TB drugs to all relevant health facilities should be in place. Anti-TB drugs should be available free of charge to all TB patients, both because many patients are poor and may find them difficult to afford, and because treatment has benefits that extend to society as a whole (cure prevents transmission to others). Legislation related to drug regulation should be in place, and use of anti-TB drugs by all providers should be strictly monitored.

5. Standardized recording and reporting - establishing a reliable monitoring and evaluation system with regular communication between the central and peripheral levels of the health system is vital. This requires standardized recording of individual patient data, including information on treatment outcomes, which are then used to compile quarterly treatment outcomes in cohorts of patients. These data, when compiled and analysed, can be used at the facility level to monitor treatment outcomes, at the district level to identify local problems as they arise, at provincial or national level to ensure consistently high-quality TB control across geographical areas, and nationally and internationally to evaluate the performance of each country. Both developed and developing countries now have additional diagnostic information at their disposal, including sputum culture, DST and HIV test results, all of which can be used to guide patient management. TB programme managers also need to monitor records and reports from public and private care providers not directly linked to the NTP. Special attention must be paid to ensuring the confidentiality of patient information.

Sources:

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Annex 3

TB – testing methods

Sputum smear microscopy

Sputum specimens should be obtained for microscopic examination from all IDUs suspected of having pulmonary TB. Microbiological diagnosis is confirmed by culturing Mycobacterium tuberculosis (or under appropriate circumstances, by identifying specific nucleic acid sequences in a clinical specimen) from any suspected site of disease. However, in many settings where resources are limited, neither culture nor rapid amplification methods are currently available or feasible. In such circumstances, the diagnosis of TB may also be confirmed by the presence of acid-fast bacilli (AFB) in sputum smear examination. Repeated sputum smear microscopy may diagnose pulmonary TB in up to two-thirds of active cases. In nearly all clinical circumstances in settings of high TB prevalence, identification of AFB by microscopic examination is highly specific for the Mycobacterium tuberculosis complex. The optimum number of sputum specimens to establish a diagnosis has been evaluated. The first specimen was found positive in 83–87 % of all patients in whom AFB are ultimately detected; the second specimen was positive in an additional 10–12 % and the third specimen in a further 3–5 %. On this basis, WHO recommends the microscopic examination of two sputum specimens (formerly three) (2). Because the yield of AFB appears to be greatest from early morning (overnight) specimens, WHO further recommends that at least one specimen should be obtained from an early morning collection.

The procedures for collecting sputum involve the production of droplets that are highly infectious if the patient has untreated pulmonary TB. Sputum collection should therefore be organised in areas with good ventilation or, if not available, outside the building. Sputum smear specimens should be examined by microscopy immediately but no later than five to seven days after they have been collected.

Culture

Sputum smear microscopy is the first bacteriological diagnostic test of choice. However, where adequate and quality-assured laboratory facilities are available, the evaluation of patients should also include culture. Culture adds extra cost and complexity but greatly increases the sensitivity and specificity of diagnosis, resulting in better case detection. Although the results of culture may not be available until after a decision to begin treatment has been made, treatment may be stopped subsequently if cultures from a reliable laboratory are negative and if the patient has not responded clinically to treatment and the clinician has sought other evidence in pursuing the differential diagnosis.

Chest X-ray

As no chest radiographic pattern is absolutely specific for pulmonary TB, the diagnosis of smear-negative TB is always presumptive and should be based on other clinical and epidemiological information, including failure to respond to a course of broad-spectrum antibiotics and exclusion of other pathology. Reliance on chest radiography as the only diagnostic test for TB results in either overdiagnosis of TB or missed diagnoses of TB and other diseases and is therefore not recommended. Radiographic examination, however, is most useful when applied as part of a systematic approach to evaluate patients whose symptoms and/or findings suggest TB but whose sputum smears are negative. The use of chest radiography to diagnose pulmonary TB may be compromised by poor film quality, low specificity and difficulties with interpretation. HIV infection diminishes the reliability of chest radiographs for the diagnosis of pulmonary TB because the disease commonly presents with an atypical pattern. Furthermore, the chest radiograph may be normal in a proportion of HIV-infected patients with sputum culturepositive TB (observed in up to 14 % of such cases). Chest radiography remains an important adjunct to the diagnosis of smear-negative pulmonary TB in people living with HIV.

Fluoroscopy results are not acceptable as documented evidence of pulmonary TB.

Sputum smear microscopy and culture require skill and experience by the healthcare provider. If healthcare providers who are doing the medical examination, testing and counselling for infectious diseases in IDUs do not have the necessary skill, or the appropriate safety precautions are not in place, TB screening should not be a part of the basic screening test and all IDUs should be referred for TB screening to competent health institutions. The screening procedures in IDUs with no signs or symptoms of TB disease can be limited to screening for latent TB. The screening methods for latent TB in asymptomatic IDUs include the tuberculin skin test and blood tests.

The tuberculin skin test (TST)

This skin test has traditionally been used to diagnose latent infection with Mycobacterium tuberculosis. However, it has several limitations, particularly poor specificity because of crossreactivity with the antigens of the Bacille Calmette Guerin (BCG) vaccine, as well as many of the nontuberculous mycobacteria. In addition, false-negative TST is more likely to occur among IDUs because of the high rate of anergy that occurs in this population, most commonly found in HIV-seropositive IDUs. For this reason, less emphasis should be put on TST results in IDUs in areas where HIV prevalence in this group is high, and more on potential exposure to TB together with signs and symptoms of the disease.

Blood tests

IFN-gamma release assays (IGRA tests) have in recent years been proposed as alternatives to the TST. The potential for false-positive tests due to cross-reactivity is significantly lower with IGRAs than with the TST. In addition, the use of this test in IDUs is more likely to diagnose latent TB infection compared with traditional TSTs (Grimes et al., 2007). However, IGRAs have as yet limited potential in high burden TB and HIV settings.

Source: Guidelines for testing HIV, viral hepatitis and other infections in injecting drug users, EMCDDA, 2010

Annex 4

Best practices (Saint Petersburg)

In Saint Petersburg at a department for TB/HIV co-infected patients, two foundations “Svecha” and “Humanitarian Action” introduced a joint project.

The objective of the project was very simple: to organize psychological support to patients, most of whom had drug dependency. Initially we spent a lot of time and efforts to make sure that at least some abstinence treatment is provided. We even succeeded to introduce a position of psychologist/expert in narcology at this department. However very soon we learnt that simply having a doctor does not mean that treatment will be offered: a permission for storing the drugs had to be obtained, as well as a license to provide substance-dependence treatment and services, etc. To this day it is not clear, what were the actual requirements and what was made up by the chief doctor. But one thing is obvious: it is a challenge to provide access to substance-dependence treatment and services at an institution not specialized for this purpose. In the meantime we slowly started implementing the project. Psychotherapist of our project offered services at the department three times a week, providing counseling and group work. It was not clear at the beginning who will come for these services. But with time people started to come. There was not much to do for them at the department anyway. And he was a good specialist too.

Social worker – we had planned that she would be responsible for linking “hospital to city”, but in fact she was like the second psychotherapist. She made a small library at the department. She created art-therapy groups and self-help groups. Along the way deputy head of the department started helping, without him nothing of course would have materialized. He was in charge of “Patients’ school”. In the evenings during his shift, he would sit down with the patients and tell them why it is important to adhere to the treatment, how drug resistance emerges, how HIV infection helps reactivate TB. Later a group of Narcotics Anonymous was established at the department.

In a nut shell, after one year of our work at the department, it was clear that substance-dependence treatment is not the only and by far not the most effective way of improving treatment adherence. In any case, percentage of defaulters at the department was more than halved, although introduction of substance-dependence treatment and services failed. This does not mean that substance-dependence treatment is not necessary at TB hospitals.

MAIN CHALLENGES:

Problem: it is very difficult to find personnel to work in TB hospital. Staff cannot be PLHIV, and even HIV negative persons rarely wanted to work there.

Solution: it is really difficult to find personnel. What helped up was discussing in details all involved risks with the deputy head of the department. We discussed the rules of preventive treatment (which was obligatory for all staff), infection control (respirators for staff, ultra violet germicidal irradiation (UVGI)). Some of the activities could be conducted outside at a park, which surrounded the TB hospital.

Problem: allocation of paid staff positions had to be discussed and agreed upon with the chief doctor of the TB hospital.

Solution: According to the current health care legislation, all in-patient TB facilities had to have paid positions of an expert in narcology, a psychologist and a social worker. Existence of similar legislation in other countries needs to be checked. In our case it turned out that the management of the TB hospital did not make any efforts to fill in the vacancies for the above mentioned positions. When we expressed willingness to find the specialists, the management welcomes this initiative. It is true though that the salaries at the TB hospital were quite humble. An alternative is to have a part-time specialist, for instance, an expert in narcology, who visits when there are requests.

Problem: team work at the department is made difficult because of the extremely negative attitude of the staff towards the patients.

Solution: Staff needed additional skills building and support. In our case, staff members were reacting very positively to training activities, especially to burn-out prevention activities. It was also very productive to offer possibilities to participate in conferences and seminars.

Annex 5

Building more effective specialist services			
Advocacy Issues	**Goals**	**Objectives**	**Indicators**
Stigma & discrimination (S&D) from staff	To reduce levels of S&D among staff and improve consumer experience	Deliver sensitivity training to staff about working with people who use drugs	Reduction in complaints Improved working relationships between staff and clients
Increase integration between TB, HIV and OST services	To improve working relationships between services to enhance effectiveness and consumer experience of using multiple related services	Deploy or develop opportunities for meaningful participation in the planning systems for HIV, TB and OST Advocate for integrated service model and promote consumer satisfaction surveys as a means of gathering intelligence from consumer population	Advocates have places at table of key HIV, TB and OST planning forums Advocates have points of influence on those engaged in policy forums Questions are raised about service integration Consumer satisfaction survey(s) undertaken testing consumer experience of care pathway
Improve treatment access	To ensure that people who use drugs have fair and equitable access to range of treatments promoted in global guidelines and based on availability within country	Advocate where people who inject drugs face barriers to TB or HIV treatment access Advocate for access to OST services as a core component of effective TB and HIV treatment Advocate for reasonable access to medicines for OST, HIV and TB without political interference or barriers from pharmaceutical companies	Number of complaints submitted Changes in clinic policy following advocacy intervention or interventions Advocacy activities that bring attention to positive effects of OST on health and wellbeing OST, HIV and TB drugs accepted as essential medicines in more countries or home country

Annex 6

Instruction ADVOCACY: PARTNERS

See below the list of possible problems which advocacy can deal with. Each group will get one problem and will work on question: What partners can be involved in solving this problem?

Problem1:
Hospitals do not provide drug-dependence treatment and services to TB patients – they do not complete their treatment

Problem2:
In prisons there are no second-line drugs to treat MDR TB

Problem 3:
TB doctors do not have the necessary skills to diagnose and treat TB in PLHIV

Problem 4:
Lack of financing to buy second line drugs and tests for MDR TB

Other problems are possible depending on group composition.