

Management of drug-resistant tuberculosis

**Training for staff working at
DR-TB management centres**

Training modules



**World Health
Organization**

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This training material is based on the WHO documents including the *Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis*. 2014 (WHO/HTM/TB/2014.11), *Guidelines for the programmatic management of drug-resistant tuberculosis: 2011 update* (WHO/HTM/TB/2011.6), *Guidelines for the programmatic management of drug-resistant tuberculosis: emergency update 2008* (WHO/HTM/TB/2008.402), *Treatment of tuberculosis: guidelines – 4th ed.* (WHO/HTM/TB/2009.420), *The use of bedaquiline in the treatment of multidrug-resistant tuberculosis: interim policy guidance* (WHO/HTM/TB/2013.6). It is designed for use in tuberculosis control programmes aligned to WHO recommendations. It is expected that this material would be adapted to the specific requirements and the policy in the country.

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Acknowledgements

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Disclaimer

The existing modules are not meant to serve as comprehensive guidelines, but only as an example of how training modules could be developed based on the respective national guidelines for the programmatic management of drug-resistant tuberculosis (PMDT). Any training modules will need to be used in conjunction with the latest national PMDT guidelines and World Health Organization (WHO) guidelines. Therefore, these generic modules can either be adapted for use in country training, keeping in view the guidelines, or may be used as examples to modify existing country modules for PMDT training. Given below is an illustrative list of steps that may be followed for adaption of modules.

- Evaluate the generic modules to check consistency with the national guidelines and whether the modules in the current form contain adequate and appropriate technical details relevant for the country. This would include the following:
 - Use of country examples for exercises: the modules provide an illustrative list of examples, but this is not comprehensive and not all may be locally relevant.
 - Screening of high-risk categories for drug resistance and subsequent diagnostic algorithms for diagnosing resistance in TB patients may be different in the country, and specifically the use of newer technologies within the algorithm.
 - Recording and reporting formats: new case definitions and treatment outcomes, formats for recording and reporting have been recommended by WHO in 2013. These may be used in exactly the same form or may have been adapted to country needs.
 - Treatment regimens may vary by country, although the basic principles of treating a DR-TB case remain the same. Accordingly, the quantification of drugs varies because of:
 - which drug combination is used
 - formulation and dosage
 - calculation of needs for duration of treatment (use of 6 doses/week formula)
 - country policy on level of buffer stock.
 - Care delivery models – hospital/facility/community based – will vary across countries. The need for and extent of hospitalization are different. Similarly, the availability of patient support varies from country to country.
 - Names used in the exercises are not specific to any country. It would be good to use names that sound familiar to those used in the country so that participants can identify themselves with these examples.
- Depending on the target audience and country context, the modules may need to be translated into the national language.
- It is always useful to pilot-test the modules with the target audience before finalization and wider usage. The pilot test could be in the form of self-reading by a group of health workers who then discuss their findings or could be actually used for training where feedback is collected from all participants on content, duration and overall organization of the training.

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Facilitator's guide



**World Health
Organization**

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Introduction

For whom is this course intended?

This course is designed for health workers who are involved in detecting cases of and managing patients with drug-resistant TB (DR-TB)^a at DR-TB management centres^b that specialize in caring for such patients. These health workers may be physicians, nurses or midwives.

What are the methods of instruction used in this course?

This course uses a variety of methods of instruction, including reading, written exercises, discussions, role-plays and demonstrations. Practice – whether through written exercises, role-plays, or in the health facility – is considered a critical element of instruction.

^a These modules focus on managing rifampicin-resistant TB (RR-TB) and multidrug-resistant TB (MDR-TB) (collectively referred to as RR/MDR-TB in several places) because of the clinical significance and need for treatment with second-line drugs in both cases. The modules do not specifically focus on extensively drug-resistant TB (XDR-TB) and polydrug-resistant TB (PDR-TB) other than RR-TB.

^b For the purpose of these modules, the term “DR-TB management centre” is used to denote any health facility where drug resistance among those presumed to have TB or known TB patients is diagnosed and treated.

How is the course conducted?

- Small groups of participants are led and assisted by facilitators as they work through the course modules (booklets that contain units of instruction). The facilitators do not deliver didactic lectures, as in traditional classrooms. The facilitator's role is to answer questions, provide individual feedback on exercises, and lead discussions and role-plays.
- The modules provide the basic information that has to be learnt. Information is also provided through demonstrations and role-plays.
- The modules are designed to help each participant develop the specific knowledge and skills necessary for detecting DR-TB and treating patients with the disease. Participants develop this knowledge and these skills as they read the modules and practise by doing written exercises, and engaging in group discussions and role-plays.
- Participants work at their own pace through the modules. In some activities, such as role-plays and discussions, the group works together.
- Each participant discusses any problem or question with the facilitator, and receives prompt feedback on completed exercises. Giving feedback involves reviewing and discussing the exercises with the participants.

To prepare for each module, you should do the following:

- Read the module and work through the exercises.
- Check your answers by referring to the answer sheets (provided in a separate packet).
- Read all the information about the module in this guide.
- Plan with your co-facilitator/s how the module will be presented and which important points will be emphasized.
- Collect any necessary supplies for exercises in the module.
- Think about sections that participants might find difficult and questions they may ask.
- Plan how to help with difficult sections and answer possible questions.
- Develop questions that will encourage participants to think about using their new skills in their own health facilities.

You are not expected to teach the content of the course through formal lectures. Nor is this a good idea, even if this is the teaching method to which you are most accustomed.

Who is a FACILITATOR?

A facilitator is a person who helps participants learn the skills presented in the course. The facilitator spends much time in discussion with participants, either individually or in small groups. For facilitators to give enough attention to each participant, a ratio of one facilitator to five or six participants is desired. If your assignment is to teach this course, YOU are a facilitator.

As a facilitator, you must be familiar with the course material. It is your job to explain, demonstrate, answer questions, talk with participants about their answers to the exercises, conduct role-plays, lead group discussions, and generally give participants any help they need to successfully complete the course.

What, then, DOES a FACILITATOR do?

The facilitator needs to do three basic things.

1. INSTRUCT

- Make sure that each participant understands how to work through the materials and what is expected in each module and each exercise.
- Answer the participant's questions as they occur.
- Explain any information that the participant finds confusing, and help the participant understand the main purpose of each exercise.
- Lead group activities, such as discussions and role-plays, to ensure that learning objectives are met.
- Promptly review each participant's work and give correct answers.
- Discuss how the participant obtained the answers in order to identify any weaknesses in the participant's skills or understanding.
- Provide additional explanations or practice to improve skills and understanding.
- Help participants understand how to use the skills taught in the course in their own health facilities.

2. MOTIVATE

- Compliment participants on correct answers, improvement and progress.

3. MANAGE

- Plan ahead and obtain all supplies and equipment needed each day so that these are in the classroom when required.
- Make sure that there are no disturbances during the learning process, such as too much noise or not enough light.
- Monitor each participant's progress.

How do you do these things?

- Show enthusiasm for the topics covered in the course and for the work that the participants are doing.
- Be attentive to each participant's questions and needs. Encourage participants to come to you at any time with questions or comments.
- Watch the participants as they work, and offer individual help if you see a participant looking troubled, staring into space, not writing answers or not turning the pages. These are clues that the participant may need help.
- Promote a friendly, cooperative relationship. Respond positively to questions (for example, by saying, "Yes, I see what you mean," or "That is a good question"). Listen to participants' questions and try to address their concerns, rather than rapidly giving the correct answer.
- Always take enough time with each participant to answer questions completely, so that both you and the participant are satisfied.

What NOT to do

- During times scheduled for course activities, do not work on other projects or discuss matters not related to the course.
- While discussing with participants, avoid using facial expressions or making comments that could cause participants to feel embarrassed.
- Do not lecture about the information that participants are about to read. Give only the introductory explanations that are suggested in the *Facilitator's guide*. If you give too much information too early, it may confuse participants. Let them read it for themselves as they work through the modules.
- Do not review the text paragraph by paragraph. This is boring and suggests that participants cannot read for themselves. When necessary, review the highlights of the text while giving individual feedback or during group discussions.
- Do not be condescending; in other words, do not treat participants as if they are children. They are adults.
- Do not talk too much. Encourage participants to speak.
- Do not be shy, nervous, or worried about what to say. This *Facilitator's guide* will help you remember what to say. Just use it.

How can this FACILITATOR'S GUIDE help you?

This *Facilitator's guide* will help you teach each of the course modules. For each module, the guide includes the following:

- a list of the procedures to complete during each module, highlighting the type of feedback to be given after each exercise;
- guidelines describing
 - how to conduct demonstrations, role-plays and group discussions
 - points to make during group discussions or individual feedback;
- answers to the exercises.

Answer sheets are also provided in a separate packet for each participant. Individual answer sheets should be detached and given to each participant after the exercises, during individual feedback or after a group discussion.

At the end of this guide are *Guidelines for all modules*. This section describes techniques to use when working with participants during the course. It provides suggestions on how to work with a co-facilitator, if applicable. It also includes important techniques to use when:

- participants are working individually;
- you are providing individual feedback;
- you are leading a group discussion;
- you are coordinating a role-play.

Checklist of instructional materials needed for each small group

Table 1 **Checklist of instructional materials needed**

ITEM NEEDED	NUMBER NEEDED
Facilitator's guide	1 for each facilitator and participant (if participants are involved in a training of trainers course [ToT])
Set of six training modules (A–F)	1 set for each facilitator and 1 set for each participant
Answer sheets in packet (optional)	1 packet for each participant, if they will be used
Copy of course schedule	1 for each facilitator and 1 for each participant

Checklist of supplies needed for the training

Supplies needed for each person include the following:

- name-tag and holder
- pen
- pencil with eraser
- paper
- highlighter
- folder or large envelope to collect answer sheets
- ruler
- calculator (optional but helpful).

Supplies needed for each group include the following:

- large paper clips (helpful to mark the place in the module while doing an exercise)
- pencil sharpener
- stapler and staples
- 1 roll masking tape (for taping pages from the flipchart to the wall)
- extra pencils and erasers
- flipchart pad and markers, or blackboard and chalk
- overhead projector (if possible), and erasable markers for writing on overhead transparencies.

Certain exercises require special supplies, such as anti-TB medicines and medicine packets. These supplies are listed in the guidelines for each module. Be sure to collect the needed supplies from your course director before conducting these exercises.

Facilitator’s guidelines for Module A: Introduction

PROCEDURES	ACTIVITY
1. Introduce yourself and ask participants to introduce themselves.	Introductions
2. Do any necessary administrative tasks.	—————
3. Distribute and introduce <i>Module A: Introduction</i> . Participants should read pages A1–A15. They do not need to read the Glossary or the lists of abbreviations and abbreviations of anti-TB medicines.	Reading
4. Answer any questions about <i>Module A: Introduction</i> .	Group discussion
5. Explain your role as a facilitator.	—————
6. Ask participants to tell the group where they work and describe briefly their responsibility for identifying patients presumed to have drug-resistant TB (DR-TB) and treating these patients.	Group discussion
7. Continue immediately to <i>Module B: Detect cases of DR-TB</i> .	—————

1. Introduce yourself and participants

- a. Introduce yourself as a facilitator of this course and write your name on the board or flipchart.
- b. As participants introduce themselves, ask them to write their names on the board or flipchart.
- c. Remind participants to wear their name-tags during the session. If possible, also have them write their names on large name cards at their places.
- d. Leave the list of names where everyone can see it. This will help you and the participants learn one another’s names.

2. Administrative tasks

There may be some administrative tasks or announcements that you need to address. For example, you may need to explain the arrangements that have been made for breaks, lunch, transportation or payment of a per diem, location of water closets/ toilets, telephones, etc.

Distribute the course schedule.

3. Introduce the module and manual

- a. Explain that *Module A: Introduction* briefly describes the importance of drug-resistant tuberculosis (DR-TB) as a health problem. It also describes the course’s methods and learning objectives.
- b. Explain that this module, like all the modules that the participants will be given, is theirs to keep. As they read, they can highlight important points or write notes on the pages if they wish.

- c. Point out the Glossary at the end of the module. Participants should refer to the Glossary when they encounter an unfamiliar term.

Ask participants to read pages A-3–A-17. They do not need to read the Glossary. Point out the lists of abbreviations and abbreviations of anti-TB medicines on pages A-26 and A-27.

4. Answer questions

When everyone has finished reading, ask if there are any questions about the module or the purpose of the course. Answer any questions.

5. Explain your role as facilitator

Explain to participants that as a facilitator (and along with your co-facilitator/s, if you have one) your role throughout this course will be as follows:

- to guide them through the course activities;
- to answer questions as they arise or find the answer if you do not know;
- to clarify information they find confusing;
- to give individual feedback on exercises where indicated;
- to lead group discussions and role-plays.

6. Discuss participants' responsibility for detecting DR-TB and treating patients with the disease

Explain to participants that you would like to learn more about their responsibilities as they relate to DR-TB. This will help you understand their situations and be a better facilitator for them. For now, ask participants to say where they work and what their job is. During the course, you will have additional discussions to determine exactly what they do at their DR-TB management centre.

To encourage informality, ask for a volunteer to share information. Ask the volunteer the two questions below. Note the answers on the board or flipchart and summarize participants' roles and responsibilities.

- What is the name of the facility where you work, and where is it?
- What is your position or responsibility for TB patients? For DR-TB patients?

*Note: Have the participants remain seated. You should ask the questions and have participants answer you, as in a conversation. It is important that the participants feel relaxed and not intimidated or put on the spot. Although it may be interesting to ask more questions, **do not do that now**. This should not be a long discussion.*

7. Continue to the next module

Proceed directly to *Module B: Detect cases of DR-TB*.

Facilitator’s guidelines for Module B: Detect cases of DR-TB

PROCEDURES	ACTIVITY
1. Distribute <i>Module B: Detect cases of DR-TB</i> . Introduce the module. Show and explain the icons and instructions that will guide participants through all of the modules.	_____
2. Have participants read pages B-5–B-15. When everyone is ready, have them turn to Exercise A on page B-48.	_____
3. Have participants do Exercise A individually.	Provide individual feedback.
4. Have participants continue reading from page B-16 until the next stop sign on page B-22. Have participants do Exercise B on page B-50 individually.	Provide individual feedback.
5. Have participants continue reading from page B-23 until the stop sign on page B-35. Have them do Exercise C on page B-52 individually.	Provide individual feedback.
6. Have participants go back to page B-35 and read until the next stop sign on page B-38. Instruct them to answer the questions for Exercise D on page B-55 as preparation for the group discussion. Lead a discussion of how RR/MDR-TB cases are detected at participants’ own DR-TB management centres.	Group discussion
7. Explain that at the end of each module there is a summary of important points and self-assessment questions. Explain the purpose of the self-assessment questions and how to complete them. Then ask participants go to page B-39, read the summary and answer the self-assessment questions.	_____
8. Participants complete the self-assessment questions and check their own answers.	Participants check their own answers.
9. Conclude the module.	_____

1. Introduce the module

Explain that this module describes how to identify and refer patients who may have drug-resistant (RR/MDR)-TB among all the patients who attend their health facility. Explain that sputum will be collected from the patient presumed to have RR/MDR-TB and the patient will be evaluated.

Review the list of objectives

Show and explain **the icons and instructions** that will guide participants through the modules. Explain that they will read part of the module then do an exercise related to the section they have just read. After completing the exercise, they will continue reading.

- When participants reach an exercise, they need to stop reading and follow the instructions for the exercise.
- Some exercises are group discussions and some are individual work. You may want to say something like the following:

- When an exercise is individual work, this means that you should work through the exercise by yourself and write the answers in your copy of the module. However, if you have a question about what to do, please ask for help.
- When you have finished the exercise, you will see an instruction in a box that says, “Review your answers with a facilitator”. This type of discussion is called individual feedback. During this discussion, we will together review your work and compare it with the answer sheet. If you have made errors, I will help clarify any misunderstandings. I am here to help you learn.

Then explain what participants should do when they have finished an exercise and are ready for feedback. Depending on the arrangement of the room, they might raise their hand for a facilitator to come to them or they may go to the facilitator.

- At the end of each exercise, participants will continue reading until they reach the next exercise; this point is indicated by stop sign.

Ask participants to begin reading the module at [page B-5](#) and continue reading until they reach the first exercise. They should follow the instructions in the box and turn to the exercise.

While participants are reading

Participants will read silently [pages B-5–B-15](#); this may be difficult for some who are not accustomed to extended reading. Watch to see if any participant is struggling. If a participant is visibly struggling, go to that individual and ask quietly if the participant has a question or needs help. Try to address any problems. Leaving a participant to struggle is likely to result in frustration and loss of motivation. You may need to explain a form.

2. Exercise A: Identify presumptive cases of drug-resistant (RR/MDR)-TB, Case 1 – group demonstration

Lead the group through Case 1, [page B-48](#), so that you are sure that participants understand how to figure out whether a patient should be presumed to have DR-TB or not. Ask participants (or explain as needed) where to look to find the necessary information. Refer to section 1 ([pages B-7–B-15](#)).

Then ask participants to do Cases 2–5 on their own.

3. Exercise A: Identify presumptive cases of drug-resistant (RR/MDR)-TB – written exercise with individual feedback

Watch as participants begin working on this individual exercise. Be sure that they are not confused about what to do. Some participants need encouragement to begin writing in the module.

When a participant has finished the exercise, go to him or her, or ask the participant to come to you. If individual feedback is new to participants, most will probably wait to see whether and how individual feedback happens. Some may decide that they would rather not have individual

feedback and will not approach you unless you prompt them. Ensure that every participant gets feedback on this exercise.

It is important to ensure that each participant's experience with individual feedback is positive, especially for this and the next few exercises. Look at each participant's work carefully. Ask if the participant has questions, and listen attentively. Answer carefully. Participants will assess whether you are really interested in helping and whether feedback is likely to be embarrassing or punitive. It is essential that you build each participant's confidence in the fact that interactions with a facilitator will be helpful and pleasant, not punitive. When interactions are positive, and participants feel that facilitators are interested in their work, they are more motivated to work well.

When a participant approaches you for feedback, sit down with the participant and look at his or her work. Compare the participant's answers to those on the answer sheet. If the participant has made errors, do not simply correct them. Instead, first ask the participant to explain his or her answers. If the participant has questions, answer them. Try to find out the reason for any misunderstanding and offer clarification. The purpose of the interaction is to give feedback on what the participant did correctly and to correct any misunderstanding. At the end of the interaction, you should feel that the participant will be able to do the exercise correctly.

Check each participant's work for Exercise A. If a participant has made errors, refer the participant back to the pages in the module (pages B-7–B-15) that explain what the participant missed, and ask him or her to reread that section. Then ask the participant for a revised answer.

At the end of the feedback session, ask the participant to name the main groups of patients who should be presumed to have DR-TB and should be screened by a rapid test followed by culture and drug-susceptibility testing (DST). These groups include those who:

- have been treated for TB previously;
- have active TB that developed after exposure to a person known to have RR/MDR-TB;
- are TB patients who remain sputum smear positive after 2–3 months of treatment.

All people living with HIV who are diagnosed with active TB should undergo presumptive testing for DR-TB, especially if they live in areas where the prevalence of multidrug resistance is moderate or high. Unrecognized DR-TB is associated with high mortality in people living with HIV. Therefore, it is important to know the HIV status of anyone presumed to have TB and TB patients, and to investigate all HIV-positive patients who have symptoms of TB for drug resistance using culture and DST.

There may be additional determinants of resistance to anti-TB medicines in your country.

If there are additional important determinants of resistance to anti-TB medicines in your country, ask for the group's attention and conduct a brief discussion on these. Write them on the flipchart.

Module B: Detect cases of DR-TB

Answers to Exercise A**Case 1**

- A case of presumptive RR/MDR-TB? *Yes.*
- If yes, why? *Previously treated for TB, returning for treatment after loss to follow up*
- Tests to request: Smear [] Xpert MTB/RIF [x] Culture [x] Drug susceptibility [x]
HIV test [x]

(Depending on country policy, in case of availability of Xpert MTB/RIF, a baseline sputum examination may not be required. Further, culture and DST may be done subsequently or in parallel with Xpert MTB/RIF testing.)

Case 2

- A case of presumptive RR/MDR-TB? *Yes.*
- If yes, why? *Relapse or failure after multiple courses of treatment, perhaps of poor quality*
- Tests to request: Smear [] Xpert MTB/RIF [x] Culture [x] Drug susceptibility [x]
HIV test [x] *(The test should be redone to obtain current results.)*

Case 3

- A case of presumptive RR/MDR-TB? *No, the patient is presumed to have drug-susceptible TB.*
- If yes, why?
- Tests to request: Smear [x] Xpert MTB/RIF [] Culture [] Drug susceptibility []
HIV test [] *(His HIV test is recent enough.)*

(Some countries may have the policy of testing new cases directly with Xpert MTB/RIF rather than sputum smear.)

Case 4

- A case of presumptive RR/MDR-TB? *Yes.*
- If yes, why? *Patient still smear positive after 3 months of retreatment regimen (likely treatment failure)*
- Tests to request: Smear [] Xpert MTB/Rif [x] Culture [x] Drug susceptibility [x]
HIV test [x]

Case 5

- A case of presumptive RR/MDR-TB? *No, but because of high mortality associated with HIV and RR/MDR-TB coinfection, all TB/HIV-coinfected cases should be screened for drug resistance.)*
- If yes, why? *Person living with HIV who has active TB*
- Tests to request: Smear [] Xpert MTB/RIF [x] Culture [x] Drug susceptibility [x]
HIV test []

4. Exercise B: Filling out a Request for examination of biological specimen for TB – written exercise with individual feedback

Be sure that participants use the *Request for examination of biological specimen for TB* provided after the case to write their answers.

When a participant comes to you for individual feedback, check the answers against the answer sheet and offer clarification as needed.

Congratulate the participant on the work.

Then ask the participant to comment on how he or she will identify patients presumed to have DR-TB and collect sputum at the DR-TB management centre.

Ask these questions:

- Who is responsible for identifying patients whose treatment regimens are failing or in danger of failing ?
- Does the participant's facility follow this schedule for collecting two sputum samples?
- What problems are encountered while detecting cases? How can they be overcome?

Then ask the participant to go back to [page B-22](#) and begin reading again. Tell the participant that sections 4 and 5 describe how to decide on a treatment regimen for a patient presumed to have DR-TB while the health worker awaits DST results – an important concept. When participants reach [page B-30](#), they should turn to Exercise C.

Note: If you think that participants may have difficulty interpreting Figure 4 Diagnosing drug-resistant tuberculosis (DR-TB) at a DR-TB management centre (page B-24), take a few minutes to go over the figure with the group. It should be clear to them which side of the flow diagram corresponds to the situation in their DR-TB management centre, but they should be aware that other situations may exist elsewhere.

Module B: Detect cases of DR-TB

Answers to Exercise B

Request for examination of biological specimen for TB

Treatment unit: Balanot DR-TB Management Centre Date of request: 14 Aug 2013

Patient name: Sophia Zakaria

Age (years): 18 Date of birth: 8 June 1995 Sex: Male Female

Patient address: 12A Second Avenue, Balanot
 Telephone: _____

Reason for examination:

Diagnosis. If diagnosis, presumptive RR-TB/MDR-TB? Yes No

OR Follow up. If follow up, month of treatment: _____ and TB registration number _____

HIV infection? Yes No Unknown

Previously treated for TB? Yes No Unknown

Specimen type: Sputum Other
 (specify): _____

Test(s) requested: Microscopy Xpert MTB/RIF
Culture Drug susceptibility Line-probe assay

Requested by (name and signature): _____

Microscopy results (to be completed in the laboratory)

Date sample collected (filled by requestor)	Specimen type	Laboratory serial number(s)	Visual appearance (blood-stained, mucopurulent or saliva)	Result (tick one)				
				Negative (0 AFB/100 HPF)	1-9/100 HPF (scanty; report no. of AFB)	+	++	+++

Examined by (name and signature): _____

Date of result: _____

Xpert MTB/RIF test result (to be completed by the laboratory)

Date sample collected: _____

M. tuberculosis: Detected Not detected Invalid / No result / Error

Rifampicin resistance: Detected Not detected Indeterminate result

Examined by (name and signature): _____

Date of result: _____

Culture results (to be completed by the laboratory)

Date sample collected	Specimen type	Laboratory serial number(s)	Result (tick one)					NTM ^m	Contaminated
			Negative (0 colonies)	1-9 (<10 colonies)	+ (10-100 colonies)	++ (>100 colonies)	+++ (Innumerable/confluent growth)		

Examined by (name and signature): _____

Date of result: _____

Drug-susceptibility test (DST) and line-probe assay (LPA) results (to be completed by the laboratory)

Date sample collected (filled by requestor)	Method ^a	Laboratory serial number(s)	Results ^b (mark for each drug)														
			H	R	E	S	Am	Km	Cm	FQ:	Other:	Other:	Other:	Other:			

^aSpecify: solid media DST; liquid media DST; direct LPA; indirect LPA

^bResults codes: R = Resistant S = Susceptible C = Contaminated - = Not done

Examined by (name and signature): _____

Date of result: _____

^c Non-tuberculous mycobacteria

5. Exercise C: Assess the likelihood of DR-TB and recommend a treatment regimen – written exercise

Individual work on written exercise

Participants will work individually on this exercise.

Individual feedback

Discuss each case with each participant. Compare the participant's work with the answer sheet (on the next page). If the participant has made errors, try to determine why and correct any misunderstandings.

Then ask the participant to read until the next stop sign on [page B-35](#) and do Exercise D on [page B-55](#).

Module B: Detect cases of DR-TB

Answers to Exercise C

Case 1: Dalia Chalco

1. What do the laboratory results tell you about Ms Chalco?
She has bacteriologically confirmed pulmonary TB.
2. Should you screen her for DR-TB? Why or why not?
Yes, because she has been exposed to a documented case of DR-TB and has developed active TB.
3. What laboratory tests will you order next for Ms Chalco?
Xpert MTB/RIF, culture and DST. You should also recommend that she be tested for HIV.
4. What is Ms Chalco's likelihood of having DR-TB?
High.
5. What regimen would you recommend for her treatment while awaiting the DST results?
A second-line drugs regimen based on her husband's resistance pattern.

Case 2: Ming Tai

1. Do her culture results confirm or exclude TB?
The results confirm TB.
2. Why did the physician send sputum for culture and DST?
Because the physician knows that Ming Tai is living with HIV and he diagnosed TB, he presumed that she would have a high risk of mortality if drug resistance is not diagnosed early. Therefore, she should be screened by rapid tests, and culture and DST.
3. Does the patient require a change of regimen at this time?
No. As she is a new case (and even though she is HIV positive) she can continue on the new-patient regimen. However, if she deteriorates clinically, she may need an empirical second-line drugs regimen.
4. What is the next step that should be taken and why?
Ming Tai has resistance to H and R; she has MDR-TB and needs a second-line drugs regimen. Her case should also be presented to the review panel.

6. Exercise D: Detecting DR-TB cases at your DR-TB management centre – group discussion

When participants have finished answering the questions on page B-55, begin the discussion. Discuss each of the questions in turn and involve all the participants. Participants working in the same DR-TB management centre should agree on their answers.

Ask participants to focus not only on how procedures are done now, but also on how they should be done. Emphasize that the training is being conducted for the purpose of improving the skills and knowledge of health staff, and improving how DR-TB is managed at DR-TB management centres.

If participants raise questions about how procedures should or will be implemented, obtain clarification from the course director, the responsible officer at the DR-TB management centre or the national TB programme.

7. Explain what happens at the end of each module and the purpose of self-assessment questions

At the conclusion of the discussion, explain that at the end of each module there are:

- a summary of important points;
- self-assessment questions; and
- answers to the self-assessment questions.

The summary provides a review of the module.

The self-assessment provides an opportunity for participants to review the important tasks taught in the module.

You may want to say something like the following:

- Self-assessment questions are a way to review the material and help you assess for yourself what you have learnt and what you have missed or forgotten. They are not a test in the usual sense because you do not receive a grade. Instead, you check your own answers against the answers given. After each answer you will be referred to the section of the module where the information was taught.
- If you answer all of the self-assessment questions correctly, you can feel satisfied and proud that you have learnt the important points that the module taught. If you miss a question, this tells you what you need to study again. Look back at the specified section of the module and reread it.
- When you answer the self-assessment questions, work carefully. Do not look ahead at the answers because this will make the review less effective. Also, if you look ahead at the answers, you will not know what you have learnt and what you need to study further.

8. Self-assessment questions (self-checked)

Watch to make sure that participants are reading and writing answers to the self-assessment questions. They are allowed to refer to the module to determine an answer. If a participant is just reading or copying the answers (without attempting to answer the questions first), speak quietly to the participant and encourage him or her to try answering the questions before referring to the module, using the module only as needed to help learn the important tasks taught.

9. Conclude the module

Ask the group how they did on the self-assessment. If there are any questions about the answers, or other questions about the module, discuss them.

Emphasize that this module has described how to detect patients with DR-TB by using a list of risk groups for patients likely to have drug-resistant strains of TB; people in these risk groups should be screened by a rapid test like Xpert MTB/RIF and subsequently confirmed for multidrug resistance by culture and DST (depending on country policy). Everyone should know the risk groups and know what to do when they presume a patient may have DR-TB.

Although a case found to have rifampicin-resistant TB (RR-TB) can be started on second-line drugs, in order to confirm MDR-TB, a culture and DST are needed, and the results of these tests may take a number of weeks to be returned. Patients presumed to have MDR-TB must be made aware of this process; health workers must be attentive to the results as they come in.

Reinforce any additional important points from this module that you want to. Thank the participants for taking part in the individual feedback.

Congratulate them on completing this module.

Facilitator's guidelines for Module C: Treat DR-TB patients

PROCEDURES	ACTIVITY
1. Distribute <i>Module C: Treat DR-TB patients</i> . Introduce the module.	_____
2. Have participants read pages C-4–C-18. When everyone is ready, they should turn to Exercise A on page C-81 and work individually. A group discussion should follow when all have finished the exercise.	Group discussion
3. Have participants read pages C-22–C-34. When participants are ready, they should turn to Exercise B on page C-83 and do the cases on their own.	Provide individual feedback.
4. Have participants read pages C-33–C-38 and then do Exercise C on page C-94 on their own; when they have completed the exercise, it should be followed by a group discussion.	Group discussion
5. Have participants read pages C-40–C-57 and then do Exercise D on page C-100 individually.	Provide individual feedback
6. Have participants read section 8, pages C-57–C-60 and then do Exercise E on page C-103 individually.	Provide individual feedback.
7. Have participants read the summary of important points and do the self-assessment on pages C-68–C-71. They should check their answers against those provided.	Participants check their own answers.
8. Conclude the module.	_____

1. Introduce the module

Explain that this module describes how to treat DR-TB patients (refer to the list of objectives). Review the objectives. Explain that some tasks involved in treating DR-TB patients are mentioned in this module but more detailed information is given in other modules, such as *Module D: Inform and educate patients about DR-TB*.

2. Exercise A: Selecting a treatment regimen for DR-TB – individual work followed by group discussion

Ask participants to read until they reach the first stop sign (page C-18). They should read the instructions for Exercise A on page C-81 and do the exercise on designing a treatment regimen, beginning with the first case. You should emphasize that while participants may not be directly responsible for deciding on a patient's regimen, it is important to know how regimens are developed and what the results of DST mean. Tell patients to refer as needed to section 1.3 and the figures on pages C-15–C-17 that outline the medicines and principles used when developing regimens for second-line drugs.

After participants have written answers to the exercise, discuss the questions below for each case. This discussion should help participants feel comfortable with the underlying rules for selecting treatment regimens based on DST results.

- a. Does the patient have at least four medicines in the proposed regimen, including an injectable agent?
- b. Are there any first-line medicines that can be used for this patient?
- c. What do you need to know from the DST results? How does the information available at this time limit your decision?
- d. Does the patient have any other conditions or characteristics that necessitate modification of the regimen?

Module C: Treat DR-TB patients

Answers to Exercise A**Selecting a treatment regimen with second-line drugs**

A basic regimen for both patients is shown below. Z should be included in the intensive phase, but is not considered one of the four effective second-line drugs that are required to treat a DR-TB case. The regimen may vary slightly depending on the specific medicines that are used in your country.

CASE	PROPOSED REGIMEN IN THE INTENSIVE PHASE OF THERAPY*	DAILY DOSE	UNITS/DAY
Case 1	Z-Km-Lfx-Pto-Cs	Z: 1500 mg Km: 750 mg Lfx: 750 mg Pto: 500 mg Cs: 500 mg	Z: 3 tablets (500 mg each) Km: 750 mg/day Lfx: 3 tablets (250 mg each) Pto: 2 tablets (250 mg each) Cs: 2 capsules (250 mg each)
Case 2	Z-Km-Lfx-Pto-Cs	Z: 2000 mg Km: 1000 mg Lfx: 1000 mg Pto: 750 mg Cs: 750 mg	Z: 4 tablets (500 mg each) Km: 1000 mg/day Lfx: 4 tablets (250 mg each) Pto: 3 tablets (250 mg each) Cs: 3 capsules (250 mg each)

* In the continuation phase, the injectable will be discontinued. Z can be stopped or could also be continued in the continuation phase.

3. Exercise B: Preparing a Second-line TB treatment card – written exercise

Individual work on written exercise

Participants will do this exercise individually. Participants may use the blank *Second-line TB treatment card* in the module or you may provide copies to them.

Individual feedback

When you check each participant's *Second-line TB treatment cards*, be sure that all appropriate spaces have been filled in (name, address, health unit, sex, age, disease site, type of patient, results of sputum-smear microscopy, culture result, DST results, treatment regimen, daily number of tablets). If any spaces were left blank, look at whether the participant missed them on both the *Second-line TB treatment cards*. If so, point out the omission. Ask the participant to fill out the cards completely and then return to discuss them with you.

Discuss each case with the participant, and compare the participant's *Second-line TB treatment cards* with the answer sheets. If the participant has made errors, do not simply correct them. Find out the reason for the misunderstanding and offer clarification.

Give the participant a copy of the answer sheets.

Ask the participant to read from page C-31 until the next stop sign on page C-42.

TB Control Programme

Second-line Registration Number: _____
 Date of second-line treatment registration: _____
 Treatment Centre: Blue Acorn DR-TB management centre
 Patient Name: Thebua Huru
 Address & Telephone: 1406 Betancourt Street, Xiadi Village
 District: Longo
 Sex (circle one): M F
 Age: 37 yrs DOB: 25/5/1975
 Initial weight (kg): 43 Kg
 Height (cm): 159 cm
 Site (circle one or both): Pulmonary Extrapulmonary
 If extrapulmonary, specify site: _____

Second-line TB treatment card

Registration Group	Choose one only
New	
Relapse	
Treatment after loss to follow up	
Treatment after failure of first treatment with first-line drugs	
Treatment after failure of retreatment regimen with first-line drugs	X
Other (previously treated without known outcome; previously treated extrapulmonary)	
Transfer in (from another second-line treatment programme)	

Transfer in (from another second-line treatment programme) if yes name of center: _____ Yes
 No

HIV INFORMATION

HIV Testing done (circle one): Y / N / Unknown
 Date of Test: 04-11-10 Result: Neg
 Started on ART (circle one): Y / N Date: _____
 Started on CPT (circle one): Y / N Date: _____

Meetings of review panel (medical commission, selection committee, consilium)

Date	Meetings of the review panel: dates and decisions
18-12-2011	Decision <u>Approve Treatment - Z-Km-Lfx-Pto-Cs</u>

Form 01

Previous Tuberculosis Treatment Episodes			
District TB Register No. (i.e. BMU register number)	Start Date (if unknown put year)	Regimen (write regimen in drug abbreviations)	Outcome
345-10	Oct 2010	2HRZE/4HR	Failed
345-10	May 2011	2HRZE5/ 1HRZE/5 HRE	Failed

Previous use of second-line drugs for more than one month?

Y / N / Unknown

If Yes, indicate in Table above

Drug Abbreviations			
First-line drugs	second-line drugs		
H=isoniazid	Am=amikacin	Eto=ethionamide	Bdq=bedaquiline
R=rifampicin	Km=Kanamycin	Pto=Prothionamide	Cif=clarithromycin
R=ethambutol	cm=capreomycin	Cs=cycloserine	Cfz=clofazimine
S=streptomycin	lfx=levofloxacin	Pas-p-amino-salicylic acid	Dim=delamanid
Z=Pyrazinamide	Mfx=Moxifloxacin	Amx/cV=amoxicillin/ clavulanate	Ipim=imipenem
	Gfx=gatifloxacin		Lzd=linezolid
			Mpm=meropenem

Transfer In (from another second-line treatment programme)

If yes name of centre: _____

TB Control Programme

Second-line Registration Number: _____
 Date of second-line treatment registration: _____
 Treatment Centre: Blue Acorn DR-TB management centre
 Patient Name: Hilda Theab
 Address & Telephone: House C12-Block 33, Sharma City
 District: Sharma
 Sex (circle one): M F
 Age: DOB: 42 yrs
 Initial weight (kg): 55 Kg
 Height (cm): 177 cm
 Site (circle one or both): Pulmonary Extrapulmonary
 If extrapulmonary, specify site: _____

Second-line TB treatment card

Registration Group	Choose one only
New	
Relapse	
Treatment after loss to follow up	
Treatment after failure of first treatment with first-line drugs	
Treatment after failure of retreatment regimen with first-line drugs	X
Other (previously treated without known outcome; previously treated extrapulmonary)	
Transfer in (from another second-line treatment programme)	

Transfer in (from another second-line treatment programme) if yes name of center: _____
 Yes
 No

HIV INFORMATION

HIV Testing done (circle one): Y / N / Unknown
 Date of Test: _____ Result: _____
 Started on ART (circle one): Y / N Date: _____
 Started on CPT (circle one): Y / N Date: _____

Meetings of review panel (medical commission, selection committee, consilium)

Date	Decision	Meetings of the review panel: dates and decisions
27 April 2013		Treatment approved - Z-Km-Mfx-Pto-PAS

Form 01

Previous Tuberculosis Treatment Episodes			
District TB Register No. (i.e. BMU register number)	Start Date (if unknown put year)	Regimen (write regimen in drug abbreviations)	Outcome
	May 2011	2HRZE/4HR	Lost to follow-up
553-12	Oct 2012	2HRZE/4HR	Failed

Previous use of second-line drugs for more than one month?

Y / N / Unknown

If Yes, indicate in Table above

Drug Abbreviations			
First-line drugs	second-line drugs		
H=isoniazid	Am=amikacin	Eto=ethionamide	Bdq=bedaquiline
R=rifampicin	Km=Kanamycin	Pto=Prothionamide	Cl=clarithromycin
R=ethambutol	cm=capreomycin	Cs=cycloserine	Ctz=clofazimine
S=streptomycin	fx=levofloxacin	"Pas=p-aminosalicylic acid"	Dlm=delamanid
Z=Pyrazinamide	Mfx=Moxifloxacin		Ip=imipenem
	Ox=ofloxacin	Amx/cOv=amoxicillin/ clavulanate	Lzd=levonolid
	Gk=gatifloxacin		Mpn=meropenem

Transfer In (from another second-line treatment programme)

if yes name of centre: _____

Second-line TB treatment card

Month of Treatment	Sputum Microscopy		Month of Treatment	Date*	Culture		Drug Susceptibility Testing (DST) Results
	Date*	Sample Number			Result	Date*	
Prior**			Prior**				
0	12-March-2013	79/81	0	12-March-2013	79		03-13
1			1				R
2			2				R (Xp)
3			3				R
4			4				R
5			5				
6			6				
7			7				
8			8				
9			9				
10			10				
11			11				
12			12				
13			13				
14			14				
15			15				
16			16				
17			17				
18			18				
19			19				
20			20				
21			21				
22			22				
23			23				
24			24				

Notation method for DST:
 R=resistant
 S=susceptible
 C=contaminated
 Unk=Unknown

§ indicate near result if initial resistance was detected on line-probe assay or Xpert MTB/RIF

Notes:
 *All dates in both tables are the dates the sputum was collected from the patient
 **The date the sputum was collected that led to the patient being registered with MDT-TB (if performed)

Notation Method for Recording Smears:

No AFB	0
1-9 AFB per 100 HPF	Scanty (and report number of AFB)
10-99 AFB per 100 HPF	+
1-10 AFB per HPF	++
>10 AFB per HPF	+++

Notation Method for Recording Cultures (solid media):

No growth reported	0
Fewer than 10 colonies	Report number of colonies (1-9)
10-100 colonies	+
More than 100 colonies	++
Innumerable or confluent growth	+++
Non-tuberculous mycobacteria	NTM
Contaminated	contaminated

Notation method for Xpert MTB/RIF results

T	= MTB detected, rifampicin resistance not detected
RR	= MTB detected, rifampicin resistance detected
TI	= MTB detected, rifampicin resistance indeterminate
N	= MTB not detected
I	= invalid / no result / error

4. Exercise C: Recording directly observed treatment on the *Second-line drugs treatment card* – written exercise and group discussion

When participants have reached page C-40, they should turn to page C-94 and complete Exercise C individually.

Individual work on written exercise

Participants can read the dates of treatment and mark the *Second-line TB treatment card* by themselves. An alternative method, which may be easier and quicker for some participants, is for the facilitator to read aloud the dates of treatment. The participants listen and mark the card, day by day (each participant marks his or her own copy). This strategy can be used only if all participants are working at more or less the same speed.

Individual feedback

Compare each participant's work with the answer sheet (on the next pages). If the participant has made errors, try to determine why and correct any misunderstandings.

Give the participant a copy of the answer sheet.

Ask the participant to prepare for the group discussion (questions on page C-99).

Answers to Exercise C

Patient's name Mr A J Annan

Second-line TB treatment card

Month of Treatment	Sputum Microscopy		Month of Treatment	Culture		Drug Susceptibility Testing (DST) Results
	Date *	Sample Number		Result	Date *	
Prior**			Prior**			
0	10-May-2013	218-13	0	10-May-2013	218-13	++
1	21-June-2013	325-13	1	21-June-2013	325-13	+
2	19-July-2013	501-13	2	19-July-2013	501-13	-
3	19-Aug-2013	657-13	3			
4	19-Sep-2013	830-13	4			
5			5			
6			6			
7			7			
8			8			
9			9			
10			10			
11			11			
12			12			
13			13			
14			14			
15			15			
16			16			
17			17			
18			18			
19			19			
20			20			
21			21			
22			22			
23			23			
24			24			

Month of Treatment	Date *	Sample Number	Result
Prior**			
0	10-May-2013	218-13	++
1	21-June-2013	325-13	-
2	19-July-2013	501-13	-
3	19-Aug-2013	657-13	-
4	19-Sep-2013	830-13	-
5			
6			
7			
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11			
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16			
17			
18			
19			
20			
21			
22			
23			
24			

Month of Treatment	Date *	Sample Number	Result
Prior**			
0	10-May-2013	218-13	++
1	21-June-2013	325-13	-
2	19-July-2013	501-13	-
3	19-Aug-2013	657-13	-
4	19-Sep-2013	830-13	-
5			
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18			
19			
20			
21			
22			
23			
24			

Month of Treatment	Date *	Sample Number	Result
Prior**			
0	10-May-2013	218-13	++
1	21-June-2013	325-13	-
2	19-July-2013	501-13	-
3	19-Aug-2013	657-13	-
4	19-Sep-2013	830-13	-
5			
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18			
19			
20			
21			
22			
23			
24			

Month of Treatment	Date *	Sample Number	Result
Prior**			
0	10-May-2013	218-13	++
1	21-June-2013	325-13	-
2	19-July-2013	501-13	-
3	19-Aug-2013	657-13	-
4	19-Sep-2013	830-13	-
5			
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7			
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Month of Treatment	Date *	Sample Number	Result
Prior**			
0	10-May-2013	218-13	++
1	21-June-2013	325-13	-
2	19-July-2013	501-13	-
3	19-Aug-2013	657-13	-
4	19-Sep-2013	830-13	-
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Month of Treatment	Date *	Sample Number	Result
Prior**			
0	10-May-2013	218-13	++
1	21-June-2013	325-13	-
2	19-July-2013	501-13	-
3	19-Aug-2013	657-13	-
4	19-Sep-2013	830-13	-
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Month of Treatment	Date *	Sample Number	Result
Prior**			
0	10-May-2013	218-13	++
1	21-June-2013	325-13	-
2	19-July-2013	501-13	-
3	19-Aug-2013	657-13	-
4	19-Sep-2013	830-13	-
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Month of Treatment	Date *	Sample Number	Result
Prior**			
0	10-May-2013	218-13	++
1	21-June-2013	325-13	-
2	19-July-2013	501-13	-
3	19-Aug-2013	657-13	-
4	19-Sep-2013	830-13	-
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Month of Treatment	Date *	Sample Number	Result
Prior**			
0	10-May-2013	218-13	++
1	21-June-2013	325-13	-
2	19-July-2013	501-13	-
3	19-Aug-2013	657-13	-
4	19-Sep-2013	830-13	-
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Month of Treatment	Date *	Sample Number	Result
Prior**			
0	10-May-2013	218-13	++
1	21-June-2013	325-13	-
2	19-July-2013	501-13	-
3	19-Aug-2013	657-13	-
4	19-Sep-2013	830-13	-
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Month of Treatment	Date *	Sample Number	Result
Prior**			
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1	21-June-2013	325-13	-
2	19-July-2013	501-13	-
3	19-Aug-2013	657-13	-
4	19-Sep-2013	830-13	-
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Month of Treatment	Date *	Sample Number	Result
Prior**			
0	10-May-2013	218-13	++
1	21-June-2013	325-13	-
2	19-July-2013	501-13	-
3	19-Aug-2013	657-13	-
4	19-Sep-2013	830-13	-
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Group discussion

Give participants time to think about and write answers to the questions before the discussion begins.

1. Ask different participants to suggest some possibilities for what could happen to the tablets. The point is that there are many possibilities, and a health worker cannot know exactly what happened. Some possibilities that could be discussed are listed below.
 - *Marti Gra could take them all correctly.*
 - *She could lose one or discard one or more that she does not like and take the others.*
 - *She could give them all away or sell them or throw them away.*
 - *They could be ruined.*
 - *She could forget to take them.*
 - *She could save them for later.*
 - *She could take them another day, and then get a double dose on that day.*
2. *The health worker should have given Ms Gra a glass of water along with the tablets and watched her swallow them. Alternatively, the health worker could have asked Ms Gra to get some water. When Ms Gra returned with the water, the health worker could have given her the tablets and watched her swallow them.*
3. Discuss the consequences that may occur when anti-TB medicines are not taken regularly. Possible consequences include the following:
 - *The patient will not be cured. The disease will be prolonged and will be more difficult or impossible to treat in the future.*
 - *The patient's strain of Mycobacterium tuberculosis may develop further resistance to some of the medicines.*

After you have checked the answers for this exercise, ask participants to return to [page C-42](#) and continue reading until [page C-58](#).

5. Exercise D: Follow-up laboratory examinations – written exercise with individual feedback

When the participants are ready (or almost ready) to do Exercise D, ask for the group's attention. Review the schedule for follow-up laboratory examinations on [page C-50](#) to be sure that participants understand how to read it. They should refer to this page in the module while they do the exercise.

To give individual feedback, discuss each case and compare each participant's answers with those on the answer sheet. If there is an error, ask how the participant arrived at a particular answer so that you can understand whether the participant does not understand how to read the schedule or has a different problem. Look at the schedule together and help the participant figure out the correct answer.

Give the participant a copy of the answer sheet.

Ask the participant to read from [page C-57](#) to [page C-64](#) in preparation for Exercise E.

Module C: Treat DR-TB patients

Answers to Exercise D**Case 1: Data Berth**

Data Berth is a diabetic with poor control of his blood sugar, whose treatment was decentralized after the third month of treatment; he then experienced worsening cough and weight loss. Below are the results of sputum smears and cultures from his *Second-line TB treatment card*.

RESULTS OF SPUTUM EXAMINATION				WEIGHT (KG)
MONTH	DATE	SMEAR	CULTURE	
0	10/5/11	+++	+	52
1	12/6/11	0	0	52
2	11/7/11	0	0	50
3	8/8/11	0	0	49
4	6/9/11	++		47
5	10/10/11	++		45

What is the appropriate action for the health worker to take for this patient now? Explain what the health worker should do and why.

Data Berth should be sent back to the DR-TB management centre so that his treatment regimen can be reconsidered and his diabetes can be managed appropriately in consultation with a specialist. Request a DST from the last positive culture. He is at risk of treatment failure.

Case 2: Little Seen

The following table shows the results of Little Seen's sputum-smear and culture examinations.

RESULTS OF SPUTUM EXAMINATION				WEIGHT (KG)
MONTH	DATE	SMEAR	CULTURE	
0	28/11/11	++	+	52
1	2/12/11	0	0	51.2
2	2/1/12	0	0	51.5
3	3/2/12	0		52.5
4	2/3/12	0		54
5				56
6				

What is the appropriate action for the health worker to take for this patient now? Explain what the health worker should do now.

The patient has had four negative smears and two negative cultures. Consider decentralizing the patient's treatment at a local health facility if not done so far. Encourage the patient and congratulate him for the good progress.

Case 3: Jasmine Tee

The following table shows the results of Jasmine Tee's sputum-smear and culture examinations.

RESULTS OF SPUTUM EXAMINATION				WEIGHT (KG)
MONTH	DATE	SMEAR	CULTURE	
0	28/9/11	+	+	44
1	10/10/11	0	+	45
2	11/11/11	0	0	46
3	12/12/11	0		47
4	1/1/12	0		47
5	2/2/12	0		47

What is the appropriate action for the health worker to take for this patient? Explain what the health worker should do now.

The patient has had five negative smears and one negative culture.

Consider shifting to the continuation phase after 3 more months of treatment if smear results and culture results continue to be negative. The patient is eligible for the continuation phase after 8 months of treatment with the injectable agent.

Case 4: Rowdy Mann

Below are the results of Rowdy Mann's smear and culture examinations. He is asymptomatic, and the chest X-ray is improving significantly. His weight is increasing.

RESULTS OF SPUTUM EXAMINATION				WEIGHT (KG)
MONTH	DATE	SMEAR	CULTURE	
0	5/5/12	+++	+	59
1	10/6/12	0	0	59
2	11/7/12	0	0	60.5
3	12/8/12	0	0	61
4	9/9/12	0	0	61
5	11/10/12	0	0	59
6	11/11/12	0	0	59.5
7	15/12/12	0	n/d	61

RESULTS OF SPUTUM EXAMINATION				WEIGHT (KG)
MONTH	DATE	SMEAR	CULTURE	
8	13/1/13	0	0	62
9	9/2/13	0	n/d	62.5
10	8/3/13	+1	pending	63

What is the appropriate action for the health worker to take for this patient now? Explain what the health worker should do and why.

Ask for another smear and another culture, and wait for the culture results from month 10 before taking action. The smear from month 10 may be an error, and the culture could have been recorded as positive if the sample was mislabelled. If the second smear is positive, send the patient to the DR-TB management centre for an evaluation.

6. Exercise E: Decide DR-TB treatment outcomes – written exercise

Compare each participant's answers with the answer sheet. If there are any errors, ask the participant about the reason for the choice of outcome. Refer to the definitions of the DR-TB treatment outcomes in the module (page C-61).

Give the participant a copy of the answer sheet.

Ask the participant to resume reading on page C-61 and work to the end of the module.

Module C: Treat DR-TB patients

Answers to Exercise E

Case 1: Data Berth

Data Berth had culture conversion after the first month of treatment, but then reconverted to smear positive and culture positive during the fourth month. He was sent back for directly observed treatment (DOT) at the DR-TB management centre. His last dose was given on 20 May 2009. Mr Berth has continued treatment for 12 months; the results of his smear and culture examinations are given below.

MONTH	DATE	RESULTS OF SPUTUM EXAMINATION		WEIGHT (KG)
		SMEAR	CULTURE	
0	10/5/11	+++	+	52
1	12/6/11	0	0	52
2	11/7/11	0	0	50
3	8/8/11	0	0	49
4	6/9/11	++	+	47
5	10/10/11	++	+	47.5
6	9/11/11	+	+	48
7	6/12/11	0	0	48
8	7/1/12	+	+	47.5
9	8/2/12	+	+	47
10	9/3/12	++	+	45
11	10/4/12	+++	+	44
12	11/5/12	++	+	42

Record the date and treatment outcome on the excerpt of his *Second-line TB treatment card*.

Treatment outcome

OUTCOME	MARK ONE	DATE
Cured		
Treatment completed		
Died		
Failed	X	5-20-12
Lost to follow up		

Case 2: Little Seen

Little Seen completed 21 months of treatment on 10 August 2010. He is compliant with treatment and asymptomatic, but he had poor compliance with sputum testing. His smear and culture results are presented below.

RESULTS OF SPUTUM EXAMINATION				WEIGHT (KG)
MONTH	DATE	SMEAR	CULTURE	
0	28/11/11	++	+	52
1	2/12/11	0	0	51.2
2	2/1/12	0	0	51.5
3	3/2/12	0	0	52.5
4	2/3/12	0	0	54
5	3/4/12	0	0	56
6	4/5/12	0	0	56.5
7		-		56.8
8		-		57.1
9	4/8/12	0	0	57.5
10		-	-	58
11	2/10/12	0	0	58
12		-		57
13		-	-	57.4
14		-	-	57
15		-	-	58
16	8/3/13	0	0	56.5
17		-	-	58
18		-	-	57
19		-	-	58
20		-	-	59.4
21	6/8/13	0		58

Record the date and treatment outcome on the excerpt of his *Second-line TB treatment card*.

Treatment outcome

OUTCOME	MARK ONE	DATE
Cured	x	10/8/13
Treatment completed		
Died		
Failed		
Lost to follow up		

Case 3: Jasmine Tee

Jasmine Tee completed 19 months of second-line drugs treatment on 7 April 2013. Below are the results of her culture examinations.

RESULTS OF SPUTUM EXAMINATION				WEIGHT (KG)
MONTH	DATE	SMEAR	CULTURE	
0	28/9/11	+	+	44
1	10/10/11	0	+	45
2	11/11/11	0	0	46
3	12/12/11	0	0	47
4	1/1/12	0	0	47
5	2/2/12	0	0	47
6	3/3/12	0	0	48
7	4/4/12	0	0	49
8	5/5/12	0	n/d	47
9	6/6/12	0	0	47
10	7/7/12	0	n/d	47
11	8/8/12	0	0	47
12	9/9/12	0	n/d	47
13	10/10/12	0	0	47
14	11/11/12	0	n/d	47
15	12/12/12	0	0	47
16	1/1/13	0	n/d	47
17	2/2/13	0	0	47
18	3/3/13	0	n/d	47
19	4/4/13	0	0	49
20	6/5/13	0	0	50

Record the date and treatment outcome on the excerpt of her *Second-line TB treatment card*.

Treatment outcome

OUTCOME	MARK ONE	DATE
Cured	x	8/5/13
Treatment completed		
Died		
Failed		
Lost to follow up		

Case 4: Rowdy Mann

It has been 2 months since Mr Mann last came for treatment on 2 June 2013. When the health worker went to his home a month ago, the apartment was vacant. The contact person told the health worker that the family had moved away. The contact person said that Rowdy Mann had told her that he had finished treatment with second-line drugs. The contact person did not know where the family had moved.

MONTH	DATE	RESULTS OF SPUTUM EXAMINATION		WEIGHT (KG)
		SMEAR	CULTURE	
0	5/5/12	+++	+	59
1	10/6/12	0	0	59
2	11/7/12	0	0	60.5
3	12/8/12	0	0	61
4	9/9/12	0	0	61
5	11/10/12	0	0	59
6	11/11/12	0	0	59.5
7	15/12/12	0	n/d	61
8	13/1/13	0	0	62
9	9/2/13	0	n/d	62.5
10	8/3/13	+	0	63
11	8/4/13	+		63
12	8/5/13	+		63
13				
14				
15				

Record the date and treatment outcome on the excerpt of his *Second-line TB treatment card*.

Treatment outcome

OUTCOME	MARK ONE	DATE
Cured		
Treatment completed		
Died		
Failed		
Lost to follow up	X	3-8-13

7. Self-assessment questions (self-checked)

8. Conclude the module

Ask the group how they did on the self-assessment. If there are any questions about the answers, or other questions about the module, discuss them.

Make any important points that you want to reinforce to these participants.

Congratulate participants on completing this important module. It is the longest module, and requires considerable persistence and concentration.

Facilitator's guidelines for Module D: Inform and educate patients about DR-TB

PROCEDURES	ACTIVITY
1. Distribute <i>Module D: Inform and educate patients about DR-TB</i> . Introduce the module.	_____
2. Have participants read pages D-4–D-11 and then do written Exercise A on page D-59.	Provide individual feedback.
3. Have participants read pages D-11–D-33. When they reach the stop sign on page D-33, they should turn to page D-61 and read the instructions for Exercise B. Lead the role-play for Exercise B (page D-61).	Lead role-play.
4. Have participants read pages D-34–D-42 and then do the written Exercise C on page D-63.	Provide individual feedback.
5. Have participants continue reading from page D-42 until page D-44 and have them do Exercise D on page D-64.	Provide individual feedback.
6. Have participants read pages D-44–D-49 until the end of the module and have them do Exercise E on page D-65.	Group discussion
7. Have participants read the summary of important points on pages D-50–D-51, and then answer the self-assessment questions. Participants check their own answers against those provided in the module.	Participants check their own answers.
8. Conclude the module.	_____

1. Introduce the module

Explain that communication with patients is a critical part of treating DR-TB. If the health worker communicates with the patient clearly, thoroughly and supportively, the patient will be more likely to continue and complete treatment.

Explain that this module focuses on using good communication skills to inform patients about DR-TB and its treatment. Patients' needs for information about DR-TB vary, because they come from different situations and have different levels of knowledge about the disease. The health worker must ask questions and LISTEN carefully in order to tailor information so that it meets each patient's specific needs.

Also explain that as this module is about communicating, one exercise will be a role-play. The role-play allows participants to practise informing patients about DR-TB using good communication skills.

2. Exercise A: Checking questions – written exercise followed by individual feedback

Participants should read pages D-4–D-11 and then turn to page D-59 and complete Exercise A. This brief exercise is an opportunity to make sure that participants understand what checking questions are.

You may want to explain that health workers should ask checking questions at the end of a meeting with a patient, or after giving important information. These questions should be asked to check the patient's understanding of what has been said. The questions should relate to the information the health worker has just given.

Compare each participant's answers with the answer sheet. Remind participants, as needed, to try to ask open-ended questions that begin with who, what, when, where, how or why, rather than questions that can be answered simply with a "Yes" or "No."

Tell participants that they should use checking questions at the end of the role-plays later in the module. After the exercise, ask participants to read pages D-11–D-33 of the module – that is, until the next stop sign.

Module D: Inform and educate patients about DR-TB

Possible answers to Exercise A

1. The participant should have listed two checking questions similar to those below.
 - *How many days a week will you have to take your anti-TB medicines?*
 - *Who will observe you taking the medicines? How often will this person observe you?*
 - *Where will you begin treatment for DR-TB? Why do you have to start there?*
 - *How many medicines will you be taking? How long will treatment last?*

2. The participant should have listed two checking questions similar to those below.
 - *How is DR-TB transmitted? What about ordinary TB?*
 - *What are some of the ways you can prevent TB and DR-TB from spreading?*
 - *What are some of the regular activities that do not spread TB and DR-TB?*
 - *When will you be non-infectious (that is, not able to spread TB to others)?*
 - *What is the best way to stop being infectious?*

3. Exercise B: Initial patient information about DR-TB – role-play**Conducting the role-play**

Divide the participants into groups of three. The groups will do their role-plays simultaneously in separate parts of the room.

Introduce the role-play by explaining that each participant will have a turn to practise informing a DR-TB patient about the disease and its treatment using the guide in the module. One person will play the patient, and one will play the health worker. The third person will observe, referring to the “Guide to providing information to DR-TB patients being enrolled for treatment” (pages D-29–D-33), and comment on the role-play using the checklist on page D-62. When the first role-play is finished, the members will switch roles and repeat the role-play.

Ask participants to read the instructions for Exercise B on page D-61 if they have not already done so.

Ask the groups to give themselves some space so that they do not distract one another. The groups may go to opposite corners of the room, or one group may go into the hall. However, the groups should not go far because the facilitator needs to observe them.

Ask participants whether they have any questions about what to do, and clarify instructions if needed. It is important that participants understand what they are supposed to do. The participant playing the health worker should feel free to refer to the “Instructions for the health worker” at any time in order to keep on track.

Ask the groups to begin, and watch as they get started. Help them as necessary. Move around so that you can observe each group and ensure that they stay on track. Give instruction and feedback as necessary.

After each role-play, when the observer is pointing out any steps that have been omitted, check that the comments are brief and related to topics in the “Guide to providing information to DR-TB patients being enrolled for treatment”. Then encourage the group to quickly switch roles and perform the role-play again. It is important to keep the role-plays moving so that participants do not become bored or frustrated.

Discussion

After all groups have finished their third role-play, gather everyone together for a discussion to reinforce the important points about providing information to a patient who is starting treatment with second-line drugs. Ask participants to close their modules and tell you from memory the important topics that need to be covered during this discussion with patients. Ask each participant to list one step as you write it down on a flipchart or chalkboard. You should be able to *quickly* construct a reasonable list with input from the group.

Ask participants to read pages D-34–D-42. Section 5 describes how to provide information about the medicines a DR-TB patient will take. After they have read section 5, they should turn to page D-63 and do Exercise C. Section 6 describes how to continue providing information about DR-TB after the patient has begun treatment.

4. Exercise C: Problem-solving – written exercise followed by individual feedback

This exercise allows participants to imagine what they would say or do in common situations that might interfere with DR-TB treatment. Remind participants that they should give information but only information that is relevant to the situation and the patient’s immediate concerns. Sometimes the first thing a health worker should do is ask a question to find out more about what the patient is thinking or feeling.

Remind participants of the need to find out the cause of a problem before identifying a solution. Note that many of the answers on the answer sheet begin, “Find out why...” or “Ask why...”. Sometimes the solution to a problem is simply to provide information to the patient or the family, but at other times the situation may be more complicated.

Participants’ answers may differ from those on the answer sheet. Refer to the answer sheet to suggest ideas that participants do not mention.

After you provide individual feedback, give each participant a copy of the answer sheet. Point out that these are possible answers; other answers may be suitable as well.

Then participants then should continue reading from page D-40 until section 7.

Module D: Inform patients about DR-TB

Possible answers to Exercise C**WHAT WOULD YOU SAY OR DO IF...? BRIEFLY WRITE YOUR IDEAS BELOW**

A patient wants to take the medicine unsupervised at home.

Discuss with the patient why he or she wants to take the medicines at home. Explain that DOT has been shown to have much better success in curing patients. The process of DOT benefits the patient; treatment for DR-TB is a long and expensive process, so everyone wants to ensure that the treatment is a success. It is also important for a health worker to see the patient to make sure there are no problems with adverse effects.

A patient has missed 1 day of treatment but reported the following day.

Give the specific day's dose only. Try to find out why the patient missed the previous day's dose. Attempt to solve any problems that might be keeping the patient from treatment. Remind the patient of the need to take all of the doses of medicine for the prescribed length of time. Missing a dose extends the total duration of treatment by an equal number of days. Explain to the patient that taking medicines irregularly may make it harder to treat the disease and may make it less likely that the patient will be cured.

A patient says her husband, who has a cough, does not have time to be tested for TB.

Find out whether the patient has told her husband about her illness. Explain that it is important for her husband to be tested. If he has DR-TB, he could spread the disease to others and reinfect her. Offer to visit her husband and explain the need for testing.

A patient has DR-TB and HIV. He is resisting admission to hospital to start treatment because he says he does not feel that bad and must work.

It is a good sign that he is not feeling too bad right now. But it is important that he starts treatment right away to prevent both diseases from getting worse. The earlier he begins treatment, the better his chances of being cured of DR-TB.

Ask the patient why he does not want to be admitted. Depending on his reasons, give information about why it is important and discuss ways to make it easier to relocate. Explain that he is contagious and should not be exposing others to DR-TB at home or at work.

When he is in hospital, the staff can watch him closely to make sure the medicines do not cause him any problems, as adverse effects can be worse in patients who have both TB and HIV. In hospital, staff will be able to give him appropriate care and support. However, if there are plausible reasons for not getting admitted, the treating physician and health workers' team should explore alternate measures of providing DOT for DR-TB, preferably at a health facility to start with and later moving to community-based observed treatment.

<p>A patient who has completed 5 months of second-line drugs treatment seems angrier each day.</p>	<p>Comment that the patient seems angry and ask sympathetically why.</p> <p>If relevant, discuss the possibility of making his treatment more convenient.</p> <p>If he is angry with a particular health worker, try to find another staff member who can observe his treatment or find another solution.</p> <p>If he is angry about something at home, discuss the situation with empathy and try to help find a solution.</p>
<p>A patient has been on treatment for 3 weeks and has nausea and vomiting. She says she cannot stand it any more and wants to stop treatment.</p>	<p>Praise the patient for continuing treatment through the nausea so far. Try to help relieve the nausea (if this has not already been done) by giving her metoclopramide or dividing the doses of the oral second-line medicines and giving them in the morning and afternoon (at least one should be directly observed by a health worker).</p> <p>Reassure her that most patients find that the nausea diminishes. Encourage her to continue treatment. Remind her that stopping treatment could lead to worsening of her illness and make it less likely that she will be cured if she decides to return to treatment later.</p>

5. Exercise D: Preparing for decentralization of treatment – written exercise followed by individual feedback

This exercise asks participants to first identify the indicators for decentralization of treatment to a local health facility. After that, participants have to think about how to discuss decentralization with the patient. Remind participants that they should give information but only information that is relevant to the situation. Sometimes, the first thing a health worker should do is ask a question to find out more about what the patient is thinking or feeling.

Participants' answers may differ from those on the answer sheet. Refer to the answer sheet to suggest ideas that participants do not mention.

After you provide individual feedback, give each participant a copy of the answer sheet. Point out that these are possible answers; other answers may be suitable as well.

Then participants then should continue reading from "9. Palliative and end-of-life care for patients in whom all the possibilities of treatment have failed" on page D-47 until the end of the module.

Possible answers to Exercise D

Possible indicators for decentralization of treatment are as follows:

- *Country policy of ambulatory treatment;*
- *The patient is able to attend a local health facility for daily treatment or has access to a trained provider of DOT;*
- *The patient is tolerating the medicines in the regimen; and*

- *The patient has been culture negative for at least 1 month and smear-negative for the past 2 months.*

Relevant information that could be included in the participants' answers:

At every visit: demonstrate a caring, respectful attitude. Praise and encourage the patient. Speak clearly and simply. Encourage the patient to ask questions.

ASK THE PATIENT QUESTIONS SUCH AS

THEN GIVE RELEVANT MESSAGES

How do you feel now that your tests show that you are unlikely to spread the disease?

Say something like the following:

Congratulations!

This is the first step along the road to being cured. When your treatment is decentralized, it means that your treatment has been going well and you are no longer contagious. You will continue to receive treatment for DR-TB but the treatment can be given closer to your home, so you can live at home.

Do you have any ideas about how decentralization may help you and your treatment?

Say something like the following:

The local facility will be easier for you to get to than the DR-TB management centre because it is nearer to your home. The staff has been trained to continue your treatment. Although you will be treated at the local facility, you will still have monthly sputum examinations. You will come back to this DR-TB management centre for monthly visits with the physician. If you have any problems or need specialized services, the local facility can send you back to this DR-TB management centre at any time so that we can help care for you.

What about the local facility's responsibilities to you?

Say something like the following:

Staff at the local facility will be responsible for providing treatment to you as well as maintaining good records of your treatment. If you have any side-effects from the medicines you are taking, or if you do not feel well, you must tell the staff at the local facility so that they can help you quickly and send you for specialized care if necessary.

You must keep your copy of the *Second-line TB treatment card* and take it with you every day that you have treatment; the staff at the local facility will record when you receive treatment. Bring your card to the DR-TB management centre when you return for your monthly visit with the physician at the DR-TB management centre.

You must continue to collect sputum for monthly examinations. You must come back to this DR-TB management centre every month to have a visit with the physician; the physician will give you a physical examination and check that your treatment is going well.

Do you have any questions? Is there anything that is not clear?

Say something like the following:

Do you have any questions or concerns about this process?

Will you have difficulty in getting to the local health facility every day for treatment?

Do you know anyone who might be able to give you treatment on the days that you cannot make it to the facility?

Say something like the following:

When your treatment is decentralized to (*provide the name of the facility*) someone must observe you taking your medicines 6 days a week as has happened here.

If necessary, we can train someone in your community to provide treatment, and you can help us choose whom to train. We will provide the medicines and supervise this person.

Discuss with the patient:

- *where the patient lives and works, whom the patient sees each day, whether transport is available, and whether the family is supportive of treatment;*
- *possible community-based treatment supporters who would be convenient and acceptable, taking into account the supporter's proximity to the patient, relationship to the patient (if any) and whether the supporter is already supervising treatment for other patients;*
- *where and when the patient could meet regularly with a treatment supporter.*

Review: ask checking questions to ensure that the patient remembers important messages and knows what to do next. Reinforce earlier messages or give more information as needed.

6. Exercise E: group discussion: at the end of treatment

This exercise allows participants to think about the situation for patients at the end of treatment. First, participants are asked to answer questions about the procedures in their own programmes regarding end of treatment. Afterwards, there will be a group discussion on the same topic.

Allow approximately 15 minutes for the initial questions and then start the group discussion.

Possible answers to Exercise E

For the individual questions, all kinds of answers can be expected. This will become clear during the group discussion.

The group discussion can be guided by using the questions that participants answered individually:

- Do you have a conversation with patients at the end of their treatment?
- If there is no conversation with patients, do you think it is important that this should be introduced?
- What do you tell patients when their treatment outcome is either cured or treatment completed?
- What do you tell patients whose treatment has failed?

Make sure all participants get an opportunity to participate in the group discussion. After all questions are discussed, summarize and conclude the discussion.

Regardless of the situations in the various programmes, whenever an interaction between the patient and health worker takes place at the end of treatment, it should include some of the information below.

Demonstrate a caring, respectful attitude. Praise and encourage the patient. Speak clearly and simply. Encourage the patient to ask questions.

ASK THE PATIENT QUESTIONS OR DISCUSS THE FOLLOWING

THEN GIVE RELEVANT MESSAGES

How do you feel about finishing treatment?

Congratulate patients who have been cured or have completed treatment.

Say something like the following:

Congratulations! You have just finished a long and difficult treatment. I am very proud of the commitment and dedication you have shown over the past 20 months. You no longer have to take any medications.

However, it is possible that the disease will come back. If you develop any symptoms of TB, such as a cough, back or chest pain, blood in the phlegm, or unexplained fever or weight loss, let us know immediately so that we can conduct the proper tests to see what the problem is.

If anyone close to you, such as family members or other people in your community, has symptoms, bring that person in; let the staff know that you had DR-TB so that they are aware that the person was in close contact with you when you had the disease.

How will you keep your body healthy?

Say something like the following:

Leading a healthy lifestyle is always good but it is especially important after you have had a long treatment, such as the treatment with second-line drugs. Exercising, eating healthy food, not smoking or drinking, and getting enough rest will help you recover, combat other illnesses and reduce the risk of TB coming back. People with weak defences get sick from TB more often than healthy people. Now that you are cured, try to maintain a healthy lifestyle.

Give support to patients whose outcome is treatment failure.

Say something like the following:

You have been through so many difficulties with your medicines. Unfortunately, they do not seem to be helping you. It is time that you take a break from your treatment. We will continue to provide medical care and support.

Because you may still spread the disease, it would be best if you avoid crowded, enclosed areas, and avoid sleeping in the same room with other people, if possible. Cover your mouth and nose when you cough or sneeze. Open the windows in your room to allow air to flow out. If possible, use an electric fan to direct the air outside.

7. Self-assessment questions (self-checked)

8. Conclude the module

Ask the group how they did on the self-assessment. If there are any questions about the answers, or any other questions about the module, discuss them.

Make any important points that you want to reinforce to the participants.

Mention specific improvements that you have noticed in their communication skills.

Congratulate participants on completing this module.

Facilitator's guidelines for Module E: A patient-centred approach to ensuring continuation of DR-TB treatment

PROCEDURES	ACTIVITY
1. Distribute Module E: A patient-centred approach to ensuring continuation of DR-TB treatment. Introduce the module.	_____
2. Have participants read pages E-4–E-17. When all participants have read the instructions and questions for Exercise A on page E-33, lead a group discussion.	Group discussion
3. Have participants read pages E-18–E-23 of the module and then do Exercise B on page E-35 individually. Once all participants have finished the exercise, lead a short group discussion.	Provide individual feedback; group discussion
4. Have participants read the summary of important points and work until the end of the module. Participants check their own answers to the self-assessment questions against those provided in the module.	Participants check their own answers.
5. Conclude the module.	_____

1. Introduce the module

Explain that as treatment with second-line drugs is a long process, it is critical to maintain contact with patients throughout their treatment and ensure that they will continue for the full duration. Every effort should be made to prevent absences from treatment and interruptions, and to maintain contact with patients even when circumstances are not favourable for this. To ensure that patients continue treatment, health workers need to provide good support, identify potential problems and help to solve those that may interfere with treatment, organize transfers and referrals, and follow up with patients who miss doses.

Ask participants to suggest some reasons why patients may miss an appointment or interrupt treatment. Mention some common situations that will be discussed in this module. See the list on page E-5 of the module.

Ask participants to read through until page E-17 and then follow the directions for Exercise A, which starts on page E-33.

2. Exercise A: Supporting DR-TB patients and ensuring continued treatment – written exercise and group discussion

When everyone has finished answering the questions, begin the discussion.

This should be a substantive discussion that allows participants to reflect on the situation at their own DR-TB management centre, and to hear about other DR-TB management centres if participants from other centres are present. The discussion should help increase participants' understanding of what is done well at their own and others' centres, and what can be improved.

Move through the questions, asking participants to describe the situation at their DR-TB management centre. It is not necessary to ask every participant to answer every question, as this will make the discussion too long. One method for keeping the discussion moving is to ask two participants for their answers to a question, and then ask the group if anyone has a different answer or has an important point to add.

When the discussion has been concluded, ask participants to continue reading from page E-18 until the next stop sign on page E-23.

3. Exercise B: Decentralizing a DR-TB patient's treatment – written exercise

In the first part of this exercise, participants complete a *Tuberculosis referral/transfer form* for a DR-TB patient named Paula Musunga. Once they have completed the form, participants should continue working individually to answer the questions on page E-37. As they complete the exercise, they should approach you for individual feedback. Compare their work with the form provided in the answer sheets. Give them a copy of the answer sheet.

For use by facility to which patient has been referred or transferred:

Name of facility _____

District _____ Date _____

Name of patient _____ District TB no. _____

The above patient reported at this facility on _____ (date)

Signature _____ Position _____

Send this part back to referring/transferring facility as soon as patient has reported.

Answers for Exercise B (continued)

1. What documents should the staff at the Blue Acorn DR-TB management centre send with the patient to the Silbe Health Centre?
 - *Two copies of the patient's Second-line TB treatment card (one for the local facility and one for the patient)*
 - *Tuberculosis referral/transfer form*
 - *Medicine delivery form (this will be described in Module F).*

2. What information should be discussed with Mrs Musunga prior to decentralization of treatment?
 - *What decentralization is and the eligibility criteria for decentralization*
 - *The benefits of receiving DR-TB services at the local health facility*
 - *The responsibilities of the patient and the local health facility*
 - *That the patient must keep his or her copy of the Second-line TB treatment card and have it available every day when receiving treatment*
 - *The schedule for monthly monitoring visits with the physician at the DR-TB management centre and the required follow-up sputum examinations that will also be done at the DR-TB management centre*
 - *The possibility that the local health facility will identify, train and supervise a community-based treatment supporter for her, if necessary.*

3. How will the staff know whether Mrs Musunga arrived at the Silbe Health Centre to continue her treatment?

They should receive the bottom part of the tuberculosis referral/transfer form from the Silbe Health Centre, completed and signed. If it does not arrive, they should call the Silbe Health Centre and ask about the patient.

4. What should be the next contact that staff at the Blue Acorn DR-TB management centre has with Mrs Musunga?

She should return to the DR-TB management centre for her monthly monitoring visit with the physician.

4. Self-assessment questions (self-checked)

Participants should read the summary of important points (pages E-24–E-25) and complete the self-assessment on pages E-26–E-27.

5. Conclude the module

Ask the group how they did on the self-assessment. If there are any questions about the answers, or any other questions about the module, discuss them.

Make any important points that you want to reinforce to the participants.

Congratulate participants on completing this module.

Facilitator’s guidelines for Module F: Manage medicines and supplies for DR-TB

PROCEDURES	ACTIVITY
1. Prepare for the exercise by obtaining and assembling the required medicines and other supplies for Exercise B.	_____
2. Distribute <i>Module F: Manage medicines and supplies for DR-TB</i> . Introduce the module.	_____
3. Have participants read pages F-4–F-17. Then have them do Exercise A on page F-35 individually.	Provide individual feedback.
4. Have participants read pages F-17–F-23 and then have them do Exercise B on page F-38, which is a practical exercise. Lead a short discussion after the exercise is concluded.	Group discussion
5. Have participants continue reading from page F-23 until the end of the module, then have them do Exercise C on page F-39.	Pair exercise, followed by group discussion
6. Participants do the self-assessment questions. Have them check their answers against those provided.	Participants check their own answers.
7. Conclude the module.	_____

1. Prepare for the exercise

To prepare for the exercise, make sure that there are enough loose medicines and other materials for the participants to use. Each group should receive a container holding:

- a. enough of the anti-TB medicines Z, E, Lfx, Pto/Eto and Cs for 6 daily doses;
Note: If these medicines are not available, use the second-line anti-TB medicines that are available, but remember that you will need to create a revised version of the second-line drugs regimen section of Jose Delgado’s treatment card (page F-38 of the module) and make copies of it for participants. In case no drugs can be made available, the last resort would be to use candies of different colours or even balls made of coloured paper (naming one for each drug and marking the strength of the tablet as per the available formulations);
- b. other materials necessary for preparing the medicine packets as done in your country.

Begin to collect the medicines at least 2 days ahead of time

If you will need to request medicines to use in Exercise B, begin the task several days beforehand so that there is time to obtain all the necessary supplies.

2. Introduce the module

Explain that this module describes how to manage medicines and other supplies used in caring for patients with DR-TB. Review the objectives on page F-5.

Ask participants to read the module through to page F-17 and then follow the directions for Exercise A, which starts on page F-35.

3. Exercise A: Determine the quantities of second-line drugs to order – written exercise

Start by explaining that in this exercise, participants will determine how many medicines to order for an upcoming quarter.

Ask participants to work individually.

Compare each participant's work with the answer sheet on the next page. If a participant has made errors, try to determine why and correct any misunderstanding.

Give the participants a copy of the answer sheet. Tell them to read pages F-17–F-23 and then turn to Exercise B.

Module F: Manage medicines and supplies for DR-TB

Answers for Exercise A

PATIENTS	DRUGS									
	Z 500 MG	E 400 MG	KM 1 G	CM 1 G	LFX 250 MG	MTX 400 MG	PTO 250 MG	CS 250 MG	PAS 4 G	B6 50 MG
1– CC	3		1		4		3	3		
2– JB	4	3			4		3	3		2
3– JV	4	3	1		4		3		2	
4										
5										
6										
Daily total (sum)	11	6	2		12		9	6	2	2
Monthly (daily x 26)	286	156	52		312		234	156	52	52
Quarterly (monthly x 3)	858	468	156		936		702	468	156	156

TB medicine requisition form

Requesting facility: Blue Acom DR-TB management centre Date requested: 1 June 2013

For the month/s of: July-August-Sept 2013

#	Description (Please specify preparation of drug)	Unit	Quarterly use	Buffer (1 month)	Quantity needed (c=a+b)	On-hand (d)	Quantity requested (e=c-d)	Units per container	# Containers sent
			(a)	(b)	(c=a+b)	(d)	(e=c-d)		
1	Z 500mg	tablet	858	286	1144	107	1037		
2	E 500mg	tablet	468	156	624	110	514		
3	Kn 1g	vial	156	52	208	46	162		
4	Lfx 250mg	tablet	936	312	1248	132	1116		
5	Mfx 400mg	tablet				113			
6	Pto 250mg	tablet	702	234	936	126	810		
7	Cs 250mg	capsule	468	156	624	102	522		
8	PAS 4 g	sachet	156	52	205	55	153		
9	B6 50 mg	tablet	156	52	205	0	205		
10									
11									
12									

Requested by: _____

(Signature and printed name/date)

4. Exercise B: Prepare daily medicine packets – practical exercise

When participants are ready for Exercise B, have them turn to page F-38 and read the instructions. Distribute the containers you prepared earlier.

When each participant has successfully prepared a daily dose for a DR-TB patient, you can lead a short discussion about preparing medicine for patients.

Ask the participants to think about the following questions.

- How is preparing medicine for DR-TB different from the system used for patients receiving regimens with only first-line medicines?
- How are injectable agents stored at their facility?
- Have they used second-line medicines for TB before?
- What kind of refrigeration is available at their facility?

When the discussion has concluded, participants should continue reading from page F-23 until the end of the module.

5. Exercise C: Pair exercise and group discussion

The first part of the exercise is done in pairs. Participants discuss the storage room(s) in their health facilities and assess if they are appropriate for TB drug storage. They are asked to apply the requirements that they have just learnt.

After the pair exercise, you facilitate a group discussion on the findings and recommendations for improvement of storage rooms.

Points to be taken into consideration are as follows:

- Temperature
- Exposure to sunlight
- Storage off the floors and walls
- Space
- Organization

Participants may come up with other issues. This is to be encouraged!!

6. Summarize important points and self-assessment questions (self-checked)

7. Conclude the module

Ask the group how they did on the self-assessment. If there are any questions about the answers, or other questions about the module, discuss them.

Make any important points that you want to reinforce to these participants.

Conclude the training course

Conclude your time with the participants by summarizing important points and answering questions from them about applying what they have learnt.

You may want to do the following:

- Congratulate participants on completing the training course.
- Briefly summarize the important information in modules A–F.
- Ask them if they have any questions about what was taught in the modules and provide (or let another participant provide) explanations as needed.

Guidelines for all modules

Facilitator's techniques

A. Techniques for motivating participants

Encourage interaction

1. During the first day, you will speak individually with each participant several times – for example, during individual feedback. If you are friendly and helpful during these first interactions, it is likely that participants:
 - will overcome their shyness;
 - will realize that you want to talk with them; and
 - will interact with you more openly and productively throughout the course.
2. Look carefully at each participant's work. Check to see whether participants are having any problems, even if they do not ask for help. If you show interest and give each participant undivided attention at the appropriate time, participants will feel more compelled to do the work. Also, if participants know that someone is interested in what they are doing, they are more likely to ask for help when they need it.
3. Be available to talk with participants as needed.

Keep participants involved in discussions

4. Frequently ask questions to check participants' understanding and keep them actively thinking and taking part. Questions that begin with "What," "Why," or "How" require more than just a few words to answer. Avoid asking questions that can be answered with a simple "Yes" or "No".

After asking a question, PAUSE. Give participants time to think and volunteer a response. A common mistake is to ask a question and then answer it yourself. If no one answers your question, rephrasing it may help break the tension of silence. But do not do this repeatedly. Some silence is productive.

5. Acknowledge all participants' responses with a comment, a "Thank you" or a definite nod. This will make participants feel valued and encourage participation. If you think a participant has missed the point, ask for clarification, or ask whether another participant has a suggestion. If a comment is ridiculed or ignored, the participant may withdraw from the discussion entirely or not speak voluntarily again.

6. Answer participants' questions willingly, and encourage them to ask questions when these arise rather than to hold the questions until a later time.
7. Do not feel compelled to answer every question yourself. Depending on the situation, you may turn the question back to the participant or invite other participants to respond. You may need to discuss the question with the course director or another facilitator before answering. Be prepared to say, "I don't know but I'll try to find out."
8. Use participants' names when you call on them to speak and when you give them credit or thanks. Use the speaker's name when you refer to a previous comment.
9. Maintain eye contact with participants so that everyone feels included. Be careful not to always look at the same participants. Looking at a participant for a few seconds will often prompt a reply, even from a shy participant.

Keep the session focused and lively

10. Keep your presentations lively.

Present information conversationally rather than reading it.

Speak clearly. Vary the pitch of your voice and speed of your words.

Use examples from your own experience, and ask participants for examples from their experience.

11. Write key ideas on a flipchart or blackboard as they are offered. This is a good way to acknowledge responses. The speaker will know that the idea has been heard and will appreciate having it recorded for the group to see.

When writing ideas, use the participant's own words if possible. If you must be brief, paraphrase the idea and check it with the participant before writing it. You want to be sure that the participant feels you understood and recorded the idea accurately.

Do not turn your back to the group for long periods as you write.

12. At the beginning of a discussion, write the main question on the flipchart or board. This will help participants to stay on the subject. When needed, walk to the flipchart and point to the question.

Paraphrase and summarize frequently to keep participants focused. Ask participants to clarify their statements if necessary. Also, encourage other participants to ask speakers to repeat or clarify statements, if necessary.

If the discussion wanders off the subject, restate the original question to the group to help them focus on the main issue. If you feel someone resists getting back on track, pause to get the group's attention, tell them that they have gone astray, and then restate the original question.

Do not allow several participants to talk at once. When this occurs, stop the talkers and assign an order for speaking. For example, say, "Let's hear Dr Concepcion's comment first,

then Dr Salvador's, then Dr Tan's". People usually will not interrupt if they know they will have a turn to talk.

Thank participants whose comments are brief and to the point.

13. Try to encourage quieter participants to speak. Ask to hear from a participant in the group who has not spoken before, or walk toward someone to encourage that person.

Manage any problems

14. Some participants may talk too much. Here are some suggestions for handling an overly talkative participant.

- Do not call on the talkative person first after asking a question.
- After a participant has gone on for some time, say, "You have had an opportunity to express your views. Let's hear what some of the others have to say." Then rephrase the question and invite other participants to respond, or call on someone else immediately by saying, "Dr Tan, you had your hand up a few minutes ago."
- When the talkative participant pauses, break in quickly and ask to hear from another member of the group, or ask a question of the group, such as, "What do the rest of you think about this point?"
- Record the participant's main idea on the flipchart or board. As the participant continues to talk about the idea, point to it on the flipchart or board and say, "Thank you, we have noted your idea." Then ask the group for another idea.
- Do not ask the talkative participant any questions. If the same participant answers all the questions directed to the group, ask for an answer from another individual specifically or from a specific subgroup. For example, ask, "Does anyone on this side of the table have an idea?"

15. Try to identify participants who may be having difficulty in understanding or speaking the language in which the course is offered. Speak slowly and distinctly so that you can be more easily understood, and encourage the participant's efforts to communicate.

Discuss with the course director any language problems that may seriously impair the ability of a participant to understand the written material or the discussions. It may be possible to arrange help for the participant.

Discuss disruptive participants with your co-facilitator, if you are working with one, or with the course director. The course director may be able to discuss matters privately with the disruptive individual.

Provide positive reinforcement to participants

16. As a facilitator, you will have your own style of interacting with participants. However, a few techniques for reinforcing participants' efforts include the following:

- Avoid the use of facial expressions or comments that could cause participants to feel embarrassed.
- Sit or bend down to be at the same level as participants when talking to them.
- Answer questions thoughtfully rather than hurriedly.
- Encourage participants to speak to you by allowing them time.

- Appear interested by saying something like, “That’s a good question” or “That’s a good suggestion.”
17. Give positive reinforcement to participants who:
- try hard;
 - ask for an explanation about a confusing point;
 - do a good job on an exercise;
 - participate in group discussions; or
 - help other participants without distracting them by talking at length about irrelevant matters.

B. Techniques for relating modules to participants’ jobs

1. Discuss how participants might use the procedures taught in the modules in their own health facilities. This will help participants to start thinking about how to apply what they are learning.
2. Give positive reinforcement to participants who discuss or ask questions about using the procedures in their own health facilities. Acknowledge and respond to their concerns.

C. Techniques for co-facilitators to work together

1. Spend some time with your co-facilitator before the course begins. Exchange information about prior teaching experiences and individual strengths, weaknesses and preferences. Agree on roles and responsibilities, and how you can work together as a team.
2. Assist each other in providing individual feedback and conducting group discussions. For example, one facilitator may lead a group discussion, and the other may record the important ideas on the flipchart or board. The second facilitator could also check the *Facilitator’s guide* and add any points that have been omitted.
3. Each day, review the teaching activities that will occur the next day (such as role-plays and discussions), and agree on who will lead the discussion, collect the supplies or attend to other tasks.
4. Work *together* on each module rather than taking turns at having sole responsibility for a module.

Guidelines for all modules

When participants are working

- Look available, interested and ready to help.
- Watch participants as they work, and offer individual help if you see a participant looking troubled, staring into space, not writing answers or not turning pages. These are clues that the participant may need help.
- Encourage participants to ask you questions whenever they need help.
- If important issues or questions arise when you are talking with an individual, make a note of them to discuss later with the entire group.
- If a question arises that you cannot answer adequately, obtain assistance as soon as possible from another facilitator or the course director.
- Review the points in this *Facilitator's guide* so that you will be prepared to discuss upcoming exercises with participants.

Guidelines for all modules

When providing individual feedback

- Before giving individual feedback, refer to the appropriate notes in this guide to remind yourself of the important points.
- Compare each participant's answers with those on the answer sheet.
- If the participant's answer to any exercise is incorrect or unreasonable, ask questions to determine why the error was made. There may be many reasons for an incorrect answer. For example, a participant may not understand the question, may not understand some of the terms used in the exercise, may be accustomed to different procedures, may have overlooked some information about a case or may not understand the process that is being taught.
- Once you have identified the reason or reasons for the incorrect answer, help the participant correct the problem. For example, you may need to only clarify the instructions. On the other hand, if the participant has difficulty in understanding the process itself, you might try using a specific case example to explain. After explaining, ask questions to be sure that the participant has understood.
- Give each participant a copy of the answer sheet, if one has been provided.
- Always provide positive reinforcement for good work, for example, by
 - commenting on how well the participant understands,
 - showing enthusiasm for the participant's ideas for applying a skill in their health facility,
 - mentioning that you enjoy discussing exercises with the participant,
 - commenting that the participant's hard work is appreciated.

Guidelines for all modules

When leading a group discussion

- Plan to conduct the group discussion at a time when you are sure that all participants will have completed the preceding work. Wait to announce this time until most participants are ready, so that others will not rush through the work.
- Before beginning the discussion, refer to the appropriate notes in this guide to remind yourself of the purpose of the discussion and the important points.
- Begin the discussion by telling the participants the purpose of the discussion.
- Often there is no single correct answer that needs to be agreed on in a discussion. Just be sure that the conclusions of the group are reasonable, and that all participants understand how the conclusions were reached.
- Try to get most of the group members involved in the discussion. Record key ideas on a flipchart as they are offered. Keep your participation to a minimum, but ask questions to keep the discussion active and on track.
- Always summarize, or ask a participant to summarize, what was discussed in the exercise. Give each participant a copy of the answer sheet, if copies have been provided.
- Provide positive reinforcement for good work, for example, by
 - praising participants for the list they have compiled,
 - commenting on their understanding of the exercise,
 - commenting on their creative or helpful suggestions for using their new skills on the job,
 - praising them for their ability to work together as a group.

Guidelines for all modules

When coordinating a role-play

- Before the role-play, refer to the appropriate notes in this guide to remind yourself of the purpose of the role-play, the background information and important points to make afterwards.
- At the beginning of the role-play –
 - review instructions for the role-play,
 - assign three participants to a group to do the role-play together,
 - give role-play participants any props needed, for example, medicines,
 - suggest that each group go to a separate corner or area to work,
- Observe each group quietly, and make notes of points to cover later with the entire group.
- Interrupt only if the players are having difficulty or have strayed from the purpose of the role-play.
- When all groups have finished their role-plays, conclude the exercise with a brief discussion. Discuss things done well and things that could be improved.
- Ask participants to describe what they have learnt from the role-plays.

Table 2 Types of training using the modules

#	TYPE OF TRAINING	DESCRIPTION	FOR WHOM	WHAT IS REQUIRED
1.	For individuals to learn in a self-study format	<ul style="list-style-type: none"> • Health-care workers can use the modules according to their needs. • They can work through them at their own pace. • Use the modules as a reference. 	<ul style="list-style-type: none"> • Participants who need to learn about managing a DR-TB management centre • As a reference material for those who have already been trained 	<ul style="list-style-type: none"> • Country modules for training on PMDT or WHO modules adapted to the country's policies and protocols • In certain instances, countries may need translated versions.
2.	As part of a 5-day facilitator-led training course OR targeted training of specific staff	<p>The self-study modules can be used as part of a training course that is led by a facilitator.</p> <ul style="list-style-type: none"> • Facilitators lead group discussions about the content, exercises and role-plays. This engaging training is valuable for answering questions and emphasizing important information. • Participants work through the modules. 	<ul style="list-style-type: none"> • Participants who need to learn about managing a DR-TB management centre • The modules can also be used separately for specific categories of staff, e.g. for community workers involved in referral, nurses/ counsellors involved in patient counselling, pharmacists managing drugs stocks. 	<ul style="list-style-type: none"> • Country modules for training on PMDT or WHO modules adapted to the country's policies and protocols • Facilitators who have <ul style="list-style-type: none"> – knowledge of the WHO training modules – experience in training adults • Assistance from WHO and technical partners to help plan and conduct the training • Identified funding source
3.	As part of a 7-day facilitator-led training-of-trainerscourse	<p>The self-study modules can be used as part of a training-of-trainers (ToT) course that is led by several facilitators.</p> <p>WHO has in earlier instances used the Centers for Disease Control and Prevention (CDC) Teachback Methodology Curriculum that focuses on providing participants with the skills necessary to teach the course. The interactive training blends the learning of course content with enhancing training skills.</p> <ul style="list-style-type: none"> • Facilitators teach a set of training skills to the participants. • The participants use the training skills to teach a portion of the course curriculum. <p>ToT is expected to work best when</p> <ul style="list-style-type: none"> • there is regional and country ownership • there are follow-up plans with an adequate budget • it guides the country human resource development plan, which in turn is part of a national strategic plan. 	<p>National and subnational trainers who would be training health-care staff delivering DR-TB services in their respective settings</p>	<ul style="list-style-type: none"> • It could be at the regional or country level. • For the regional level, generic modules to be used while for country trainings, country modules for training on PMDT or WHO modules adapted to the country's policies and protocols • ToT curriculum (e.g. CDC Teachback Methodology Curriculum) • Facilitators who have <ul style="list-style-type: none"> – experience in teaching the training modules to others – experience in training trainers • Assistance from WHO and CDC to help plan and conduct the training • Identified funding source

Sample schedule for the course

The following agenda provides approximate times for the different training activities. For each module, the time given allows for participants to read through the content, work through the exercises, and discuss the content and exercises. However, the schedule can be adapted based on country needs and the context in which the training is undertaken.

DAY	ACTIVITY	APPROXIMATE TIME
Day 1	Registration	0.5 hour
	Opening presentation and introductions (welcome, introductions and importance of this training)	1 hour
	Course overview (agenda, materials, ground rules, parking lot and housekeeping)	0.5 hour
	Module A: Introduction	0.5 hour
	Module B: Detect cases of DR-TB	3.5 hours
Day 2	Module C: Treat DR-TB patients	5.75 hours
Day 3	Module D: Inform and educate patients about DR-TB	5 hours
	Module E: A patient-centred approach to ensuring continuation of DR-TB treatment	1 hour
Day 4	Module E: A patient-centred approach to ensuring continuation of DR-TB treatment	2 hours
	Module F: Manage medicines and supplies for DR-TB	4 hours
Day 5	Module F: Manage medicines and supplies for DR-TB	1 hour
	Next steps	1.5 hours
	<i>This would be a discussion and could include subjects such as:</i> <ul style="list-style-type: none"> • <i>creating an action plan for what participants will do</i> • <i>discussing the action plans</i> • <i>discussing challenges and solutions for implementing an MDR-TB programme in your setting</i> • <i>creating a network for sharing implementation issues</i> 	(could be longer – especially if action plans are included)
	Closing session	1 hour (could be just 0.5 hour)

Management of drug-resistant tuberculosis

**Training for staff working at
DR-TB management centres**

Module A: Introduction



**World Health
Organization**

MODULE A

Introduction

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Introduction

This module provides a general discussion of multidrug-resistant tuberculosis and this training course. It also describes the methods and materials used, the learning objectives and the programmatic assumptions that underlie this course. A glossary and a list of abbreviations are included.

What is drug-resistant tuberculosis?

Tuberculosis (TB) and other forms of drug-resistant (DR)-TB, such as multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB), are all caused by the same organism, *Mycobacterium tuberculosis*. In general, TB is considered to be drug

resistant when the organism is not killed by anti-TB medicines during a laboratory test called drug-susceptibility testing (DST). This means that the laboratory reports show growth of bacilli in the culture medium despite the presence of the medicine. Newer and faster genotypic tests to find drug resistance are the Xpert MTB/RIF and line-probe assay (LPA), which identify genetic mutations in bacilli that make them resistant to anti-TB drugs.

The two most effective first-line anti-TB medicines are isoniazid and rifampicin. These are considered most important when determining resistance patterns in tubercle bacilli. The following are the different forms of DR-TB.

- In **monoresistant TB**, the strain of *M. tuberculosis* is resistant to one first-line anti-TB medicine only, out of the first-line anti-TB medicines – isoniazid (H), rifampicin (R), pyrazinamide (Z), ethambutol (E) and streptomycin (S).
- In **polyresistant TB**, the strain of *M. tuberculosis* is resistant to more than one first-line anti-TB medicine other than both isoniazid and rifampicin.
- In **multidrug-resistant TB (MDR-TB)**, the strain of *M. tuberculosis* is resistant to at least both isoniazid and rifampicin – and may or may not be resistant to other first-line anti-TB medicines.
- In **extensively drug-resistant TB (XDR-TB)** – a severe form of MDR-TB – the strain of *M. tuberculosis* is multidrug resistant and has also resistance to any of the fluoroquinolones (ofloxacin, levofloxacin, moxifloxacin or gatifloxacin) and to any one of the second-line injectable agents (kanamycin, amikacin or capreomycin).
- In **rifampicin resistance (RR-TB)**, the strain of *M. tuberculosis* is resistant to rifampicin detected using rapid diagnostic methods (phenotypic or genotypic), with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, in the form of monoresistance, multidrug resistance, polydrug resistance or extensive drug resistance.

These modules focus on managing RR-TB and MDR-TB (collectively referred to as RR/MDR-TB) because of the clinical significance and need for treatment with second-line drugs in both cases.

TB and DR-TB are both spread in the same manner – by aerosol. When a person with pulmonary TB coughs or sneezes, tubercle bacilli are spread into the air in tiny droplets. Other people who breathe in these droplets may become infected. Not all people who are infected with tubercle bacilli will develop TB disease.

The symptoms of TB and DR-TB are the same. The main symptom is a cough lasting for two weeks or more; additionally, the patient may have fever; chest or back pains, or both; haemoptysis and/or weight loss. Other symptoms include sweating, fatigue, malaise and shortness of breath.

^a While it has been the practice until now to limit the definitions of monoresistance and polydrug resistance to first-line drugs only, future drug regimens may make it important to classify patients by their strain resistance patterns to fluoroquinolones, second-line injectable agents as well as any other anti-TB drug for which reliable DST becomes available.

Managing DR-TB is more complex than managing drug-susceptible TB because of the following reasons:

- Confirming RR/MDR-TB requires a rapid molecular diagnostic test and/or quality-assured culture and DST, in addition to the sputum-smear microscopy.
- Treating RR/MDR-TB requires a larger number of costlier, more toxic second-line anti-TB medicines, which need to be taken at least 6 days a week usually for 20 months or longer, and treatment needs to be strictly supervised.
- Strategies to manage RR/MDR-TB require more resources (logistical, human and financial) than TB that is susceptible to first-line medicines.

The emergence of DR-TB is a human-induced phenomenon. The selection of DR bacilli is typically favoured by inadequate or poorly administered treatment, although DR-TB can also spread from person to person. Some of the many factors that can contribute to resistance include the following:

- poor selection of treatment regimens
- incomplete or irregular treatment
- poor quality or irregular supply of medicines, or both
- barriers to treatment (social, economic, transportation difficulties)
- poor monitoring of treatment and failure to directly observe treatment
- poorly organized or poorly funded TB control programmes
- poor infection control practices, especially in health-care facilities.

It is essential to manage DR-TB in the proper setting to increase the chances of cure, prevent the spread of infection and avoid the acquisition of additional resistance.

TB and DR-TB as public health problems

The World Health Organization (WHO) declared TB a global emergency in 1993 in recognition of the growing importance of TB as a public health problem. About one third of the world's population is infected with *M. tuberculosis*. Globally, in 2012, there were an estimated 8.6 million new cases of TB disease, of which 5.7 million were notified, and there were 1.3 million deaths among TB patients.¹ Geographically, the burden of TB is highest in Asia and Africa. India and China combined have almost 40% of the world's TB cases. The African Region has approximately one quarter of the world's cases, and the highest TB notification and death rates relative to population, largely as a result of concomitant HIV infection.

The emergence of resistance to the medicines used to treat TB, and particularly MDR-TB, has become a significant public health problem in a number of countries and an obstacle to the effective global control of TB. By the end of 2012, 136 countries had data on anti-TB drug resistance. Worldwide, an estimated 450 000 people developed MDR-TB and at least 170 000 deaths were caused by the disease in 2012. XDR-TB has now been reported in 92 countries. In 2012, there was a 42% increase in the number of RR/MDR-TB cases detected and reported to WHO, from around 66 000 in 2011 to around 94 000 in 2012. These increases have to be matched with treatment capacity. In 2012, only around 77 000 eligible patients were actually put on treatment for MDR-TB. This means that a significant number of patients

did not receive appropriate second-line treatment. Furthermore, the treatment success rates of MDR-TB remain low at 48% globally, ranging between 30% and 60% in most countries, even when second-line drugs are available.

The importance of universal access to DR-TB management is well known to country programmes and partners, but progress has been slow. Achieving universal access to treatment as envisaged in the 2009 World Health Assembly Resolution WHA62.15 requires a bold and concerted drive on many fronts of TB care.¹

In countries where resistance has been identified, WHO recommends implementing specific measures within TB control programmes using a country-specific framework known as the programmatic management of drug resistant-TB (PMDT).

The Stop TB Strategy

*The Stop TB Strategy*² builds on the successes of directly observed treatment, short-course (DOTS, the basic package of interventions that underpins the strategy) while addressing the key challenges to controlling TB. This strategy underpins the Global Plan to Stop TB 2011–15² and contains six elements.

- **Pursue high-quality DOTS expansion and enhancement**
 - a. Secure political commitment, with adequate and sustained financing.
 - b. Ensure early case detection and diagnosis through quality-assured bacteriology.
 - c. Provide standardized treatment with supervision and patient support.
 - d. Ensure effective medicine supply and management.
 - e. Monitor and evaluate performance and impact.
- **Address TB/HIV, MDR-TB and the needs of poor and vulnerable populations**
 - a. Scale up collaborative activities.
 - b. Scale up prevention and management of MDR-TB.
 - c. Address the needs of TB contacts, and of poor and vulnerable populations.
- **Contribute to health systems strengthening based on primary health care**
 - a. Help improve health policies, human resource development, financing, supplies, service delivery and information.
 - b. Strengthen infection control in the health services, other congregate settings and households.
 - c. Upgrade laboratory networks and implement the Practical Approach to Lung Health.
 - d. Adapt successful approaches from other fields and sectors, and foster action on the social determinants of health.
- **Engage all care providers**
 - a. Involve all public, voluntary, corporate and private providers through public–private mix approaches.
 - b. Promote use of the International Standards for Tuberculosis Care.³

- **Empower people with TB and communities through partnerships**
 - a. Pursue advocacy, communication and social mobilization.
 - b. Foster community participation in TB care, prevention and health promotion.
 - c. Promote use of the Patients' Charter for Tuberculosis Care.⁴
- **Enable and promote research**
 - a. Conduct programme-based operational research.
 - b. Advocate for and participate in research to develop new diagnostics, medicines and vaccines.

Applying the basic TB control framework to the management of MDR-TB

The framework for the programmatic management of MDR-TB is organized around the five basic components of TB control because the underlying principles are the same:

- Sustain political commitment.
- Use a rational case-finding strategy that includes accurate, timely diagnosis made using quality-assured culture and DST.
- Implement appropriate treatment strategies that use second-line medicines under proper case-management conditions.
- Ensure an uninterrupted supply of quality-assured first-line and second-line anti-TB medicines.
- Standardize the recording and reporting systems for controlling drug-resistant TB.

Each of the components involves more complex and costly operations than those for controlling drug-susceptible TB. However, addressing MDR-TB strengthens national TB control programmes.

Post-2015 End TB strategy

The Sixty-seventh World Health Assembly adopted the post-2015 Global TB strategy and targets for TB on 19 May 2014.⁵

Background

Ending the global TB epidemic is feasible, with the dramatic decline in TB deaths and cases, as is elimination of the economic and social burden of TB. Failure to do so will carry serious individual and global public health consequences.

Achievement of this goal by 2035 requires the following:

1. **expanding the scope and reach of interventions** for TB care and prevention, with a focus on high-impact, integrated and patient-centred approaches;
2. **eliciting full benefits of health and development policies and systems**, through engaging a much wider set of collaborators across government, communities and the private sector;
3. **pursuing new scientific knowledge and innovations** that can dramatically change TB prevention and care.

To ensure full impact, these actions must build on the principles of government stewardship, engagement of civil society, human rights and equity, and adaptation to the unique context of diverse epidemics and settings.

Purpose of this training course

As more countries begin to treat larger numbers of patients with RR/MDR-TB, major challenges in the development of human resources will need to be addressed in order to successfully scale up control of the disease. These challenges include:

- ensuring that staff are available;
- ensuring that staff are competent;
- ensuring that the workforce is motivated; and
- ensuring that the support needed to complete tasks is available.

Standardizing operational procedures and training staff in the knowledge and skills that are necessary to manage RR/MDR-TB are therefore becoming increasingly important. Countries need *competency-based training materials* that train staff in tasks that go beyond simply reading guidelines on RR/MDR-TB management.

This course is designed to give **health workers** at **DR-TB management centres** the knowledge, skills and attitudes they need to complete the following tasks: detect cases of DR-TB; treat DR-TB patients; inform patients, their families and close contacts about DR-TB; and manage first-line and second-line anti-TB medicines. The term “health workers” includes physicians, nurses, midwives and other health-care professionals in the public and private sectors. For the purpose of these modules, the term **DR-TB management centre** is used to denote any health facility where drug resistance is diagnosed and treated among those presumed or known to have TB. The actual nomenclature and setting in various countries may vary, including the possibility of having a diagnostic centre at a different location. However, these are generic modules and, as described in the facilitator’s guidelines, need to be adapted to country circumstances.

These training modules are intended for programmes developing and/or expanding the DR-TB component of their national TB programmes (NTPs) and that already have the basic requirements of a TB control programme in place. *It is expected that the content and methods will be adapted by the trainers to the policies and practices applicable in the respective countries.*

The general principles and teaching methods covered in this course may be applicable to drug-susceptible TB as well as to all forms of DR-TB.

Further information about different aspects of the programmatic management of MDR-TB can be found in the “Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. 2014”⁶ “Guidelines for the programmatic management of drug-resistant tuberculosis: emergency update 2008”⁷ and the update in 2011.⁸

Course methods and materials

This course uses a variety of methods of instruction, including reading assignments, written exercises, discussions, role-plays and demonstrations. Practice is considered a critical element of instruction and is conducted through written exercises and role-plays.

The complete course includes six training modules (booklets containing units of instruction) and one reference booklet. Depending on the structure of your course, you may use some or all of the following modules:

A: Introduction (includes a list of abbreviations and a glossary)

B: Detect cases of DR-TB

C: Treat DR-TB patients

D: Inform patients about DR-TB

E: Ensure continuation of DR-TB treatment

F: Manage medicines and supplies for DR-TB

The course is designed for small groups of participants who are led and assisted by facilitators as they work through the modules. The facilitators will not deliver didactic lectures as in a traditional classroom. Their role is to answer questions, provide feedback on exercises, lead discussions and structure role-plays. For the most part, participants work through the modules at their own pace; in some activities, such as role-plays and discussions, small groups work together. There is no module on infection control in this course; information on infection control practices is contained in module 1 of “Management of tuberculosis: training for health facility staff”⁹ and may be adapted by countries. Similarly, countries can add a module on monitoring DR-TB patients (including recording and reporting), and any other topic considered relevant.

The modules may be used to train staff in several different ways (refer to Table 2, page 71 in the facilitators’ guide).

- All of the modules may be completed in sequence without interruption, for example, in a 5-day training session. This will be the format most often used.
- One module at a time may be used in a series of short training sessions, for example, one module per week.
- Selected modules may be used in a training session to teach specific needed skills.
- Modules may be used to train staff on the job for specific activities.
- Motivated health workers may work through the modules on their own to teach themselves.
- The modules may be used as a reference.

Assumptions for this training course

Across the globe, projects and programmes to treat DR-TB are organized differently and reflect different management decisions, such as whether standardized or individualized treatment is offered, the frequency of sputum culture, and whether treatment is offered in the inpatient or ambulatory setting.

In order to create generic training material for DR-TB management – that is, material that can be used in many countries – certain assumptions were made about how programmes function. These assumptions are based on a number of factors, including how programmes are organized and prevailing programmatic conditions.

Note: These assumptions have been used to facilitate the training process and do not represent the opinion of WHO or an endorsement of a certain project or programme design. They are intended to facilitate the training of staff in the management of DR-TB.

For example, your country may have its own list of patient groups considered to be at high risk for DR-TB who are recommended to be screened using DST. Your programme may provide ambulatory care for DR-TB patients during the first few months instead of hospitalization. Such variations will not impact the tasks that need to be completed to detect DR-TB and treat these patients. If your programme uses only standardized treatment, you do not have to be concerned about selecting treatment regimens or performing DST for second-line medicines; however, it is useful to know how these are done.

In this course, the following terms are used.

Local health facilities are public or private facilities that are responsible for referring patients presumed to have DR-TB to DR-TB management centres, where appropriate laboratory facilities for diagnosing resistance are available and patients found to have DR-TB can begin treatment.

DR-TB management centres are specialized public or private health facilities that offer comprehensive management for DR-TB patients. Through their links with laboratories and specialized medical services, DR-TB management centres are able to detect, confirm, treat and monitor patients with DR-TB. Typically, these centres have inpatient facilities or are linked to a hospital with wards for patients with DR-TB. Patients in whom DR-TB is diagnosed are registered at DR-TB management centres where treatment is started and continued for as long as patients remain sputum smear-positive; DR-TB management centres provide a complete package of services. After a certain period of treatment, the patients with DR-TB return to the care of local health facilities to continue their treatment closer to home; this process is called decentralization.

This course uses as examples WHO's recording and reporting forms contained in its guidelines on DR-TB. Some additional forms are included, which have been adapted from those used in countries implementing the programmatic management of DR-TB.

Local health facilities manage a small number of DR-TB patients and offer a basic package of services; they provide continuing care to patients who have been returned to their facility by DR-TB management centres to complete their treatment. During this time, patients visit DR-TB management centres monthly and remain under their centre's supervision and overall responsibility.

While there are differences in the scope of services available at DR-TB management centres and local health facilities, their common functions include directly observing patients taking all doses of their anti-TB medicines, specifically during the intensive phase when injections are required. Depending on patient convenience, direct observation may continue at the health facility or through community-based support carried out by approved observers in the community. Local health facilities also provide health education, and actively trace patients who interrupt treatment. Some of these roles and responsibilities are summarized in *Table 1*.

Table 1 Roles and responsibilities of DR-TB management centres and local health facilities in treating patients with drug-resistant tuberculosis (DR-TB)

DR-TB MANAGEMENT CENTRES	LOCAL HEALTH FACILITIES
Identify presumptive cases of DR-TB	Identify presumptive cases of DR-TB Transfer presumptive cases or arrange to send the sputum sample to the DR-TB management centre
Diagnose DR-TB cases (using culture and drug-susceptibility testing and other available tools such as Xpert MTB/RIF) Investigate household contacts of patient	Investigate household contacts of patient
Register patient and initiate treatment Provide directly observed treatment	Continue directly observed treatment for DR-TB patients decentralized by DR-TB management centres
Provide bacteriological follow up of response to treatment using microscopy and culture	Provide bacteriological follow up of response to treatment using microscopy
Provide early detection, monitoring and management of adverse effects of treatment, including serious and uncontrolled adverse effects Provide referral to specialists	Ensure early detection of adverse effects of treatment Manage minor adverse effects and refer patients with serious and uncontrolled adverse effects to DR-TB management centres
Actively trace patients who are lost to follow up	Actively trace patients who are lost to follow up
Refer patients to local facilities for community-based TB care (this process is known as decentralization)	Receive patients from DR-TB management centres
Ensure that a physician clinically monitors each patient at least monthly	Ensure that patients return to the DR-TB management centre for monthly monitoring visit
Supervise and monitor patients and treatment supporters	Supervise community-based DR-TB treatment supporters
Manage stocks of medicines used for treatment, including buffer stock Supply medicines to the local health facility	Manage stock of medicines used for patients on treatment

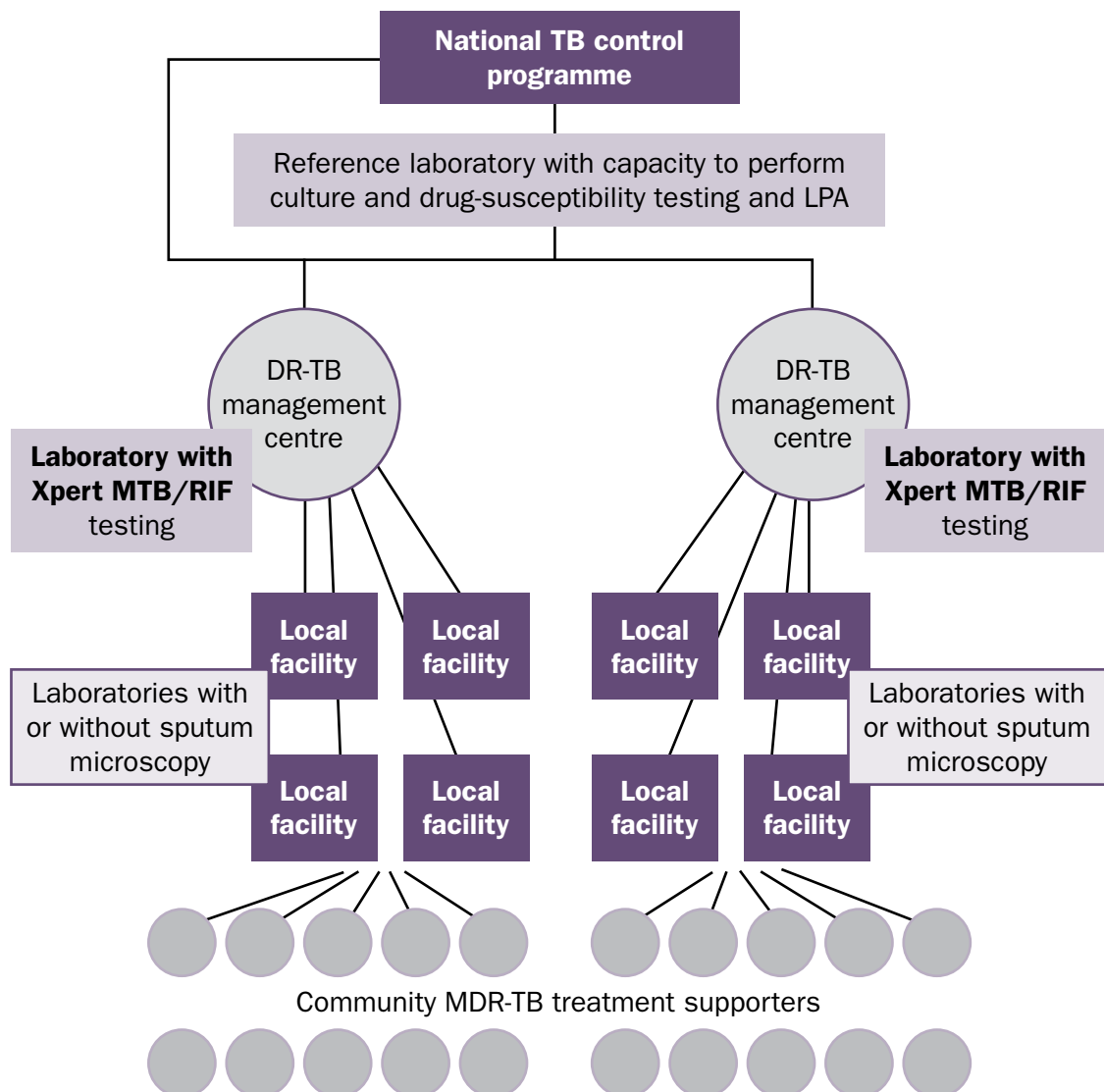
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DR-TB MANAGEMENT CENTRES	LOCAL HEALTH FACILITIES
Provide counselling and information on treatment to people undergoing diagnostic tests for DR-TB and to those who have already been diagnosed	Continue to provide information to patients about their treatment
Provide psychosocial support services	Refer patients for/provide psychosocial support services
Record and report treatments observed and clinical progress made	Record and report treatments observed

The management of DR-TB patients is expected to be increasingly decentralized from DR-TB management centres to facilities in the community. *Figure 1* shows the organization of the health-care delivery system for DR-TB management envisioned in this course.

Figure 1 Possible structure of a health-care delivery system for managing drug-resistant tuberculosis (DR-TB) as envisioned in these modules



In addition to the delivery system for treatment shown above, each module makes certain assumptions about how the management of patients will be organized.

For Module B, this course makes the assumptions described below.

- People falling into any of the groups listed below should be tested for RR/MDR-TB using Xpert MTB/RIF test or LPA and/or culture and DST, as per the country's policy. Therefore, the following cases should be referred to a DR-TB management centre for evaluation and diagnosis:
 - any patient before the start of a retreatment regimen (those having failed a regimen, relapsed or returned after loss to follow up, other previously treated cases including chronic cases);
 - close contacts of DR-TB patients who have been diagnosed with active TB;
 - patients not responding to first-line anti-TB treatment (remaining sputum smear-positive at the end of the intensive phase of a first-line anti-TB drug regimen);
 - HIV-positive patients with active TB;
 - cases from congregate settings where transmission rates of TB and hence DR-TB as well are high, e.g. prisoners, mine-workers, etc.;
 - any TB patient coming from a group determined by the programme to have a significant risk for DR-TB, such as:
 - patients with co-morbid conditions associated with malabsorption or rapid-transit diarrhoea;
 - residents of areas with high DR-TB prevalence (DR-TB rates in many areas of the world can be high enough to justify routine DST in all new cases).
- Two sputum samples will be collected from people presumed to have DR-TB and sent to the laboratory.^b If the test is positive for TB and rifampicin resistance using the rapid genotypic tests, the samples will be sent to a laboratory with the capability for performing cultures and DST to confirm MDR-TB.
- Rifampicin resistance diagnosed using Xpert MTB/RIF testing is a strong indicator of MDR-TB. When the patient is found to be rifampicin resistant, culture and DST may be done to confirm MDR-TB in patients considered to be at low risk for drug resistance, e.g. new TB cases starting treatment for the first time. The algorithm for use of the Xpert MTB/RIF test and follow up of the result is provided in detail in Module B and may be adapted by countries as per the local needs and disease epidemiology. However, the patient does not have to wait in all cases for the results of culture and DST to start MDR-TB treatment. The DST will include testing for at least the most important first-line medicines, isoniazid and rifampicin.
- The physician at the DR-TB management centre will present all patients for whom MDR-TB treatment is proposed (either an empirical regimen or a regimen for MDR-TB confirmed by DST) to the appropriate review panel for treatment decisions.
- Investigations of contacts will be carried out for all close contacts of the patient; investigations will include clinical examination of all symptomatic contacts.

^b Two samples should be collected if performing AFB microscopy and a single sample for Xpert.

For Module C, this course makes the assumptions described below.

- There will be a committee called a review panel, which is made up of experts in DR-TB, and the committee will make decisions about diagnosis, treatment regimens, decentralization, modification of regimens and evaluation of outcomes. However, once the diagnosis of RR/MDR-TB is made, there should be no delay in initiation of treatment because of waiting for the committee to meet.
- RR/MDR-TB may be treated with a standardized or individualized regimen. However, the individualized regimen (laboratory-based or empirical) requires DST for second-line drugs and specialized decisions.
- Each dose is given under directly observed therapy (DOT) throughout the treatment, 6–7 days a week.
- Standard DOTS notation will be used to mark the *TB and Second-line TB treatment card*.
- The *Second-line TB treatment register* will be kept at the DR-TB management centre and will be the basis for monitoring and data analysis.
- The *Second-line TB treatment register* will follow the format recommended in the 2013 revised definitions and framework document.
- The injectable agent is generally administered for at least four months past culture conversion and for not less than 8 months. After this point, the patient is usually eligible for the continuation phase of treatment depending on culture conversion and decisions of the review panel. During the continuation phase, the injectable agent is discontinued and the patient continues to take the other medicines in the regimen, usually for at least 12 months past culture conversion.
- The total length of treatment is expected to be 20 months in most patients not previously treated for MDR-TB.
- Depending on the country policy, ambulatory treatment should be initiated as soon as possible.
- Patients who have begun treatment at a local health facility will make a monthly monitoring visit to a physician at the DR-TB management centre and will continue having monthly sputum-smear and culture examinations in the intensive phase and culture examination once in two months during the continuation phase.

For Module D, this course makes the assumption described below.

- Patients will be counselled about HIV and referred for HIV testing.

For Module E, this course makes the assumptions described below.

- Patient support measures such as incentives and enablers may be provided as per country policy for DR-TB patients who are deemed to need them.
- DR-TB patients are generally not to be given doses for self-administration, such as during travel. Missed doses count as absences.
- If a patient misses a scheduled dose for more than 24 hours, a health worker will contact the patient by telephone; if that is not successful, a health worker will find the patient by making a home visit or having a health worker from a local health facility do so.

- If a patient wants to stop treatment, the patient should be counselled and all efforts made to remove any barriers to convenient treatment. However, if the patient still insists on discontinuing the treatment, a meeting should be held with the patient and a waiver should be signed. The waiver should say that the patient has been informed of the consequences of discontinuing treatment and has been offered alternatives to facilitate treatment, but has made up his or her mind to discontinue treatment and thereby currently waives his or her rights to seek a cure for DR-TB.
- Treatment supporters may be used, but they must receive special training to administer medicines to patients. The local health facility is responsible for identifying, preparing and supervising a community-based DR-TB treatment supporter, if necessary.

For Module F, this course makes the assumptions described below.

- Medicines for DR-TB patients will be kept at a central pharmacy with sufficient buffer stocks.
- Staff at the DR-TB management centre will request replenishment of stocks from the central pharmacy each quarter using a *TB medicine requisition form*.
- Local health facilities will receive anti-TB medicines quarterly only for the number of decentralized patients receiving treatment there.
- Staff at the local health facility and the DR-TB management centre will be responsible for putting together the daily treatment dose for each patient they treat.
- The administration of safe injections will not be discussed in these modules as health workers are assumed to have this knowledge.
- Other medicines included in antiretroviral therapy or co-trimoxazole preventive therapy will be managed in coordination with the HIV programme.
- Other supplies (such as syringes and sputum containers) will be procured in the same manner as they are for patients who do not have DR-TB.

Learning objectives

The learning objectives are specified after the introduction in each module. The modules provide information and examples, and allow you to practise the skills necessary for detecting RR/MDR-TB, managing cases and monitoring progress. Exercises are provided at the end of each module. After completing each module, participants will be able to accomplish the tasks described below.

Module B: Detect cases of RR/MDR-TB

- Identify presumptive cases of RR/MDR-TB who should be tested by rapid tests and/or culture and DST.
- Collect sputum samples from the presumptive RR/MDR-TB case.
- Fill out the *Request for examination of biological specimen for TB*.
- Inform the presumptive case about the possible diagnosis of RR/MDR-TB and steps to be taken.
- Determine whether DST results will be available soon enough to guide the choice of a treatment regimen;

- Understand how a physician will select an empirical treatment regimen based on the patient's likelihood of having RR/MDR-TB;
- Read the results of smear microscopy, culture and DST and/or a rapid test, and decide on the appropriate response;
- Choose an appropriate regimen based on the DST results; and
- Investigate close contacts of RR/MDR-TB patients.

Module C: Treat RR/MDR-TB patients

- Use treatment history, DST results and other information to propose an RR/MDR-TB treatment regimen.
- Prepare a patient's *Second-line TB treatment card* and include treatment history and laboratory results.
- Give directly observed treatment and record it on the *Second-line TB treatment card*.
- Monitor the patient for adverse effects and identify appropriate actions to be taken if they occur.
- Determine when the patient is due for follow-up examinations.
- Record the results of laboratory examinations.
- Identify when a patient is eligible for decentralization or shifting to the continuation phase of treatment.
- Record changes to the treatment regimen in the *Second-line TB treatment card*.
- Update the *Second-line TB register* throughout the duration of treatment.
- Determine the treatment outcome of an RR/MDR-TB patient.

Module D: Inform patients about RR/MDR-TB

- Use good communication skills when informing patients about their diagnosis and treatment.
- Inform the patient with presumptive RR/MDR-TB about the diagnostic process and when the results will be received.
- Counsel the patient about HIV and TB.
- At enrolment for RR/MDR-TB treatment, counsel the patient and, if possible, the family, about the disease and how it is treated.
- Provide information about the specific medicines the patient will take.
- Throughout treatment, provide information and support to the patient about adverse effects, the need to continue treatment, and monthly sputum examinations and monitoring visits.
- Provide information about the decentralization process.
- Provide information at the end of treatment.

Module E: Ensure continuation of RR/MDR-TB treatment

- Support RR/MDR-TB patients when giving them DOT.
- Identify problems that may hinder DOT and help to solve them; take steps to prevent them in the future.
- Decentralize an RR/MDR-TB patient's treatment.
- Take action to trace an RR/MDR-TB patient who has missed treatment.

- Coordinate RR/MDR-TB patients' medical referrals and transfers between treatment facilities.
- Complete a *tuberculosis referral/transfer form*.

Module F: Manage medicines and supplies for RR/MDR-TB

- Ensure adequate supplies of RR/MDR-TB medicines for your DR-TB management centre.
- Order medicines and supplies for RR/MDR-TB patients.
- Plan for other necessary supplies.
- Prepare medicines for RR/MDR-TB patients.
- Use good medicine-management procedures to maintain the stock of anti-TB medicines.

References

1. Global tuberculosis report 2013. Geneva: World Health Organization; 2013 (WHO/HTM/TB/2013.11).
2. The Stop TB Strategy: building on and enhancing DOTS to meet the TB-related Millennium Development Goals. Geneva: World Health Organization; 2006 (WHO/HTM/TB/2006.368).
3. International standards for tuberculosis care (ISTC), 3rd ed. The Hague: Tuberculosis Coalition for Technical Assistance; 2014.
4. Patients' charter for tuberculosis care: patients' rights and responsibilities. Geneva, World Care Council, 2006.
5. The end TB strategy. Geneva: World Health Organization, 2014. (http://www.who.int/tb/post2015_TBstrategy.pdf, accessed 30 October 2014).
6. Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. Geneva: World Health Organization; 2014 (WHO/HTM/TB/2014.11).
7. Guidelines for the programmatic management of drug-resistant tuberculosis: emergency update 2008. Geneva: World Health Organization; 2008 (WHO/HTM/TB/2008.402).
8. Guidelines for the programmatic management of drug-resistant tuberculosis: update 2011. Geneva; World Health Organization; 2011 (WHO/HTM/TB/2011.6).
9. Management of tuberculosis: training for health facility staff, 2nd ed. Geneva: World Health Organization; 2009 (WHO/HTM/TB/2009.423).

Glossary

The definitions provided here refer to the use of terms in the content of this course and are not necessarily valid in other contexts. The definitions given here apply specifically to the management of DR-TB and may vary from the same terms used when discussing drug-susceptible TB.

acid-fast bacilli (AFB)	bacilli that hold the colour of the stain even after washing with acid. Tubercle bacilli are acid fast.
active TB case	a patient with current disease due to Mycobacterium tuberculosis
adherence	for a TB patient, adherence means taking anti-TB medicines as scheduled.
adverse drug reaction (ADR)	a response to a medicine which is noxious and unintended, and which occurs at doses normally used in humans
anorexia	loss of appetite
approved MDR-TB case	a patient whose case has been considered by the review panel and whose treatment has been approved to begin, regardless of whether the patient has actually begun treatment
bacilli	rod-shaped bacteria
buffer stock	extra stock kept by a health facility to ensure adequate supplies even if there is increased use or a delay in the delivery of medicines
checking question	a question asked after giving instruction, which is intended to check the learner's understanding, so that more information can be given if needed
chronic case	a patient whose sputum tests positive by microscopy at the end of a retreatment regimen. This term is to be avoided. See also retreatment regimen.
cohort	a group of patients discussed or analysed collectively because they have a characteristic/s in common
colony	growth of Mycobacterium tuberculosis bacilli in a culture medium
confirmed case of MDR-TB	a patient with a positive culture for Mycobacterium tuberculosis whose infecting strain has been confirmed through a drug-susceptibility test to be resistant in vitro to at least isoniazid and rifampicin
close contact	a person who is not in the household but shared an enclosed space, such as a social gathering place, workplace or facility, for extended periods during the day with the index case during the 3 months before commencement of the current treatment episode. See also household contact.

continuation phase	the phase of TB treatment after the intensive phase. The continuation phase for RR/MDR-TB patients generally starts after no less than 8 months of treatment with the injectable agent; the injectable agent is generally administered for at least four months past culture conversion. This phase usually lasts for at least 12 months past culture conversion. See intensive phase.
conversion	a change from sputum smear-positive to sputum smear-negative or from culture-positive to culture-negative. Culture conversion is the most useful indicator that treatment for RR/MDR-TB has been effective.
conversion rate	the proportion of sputum smear-positive or culture-positive cases, or both, that are shown to be sputum smear-negative or culture-negative, or both, for two consecutive months during RR/MDR-TB treatment. The most important interim indicator of treatment success is culture conversion.
cross-resistance	resistance to one anti-TB medicine conferred to some or all members of the same family of medicines or, less commonly, to members of different families of medicines, e.g. kanamycin and amikacin have high cross-resistance – that is, if a strain is resistant to one of these medicines, it is also resistant to the other.
culture	a method of diagnosis in which bacteria are grown in a special medium conducive to their growth. See also drug-susceptibility test.
cured (treatment outcome for MDR-TB)	treatment completed as recommended by the national policy without evidence of failure AND three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase
decentralization	the process of moving a patient from care at a DR-TB management centre to care at a local facility/community to continue RR/MDR-TB treatment and monitoring after the patient has fulfilled a set of criteria
diagnostic sputum smear examination	a sputum smear examined under the microscope to diagnose pulmonary TB
died (treatment outcome)	a patient who dies for any reason during the course of treatment
directly observed treatment	treatment observed by a health worker or a community-based TB treatment supporter. The health worker or treatment supporter watches the TB patient swallow each dose of medicine. See treatment supporter.
drug rechallenge	removing from treatment a medicine that has caused an adverse effect and then reintroducing it while monitoring for adverse effects
drug resistance	the adaptation of microorganisms so that they are not killed by antimicrobials
drug-resistant TB	TB shown to be caused by bacilli resistant to any anti-TB medicine

drug-susceptibility testing (DST)	the isolation and identification of bacterial agents from clinical specimens using standardized testing techniques to determine the susceptibility or resistance of the bacteria to certain antimicrobials
drug-susceptible TB	TB caused by bacilli that are killed by anti-TB medicines
empirical	guided by observation and experience. In these guidelines, empirical means providing treatment before (or without) confirming whether the organisms causing TB in the patient are resistant to medicines.
enrolled MDR-TB case	a patient who has begun treatment with an RR/MDR-TB regimen
extensively drug-resistant TB (XDR-TB)	a form of TB caused by bacilli resistant to at least isoniazid and rifampicin (thus, multidrug-resistant or MDR) and also resistant to any fluoroquinolone and any one of the second-line injectable agents (amikacin, capreomycin or kanamycin)
extrapulmonary TB	TB affecting organs other than the lungs, for example, the lymph nodes, bones, joints, genitourinary tract, meninges, pleura or intestines
failed (treatment outcome for MDR-TB)	treatment terminated or need for permanent regimen change of ≥ 2 anti-TB drugs because of lack of conversion in the continuation phase, OR bacteriological reversion in the continuation phase after conversion to negative, OR evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs, OR adverse drug reactions (ADRs)
first-line anti-TB medicines	the medicines normally used to treat TB cases when the bacilli are still considered susceptible to these drugs. See also second-line anti-TB medicine.
fixed-dose combination (FDC)	two or more medicines combined in one pill or capsule in specific doses to facilitate the correct intake of medicines. Currently, there are no FDCs for second-line anti-TB medicines.
haemoptysis	coughing up blood
household contact	a person who shared the same enclosed living space for one or more nights or for frequent or extended periods during the day with the index case during the 3 months before commencement of the current treatment episode
incidence	the number of new cases of a disease occurring in a defined population during a given period
indicator	a measurable number, proportion, percentage or rate that monitors the extent of a programme's achievement or the level of some condition among the population
intensive phase	the first phase of treatment for RR/MDR-TB, lasting no less than 8 months of treatment and for at least four months past culture conversion and consisting of oral medicines and an injectable agent. During this phase, conversion of sputum smears and cultures usually occurs, and clinical symptoms improve. See also conversion.

in vitro	describes the drug-susceptibility testing process performed in a laboratory as opposed to in a patient
jaundice	yellow skin or eyes caused by damage to or failure of the liver
line-probe assay	rapid molecular test for detection of multidrug-resistant tuberculosis (RR/MDR-TB). Line-probe assay (LPA) can give a test result within 1–2 days. LPA was endorsed by WHO in 2008.
local health facility	a public or private health facility that provides a basic package of management services for a small number of patients who have been decentralized from a DR-TB management centre
lost to follow up (treatment outcome)	a patient whose treatment was interrupted for 2 consecutive months or more. (This category was previously known as defaulted.)
DR-TB management centre	a specialized public or private health facility that provides comprehensive management for patients with DR-TB. Through the facilities' links with laboratories and specialized medical services, DR-TB management centres are able to detect, confirm, treat and monitor patients with DR-TB.
MDR-TB regimen	a regimen designed to treat RR/MDR-TB patients
mild adverse effect	an adverse reaction to, or side-effect of, a medicine that does not warrant discontinuation of the medicine
monoresistant TB	a form of DR-TB in which <i>Mycobacterium tuberculosis</i> is resistant to only one anti-TB medicine
mucopurulent	containing both mucus and pus
multidrug-resistant tuberculosis (MDR-TB)	active TB in which the bacilli are resistant in vitro to at least rifampicin and isoniazid, the two most powerful first-line anti-TB medicines
<i>Mycobacterium tuberculosis</i>	the bacillus that causes all forms of tuberculosis, whether drug-susceptible, multidrug-resistant or extensively drug-resistant
new (type of patient)	a patient who has never had treatment for TB or who has been treated with anti-TB medicines for less than 1 month
open-ended question	a question that cannot be answered by a simple “yes” or “no” but requires further response. For example, questions that begin with “why” or “how” are open-ended.
other previously treated patient (type of patient)	a patient who has been previously treated for TB but with an unknown or undocumented outcome for their most recent treatment episode
ototoxicity	the tendency of certain medicines to cause functional impairment and cellular degeneration of the inner ear and of the eighth cranial nerve. Ototoxicity may be reversible or irreversible.

not evaluated (treatment outcome)	a TB patient for whom no treatment outcome is assigned. (This includes cases “transferred out” to another treatment unit and where the treatment outcome is unknown to the reporting unit.)
percentage	a part of a whole expressed in hundredths. If 50% of a population is female, it means that 50 out of 100 people are female. The following examples show different ways of expressing the same meaning: 50% = 0.50 = 50/100; 4% = 0.04 = 4/100.
peripheral neuropathy	a condition of the nervous system that usually begins in the hands or feet, or both, and is accompanied by symptoms of numbness, tingling, burning or weakness
pleura	the membrane that contains and covers the lungs and wall of the chest cavity
polyresistant TB	a form of drug-resistant TB in which Mycobacterium tuberculosis is resistant to more than one first-line anti-TB drug, other than both isoniazid and rifampicin
positive culture	for the purpose of diagnosing TB, a culture is considered positive when Mycobacterium tuberculosis is growing, regardless of the number of colonies
presumptive RR/MDR-TB	case a person in one of the risk groups for RR/MDR-TB; the definition of a risk group depends on the criteria specified by the national TB control programme
prevalence	the number of all cases of a disease or a condition existing in a defined population at a specific point in time or during a given period
prognosis	the predicted course that a disease will take; expectations for a patient’s recovery or decline
programmatic	the TB programme activities and resources required to ensure
management of drug-resistant TB (PMDT)	the coordinated management of patients with drug-resistant TB
proportion	the relationship of a part to a whole, often written as a decimal fraction or percentage (for example, 0.17 or 17%).
pulmonary TB	TB affecting the lungs
radiographic abnormalities	abnormalities seen on X-rays
rate	a measure of the frequency of some event in a defined population during a given period expressed, for example, as 1.5/100 000.
referral	sending a patient to another health facility or to a clinician. For example, patients may be referred for diagnosis, initiation of treatment, special care or hospitalization for complications or toxicity, or for other reasons.
regimen	a plan of treatment specifying which medicines are to be given, and the dose, frequency and duration of treatment for each medicine

relapse (type of patient)	a patient previously treated for TB, who was declared cured or treatment completed at the end of the most recent treatment episode and is now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection)
reserve stock	extra stock of medicines kept by a health facility to ensure adequate supplies even if there is an increase in use or a delay in their delivery. See also buffer stock.
retreatment regimen	a regimen of first-line anti-TB medicines given to a TB patient whose previous treatment has failed. It may also be given for cases returning after loss to follow up (having had at least 4 weeks of treatment) and relapse cases after an initial first-line treatment regimen.
reversion	a change from a negative culture to a positive culture after an initial conversion, and when two consecutive cultures taken at least 30 days apart are found to be positive. For the purpose of defining “treatment failure”, reversion is only considered when it occurs in the continuation phase.
review panel	a case-management team that comprises a multidisciplinary group of programme staff, physicians, nurses and other relevant health-care workers who have expertise in managing DR-TB. The panel meets regularly to confirm diagnoses and determine treatment regimens, and to assess responses to treatment and treatment outcomes through consensus, utilizing WHO’s guidelines for DR-TB and their country’s national guidelines for the programmatic management of DR-TB.
second-line anti-TB medicine	a therapeutic agent that is not the medicine of choice or the first medicine normally used to treat TB. Generally, second-line agents are used when standard “first-line” therapy fails. RR-TB regimens use second-line medicines. See also first-line anti-TB medicine.
severe adverse effect	a severe reaction to a medicine or a side-effect that needs prompt medical intervention and often necessitates discontinuation of the medicine suspected to have caused the reaction
smear conversion	a change from sputum smear-positive to sputum smear-negative
specimen	a biological sample taken for testing purposes (for example, of urine, lymph node or sputum)
sputum-smear microscopy	examination of sputum with a microscope to determine whether acid-fast bacilli are present
sputum smear-negative cases	pulmonary TB patients whose sputum does not contain enough tubercle bacilli to be detectable by microscopy
sputum smear-positive cases	pulmonary TB patients with sputum containing tubercle bacilli that are detectable by microscopy

stock card	a card kept with each medicine and each different strength of a medicine in the storeroom. The stock card is updated whenever medicines are received or dispensed so that it always shows the actual balance in stock.
stock on-hand	actual quantity of a medicine or other supply at a facility at a particular time (includes buffer stock)
transfer	as used in this course, changing the facility at which a patient with RR/MDR-TB is treated to accommodate a patient's household move
transfer in (type of patient)	a patient who has been transferred from another TB reporting unit (TB register) to continue treatment
transmission	the transfer of infection or disease from one person to another
treatment after failure (type of patient)	a patient who was previously treated for TB and whose treatment failed at the end of their most recent treatment episode. See also retreatment regimen.
treatment after lost to follow up (type of patient)	a patient previously treated for TB and declared "lost to follow up" at the end of the most recent treatment episode. (This was previously known as "treatment after default".)
treatment completed (RR/MDR-TB treatment outcome)	treatment completed as recommended by the national policy without evidence of failure BUT no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase
treatment success	the sum of cured and treatment completed.
treatment supporter	a trained health worker or trained and supervised community member who directly observes a TB or RR/MDR-TB patient's treatment. When it is not convenient for a patient to visit a health facility during regular hours, a community-based treatment supporter may be selected to directly observe a patient's treatment at a more convenient place and time. See also directly observed treatment.
tubercle bacilli	the bacilli that cause tuberculosis (<i>Mycobacterium tuberculosis</i>)
tuberculin skin test (TST)	intradermal injection of 0.1 ml of tuberculin (protein extracted from TB bacilli). A positive test result indicates TB infection but not disease. In an individual infected with TB, a hardening of the skin (or induration) can be observed at the injection site within 48–72 hours.
tuberculosis (TB)	a disease caused by the organism <i>Mycobacterium tuberculosis</i> . Not everyone infected with <i>M. tuberculosis</i> develops symptoms of TB disease, which may include cough, bloody sputum (haemoptysis), night sweats, fever and weight loss (in pulmonary TB). In this course, TB refers to TB disease rather than the infection without disease.
Xpert MTB/RIF	rapid molecular test to diagnose TB and rifampicin resistance. The Xpert MTB/RIF gives a result within a few hours. WHO endorsed Xpert MTB/RIF in 2010.

Abbreviations

ADR	adverse drug reaction
AFB	acid-fast bacilli
ART	antiretroviral therapy
BCG	Bacillus Calmette–Guérin
CPT	co-trimoxazole preventive therapy
DOTS	directly observed therapy, short-course (the internationally recommended approach to TB treatment)
DR-TB	drug-resistant TB
DST	drug-susceptibility testing
FDC	fixed-dose combination
HIV	human immunodeficiency syndrome
FEFO	first expiry, first out
FQ	fluoroquinolones
IPT	isoniazid preventive therapy
LPA	line-probe assay
MDR-TB	multidrug-resistant tuberculosis
MTBc	Mycobacterium tuberculosis complex
NTP	national tuberculosis programme
PMDT	programmatic management of drug-resistant tuberculosis
PTB	pulmonary TB
RR-TB	rifampicin-resistant TB
TB	tuberculosis
TOT	training of trainers
TST	tuberculin skin test
WHO	World Health Organization
WRD	WHO-approved rapid diagnostics
XDR-TB	extensively drug-resistant tuberculosis

Abbreviations of anti-TB medicines

Am	amikacin
Amx/Clv	amoxicillin/clavulanate
Bdq	bedaquiline
Cfz	clofazimine
Clr	clarithromycin
Cm	capreomycin
Cs	cycloserine

Dlm	delamanid
E	ethambutol
Eto	ethionamide
H	isoniazid
Ipm/Cln	imipenem/cilastatin
Km	kanamycin
Lfx	levofloxacin
Lzd	linezolid
Mfx	moxifloxacin
Ofx	ofloxacin
PAS	para-aminosalicylic acid
PAS-Na	p-aminosalicylate sodium
Pto	prothionamide
R	rifampicin
S	streptomycin
Z	pyrazinamide

Management of drug-resistant tuberculosis

**Training for staff working at
DR-TB management centres**

Module B: Detect cases of DR-TB



**World Health
Organization**

MODULE B

Detect cases of DR-TB

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Introduction

Detecting a case of drug-resistant tuberculosis (DR-TB) is more complex and time-consuming than detecting a case of TB that is susceptible to first-line medicines. People with pulmonary TB excrete tubercle bacilli that can be detected by examining their sputum under a microscope – that is, by sputum-smear microscopy. However, drug resistance^a cannot be diagnosed with sputum-smear microscopy. This is because a positive smear of DR-TB looks the same as a positive smear of drug-susceptible TB. They are caused by the same organism, *Mycobacterium tuberculosis*.

A definitive diagnosis of DR-TB requires that *Mycobacterium tuberculosis* bacteria be detected and resistance to anti-TB drugs determined. This can be done by isolating the bacteria by culture, identifying it as belonging to the *M. tuberculosis* complex (MTBc), and conducting drug-susceptibility testing (DST) using solid or liquid media, or by performing a WHO-endorsed molecular test to detect the DNA and mutations associated with resistance in tubercle bacilli. Conventional or phenotypic DST determines whether the *M. tuberculosis* strain will grow in the presence of different anti-TB medicines or whether the medicines will stop its growth. If the strain grows in the presence of a medicine, it is said to be resistant to that medicine. Molecular or genotypic testing detects mutations in the TB genome associated with specific drug resistance. Currently, molecular tests, such as Xpert MTB/RIF and line-probe assay (LPA), are endorsed by WHO. Specimens from all people presumed to have DR-TB must therefore be tested using rapid molecular tests, where available, or molecular tested and/or cultured, and undergo DST to confirm whether multidrug resistance or any other type of resistance is present.

Patients with pulmonary TB (including DR-TB) are usually infectious because they discharge tubercle bacilli into the air by coughing and sneezing. Close contacts of patients with DR-TB may become infected with a drug-resistant strain of TB when they breathe in resistant tubercle bacilli. The longer that people with DR-TB remain untreated, the greater the likelihood that they will infect their close contacts, just like people with susceptible TB.

Early identification of presumptive cases of DR-TB should be a priority for every health-care facility. It is critical to detect DR-TB because standard TB regimens using first-line medicines^b are no longer effective in treating it: treatment regimens for DR-TB use second-line medicines. If patients with DR-TB are not detected and treated correctly with second-line medicines,^c they will have poor treatment outcomes, spread DR-TB in their communities and the resistance of bacilli harboured by such patients may amplify. Early treatment of these cases with an appropriate DR-TB regimen increases the likelihood of a good outcome and minimizes

^a Although in these modules drug resistance refers to *M. tuberculosis* that is resistant to the first-line anti-TB drugs, the modules focus on the management of rifampicin and/or isoniazid, i.e. RR or MDR-TB (RR/MDR-TB) because of its clinical significance and the need to use second-line drugs in such cases.

^b First-line treatment refers to the first drug normally used to treat a particular condition. The standard new-patient regimen for TB treatment (formerly category I or III treatment) is given to patients who have never taken any medicines for treatment of TB or have taken these medicines for less than 1 month. The standard retreatment regimen (formerly category II treatment) is given to patients who have been previously treated for TB; it lasts longer and includes more medicines. Both of these regimens use first-line medicines only.

^c Second-line medicines are therapeutic agents that are not the first medicine of choice normally used to treat a condition. Generally, second-line agents are used when standard first-line therapy fails.

destruction of the lungs by the microorganism. It also limits the amplification of resistance and prevents the emergence of extensively drug-resistant TB (XDR-TB).

Ideally, specimens from all people presumed to have TB should undergo sputum-smear microscopy or rapid molecular testing, culture and DST. However, given the limited resources in many countries, this is often not possible for all presumptive TB cases.

People presumed to have DR-TB may be identified from among patients already diagnosed with TB or from people presumed to have TB who present at a DR-TB management centre; they may also be referred by first-level health facilities in the area. Before selecting the treatment regimen for a TB patient, the health worker at the first-level facility will consider whether the patient has previously taken any anti-TB medicines and the likelihood that the TB patient may have DR-TB. A TB patient with a risk of DR-TB is a “presumptive DR-TB case” and should be sent to a DR-TB management centre for evaluation and treatment.

Objectives of this module

After completing this module participants will be able to do the following: Section:

- ▶ Identify presumptive cases of DR-TB who should be screened by rapid molecular methods, culture and DST 1
- ▶ Collect sputum samples from the presumptive DR-TB case 2
- ▶ Fill out the Request for sputum examination form..... 2.3
- ▶ Inform the presumptive case about the possible diagnosis of DR-TB and steps to be taken..... 3.2
- ▶ Determine whether DST results will be available soon enough to guide the choice of a treatment regimen 4
- ▶ Understand how a physician selects an empirical TB treatment regimen based on the patient’s likelihood of having DR-TB 5
- ▶ Read the results of smear microscopy, culture and DST, and decide on an appropriate response 6
- ▶ Choose an appropriate regimen based on the DST results 7
- ▶ Use rapid molecular DST results to guide the choice of regimen from the start of treatment (where rapid DST is available) 8
- ▶ Investigate close contacts of DR-TB patients 9

If you need to look up an unfamiliar word, refer to the Glossary at the end of Module A.

1. Identify presumptive or diagnosed TB cases who should be screened for DR-TB^d

The symptoms of pulmonary DR-TB are the same as for pulmonary TB sensitive to first-line anti-TB medicines, in particular, cough lasting for two weeks or longer. Other symptoms of TB and DR-TB include fever, chest or back pain, haemoptysis, weight loss, and general symptoms such as night sweats, fatigue, malaise and shortness of breath. All people presenting at health facilities with any of these symptoms should be screened for TB by sputum-smear microscopy. All patients with TB should be further assessed to determine whether they are likely to have DR-TB. For persons at risk of DR-TB, WHO recommends the use of Xpert MTB/RIF as the initial diagnostic test rather than microscopy, culture and DST.^e

At the DR-TB management centre, presumptive cases of TB may present at the outpatient department (for example, a person may attend the facility because of cough) and you may decide that the patient should be screened for DR-TB. On the other hand, presumptive cases of DR-TB may be referred from local health facilities (for example, a TB patient for whom treatment has failed – that is, someone who is smear-positive after 5 months or more of treatment). You may presume that a TB patient has DR-TB if he or she has certain characteristics indicating a higher risk of the disease or if he or she is not responding to treatment.

If a patient has bacteriologically confirmed TB, or has been clinically diagnosed to have TB,^f you should assess the likelihood that the patient has DR-TB. In certain cases, a presumptive TB case may also be a presumptive case of drug resistance, e.g. a close contact with a known case of drug resistance. As the diagnosis of DR-TB is more complex and depends on different factors, you need to conduct a more in-depth interview with the patient to assess the likelihood that he or she has DR-TB.

By evaluating findings from pilot projects, WHO has compiled a list of risk factors for DR-TB. Persons who present with any of the risk factors listed below should be presumed to have DR-TB, and need an Xpert MTB/RIF test or LPA, culture and DST before, or at the start of, treatment; they should be referred to a DR-TB management centre for evaluation and diagnosis.

^d Patients likely to have MDR-TB should ideally be screened with rapid DST (Xpert MTB/Rif or LPA), which gives results in hours or days and can be done without culture. However, access to these tests is limited; hence this module also includes information on screening for MDR-TB using conventional methods, such as culture and DST using solid or liquid media.

^e Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF system for the diagnosis of pulmonary and extrapulmonary TB in adults and children: policy update. Geneva: World Health Organization; 2013.

^f A bacteriologically confirmed TB case is one from whom a biological specimen is positive by smear microscopy, culture or WHO-approved rapid diagnostics (WRD, such as Xpert MTB/Rif). All such cases should be notified, regardless of whether TB treatment has started.

A clinically diagnosed TB case is one who does not fulfil the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. This definition includes cases diagnosed on the basis of X-ray abnormalities or suggestive histology, and extrapulmonary cases without laboratory confirmation. Clinically diagnosed cases subsequently found to be bacteriologically positive (before or after starting treatment) should be reclassified as bacteriologically confirmed.

The list includes the following risk factors:

(The list and priority may vary in some countries depending on the epidemiology.)

- any patient before the start of a retreatment regimen (those having failed a regimen, relapsed or returned after loss to follow up, other previously treated cases);
- close contacts of DR-TB patients who have been diagnosed with active TB;
- patients not responding to first-line anti-TB treatment (remaining sputum smear-positive at the end of the intensive phase of a first-line anti-TB drug regimen);
- HIV-positive patients with active TB;
- cases from congregate settings where transmission rates of TB and hence DR-TB as well are high, e.g. prisoners, mine-workers, etc.;
- any TB patient coming from a group determined by the programme to have a significant risk for DR-TB, such as
 - patients with co-morbid conditions associated with malabsorption or rapid-transit diarrhoea;
 - residents of areas with a high DR-TB prevalence (DR-TB rates in many areas of the world can be high enough to justify routine DST in all new cases).

It is also important to investigate all HIV-positive patients who have symptoms of TB for drug resistance. HIV is not always a risk factor for DR-TB; however, TB may be missed when HIV-positive patients have negative sputum-smear microscopy results. Undiagnosed resistance may also lead to increased mortality in HIV-positive individuals.

Specimens from these at-risk patients should undergo Xpert MTB/RIF, culture and DST *before or at the start of treatment*.[§] An LPA may be used as per country policy if a sputum examination has already been done and found positive.

WHO also recommends that an Xpert MTB/RIF assay or culture and DST be performed *during treatment* for new and previously treated patients who remain sputum smear-positive at the end of the intensive phase of first-line treatment. Treatment is considered likely to be failing in these patients. The purpose of performing rapid or conventional DST at this stage is to detect drug resistance without waiting until the fifth month to change to appropriate therapy.

1.1 Determine whether the TB patient has previously taken anti-TB medicines and the outcome of previous treatment

All patients previously treated for TB are at high risk of having DR-TB.

First, the attending health-care worker needs to ask whether the patient has ever taken any medicine for the treatment of TB. If so, find out for how long the medicines were taken and

[§] Use these groups until you know which groups your national TB control programme considers to be most at risk based on country-specific data from surveillance for drug resistance. It is strongly recommended that TB control programmes collect representative data on drug resistance in new patients and for the different categories of retreatment patients (those for whom a new-patient regimen has failed, those for whom a retreatment regimen has failed, those who have defaulted and those who have relapsed), as well as other high-risk groups. The prevalence of resistance in specific risk groups may vary greatly across settings. Programmes should examine data on drug resistance in risk groups, as well as their own technical capacity and resources, to determine which groups should routinely have DST or MDR-TB regimens, or both.

whether the full regimen was completed, or at what point the treatment was stopped. A patient who has never taken anti-TB medicines (or who has taken them for less than 1 month) is considered a new case. Previously treated patients are those who have received 1 month or more of anti-TB treatment in the past. They are further classified by the outcome of their most recent course of treatment, as shown in *Figure 1*.

Figure 1 Patients previously treated for tuberculosis but who have active tuberculosis, classified by the outcome of their most recent treatment (patient registration group)

IF the outcome of the most recent course of treatment was	THEN the type of patient is
Cure or treatment completed	Relapse
Lost to follow up	Treatment after loss to follow up
Treatment failure	Treatment after failure
Unknown or undocumented	Other previously treated

The initial interview with the patient must be thorough to enable you to correctly assess the patient’s risk of DR-TB. It is critical to determine whether a patient has previously been treated for TB and may have acquired drug resistance. Take time to talk with the patient and listen carefully. Ask several questions to find out about all previous treatment, and explain why this information is important.

Ask:

- **Have you ever been treated for TB?**
- **Have you ever taken injections for more than 1 or 2 weeks for TB or symptoms suggestive of TB? Why?**
- **Have you ever taken a medicine that turned your urine orange or red?**

If a patient has had a course of injections lasting longer than 1 or 2 weeks, it is likely that the medicine administered was streptomycin. If the patient has taken a medicine that turned the urine orange or red, the medicine is likely to have been rifampicin. If you think a patient is hiding past treatment for TB, explain that new patients do not receive better medicines than previously treated patients. Explain that patients who have been previously treated need a stronger regimen to be cured than new patients do.

If a patient has been previously treated for TB, ask about the outcome of that treatment. Ask to see any documentation/records that the patient may have, such as a *Tuberculosis identity card* or *TB registration number* or a copy of the *TB treatment card*.

Ask the patient the following questions.

- **For how many months were you treated for TB?**
- **Did you complete the TB treatment or did you stop before completing it?**
 - If the patient stopped – **How long ago did you stop?**
 - If the patient completed treatment – **Did the health staff tell you that you were cured?**
- **Did a health worker tell you that your treatment did not work or that it had failed?**
- **Was that the first time you had been treated for TB?**
- **If not, how many different times have you been treated for TB?**
- **By whom were you treated (each time) and where?**
- **Do you have any records of your treatment(s)?**

Listen to the patient's answers carefully and ask follow-up questions to fully understand the patient's TB treatment history. If your facility has access to a register or records of previous treatment, use these to find out more about the patient's treatment history (*Figure 2*).

Not all patients in whom a regimen fails have DR-TB, and the percentage of those with DR-TB may depend on a number of factors, including quality of medicines used and whether directly observed treatment (DOT) was used throughout treatment. Whether the different types of previously treated patients (those who are lost to follow up, relapsed or for whom treatment has failed) are presumed to be moderately likely or highly likely to have DR-TB is decided by your national TB control programme using the best available data.

In most settings, a patient in whom treatment has previously failed is **highly likely** to have DR-TB. Patients who return to treatment after defaulting, or because they have relapsed after one course of treatment, are only moderately likely to have DR-TB. However, patients who return to treatment after defaulting from a **second or subsequent course** of treatment, or because they have relapsed after a **second or subsequent course**, are **highly likely** to have DR-TB.

If the patient has relapsed or is returning for treatment after being lost to follow up, find out whether the patient relapsed or was lost to follow up after one course of treatment or after a second or subsequent course of treatment.

Figure 2 Classification of tuberculosis (TB) patients according to history of previous treatment

TYPE OF TB PATIENT		DEFINITION
New		A patient who has never had treatment for TB, or has taken anti-TB drugs for less than 1 month
Previously treated	Relapse	A patient who was previously treated for TB, was declared cured or treatment completed at the end of their most recent treatment episode and is now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection)
	Treatment after failure	A patient who was treated for TB and whose treatment has failed
	Treatment after loss to follow up	A patient who was treated for TB and declared lost to follow up at the end of his/her most recent treatment episode
Other previously treated patients		Patients previously treated for TB but with an unknown or undocumented outcome for their most recent treatment episode

Patients with unknown previous TB treatment history do not fit into any of the categories listed above.

1.2 Determine the HIV status of the TB patient

All people living with HIV who are diagnosed with active TB should undergo presumptive testing for DR-TB, especially if they live in areas where the prevalence of MDR-TB is moderate or high. WHO recommends Xpert MTB/RIF as a primary diagnostic test for all adults and children living with HIV who have signs or symptoms of TB. Unrecognized DR-TB is associated with high mortality in people living with HIV. Therefore, it is important to know the HIV status of anyone presumed to have active TB and of known TB patients. Generally, HIV is not by itself a risk factor for DR-TB; however, TB may be missed when HIV-positive patients have negative sputum-smear microscopy results. Therefore, many programmes consider HIV-positive patients to have a high likelihood of having RR/MDR-TB, and perform an Xpert MTB/RIF test for all HIV-positive patients with presumptive TB. All patients diagnosed with HIV-associated TB should receive a rapid molecular test, including Xpert MTB/RIF or LPA, for the detection of potential drug resistance.^h HIV-infected patients with RR/MDR-TB should be tested for second-line anti-TB drug resistance.³

Ask the TB patient about his or her HIV status:

- **Do you know your HIV status?**
- **Do you have a written record of the test result?**

^h In case access to rapid molecular tests is limited, then all HIV-positive patients with presumptive TB or confirmed TB disease should be investigated for drug resistance using conventional culture and DST. Programmes without facilities or resources to test all HIV-positive patients suffering from TB for DR-TB should put significant efforts into establishing such capacity, especially if DR-TB rates are moderate or high.

If a patient knows his or her HIV status, ask to see written documentation of the test result and record the result and date of the test in the registerⁱ where you record presumptive TB cases in your facility. HIV status should be recorded only if written documentation is available. If the patient has not been tested, or if there is no documentation, or if the TB patient tested negative more than 3 months ago (a negative HIV test result from earlier than 3 months previous may be obsolete), recommend that the patient be tested (or retested) for HIV during the visit (*Figure 3*). Follow your national TB control programme's guidelines on recommending HIV testing to TB patients, and provide the appropriate counselling and testing for HIV.

HIV testing should be recommended on the same day as the initial sputum sample is collected for microscopy. Depending on the DR-TB management centre's capabilities, the patient may be tested and receive the result on the same day or may receive the results at the same time as the microscopy results become available.^j

If the patient is HIV-positive, ask whether the patient is taking medicines.

- **Are you receiving care for HIV?**
- **Are you on antiretroviral therapy (ART)?**
- **Are you taking daily co-trimoxazole (known as co-trimoxazole preventive therapy or CPT)?**
- **Are you taking daily medicine to prevent TB (isoniazid preventive therapy or IPT)?**

Ask for any documentation that the patient has about HIV treatment, for example, on an *HIV care/ART care card*, or obtain information from the clinic providing HIV care.

There may be problems in obtaining this information. A patient may not wish to reveal his or her HIV status. An HIV clinic may not provide information because of concerns about confidentiality. The patient may not know the date that he or she started ART or CPT. If the HIV clinic is not based at the DR-TB management centre, you may need to contact your coordinator about obtaining information from the clinic.

However, knowing the HIV status of a TB patient is important for making decisions about TB treatment; the patient's HIV status affects the likelihood of having DR-TB and determines whether the patient needs ART or CPT. If a TB patient is on ART, this affects the choice of anti-TB medicines and may affect where treatment is provided and who acts as a treatment supporter. Knowledge of a patient's HIV status is also important so that appropriate counselling and advice on DR-TB and HIV can be offered about prognosis, side-effects and associated diseases.

ⁱ Such a register may not be available in all settings.

^j Offer HIV testing *only if* your facility is capable of providing the appropriate counselling and testing. Staff at the facility *must* receive training and supervision to enable them to do the following:

- Give individuals sufficient information to make an informed and voluntary decision to be tested for HIV (that is, provide pretest counselling).
- Maintain patient confidentiality.
- Perform post-test counselling.
- Refer the patient to the appropriate services (in case of a positive HIV result).

Providing separate clinical evaluation for TB and HIV means that patients will make more visits.

Figure 3 **Recommending HIV testing during the diagnostic process to patients presumed to have drug-resistant tuberculosis (DR-TB)**

Ask the TB patient about his or her HIV status. If the patient has not been tested, or if there is no documentation, recommend that the patient be tested (or retested) during the visit. Inform the patient that a previous negative HIV test result may be obsolete. If the TB patient tested negative more than 3 months ago, recommend another HIV test.

A clinician, nurse, antiretroviral therapy aide or other counsellor, or another health worker who has been trained for this task, can provide the pretest information, obtain informed consent and do the test in the clinic. This is more efficient than referring patients elsewhere for testing and counselling, and it is more likely that patients will be tested. Group education sessions may be used to provide pretest information and counselling.

Advising a person suspected of having DR-TB or a DR-TB patient to have an HIV test includes several important components, often referred to as the 3C's: counselling, confidentiality and consent. When giving pretest information, the health worker:

1. provides key information on HIV/AIDS and its interaction with TB;
2. provides key information about HIV testing, such as the clinical and preventive benefits of knowing one's HIV status, information on confidentiality, and the available services and costs;
3. confirms the willingness of the patient to proceed with the test and seeks informed consent; if needed, the health worker should also provide additional information and refer the patient for additional counselling.

When the results of the test become available, inform and counsel the patient accordingly. All patients **must** be counselled when the test results are given, regardless of the result. Also, record the test result in the *Register of TB suspects* as:

(Pos.) positive

(Neg.) negative

(I) discordant or inconclusive (when two tests are done and one is positive and the other is negative)

(ND) not done.

1.3 Determine whether the TB patient was exposed to a case with documented DR-TB

People who develop active TB after exposure to a patient with documented DR-TB should be presumed to have DR-TB. A new TB case who is a close contact of a known case with DR-TB has a **high likelihood** of having DR-TB. A close contact refers to a person who is not in the household but has shared an enclosed space, such as a social gathering place, workplace

or facility, for extended periods during the day with the index case during the 3 months before commencement of the current treatment episode.

A household contact refers to a person who has shared the same enclosed living space for one or more nights or for frequent or extended periods during the day with the index case during the 3 months before commencement of the current treatment episode. Determine whether the TB patient is, or may be a contact of, someone who has or had DR-TB.

Ask the patient the following questions.

- **Has anyone in your family ever had TB or DR-TB?** (*Ensure that the patient understands that you would like to know about this even if someone was diagnosed long ago.*)
- **Has any close contact, for example, someone that you work with each day, ever had TB or DR-TB?**
- **If yes, where and by whom was this person treated? How long did the treatment last?**
- **If yes, what were the results of treatment?**

You may also presume that someone has DR-TB when you investigate close contacts of DR-TB patients who are enrolled in treatment at your DR-TB management centre. If a DR-TB patient mentions that a household member or other close contact has developed TB symptoms, you must quickly investigate.

1.4 Determine the quality of the TB patient's previous treatment

A patient whose treatment was of poor quality has an increased risk of DR-TB. Patients treated in the private sector often encounter barriers to good treatment.

Ask the patient the following questions.

- **Were you treated at a public clinic or by a private provider?**
- **If by a private provider then are there any records of the drugs prescribed and source of those drugs?**
- **Was your treatment taken regularly or was it "on and off"?**
- **Was your treatment directly observed? Who observed your treatment? How many days per week did this person observe your treatment? For example, was your treatment observed for every dose, every second dose, once per week?**
- **How many medicines did you take?**
- **Where did you get the medicines? Did you have to buy them?**

Listen to the patient's answers carefully and ask follow-up questions to fully understand the quality of the patient's previous TB treatment. If the patient took medicines irregularly, if the treatment was not directly observed, if the patient had to purchase the medicines, if the patient took fewer medicines than recommended, if the patient received treatment from a private provider who may not have used a standard treatment regimen, or if the patient used medicine of questionable quality, it is likely that the previous treatment created drug resistance. If you decide that the previous treatment seems to have been of **poor quality**, consider that the patient is **likely** to have DR-TB.

1.5 Ask other questions to identify presumptive cases of DR-TB

In your country, there may be additional important factors that make it likely that a patient has developed DR-TB. TB patients observed to have an increased risk of RR/MDR-TB in certain settings are those:

- treated in a programme that operates poorly (especially with recent or frequent problems with the continuous availability of medicines);
- with a history of using anti-TB medicines of poor or unknown quality;
- whose treatment in the private sector failed;
- who are exposed in institutions where there was an outbreak of DR-TB or a high prevalence of the disease (such as prisons or mines);
- with co-morbid conditions associated with malabsorption or rapid-transit diarrhoea;
- who have type-2 diabetes mellitus.

Ask TB patients questions about any of the factors described above or other factors that are important determinants of drug resistance in your country to ascertain whether the patient is likely to have DR-TB and should be screened with Xpert MTB/RIF.



Now do Exercise A – written exercise

When you reach this point in the module, turn to Exercise A, and read the instructions. When you have finished, review your answers with a facilitator.

2. Collect and send sputum samples for testing for drug resistance

Collect two sputum samples (also called specimens) as described below from a presumptive case of DR-TB and send the samples to the laboratory for Xpert MTB/RIF, culture and DST. If the laboratory is easily accessible, you may send the presumptive case directly to the laboratory instead. If the patient is very ill, refer him or her immediately to a clinician (or the nearest hospital) for assessment and care, with instructions for preventing the spread of infection, specifically cough etiquette and use of a mask. Do not delay the treatment of a very ill patient in order to obtain sputum samples.

2.1 Obtain cooperation from the person presumed to have DR-TB

When a person is presumed to have DR-TB, explain the reason for sputum examination and enlist the person's cooperation for obtaining sputum for testing. Explain that Xpert MTB/RIF and culture testing are essential for detecting TB; they are also the first two steps needed to run DST, the test that determines whether the patient's strain of TB is resistant to first-line medicines.

2.2 Collect sputum samples from the presumptive DR-TB case

Follow your country's guidelines on sputum collection. General guidelines and a schedule are given in Annex A. Two sputum samples are needed for baseline investigations of DR-TB^k for performing sputum microscopy as well as rapid molecular testing. (Only one sample will be required for follow up.) Collect the samples in a single day or over a 2-day period.^l

The first sample should be collected "on the spot", while the person is still at the DR-TB management centre. Give the presumptive case instructions on how to produce and collect sputum. Explain why the sputum is needed, and show the patient how to cough up sputum and handle the container. The patient should go outdoors or to a well-ventilated area to collect the sample, thereby reducing the risk of exposing health-care workers and other patients to the disease. If possible, observe and guide the patient during sample collection, but do not stand in front of the patient while he or she coughs up the sputum. The patient should give the sample to you. Give the presumptive case another labelled container for a second sample for same-day collection or to take home and use the next morning.

Example

TB specimen	
Facility:	<u>Veld DR-TB management centre</u>
Lab no.:	_____
Name:	<u>Sam Belhow</u>
Date collected:	<u>1 Feb 2013</u>

^k Two samples should be collected if performing AFB microscopy, or a single sample for Xpert according to the country policy.

^l These modules assume that two samples will be collected during 2 days. However, WHO also recommends front-loaded smear microscopy in which two specimens are collected and examined on the same day that a patient presents; the advantage of this is that patients who are diagnosed with TB can begin treatment on the same day. Patients with negative smears can be asked to return with a morning specimen the next day. This method reduces the cost of visits incurred by patients and reduces the proportion of patients dropping out of the diagnostic process.

Sample two should be collected by the presumptive TB or DR-TB case upon waking up the next morning. The presumptive TB or DR-TB case brings this second sample to you at the health facility.

Remember:

- **Label the containers (not the lids) before collecting the sputum samples.**
- **Collect sputum in a well-ventilated area, preferably outdoors or in a sputum-collection booth, away from other people.**
- **Check whether the sample contains sufficient sputum, not just saliva. If it does not, ask the presumptive case to add more.**
- **After collecting the sputum, be sure that the lid is closed tightly. Wipe off the outside of the container with disposable tissue, if needed.**
- **Wash your hands thoroughly with soap and water.**

Tell the person presumed to have DR-TB when to return to the health facility for the results. Also explain that culture examination may be performed regardless of the results of the Xpert MTB/RIF test.

Some people presumed to have DR-TB may not be able to produce sputum for examination. This often occurs with children, patients with minimal cough and some HIV-positive patients. In these cases, alternative measures to collect sputum should be used, and the presumptive case should be referred to a specialized facility where these procedures can be performed. It is beyond the scope of this module to describe these measures.

2.3 Fill out the Request for examination of biological specimen for TB

The *Request for examination of biological specimen for TB* form is used to request laboratory tests to detect TB or DR-TB. One form can be used to request for all the tests for one presumptive TB or DR-TB case. Specimens other than sputum, obtained from other parts of the body, may also be sent for microscopy, culture and DST using this form.

Complete the top part of the form. Under the heading “Reason for examination” tick (✓) the box for diagnosis, and tick when the patient is a presumptive RR/MDR-TB case. Tick the boxes of the tests requested. Indicate what kind of specimen was collected (sputum or other). Specimens should be sent for laboratory testing on the day of collection.

In the next example, the presumptive TB case was referred as lost to follow up; the health worker marked Xpert MTB/RIF, culture and DST along with the diagnosis box. The laboratory will fill out the bottom portion with the results as they become available.

Example 1

Request for examination of biological specimen for TB

Treatment Unit: Veld DR-TB management centre Date of request: 1 February 2013
 Patient Name: Sam Belhow
 Age (years): Sam Belhow Date of Birth: 28 Jan. 1989 Sex (mark one): M F
 Patient Address: 1220 Old Mail Road, Centre City, House number 36
 Patient Telephone: 01234567

Reason for examination (mark one):
 Diagnostic Presumptive RR-TB/MDR-TB: Y N
 Follow-up If follow-up, month of treatment: _____
 Sputum Other (specify): _____
 HIV infection Y N Unknown

Patient previously treated for TB (mark one): Yes No Unknown

If information available specify if

New	After failure of 1st treatment with 1st-line drugs
Relapse	After failure of retreatment regimen with 1st-line drugs
After Loss to follow-up	Other

Tick diagnosis for presumptive cases of RR-TB/ MDR-TB.

Test requested: Microscopy Xpert MTB/RIF Culture Drug susceptibility Line probe assay

Name, signature and telephone of requestor: Dr Morse

RESULTS (to be completed in the laboratory)

Microscopy results

Date sample collected (to be filled by requestor)	Specimen type	Laboratory serial number/s	Visual appearance (blood-stained, mucopurulent or saliva)	Result (check one)				
				Negative (0 AFB/100HPF)	1-9/100HPF (scanty; report number of AFB)	+ 10-99 AFB/100HPF	1-10 AFB/HPF	>10 AFB/HPF

Tick all the required laboratory tests

Examined by (Name & signature): _____ Date of result: _____

Xpert MTB/RIF test result (to be completed in the laboratory)

Date collected (to be filled by requestor)

M. tuberculosis			Rifampicin resistance		
Detected	Not detected	No result / Invalid / Error	Detected	Not detected	Indeterminate result

Examined by (Name & signature): _____ Date of result: _____

Culture results (to be completed in the laboratory)

Date sample collected (to be filled by requestor)	Media used (liquid or solid)	Laboratory serial number/s	Result (check one)						
			Negative (0 colonies)	1-9 <10 colonies	+ 10-100 colonies	++ >100 colonies	+++ Innumerable / confluent growth	NTM ¹	Contaminated

Examined by (Name & signature): _____ Date of result: _____

Drug-susceptibility test (DST) and line-probe assay (LPA) results (to be completed in the laboratory)

Date sample collected (to be filled by requestor)	Media used (liquid or solid media; direct or indirect LPA)	DST laboratory serial number/s	H	R	E	S	Am	Km	Cm	FQ	Other	Other	Other	Other

R: Resistant; S: Susceptible; C: Contaminated; - Not done

Examined by (Name & signature): _____ Date of result: _____

¹ Non-tuberculous mycobacteria

2.4 Pack the samples and send them to the laboratory

Keep the sputum samples in a refrigerator or in as cool a place as possible until they are transported to the laboratory. Samples should be sent to the laboratory as single specimens, each sample in a separate container. Send the samples to the laboratory as soon as possible.

From the refrigerator, transfer the sputum containers into a transport box. The sputum samples will go with the individual *Request for examination of biological specimen for TB* form for each patient. The delivery process should ensure that the specimens reach the laboratory within 24 hours of collection. If the samples will not be picked up by the messenger on the same day, keep the samples refrigerated or in the transport box with refrigerants. Make sure the refrigerants are replaced periodically to keep the specimens cool.

Prepare a dispatch list to accompany each transport box. The dispatch list should identify the sputum samples contained in the box. Before sending the box to the laboratory, do the following:

- Check that all containers have been closed and wiped clean.
- Check that the dispatch list states
 - the correct total number of sputum containers in the box,
 - the identification numbers on the containers, and
 - the name of each patient.
- Check that a *Request for examination of biological specimen for TB* form has been enclosed for each patient.
- Close the box carefully.
- Write the date on the dispatch list.
- Put the dispatch list in an envelope and attach the envelope to the outside of the transport box.

2.5 Record data in the presumptive TB and DR-TB case register or on the TB or Second-line TB treatment card

Your DR-TB management centre may keep a register of presumptive cases of TB or for TB and DR-TB cases, or both. The presumptive TB and DR-TB case register is a record of the people seen at a facility who are presumed to have TB; this register is particularly useful for monitoring case-detection activities and the results of all sputum examinations. Record the presumptive DR-TB case in the register if he or she is not presently receiving TB treatment. Be sure to write down a complete name and address so that the presumptive TB or DR-TB case can be located if the result is positive, but he or she does not return. An example of a presumptive TB and DR-TB case register can be found in Annex B.

For presumptive DR-TB cases that are already receiving treatment for TB, find the patient's *TB treatment card* and note in the "Comments" section that sputum was sent for Xpert MTB/RIF, culture and DST.

2.6 Complete and return the bottom part of the presumptive DR-TB referral form (if the presumptive DR-TB case was referred from another facility)

When a local health facility refers a person presumed to have DR-TB to a DR-TB management centre for evaluation, a health worker completes and sends a referral letter and the patient's *TB treatment card* along with the patient. Please see an example of a *DR-TB referral form* below.

When a person presumed to have DR-TB is received at the DR-TB management centre with this form (or one similar to it), complete the bottom section of the form and send it back to the local health facility. This lets the staff there know that the referral was successfully completed.

In the example of the *DR-TB referral form*, the top section was completed by the health facility, and the bottom section by the DR-TB management centre. It should be detached and sent back to the health facility.

3. Collect and record data about the presumptive DR-TB case

Health-care workers at the DR-TB management centre perform the steps in this section when they identify a presumptive case of DR-TB or receive a presumptive case that has been referred by a local health facility. They will

- (1) record information about the state of investigation of the DR-TB case, the person's condition and medical details in the patient's medical record; and
- (2) update the results in the centre's *Register of presumptive TB and DR-TB cases* (see an example of such a register in Annex B).

Example of a form that can be used to refer patients being evaluated for DR-TB

Presumptive DR-TB referral form

Date of Referral (dd/mm/yy) 05/05/2013

Name of patient Josephus Esna

Age 34 Last Sex: M F First Middle

Address 77 Kingsway Park, Veld Tel. No. _____

Referring facility

Name and address Panola Health Centre, 766 Auburn Street

Tel. No. 2354-266 Fax No. 2354-266

City Veld Referring MD Dr. Jansen

Name of DR-TB management centre where patient will be sent Veld DR-TB management centre

DR-TB Risk Group:

Type of MDR-TB suspect. Please tick.

- New patient regimen failure
- HIV-positive TB patient
- Retreatment regimen failure
- Likely Failure of Retreatment regimen
- Lost to follow up
- Active TB after contact with MDR-TB case
- Relapse of New patient regimen
- Treatment failure of privately treated case
- Relapse of Retreatment regimen
- Other (specify)

TB Treatment History:

TB Diagnosis and treatment

Date diagnosed	Where	By whom	Anti-TB drugs taken	Duration	Outcome
1 May 2013	Panola Health C.		New patient regimen started 1 May 2013		

Attach a copy of the patient's present TB treatment card (if it exists)



To be completed by DR-TB management centre receiving referred patient:

Name of DR-TB management centre Veld DR-TB management centre

District Veld Date 8 May 2013

Name of patient Esna Josephus District TB No. _____

The above patient reported at this facility on 7 May 2013 (date)

Signature Lillian Kuwebe Position Nurse Sup.

Send this part back to the referring or transferring facility as soon as patient has reported.

3.1 Inform the presumptive TB case about the possible diagnosis of DR-TB and steps to be taken

The person presumed to have DR-TB may be scared or nervous about what disease he or she may have. Think about how you might feel if you were the patient. All communication must be kind, supportive and medically correct.

People presumed to have the disease should be informed clearly and sensitively about the possibility that they have DR-TB. Explain in simple terms what drug resistance is and what it means for treatment. Reassure the patient that DR-TB can be cured, but that it will take dedication and many months of treatment. DR-TB is a serious disease and treatment is given free of charge. It is important to ensure that the patient will be ready to start treatment once it is approved by the review panel. Explain that the approval process may take some time (give the patient an idea of how long this may be) but the patient should be ready to begin treatment in the near future.

This is an important meeting with the patient who may have DR-TB. At this initial discussion, you will begin to provide important information and support, and tell the patient about the treatment. This is the beginning of a long relationship with the patient, one that is essential for the successful treatment of the disease. You should provide information on the following:

- the diagnosis of DR-TB;
- the diagnostic and baseline tests that may be done (Xpert MTB/RIF, microscopy, culture, DST and others);
- timelines for receiving results;
- the next steps to be taken (after approval from the review committee, the patient may continue his or her present treatment, begin treatment with second-line drugs, or begin a retreatment regimen);
- what treatment is like;
- ways to prevent transmission of TB and DR-TB to close contacts.

See Module D for more information.



Now do Exercise B – written exercise

When you reach this point in the module, turn to Exercise B and read the instructions. When you have finished, review your answers with a facilitator.

4. Determine whether DST results will be available soon enough to guide the choice of a treatment regimen

The laboratory capacity and type of test performed in each country will determine when the DST results will be available for confirming or excluding a diagnosis of DR-TB and thereby for deciding the best regimen for an individual patient. In settings where rapid DST is used, results are available within hours or days, and those results should guide the choice of a treatment regimen. If RR-TB or MDR-TB is confirmed, the patient can be prescribed a standardized or individualized MDR-TB regimen. If RR-TB or MDR-TB is excluded, a standard first-line anti-TB treatment regimen can be begun.

In several settings, however, only conventional DST is available, and it provides results in months. In these cases, the physician must consider treatment options at two points: when multidrug resistance is presumed but laboratory confirmation is pending, and after multidrug resistance has been confirmed. Initially, a treatment regimen must be selected based on the **presumed likelihood** of DR-TB in that patient. The patient may need to start an empirical second-line drugs regimen while DST results are awaited. These modules use the term “empirical” to refer to the initiation of treatment prior to determination of a firm diagnosis of DR-TB. Empirical regimens can be used for both standardized and individualized treatment strategies. When DST results are received (weeks or months later), if they indicate that a change in regimen is needed, the regimen can be modified at that time.

Now study *Figure 4*. The diagram shows how diagnosis and treatment are intertwined in a setting where conventional DST is used because the TB patient must start treatment before the diagnosis of MDR-TB is confirmed.

- If rapid DST is available in your DR-TB management centre, the physician will use those results to make a diagnosis and prescribe an anti-TB regimen. This is the situation shown on the left side of *Figure 4* in shaded boxes and described in section 8.
- If only conventional DST is available in your DR-TB management centre, the physician will prescribe an empirical treatment regimen based on the patient’s presumed risk of DR-TB, clinical condition and country policy, and await the results of DST. When the results are received, the regimen can be adjusted if needed. These steps are shown on the right side of *Figure 4* and described in sections 5–7 below.

Figure 4 **Diagnosing drug-resistant tuberculosis (DR-TB) at a DR-TB management centre**

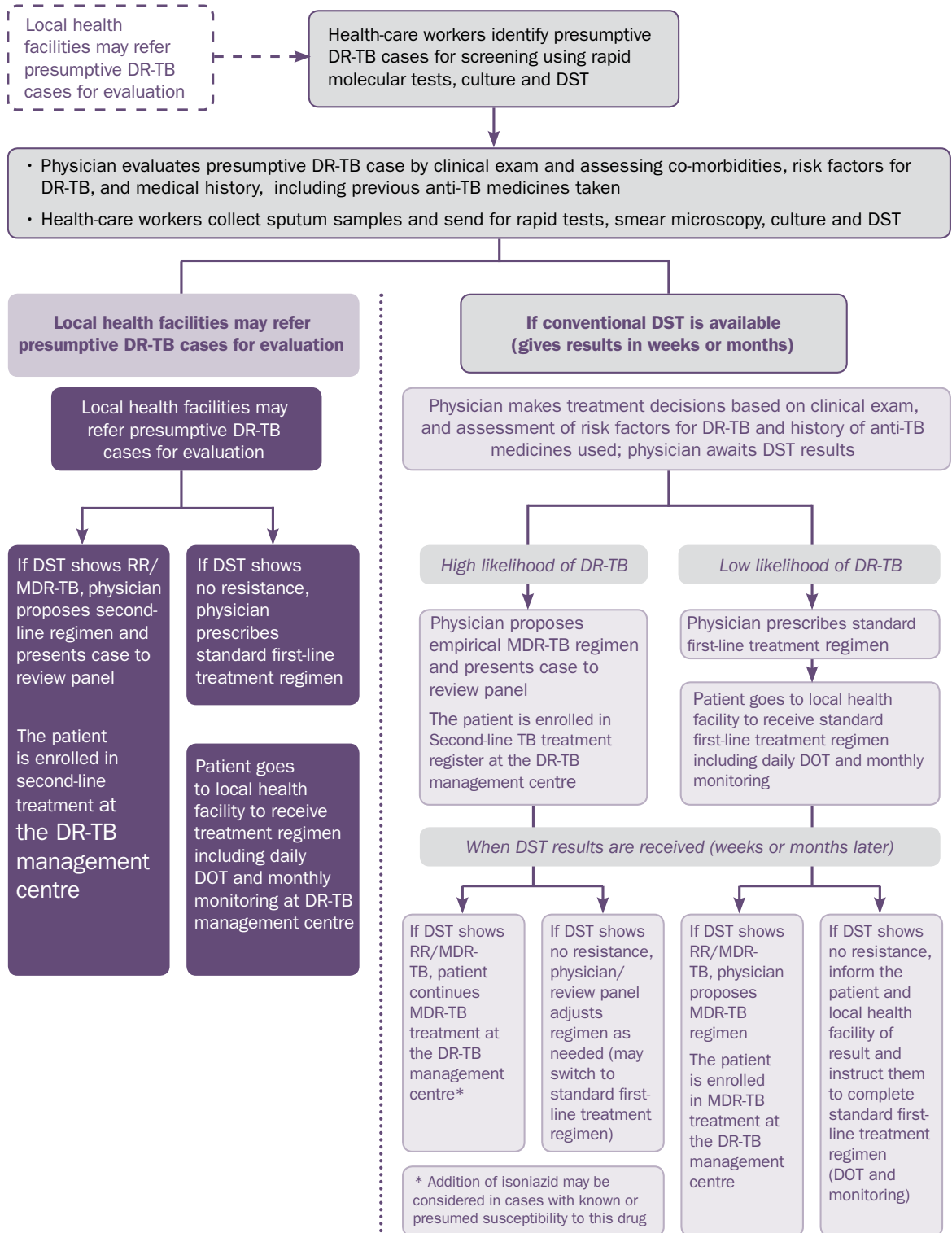
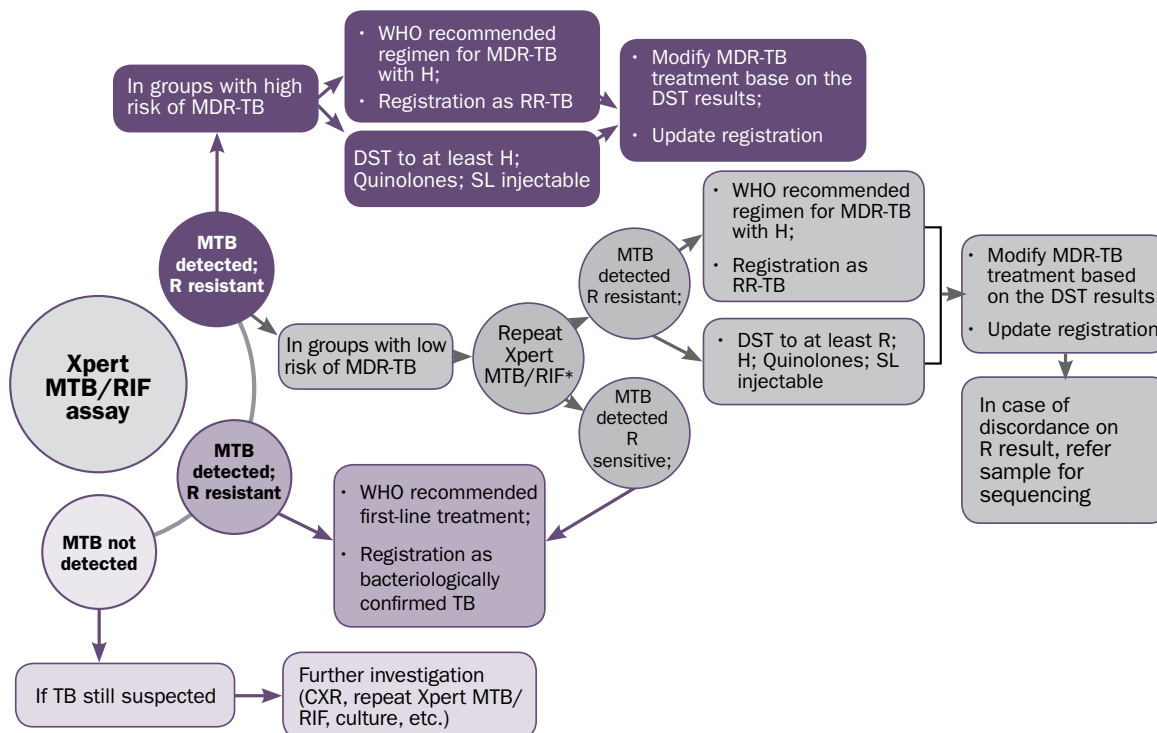


Figure 5 **Triage of individuals presumed to have TB using Xpert MTB/RIF where available⁴**



* Done on a fresh sample. If LPA is available at the site and sample is smear positive, LPA can be used for the repeated testing

5. While awaiting DST results, the physician makes treatment decisions

The DR-TB management centre physician, who is in charge of the case, makes treatment decisions while awaiting the DST results; these decisions are based on the clinical examination of the patient and assessment of risk factors for DR-TB, and whether the patient has previously taken anti-TB medicines. Obtaining specimens for culture and DST, and awaiting the results should not delay the start of therapy, specifically in settings where a WHO-approved rapid diagnostic (WRD) test^m like Xpert MTB/RIF is not available. Empirical regimens should be started promptly. This is especially important if the patient is seriously ill or the disease is progressing rapidly. Placing a patient on an empirical regimen is done to prevent clinical deterioration in groups of patients that are **highly likely** to have disease that is drug resistant. The therapy should also make the patient less infectious, thus decreasing the risk of transmission to contacts.

^m Most commonly available WRD include Xpert MTB/Rif and line-probe assay (LPA). However, for performing LPA, it is essential to have a prior positive sputum microscopy result.

WHO recommends administering a regimen with first-line medicines to groups of patients that are **moderately likely or unlikely** to have disease that is drug resistant. The physician in charge of the case will decide the patient's likelihood of having DR-TB and propose a regimen to begin treatment while awaiting the DST results.

5.1 If the patient has a high likelihood of RR/ MDR-TB, the physician should take steps to start an appropriate regimen promptly

If it is highly likely that a patient has RR- or MDR-TB then the physician should start an appropriate regimen promptly. The physician should take the steps described below (these steps are described in detail in Module C).

- The physician proposes an appropriate empirical regimen (may be standardized or individualized based on whether the patient has been previously treated for TBⁿ).
- The physician presents the patient's case to the review panel for approval of a regimen consisting of second-line drugs (presentation includes information on the patient's clinical condition and history).
- The patient is enrolled in the *Second-line TB treatment register* at the DR-TB management centre.

(In the case of an emergency, a physician may start a patient on treatment and present the case to the review panel afterwards.)

5.2 If the patient is moderately likely or unlikely to have DR-TB, start a standard first-line anti-TB treatment regimen

A standard regimen with first-line drugs should be started if the patient is only moderately likely to have DR-TB or is unlikely to have it. In these cases, the physician or other health worker:

- prescribes a standard first-line anti-TB treatment regimen;
- informs the patient that when the results of DST are available, he or she will be informed and, if needed, the regimen will be adjusted;
- sends the patient back to the local health facility for the standard first-line anti-TB treatment regimen or treats the patient as an outpatient at the DR-TB management centre.

ⁿ Patients being treated for MDR-TB may have regimens that are standardized – that is, a fixed regimen based on the results of DST for a sample of patients in the country or region, and that is similar to WHO's recommended standard treatment regimens – or regimens that are individualized – that is, designed to take account of the specific patient's DST results, history of treatment with anti-TB medicine, DST results of the index case, etc.

Figure 6 **Selecting an empirical tuberculosis (TB) treatment regimen**

IF →		AND →	THEN
the TB patient is		the likelihood of RR/ MDR-TB is	the recommended regimen is
New		Low	New-patient INITIAL FLD regimen (Refer if on ART) ^a
		But if the patient is a contact of a known RR/MDR-TB case, the likelihood is high	MDR-TB regimen
Previously treated	Treatment after failure	High	MDR-TB regimen
	Treatment after being lost to follow up	High	MDR-TB regimen
	Relapse after second or subsequent course of treatment	High	MDR-TB regimen
Transfer in		Continue current treatment regimen	
Other previously treated patients		Estimate using best information about the outcome of the patient's previous treatment	If the risk is low, then use new-patient regimen If the risk is moderate, then use retreatment regimen (refer if on ART; ^a refer if pregnant ^b) If the risk is high, then use MDR-TB regimen

ART – antiretroviral therapy; FLD – first-line drugs; MDR-TB – multidrug-resistant TB; RR-TB – rifampicin-resistant TB

^a If the patient is already on ART, refer to a clinician for prescription of an anti-TB treatment regimen; the clinician should consider the possibility of interaction between ART and anti-TB medicines.

^b Streptomycin is not safe for use during pregnancy; only a clinician should prescribe a regimen for a woman who is or may be pregnant.

6. Receive the results of diagnostic tests

The laboratory will send the report of the rapid DST or smear microscopy results and later, the culture and DST results. Whenever you receive results, you should record them in the appropriate records at the DR-TB management centre, and consider the implications of the results for the care of the patient.

6.1 Record the laboratory results

Read the Results section on the *Request for examination of biological specimen for TB* form. This provides information on whether each sample (or specimen) was found positive or negative for acid-fast bacilli (AFB).

Find the presumptive TB case's entry in the *Register of presumptive TB and DR-TB cases* (see Annex B). Record the results for each of the samples in the columns labelled *Results of Xpert MTB/RIF* and *sputum examinations*. If an HIV test result has been received during the time since you first entered the presumptive TB case in the register, record it.

For a presumptive DR-TB case who is already receiving treatment for TB, record the smear results on the patient's *TB treatment card*.

Example of a laboratory report of microscopy results

Microscopy results (to be completed in the laboratory)

Date sample collected (filled by requestor)	Specimen type	Laboratory serial number(s)	Visual appearance (blood-stained, mucopurulent or saliva)	Result (tick one)				
				Negative (0 AFB/100 HPF)	1-9/100 HPF (scanty; report no. of AFB)	+	++	+++
31 Jan 2013	Sputum	63	MP			✓		
1 Feb 2013	Sputum	67	MP				✓	

Find the smear results here.

Examined by (name and signature): _____

Record this date on the *TB treatment card* or register of presumptive cases.

Date of result: 4 Feb 2013

6.2 Take appropriate action in response to the laboratory results (see Figure 5)

- **If the Xpert MTB/RIF result is positive for TB**, this means that the presumptive TB case has been confirmed to have pulmonary TB.
- **If the Xpert MTB/RIF result is also positive for rifampicin resistance**, this means the TB case is also highly likely to have DR-TB if previously treated or otherwise considered to be at high risk of DR-TB based on country epidemiology. The patient should be registered as an RR-TB case and treated with second-line drugs while awaiting culture and DST results for additional resistance patterns. In cases considered at low risk of DR-TB, the initial rapid test may be followed by another rapid test (Xpert MTB/RIF or LPA) on a different

sputum sample to eliminate any pre- or post-analytical errors that may have occurred while performing the initial test, depending on the country policy.

- **If any of the sputum specimens are smear positive**, this means that the presumptive DR-TB case has infectious pulmonary TB. The patient should be treated for TB while awaiting the DST results. Inform the patient about infection control precautions that should be used while at home to avoid spreading TB to those around him or her. Important messages to give to the patient are described in Module D.
- **If all specimens are smear negative**, this means that the patient is not highly infectious but may still have TB (either drug susceptible or drug resistant). This will be confirmed by the result of the rapid molecular test or conventional culture and DST.

In case rapid molecular tests are not available and the smear microscopy results are negative, the laboratory will process the specimens to isolate and identify *M. tuberculosis* by culture and perform DST to anti-TB drugs. Because there are many cases of smear-negative but culture-positive TB, this step is important for diagnosing active TB. When DR-TB is presumed, it is critical to confirm or exclude the suspicion with DST, which can be done from a positive culture. Rapid DST (an LPA) can be performed from a positive smear or positive culture.

6.3 Record the Xpert MTB/RIF, LPA or culture results in the presumptive TB and DR-TB case register or on the patient’s TB or Second-line TB treatment card

Upon receiving the results of a presumptive case that has not yet been diagnosed with TB or DR-TB, find the case’s name in the presumptive TB and DR-TB case register. Record the results in the columns under the label “*Results of Xpert MTB/RIF and sputum examinations*”. In the “Observations” column write the date that the sputum was collected for **Xpert MTB/RIF test and note that it was Xpert MTB/RIF**.

For a presumptive DR-TB case that is already receiving treatment for TB, record Xpert MTB/RIF results on the patient’s *TB treatment card* (see example below).

When the culture results for a presumptive case become available, find the case’s name in the presumptive TB and DR-TB case register. Record the culture results in the “Culture” column, and also write down the date and the sample number.

Example of a laboratory report of culture results

Culture results (to be completed by the laboratory)

Date sample collected (filled by requestor)	Media used (liquid or solid)	Laboratory serial number(s)	Result (tick one)					NTM	Contaminated
			Negative (0 colonies)	1-9 (<10 colonies)	+(10-100 colonies)	++ (>100 colonies)	+++ (Innumerable/confluent growth)		
31 Jan 2013	Liquid	63				✓			
1 Feb 2013	Liquid	67				✓			

Examined by (name and signature): _____

Date of result: 16 Feb 2013

Both samples were culture positive for *M. tuberculosis*.

Example of sputum and culture results recorded on patient’s TB treatment card

Month of Treatment	Sputum Microscopy			Month of Treatment	Culture		
	Date	Sample Number	Result		Date	Sample Number	Result
Prior				Prior			
0	31-1-2013	63/67	++	0	31-1-2013	63/67	++
1				1			
2				2			
3				3			
4				4			
5				5			
6				6			
7				7			
8				8			
9				9			

6.4 Take appropriate action in response to the laboratory results

- **If a patient has an Xpert MTB/RIF test result that is positive for *M. tuberculosis* and negative for rifampicin resistance**, this means that the presumptive DR-TB case has been confirmed to have pulmonary TB but does not have RR/MDR-TB.

 - Explain to the patient that the Xpert MTB/RIF test was positive for TB but that the illness is not RR-TB or MDR-TB.
 - If the patient has not yet started TB treatment, locate the patient, open a *TB treatment card* and begin first-line treatment according to the national guidelines.
 - If the patient is on TB treatment with first-line medicines, continue the treatment.
 - A patient who has already begun DR-TB treatment requires a change to a first-line treatment at this point.

- **If a patient has an Xpert test result that is positive for *M. tuberculosis* and positive for rifampicin resistance**, this means that the presumptive DR-TB case has been confirmed to have rifampicin resistance, which is a strong indicator of MDR-TB.

 - Explain to the patient that the rapid test was positive for TB and that the illness is drug resistant.
 - If the patient has not yet started second-line treatment, locate the patient, present his or her case to the review panel, open a *Second-line TB treatment card* and begin a treatment regimen with second-line drugs.
 - If the patient is on TB treatment with first-line medicines, a change in treatment regimen is required. The physician will consult the review panel for the appropriate change in regimen.
 - A patient who has already begun MDR-TB treatment requires no change at this point.

- **If a patient has at least one sputum culture that is positive for *M. tuberculosis***, this means that the presumptive DR-TB case has been confirmed to have pulmonary TB.

 - Explain to the patient that the culture was positive, and that the final stage of diagnostic testing will be performed in the following weeks to determine whether the patient’s illness is drug resistant. Let the patient know that he or she will be contacted as soon as the DST results are available.

- If the patient has not yet started TB treatment, locate the patient, open a *TB treatment card* and begin treatment according to the national guidelines. Continue to monitor the patient in case he or she needs to begin an empirical MDR-TB regimen based on the criteria in national guidelines^o before the DST results are available.
- If the patient is on TB treatment with first-line medicines, continue to monitor the patient in case he or she needs to begin an MDR-TB regimen before the DST results are available.
- A patient who has already begun MDR-TB treatment requires no change at this point.

If all the test results were negative, the review panel will have to decide about whether or not to start treatment.

6.5 Record (rapid) DST results on the patient's TB treatment card

The laboratory must ensure that (rapid) DST results that confirm cases of RR- or MDR-TB are reported by the fastest method, such as a telephone call, with the *Result* form to follow.

To record the (rapid) DST results, find the patient's *TB treatment card* or *Second-line TB treatment card*. Record the results on the patient's card (in the DST section in countries that use routine culture or in the Comments section in those countries that do not use routine culture).

Example of a laboratory report of Xpert MTB/RIF results

Xpert MTB/RIF test result (to be completed by the laboratory)

Date sample collected: 5 April 2013

M. tuberculosis: Detected Not detected Invalid / No result / Error

Rifampicin resistance: Detected Not detected Indeterminate result

Examined by (name and signature): John Davis

Date of result: 7 April 2013

Example of a laboratory report of DST results

Please refer to the Glossary in Module A for an explanation of the abbreviations used for the medicines in this example.

^o In some high-risk groups, such as those with failure of retreatment regimen, contacts of known MDR-TB cases, failure of first-line treatment, the national guidelines may recommend starting second-line treatment before the DST results are available.

Drug-susceptibility test (DST) and line-probe assay (LPA) results (to be completed by the laboratory)

Date sample collected (filled by requestor)	Method ^a	Laboratory serial number(s)	Results ^b (mark for each drug)													
			H	R	E	S	Am	Km	Cm	FQ:	Other:	Other:	Other:	Other:		
31 Jan 2013	Liquid media DST		R	R	R	S										

This patient has a strain of TB that is resistant to isoniazid, rifampicin and ethambutol, and susceptible to streptomycin.

^a Specify: solid media DST; liquid media DST; direct LPA; indirect LPA

^b Results codes: R = Resistant S = Susceptible C = Contaminated - = Not done

Examined by (name and signature): _____

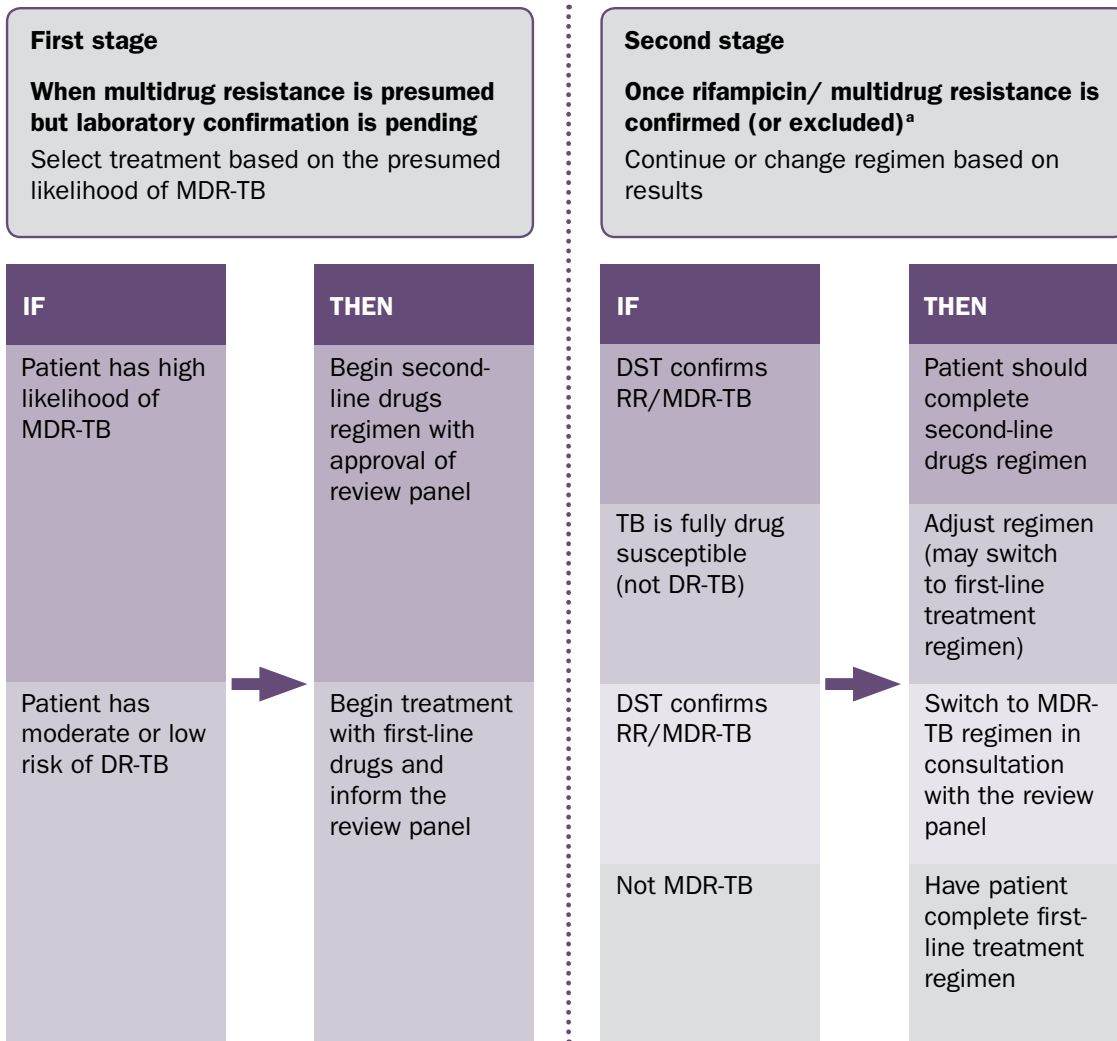
Date of result: 2 March 2013

7. Choose an appropriate regimen based on the DST results

The DST results will confirm or exclude the diagnosis of DR-TB in the patient and will provide specific information on which medicines the patient’s strain is susceptible or resistant to. At a minimum, the laboratory should provide DST for isoniazid and rifampicin. Depending on the capability of the laboratory, DST may be provided for other first-line medicines: streptomycin, ethambutol and pyrazinamide. In settings where XDR-TB is a concern, DST to second-line injectable agents and fluoroquinolone drugs will be needed in order to rapidly allow the identification of XDR-TB patients. Currently, DST for second-line medicines is usually done at the national reference laboratory level with quality assurance through the WHO TB supranational reference laboratory network.

Because conventional DST does not provide results until weeks or months later, the physician sometimes has to choose an empirical regimen for the patient’s first stage of treatment if multidrug resistance is presumed but laboratory confirmation is pending. Once the DST results are received, the physician will know whether RR/MDR-TB has been confirmed and whether the patient needs treatment with a regimen of second-line drugs. This decision-making process is shown in *Figure 7*.

Figure 7 **Selecting a tuberculosis (TB) treatment regimen in two stages**



MDR, multidrug-resistant

^a Cases with drug-resistance patterns other than rifampicin/multidrug resistance will be detected by DST and should be treated as per guidelines. However, the design of regimens for mono-resistant and poly-resistant cases of TB is not discussed in these modules.

7.1 If DST results show RR/ MDR-TB, the patient needs a second-line drugs regimen

If the patient is on a second-line drugs regimen

- the patient continues treatment with an approved regimen;
- the physician may propose an adjustment to the regimen if an individualized approach is being used;
- the physician will present the case and the DST results to the review panel for possible adjustment of regimen.

If the patient is currently on a first-line treatment regimen

- locate the patient with confirmed RR/MDR-TB (the patient may be receiving TB treatment as an outpatient at the DR-TB management centre or the local health facility or may not be receiving treatment) and invite the patient to the DR-TB management centre;
- inform the patient of the confirmed diagnosis of RR/MDR-TB and the next steps to be taken;
- collect sputum and send for culture and DST;^P
- mark the outcome of the current regimen as a failure;
- have a physician evaluate the DR-TB patient;
- have the physician propose a second-line drugs regimen;
- have the physician present the case to the review panel for approval of the treatment regimen;
- enrol the patient in second-line drugs treatment at the DR-TB management centre.

The review panel will make the final decisions on whether a standardized or individualized second-line drugs regimen is appropriate. (See Module C for more information about how the regimens are designed and the role of the review panel.)

7.2 If DST does not show rifampicin resistance, the patient needs a first-line treatment regimen

If the patient is on a second-line drugs regimen

- present the DST results to the review panel so that the regimen can be adjusted as needed (for example, the patient may be switched to a first-line treatment regimen); and
- refer the patient to a local health facility to complete treatment, including DOT and monitoring.

If the patient is on a retreatment regimen

- inform the patient and the local health facility of the DST result (no drug resistance) and that the patient needs to complete the first-line treatment regimen.

7.3 Trace a patient with confirmed RR/MDR-TB who does not return for test results

Many patients with presumed DR-TB will be on treatment while awaiting the results of culture and DST. However, if a presumptive DR-TB case cannot be located and DST results show drug resistance, it is essential that a highly proactive search be conducted to find the patient. All efforts should be made to contact or locate the patient as soon as possible. Call the patient or his or her contacts using the information recorded in the *Presumptive TB and DR-TB case register* or on the *TB treatment card*. You should also contact the referring health facility to help locate the patient. You may also need to visit the patient's home. Patients with DR-TB

^P This is done to check for a potential amplification of resistance caused by using an inappropriate regimen (that is, one that uses first-line drugs).

who are left untreated can infect many others; moreover, delays in treatment can lead to worse outcomes. Hence, it is imperative not to lose contact with patients confirmed to have DR-TB before treatment begins.

8. If a DR-TB management centre performs rapid DST (results available within hours or days), use the results to guide the choice of regimen

With rapid DST using WRD, drug resistance can be confirmed or excluded within 1–2 days, which allows the result to guide the regimen from the start of therapy.

- If rapid DST results show RR/MDR-TB:
- the physician proposes an appropriate second-line drugs regimen;
- the physician presents the case to the review panel for approval;
- the patient is informed of the next steps in the process;
- the patient is enrolled in treatment at the DR-TB management centre.

If rapid DST results show no resistance, prescribe the first-line treatment regimen and send the patient to a local health facility to receive the regimen; the medicines should be provided using DOT, and patients should visit the local health facility for monthly monitoring.



Now do Exercise C – written exercise

When you reach this point in the module, turn to Exercise C and read the instructions. When you have finished, review your answers with a facilitator.

9. Investigate close contacts of DR-TB patients

A close contact is defined as a person who is not in the household but has shared an enclosed space, such as a social gathering place, workplace or facility, for extended periods during the day with the index case during the 3 months before commencement of the current treatment episode. On the other hand, a household contact is a person who has shared the same enclosed living space for one or more nights or for frequent or extended periods through the day with the index case during the 3 months before commencement of the current treatment episode. Data indicate that close contacts of DR-TB patients who develop active TB most commonly have drug-resistant disease. All close contacts of DR-TB patients should be identified through contact tracing, and evaluated for active TB by a health-care provider.

9.1 Obtain the names of a DR-TB patient's close contacts

Inform the patient of the possibility that his or her close contacts may have been infected with a drug-resistant strain of TB. Explain the need to interview and examine all of these close contacts and, in particular, the following:

1. All children younger than 5 years

Studies have shown that children who are younger than 5 years and who live in the same household as the patient have increased vulnerability to TB; these children also are more likely to progress to disease after infection. Children who are younger than 5 years should be screened even if they do not have symptoms and should receive clinical evaluation every 6 months for two years after their last DR-TB exposure, whether or not they are symptomatic.

2. People of all ages living with HIV

People of all ages living with HIV are vulnerable to TB and DR-TB and should be screened even if they do not have symptoms. HIV-infected people should receive clinical evaluation every 6 months for two years after their last MDR-TB exposure, whether or not they are symptomatic.

3. People older than 5 years who have symptoms suggestive of TB

Cough is one of the important symptoms of TB. However, contacts of TB patients may present with other symptoms as well. Investigate any close contact/household contact, regardless of age, who has any symptoms suggestive of TB. Close contacts of MDR-TB patients with TB symptoms should receive a more aggressive diagnostic work-up than those in whom drug-susceptible TB is suspected.

As with any clinical procedure, information about the patient is confidential; care should be taken when tracing contacts to avoid revealing the patient’s information to the community.

9.2 Complete the list of the DR-TB patient’s contacts on the Contact investigation section of the Second-line TB treatment card, and conduct interviews

In the “Contact investigation” section of the *Second-line TB treatment card*, record all of the patient’s close contacts. Then interview the contacts, and evaluate them for active TB. An example of a completed “Contact investigation” section is shown below.

Example – contact investigation section

Contact investigations

First names and surnames	Relationship to case	Age	Date seen	Symptoms	Result
<i>Osa Abatu</i>	<i>husband</i>	25	25/10	<i>Cough 2 weeks</i>	<i>Smear neg 28/10</i>
<i>Luca Abatu</i>	<i>son</i>	1	20/10	<i>No symptoms</i>	<i>Screened no TB</i>
<i>Keema Onyango</i>	<i>mother</i>	40	20/10	<i>No symptoms</i>	
<i>Ruth Purefoy</i>	<i>co-worker</i>	17	22/10	<i>No symptoms</i>	

List all close contacts of the patient.

9.3 Provide information to asymptomatic adults who are close contacts

Inform all adults who are close contacts about the symptoms of TB, including cough of any duration, night sweats and fever. Instruct them to go to the local health facility or the DR-TB management centre immediately **if** they experience any TB symptoms; ensure that they understand that it is important to let health workers know that they are a contact of a DR-TB patient.

9.4 Instruct symptomatic close contacts on appropriate care and follow up

A close contact of a DR-TB patient who has symptoms suggestive of TB is at high risk for DR-TB. A symptomatic close contact must begin the diagnostic process just as other patients at high risk for the disease do – that is, a chest X-ray examination should be done and sputum specimens must be collected and sent for testing by rapid diagnostic methods, such as Xpert MTB/RIF, or if not available, smear microscopy, culture and DST. In areas with a high HIV prevalence, a close contact should undergo HIV testing. HIV testing should be also done if anyone in the household is known to be HIV positive. The patient should be evaluated and empirical treatment started as described in this module.

9.5 Evaluate children by physical examination, chest X-ray and skin test

For children who are younger than 5 years with or without symptoms, the following procedures should be done:

- an evaluation by a physician, including history and physical examination;
- a tuberculin skin test (TST);
- a chest X-ray (anteroposterior and lateral positions);
- sputum investigations (ideally, a rapid diagnostic method such as Xpert MTB/RIF⁵ or, if not available, sputum smear microscopy, culture and DST);
- HIV counselling (of child or parents, depending on the age of the child) and testing in areas where the prevalence of HIV is high or if the parents are known or suspected to be HIV positive.

TB and, to a greater extent, DR-TB are difficult to diagnose in children. Evaluate all children who are close contacts of DR-TB patients to detect those who are infected and those who have active TB disease. Perform a TST to determine whether they are infected. If the TST induration is 10 mm or greater, the test is positive. On the basis of the currently available evidence, the universal use of second-line anti-TB drugs for the treatment of latent TB in MDR-TB contacts is not recommended.

If the X-ray is abnormal, TB should be considered as a possible diagnosis. Most young children will not be able to produce adequate sputum specimens upon request. Sputum induction with nebulized hypertonic saline may facilitate collection of tracheobronchial secretions, especially in children who have a dry cough or no cough. Nebulization also may often be unsuccessful in young children. In this situation, gastric lavage is the most common procedure for collecting specimens for Xpert MTB/RIF or culture and DST.³

If the child has three of the five symptoms listed below, or has an X-ray consistent with TB disease, he or she may need to be treated for TB:

1. chronic cough or wheeze for 2 weeks or more;
2. unexplained fever for 2 weeks or more;
3. weight loss, failure to gain weight or loss of appetite;
4. failure to respond to a 2-week course of an appropriate antibiotic for an infection of the lower respiratory tract;
5. failure to regain the previous state of health 2 weeks after a viral infection or measles.

Any child who has three of the five symptoms described above may also have extrapulmonary TB and should be examined by a specialist.

DR-TB should be suspected in children with active TB if the child:

- is a close contact of a DR-TB patient;
- is a contact of a TB patient who died while being treated if there are reasons to suspect that the patient's disease was DR-TB;
- has bacteriologically proven TB that is not responding to first-line medicines given by DOT.

Once a child is suspected of having DR-TB then, in addition to a physician's evaluation, TST, X-ray and Xpert MTB/RIF, the following should be done:

- sputum smear, culture and DST;
- HIV counselling (of child or parents, depending on the age of the child) and testing in areas where the prevalence of HIV is high or if the parents are known or suspected to be HIV positive.



Now do Exercise D – discussion

When you reach this point in the module, turn to Exercise D and read the questions. When everyone is ready, your facilitator will lead a group discussion.

Summary

- Early identification of presumptive cases of DR-TB should be a priority for every health-care facility. It is critical to detect DR-TB because standard TB regimens that use first-line medicines are ineffective in treating RR/ MDR-TB. If patients with DR-TB are not detected and treated correctly with second-line medicines, they will have poor outcomes and spread the disease in their communities.
- Persons who present with any of the risk factors listed below are likely to have DR-TB and need either an Xpert MTB/RIF test or culture and DST before, or at the start of, treatment; they should be referred to a DR-TB management centre for evaluation and diagnosis.

The list includes the following risk factors:

- any patient before the start of a retreatment regimen (those having failed a regimen, relapsed or returned after loss to follow up, other previously treated cases);
 - close contacts of DR-TB patients who have been diagnosed with active TB;
 - patients not responding to first-line anti-TB treatment (remaining sputum smear-positive at the end of the intensive phase of a first-line anti-TB drug regimen);
 - HIV-positive patients with active TB;
 - cases from congregate settings where transmission rates of TB and hence DR-TB as well are high, e.g. prisoners, mine-workers, etc.;
 - any TB patient coming from a group determined by the programme to have a significant risk for DR-TB, such as:
 - patients with co-morbid conditions associated with malabsorption or rapid-transit diarrhoea;
 - residents of areas with high DR-TB prevalence (DR-TB rates in many areas of the world can be high enough to justify routine DST in all new cases).
- Ask questions to find out whether the TB patient has previously taken any anti-TB medicines, the outcome of previous treatment, the patient's HIV status, whether the patient was exposed to a known case of DR-TB, the quality of previous treatment for TB, and about any additional factors that affect the likelihood of a person becoming infected with DR-TB in your country.
 - Unrecognized DR-TB is associated with high mortality in people living with HIV. Therefore, it is important to know the HIV status of all people presumed to have TB and all those known to have TB, and to investigate all HIV-positive patients who have symptoms of TB for drug resistance using rapid DST, culture and DST. Generally, HIV is not by itself a risk factor for DR-TB; however, TB may be missed when HIV-positive patients have negative results for sputum-smear microscopy. Therefore, it is essential to perform rapid DST, and if necessary, culture and DST for all HIV-positive patients with active TB.
 - Collect two sputum samples⁹ from every presumptive DR-TB case and send the samples to the laboratory as per country policy for Xpert MTB/RIF, microscopy examination, culture and DST. Send a completed *Request for examination of biological specimen for TB* form with the samples. Keep the samples cool at all times.

⁹ Two samples if doing AFB microscopy. For Xpert MTB/ RIF, one sample would be sufficient.

- Inform the patient about the possible diagnosis of DR-TB and the next steps in the process of diagnosis and treatment. All communication must be kind, supportive and medically correct. Explain what drug resistance is, and what it means for treatment. Reassure the patient that DR-TB can be cured, but explain that it will take many months of treatment.
- The laboratory capacity of your country will determine whether DST results will be available early enough to guide the choice of a treatment regimen. Rapid DST can confirm or exclude RR or MDR-TB within hours or days so that an appropriate regimen is chosen immediately. Conventional DST provides results in weeks or months. Therefore, if the physician is awaiting DST results, he or she must choose an empirical regimen based on the suspected case's likelihood of having DR-TB.
- WHO recommends administering an empirical RR/MDR-TB regimen to groups of patients who have a **high likelihood** of having RR/MDR-TB. The empirical treatment regimens can be standardized or individualized, as per national policy. Standard treatment regimens using first-line medicines are recommended for groups that are moderately likely or unlikely to have the disease. Obtaining specimens for culture and DST, and awaiting the results, should not delay the start of therapy. Empirical regimens should be started promptly. This is especially important if the patient is seriously ill or the disease is progressing rapidly.
- When the results of smear microscopy, rapid DST, culture and DST are received at the DR-TB management centre, record them in the patient's records and decide on the appropriate action to be taken in response to the results. When a patient is confirmed to have TB by smear, rapid DST or culture, be sure that the patient is located and that treatment is started.
- When rapid DST results confirm or exclude the diagnosis of RR/MDR-TB in the patient, the physician knows whether the patient needs a second-line drugs regimen. If rapid DST confirms RR/MDR-TB, the patient should continue or switch to an MDR-TB regimen. If rapid DST shows that the patient's disease is not resistant to first-line medicines, the patient should continue the current regimen or be switched to a standard first-line treatment regimen.
- Close contacts of DR-TB patients who develop active TB most commonly have drug-resistant disease. All close contacts of DR-TB patients should be identified through contact tracing, and they should be evaluated for active TB by a health-care provider. In particular, interview and examine:
 - all children in the household younger than 5 years;
 - people of all ages living with HIV;
 - any close contact regardless of age who has symptoms of TB.

Self-assessment questions

Answer the self-assessment questions below to check what you have learnt. Then compare your answers to those on pages B-39–B-40.

1. Write a “T” for true or “F” for false by the following statements:
 - ___ A drug-susceptibility test (DST) is required to confirm a diagnosis of MDR-TB.
 - ___ An Xpert MTB/RIF and/or culture and DST should be done for people presumed to have DR-TB, even if the smears are negative.
 - ___ An HIV-positive patient with smear-negative TB cannot have DR-TB.
 - ___ All patients with confirmed MDR-TB have strains of TB that are resistant to at least isoniazid and rifampicin.
 - ___ All patients must have DST results showing resistance before they can be started on second-line drugs.

2. List five different groups at high risk for DR-TB who should be screened by Xpert MTB/RIF, and/or culture and DST.
 -

 -

 -

 -

 -

3. How many sputum samples need to be examined to arrive at a diagnosis?

When and where should this sample/these samples be collected?

Answers to self-assessment questions

If you had difficulty answering any question, turn back and study the section indicated. If you do not understand something, discuss it with a facilitator.

1. Write a “T” for true or “F” for false by the following statements:

- T A drug-susceptibility test (DST) is required to confirm a diagnosis of MDR-TB.
- T An Xpert MTB/RIF and/or culture and DST should be done for people presumed to have DR-TB, even if the smears are negative.
- F An HIV-positive patient with smear-negative TB cannot have DR-TB.
- T All patients with confirmed MDR-TB have strains of TB that are resistant to at least isoniazid and rifampicin.
- F All patients must have DST results showing resistance before they can be started on second-line drugs.

2. List five different groups at high risk for DR-TB who should be screened by Xpert MTB/RIF, and/or culture and DST.

- *any patient before the start of a retreatment regimen (those having failed a regimen, relapsed or returned after loss to follow up, other previously treated cases);*
- *close contacts of DR-TB patients who have been diagnosed with active TB;*
- *patients not responding to first-line anti-TB treatment (remaining sputum smear-positive at the end of the intensive phase of a first-line anti-TB drug regimen);*
- *HIV-positive patients with active TB;*
- *cases from congregate settings where transmission rates of TB and hence DR-TB as well are high, e.g. prisoners, mine-workers, etc.*

(See section 1.)

3. How many sputum samples need to be examined to arrive at a diagnosis?

Two samples are needed for diagnosis.^a

When and where should this sample/these samples be collected?

The first sample is collected at the DR-TB management centre during the first visit when the patient is suspected of having MDR-TB. The second sample is collected by the patient at home upon waking up the next morning.^b

(See section 2.)

^a Two samples should be collected if performing AFB microscopy, else a single sample for Xpert.

^b WHO also recommends front-loaded smear microscopy in which two specimens are collected and examined on the same day that a patient presents.

4. What difference does it make to the physician at the DR-TB management centre if rapid DST is or is not available?

Rapid DST can confirm or exclude RR/MDR-TB within hours or days so that an appropriate regimen can be chosen at the start of treatment. If a physician must wait for the results of conventional DST to confirm MDR-TB, then he or she must choose an empirical regimen based on the likelihood of the patient having MDR-TB. When DST results are available months later, the regimen may have to be adjusted.

(See section 4.)

5. Under what circumstances can a patient be enrolled on second-line treatment before results from culture and DST are available?

If the TB patient has a high likelihood of DR-TB (based on TB treatment history and other factors), the physician may decide to initiate the case on second-line drugs and present the case to the review panel for approval of a second-line drugs regimen. If the review panel approves the treatment, the patient will be enrolled in second-line treatment at the DR-TB management centre before results of culture and DST are available.

(See sections 4 and 5.)

6. Culture results show that a person suspected of having DR-TB is positive for TB, and the DST results show resistance to isoniazid and rifampicin. However, the patient defaulted on treatment before these results were available. What should the DR-TB management centre staff do?

A highly proactive search to find the patient needs to be made. All efforts should be made to contact or locate the patient as soon as possible. Call the patient or the patient's contacts using the numbers recorded in the presumptive TB and DR-TB register. Also contact the local health facility near the patient's residence for help in tracing the patient; the local facility may be able to visit the patient's home.

Why is it important for the staff to take this action?

Patients with DR-TB who are not treated can infect many other people. In addition, delaying treatment may lead to further clinical deterioration, increased damage to the lungs and a worse outcome.

(See section 7.3.)

7. A patient suspected of having DR-TB who is put on a second-line regimen may have already infected other people. Who should this patient ask to come to the DR-TB management centre to be screened for DR-TB?

*Ask **all** close contacts to come to the DR-TB management centre for evaluation; emphasize to adult contacts that this includes children who are younger than 5 years and others who have symptoms suggestive of TB.*

(See section 9.)



The End

Congratulations on finishing this module!

References

1. Guidelines for the programmatic management of drug-resistant tuberculosis: emergency update 2008. Geneva: World Health Organization; 2008 (WHO/HTM/TB/2008.402).
2. Guidelines for the programmatic management of drug-resistant tuberculosis: 2011 update. Geneva: World Health Organization; 2011 (WHO/HTM/TB/2011.6).
3. Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. Geneva: World Health Organization; 2014 (WHO/HTM/TB/2014.11).
4. Xpert MTB/RIF implementation manual: technical and operational 'How-to'; practical considerations. 2nd edition. Geneva: World Health Organization; 2014 (WHO/HTM/TB/2014.1).
5. Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulmonary TB in adults and children. Policy update. Geneva: World Health Organization; 2013 (WHO/HTM/TB/2013.16).

Exercises for Module B: Detect cases of MDR-TB

Exercise A

Written exercise: Identify presumptive cases of RR/MDR-TB

In this exercise you will identify those patients at your DR-TB management centre who should be suspected of having RR/MDR-TB and screened by rapid DST or microscopy, culture and DST.

Read each of the cases below. For each case, decide whether the patient should be suspected of having RR/MDR-TB. If the disease should be suspected, state the patient's group or factor that makes this patient a suspected case. Then list the sputum examination tests that should be requested for the patient.

Case 1

A 34-year-old female patient complains of a persistent cough for 4 weeks; she also has back pain, haemoptysis and weight loss. She is receiving treatment for diabetes mellitus. When you interview her, she explains that she had been treated for TB but quit the treatment after several months because she was feeling better. She shows you a *TB identity card* from that treatment. She had about 4 months of new-patient treatment before discontinuing the medicines. She was sputum smear-negative after 2 months of treatment. She says that she is HIV-negative but does not have any documentation.

- A case of presumptive RR/MDR-TB?
- If yes, why?
- Tests to request: Smear [] Xpert MTB/RIF [] Culture []
Drug susceptibility [] HIV test []

Case 2

A 43-year-old female patient has been sent from a local health facility to the DR-TB management centre for evaluation. She has received three courses of TB medications from a private doctor over a period of years but no longer has money to pay for treatment. The patient said that she took all of the medicines each time but now she has cough and fears it may again be TB. She has also lost weight, occasionally has a fever, and has chest pain and night sweats. She shows you her HIV test results from about 1 year ago; she was HIV negative.

- A case of presumptive RR/MDR-TB?
- If yes, why?
- Tests to request: Smear [] Xpert MTB/RIF [] Culture []
Drug susceptibility [] HIV test []

Case 3

A 20-year-old male medical student at a nearby university has come to the DR-TB management centre because he has had a cough for more than a month and a fever for 6 days. He has never

been diagnosed or treated for TB. He mentions that he has been working in a small clinic for the past 3 months where they are treating TB patients. He has documentation of a negative HIV test done 2 months ago.

- a. A case of presumptive RR/MDR-TB?
- b. If yes, why?
- c. Tests to request: Smear [] Xpert MTB/RIF [] Culture []
Drug susceptibility [] HIV test []

Case 4

A 53-year-old man is sent to the DR-TB management centre by a local health facility. He has finished the third month of a retreatment regimen and is still smear positive. He also has a cough and back pain, and has been losing weight. The patient has had no adverse effects from treatment and has complied with the treatment schedule. He has never had an HIV test and says that he does not need one.

- a. A case of presumptive RR/MDR-TB?
- b. If yes, why?
- c. Tests to request: Smear [] Xpert MTB/RIF [] Culture []
Drug susceptibility [] HIV test []

Case 5

A female patient, 18 years old, receives ART and HIV care at the university hospital clinic. She recently developed a cough and fever, and has lost weight. The staff at the clinic suspected that she had developed TB and did a sputum-smear microscopy examination, which was positive. They have sent her to the DR-TB management centre for a prescription of anti-TB medicines. She went to a private doctor some years ago and thinks that she might have had some anti-TB medicines then.

- a. A case of presumptive RR/MDR-TB?
- b. If yes, why?
- c. Tests to request: Smear [] Xpert MTB/RIF [] Culture []
Drug susceptibility [] HIV test []

When you have finished this exercise, review your answers with a facilitator.



GO BACK and read section 2 and work to the next stop sign.

Exercise B

Written exercise: Filling out a Request for examination of biological specimen for TB

In this exercise you will complete the *Request for examination of biological specimen for TB* form for one of the patients identified as a suspected RR/MDR-TB case in Exercise A (Case 5).

Read the information below and use it to complete the form on the next page.

Background information

You work at the DR-TB management centre at Balanot University Hospital. You have collected two sputum samples from the patient to send to the laboratory.

Today is 14 August 2013.

Patient's information

Name: Sophia Zakaria. She was described as follows in Exercise A:

A female patient, 18 years old, receives ART and HIV care at the university hospital clinic. She recently developed a cough and fever, and has lost weight. The staff at the clinic suspected that she had developed TB and did a sputum-smear microscopy examination, which was positive. They have sent her to the DR-TB management centre for a prescription of anti-TB medicines. She went to a private doctor some years ago and thinks that she might have had some anti-TB medicines then.

Her address is 12A Second Avenue, Balanot.

Recent information:

Sophia Zakaria was entered in the *Presumptive TB and DR-TB case register* at the Balanot University Hospital. She does not yet have any TB registration number.

Now use the above information to complete the blank form on the next page.

When you have finished this exercise, review your answers with a facilitator.



GO BACK and read section 4 and work to the next stop sign.

Request for examination of biological specimen for TB

Treatment Unit: _____ Date of request: _____

Patient Name: _____

Age (years): _____ Date of Birth: _____ Sex (mark one): M F

Patient Address: _____ Patient Telephone: _____

Reason for examination (mark one):	Diagnostic	Presumptive RR-TB/MDR-TB: <input type="checkbox"/> Y <input type="checkbox"/> N	Patient previously treated for TB (mark one): <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
	Follow-up	If follow-up, month of treatment: _____	
Specimen type:	Sputum	Other (specify): _____	If information available specify if
		HIV infection <input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> Unknown	
			Relapse: After failure of retreatment regimen with 1st-line drugs
			After Loss to follow-up: Other

Test requested:

Microscopy	Xpert MTB/RIF	Culture	Drug susceptibility	Line probe assay
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Name, signature and telephone of requestor: _____

RESULTS (to be completed in the laboratory)

Microscopy results

Date sample collected (to be filled by requestor)	Specimen type	Laboratory serial number/s	Visual appearance (blood-stained, mucopurulent or saliva)	Result (check one)				
				Negative (0 AFB/100HPF)	1-9/100HPF (scanty; report number of AFB)	+ 10-99 AFB/100HPF	++ 1-10 AFB/HPF	+++ >10 AFB/HPF

Examined by (Name & signature): _____ Date of result: _____

Xpert MTB/RIF test result (to be completed in the laboratory)

Date collected (to be filled by requestor)

M. tuberculosis			Rifampicin resistance		
Detected	Not detected	No result / Invalid / Error	Detected	Not detected	Indeterminate result

Examined by (Name & signature): _____ Date of result: _____

Culture results (to be completed in the laboratory)

Date sample collected (to be filled by requestor)	Media used (liquid or solid)	Laboratory serial number/s	Result (check one)						NTM ¹	Contaminated
			Negative (0 colonies)	1-9 <10 colonies	+ 10-100 colonies	++ >100 colonies	+++ Innumerable / confluent growth			

Examined by (Name & signature): _____ Date of result: _____

Drug-susceptibility test (DST) and line-probe assay (LPA) results

(to be completed in the laboratory)

Date sample collected (to be filled by requestor)	Media used (liquid or solid media; direct or indirect LPA)	DST laboratory serial number/s	H	R	E	S	Am	Km	Cm	FQ	Other	Other	Other	Other

R: Resistant; S: Susceptible; C: Contaminated; - Not done

Examined by (Name & signature): _____ Date of result: _____

¹ Non-tuberculous mycobacteria

Exercise C

Written exercise: Assess the likelihood of MDR-TB and recommend an empirical TB treatment regimen

In this exercise you will read and interpret laboratory results to decide on appropriate actions. Read each case below and answer the numbered questions.

Case 1

Dalia Chalco is a 36-year-old married female. Her husband has recently been diagnosed as an MDR-TB patient; he is being treated at your DR-TB management centre. She came in last week complaining of cough and fever, and is fearful that she has TB. She has never been treated for TB. Her smear results have just come back from the laboratory and are found below. She has never been tested for HIV.

SMEAR RESULTS

Microscopy results

Date sample collected (filled by requestor)	Specimen type	Laboratory serial number(s)	Visual appearance (blood-stained, mucopurulent or saliva)	Result (tick one)				
				Negative (0 AFB/100 HPF)	1-9/100 HPF (scanty; report no. of AFB)	+	++	+++
22 Sept 2013	Sputum	1031	MP				✓	
23 Sept 2013	Sputum	1039	MP					✓

Examined by (name and signature): BJ Ranch

Date of result: 24 Sept 2013

Continue reading below and answer the numbered questions.

1. What do the laboratory results tell you about Ms Chalco?
2. Should you screen her for MDR-TB? Why or why not?
3. What laboratory tests will you order next for Ms Chalco?

Your DR-TB management centre sends sputum samples to a laboratory that does culture and conventional DST. You usually receive culture results after 3 weeks and DST results after 2 months, so you will not know whether Ms Chalco has MDR-TB for a couple of months.

She needs to start TB treatment soon; an empirical regimen will be chosen based on the likelihood that she has MDR-TB and the physician’s assessment.

4. What is Ms Chalco’s likelihood of having MDR-TB?

5. What regimen would you recommend for her treatment while awaiting the DST results?

Case 2

Ming Tai is a 25-year-old woman who is living with HIV. Her physician suspected that she had TB. He collected two sputum samples and sent them for smear, culture and DST on 9 March 2013, and also took an X-ray. Her sputum results were negative; her physician diagnosed smear-negative pulmonary TB. She began a new-patient regimen on 16 March 2013.

Her culture results were available 3 weeks later.

CULTURE RESULTS

Culture results *(to be completed by the laboratory)*

Date sample collected (filled by requestor)	Media used (liquid or solid)	Laboratory serial number(s)	Result (tick one)					NTM	Contaminated
			Negative (0 colonies)	1-9 (<10 colonies)	+ (10-100 colonies)	++ (>100 colonies)	+++ (Innumerable/confluent growth)		
8/3/2013	<i>solid</i>	198							✓
9/3/2013	<i>solid</i>	211				✓			

Examined by (name and signature): BJ Ranch

Date of result: 2 April 2013

1. Do her culture results confirm or exclude TB?

2. Why did the physician send sputum for culture and DST?

3. Does the patient require a change of regimen at this time?

Some weeks later, the patient’s DST results become available. Her results are shown below.

Drug-susceptibility test (DST) and line-probe assay (LPA) results

Date sample collected (filled by requestor)	Method ^a	Laboratory serial number(s)	Results ^b (mark for each drug)											
			H	R	E	S	Am	Km	Cm	FQ:	Other:	Other:	Other:	Other:
9 March 2013	Solid	211	R	R	S	R								

^aSpecify: solid media DST; liquid media DST; direct LPA; indirect LPA

^bResults codes: R = Resistant S = Susceptible C = Contaminated – = Not done

Examined by (name and signature): BJ Ranch

Date of result: 14 May 2013

4. What is the next step that should be taken and why?

When you have finished this exercise, review your answers with a facilitator.



GO BACK and read section 9 and work to the next stop sign.
When everyone is ready, there will be a group discussion.

Exercise D

Group discussion: Detecting MDR-TB cases at your DR-TB management centre

In this exercise, the group will discuss how the procedures described in this module can be carried out at your DR-TB management centre. Write answers to the questions below in preparation for the discussion.

1. What laboratory does your DR-TB management centre use for Xpert MTB/RIF sputum-smear microscopy, culture and DST? Where is it located?
2. How long does it take to receive results back from the laboratory for:
 - sputum smear microscopy?
 - culture?
 - DST?
3. Is rapid DST or conventional DST available to your DR-TB management centre?
4. Is HIV testing available in your DR-TB management centre or must patients go elsewhere for counselling and testing?
5. Is there a review panel at your DR-TB management centre as described in the module? How often do they meet?
6. Who can prescribe an empirical RR/MDR-TB regimen at your DR-TB management centre?
7. What procedures described in this module are done differently at your DR-TB management centre? Do adjustments need to be made?

When everyone is ready, there will be a group discussion on these questions.

Annexes

Annex A: Collect sputum samples for examination _____ B-58

Annex B: Register of presumptive TB and DR-TB cases _____ B-60

Annex C: Request for examination of biological specimen for TB _____ B-61

Annex A: Collect sputum samples for examination

- **Explain** that the patient with suspected TB needs a sputum examination to determine whether there are TB bacilli in the lungs and, if so, whether they are resistant to some anti-TB medicines.

List the name and address of the person presumed to have TB in the *Register of presumptive TB cases*.

- **Label** the sides of the sputum containers (not the lids).

Two samples are needed for the diagnosis of TB. Two samples should be collected if performing AFB microscopy or a single sample for Xpert.

One sample is needed for follow-up examinations.

- **Fill out the *Request for sputum smear microscopy examination form*.**
- **Explain and demonstrate, fully and slowly, the steps for collecting sputum.**
 - Show the suspected TB case how to open and close the container.
 - Breathe deeply and demonstrate a deep cough. The presumptive TB case must produce sputum, not saliva alone.
 - Explain that the presumptive TB case should cough deeply to produce sputum and spit it carefully into the container.
- **Collect**
 - Give the presumptive TB case the container and lid.
 - Send the presumptive TB case outside to collect the sample in the open air if possible or to a well-ventilated place, away from other people and with sufficient privacy.
 - When the presumptive TB case returns with the sample, look at it. Is there a sufficient quantity of sputum (not just saliva)? If not, ask the presumptive TB case to add more.
 - Explain when the presumptive TB case should collect the next sample, if needed.

TB specimen

Name: _____

Health facility: _____

Date: _____

Specimen no.: _____

In many health facilities, the specimen number is the presumptive TB case's number or the patient's district TB number, followed by -1 or -2.

Schedule for collecting two sputum samples

Day 1:

- Collect an on-the-spot sample as instructed above (**Sample 1**).
- Instruct the presumptive TB case about how to collect an early morning sample the next day (first sputum after waking). Give the presumptive TB case a labelled container to take home. Ask the presumptive case to bring the sample to the health facility the next day.

Day 2:

- Receive the early morning sample from the presumptive TB case (**Sample 2**).

- **When you collect the second sample, tell the presumptive case when to return for the results.**
- **Store**
 - Check that the lid is tight. Wipe off the outside of the container, if needed.
 - Isolate each container in its own plastic bag if possible, or wrap in newspaper.
 - Store in a cool place. (If samples are to be sent for culture, keep refrigerated.)
 - Wash your hands.
- **Send**
 - Send the samples from the health facility to the laboratory.
 - The total time from collection until reaching laboratory should be no more than 5 days. (Samples sent for culture should be sent promptly and reach the laboratory within 1–2 days.)

Annex B: Register of presumptive TB and DR-TB cases

(This register is not part of the standard PMDT stationery)

Year: _____ Facility: _____

Date (dd/mm)	TB number	Name of patient	Age		Complete address & telephone number	Result of HIV test*	Date first sputum collected	Date sputum sent to laboratory	Date results received	Results of Xpert MTB/RIF and sputum examinations		Culture and DST results	TB Treatment card opened (record date)	Observations/ Clinician's diagnosis
			M	F						1	2			

* Documented evidence of HIV testing during or before anti-TB treatment is reported here. Results are denoted as Pos (positive); Neg (negative); I (discordant/inconclusive); ND (not done or unknown); RR (rifampicin resistant). Xpert= Xpert MTB/RIF test result.

† The Xpert MTB/RIF test may not be accessible to presumptive TB cases in all countries.

Annex C: Request for examination of biological specimen for TB

Treatment Unit: _____ Date of request: _____

Patient Name: _____

Age (years): _____ Date of Birth: _____ Sex (mark one): M F

Patient Address: _____ Patient Telephone: _____

Reason for examination (mark one):	Diagnostic	Presumptive RR-TB/MDR-TB: <input type="checkbox"/> Y <input type="checkbox"/> N	Patient previously treated for TB (mark one): <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown	
	Follow-up	If follow-up, month of treatment: _____		
Specimen type:	Sputum	Other (specify): _____	If information available specify if	
		HIV infection <input type="checkbox"/> Y <input type="checkbox"/> N <input type="checkbox"/> Unknown		
			New	After failure of 1st treatment with 1st-line drugs
			Relapse	After failure of retreatment regimen with 1st-line drugs
			After Loss to follow-up	Other

Test requested: Microscopy Xpert MTB/RIF Culture Drug susceptibility Line probe assay

Name, signature and telephone of requestor: _____

RESULTS (to be completed in the laboratory)

Microscopy results

Date sample collected (to be filled by requestor)	Specimen type	Laboratory serial number/s	Visual appearance (blood-stained, mucopurulent or saliva)	Result (check one)					
				Negative (0 AFB/100HPF)	1-9/100HPF (scanty; report number of AFB)	+ 10-99 AFB/100HPF	++ 1-10 AFB/HPF	+++ >10 AFB/HPF	

Examined by (Name & signature): _____ Date of result: _____

Xpert MTB/RIF test result (to be completed in the laboratory)

Date collected (to be filled by requestor)

M. tuberculosis			Rifampicin resistance		
Detected	Not detected	No result / Invalid / Error	Detected	Not detected	Indeterminate result

Examined by (Name & signature): _____ Date of result: _____

Culture results (to be completed in the laboratory)

Date sample collected (to be filled by requestor)	Media used (liquid or solid)	Laboratory serial number/s	Result (check one)						NTM ¹	Contaminated
			Negative (0 colonies)	1-9 <10 colonies	+ 10-100 colonies	++ >100 colonies	+++ Innumerable / confluent growth			

Examined by (Name & signature): _____ Date of result: _____

Drug-susceptibility test (DST) and line-probe assay (LPA) results

(to be completed in the laboratory)

Date sample collected (to be filled by requestor)	Media used (liquid or solid media; direct or indirect LPA)	DST laboratory serial number/s	H	R	E	S	Am	Km	Cm	FQ	Other	Other	Other	Other

R: Resistant; S: Susceptible; C: Contaminated; - Not done

Examined by (Name & signature): _____ Date of result: _____

¹ Non-tuberculous mycobacteria

Management of drug-resistant tuberculosis

**Training for staff working at
DR-TB management centres**

Module C: Treat DR-TB patients



**World Health
Organization**

MODULE C

Treat DR-TB patients^a

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^a These modules focus on managing rifampicin-resistant TB (RR-TB) and multidrug-resistant TB (MDR-TB) (collectively referred to as RR/MDR-TB in several places) because of the clinical significance and need for treatment with second-line drugs in both cases. The modules do not specifically focus on extensively drug resistant TB (XDR-TB) and polydrug-resistant TB (PDR-TB) other than RR-TB.

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Introduction

In Module B, you learnt how to identify people presumed to have drug-resistant tuberculosis (DR-TB) and how to determine whether they have the disease. This module describes how to treat persons with DR-TB.

As with drug-susceptible TB, there are two phases of treatment for DR-TB during which patients take specific combinations of medicines: the intensive phase and the continuation phase. Treatment regimens using second-line drugs can be standardized or individualized. Standardized means that a fixed regimen is applied, based on the results of drug-susceptibility testing (DST) from a sample of patients in your country or region and aligned to the World Health Organization (WHO)'s recommendations. An individualized regimen is based on the patient's previous history of anti-TB treatment and individual DST results.

Most of the WHO recommendations on the composition and duration of treatment for rifampicin-resistant/multidrug-resistant (RR/MDR)-TB are conditional and based on very low-quality evidence^b (refer to Annex D for an overview of grading terminologies). The duration of treatment for RR/MDR-TB is much longer than treatment for drug-susceptible TB. **Treatment generally lasts for at least 20 months for most patients and the duration may be modified according to the patient's response to therapy.** The physician at the DR-TB management centre, along with the members of the review panel (a case-management committee composed of health-care workers with expertise in managing DR-TB), decides on the appropriate medicines to be used in the patient's regimen.

It is vital that patients with DR-TB take all medications in the regimen correctly in order to increase the probability of being cured and minimizing the risk of relapse. **Once patients have been diagnosed with DR-TB, treatment represents the best opportunity for them to be cured.** Patients with MDR/extensively drug-resistant (XDR)-TB have high mortality rates, if untreated. If DR-TB patients are left to take medicines by themselves, a large proportion will find it difficult to take treatment as prescribed. Predicting who will or will not adhere to treatment is difficult because the factors that cause non-adherence may be related to the facility/services, to personal reasons of the patient, and other reasons beyond the immediate control of the patient and health-care provider.

All health workers must play an active role in ensuring that every patient takes the recommended medicines in the right combinations, in the correct schedule and for the appropriate duration. The best way to ensure this is for a health worker or a community-based TB treatment supporter to observe each patient take the medicines through a patient-centred approach. A patient-centred approach to directly observed treatment (DOT) consists of assessing the needs and values of the patient that influence adherence to treatment; coordinating with relatives, community members and other health-care workers for an effective response that removes the barriers to adherence that were identified (from material needs to discrimination due to stigma); and preventing and providing relief of all suffering associated with the disease and its treatment, including effective management of adverse drug reactions. This is discussed in

^b See the WHO guidelines for more details about the evidence on which these recommendations were based.

further details in Module E (A patient-centred approach to ensuring continuation of DR-TB treatment).

Patient-centred DOT should continue throughout the entire period of treatment. DR-TB treatment takes place in different settings, depending on the country's situation and guidelines. **These modules need to be adapted in order to train health-care workers in the methods most appropriate to the local situation.** In some countries, DR-TB treatment initially takes place in a specialized management centre (like a hospital) where patients are admitted and given daily treatment as inpatients (or, depending on the country's procedures, patients may receive daily treatment as outpatients, sometimes after relocating to temporary housing near the DR-TB management centre). During the initial period at the DR-TB management centre, patients start DR-TB treatment, and are monitored closely for early detection and management of adverse events, while receiving education and information about the disease and its treatment. When a patient tolerates the medicines, treatment may be decentralized (or transferred) to a local health facility, or the patient may continue treatment at the DR-TB management centre. If a patient's treatment is decentralized, the patient receives treatment at his or her local health facility or from a community treatment supporter for the remainder of the regimen.

In other countries, DR-TB treatment can be **fully ambulatory**, meaning that both the intensive and the continuation phase take place at a local health facility near the patient's home or with assistance from a community treatment supporter.

In both situations, the patient continues to have monthly sputum examinations and is also evaluated monthly by the physician at the DR-TB management centre .

To provide patient-centred DOT, the health worker coordinates a place and time convenient to both the patient and the health worker or a community-based treatment supporter at a local health facility. At each visit, the health worker:

- greets the patient and asks about any adverse events and other problems since the last visit;
- administers treatment, including watching that the medicines are swallowed and giving the injection;
- records the treatment observed and the date on the *Second-line TB treatment card*;
- notes immediately whether treatment has been interrupted and takes action, such as tracing the patient and encouraging the patient to resume treatment;
- establishes and maintains a supportive relationship with the patient. A good relationship enables the patient to discuss any questions or fears about the disease and treatment, and report any problems; it allows the health worker to identify the needs of the patient and establish linkages with those who can provide meaningful support for continuing the treatment.

The first-line anti-TB medicines used to treat drug-susceptible TB are efficacious and tolerable, whereas the second-line medicines used to treat DR-TB may be less efficacious and cause more adverse effects. The adverse effects occur mainly during the first few months of treatment. However, very serious adverse effects are uncommon. Some adverse effects are self-limiting

and resolve after a short time; others can be treated with medicines to alleviate the patient’s symptoms. All adverse effects must be swiftly and effectively managed or treated until the patient develops a tolerance for these effects or until the adverse effects resolve. Reducing the dose of a medicine, or withdrawing or replacing it should occur only as the last possible course of action. For patients who have resistance to multiple medicines so that only a few medicines can be used, stopping any of these medicines may result in treatment failure.

The progress of RR/MDR-TB treatment in a patient with pulmonary TB must be monitored by follow-up sputum-smear examination, culture and DST, if necessary, in addition to monthly clinical monitoring. Negative sputum smears and negative cultures at specific times indicate good treatment progress, which encourages the patient to continue treatment and motivates the health worker responsible for supervising the treatment. Culture examinations are also required to determine whether the patient is cured.

Objectives of this module

After completing this module participants will be able to do the following:	Section:
▶ Use the treatment history, DST results and other information to propose an RR/MDR-TB regimen	1
▶ Prepare a patient’s Second-line TB treatment card and include the treatment history and laboratory results	3.1
▶ Give DOT and record it on the Second-line TB treatment card.....	5
▶ Monitor the RR/MDR-TB patient for adverse effects and identify appropriate actions that can be taken if they occur	6
▶ Determine when the patient is due for follow-up examinations.....	7.1
▶ Record the results of laboratory examinations.....	7.3
▶ Identify when a patient is eligible for decentralization or shifting to the continuation phase of treatment	7.5
▶ Record changes to the treatment regimen on the Second-line TB treatment card.....	8
▶ Update the Second-line TB treatment register throughout the duration of treatment	3.3, 7.3, 9.4
▶ Determine the treatment outcome for an RR/MDR-TB patient	9

Note: Some steps of these procedures are described in this module in the appropriate place, but more detail is provided in other modules:

- Providing information about DR-TB to patients and their families is described in Module D.

- Dealing with problems, such as when a patient stops coming for treatment, is described in Module E.
- Preparing a patient's medicines is described in Module F.

If you need to look up an unfamiliar word, refer to the Glossary at the end of Module A.

1. Design a treatment regimen for an RR/MDR-TB patient

There are two treatment regimens: standardized and individualized.

- **Standardized treatment:** drug resistance surveillance (DRS) data from representative patient populations are used to base regimen design in the absence of individual DST. All patients in a defined group or category receive the same regimen. Presumptive DR-TB should be confirmed by DST whenever possible.
- **Individualized treatment:** each regimen is designed based on the patient's past history of TB treatment and individual DST results.

Usually, the patient will begin a standardized regimen. The standardized regimen can be adjusted once the DST results are available, particularly for fluoroquinolones and second-line injectable drugs.

In case the treatment has to be initiated prior to the determination of a firm diagnosis of DR-TB, the "empirical" treatment regimen could be used. Empirical regimens can be used for both standardized and individualized treatment strategies. For example, an empirical MDR-TB regimen can be used when initiating treatment of close contacts of an MDR-TB patient before the diagnosis of MDR-TB is made.

If, after evaluating a patient, the physician concludes that the patient should begin a second-line regimen, the physician may choose the standardized treatment or design an individualized treatment regimen if DST results are available. The physician will then present the case and the proposed regimen to the review panel for authorization before the patient begins treatment.

There are many decisions to be made while designing a regimen for a DR-TB patient. This section provides the basic information on designing such regimens. However, it is important to note that this guide alone will not provide sufficient information to design a treatment regimen, and the review panel will always make the final decisions based on the national guidelines.

1.1 Anti-TB medicines

All health workers involved in caring for patients with DR-TB should be familiar with the different medicines that can be used to treat patients with DR-TB. These medicines are classified into five groups (refer to Table 1 for further details):

group 1 – first-line oral anti-TB agents;

group 2 – injectable anti-TB agents;

group 3 – fluoroquinolones;

group 4 – oral bacteriostatic second-line anti-TB medicines;

group 5 – anti-TB drugs with limited data on efficacy and/or long-term safety in the treatment of DR-TB. This group includes new anti-TB agents.

The physician uses these groups to select a regimen. Group 1 medicines, the most effective and the best tolerated, should be used if there is good laboratory evidence and a clinical history to suggest that an agent from this group will be effective. It is recommended to add pyrazinamide (Z) in all cases for the intensive phase of treatment, though it is not counted among the list of four effective medicines. All patients should receive an injectable agent from group 2 if susceptibility has been documented or is presumed. All patients should receive a medication from group 3 if the strain is susceptible or if the medication is thought to be effective. Agents in group 4 are added after considering the estimated susceptibility, previous use of anti-TB medicines, side-effect profile and cost. Agents in group 5 are not recommended by WHO for routine use in treating drug-resistant TB because their effectiveness or safety profile are unclear.

In general, the intensive phase of MDR-TB treatment regimens should consist of at least four second-line anti-TB drugs likely to be effective, as well as pyrazinamide. The **intensive phase** (i.e. the initial part of treatment during which a group 2 injectable agent is used) lasting for about eight months is conditionally recommended for most patients, but the duration can be modified according to the patient's response to treatment. MDR-TB regimens should include at least pyrazinamide, a fluoroquinolone (preferably later-generation), an injectable anti-TB drug, ethionamide (or prothionamide) and either cycloserine or PAS (*p*-aminosalicylic acid). The injectable is given 5–7 days a week and all other drugs are given 6–7 days a week. For patients newly diagnosed with MDR-TB (i.e. not previously treated for MDR-TB), a total treatment duration of 20 months is suggested for most patients; the duration may be modified according to the patient's response to therapy. During the continuation phase, the patient takes all of the same medicines but the injectable agent is discontinued.^c Each dose is given under direct observation with proper patient-centred support throughout the treatment.

Table 1 provides a summary of the different anti-TB medicines and their abbreviations.

^c Certain group 5 medicines, when added to reinforce the treatment regimen, are given for a limited period (e.g. bedaquiline for 6 months).

Table 1 **Groups of anti-tuberculosis (TB) medicines**

GROUP NAME	ANTI-TB AGENT	ABBREVIATION
Group 1. First-line oral agents	Isoniazid	H
	Rifampicin	R
	Ethambutol	E
	Pyrazinamide	Z
	Rifabutin ^a	R
	Rifapentine ^a	Rpt
Group 2. Injectable anti-TB drugs (injectable agents or parenteral agents)	Streptomycin ^b	S
	Kanamycin	Km
	Amikacin	Am
	Capreomycin	Cm
Group 3. Fluoroquinolones (FQs) ^d	Levofloxacin	Lfx
	Moxifloxacin	Mfx
	Gatifloxacin ^c	Gfx
Group 4. Oral bacteriostatic second-line anti-TB drugs	Ethionamide	Eto
	Prothionamide	Pto
	Cycloserine	Cs
	Terizidone ^e	Trd
	Para-aminosalicylic acid	PAS
	Para-aminosalicylate sodium	PAS-Na
Group 5. Anti-TB drugs with limited data on efficacy and/or long-term safety in the treatment of drug-resistant TB (This group includes new anti-TB agents)	Bedaquiline	Bdq
	Delamanid	Dlm
	Linezolid	Lzd
	Clofazimine	Cfz
	Amoxicillin/clavulanate	Amx/Clv
	Imipenem/cilastatin ^f	Ipm/Cln
	Meropenem ^f	Mpm
	High-dose isoniazid	High dose H
	Thioacetazone ^g	T
	Clarithromycin ^g	Clr

^a Rifabutin and rifapentine have similar microbiological activity as rifampicin. Rifabutin is not on the WHO list of essential medicines; however, it has been added here as it is used routinely in patients on protease inhibitors in many settings. Rifapentine is part of a course of latent TB infection and active TB treatment in some countries, but to date, is not part of any WHO-endorsed treatment regimens.

^b There are high rates of streptomycin resistance in strains of MDR-TB; therefore, streptomycin is not considered a second-line anti-TB injectable agent.

^c Gatifloxacin can have “life-threatening” side-effects including serious diabetes (dysglycaemia). The drug has been removed from the formula of a number of countries. Safer alternatives are discussed below in the section on group 5 drugs.

^d Ofloxacin is considered a weaker agent with less activity against TB than other fluoroquinolones and has been removed as a choice in group 3 drugs (*see* section 1.3.4 on group 3 – Select a medicine from group 3 for more information).

^e Terizidone has limited programme and effectiveness data as compared to cycloserine.

^f Clavulanate (Clv) is recommended as an adjunctive agent to imipenem/cilastatin and meropenem.

^g Limited data on the role of thioacetazone and clarithromycin in MDR-TB treatment has resulted in many experts not including these drugs as options for group 5.

1.2 Determine whether there are special circumstances that affect the regimen

A number of conditions should be investigated to ensure that proper treatment is provided. These conditions or circumstances should have been noted in the patient's medical file and in the register of presumptive TB and DR-TB cases (*see* Module B). Be sure to check all the patient records as you decide how to design the patient's regimen. Each patient's situation is different and must be taken into account before treatment begins to ensure the best outcomes. Interview the patients and review their medical file to detect any of the following conditions or situations that **may require** individualized decisions to be made about treatment.^{1,2}

HIV infection: among HIV-positive patients in general, TB is the most prevalent coinfection. Patients who have TB and HIV, and particularly patients who have DR-TB and HIV, present a challenge for treatment. The patient with DR-TB and HIV co-morbidity requires intensive medical care, including prompt initiation of antiretroviral therapy (ART) and co-trimoxazole preventive therapy (CPT) if the patient is not already on these regimens, intensive monitoring of both the response to therapy and potential adverse effects, and management of adverse effects. Care should also include additional nutritional and socioeconomic support as well as infection control. Care and treatment must be coordinated between the team treating the patient for DR-TB and the HIV control programme.

Substance dependence: patients with substance-dependence disorders should be offered therapy for overcoming their addictions. Strongly encourage patients to completely abstain from alcohol or other substances. Patients who take cycloserine and are dependent on alcohol or other substances have a higher incidence of adverse effects, including a higher incidence of seizures. If cycloserine is important to the regimen, it may be used but the patient should be closely observed for adverse effects, and these must be adequately treated.

Psychiatric disorder: adverse effects from cycloserine may be more prevalent in patients with psychiatric disorders, but the benefits of using this medicine may outweigh the potential higher risk. Hence, the use of cycloserine is not absolutely contraindicated in these patients. However, close monitoring is recommended when cycloserine is used in patients with psychiatric disorders or in other patients who have shown a tendency towards depression (or are at risk of suicide, as a rare adverse effect of this medicine is suicidal ideation).

Liver disorder: patients with a history of liver disease can receive the usual DR-TB regimens provided there is no clinical evidence of chronic active liver disease, acute viral hepatitis or excessive alcohol consumption. Otherwise, avoid pyrazinamide and use other medicines known to cause hepatotoxicity with caution; liver enzymes should be monitored closely.

Seizure disorder: avoid cycloserine in patients with active seizure disorders that are not well controlled with medication. However, in cases where cycloserine is a crucial component of the treatment regimen, it can be given and the seizure medication adjusted as needed.

Renal insufficiency: patients with renal insufficiency require close supervision and modification of the doses of certain medicines. Monitor serum creatinine and electrolytes every 1–2 weeks

while the patient is on the injectable agent. (See Chapter 7 of the Companion handbook for information on adjusting the dose of medicines for patients with renal insufficiency.¹)

Diabetes mellitus: patients with diabetes require close supervision and co-management with the physician who manages the patient's diabetes. The presence of diabetes mellitus may multiply the adverse effects of anti-TB medicines, especially renal dysfunction and peripheral neuropathy. Ethionamide or prothionamide may make it more difficult to control insulin levels. Monitor creatinine and potassium concentrations more frequently than usual, preferably weekly during the first month of treatment and at least monthly thereafter.

Children: the dose of anti-TB medicines should be administered according to the child's weight: weight should be monitored monthly and doses adjusted as the child grows and gains weight (refer to the recommended weight-based dosing for second-line medicines for children in Annex 3 of the Companion handbook¹). A child is often presumed to have the same pattern of drug susceptibility as the contact with DR-TB, but this may not be the case. Therefore, every effort must be made to confirm drug resistance and avoid unnecessarily exposing the child to toxic medicines. However, a paediatric patient may have a negative culture, and regimens can be designed only on the contact's DST results and history of exposure to anti-TB medicines. Although no long-term studies have proven the safety of anti-TB medicines given for prolonged periods to children, DR-TB is life-threatening and the risks and benefits of treatment should be discussed with the family. There is no anti-TB medicine that is absolutely contraindicated in children, including the fluoroquinolones, whose benefits outweigh their risks.

Breastfeeding: anti-TB medicines are found in breast milk in concentrations that equal only a small fraction of the therapeutic dose for an infant, but there are limited data on the effects of prolonged exposure of infants to the medicines in a second-line drugs regimen. Therefore, when resources and training are available, babies of mothers who have DR-TB may be fed with formula. The decision about whether to breastfeed should be discussed with the mother. If she decides to breastfeed, she may be asked to wear a surgical mask or at least cover her face with a cloth while nursing until she becomes smear negative. While the mother is smear positive, it is best for other family members to take care of the baby to prevent transmission. When mother and infant are together, their time should be spent in well-ventilated areas or outdoors.

Use of oral contraception: patients generally have no problems in continuing to use oral contraceptives unless they vomit within 2 hours after taking the contraceptive; this may lead to poor absorption of the contraceptive and decreased efficacy. Contraceptive pills can also interact with rifampicin, which is used to treat rifampicin-susceptible cases of DR-TB, leading to decreased contraceptive efficacy. In these situations, patients should be advised to use other forms of contraception.

Pregnancy: treatment for DR-TB is not contraindicated during pregnancy. However, since there have only been a limited number of studies on the effects of second-line medicines on pregnant patients, and particularly on the fetus, treatment may be postponed until the second trimester as most teratogenic effects occur during the first trimester. However, if the mother's DR-TB is severe or life threatening, treatment should be started sooner. The regimen for

a pregnant patient should include three to four oral medicines deemed to be effective but exclude the following:

- injectable agents (group 2), because they are particularly toxic to the developing fetal ear (ototoxic), specifically during the first trimester. However, if the use of an injectable is unavoidable, capreomycin may be considered as an alternative; and
- ethionamide (group 4), because of an increased risk of nausea and vomiting, and possible teratogenic effects.

There are limited data on the safety and long-term use in pregnancy of fluoroquinolones, cycloserine, PAS and amoxicillin/clavulanate, but these are considered the drugs of choice for MDR-TB treatment in pregnancy. Immediately after delivery, therapy should be reinforced with an injectable agent or other medicines if necessary.

Consider termination of the pregnancy if the mother's life is compromised.

1.3 Design the proposed second-line regimen

Many countries use standardized regimens to treat RR/MDR-TB and hence the health worker's role is in careful administration of the prescribed standardized regimen. However, when patients have previously taken any of the medicines included in the standardized regimen, have DST results documenting resistance, or show intolerance to a medicine, some modification may be necessary and these facts should be presented to the review panel. Medicines are selected based on the results of DST, the patient's treatment history, and the medicine's efficacy, adverse effects profile, availability and cost.

First and foremost, all treatment regimens for DR-TB patients should consist of **at least four** medicines that have certain, or almost certain, effectiveness, plus pyrazinamide. Often, more than four agents may be started if the pattern of drug susceptibility is unknown, or if the effectiveness of one or more agents is questionable.

The physician at the DR-TB management centre will design a treatment regimen for each DR-TB patient by following the steps described below.

1.3.1 Review the patient's DST results

Review the patient's DST results, making sure that the DST has been done in a quality-assured laboratory. If the DST results **show resistance to a certain medicine**, it should not be included. Only agents documented to have certain or almost certain effectiveness should be used. If the evidence about an agent's effectiveness is unclear, the agent may be included in the regimen but it should not be counted as one of the four effective medicines.

1.3.2 Confirm the patient's history of anti-TB treatment

Every effort should be made to supplement what the patient remembers about previous treatments with objective records from health-care providers to determine which anti-TB agents have been used. A detailed clinical history may indicate which medicines are likely to

be ineffective. The probability of acquiring resistance to a medicine increases with the length of time that it has been used. If a patient was treated with a medicine for longer than 1 month and persistently had positive smears or cultures, the strain should be considered as “probably resistant” to that medicine.

1.3.3 Select one injectable agent from group 2

Always use one injectable agent from group 2, either kanamycin or amikacin or capreomycin. Generally, the injectable agent should be used for at least the first 8 months (and at least 4 months past culture conversion) along with the other drugs constituting the intensive phase of treatment. Kanamycin is generally selected due to its lower cost. Kanamycin and amikacin have a high frequency of cross-resistance – that is, if a strain is resistant to one of these medicines, it is likely to be resistant to other medicines in the same family. If an isolate is resistant to kanamycin and amikacin, then capreomycin should be used. Given the high rates of streptomycin resistance in patients with MDR-TB and its extensive use as a first-line agent in many countries, streptomycin is not often used in regimens for treating MDR-TB, even if DST shows susceptibility to it. However, in cases where the strain is resistant to all the second-line injectable drugs (amikacin, kanamycin, and capreomycin), but it is susceptible to streptomycin, streptomycin should be considered, as there is little cross-resistance between streptomycin and the other injectable agents.

1.3.4 Select a medicine from group 3

Always use one later-generation fluoroquinolone (levofloxacin or moxifloxacin) from group 3. Levofloxacin or moxifloxacin are considered to be more effective against *Mycobacterium tuberculosis* than ofloxacin. If levofloxacin (or ofloxacin) resistance is documented, use moxifloxacin, but do not rely upon it as one of the four core medicines. Avoid moxifloxacin if possible when using bedaquiline. Gatifloxacin has been associated with serious side-effects, such as hypoglycaemia, hyperglycaemia and new-onset diabetes. Until more valid data clarify the safety profile of gatifloxacin in the treatment of MDR-TB, moxifloxacin or levofloxacin are the preferred fluoroquinolones.

1.3.5 Select medicines from group 4

Add two or more group 4 drugs until you have at least 4 second-line anti-TB drugs likely to be effective. Ethionamide/prothionamide is considered the most effective group 4 drug. Cycloserine and/or PAS should be included in regimens for MDR-TB. Consider treatment history, side-effect profile and cost. DST is not considered reliable for the drugs in this group. As the combination of ethionamide or prothionamide with PAS causes a high incidence of adverse gastrointestinal effects and may lead to hypothyroidism, these two agents are commonly used together only when all three agents in group 4 are needed.

The drug in the group 4 should be started at a low dose for a few days and then gradually increased until the full dose is reached. It should be noted, however, that PAS requires cold-chain storage (not required for sodium PAS), making it less convenient to use.

1.3.6 Select additional medicines from group 1

Based on the criteria discussed above and depending on the circumstances of the patient as described in section 1.2, produce a list of the medicines that may be used for the patient's regimen. Pyrazinamide is routinely added in most regimens; ethambutol can be added if the criteria for an effective drug are met. If DST for isoniazid is unknown or pending, it can be added to the regimen until the DST results are available.

1.3.7 Select additional medicines from group 5 if necessary

Group 5 drugs are not recommended by WHO for routine use in MDR-TB treatment. Although all of them have demonstrated some activity in vitro or in animal models, the evidence of their efficacy in humans for the treatment of DR-TB varies. Most of these drugs are, with the exception of bedaquiline and delamanid, not registered for the treatment of MDR-TB, making their use “off-label.”^d In some cases, the drugs are costly and they require intravenous administration (imipenem and meropenem). However, they remain as options in cases where adequate regimens are impossible to design with the medications from groups 1–4. If a situation requires the use of group 5 drugs, experts will often recommend using two to three drugs from the group, given the limited knowledge of efficacy.

WHO recommends that bedaquiline and delamanid may be added to a WHO-recommended regimen in adult patients with pulmonary MDR-TB (conditional recommendation, very low confidence in estimates of effects). Given the limited data available on bedaquiline and its use under the various situations that may be encountered in different clinical settings, adequate provisions for safe and effective use of the drug must be in place.³

Countries that have introduced bedaquiline and delamanid may be following a different treatment algorithm and need to refer to Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis,¹ or the national guidelines for the purpose.

1.3.8 Calculate doses

Once the regimen has been designed, calculate the correct doses based on the patient's weight and age. Annex A provides the recommended daily doses of each medicine for different patients of different weights, and the most common presentations of each medicine.

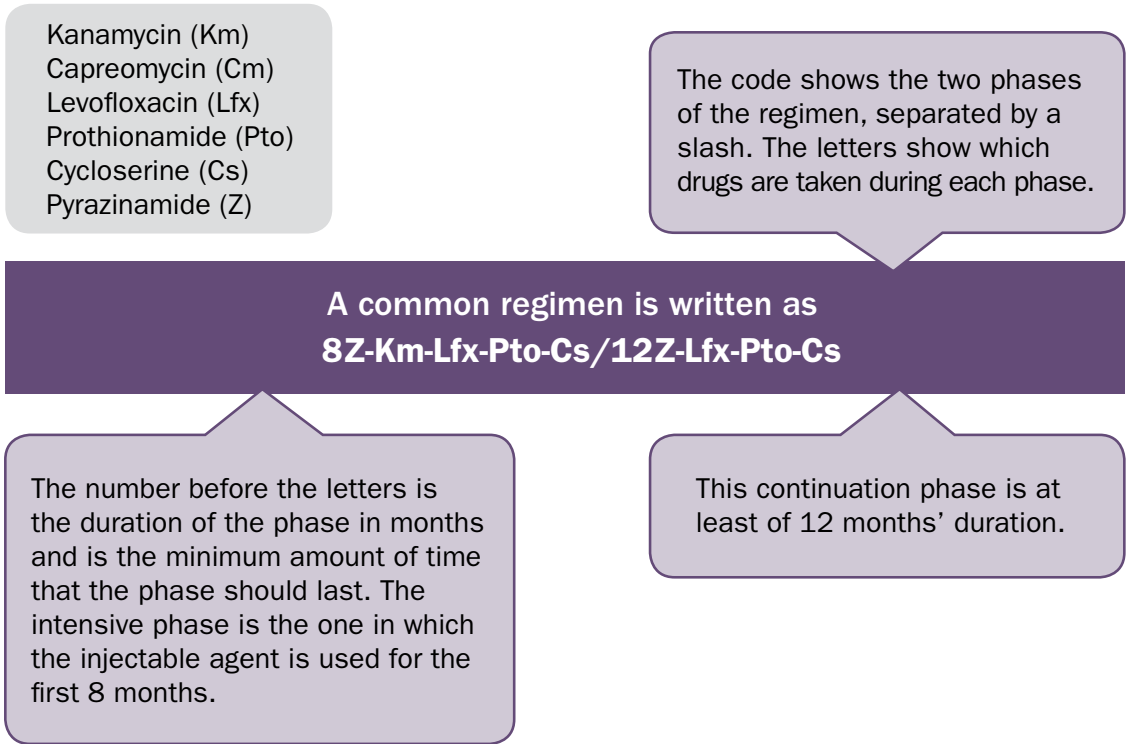
The physician may adjust the doses if other circumstances are present, such as renal insufficiency (*see* Annex B).

The treatment regimen prescribed for an MDR-TB patient is finally recorded as a prescription. Figure 1 describes how to read the medicine code for treatment regimens, while Figure 2 gives the basic principles for designing regimens for DR-TB.

^d **Off-label use** is the practice of prescribing a *drug* to treat a medical condition for which a stringent drug regulatory body has not approved the indication. It may also include using the drug in an age group in whom the drug has not yet been approved or in a dosage or form of administration different from the original approval.

Figure 1 How to read the medicine code for treatment regimens for drug-resistant tuberculosis

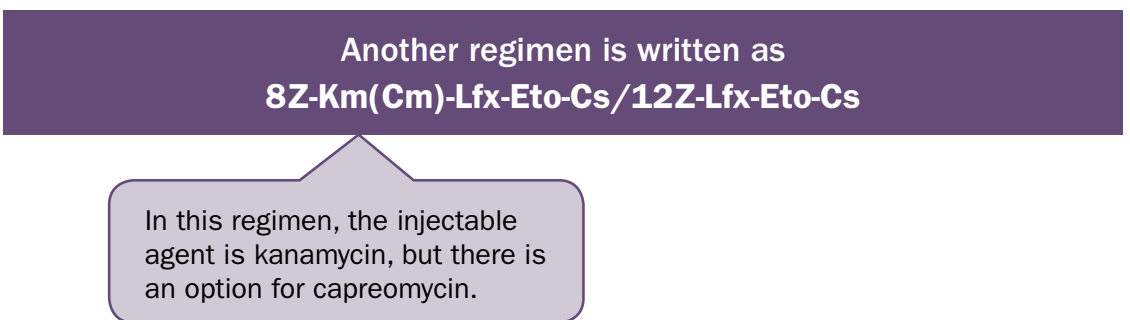
TB treatment regimens are described using a standard code in which each anti-TB medicine has an abbreviation. The abbreviations for the regimens in the example are provided.



In the regimen shown above, the intensive phase of treatment uses four oral medicines (including Z) plus the injectable agent for 8 months. In the continuation phase, the patient takes four oral medicines (including Z) oral medicines without the injectable agent for about 12 months.

The duration of a second-line regimen is at least 20 months (in previously untreated RR-/MDR-TB patients). The duration of the intensive phase or the continuation phase, or both, may be varied, depending on the patient's response to treatment.

When an alternative medicine is specified in a regimen, it appears as a letter in parentheses (*see below*).



Example

Selecting a treatment regimen for MDR-TB^{a,b}

Ali Jafar is a 33-year-old male patient who has been treated for TB by a private practitioner and has never had sputum conversion. He has received RHZES for a number of months. His DST results show resistance to R, H and S, as well as susceptibility to E. He weighs 45 kg.

1. Review the patient's DST results

The DST results show resistance to R, H and S and susceptibility to E.

2. Confirm the patient's history of anti-TB treatment

The patient received RHZES for 5 months before being declared a treatment failure.

3. Select one drug from group 2

Select Km from group 2 because it has never been used. This is the first reliable drug among the four core drugs in the regimen.

4. Select one drug from group 3

Select Lfx from group 3. This is the second reliable drug among the four core drugs in the regimen.

5. Select additional drugs from group 4

Select Pto **or** Eto and Cs from group 4 as two additional drugs. These are the third and fourth drugs that complete the four core drugs in the regimen.

6. Select all drugs from group 1

Select all drugs that may be effective in treating the patient but they should not count towards the 4 effective drugs because they were used for more than a month (used for 5 months). Commonly, Z should be included. E can be included as there is no proof of resistance.

7. Select additional drugs from group 5

This step is unnecessary as you have already chosen four core drugs.

Regimen and dose per day

The regimen will be 8E-Z-Km-Lfx-Pto-Cs/12E-Z-Lfx-Pto-Cs, with Km, Lfx, Pto and Cs being the four core drugs. To determine how many tablets or capsules of each drug to give, divide the recommended dose (mg/day) by the number of milligrams per tablet in common preparations. Hence, a patient who weighs 45 kg will be given daily:

- E 1200 mg/day = 3 tablets of 400 mg per day
- Z 1500 mg/day = 3 tablets of 500 mg per day
- Km 750 mg (injectable) per day = 3/4 of a 1 g vial per day
- Lfx 750 mg/day = 3 tablets of 250 mg per day
- Pto 500 mg/day = 2 tablets of 250 mg per day
- Cs 500 mg/day = 2 capsules of 250 mg per day.

^a Abbreviations for all of the anti-TB medicines are spelt out in Table 1.

^b Among the first-line drugs, DST is considered less reliable and reproducible for streptomycin, ethambutol and pyrazinamide (pyrazinamide testing can be performed only on liquid media after appropriate pH adjustment).

Figure 2 **Basic principles for designing treatment regimens for drug-resistant tuberculosis**

- Regimens should consist of at least four second-line medicines that have certain or almost certain effectiveness along with pyrazinamide (Z) in the intensive phase. If evidence about the effectiveness of a medicine is unclear, the medicine may be included in the regimen but it should not be counted as one of the four core drugs.
- If the pattern of drug susceptibility is unknown or if the effectiveness of a medicines or medicines is unclear, then the treatment may be started with more than four medicines.
- Always use one group 2 agent – an injectable agent – either kanamycin or amikacin or capreomycin during the initial phase, which should last at least 8 months and at least 4 months past culture conversion.
- Always use one fluoroquinolone from group 3. Levofloxacin is the agent of choice.
- Use two or three group 4 agents – the oral bacteriostatic second-line drugs – to ensure there are at least four reliable agents in the regimen. Prothionamide and ethionamide have proven efficacy and low cost; select one of them. Cycloserine and/or PAS should be included in regimens to treat MDR-TB.
- Always use group 1 medicines – the first-line anti-TB medicines – whenever there is no proof of resistance or if the patient’s clinical history suggests that they will be efficacious. Pyrazinamide should **always** be included. However, these drugs are not counted in the four effective drugs required.
- Use agents from group 5 only if the core regimen of four reliable agents cannot be formed using agents from groups 1–4 because of resistance, previous use or adverse effects.

Other points to remember

- Early detection of MDR-TB and prompt initiation of treatment are important factors in achieving successful outcomes.
- Regimens should be based on the national standardized regimen or pattern of drug susceptibility, and the medicines previously taken by the patient, particularly any first-line anti-TB medicines.
- The intensive phase is generally recommended for 8 months (subject to response to treatment), and for at least 4 months past culture conversion.
- The total length of treatment is expected to be continued for at least 12 months past the point at which culture converts to negative and not less than 20 months in total.
- Injectable drugs can be given 5–7 days a week, depending on the availability of a skilled medical person to give the intramuscular (IM) injection. Injectable anti-TB drugs should be given once daily. If adverse effects are problematic in a patient, the injectable agent may be given three times a week after culture conversion.
- Oral drugs are to be given 6–7 days a week under DOT.
- When possible, pyrazinamide, ethambutol and the fluoroquinolones should be given once per day. This dosing may be more efficacious, and it facilitates DOT. However, for children, the recommendation is to give fluoroquinolones twice a day. Ethionamide, prothionamide, cycloserine and para-aminosalicylic acid are preferably given in one dose. However, if circumstances so dictate, they may be given in divided doses as long as each dose is directly observed.
- Pyrazinamide may be used for the entire treatment if it is judged to be effective. Many MDR-TB patients have chronically inflamed lungs that theoretically produce the acidic environment in which pyrazinamide is active.
- The dose should be determined by the patient’s weight. A suggested weight-based dosing scheme is shown in Annex A.

These principles are taken from the Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. Geneva: World Health Organization; 2014 (WHO/HTM/TB/2014.11).



Now do Exercise A – written exercise

When you reach this point in the module, turn to Exercise A, and read the instructions. Complete both cases by yourself and discuss your answers as a group after everyone has finished.

2. Present the case to the review panel for approval of the second-line drugs regimen

The review panel is a case-management committee composed of health-care workers with expertise in managing DR-TB. The committee meets regularly (at least monthly) to discuss cases; their duties include the following:

- Reviewing the presentation of DR-TB cases for enrolment in treatment, and approving proposed treatment regimens;
- During treatment, assessing the patient’s response and approving any change in regimen, treatment outcome or action point relevant to the case presented;
- Arriving at a consensus on decisions when the management of a DR-TB patient is unclear and complicated.

The committee makes decisions by consensus using standards based on WHO guidelines for the programmatic management of drug-resistant tuberculosis.² *Figure 3* illustrates how the review panel manages DR-TB patients.

The review panel should evaluate second-line treatment for all patients. Patients’ cases are presented to the review panel if:

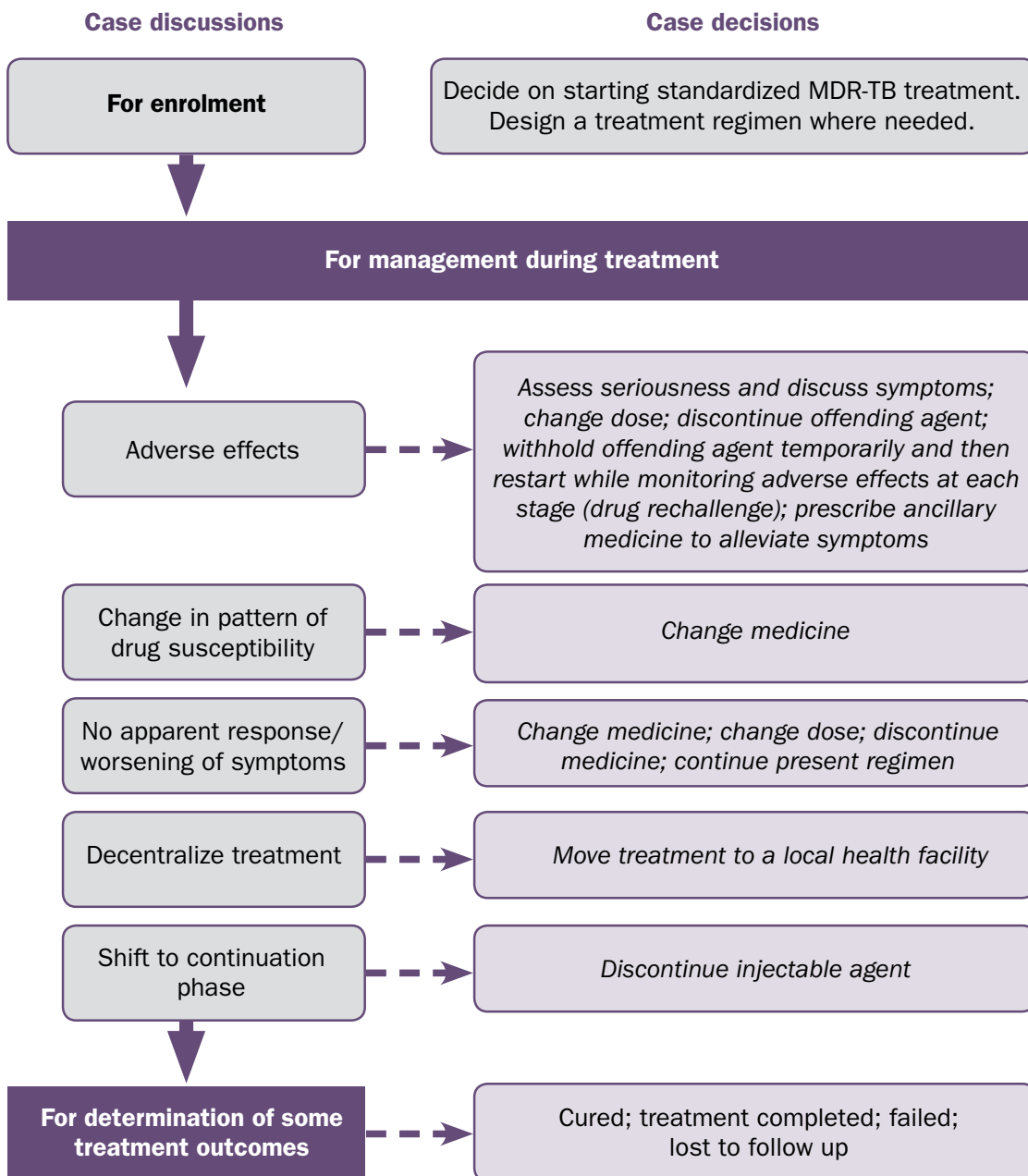
- they have been confirmed to have RR/ MDR-TB by Xpert MTB/RIF or culture and DST as the case may be; or
- there is a high likelihood that the patient has MDR-TB and needs treatment while waiting for the DST results.

When the physician at the DR-TB management centre believes that a patient should receive a second-line regimen, he or she schedules the case for presentation at the review panel’s next meeting. The physician prepares the documents necessary to present the case, including the medical records of previous treatment and testing, laboratory results, X-ray films and the proposed regimen.

Sometimes, for patients presumed to have DR-TB who are awaiting DST results, the review panel or a trained physician may approve a standard second-line drugs regimen to begin right away (“empirical treatment”). At other times, the panel may decide that patients with presumptive MDR-TB should continue their present treatment while awaiting confirmation of the diagnosis.

However, a delay in meeting of the review panel should not delay the start of treatment of patients with proven or a high likelihood of DR-TB. Occasionally, there are emergency situations, such as when the patient with suspected DR-TB is critically ill at the time of first consultation. The physician, after interviewing and examining the patient, and reviewing the clinical history, may assess the patient’s general condition and determine that treatment needs to begin before the review panel’s next meeting. There are also good examples from some countries where nurses initiate MDR-TB treatment based on a set of defined criteria to avoid delays. This is specifically important in case of co-morbidities like HIV where MDR-TB treatment in eligible patients should be initiated at the soonest. Your country’s review panel defines the criteria for the physician’s decision.

Figure 3 **The process followed by the review panel**



3. Enrol the DR-TB patient in treatment at the DR-TB management centre

Once the decision to start the patient on second-line drugs for the treatment of DR-TB has been taken, every effort must be made to locate the patient and start the regimen promptly. Contact the patient or ask the local health facility to find and inform the patient of the schedule for starting treatment.

3.1 Prepare the patient's *Second-line TB treatment card*

To enrol a DR-TB patient on treatment, open a *Second-line TB treatment card*. See the example in section 3.1.3 for a patient who has recently enrolled and begun treatment. Refer to the example as you read this section.

The original *Second-line TB treatment card* will be kept at the DR-TB management centre or local health centre, depending on where the patient will start DR-TB treatment. It is essential that the card is completed accurately, and then kept up to date throughout treatment.

3.1.1 Record the patient's general information

Write the patient's general information in the upper portion of the front of the treatment card. Write the patient's name and district TB registration number (if the patient is currently being treated).

Be sure to record the patient's complete address. The address refers to the residence where the patient has been staying on a long-term basis before starting treatment with second-line drugs. Ask the patient for the name and address of someone you could contact if you need to get in touch with him or her; these are known as the contact name and address. This is the person you would get in touch with if, for example, the patient does not report for a scheduled visit. The contact person should be someone such as a family member, neighbour or friend who will know how and where to find the patient if he or she is not at home.

Record the patient's sex, age, weight and disease site at the initial visit. Weigh the patient to determine his or her current weight, which may have changed in the interval between the physician's examination at the DR-TB management centre and the time when treatment begins.

Once the patient starts treatment, an RR/MDR-TB registration number is created. This number may be given in the format RC-NN-YY, where RC refers to the code for the DR-TB management centre, NN refers to a chronological case number at the centre (the first patient each year is 01 and patients enrolled subsequently are numbered sequentially), and YY refers to the year patient is enrolled. The RR/MDR-TB registration number is entered onto the treatment card as well as in the *Second-line TB treatment register*.

3.1.2 Record previous anti-TB treatment, registration group, HIV information and the review panel's decisions

Refer to the patient's *screening form* for information on previous anti-TB treatment. Completing the section on "Previous TB treatment" is crucial for ensuring that patients with DR-TB are

classified correctly, and it should be as accurate as possible. Make sure you complete the data on first-line and second-line agents taken by the patient. Keep in mind that patients who took anti-TB medicines for less than 1 month should not be registered as having taken the medicines. For the purposes of registration on second-line treatment for RR/MDR-TB, patients are considered “new” if DST was performed within one month of the start of treatment, even if they had received more than one month of first-line drug treatment for TB by the time that the DST results returned and they were registered for second-line TB treatment.

Example: Second-line TB treatment card: record previous anti-TB treatment

Previous Tuberculosis Treatment Episodes				Drug Abbreviations			
District TB Register No. (i.e. BMU register number)	Start Date (if unknown put year)	Regimen (write regimen in drug abbreviations)	Outcome	First-line drugs	second-line drugs		
51-10-168	8/9/10	2 HRZE/ 4 HR	Lost to follow up	H=isoniazid	Am=amikacin	Eto=ethionamide	Bdq=bedaquiline
51-11-83	16/6/11	2 SHRZE/ 1 HRZE/ 5 HRE	Treatment failure	R=rifampicin	Km=Kanamycin	Pto=Prothionamide	Clr=clarithromycin
				R=ethambutol	cm=capreomycin	Cs=cycloserine	Cfz=clofazimine
				S=streptomycin	lfx=levofloxacin	Pas=p-amino-salicylic acid	Dlm=delamanid
				Z=Pyrazinamide	Mfx=Moxifloxacin		lpm=imipenem
					Ofx=ofloxacin	Amx/ cCv=amoxicillin/ clavulanate	Lzd=linezolid
					Gfx=gatifloxacin		T=thiacetazone

Previous use of second-line drugs for more than one month?

Y / N / Unknown

If Yes, indicate in Table above

Use the information on the *screening form* about previous anti-TB treatment and its outcome to determine the patient’s registration group. Definitions for DR-TB registration groups are shown in *Figure 4*. Mark the appropriate box for registration group as shown below.

Example: Second-line TB treatment card: determine registration group

Registration Group	Choose one only
New	
Relapse	
Treatment after loss to follow up	
Treatment after failure of first treatment with first-line drugs	
Treatment after failure of retreatment regimen with first-line drugs	X
Other (previously treated without known outcome; previously treated extrapulmonary)	
Transfer in (from another second-line treatment programme)	

Figure 4 **Definitions of registration groups for patients with drug-resistant tuberculosis (RR/MDR-TB)**

DR-TB registration group	Definition
New	A patient who has received no anti-TB treatment or less than 1 month of anti-TB treatment ^a
Relapse	A patient who was previously treated for TB, was declared cured or treatment completed at the end of the most recent treatment episode and is now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection)
Treatment after loss to follow up	A patient who was previously treated for TB and was declared lost to follow up at the end of their most recent treatment episode (these were previously known as treatment after default patients)
Treatment after failure of initial/retreatment regimen	A patient who was previously treated for TB with first-line drugs and whose treatment failed at the end of the most recent treatment episode
Other previously treated patient	A patient who was previously treated for TB but with an unknown or undocumented outcome for the most recent treatment episode

^a For the purposes of registration on second-line treatment for MDR-TB, patients are considered “new” if DST was performed within one month of the start of treatment, even if they had received more than one month of first-line drug treatment for TB by the time that the DST results became available and they were registered for second-line TB treatment.

Patients with unknown previous TB treatment history do not fit into any of the categories listed above.

In the HIV information box, write the date of HIV testing and the results, if available. If the patient is HIV positive, record whether the patient has started ART or CPT and, if so, the dates that treatment started. This information is obtained from the patient.

Example: Second-line TB treatment card: record HIV information

HIV INFORMATION	
HIV Testing done (circle one):	<input checked="" type="radio"/> Y / <input type="radio"/> N / <input type="radio"/> Unknown
Date of Test: <u>12 Nov 2012</u>	Result: <u>Neg</u>
Started on ART (circle one):	<input type="radio"/> Y / <input type="radio"/> N Date: _____
Started on CPT (circle one):	<input type="radio"/> Y / <input type="radio"/> N Date: _____

In the box for Review panel meetings, record the date of the meeting when the decision was made to enrol the patient and any other decisions made at that time. During the course of treatment, whenever the patient’s case is presented to the review panel for decisions on case management or treatment outcome, record the date, the purpose of the presentation and the decisions.

Example: Second-line TB treatment card: record decisions made by the review panel

Meetings of the review panel: dates and decisions		
Date	Decision	Next Date
24-1-13	Treatment Approved - Standard Regimen Z-Km-Lfx-Pto-Cs	

3.1.3 Record Xpert MTB/RIF, smear, culture and DST, line-probe assay (LPA) results

Find any results of sputum-smear microscopy, culture and DST that were sent by the laboratory or forwarded from the local health facility. Use the row labelled Prior on page 2 of the treatment card to record the date, specimen number and results of sputum-smear microscopy and culture that are more than 30 days old. Baseline results are the results that determined the patient’s diagnosis. Enter baseline results in the row labelled “0”.

Example: Second-line TB treatment card: record results of sputum-smear microscopy and culture

Month of Treatment	Sputum Microscopy			Month of Treatment	Culture		
	Date	Sample Number	Result		Date	Sample Number	Result
Prior				Prior			
0	23 Dec 12	727	++	0	23 Dec 12	727	++
1	24 Dec 12	899	+	1			
2				2			
3				3			
4				4			
5				5			
6				6			
7				7			
8				8			
9				9			

Smear results at baseline

Date sputum was collected

Culture results at baseline

In the section for Drug susceptibility testing, record the date that the result was released by the laboratory and the specimen number, both of which are found in the results sent by the laboratory.

Drug-susceptibility test (DST) and line-probe assay (LPA) results

Date sample collected (filled by requestor)	Method ^a	Laboratory serial number(s)	Results ^b (mark for each drug)												
			H	R	E	S	Am	Km	Cm	FQ:	Other:	Other:	Other:	Other:	
23 Dec 2012	Liquid media DST		R	R	R	S									

This patient has a strain of TB that is resistant to isoniazid, rifampicin and ethambutol, and susceptible to streptomycin.

^a Specify: solid media DST; liquid media DST; direct LPA; indirect LPA

^b Results codes: R = Resistant S = Susceptible C = Contaminated - = Not done

Examined by (name and signature): _____

Date of result: 31 Jan 2013

Second-line TB treatment card

TB Control Programme

Second-line Registration Number: HH07-13
 Date of second-line treatment registration: 4/2/2013
 Treatment Centre: Hillmore Hospital
 Patient Name: James Shore
 Address & Telephone: 2499 Longbow Way House 3
 District: Longoria
 Sex (circle one): M F
 Age: 29 yrs DOB: 31/1/1984
 Initial weight (kg): 59 kg
 Height (cm): 176 cm
 Site (circle one or both): Pulmonary Extrapulmonary
 If extrapulmonary, specify site: _____

Registration Group	Choose one only
New	
Relapse	
Treatment after loss to follow up	
Treatment after failure of first treatment with first-line drugs	
Treatment after failure of retreatment regimen with first-line drugs	X
Other (previously treated without known outcome; previously treated extrapulmonary)	
Transfer in (from another second-line treatment programme)	

Transfer in (from another second-line treatment programme) If yes name of center: _____
 Yes
 No

HIV INFORMATION

HIV Testing done (circle one): Y / N / Unknown
 Date of Test: 04-11-10 Result: NEG
 Started on ART (circle one): Y / N Date: _____
 Started on CPT (circle one): Y / N Date: _____

Meetings of review panel (medical commission, selection committee, consilium)

Date	Decision	Meetings of the review panel: dates and decisions
01-02-13	Treatment Approved - Standard Regimen 8Z-Km-Lfx-Pto-Cs	Next Date 05-3-13

Previous Tuberculosis Treatment Episodes			
District TB Register No. (i.e. BMU register number)	Start Date (if unknown put year)	Regimen (write regimen in drug abbreviations)	Outcome
51-10-168	8/9/10	2HRZE/4HR	Lost to follow up
51-11-83	16/6/11	2 SHRZE/ 1 HRZE/ 5 HRE	Treatment failure

Previous use of second-line drugs for more than one month?

Y / N / Unknown

If Yes, indicate in Table above

Drug Abbreviations			
First-line drugs	second-line drugs		
H=isoniazid	Am=amikacin	Eto=ethionamide	Bdq=bedaquiline
R=rifampicin	Km=kanamycin	Pto=Prothionamide	Clr=clarithromycin
R-ethambutol	cm=capreomycin	Cs=cycloserine	Cfz=clofazimine
S=streptomycin	lfx=levofloxacin	Pas=p-aminosalicylic acid	Dim=delamanid
Z=Pyrazinamide	Mfx=Moxifloxacin	lpm=imipenem	Lzd=linezolid
	Ofx=ofloxacin	Amx/cV=amoxicillin/ clavulanate	Mpm=meropenem
	Gfx=gatifloxacin		

Transfer In (from another second-line treatment programme)

If yes name of centre: _____

Second-line TB treatment card

Month of Treatment	Sputum Microscopy		Month of Treatment	Culture		Drug Susceptibility Testing (DST) Results§	
	Date*	Sample Number		Result	Date*	Sample Number	Result
Prior**			Prior**				
0	23 Dec 12	727	0	23 Dec 12	727		23/12/13
1	24 Dec 12	899	1			H	R
2			2			R	R
3			3			E	R
4			4			S	S
5			5			Am	
6			6			Km	
7			7			Cm	
8			8			FQ	
9			9			Other	
10			10			Other	
11			11			Other	
12			12			Other	
13			13			Other	
14			14			Other	
15			15			Other	
16			16			Other	
17			17			Other	
18			18			Other	
19			19			Other	
20			20			Other	
21			21			Other	
22			22			Other	
23			23			Other	
24			24			Other	

Notation method for DST:
 R=resistant
 S=susceptible
 C=contaminated
 Unk=Unknown

§ indicate near result if initial resistance was detected on line-probe assay or Xpert MTB/RIF

Notes:

*All dates in both tables are the dates the sputum was collected from the patient
 **The date the sputum was collected that led to the patient being registered with MDT-TB (if performed)

Notation Method for Recording Smears:

No AFB	0
1-9 AFB per 100 HPF	Scanty (and report number of AFB)
10-99 AFB per 100 HPF	+
1-10 AFB per HPF	++
>10 AFB per HPF	+++

Notation Method for Recording Cultures (solid media):

No growth reported	0
Fewer than 10 colonies	Report number of colonies (1-9)
10-100 colonies	+
More than 100 colonies	++
Innumerable or confluent growth	+++
Non-tuberculous mycobacteria	NTM
Contaminated	contaminated

Notation method for Xpert MTB/RIF results

T	= MTB detected, rifampicin resistance not detected
RR	= MTB detected, rifampicin resistance detected
TI	= MTB detected, rifampicin resistance indeterminate
N	= MTB not detected
I	= invalid / no result / error

3.1.4 Request baseline Xpert MTB/RIF, LPA, smear, culture, DST, chest X-ray and blood tests

If the laboratory tests were done more than 30 days prior to the start of treatment, request new smear, and culture and DST examinations for a baseline. For example, if the patient has been waiting for approval of second-line drugs treatment for 3 months, new baseline examinations are necessary. However, the patient can be started on treatment based on the previous results while the new sample is being processed. Follow the process of collecting sputum for laboratory testing for smear examination, culture and DST described in Module B. Chest X-rays and blood tests should be requested using your country's forms.

3.2 Inform the patient about enrolling for treatment

When the patient reports to the DR-TB management centre for enrolment, you should provide information on the following:

- DR-TB and the difference between treatment for drug-susceptible TB and DR-TB;
- the second-line drugs regimen (due attention to any new drugs in the regimen and any need for informed consent);
- the necessity of having someone directly observe the treatment;
- the need for hospitalization (if relevant);
- preventing the spread of the disease;
- patients' rights and responsibilities;
- support services available at the DR-TB management centre or at other governmental offices providing social protection services for which the patient is eligible;
- the reasons for tracing close contacts of the patient;
- what the patient can expect and what he or she will need to do next.

At the conclusion of the counselling session, confirm that the patient agrees to undergo treatment for DR-TB; ensure that the patient understands that this requires:

- DOT 6(7) days per week for at least 20 months;
- monthly follow-up sputum examinations; and
- attendance at monthly monitoring visits with a physician at the DR-TB management centre.

See Module D to learn more about the messages to give patients.

3.3 Enter the patient in the *Second-line TB treatment register*

Once a patient has begun treatment, register the patient in the *Second-line TB treatment register*. Complete the required data as shown in the example. This is mostly the same information that you have filled out in more detail on the *Second-line TB treatment card*.

Copy the patient's demographic and background information from his or her *treatment card*. In the first column, write the patient's RR/MDR-TB registration number, for example, HH-05-10 (DR-TB management centre code, case number, year).

Enter the date that the patient started treatment in the "Date treatment start" column.

Example: Second-line TB treatment register (page 1 of 4)

Unique Second-line TB Treatment Register No.	Date Entered in Second-line TB treatment register	Name	Sex (M/F)	Age/Date of Birth D/M/Y	Address	Date entered in BMU TB Register	BMU TB Register No	Site of Disease (P/EP/Both)	Registration Group*	Second-line Drugs received previously (Y/N/Unk)	Date Sample taken for DST	Result of Drug Susceptibility Testing (DST) **												
												H	R	E	S	Amk/Km	Cm	FQ	Other	Other	Other			
HH-01-13	6 Jan 2013	Elena Fari	F	43	22 Market St, upstairs, Nikobo			P	3	N	18 Nov 2012	R	R	R	S	-	-	-	-	-	-	-	-	
HH-02-13	18 Jun 2013	Resuma Rasel	M	23	142 Tower Road, Nikobo			P	5	N	20 Nov 2012	R	R	R	S	-	-	-	-	-	-	-	-	
HH-03-13	30 Jan 2013	Sonroy Patel	M	67	38 Town Park, Nikobo			P	5	N	1 Dec 2012	R	R	R	R	-	-	-	-	-	-	-	-	
HH-04-09	8 Feb 2013	Joseph Abanya	M	28	Station Sq, above jeweler, Nikobo			P	4	Y (FQ)	3 Dec 2012	R	R	R	S	-	S	-	-	-	-	-	-	
5				/ /																				
6				/ /																				
7				/ /																				

* 1=New; 2=Relapse; 3=After Loss to follow-up; 4=After failure of first treatment with first-line drugs; 5=After failure of retreatment with first-line drugs; 6=Transfer in (from another Second-line TB treatment centre)

** Enter DST result that led to the patient being registered for second-line treatment. If DST is pending, complete when the results become available

Drug Abbreviations			
First-line Drugs	Second-line Drugs		
H=Isoniazid	Amk=Amikacin	Eto=Ethionamide	Bdq=Bedaquiline
R=Rifampicin	Km=Kanamycin	Pto=Prothionamide	Cfz=Clofazimine
E=Ethambutol	Cm=Capreomycin	Cs=Cycloserine	
S=Streptomycin	Lfx=Levofloxacin	"PAS=p-aminosalicylic acid"	lpm=Imipenem
Z=Pyrazinamide	Mfx=Moxifloxacin		Lzd=Linezolid
	Ofx=Ofloxacin	Amy/Clv=Amoxicillin/clavulanate	T=Thiacetazone
	Gfx=Gatifloxacin		

Enter the date the review panel approved treatment under the heading “Approval date”. Fill in the patient’s full name, sex, age and address (this should be an address that you could use to visit the patient if necessary).

Using information from the *Second-line TB treatment card*, fill in the columns headed “HIV status”, “Registration group” and “Second-line drugs received previously”. Find the **baseline** smear and culture results (for month 0) and DST results, as well as the patient’s approved treatment regimen, on the *treatment card*, and copy them into the *Second-line TB treatment register*.

3.4 Make a home visit

Visiting the patient’s home will allow you to verify that the patient lives at the address stated in the records and record other relevant addresses (for example, those of a partner or spouse, parents, place of work or study, or private doctor who may be consulted). This maximizes the likelihood of being able to locate a patient who interrupts treatment. Also ask for mobile phone numbers of the patient and family members; these have proved valuable in many settings.

A home visit provides an opportunity to arrange screening for household contacts, especially children who are younger than 5 years and people of any age who may have symptoms of TB or be living with HIV. While at the residence, suggest ways to improve ventilation in the house and practices that the patient should observe to avoid infecting others.

This visit should provide time to discuss with the patient and family members the nature of the disease and its treatment, the infection control measures to apply, the measures to prevent stigmatization and discrimination, the duration of treatment and the need to notify the health facility ahead of time if their address changes. Interview the patient and his or her relatives about their socioeconomic conditions to determine the need for providing appropriate enablers to ensure the patient’s adherence to treatment, if necessary. With this information, you can make an assessment and give recommendations to the responsible person at the DR-TB management centre about what additional steps should be taken to ensure that the patient has appropriate support for treatment. Some possible incentives and enablers are listed in Module E.

3.5 Complete the *Second-line TB treatment card* with additional information

Complete the *Second-line TB treatment card* with the patient’s current weight, treatment regimen and doses of each medicine.

3.5.1 Weigh the patient and adjust doses of individual medicines as necessary

The patient might have gained or lost weight in the interval between the initial screening for DR-TB and the review panel’s approval of treatment. This can affect the dose of each medicine. Weigh the patient and correct any dose that needs to be altered. (*See Annex A* to learn about the specific doses for each medicine.)

3.5.2 Record the second-line treatment regimen and doses

When treatment is approved, record the regimen's abbreviation on the *treatment card* under the heading "Second-line treatment regimen". Record the date when the patient starts treatment in the first row as well as the dose of each of the medicines; doses should be stated as the number of tablets, capsules or sachets for oral medicines. For injectable agents, write the number of milligrams to be administered. One full daily dose consists of each the medicines in the correct amounts that the patient should take in a day.

Most medicines should be started at the full daily dose prescribed for the patient. Cycloserine, ethionamide and para-aminosalicylic acid (group 4 drugs) may be started at lower doses and increased over 2 weeks to reduce the frequency or severity of side-effects; however, the review panel and the physician will dictate this.



Now do Exercise B – written exercise

When you reach this point in the module, turn to Exercise B and read the instructions. When you have finished the exercise, review your answers with a facilitator.

4. Obtain medicines for the patient

Obtain the supply of medicines in packets along with the injectable agent, all of which will be prepared by the DR-TB management centre's pharmacist and labelled with the patient's name. Each packet contains the patient's daily dose of the treatment (excluding para-aminosalicylic acid if it is part of the regimen because it must remain refrigerated). Depending on the country policy, the pharmacist will replenish the packets and the injectable agent every week or fortnight. (*See* Module F for more information about how and when to prepare the medicines. As different medicines may be received in different packaging, daily packets for individual patients may need to be made. This is also discussed further in Module F.)

Be sure that you have obtained the correct regimen for the patient as specified on the *Second-line TB treatment card* and that you have the medicines and doses required for 1 week of treatment.

Give the patient information about the anti-TB medicines that he or she will be taking. Let the patient know what the different medicines look like, the number of pills that he or she will be taking each day and the frequency and possibility of adverse effects or reactions. (*See* Module D for more information about adverse effects.)

5. Directly observe treatment and record it on the treatment card

Observe the patient take all of the anti-TB medicines every day. **This means that every day, you must observe that the patient actually swallows each of the medicines and, during the intensive phase, receives the injectable agent.** Generally, medicines should not be given to a patient for self-administration because sometimes patients have reasons to postpone or even not take the medicine as prescribed, which is absolutely essential for the medicines to work.

The primary way **to prevent transmission of MDR-TB to the community** is for MDR-TB patients to take their drugs regularly. Generally, they will then become noninfectious in a few months.

5.1 Receive the DR-TB patient each day

When supervising treatment, make it as quick and easy for the patient as possible. Do not make ambulatory patients wait in line. Prioritize patients once they arrive, and prioritize DOT over other activities, such as providing information on adverse effects or well-being. All health-care workers must understand that it is not acceptable for patients to wait in line for treatment. The patients should be treated in settings with proper infection control measures in place to reduce the risk of transmission of DR strains. Delays discourage patients from continuing treatment.

Administering DOT includes greeting the patient by name and asking about his or her well-being and any adverse reactions (*see* section 6), as well as personal or social problems. If there is a problem that you cannot resolve, refer the patient for appropriate help. If there is a need for further management by specialists, this should be coordinated by the physician in the DR-TB management centre. (*See* Module E for additional information.)

5.2 Administer and directly observe the patient taking the anti-TB medicines

The steps involved in administering DOT to a DR-TB patient are described in *Figure 5*.

Sometimes a patient will not be able to come for DOT because of a conflict, such as the need to travel or attend a family event. This will be counted as an absence and should be avoided if at all possible while the patient is undergoing treatment. The doses missed during these absences will be made up by extending the duration of treatment. **Generally, medicines for DR-TB are not to be given to a patient for self-administered treatment.** However, the treating physician may take an exceptional decision when absence is not a regular feature and there is enough ground to believe that the patient will take the medicines, e.g. a community treatment supporter at the place of visit.

Some patients may not understand this policy. It is vital that you explain why DOT is so important. Patients must comply strictly with treatment because it may be their last

Figure 5 How to directly observe treatment for drug-resistant tuberculosis (RR/MDR-TB)

1. Greet the patient cordially, addressing the patient by his or her name. Ask how the patient is feeling and whether the patient has had any problems since the last visit.
2. Take out the patient's *Second-line TB treatment card*.
3. Open the patient's packet of medications for the day. Check the prepackaged medications against the *treatment card* to verify that they are correct before giving them to the patient.
4. Put the tablets into the patient's medicine cup and provide water to assist in swallowing. Watch the patient swallow each of the tablets. If the patient has difficulty swallowing them one after the other, the patient may pause briefly.
 - Fluoroquinolones should not be taken within 2–3 hours of a meal containing milk or any product containing calcium, magnesium, aluminium or iron, so advise the patient not to consume these products during this time. Examples of foods containing these are yogurt, antacids and nutritional supplements. For inpatients, medicines may be given before breakfast if the meal does not contain these products; otherwise breakfast should be postponed. Sprinkle PAS granules over applesauce or swirl in acidic juices to decrease gastrointestinal discomfort and diarrhoea.



If the patient becomes nauseated while taking the medicines, suggest taking them with food or drink.

5. To administer the injectable agent, use a sterile needle and syringe. **Check the Second-line TB treatment card to verify the correct dose of the injectable agent.** Follow the manufacturer's instructions for preparation. (It is a practice in some countries to give the injectable before giving oral drugs.)
6. Document the doses observed on the *Second-line TB treatment card*.
7. Verify that the patient feels well and confirm the next day's appointment.

opportunity to be cured. This discussion should be conducted with utmost respect for the patient, emphasizing the fact that the ultimate concern is for his or her cure.

Explain to the patient that experience has shown that DOT has a much better chance of curing patients than self-administered treatment. It ensures that no doses are forgotten, and no medications are omitted because they are lost or ruined. If the patient experiences any adverse effects, the treatment observer can learn about this right away and help the patient understand why the effect is occurring and provide supportive treatment.

Explain that in countries all over the world, DOT has been shown to have much better success in curing patients. DOT is administered for the benefit of the patient and the community. As treatment for DR-TB is expensive and the process is long, every measure must be taken to ensure that the treatment is a success.

If a patient misses a scheduled day but comes the next day, give the patient only 1 day's medicine to take in front of you. Do not give a double dose. As the patient must complete a certain number of doses, each missed dose will delay or extend the completion of the phase and the treatment by a day.

5.3 Mark the *Second-line TB treatment card* for each treatment observed

On the first day that you give DOT, begin marking it in the “Administration of drugs” section on page 3 of the *Second-line TB treatment card*. In the example on page C-41, the numbers in the top row represent the days of the month. Write the month and year when the patient started treatment in the left column and the months following in the succeeding rows. For example, if the first day of treatment is 25 October 2010, write “Oct ’10” in the first column and use the appropriate code under “25” in this row as shown in *Figure 6*.

If treatment of patients is decentralized to a local health facility, a copy of the treatment card will be prepared. The staff providing DOT will mark both copies of the *Second-line TB treatment card* (the facility's copy and the patient's copy). When the patient returns to the DR-TB management centre for a monthly monitoring visit, the patient's copy will let the physician at the DR-TB management centre know about treatment compliance as well as provide other significant information.

Figure 6 How to mark the *Second-line TB treatment card*

Tick (✓) the box for the month and day

Each day that you observe the patient swallowing the medicines and receiving the injection, tick the box under the corresponding date.

“0” or “Ø” for missed doses

If the patient does not show up for an appointment, put a “0” under that date to indicate that a dose was missed.

“I” for incomplete doses

If a patient takes only some of the medicines, write “I” for “incomplete” in red under the date. Make a note in the observations section of the treatment card of the reason why the patient did not take all of the medicines.

Dash “-” for holidays from treatment

It is useful to mark the holidays for the following month ahead of time to facilitate marking the card correctly when treatment is observed.

The total number of doses taken monthly and cumulatively is reflected in the last two columns. This will guide you in determining whether a patient is ready for the continuation phase or is eligible for treatment completion. *See* section 7.5.2 for information about eligibility for the continuation phase.

5.4 Continue providing a patient-centred approach to care

Assess regularly the evolution of patients' beliefs, values and needs related to adherence to treatment. Reinforce those beliefs, behaviours and values that prevent TB transmission, promote adherence to treatment, and prevent stigma and discrimination. Reinforce messages about the treatment for DR-TB each time that you administer DOT. Encourage the patient so that he or she will continue taking the medicines on schedule and will complete all required doses. Inform the patient about the dangers of irregular or incomplete treatment. (*See* Module D.)

Review the following whenever appropriate:

- whether the patient is following infection control measures;
- whether the relatives and other caregivers are an effective source of support;
- if the patient perceives stigma and discrimination due to the disease;
- how the patient is coping with the regimen;
- whether the patient has had any adverse effects from the medicines or whether you have observed any adverse effects); encourage the patient to continue treatment by reminding him or her that adverse effects usually go away in a few weeks;
- if the regimen is changed, review the type, colour and quantity of medicines, and the frequency of doses;
- emphasize the importance of continuing treatment and the danger of irregular treatment;
- what should be done if the patient is planning to travel or move;
- emphasize the frequency and importance of required sputum examinations and monthly monitoring visits with the physician;
- when the treatment of a patient will be eligible for decentralization.

Remind the patient to inform you if he or she is going to move away, so that you can coordinate a transfer to another health facility for treatment. It is far better to prevent a loss of contact than to have to locate and convince a patient to resume treatment after an interruption.

Example: Second-line TB treatment card

This patient began treatment on 25 October 2012. She has treatment daily except Sundays in October.

		Administration of Drugs (one line per month), NAME OF DRUG:																														Wt (kg), Lab, X-ray			
Month	Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31			
Oct '12		✓	✓	✓	✓	✓	✓	-	✓	⊕	⊕	✓		-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	-			
Nov '12																																		51	52.8

She missed her appointments on 9 and 10 November.

She had an incomplete dose on 13 November.

She had split doses on 22-24 November.

5.5 Mark the patient's attendance on the *DR-TB daily attendance sheet*

Complete the *DR-TB daily attendance sheet* (given below) at the end of each day or after seeing each patient. Mark the patients who came for DOT, and identify any who did not arrive at the DR-TB management centre's clinic for their treatment. As shown in the example, a tick (✓) means that the patient received DOT; a "0" or "Ø" means that the patient did not come for the day's treatment. This same form can be used in hospitals as a daily tracking sheet for DOT.

If a patient has not come for treatment, efforts must be made to contact the patient to find out the reason for the absence and to ensure that no other doses are missed.

If your facility treats only a small number of patients (less than five or six), then using this form is not necessary: you can use the patient's *Second-line TB treatment card* to determine quickly whether he or she attended treatment.

5.6 Weigh the patient monthly, and report any significant change in weight to the physician for dose adjustment

Every month, weigh the patient to track his or her progress, or earlier if reduction or increase in weight is easily noted by patient or health-care worker. On page 3 of the *Second-line TB treatment card* under the heading "Administration of drugs", document the patient's weight each month in the column marked "Weight (kg)".

Many times, weight gain is a sign of improvement for TB patients, but weight loss may signal that there is a problem. The dose of the medications may need to be altered when there is significant weight gain or loss. Every time the patient is weighed, refer to the recommended doses for that weight band to determine whether an adjustment needs to be made to the daily number of tablets or capsules or sachets.

When a change in dose is needed, the physician will order the change (*see* section 8).



Now do Exercise C – written exercise followed by a group discussion

When you have studied the attendance sheet on the next page, you are ready to do Exercise C. Follow the instructions and do this exercise by yourself. When everyone has finished, discuss your answers as a group.

6. Monitor patients for adverse effects

The treatment of DR-TB involves the use of multiple medicines. Many patients experience difficulties or intolerance related to the medicines. Health workers cannot predict whether a patient will experience an adverse effect from an anti-TB agent. The use of a medicine should not be restricted because it might cause a reaction. Some elderly patients or patients who are seriously ill may tolerate the medications well. However, others could have serious problems with relatively simple regimens. Most reactions occur during the first few months of treatment. Some resolve over time; others can be treated with ancillary medicines depending on the patient's symptoms. Experiencing adverse effects is one of the main reasons that patients default from treatment, so the timely detection and adequate management of adverse effects is vital. Some patients may need additional support, especially at the beginning of treatment when adverse effects may be more severe.

6.1 Continually assess patients for adverse effects

Monitor the patient closely to ensure that any adverse effects from second-line medicines are recognized quickly. The ability to monitor patients for adverse effects daily is one of the major advantages of DOT.

The majority of adverse effects are easy to recognize. Commonly, patients will voluntarily inform that they are experiencing adverse effects. However, it is important to have a systematic method of interviewing patients, as some may be reticent about reporting even severe adverse effects. Other patients may be distracted by one adverse effect and forget to report another.

Prior to giving the patient his or her daily dose of medicines, ask the patient how he or she is feeling. Listen carefully to the answer, and note any complaints that may indicate adverse effects from the anti-TB medicines. Also look carefully at the patient to see whether you observe any signs of adverse reactions. Screen patients regularly for symptoms of common adverse effects: rashes, gastrointestinal symptoms (nausea, vomiting, diarrhoea), psychiatric symptoms (psychosis, depression, anxiety, suicidal thoughts), jaundice, ototoxicity, peripheral neuropathy and symptoms of electrolyte depletion (muscle cramping, palpitations).

An adverse reaction may be mild or severe. *See* the lists of mild adverse effects in *Table 2* and of moderate-to-severe adverse effects in *Table 3*. All health-care workers should be familiar with the common adverse effects of treatment for DR-TB. Keep in mind that adverse effects occur more commonly in HIV-positive people, in elderly people and in those with co-morbidities.

6.2 Explain to the patient the probable cause of adverse effects and what can be done

Patients who experience adverse reactions may be frightened, may feel worse and may want to discontinue the anti-TB treatment. Patients are more likely to have fear and anxiety about an adverse effect if they do not understand why it is happening. Discuss with the patient the possible reasons for the adverse effects and what steps can be taken to try to alleviate them. In general, adverse effects should be treated to the extent possible, and the patient should be encouraged to tolerate these effects until they resolve. Also explain that although most patients

experience some kind of minor side-effects, these generally do not last more than a few weeks and will probably go away.

As most adverse reactions occur during the early months of treatment and diminish with time, informing patients of this fact may reassure them. Educate the patient about the adverse effect and encourage the patient to continue treatment. Explain to the patient that although the adverse effects of treatment may be difficult, they are generally much less severe than stopping treatment and continuing to be sick.

Even though some adverse effects may persist, the patient needs to continue treatment to prevent increased drug resistance and possibly death. If the patient continues to complain about a minor effect even after you have provided advice and information about the side-effect, ask the patient to see the physician at the DR-TB management centre for a follow-up examination.

6.3 Manage mild adverse effects

In *Table 2*, a number of common mild adverse reactions are listed along with a description of how to manage them and the medicines suspected of causing them. Medicines listed in **bold** type are more strongly associated with the adverse effect.

If the patient has mild adverse effects, continue providing anti-TB treatment. Give symptomatic relief to counteract the adverse effects, and assist the patient in tolerating them to the extent possible, perhaps by seeing the patient more often or making home visits if appropriate. Symptomatic treatment may include giving antihistamines for mild allergies, for example, or advice on non-pharmacological measures, such as using a cold compress for pain at the injection site. Giving ancillary medicines free of charge for symptomatic treatment – for example, an anti-emetic for nausea or a pain reliever – is a necessary and helpful step for most patients. However, even though some ancillary medicines help alleviate mild adverse reactions, in general, patients must tolerate them, considering the possibility that they will soon resolve.

Table 2 Mild adverse effects of treatment regimens for drug-resistant tuberculosis

Adverse reaction	Suspected agents	Suggested management
Anorexia	Z, Pto, Eto	Appetite stimulant
Arthralgia	Z	Nonsteroidal anti-inflammatory drugs (NSAIDs); paracetamol; exercise
Change in behaviour (talkativeness, irritability)	Cs, Ofx	Haloperidol; pyridoxine 50 mg/250 mg of Cs, up to 200 mg/day maximum
Cutaneous reaction	H, R, Z, E, Pto, Eto, Cs, PAS, S and other aminoglycosides	Antihistamines; hydrocortisone creams
Depression	Cs, H, Pto, Eto	Selective serotonin reuptake inhibitors (fluoxetine, sertraline); tricyclic antidepressants (amitriptyline)

Continues...

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Adverse reaction	Suspected agents	Suggested management
Diarrhoea	PAS	Rehydration; loperamide
Excessive salivation	Eto, Pto	Ice chips; metoclopramide
Flu-like syndrome	R	Paracetamol
Gastritis	PAS, Pto, Eto	Antacids (for example, calcium carbonate); H2 blockers; proton pump inhibitors
Gynaecomastia	Pto, Eto	Reassurance; surveillance
Headache	Pto, Eto	NSAIDs; paracetamol; exercise
Insomnia	Ofx, Lfx, Mfx	Antihistamine
Metallic taste	Pto, Eto	Reassurance
Musculoskeletal pain	No specific medicine	NSAIDs; paracetamol
Nausea and vomiting	Pto, Eto, PAS, R H, Z, E	Rehydration; metoclopramide; divide dose (morning and afternoon) only if both doses can be supervised
Olfactory hallucination	Pto, Eto	Reassurance
Peripheral neuropathy	Cs, S, Km, Pto, Eto, FQ	Increase pyridoxine to maximum daily dose (200 mg/day); tricyclic antidepressants (for example, amitriptyline)
Pain at injection site	S, Km, Am, Cm	Cold compress
Photophobia	Pto, Eto	Reassurance
Vertigo or dizziness	S, Km, Cm, Pto, Eto	Betahistine; cinnarizine

Am, amikacin; Amx/Clv, amoxicillin/clavulanate; Cfz, clofazimine; Cm, capreomycin; Cs, cycloserine; E, ethambutol; Eto, ethionamide; H, isoniazid; Km, kanamycin; Lfx, levofloxacin; Mfx, moxifloxacin; Ofx, ofloxacin; PAS, para-aminosalicylic acid; Pto, prothionamide; R, rifampicin; S, streptomycin; Z, pyrazinamide

6.4 Refer the patient to a specialist physician for moderate or severe adverse effects

If a patient has any of the moderate or severe adverse effects listed in *Table 3*, a physician should examine the patient immediately and take appropriate action. Refer the patient to a physician at the DR-TB management centre. In *Table 3*, medicines listed in **bold** are more strongly associated with the adverse effect.

It is important to detect these moderate-to-severe adverse effects at an early stage and refer the patient to a physician as soon as possible for assessment and further action. Adjustments to doses or withdrawal of anti-TB medicines must always be done at the DR-TB management centre and with the approval of the review panel.

Reminder: If at any time the patient's condition worsens significantly; refer the patient to a physician at the DR-TB management centre for further assessment and treatment.

6.5 Document adverse effects on the *Second-line TB treatment card*

Document all adverse effects, treatment interruptions, actions taken and other significant events related to the patient's treatment in the "Comments" section of the *Second-line TB treatment card*. Write down the type of problem the patient experienced – for example, gastritis or hearing loss – and the medicine suspected of causing the effect or document the patient's absence from DOT. Then note the action taken, for example, prescribing symptomatic treatment, making a home visit, or sending the patient to the physician at the DR-TB management centre.

Table 3 Moderate-to-severe adverse effects of treatment regimens for multidrug-resistant tuberculosis

Adverse reactions	Suspected agents	Suggested management
Acute renal failure	S, Km, Am, Cm	Discontinue medicine suspected of causing the effect; consider using Cm if an aminoglycoside had been the prior injectable agent in the regimen; consider dosing 2–3 times/ week if agent is essential to regimen and patient can tolerate (closely monitor creatinine concentrations); adjust doses of all anti-TB agents according to creatinine clearance.
Electrolyte abnormalities (decreased blood concentrations of potassium, magnesium and calcium)	Cm, Km, Am, S	Check electrolytes (K, Mg, Ca); replace electrolytes as needed.
Generalized hypersensitivity (including Stevens–Johnson syndrome)	Any medicine	Withdraw the medicines and refer to specialist.
Hearing loss	S, Km, Am, Cm, Clr	Document hearing loss and compare with baseline audiometry if available; change parenteral treatment to Cm if appropriate (that is, no resistance is confirmed or suspected); decrease frequency or lower dose, or both, of suspected agent if it can be done without compromising regimen; discontinue agent suspected of causing the effect if this can be done without compromising the regimen.
Haemolysis	R	Discontinue medicine and refer to specialist.
Hepatitis or jaundice	Z, H, R, Pto, Eto, PAS, E	Discontinue therapy pending resolution of hepatitis; eliminate other potential causes of hepatitis; consider suspending agent most likely to have caused adverse effect permanently; reintroduce remaining agents, one at a time, using the most hepatotoxic agents first and monitoring liver function.
Hypothyroidism	PAS, Pto, Eto	Initiate thyroxine therapy.

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Adverse reactions	Suspected agents	Suggested management
Intractable vomiting	Pto, Eto, PAS, H, E, Z	Assess for dehydration and initiate rehydration if indicated; divide the dose (morning and afternoon) only if both can be directly observed; discontinue agent suspected of causing adverse effect if this can be done without compromising the regimen.
Optic neuritis	E	Discontinue medicine and refer to ophthalmologist.
Psychosis or psychotic symptoms (violent or suicidal tendencies)	Cs, H	Discontinue agent suspected of causing the adverse effect for a short time (1–4 weeks) while psychotic symptoms are brought under control; initiate antipsychotic treatment and refer to psychiatrist; lower the dose of the agent suspected of causing the adverse effect if this can be done without compromising the regimen.
Purpura	R	Discontinue medicine and refer to specialist.
Seizures	Cs, H	Discontinue agent suspected of causing adverse effect pending resolution of seizures; initiate anticonvulsant therapy (phenytoin, valproic acid); permanently discontinue agent suspected of causing adverse effect if this can be done without compromising regimen.

Am, amikacin; Clr, clarithromycin; Cm, capreomycin; Cs, cycloserine; E, ethambutol; Eto, ethionamide; H, isoniazid; Km, kanamycin; PAS, para-aminosalicylic acid; Pto, prothionamide; R, rifampicin; S, streptomycin; Z, pyrazinamide

6.6 Exhaust all options before changing the second-line regimen when a patient has adverse effects

All attempts must be made to help the patient handle a mild or moderate adverse effect in the hope that the effect will resolve or the patient will learn to tolerate it. It is important for both the patient and the health worker to be aware that without adequate treatment, mortality from DR-TB is high. When a patient has resistance to multiple medicines, and therefore only a few medicines can be used, withdrawing one of them may result in treatment failure.

There are some ways to modify the administration of treatment, which may help with adverse effects, in particular, those caused by oral second-line medicines.

If the patient experiences intolerance, try giving small doses of oral second-line medicines and then slowly increase the dose until the full dose is reached.

Splitting the dose into morning and afternoon doses is an alternative for the toxic oral second-line medicines as long as at least one dose can be directly observed. However, the doses of pyrazinamide, ethambutol and the fluoroquinolones cannot be split.

Reducing the dose to a lower acceptable dose may also be an alternative (subtherapeutic dosing to be avoided).

The medicine may be withdrawn as long as it does not compromise the regimen – that is, four reliable medicines must still be included; otherwise, another medicine should be given as a replacement. Discontinuing a medicine is the last course of action.

If all possibilities for modifying the regimen have been tried but the patient still cannot tolerate the medicine, or if the patient has a severe adverse effect that needs immediate attention, a change in regimen may be warranted. (Section 8 describes how the review panel may approve a change in regimen and how a change is recorded.)

7. Monitor the progress of treatment during monthly visits and with laboratory examinations

Monitor patients who have pulmonary DR-TB with periodic laboratory examinations, including sputum-smear microscopy, culture and DST. These examinations are important to help in determining whether a patient's treatment is progressing as expected and make decisions about care. When regimens have been designed correctly and anti-TB treatment is taken regularly, sputum-smear and culture tests will generally convert to negative. For a patient with DR-TB, **culture conversion** is the best indicator that the treatment has been taken regularly and has been effective.

The physician at the DR-TB management centre should examine all DR-TB patients monthly; this examination is called the monthly monitoring visit. The physician uses the results of sputum smears and cultures, as well as clinical evaluation, to monitor the patient's health and the need for other interventions. The physician can evaluate clinical improvement, answer any questions that the patient may have about the disease or treatment, and provide support for continuing the treatment.

For patients with **extrapulmonary** DR-TB, the physician monitors the progress of treatment by assessing clinical status. Increase in a patient's weight is also a useful indicator of improvement.

7.1 Determine when the patient is due for follow-up examinations

For all DR-TB patients, sputum tests and other procedures follow the schedule shown in *Table 4*.

Table 4 **Schedule for follow-up examinations**

Monitoring evaluation	Recommended frequency
Serum creatinine	At baseline; then monthly if possible while receiving an injectable agent. Every 1–3 weeks in HIV-infected patients, those with diabetes and other high-risk patients
Serum potassium	Monthly while receiving an injectable agent. Every 1–3 weeks in HIV-infected patients, those with diabetes and other high-risk patients
Serum magnesium and calcium	Check blood levels of magnesium and calcium whenever hypokalaemia is diagnosed. At baseline and then monthly if on bedaquiline. Repeat if any electrocardiogram (ECG) abnormalities develop (prolonged QT interval).
Thyroid-stimulating hormone (TSH)	Every 3 months if receiving ethionamide/prothionamide and <i>p</i> -aminosalicylic acid (PAS). Every 6 months if receiving ethionamide/prothionamide or PAS, but not both together. TSH is sufficient for screening for hypothyroidism and it is not necessary to measure thyroid hormone levels. Monthly monitoring for clinical signs/symptoms of hypothyroidism is also necessary.
Liver serum enzymes (SGOT, SGPT)	Periodic monitoring (every 1–3 months) in patients receiving pyrazinamide for extended periods or for patients at risk for, or with symptoms of, hepatitis. For HIV-infected patients, monthly monitoring is recommended. For patients on bedaquiline, monitor monthly. For patients with viral hepatitis, monitor every 1–2 weeks for the first month and then every 1–4 weeks.
HIV testing	At baseline, and repeat if clinically indicated
Pregnancy tests	At baseline for women of childbearing age, and repeat if indicated
Haemoglobin and white blood cell count	If on linezolid, monitor weekly at first, then monthly or as needed, based on symptoms; there is little clinical experience with prolonged use of linezolid. For HIV-infected patients on zidovudine, monitor monthly initially and then as needed, based on symptoms.
Lipase	Indicated for work-up of abdominal pain to rule out pancreatitis in patients on linezolid, bedaquiline, stavudine (d4T), didanosine (ddI) or zalcitabine (ddC). Baseline lipase is recommended for patient on bedaquiline.
Lactic acid	Indicated for work-up of lactic acidosis in patients on linezolid or antiretroviral treatment (ART)
Serum glucose	If receiving gatifloxacin, monitor fasting blood glucose at baseline and monitor monthly. Educate/remind patients of signs and symptoms of hypoglycaemia and hyperglycaemia monthly.
Audiometry (hearing test)	Baseline audiogram and then monthly while on an injectable agent. Ask patients about changes in hearing at every clinic visit and evaluate their ability to participate in normal conversation.

Monitoring evaluation	Recommended frequency
Vision tests	For patients on long-term ethambutol or linezolid, perform at least a visual acuity test with Snellen charts and colour vision test at baseline (as a small percentage of the population has colour blindness). Repeat the test for any suspicion of change in acuity or colour vision.
Psychosocial consultation	At baseline by personnel trained in psychosocial management; during treatment and repeat as indicated. Refer to psychiatrist when indicated.
ECG	For patients on bedaquiline, at baseline then weeks 2, 12 and 24 after starting treatment. More frequent if heart conditions, hypothyroidism or electrolyte disturbances are present.

This schedule is meant for patients who progress through treatment as planned. The physician may request culture, DST, a chest X-ray or blood test at any time.

During the continuation phase, if a smear examination is positive, the DR-TB management centre's staff should collect another specimen for smear and culture (even if there is no culture scheduled).

7.2 Collect sputum for follow-up examinations

Remember to collect one sputum sample for follow-up sputum examination **monthly** so that the results will be available at regular intervals, and there will be no delays in receiving culture results.

Sputum should be collected *every month* during treatment, one week before the monthly monitoring visit, so that the results will be available to the physician during the patient's visit.

Complete a *Request for examination of biological specimen for TB* form to send with the sample. Complete the form as for a diagnostic examination, except **be sure to tick the box for follow up**, and indicate the month of treatment (that is, the number of months the patient has been treated, for example, second month, fifth month). Indicate whether the specimen is for **smear only**, **smear and culture only** or **includes DST** following the schedule for follow-up examinations shown in *Table 4*.

Remember

- Collect sputum in a well-ventilated area, preferably outdoors or in a sputum-collection booth.
- Check whether the sample contains sufficient sputum, not just saliva. If it does not, ask the patient to add more.
- After collecting the sputum, be sure that the lid is closed tightly.
- Store in a refrigerator or in a box with refrigerants if the sputum will not be processed immediately.
- Wash your hands thoroughly with soap and water.

7.3 Record the results of laboratory examinations

The technician at the laboratory will record the results in the laboratory’s register and on the bottom of the *Request for examination of biological specimen for TB* form, which will be sent back to the DR-TB management centre. All results received at the DR-TB management centre should be recorded in the patient’s *Second-line TB treatment card* and in the *Second-line TB treatment register*. If patients are receiving treatment at a local health facility, the staff there should copy the laboratory results from the patient’s *treatment card* onto the facility’s card.

Example: Bottom section of the *Request for examination of biological specimens for TB* form

Microscopy results (to be completed in the laboratory)

Date sample collected (filled by requestor)	Specimen type	Laboratory serial number(s)	Visual appearance (blood-stained, mucopurulent or saliva)	Result (tick one)				
				Negative (0 AFB/100 HPF)	1-9/100 HPF (scanty; report no. of AFB)	+	++	+++
31 Jan 2013	Sputum	63	MP			✓		
1 Feb 2013	Sputum	67	MP				✓	

Examined by (name and signature): _____

Date of result: 4 Feb 2013

This patient’s sample tested positive on smear microscopy.

Xpert MTB/RIF test result (to be completed by the laboratory)

Date sample collected: 2 Feb 2013

M. tuberculosis: Detected Not detected Invalid / No result / Error

Rifampicin resistance: Detected Not detected Indeterminate result

Examined by (name and signature): _____

Date of result: 7 April 2013

This patient’s sample tested positive for Rif resistance.

Culture results (to be completed by the laboratory)

Date sample collected (filled by requestor)	Media used (liquid or solid)	Laboratory serial number(s)	Result (tick one)						
			Negative (0 colonies)	1-9 (<10 colonies)	+ (10-100 colonies)	++ (>100 colonies)	+++ (Innumerable/confluent growth)	NTM	Contaminated
1 Feb 2013	Liquid	265				<input checked="" type="checkbox"/>			

The culture result was released ~2 weeks after the smear results and was positive.

Examined by (name and signature): _____

Date of result: 16 Feb 2013

Drug-susceptibility test (DST) and line-probe assay (LPA) results (to be completed by the laboratory)

Date sample collected (filled by requestor)	Method ^a	Laboratory serial number(s)	Results ^b (mark for each drug)													
			H	R	E	S	Am	Km	Cm	FQ:	Other:	Other:	Other:	Other:		
1 Feb 2013	Liquid	103	R	R												

The DST result was released 2 weeks after the culture result and showed resistance to H and R.

^aSpecify: solid media DST; liquid media DST; direct LPA; indirect LPA
^bResults codes: R = Resistant S = Susceptible C = Contaminated - = Not done

Examined by (name and signature): _____

Date of result: 4 March 2013

Record the results of the follow-up smear and culture on page 2 of the patient’s *Second-line TB treatment card* in the corresponding “Month of treatment” row, along with the date the specimen was collected. Culture is considered to have converted to negative when two consecutive cultures, taken at least 30 days apart, are found to be negative. In such a case, the specimen collection date of the first negative culture is used as the date of conversion. Culture is considered to have reverted to positive when, after an initial conversion, two consecutive cultures, taken at least 30 days apart, are found to be positive. For the purpose of defining “Treatment failed”, reversion is considered only when it occurs in the continuation phase.

The example below shows sputum monitoring starting at baseline (month 0) until month 6 of treatment. This example shows positive baseline bacteriology (smear and culture). At month 1, the smear examination was positive and the culture was negative. The smear examination results from month 2 until month 6 were negative; the culture results through month 4 were negative.

Example: Recording the results of follow-up laboratory tests in the Sputum microscopy section of the Second-line TB treatment card

Month of Treatment	Sputum Microscopy		Month of Treatment	Culture	
	Date	Sample Number / Result		Date	Sample Number / Result
Prior			Prior		
0	29-7-12	++	0	29-7-12	++
1	29-8-12	+	1	29-8-12	neg
2	30-9-12	neg	2	30-9-12	neg
3	31-10-12	neg	3	31-10-12	neg
4	27-11-12	neg	4	27-11-12	neg
5	1-1-12	neg	5		
6		neg	6		
7			7		
8			8		
9			9		

Smear conversion (indicated by a blue box and arrow pointing to the transition from '++' to 'neg' in the Smear column)

Culture conversion (indicated by a blue box and arrow pointing to the transition from 'neg' to 'neg' in the Culture column)

Sputum and culture conversion

When a patient who was sputum-smear positive changes to sputum-smear negative, there has been smear conversion. When a patient who was culture positive changes to culture negative, there has been culture conversion. Culture conversion is the most important indicator of treatment success for MDR-TB patients.

Example: Results recorded in the Second-line TB treatment register

Reasons for Registering on Second-line TB Treatment (tick)	Second-line TB Treatment	Smear (S) Culture (C) or Xpert MTB/RIF (X) Results (if more than one smear or culture done in a month, enter in the most recent positive result. Xpert MTB/RIF only for Month 0. Dates are for the sample collection)																											
		Start of treatment Month 0	Month 1		Month 2		Month 3		Month 4		Month 5		Month 6		Month 7		Month 8		Month 9		Month 10		Month 11		Month 12		Month 13		
Presumptive RR-TB / MDR-TB (as per national policy)	Regimen (in drug initials) Date started (D/M/Y)	S C X	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	S C S	
RR-TB confirmed	ZKm Lfx PtoCs Date: 5-Jan-13	++	RR	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RR-TB confirmed	ZKm Lfx PtoCs Date: 10-Jan-13	++	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RR-TB confirmed	ZKm Lfx PtoCs Date: 25-Jan-13	Sc	++	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RR-TB confirmed		(S)	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RR-TB confirmed		26-Nov-2012	27-Dec-2012	25-Jan-2013	28-Feb-2013																								

The patient's bacteriology results (smears and cultures) are recorded monthly. (indicated by a blue box and arrow pointing to the monthly data entries)

7.4 Ensure that the patient is able to attend monthly monitoring visits with the physician at the DR-TB management centre

The physician at the DR-TB management centre takes the following actions during the monthly monitoring visit:

- evaluates the patient's clinical condition and response to treatment by physical examination, including assessing weight, history and any other measures needed (for example, blood tests);
- reviews the *Second-line TB treatment card* to confirm that the patient has adhered to treatment and that the treatment has been directly observed. If the patient is not taking the medicines as needed, every effort must be made to ensure compliance. (See Module E for suggestions on how to maintain contact with patients and minimize interruption);
- for patients whose treatment has been transferred to the local health facility (decentralized), the physician transcribes information from the patient's *treatment card* onto the DR-TB management centre's *treatment card*, including any new results from laboratory tests, the marks for DOT and comments. The physician reviews the card to learn about the patient's compliance, and any problems encountered during visits to the local facility. If a patient has attended the local health facility irregularly, the physician and other staff should talk with the patient to reinforce the importance of adhering to treatment and the consequences of missing doses. Information added to the card by the DR-TB management centre about observations, physician's recommendations or laboratory results will later be transcribed by the local health facility onto their copy of the card;
- reviews the results of bacteriological testing. Often, the results of smears and cultures are the strongest evidence of a patient's response to therapy. However, one single positive culture in the presence of an otherwise good clinical response may have been caused by laboratory error or contamination. In this case, subsequent cultures that are negative, or in which the number of colonies is decreasing, may help to prove that the apparently positive culture result did not reflect treatment failure;
- reviews the progress of treatment and the regimen in relation to the patient's medical history, close contacts and all DST reports. If the regimen is deemed inadequate, a new regimen needs to be designed and presented for approval to the review panel;
- discusses treatment progress with the patient and answers the patient's questions. It is important that the patient has an opportunity to share any concerns with the physician, and that the physician treats these concerns with respect.

7.5 Make treatment decisions based on the results of physical examination, laboratory tests and attendance

To take the appropriate actions for the patient, it is necessary to assess how the patient is responding to treatment, when the laboratory examinations were done (that is, during which month of treatment), and whether the results of cultures are negative or positive. Meet with the patient to explain the results of the follow-up examinations and the next step of treatment.

Two expected steps in the treatment process may occur when the patient's treatment is progressing well (that is, the patient is culture negative).

- The treatment may be decentralized to a local health facility to continue treatment.
- The patient may begin the continuation phase of treatment.

If the patient's treatment is not progressing well, the patient will be re-examined, and the regimen may need to be adjusted.

The review panel needs to approve of any of these steps.

7.5.1 Determine when the treatment of a patient may be decentralized

Treatment for DR-TB begins in the DR-TB management centre or hospital and continues at one of these locations as per the country policy or as long as considered necessary because of the medical condition of the patient. For ambulatory treatment, he or she may continue the treatment at a local health facility, which may be more conveniently located for the patient. This process of transferring a patient's care is called decentralization.

The physician at the DR-TB management centre reviews the records of patients who meet these criteria and presents their cases to the review panel. Once the review panel approves, the patient's care can be decentralized.

When a patient is eligible for treatment at a local health facility, carry out the procedures described below.

- Coordinate with the District TB Officer to ensure that staff at the local health facility has been trained and are able to receive the patient and supervise continuing treatment for DR-TB. If the patient is in the intensive phase of treatment, the treatment supporter providing DOT must be trained to give injections.
- Inform the patient that treatment is progressing well, and that he or she is eligible to receive treatment at a local health facility as soon as other criteria for decentralization (listed in the previous sections) are met. Remind the patient that many months of treatment are still needed, and emphasize the importance of continuing treatment.
- Explain the process of decentralization – that is, the care will remain the same except that the patient will be able to go to a facility closer to home for daily treatment. It will still be necessary to visit the DR-TB management centre for monthly monitoring and follow up.
- If the patient lives far from the local facility, a community treatment supporter may be needed to directly observe treatment. If the local health facility is open only 5 days each week, local facility staff or a community-based treatment supporter may need to provide the treatment on the sixth day each week. The local health facility is responsible for identifying, training and supervising a community-based treatment supporter, if needed.
- Prepare the medicines, supplies, forms and personal history of the patient to be sent to the local health facility.
 - Prepare two copies of the patient's *Second-line TB treatment card* (one for the local facility and one for the patient). The starting date for treatment by the local facility will be the day on which the patient is referred. Keep the original *treatment card* at the DR-TB management centre. The patient must carry the patient's copy of the treatment card at all times while receiving treatment.

- Prepare three copies of the *Tuberculosis referral/transfer form*. (See Module E for directions on completing this form.) One copy will stay at the DR-TB management centre. One copy will be received by and stay at the receiving local health facility and one copy will be sent to the District TB Officer. After the patient has arrived, the receiving facility should sign and date the form to acknowledge the transfer, and then cut off the bottom part of the form and return it to the DR-TB management centre to acknowledge that the patient has presented at the facility.
 - Reiterate that it is important for the patient to keep the copy of the *Second-line TB treatment card*. It will serve as the link between the DR-TB management centre and the local facility, and will be used to update the DR-TB management centre's original card during the monthly monitoring visits.

7.5.2 Determine when a patient may begin the continuation phase of treatment

When a patient's treatment is progressing well, the physician will use the results of laboratory tests, the patient's response to treatment and attendance record to decide whether to begin the continuation phase.

The criteria for beginning the continuation phase are as follows:

- The patient has received the injectable agent for the expected duration of the intensive phase, generally about 8 months.
- The patient has had culture conversion and is no longer infectious.

The physician at the DR-TB management centre will review the records of patients who meet these criteria and present their cases to the review panel. Once approved by the panel, these patients can begin the continuation phase of treatment.

- Explain to the patient who meets the criteria for the continuation phase that treatment has worked well. The patient is no longer infectious and is ready to begin the next phase of treatment. Congratulate the patient.
- Explain to the patient that in the continuation phase of treatment, the injection will no longer be given (unless there are no other treatment options) but the oral medicines will continue. Explain how long this phase is likely to last (at least 12 months). Emphasize the importance of continuing treatment.
- Be sure that the patient finishes all required doses of the intensive-phase regimen before beginning the continuation phase.

7.5.3 Take necessary action for patients who are not progressing as planned

Patients who are **not** progressing well after 4 months of treatment are at high risk for treatment failure and should undergo additional DST. A patient's treatment is not progressing well if, by month 4 the patient:

- has not had culture conversion; or
- had culture conversion but then reverted to culture positive; or
- has not improved clinically (symptoms have worsened or symptoms disappear and then reappear).

Poor treatment progress may be caused by one or more of the following:

- A patient-centred approach was not followed; barriers to adherence were not identified and removed; and enablers were not provided in a timely fashion.
- The treatment was poorly supervised and medicines were not taken correctly or on schedule. Stock-out of drugs may be a problem.
- There has been a delay in sputum conversion – for example, if a patient had widespread destruction of lung tissue and a heavy bacillary load initially or if there has been a problem with medicine absorption.
- The patient’s regimen is not adequate, and the bacilli may have resistance to the medicines the patient is receiving.
- The patient has poor tolerance to treatment with severe adverse reactions.

If a patient is at high risk for treatment failure, the physician at the DR-TB management centre should do the following:

- Request DST for second-line medicines from the last positive culture.
- Present the case again to the review panel to discuss possible changes to the regimen.
- Explain to the patient that the positive results of laboratory tests or clinical examination mean that the medicines do not seem to be working as hoped.
- If the treatment of the patient has been decentralized, explain that treatment will be moved back to the DR-TB management centre.
- Continue to give DOT with the prescribed regimen until a decision has been made to change it.

If the review panel recommends changing the regimen, request the new medicines and discontinue the others.

When the DST results are received, if they have changed from baseline and show further or a different resistance:

- explain to the patient that the laboratory results mean that the medicines may not be effective in killing the TB bacilli. The patient will have to see a physician at the DR-TB management centre for a physical examination and so that changes can be made to the regimen if needed;
- the physician at the DR-TB management centre will present the case again to the review panel to consider possible regimen changes after
 - conducting a physical examination and assessing the progress of the patient;
 - reviewing the regimen in relation to the patient’s medical history, previous treatment, contacts and all DST reports;
- continue to give DOT with the prescribed regimen until a decision has been made to change it;
- if the review panel recommends a change, request the new medicines and discontinue the others; retrieve the unused medicines from the local facility. Depending on the patient’s progress and his or her physical state and needs, refer the patient to the psychosocial services team at the DR-TB management centre.



Now do Exercise D – written exercise

When you reach this point in the module, turn to Exercise D and read the instructions.
When you have finished the exercise, review your answers with a facilitator.

8. Change the second-line drug dosage or regimen when required and with the approval of the review panel

During the course of treatment for DR-TB, a patient's drug dosage or the regimen may need to be changed in the following cases:

Drug dosage

- An increase or decrease in the patient's weight necessitates a corresponding change in the dose of medication.

Treatment regimen

- The injectable agent will be discontinued at the start of the continuation phase.
- The patient has a severe adverse effect (changing the regimen for this reason should occur only when no other course of action is possible).
- There is a change in the pattern of drug susceptibility.
- Sputum conversion does not occur or there is bacteriological reversion after conversion.

A decision to modify a treatment regimen can be made only by a physician at the DR-TB management centre with agreement from the review panel. It is worth noting here that changes in regimen may be forced upon the clinicians by external factors such as stock-outs. These do not qualify for the *Treatment failure* outcome definition.

8.1 Propose a regimen change and present it to the review panel for approval

When a patient has resistance to multiple medicines, and therefore only a few can be used, withdrawing one of them may result in treatment failure.

For an increase or decrease in the patient's weight

Every month, each patient is weighed and his or her weight is recorded on the *Second-line TB treatment card*. When a significant change in weight is noted, the physician should refer to information on the recommended doses to determine whether an adjustment needs to be made to the daily number of tablets or capsules or sachets according to the patient's weight. If so, the physician presents the case to the review panel to approve the adjustment.

For discontinuation of the injectable agent at the start of the continuation phase

The physician at the DR-TB management centre identifies patients who meet the criteria to begin the continuation phase (that is, a patient who has usually received the injectable agent

for 8 months and has had culture conversion). The physician presents these cases to the review panel. Once the review panel approves the change, the patient can begin the continuation phase of treatment (that is, discontinue the injectable agent and continue taking oral treatment for at least 12 more months).

For a severe adverse effect

The physician at the DR-TB management centre who has evaluated the patient with a severe adverse effect should present the case and the proposed regimen change to the review panel. A medicine will be withdrawn because of an adverse effect only when four reliable medicines can still be included in the regimen and there is no other course of action. The review panel must approve all regimen changes unless there is an emergency. In emergency cases, the panel should review the change as soon as possible afterwards.

For a change in the pattern of drug susceptibility

If DST results show MDR-TB, and the patient has been on a retreatment regimen (first-line agents) for a number of months while awaiting those results, another DST may be requested to check for a potential amplification of resistance caused by the use of an inappropriate regimen. If later DST results show that the pattern of resistance has changed, the physician will propose a change in the regimen to address the new pattern.

Lack of culture conversion or bacteriological reversion

As already discussed in section 7.5.3 of the module, lack of culture conversion or bacteriological reversion are signs of failure of the treatment regimen. These cases need to be assessed accordingly and a change in regimen may be required as per the country policy, if at least four effective drugs are still available based on the most recent DST pattern.

8.2 Record changes to the regimen on the *Second-line TB treatment card*

As soon as the review panel approves a regimen change, or as soon as the decision to change it is made (for example, in an emergency situation), the physician at the DR-TB management centre should record the change on the patient’s *Second-line TB treatment card* as described below. The new medicines must be requested immediately. All medicines that are discontinued must be returned to the pharmacist or to designated staff at the DR-TB management centre.

Record any regimen change, including a discontinuation or change in dose, on page 3 of the *treatment card*. On the row under “Second-line regimen”, write the date of the change and specify the change being made to one or more medicines. Mark an X under a medicine that has been discontinued; record the new dose under any medicine that has been changed. Complete the “Comments” box beside the doses to document the reason for every change in regimen or dose. Also, in the “Administration of drugs” section, circle the date when the revision was made. This allows anyone to easily see that there has been a change in the regimen.

Under “Administration of drugs”, circle the date on which the change in regimen occurred. This makes it easy to track when a change took place.

The examples described below show how to mark the *treatment card* to record a change in the regimen and the date that the change was made.

Example 1: Change in drug dosage due to weight gain

A patient’s weight has increased from 44 kg to 52 kg, and this change was recorded on the *Second-line TB treatment card*. The physician noted the increase during the monthly monitoring visit on 15 December 2013, and decided that the doses of medicines should be increased. At the next meeting of the review panel on 22 December, the physician presented the proposed changes and these were approved. In Example 1, the second row indicates that on 23 December, the dose of pyrazinamide was increased from three tablets to four, kanamycin from 750 mg to 1000 mg, prothionamide from two tablets to three, and cycloserine from two capsules to three. In the box for “Comments”, the reason for the change is documented. In the “Administration of drugs” section, the cell corresponding to 23 December is circled.

Example 2: Change in regimen due to adverse effects

During 16–19 March 2013, a patient was absent from treatment. Note the “O” or “Ø” in the boxes corresponding to these dates. It was learnt that the patient had been depressed and quiet for a few days previously, and had had a decreased appetite. On 19 March, a staff member from the DR-TB management centre made a home visit and found the patient lying on the bed in his room and he had not been out of the house. After a long discussion, the patient agreed to return to treatment. The patient returned to the DR-TB management centre on 20 March; the physician ordered that cycloserine be discontinued. On the second row of the “Second-line drugs regimen” section, cycloserine has an “X” indicating that it has been discontinued. To maintain the standard of including four reliable medicines, para-aminosalicylic acid was added. In the box for “Comments”, the reason for the change is documented. In the “Administration of drugs” section, 20 March has been circled, indicating that a change in regimen occurred on that day. At the next meeting of the review panel, the change in regimen will be presented for approval.

Example 1: Change in regimen due to weight gain

MDR treatment regimen (date of treatment start and dosage [mg], change of dosage and cessation of drugs)

Date	Second-line Treatment Regimen (Date treatment started and dosage (mg), change of dosage and cessation of drugs):											Comments			
	H	R	E	S	Z (500mg)	Amk (vial – 1 g)	Km (vial – 1 g)	Cm	FQ (250 mg)	Pto/Eto (250 mg)	CS (250 mg)		PAS	Other	Other
09/11/2012					3 tab	750 mg			Lfx 3 tab	Pto – 2 tab	2 tab				
18/1/2013					4 tab	1 vial			Lfx 4 tab	Pto -3 tab	3 tab				Weight increase

Administration of Drugs (one line per month), NAME OF DRUG:

Month	Day																															Wt (kg), Lab, X-ray	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31		
Nov '12								✓	✓	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	44
Dec '12	✓	-	✓	✓	✓	✓	✓	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	46	
Jan '13	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	52		

Example 2: Change in regimen due to adverse effects

MDR treatment regimen (date of treatment start and dosage [mg], change of dosage and cessation of drugs)

Date	Second-line Treatment Regimen (Date treatment started and dosage (mg), change of dosage and cessation of drugs):											Comments			
	H	R	E	S	Z (500mg)	Amk (vial – 1 g)	Km (vial – 1 g)	Cm	FQ (250 mg)	Pto/Eto (250 mg)	CS (250 mg)		PAS	Other	Other
25/02/2013					3 tab	750 mg			Lfx 3 tab	Pto – 2 tab	2 tab				
20/03/2013					4 tab	1 vial			Lfx 4 tab	Pto -3 tab	X	2 sac			Adverse reaction - psychosis

Administration of Drugs (one line per month), NAME OF DRUG:

Month	Day																															Wt (kg), Lab, X-ray		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31			
Feb '13																																		
Mar '13	✓	-	✓	✓	✓	✓	✓	✓	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	58.7		

9. Determine the treatment outcome for a DR-TB patient

The possible treatment outcomes for DR-TB are similar to those for drug-susceptible TB. The table below defines the six possible treatment outcomes for DR-TB patients. Monitor all patients' progress to determine if they meet the criteria for any of the definitions. A patient must have completed the prescribed treatment **before being considered cured**. The results of laboratory tests, specifically cultures, are used to determine the outcomes "cured" and "failed".

Table 5 Treatment outcomes for patients with drug-resistant tuberculosis (RR/MDR-TB)*

Treatment outcome	Definition
Cured	Treatment completed as recommended by the national policy without evidence of failure AND three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase
Treatment completed	Treatment completed as recommended by the national policy without evidence of failure BUT no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase
Treatment failed	Treatment terminated or need for permanent regimen change of ≥ 2 anti-TB drugs because of <ul style="list-style-type: none"> – lack of conversion by the end of the intensive phase, or – bacteriological reversion in the continuation phase after conversion to negative, or – evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs, or – adverse drug reactions (ADRs)
Died	A TB patient who died for any reason before starting or during the course of treatment.
Lost to follow up	A patient whose treatment was interrupted for 2 consecutive months or more (This category was previously known as "defaulted".)
Not evaluated	A TB patient for whom no treatment outcome is assigned (This includes cases "transferred out" to another treatment unit and where the treatment outcome is unknown to the reporting unit.)
Treatment success	The sum of cured and treatment completed.

* Refer to the Companion Handbook (Chapter 2) for more details on the definition of certain terms and parameters.

9.1 Present cases to the review panel for determination of outcome (cured, treatment completed or failed)

Use the outcome definitions described in *Table 5* to identify each patient who may be eligible for assessment of treatment completion and final outcome. The clinical history of each patient who has fulfilled the definition of cured, treatment completed or failed must be presented

by the treating physician to the review panel for approval of the final outcome. The DR-TB management centre declares the final outcome of cured, treatment completed or failed.

If a patient fulfils the criteria described in one of the definitions above, take the following actions. If the patient is classed as:

- **Cured, treatment completed, or failed:** present the patient's case to the review panel along with supporting documentation for outcome determination. The review panel will give final approval of the outcome decision.

An outcome of lost to follow up, died or not evaluated may be declared at whichever health facility is treating the patient at the time. Appropriate actions should be taken as described below.

- **Lost to follow up:** a patient who has stopped attending treatment for 2 consecutive months or more is classified as lost to follow up. Inform the DR-TB management centre that the patient could not be traced. Also inform the DR-TB management centre of the date when the patient was considered to have missed 2 consecutive months of treatment. The DR-TB management centre should be notified about this non-adherence before the second month of missed treatment occurs. The date when the last dose was given should be recorded as the date of the outcome.
- **Died:** inform the DR-TB management centre's physician that the patient has died, the cause of death (if known) and date.
- **Not evaluated:** this outcome is assigned when the patient's definitive outcome is not known because of any of the reasons including transfer out to another facility. When a patient is transferred from one DR-TB management centre to another, record the date and mark the outcome "not evaluated" on the *Second-line TB treatment card*. You will enquire later about the patient's treatment outcome. When the other DR-TB management centre sends information on the patient's outcome, it should be presented by the treating physician to the review panel for approval of the final outcome. Only if you cannot determine another outcome will you leave the outcome as not evaluated.

9.2 Initiate counselling for treatment failures before terminating treatment

Some patients' treatments will fail. For patients whose treatment has failed while they were on a standard second-line regimen, there may be the possibility that an individualized regimen will work. The review panel will know what is feasible and make a decision, and should assess a patient in this situation.

If there is no possibility of adjusting or designing a new regimen considered to be effective, the review panel may recommend terminating treatment for the patient. In this case, initiate counselling through a psychologist or psychosocial services team before terminating the treatment (*see* chapter 13 in the Companion Handbook to the WHO policies for MDR-TB,¹ or corresponding section in national guidelines). Treatment failure when all other therapeutic options are exhausted may be devastating to a patient, and must be handled with utmost care.

The patient may die or may have a debilitating chronic disease with respiratory insufficiency. End-of-life care must be provided and proper infection control measures must be followed.

9.3 Record the final treatment outcome on the *Second-line TB treatment card*

On the last page of the *Second-line TB treatment card* is a section where the outcome should be recorded. Record the date next to the designated outcome. For most patients, the **date will be the last day of treatment**. For patients with the interim outcome of transferred out, the final outcome will be dated as the last day that treatment was documented.

A patient is usually classified as cured, treatment completed or failed after the review panel has approved the treatment outcome designation. A patient with DR-TB who completed treatment but did not have the necessary number of negative culture examinations may be classified only as treatment completed. Likewise, a patient who had a negative culture at baseline and has remained culture-negative throughout treatment may be classified only as treatment completed.

If a patient was transferred to your DR-TB management centre from another DR-TB management centre, the patient was registered as a transfer-in in the *Second-line TB treatment register* using the patient's RR/MDR-TB registration number. When the patient completes treatment or reaches some other outcome, your DR-TB management centre should send information on the patient's final outcome to the centre that initially transferred the patient.

The treatment outcome of every DR-TB patient is important for monitoring your facility's success.

Example: Treatment outcomes in *Second-line TB treatment card*

Treatment outcome

OUTCOME	MARK ONE	DATE
Cured		
Treatment completed	X	21 June 2012
Died		
Failed		
Lost to follow up		

9.4 Record the final treatment outcome in the *Second-line TB treatment register*

Fill out the *Second-line TB treatment register* with the final outcome and the last date the patient had treatment. If the patient did not complete treatment, record information about that in the column headed “Treatment outcome”, record the cause of death, whether the patient was lost to follow up (record the reason), or was not evaluated (record the facility to which the patient was transferred).

Example: Treatment outcome recorded in *Second-line TB register*

C) nt ure done : recent ED	Final outcome (Cured, Completed, Treatment failed, Died, Loss to follow-up, Not evaluated)	TB/HIV Activities			Remarks
		HIV infection (Y/ N/ Unk)	On ART (Y/N)	On CPT (Y/N)	
Month 36					
S	C				
(D/M/Y)					
	<i>Treatment completed</i>	<i>N</i>			
/ /	<i>21/06 /13</i>				
/ /	/ /				

9.5 Provide education after treatment ends

Provide education to patients who are cured or have completed treatment. Ensure that they know the following:

- the symptoms of TB and that they should to seek attention immediately if symptoms develop;
- close contacts should seek care if they develop symptoms;
- the importance of a healthy lifestyle (taking exercise, eating well, not using tobacco or alcohol, and getting enough rest) to help them recover, combat other illnesses and reduce the risk of relapse.

Give support to patients whose outcome is treatment failure.

See Module D to learn what information should be provided during this meeting.



Now do Exercise E – written exercise

When you reach this point in the module, turn to Exercise E and read the instructions. When you have finished the exercise, review your answers with a facilitator.

Summary

- Many countries recommend a standardized regimen for the use of second-line drugs in RR/MDR-TB patients. Standard regimens are based on the prevalent pattern of drug resistance in the community and decided at the national level by the TB control programme. In some instances, individualized regimens based on previous history of TB treatment and individual second-line DST patterns could also be used.
- Regimens for RR/MDR-TB should consist of at least four effective medicines plus pyrazinamide. The treatment regimen should include an injectable agent from group 2; a later-generation fluoroquinolone from group 3 if the strain is thought to be susceptible; and two or three oral bacteriostatic second-line agents from group 4. All first-line agents in group 1 to which the patient's strain of DR-TB is expected to be susceptible should be added. If a regimen cannot be constructed, recourse may be needed to the group 5 class of drugs.
- Through interviews with the patient and a review of the patient medical records, identify any condition or situation that may require individualized treatment decisions, such as excluding some medicines from the regimen.
- The physician at the DR-TB management centre will design a treatment regimen for each DR-TB patient and present the case to the review panel for approval.
- For the treatment of DR-TB, the review panel:
 - reviews the cases presented for enrolment;
 - approves the proposed treatment regimen;
 - approves changes to the regimen, decentralization, treatment outcome or any action point relevant to the case presented;
 - arrives at a consensus on decisions when management of a DR-TB patient is unclear and complicated.
- Once the regimen has been designed, calculate the correct doses for the patient taking into account the patient's weight, age and medical circumstances, such as renal insufficiency.
- Whenever a DR-TB patient is enrolled for treatment, open a *Second-line TB treatment card*. It is essential that the card is filled out completely and accurately and then kept up to date throughout treatment.
- Once a patient has begun treatment, register the patient's information in the *Second-line TB treatment register*.
- The team in charge of care and treatment delivery must follow a patient-centred approach, especially for DOT. DOT should be provided to the patient 6 (or 7) days each week. **This means that you must observe and support the patient swallowing the medicines each day that he or she presents for treatment; identify any barrier to adherence to treatment; and coordinate with other health-care workers to find a proper solution to the barrier identified.**
- Directly observing treatment helps prevent interruptions because the observer knows right away when a patient misses a dose, and can discuss the reasons for this and address them.
- On the first day that you give DOT, begin marking the treatment in the "Administration of drugs" section of the *Second-line TB treatment card*. Mark each time you give DOT by ticking (✓) the date. (Record Ø or 0 for a missed dose.)

- Assess the patient’s close contacts for possible TB or DR-TB, and record the results of your assessments on the back of the *Second-line TB treatment card*.
- Monitor adverse effects by asking patients daily, “How are you feeling? Have you had any problems?” Listen carefully to their answers, and note any complaints that may indicate adverse effects from the anti-TB medicines. Also look carefully at the patient to see whether you observe any signs of adverse reactions. An adverse effect may be mild or severe. Keep in mind that adverse effects are more common in people who are HIV positive, in elderly people and in those with co-morbidities.
- If the adverse effects are mild, take steps to help the patient continue treatment. Educate the patient about the adverse effect and why it is happening. Reassure the patient that most adverse effects occur during the early months of treatment and diminish with time. Provide symptomatic relief, including ancillary medicines, (for example, for allergies or nausea) free of charge. Encourage the patient to continue treatment.
- If a patient has moderate-to-severe adverse effects, refer the patient to a physician at the DR-TB management centre for immediate examination and care.
- For all DR-TB patients, laboratory examinations and other procedures follow the schedule below:
 - sputum-smear microscopy examinations are conducted monthly until treatment is completed;
 - cultures are taken monthly (in case of limited resources, every other month during the continuation phase of treatment);
 - DST is run every 4 months while the patient remains culture positive if an individualized regimen is being used;
 - chest X-rays should be taken every 6 months;
 - weight measured monthly; and
 - height measured monthly for children;
 - blood tests should be performed as requested by the physician during monthly monitoring visits (as a minimum, every 6 months for patients younger than 50 years or every 3 months for patients aged 50 years and older).
- Use follow-up examinations to determine whether the patient is ready for decentralization (have care transferred to a local facility) or the continuation phase of treatment (if the patient is taking ambulatory DR-TB treatment). Before starting the continuation phase, a patient must have received an injectable agent for the full duration of the intensive phase.
- Patients who are **not** progressing well after 4 months of treatment are at high risk for treatment failure and should have additional DST. A patient’s treatment is not progressing well if, by month 4, the patient:
 - has not had culture conversion; or
 - had culture conversion but then reverted to being culture positive; or
 - does not improve clinically (symptoms get worse, or symptoms disappear and then reappear).
- During the course of treatment for DR-TB, a patient’s drug dosage or regimen may need to be changed when:
 - an increase or decrease in the patient’s weight necessitates a corresponding change in the dose of medication;
 - the injectable agent is discontinued at the start of the continuation phase;

- the patient has a severe adverse effect (changing the regimen for this reason should occur only when no other course of action is possible);
 - there is a change in the pattern of drug susceptibility;
 - there is a lack of sputum conversion or bacteriological reversion after conversion.
- A decision to modify a treatment regimen can be made only by a physician at the DR-TB management centre, with agreement from the review panel. However, in emergency situations, such as if there is a severe adverse effect, the attending physician may change the regimen immediately and present it to the review panel at their next meeting. On the *Second-line TB treatment card*, record any change in medicines or doses, and circle the date that the change occurred. This provides an easy way to track treatment changes.
 - The possible DR-TB treatment outcomes are: *cured, treatment completed, failed, died, lost to follow up* and *not evaluated*. A patient must complete of the full duration of prescribed treatment (at least 20 months) before a treatment outcome of cured can be considered.

Self-assessment questions

Answer the self-assessment questions below to check what you have learnt. Then compare your answers with those given on pages C-74–C-73 below.

1. a) Initially, the regimen for a patient with confirmed MDR-TB should include: (tick all that apply)
 - at least four medicines with certain or almost certain effectiveness, plus pyrazinamide in intensive phase
 - first-line anti-TB medicines whenever there is no proof of resistance
 - one medicine from each group of medicines (groups 1–5)
 - an injectable agent
 - isoniazid and rifampicin, the two most powerful anti-TB medicines.
- b) How long does treatment for RR/MDR-TB usually last? Why?
2. A patient returns after loss to follow up from a retreatment regimen and is likely to have DR-TB. On 12 March 2013, the patient submitted two sputum samples. The patient did not return for the results and did not begin treatment. The local facility was able to reach the patient at his house on 29 March and convince him to return to begin treatment. A regimen of second-line drugs was approved on 19 April and the patient began the enrolment process on 22 April.

List five things that you should consider when enrolling this patient for treatment.

-
-
-
-
-

3. Under which circumstances may a DR-TB patient receive medicines for self-administration? (Tick all that apply.)
- when the patient has to travel
 - when the patient has a family emergency
 - when the patient cannot come to the health centre for DOT because she or he feels sick
 - when the patient has completed the intensive phase
 - when a patient has never missed a dose
 - none of the above
4. a) What are the critical aspects of DOT?
- i. talking to the patient and giving support
 - ii. providing medicines to the patient
 - iii. watching the patient swallow the medicines
 - iv. recording the treatment on the treatment card
- b) If a DR-TB patient missed an appointment yesterday, what medicines should be given at today's appointment?
5. The following patients are being treated at your DR-TB management centre and are having some problems with treatment.
- a) A DR-TB patient complains of tolerable headache in the evenings after work and dizziness, both of which are relieved by lying down. What should you do?
- b) A DR-TB patient taking para-aminosalicylic acid complains of gastritis and diarrhoea. What can you do?
- c) A DR-TB patient taking ethambutol complains of blurred vision. What should you do?

9. a) Which treatment outcomes have a different definition for DR-TB than for patients receiving first-line medicines? (Tick all that apply)

cured

treatment completed

failed

lost to follow up

died

not evaluated

b) How is the outcome “cured” defined for DR-TB patients?

Now compare your answers with those on the next page.

Answers to self-assessment questions

If you had difficulty answering any question, turn back and study the section indicated. If you do not understand something, discuss it with a facilitator.

1. a) Initially, the regimen for a patient with confirmed MDR-TB should include: (tick all that apply)

at least four medicines with certain or almost certain effectiveness, plus pyrazinamide in intensive phase

first-line anti-TB medicines whenever there is no proof of resistance

one medicine from each group of medicines (groups 1–5)

an injectable agent

isoniazid and rifampicin, the two most powerful anti-TB medicines.

(See sections 1.1 and 1.3.)

b) How long does treatment for RR/MDR-TB usually last? Why?

Twenty months or more. The intensive phase of treatment generally includes at least 8 months of the regimen using the injectable agent and at least 4 months past culture conversion. The continuation phase usually includes 12 months of treatment with the continuation-phase agents, provided the patient remains culture negative.

Resistant bacilli take longer to kill because the second-line agents that are used are less effective than first-line agents, and the physician must ensure that all bacilli are killed in order to lessen the chances of a relapse or further increases in resistance.

(See section 1.1.)

2. A patient returns after loss to follow up from a retreatment regimen and is likely to have DR-TB. On 12 March 2013, the patient submitted two sputum samples. The patient did not return for the results and did not begin treatment. The local facility was able to reach the patient at his house on 29 March and convince him to return to begin treatment. A regimen of second-line drugs was approved on 19 April and the patient began the enrolment process on 22 April.

List five things that you should consider when enrolling this patient for treatment.

You should have listed 5 of the items below:

- *Prepare the patient's Second-line TB treatment card.*
- *Inform the patient of the enrolment procedures.*
- *Complete the Second-line TB treatment register with the patient's information.*
- *Report the approval of treatment with second-line drugs to the District TB Officer.*
- *Request baseline smear (or Xpert MTB/RIF directly), culture, as well as DST, because it has been more than 30 days since the last tests.*
- *Make a home visit.*

(See section 3.)

3. Under which circumstances may a DR-TB patient receive medicines for self-administration? (Tick all that apply.)

- when the patient has to travel
- when the patient has a family emergency
- when the patient cannot come to the health centre for DOT because she or he feels sick
- when the patient has completed the intensive phase
- when a patient has never missed a dose
- none of the above

There are generally very few circumstances under which DR-TB patients can receive medicines for self-administered treatment.

(See section 5.)

4. a) What are the critical aspects of DOT?

- i. talking to the patient and giving support
- ii. providing medicines to the patient
- iii. watching the patient swallow the medicines
- iv. recording the treatment on the treatment card

- b) If a DR-TB patient missed an appointment yesterday, what medicines should be given at today's appointment?

Give the patient today's dose. Do not give a double dose.

(See section 5.)

5. The following patients are being treated at your DR-TB management centre and are having some problems with treatment.

- a) A DR-TB patient complains of tolerable headache in the evenings after work and dizziness, both of which are relieved by lying down. What should you do?

You should reassure the patient that the adverse effects will probably lessen over time. Do a basic examination like a blood pressure check and, if nothing abnormal is found, tell the patient to continue to take the medicines, and give him or her symptomatic treatment – for example, non-steroidal anti-inflammatory drugs for the headache. Instruct the patient to let you know if the symptoms get worse.

- b) A DR-TB patient taking para-aminosalicylic acid complains of gastritis and diarrhoea. What can you do?

Send the patient to the physician at the DR-TB management centre for ancillary medicines for gastritis or for possible referral to a specialist – for example, if the gastritis is causing bleeding. You may split the dose so that it can be delivered twice a day as long as at least one dose is directly observed. The patient should take para-aminosalicylic acid with an acidic liquid. Assess the state of hydration; give oral rehydration fluids for mild or moderate dehydration; refer for inpatient care including intravenous (IV) fluids if dehydration is severe.

- c) A DR-TB patient taking ethambutol complains of blurred vision. What should you do?

Stop ethambutol immediately and send the patient to the ophthalmologist at the DR-TB management centre.

(See section 6.)

6. When should a DR-TB patient have a first follow-up sputum examination? What tests should be done that month?

At the end of the first month of treatment the patient should have a sputum-smear examination and culture.

(See section 7.1.)

7. Under what circumstances can decentralization to a local health facility take place?

Treatment of patients may be decentralized if they have been culture negative for at least 1 month and the latest consecutive monthly sputum-smear examinations have been negative for 2 months. Patients must also be able to attend a local health facility for daily treatment or have access to a trained provider of DOT. The local facility must have staff trained to provide treatment with second-line drugs and be supplied with the patient's medicines.

(See section 7.5.1.)

8. Make treatment decisions for the following cases.

- a) Treatment of a DR-TB patient has been decentralized; the patient has been treated for 8 months and has been culture negative for the past 4 months. The patient has been taking all of the medicines with minimal absences and no important adverse effects. What treatment decision do you make at this time?

The patient is eligible to begin the continuation phase of treatment after his or her status has been reviewed, and the change approved by the review panel.

- b) A DR-TB patient at a DR-TB management centre has had treatment for 3 months. His smear results were positive for the first month and negative for the second month. You are waiting for the third month's results. The result of the first month's culture is negative. The patient has been taking all of the medicines with minimal absences and no important adverse effects. What treatment decision do you make at this time?

No change at the moment; just continue treatment.

- c) Treatment of a DR-TB patient has been decentralized; the patient has received treatment for 6 months and has been culture negative for the past 3 months. The patient has been taking all of the medicines with minimal absences and no important adverse effects. What treatment decision do you make at this time?

No change at the moment. In order to be eligible for the continuation phase of treatment, the patient must have received an injectable agent for at least 8 months.

(See section 7.5.2.)

- d) Treatment of a DR-TB patient has been decentralized; the patient has received treatment for 6 months and has been smear negative and culture negative since month 2. The culture for month 4 came back positive, and the patient has been complaining of feeling generally worse. The patient has been taking all of the medicines with minimal absences and no important adverse effects. What treatment decision do you make at this time?

This patient is at high risk of treatment failure and immediate action should be taken. The physician at the DR-TB management centre should:

- *request DST for second-line medicines from the last positive culture;*
- *present the case again to the review panel to consider the possibility of changing the regimen;*
- *explain to the patient that the positive results from the laboratory or clinical examination mean that the medicines do not seem to be working as hoped;*
- *continue to give DOT to the patient with the prescribed regimen until a decision has been made to change it.*

(See section 7.5.3.)

9. a) Which treatment outcomes have a different definition for DR-TB than for patients receiving first-line medicines? (Tick all that apply)

- cured
- treatment completed
- failed
- lost to follow up
- died
- not evaluated

The definitions for lost to follow up, died and not evaluated are the same as for cases of TB.

(See Table 5, section 9.)

- b) How is the outcome “cured” defined for DR-TB patients?

You may have used your own words, but check that your answer includes the main points in the definition below:

Cured: *treatment completed as recommended by the national policy without evidence of failure AND three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.*



The End

Congratulations on finishing this module!

References

1. Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. Geneva: World Health Organization; 2014 (WHO/HTM/TB/2014.11).
2. WHO guidelines for the programmatic management of drug-resistant tuberculosis: emergency update 2008. Geneva: World Health Organization; 2008 (WHO/HTM/TB/2008.402).
3. The use of bedaquiline in the treatment of multidrug-resistant tuberculosis: interim policy guidance. Geneva: World Health Organization; 2013 (WHO/HTM/TB/2013.6).

Exercises for Module C: Treat DR-TB patients

Exercise A

Individual work and group discussion: Selecting a treatment regimen for DR-TB

In this exercise, you will design two second-line treatment regimens. Use the information presented below and refer to section 1.3 of this module to propose a treatment regimen for each patient. Work individually on this exercise. Ask your facilitator for help if you do not understand what to do.

Case 1

Rolanda Ramirez Reloz is 43 years old and weighs 43.7 kg. She was treated for TB in the private sector three different times:

- started treatment August 2009 – HR for 6 months;
- second treatment in August 2010 – SRE for 6 months;
- third treatment in December 2010 – HRZE for 4 months.

She presented at the DR-TB management centre complaining of loss of weight, coughing up blood, and occasional fever, chest pain and night sweats. Chest X-rays showed a cavitory lesion in the right upper lobe and infiltrates in the left lower lobe.

Her sputum sample was collected on 3 September 2012 and the following results were received from the laboratory:

- sample 3454–10; smear: +++; culture ++;
- DST results show resistance to H, R, S.

1. Review the patient's DST results and the patient's history of treatment with anti-TB medicines. Then select medicines for the proposed treatment regimen. List them in the table below.
2. Calculate the daily dose for this patient for each medicine. (Refer to Annex A.) Then determine the number of units needed daily.

Proposed regimen	Daily dose	Units/day

Case 2

Ahab Jaleel is 34 years old and weighs 64.3 kg. He has failed Category II treatment (a retreatment regimen).

He completed a new-patient regimen (outcome: treatment completed) that started on 22 September 2009. However, he was found to be smear-positive on 3 September 2011, and the retreatment regimen was started. Sputum was collected on 3 December 2011 and the following results were received from the laboratory:

- sample 3492-09; smear: +++; culture ++;
 - DST results show resistance to H and R and sensitivity to S, E and Z.
1. Review the patient's DST results and the patient's history of treatment with anti-TB medicines. Then select medicines for the proposed treatment regimen. List them in the table below.
 2. Calculate the daily dose for this patient for each medicine. (Refer to Annex A.) Then determine the number of units needed daily.

Proposed regimen	Daily dose	Units/day

When you have finished this exercise, review your answers with a facilitator.
There will be a group discussion when everyone has finished.



When the group has finished the discussion, **GO BACK** and read sections 2 and 3, and work until the next stop sign.

Exercise B

Written exercise: Preparing a *Second-line TB treatment card*

The purpose of this exercise is to practise preparing *Second-line TB treatment cards* for patients who are beginning treatment.

Use the information provided below to prepare pages 1 and 2 of a *Second-line TB treatment card* for each patient. To fill in each card, carry out the following steps:

1. Record all of the patient's general information on the top section of the card using the available data.
2. Record any previous anti-TB treatment.
3. Mark the registration group.
4. Complete the information related to HIV status and care, if known.
5. Record any decisions made by the review panel.
6. On page 2, record the results of the screening sputum-smear and culture examinations in the "Sputum monitoring" section.
7. Record any DST results.

If any of the instructions are unclear, ask a facilitator for assistance.

Case 1

You work at the Blue Acorn DR-TB management centre.

Thelma Huru is a 34-year-old female with pulmonary TB who is starting second-line treatment on the day you see her, 23 December 2011. She does not have an MDR-TB registration number. Her date of birth is 25 May 1975. She weighs 43 kg. Ms Huru lives at 1406 Betancourt Street, Xioli Village in Longo district. Her aunt is her contact person: Iris Sambar lives on Long Way, house number 888. Ms Huru had an HIV test on 4 November 2010; it was negative.

Ms Huru's two prior treatments for TB have failed. She started Category I (new patient) treatment in October 2010, and began Category II treatment (retreatment) in May 2011. Her district TB register number is 345-10.

The review panel approved treatment with second-line drugs on 18 December 2011 with the following regimen: Z-Km-Lfx-Pto-Cs. Her smears were collected on 9 December (sample number 1655) with the result ++. The culture and DST results are not available yet and Xpert MTB/RIF testing is not available.

Use the information above to complete Ms Huru's *Second-line TB treatment card* on the next four pages.

TB Control Programme

Second-line Registration Number: _____
 Date of second-line treatment registration: _____
 Treatment Centre: _____
 Patient Name: _____
 Address & Telephone: _____
 District: _____
 Sex (circle one): M F
 Age: _____ DOB: _____
 Height (cm): _____
 Site (circle one or both): Pulmonary Extrapulmonary
 If extrapulmonary, specify site: _____

Second-line TB treatment card

Registration Group	Choose one only
New	<input type="checkbox"/>
Relapse	<input type="checkbox"/>
Treatment after loss to follow up	<input type="checkbox"/>
Treatment after failure of first treatment with first-line drugs	<input type="checkbox"/>
Treatment after failure of retreatment regimen with first-line drugs	<input type="checkbox"/>
Other (previously treated without known outcome; previously treated extrapulmonary)	<input type="checkbox"/>
Transfer in (from another second-line treatment programme)	<input type="checkbox"/>

Transfer in (from another second-line treatment programme) if yes name of center: _____
 Yes No

HIV INFORMATION

HIV Testing done (circle one): Y / N / Unknown
 Date of Test: _____ Result: _____
 Started on ART (circle one): Y / N Date: _____
 Started on CPT (circle one): Y / N Date: _____

Meetings of review panel (medical commission, selection committee, consilium)

Date	Decision	Next Date

Form 01

Previous Tuberculosis Treatment Episodes			
District TB Register No. (i.e. BMU register number)	Start Date (if unknown put year)	Regimen (write regimen in drug abbreviations)	Outcome

Previous use of second-line drugs for more than one month?

Y / N / Unknown

If Yes, indicate in Table above

Drug Abbreviations			
First-line drugs	second-line drugs		
H=isoniazid	Am=amikacin	Eto=ethionamide	Bdq=bedaquiline
R=rifampicin	Kn=Kanamycin	Pto=Prothionamide	Clf=clarithromycin
R=ethambutol	cm=capreomycin	Cs=cycloserine	Ctz=clofazimine
S=streptomycin	lk=levofloxacin	Pas=p-aminosalicylic acid	Dim=delamanid
Z=Pyrazinamide	Mfx=Moxifloxacin	Imp=imipenem	Lzd=linezolid
	Ofx=ofloxacin	Amx/cv=amoxicillin/ clavulanate	
	Gfx=gatifloxacin		Mprn=meropenem

Transfer In (from another second-line treatment programme) if yes name of centre: _____

Second-line TB treatment card

Month of Treatment	Sputum Microscopy		Date*	Sample Number	Result	Month of Treatment	Date*	Sample Number	Result	Drug Susceptibility Testing (DST) Results§	
	Date*	Sample Number								Result	Date specimen (e.g. sputum) collected
Prior**											
0											
1											
2											
3											
4											
5											
6											
7											
8											
9											
10											
11											
12											
13											
14											
15											
16											
17											
18											
19											
20											
21											
22											
23											
24											

Notation method for DST:
 R=resistant
 S=susceptible
 C=contaminated
 Unk=Unknown

§ indicate near result if initial resistance was detected on line-probe assay or Xpert MTB/RIF

Notes:

*All dates in both tables are the dates the sputum was collected from the patient
 **The date the sputum was collected that led to the patient being registered with MDT-TB (if performed)

Notation Method for Recording Smears:

No AFB	0
1-9 AFB per 100 HPF	Scanty (and report number of AFB)
10-99 AFB per 100 HPF	+
1-10 AFB per HPF	++
>10 AFB per HPF	+++

Notation Method for Recording Cultures (solid media):

No growth reported	0
Fewer than 10 colonies	Report number of colonies (1-9)
10-100 colonies	+
More than 100 colonies	++
Innumerable or confluent growth	+++
Non-tuberculous mycobacteria	NTM
Contaminated	contaminated

Notation method for Xpert MTB/RIF results

T	= MTB detected, rifampicin resistance not detected
RR	= MTB detected, rifampicin resistance detected
TI	= MTB detected, rifampicin resistance indeterminate
N	= MTB not detected
I	= invalid / no result / error

Case 2

You work at the Blue Acorn DR-TB management centre.

Hildo Theab is a 42-year-old male patient with pulmonary TB. He is starting DR-TB treatment on the day you see him, 1 May 2013. He weighs 55 kg. He lives at House C12, Block 33 in Sharma City, Sharma District. His contact person is his brother Magro who lives in House E71 in the same block. Mr Theab does not want to have an HIV test.

Mr Theab has been treated previously. He started a new-patient regimen in May 2011. After 15 days of treatment he stopped taking medicines and could not be traced. On 18 October 2011 he again reported with chest symptoms, sputum was collected and sent for smear. The results were smear positive (+). In October 2012, he was placed on a new treatment regimen, which he is currently receiving.

His district TB number is 553–12; the date of registration was 7 November 2012. His follow-up smear examination results after 5 months of treatment (12 March 2013) were positive. He underwent sputum test with Xpert MTB/RIF and was found positive for rifampicin resistance. His culture results from the March sample were released in April 2013 and were positive, and the DST results showed resistance to H, R and S. The review panel approved treatment with second-line drugs on 27 April with the following regimen: Z-Km-Mfx-Pto-PAS.

Use the information above to complete Mr Theab's *Second-line TB treatment card* on the next four pages.

Second-line TB treatment card

Month of Treatment	Sputum Microscopy		Month of Treatment	Culture		Drug Susceptibility Testing (DST) Results	
	Date*	Sample Number		Result	Date*	Sample Number	Result
Prior**			Prior**				
0			0				
1			1				
2			2				
3			3				
4			4				
5			5				
6			6				
7			7				
8			8				
9			9				
10			10				
11			11				
12			12				
13			13				
14			14				
15			15				
16			16				
17			17				
18			18				
19			19				
20			20				
21			21				
22			22				
23			23				
24			24				

Notation method for DST:

- R=resistant
- S=susceptible
- C=contaminated
- Unk=Unknown

§ indicate near result if initial resistance was detected on line-probe assay or Xpert MTB/RIF

Notes:

- *All dates in both tables are the dates the sputum was collected from the patient
- **The date the sputum was collected that led to the patient being registered with MDT-TB (if performed)

Notation Method for Recording Smears:

No AFB	0
1-9 AFB per 100 HPF	Scanty (and report number of AFB)
10-99 AFB per 100 HPF	+
1-10 AFB per HPF	++
>10 AFB per HPF	+++

Notation Method for Recording Cultures (solid media):

No growth reported	0
Fewer than 10 colonies	Report number of colonies (1-9)
10-100 colonies	+
More than 100 colonies	++
Innumerable or confluent growth	+++
Non-tuberculous mycobacteria	NTM
Contaminated	contaminated

Notation method for Xpert MTB/RIF results

T	= MTB detected, rifampicin resistance not detected
RR	= MTB detected, rifampicin resistance detected
TI	= MTB detected, rifampicin resistance indeterminate
N	= MTB not detected
I	= invalid / no result / error

When you have finished preparing *Second-line TB treatment cards* for both cases, discuss your answers with a facilitator.



GO BACK and read sections 4 and 5, and work until the next stop sign.

Exercise C

Written exercise and group discussion: Recording directly observed treatment on the *Second-line TB treatment card*

In this exercise you will record directly observed treatment on a patient's *Second-line TB treatment card*. Use the *Second-line TB treatment card* on pages C-96–C-98 for Mr AJ Annan.

Read the information below and mark Mr Annan's *Second-line TB treatment card* to show when he received DOT. Also record the results of the sputum examinations and discuss the future course of action on treatment.

Mr Annan began his treatment on Tuesday, 14 May 2013. He came and received DOT on the following days: 14, 15, 16, 17, 18 May; 19 May was a Sunday.

Mr Annan complained of dizziness for a week; it seemed manageable and he continued with his treatment.

He received DOT on 20, 21, 22, 23, 24, 25 May; 26 May was a Sunday and then till 1 June.

He did not come on 3, 4 and 5 June. DR-TB management centre staff telephoned his cousin and found out that he had moved to the house of another relative because of a family conflict. Staff at the DR-TB management centre contacted the nearest health facility and asked them to make a home visit.

Early in the morning on 6 June, the health-centre worker visited Mr Annan and found that he had been sick; he complained of severe nausea and dizziness. The health worker was able to convince him to report to the DR-TB management centre that same day.

On 6 June, because of his severe symptoms, the physician at the DR-TB management centre gave him ancillary medicines; the physician decided to present the case to the review panel and proposed replacing prothionamide with 8 g of para-aminosalicylic acid (2 sachets).

Mr Annan received DOT without prothionamide. The physician emphasized to Mr Annan the importance of not missing treatment, and Mr Annan promised to continue taking his medicines. He also expressed interest in being decentralized to the local health centre.

Mr Annan received DOT on 6, 7, 8, 10, 11, 12, 13, 14 and 15 June; 9 June and 16 were Sundays.

Meanwhile, on 11 June, the review panel approved the change in regimen suggested by the physician at the DR-TB management centre. Prothionamide was discontinued and Mr Annan was instead given para-aminosalicylic acid daily beginning on 12 June.

He weighed 51 kg.

He received DOT from 17 to 29 June; 23 and 30 June were Sundays.

On 25 June 2013, the facility received the results of the first follow-up sputum smear of specimen number 325–13 that was collected on 21 June 2013, and the result was negative.

After taking his medicines on 29 June, Mr Annan told the nurse at the DR-TB management centre that he planned to visit his mother for four days. The nurse explained to him the possible consequences of interrupting treatment and that he would not be given any medicines for self-administration. Mr Annan went ahead with his planned visit.

He returned to the DR-TB management centre and received DOT on 4 July till 20 July; 7, 14 and 21 July were Sundays. He weighed 52.8 kg on 18 July.

He continued DOT from 22 to 27 July; 28 July was a Sunday.

The DR-TB management centre received the results of the sputum-smear examination from the July follow-up visit. Sputum specimen number 501–13 was collected on 19 July, and the result was negative.

From 29 July to 28 September 2013, the patient received DOT at the DR-TB management centre 6 days each week except for Sundays.

The baseline culture result from sputum collected 10 May was positive (++) . The sample number was 238–13.

The smear results for 19 August (sample number 657–13) and 19 September (sample number 830–13) were both negative. His weight was 53.4 kg in August and 54 kg in September.

The culture result for the specimen collected in June was released in July and was positive (+) for TB. The culture result for the specimen collected in July was released in August and was negative.

When you have finished marking the *Second-line TB treatment card*, review your work with a facilitator. Also write answers to the questions on [page C-99](#) in preparation for a group discussion.

Patient's name Mr A J ANMAN

Second-line TB treatment card

Month of Treatment	Sputum Microscopy		Month of Treatment	Culture		Drug Susceptibility Testing (DST) Results	
	Date *	Sample Number		Result	Date *	Sample Number	Result
Prior**			Prior**				
0	10-May-2013	218-13	0	10-May-2013	218-13	++	10-05-2013
1			1				R
2			2				R
3			3				S
4			4				R
5			5				
6			6				
7			7				
8			8				
9			9				
10			10				
11			11				
12			12				
13			13				
14			14				
15			15				
16			16				
17			17				
18			18				
19			19				
20			20				
21			21				
22			22				
23			23				
24			24				

Notation method for DST:
 R=resistant
 S=susceptible
 C=contaminated
 Unk=Unknown

S indicate near result if initial resistance was detected on line-probe assay or Xpert MTB/RIF

Notes:

*All dates in both tables are the dates the sputum was collected from the patient
 **The date the sputum was collected that led to the patient being registered with MDT-TB (if performed)

Notation Method for Recording Smears:

No AFB	0
1-9 AFB per 100 HPF	Scanty (and report number of AFB)
10-99 AFB per 100 HPF	+
1-10 AFB per HPF	++
>10 AFB per HPF	+++

Notation Method for Recording Cultures (solid media):

No growth reported	0
Fewer than 10 colonies	Report number of colonies (1-9)
10-100 colonies	+
More than 100 colonies	++
Innumerable or confluent growth	+++
Non-tuberculous mycobacteria	NTM
Contaminated	contaminated

Notation method for Xpert MTB/RIF results

T	= MTB detected, rifampicin resistance not detected
RR	= MTB detected, rifampicin resistance detected
TI	= MTB detected, rifampicin resistance indeterminate
N	= MTB not detected
I	= invalid / no result / error

Discussion

Write answers to the questions below. When everyone is ready, there will be a group discussion on these questions.

1. A health worker was very busy and a line of people was waiting. The health worker recognized a DR-TB patient, Marti Gra, and did not want to keep her waiting. She signalled to Ms Gra to come to the front of the queue, and handed her the day's tablets. She told Ms Gra to take the tablets home and swallow them when she found something to drink.

What could happen to the tablets? (List five different possibilities.)

2. What should the health worker have done when handing the tablets to Marti Gra?
3. If a patient with DR-TB does not take the TB medicines correctly or on schedule over a period of time, what might be the consequences?



When the discussion is over, **GO BACK** to sections 6 and 7, and work until the next stop sign.

Exercise D

Written exercise: Follow-up laboratory examinations

In this exercise, you will practise making decisions based on the results of different follow-up laboratory tests. For each of the cases listed below, decide what action to take. You may refer to *Table 4* on page C-50.

Case 1: Data Berth

Treatment of Data Berth, a patient with diabetes with poor control of his blood sugar, was decentralized after the third month of treatment; he then experienced worsening cough and weight loss. Below are the results of sputum smears and cultures from his *Second-line TB treatment card*.

Results of sputum examination				Weight (kg)
Month	Date	Smear	Culture	
0	10/5/11	+++	+	52
1	12/6/11	0	0	52
2	11/7/11	0	0	50
3	8/8/11	0	0	49
4	6/9/11	++		47
5	10/10/11	++		45

What is the appropriate action for the health worker to take for this patient now? Explain what the health worker should do and why.

Case 2: Little Seen

The following table shows the results of Little Seen's sputum-smear and culture examinations.

Results of sputum examination				Weight (kg)
Month	Date	Smear	Culture	
0	28/11/11	++	+	52
1	2/12/11	0	0	51.2
2	2/1/12	0	0	51.5
3	3/2/12	0	0	52.5
4	2/3/12	0	0	54
5				

What is the appropriate action for the health worker to take for this patient? Explain what the health worker should do now.

Case 3: Jasmine Tee

The following table shows the results of Jasmine Tee's sputum-smear and culture examinations.

Results of sputum examination				Weight (kg)
Month	Date	Smear	Culture	
0	28/9/11	+	+	44
1	10/10/11	0	+	45
2	11/11/11	0	0	46
3	12/12/11	0	0	47
4	1/1/12	0	0	47
5	2/2/12	0	0	47

What action is the appropriate action for the health worker to take for this patient? Explain what the health worker should do now.

Case 4: Rowdy Mann

Below are the results of Rowdy Mann's smear and culture examinations. He is asymptomatic, and the chest X-ray is improving significantly. His weight is increasing.

Results of sputum examination				Weight (kg)
Month	Date	Smear	Culture	
0	5/5/12	+++	+	59
1	10/6/12	0	0	59
2	11/7/12	0	0	60.5
3	12/8/12	0	0	61
4	9/9/12	0	0	61
5	11/10/12	0	0	59
6	11/11/12	0	0	59.5
7	15/12/12	0	n/d	61
8	13/1/13	0	0	62
9	9/2/13	0	n/d	62.5
10	8/3/13	+	pending	63

What is the appropriate action for the health worker to take for this patient now? Explain what the health worker should do and why.

When you have finished this exercise, review your answers with a facilitator.



GO BACK and read sections 8 and 9,
and work until the next stop sign.

Exercise E

Written exercise: Decide DR-TB treatment outcomes

The purpose of this exercise is to practise determining treatment outcomes. You will decide and record the outcomes of the patients in Exercise D. Although the review panel must approve all treatment outcomes, you will help recognize cases that have reached an outcome and present them for approval.

Case 1: Data Berth

Data Berth had culture conversion after the first month of treatment, but then reconverted to smear positive and culture positive during the fourth month. He was sent back for DOT at the DR-TB management centre. His last dose was given on 20 May 2012. Mr Berth has continued treatment for 12 months; the results of his smear and culture examinations are given below.

Results of sputum examination				Weight (kg)
Month	Date	Smear	Culture	
0	10/5/11	+++	+	52
1	12/6/11	0	0	52
2	11/7/11	0	0	50
3	8/8/11	0	0	49
4	6/9/11	++	+	47
5	10/10/11	++	+	47.5
6	9/11/11	+	+	48
7	6/12/11	0	0	48
8	7/1/12	+	+	47.5
9	8/2/12	+	+	47
10	9/3/12	++	+	45
11	10/4/12	+++	+	44
12	11/5/12	++	+	42

Record the date and treatment outcome on the excerpt of his *Second-line TB treatment card*.

Outcome	Mark one	Date
Cured		
Treatment completed		
Died		
Failed		
Lost to follow up		
Not evaluated		

Case 2: Little Seen

Little Seen completed 21 months of treatment on 10 August 2013. He is compliant with treatment and asymptomatic, but he had poor compliance with sputum testing. His smear and culture results are presented below.

Results of sputum examination				Weight (kg)
Month	Date	Smear	Culture	
0	28/11/11	++	+	52
1	2/12/11	0	0	51.2
2	2/1/12	0	0	51.5
3	3/2/12	0	0	52.5
4	2/3/12	0	0	54
5	3/4/12	0	0	56
6	4/5/12	0	0	56.5
7		-		56.8
8		-		57.1
9	4/8/12	0	0	57.5
10		-	-	58
11	2/10/12	0	0	58
12		-		57
13		-	-	57.4
14		-	-	57
15		-	-	58
16	8/3/13	0	0	56.5
17		-	-	58
18		-	-	57
19		-	-	58
20		-	-	59.4
21	6/8/13	0		58

Record the date and treatment outcome on the excerpt of his *Second-line TB treatment card*.

Outcome	Mark one	Date
Cured		
Treatment completed		
Died		
Failed		
Lost to follow up		
Not evaluated		

Case 3: Jasmine Tee

Jasmine Tee completed 19 months of DR-TB treatment on 7 April 2013. Below are the results of her culture examinations.

Results of sputum examination				Weight (kg)
Month	Date	Smear	Culture	
0	28/9/11	+	+	44
1	10/10/11	0	+	45
2	11/11/11	0	0	46
3	12/12/11	0	0	47
4	1/1/12	0	0	47
5	2/2/12	0	0	47
6	3/3/12	0	0	48
7	4/4/12	0	0	49
8	5/5/12	0	n/d	47
9	6/6/12	0	0	47
10	7/7/12	0	n/d	47
11	8/8/12	0	0	47
12	9/9/12	0	n/d	47
13	10/10/12	0	0	47
14	11/11/12	0	n/d	47
15	12/12/12	0	0	47
16	1/1/13	0	n/d	47
17	2/2/13	0	0	47
18	3/3/13	0	n/d	47
19	4/4/13	0	0	49
20	6/5/13	0	0	50

Record the date and treatment outcome on the excerpt of her *Second-line TB treatment card*.

Outcome	Mark one	Date
Cured		
Treatment completed		
Died		
Failed		
Lost to follow up		
Not evaluated		

Case 4: Rowdy Mann

It has been 2 months since Mr Mann last came for treatment on 2 June 2009. When the health worker went to his home a month ago, the apartment was vacant. The contact person told the health worker that the family had moved away. The contact person said that Rowdy Mann told her that he had finished treatment with second-line drugs. The contact person did not know where the family had moved.

Results of sputum examination				Weight (kg)
Month	Date	Smear	Culture	
0	5/5/12	+++	+	59
1	10/6/12	0	0	59
2	11/7/12	0	0	60.5
3	12/8/12	0	0	61
4	9/9/12	0	0	61
5	11/10/12	0	0	59
6	11/11/12	0	0	59.5
7	15/12/12	0	n/d	61
8	13/1/13	0	0	62
9	9/2/13	0	n/d	62.5
10	8/3/13	+	0	63
11	8/4/13	+		63
12	8/5/13	+		63
13				
14				
15				

Record the date and treatment outcome on the excerpt of his *Second-line TB treatment card*.

Outcome	Mark one	Date
Cured		
Treatment completed		
Died		
Failed		
Lost to follow up		
Not evaluated		

When you have finished this exercise, review your work with a facilitator.



GO BACK and read the *Summary* and work until the end of the module.

Annexes

Annex A: Recommended doses of anti-TB medicines by patient's weight _____ C-108

Annex B: Adjusting anti-tuberculosis medicines in renal insufficiency _____ C-110

Annex C: Paediatric dosing of second-line anti-tuberculosis medicines _____ C-112

Annex D: Assessment of evidence and its grading _____ C-113

Annex A: Recommended doses of anti-TB medicines by patient's weight

Weight-based oral anti-TB drug daily dosing in adults ≥ 30 kg

DRUGS	DAILY DOSE	30–35 kg	36–45 kg	46–55 kg	56–70 kg	>70 kg
Isoniazid	4–6 mg/kg once daily	150 mg	200 mg	300 mg	300 mg	300 mg
Rifampicin	8–12 mg/kg once daily	300 mg	450 mg	450 mg	600 mg	600 mg
Pyrazinamide	20–30 mg/kg once daily	800 mg	1000 mg	1200 mg	1600 mg	2000 mg
Ethambutol	15–25 mg/kg once daily	600 mg	800 mg	1000 mg	1200 mg	1200 mg
Rifabutin	5–10 mg/kg once daily	300 mg	300 mg	300 mg	300 mg	300 mg
Levofloxacin	750–1000 mg once daily	750 mg	750 mg	1000 mg	1000 mg	1000 mg
Moxifloxacin	400 mg once daily	400 mg	400 mg	400 mg	400 mg	400 mg
Ethionamide	500–750 mg/day in 2 divided doses	500 mg	500 mg	750 mg	750 mg	1000 mg
Prothionamide	500–750 mg/day in 2 divided doses	500 mg	500 mg	750 mg	750 mg	1000 mg
Cycloserine	500–750 mg/day in 2 divided doses	500 mg	500 mg	500 mg	750 mg	750 mg
p-aminosalicylic acid^a	8 g/day in 2 divided doses	8 g	8 g	8 g	8 g	8–12 g
Bedaquiline	400 mg once daily for 2 weeks then 200 mg 3 times per week					
Clofazimine	200–300 mg (2 first months) then 100 mg					
Linezolid	600 mg once daily	600 mg	600 mg	600 mg	600 mg	600 mg
Amoxicillin/clavulanic acid^b 7/1	80 mg/kg/day in 2 divided doses	2600 mg	2600 mg	2600 mg	2600 mg	2600 mg
Amoxicillin/clavulanic acid^b 8/1	80 mg/kg/day in 2 divided doses	3000 mg	3000 mg	3000 mg	3000 mg	3000 mg
High-dose isoniazid	16–20 mg/kg once daily	600–1000 mg	1000–1500 mg			

DRUGS	DAILY DOSE	30–35 kg	36–45 kg	46–55 kg	56–70 kg	>70 kg
Imipenem/cilastatin	1000 imipenem/1000 mg cilastatin twice daily					
Meropenem	1000 mg three times daily (alternative dosing is 2000 mg twice daily)					

Weight-based injectable anti-TB drug daily dosing in adults ≥30 kg

DRUGS	DAILY DOSE	30–33 kg	34–40 kg	41–45 kg	46–50 kg	51–70 kg	>70 kg
Streptomycin	12–18 mg/kg once daily	500 mg	600 mg	700 mg	800 mg	900 mg	1000 mg
Kanamycin	15–20 mg/kg once daily	500 mg	625 mg	750 mg	875 mg	1000 mg	1000 mg
Amikacin	15–20 mg/kg once daily	500 mg	625 mg	750 mg	875 mg	1000 mg	1000 mg
Capreomycin	15–20 mg/kg once daily	500 mg	600 mg	750 mg	800 mg	1000 mg	1000 mg

^a Adapted from Tuberculosis: practical guide for clinicians, nurses, laboratory technicians and medical auxiliaries. Médecins Sans Frontières and Partners In Health; 2013.

Annex B: Adjusting anti-tuberculosis medicines in renal insufficiency^a

Drug	Recommended dose and frequency for patients with creatinine clearance <30 ml/min or for patients receiving haemodialysis (unless otherwise indicated, dose after dialysis)
Isoniazid	No adjustment necessary
Rifampicin	No adjustment necessary
Pyrazinamide	25–35 mg/kg per dose three times per week (not daily)
Ethambutol	15–25 mg/kg per dose three times per week (not daily)
Rifabutin	Normal dose can be used; if possible, monitor drug concentrations to avoid toxicity
Rifapentine	No adjustment necessary
Streptomycin	12–15 mg/kg per dose two or three times per week (not daily) ^b
Capreomycin	12–15 mg/kg per dose two or three times per week (not daily) ^b
Kanamycin	12–15 mg/kg per dose two or three times per week (not daily) ^b
Amikacin	12–15 mg/kg per dose two or three times per week (not daily) ^b
Ofloxacin	600–800 mg per dose three times per week (not daily)
Levofloxacin	750–1000 mg per dose three times per week (not daily)
Moxifloxacin	No adjustment necessary
Gatifloxacin	400 mg three times a week
Cycloserine	250 mg once daily, or 500 mg/dose three times per week ^c
Terizidone	Recommendations not available
Prothionamide	No adjustment necessary
Ethionamide	No adjustment necessary
Para-aminosalicylic acid	4 g/dose, twice daily maximum dose ^d
Bedaquiline	No dosage adjustment is required in patients with mild-to-moderate renal impairment (dosing not established in severe renal impairment, use with caution)
Linezolid	No adjustment necessary
Clofazimine	No adjustment necessary
Amoxicillin/clavulanate	For creatinine clearance 10–30 ml/min, dose 1000 mg as amoxicillin component twice daily; for creatinine clearance <10 ml/min, dose 1000 mg as amoxicillin component once daily
Imipenem/cilastatin	For creatinine clearance 20–40 ml/min, dose 500 mg every 8 hours; for creatinine clearance <20 ml/min, dose 500 mg every 12 hours

Drug	Recommended dose and frequency for patients with creatinine clearance <30 ml/min or for patients receiving haemodialysis (unless otherwise indicated, dose after dialysis)
Meropenem	For creatinine clearance 20–40 ml/min, dose 750 mg every 12 hours; for creatinine clearance <20 ml/min, dose 500 mg every 12 hours
High-dose isoniazid	Recommendations not available
Clarithromycin	500 mg daily

^a From Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. Geneva: World Health Organization; 2014 (WHO/HTM/TB/2014.11).

^b Caution should be used with injectable agents in patients with renal function impairment because of the increased risk of both ototoxicity and nephrotoxicity. If on dialysis, dose after dialysis.

^c The appropriateness of 250 mg daily doses has not been established. There should be careful monitoring for evidence of neurotoxicity (if possible, measure serum concentrations and adjust accordingly).

^d Sodium salt formulations of PAS may result in an excessive sodium load and should be avoided in patients with renal insufficiency. Formulations of PAS that do not use the sodium salt can be used without the hazard of sodium retention and are the preferred formulation in patients with renal insufficiency.

Annex C: Paediatric dosing of second-line anti-tuberculosis medicines

Medicine	Daily dose (mg/kg)	Frequency	Maximum daily dose
Streptomycin	20–40	Once daily	1 g
Kanamycin	15–30	Once daily	1 g
Amikacin	15–22.5	Once daily	1 g
Capreomycin	15–30	Once daily	1 g
Ofloxacin	15–20	Twice daily	800 mg
Levofloxacin	7.5–10	Once daily	750 mg
Moxifloxacin	7.5–10	Once daily	400 mg
Ethionamide	15–20	Twice daily	1 g
Prothionamide	15–20	Twice daily	1 g
Cycloserine	10–20	Once or twice daily	1 g
Para-aminosalicylic acid	150	Twice or thrice daily	12 g

Annex D: Assessment of evidence and its grading

The tables below provide a short overview of the terminologies used by the Guideline Development Group and their implications for adopting the recommendations.

Table 1. Quality of evidence and definitions

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 estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain

Table 2. Assessment of the strength of a recommendation

Strong	The Guideline Development Group is confident that the desirable effects of adherence to the recommendation outweigh the undesirable effects.
Conditional	The Guideline Development Group concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects.

Table 3. Implications of the strength of a recommendation for different users

Perspective	Strong recommendation	Conditional recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Adherence to this recommendation according to the guidelines could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients, and that patients must be helped to arrive at a management decision consistent with their values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their values and preferences.
For policy-makers	The recommendation can be adopted as policy in most situations.	Policy-making will require substantial debate and involvement of various stakeholders.

Management of drug-resistant tuberculosis

Training for staff working at DR-TB management centres

Module D: Inform and educate patients
about DR-TB



**World Health
Organization**

MODULE D

Inform and educate patients about DR-TB^a

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^a These modules focus on managing rifampicin-resistant TB (RR-TB) and multidrug-resistant TB (MDR-TB) (collectively referred to as RR/MDR-TB in several places) because of the clinical significance and need for treatment with second-line drugs in both cases. The modules do not specifically focus on extensively drug-resistant TB (XDR-TB) and polydrug-resistant TB (PDR-TB) other than RR-TB.

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Introduction

Informing and educating patients and their families about drug-resistant tuberculosis (DR-TB) is a critical part of treatment. Because of the complexity of the diagnostic and treatment process, it is important that health workers take sufficient time to provide adequate information and answer questions in a clear and supportive manner to facilitate education. It is also essential to identify and address the key concerns and priorities for the patient at every stage of their diagnosis and treatment, and check that they have understood the information that they have been given. Before giving information, it is important to check what the patient already understands or has heard about DR-TB so that information can be provided at an appropriate level and any misconceptions corrected.

When a patient is presumed to have DR-TB, it is necessary during the initial meeting to discuss the process of diagnosis and treatment. Information on how TB and DR-TB are spread should be provided so that patients can take precautions to avoid transmitting the disease to others. Measures to prevent or mitigate stigma and discrimination should be addressed, preferably together with the patient's family. The patient should also be asked whether anyone they know has similar symptoms, is receiving or has ever received treatment for TB.

At the time of diagnosis or start of an empirical second-line TB regimen, patients need basic information about the disease, the process of being enrolled for treatment, and their rights and responsibilities. They may have questions about how they have become infected, the difference between TB and DR-TB, the implications of a diagnosis of TB on the quality of life and the options to reduce its impact. Patients most likely will be anxious, and need reassurance that the disease can be cured in most instances with correct, uninterrupted treatment. The patient and the family need to understand, though, that DR-TB is not always possible to cure, and treatment options may become limited.

Before beginning treatment, the patient needs to understand the medicines to be taken, the treatment process and the necessity of directly observed treatment (DOT) to monitor the treatment and offer regular support. It is necessary to obtain the agreement of the patient to undertake DR-TB treatment and to make clear that the patient will require DOT 6 (or 7) days per week for at least 20 months. Any potential difficulty the patient foresees in their ability to attend for DOT should be assessed and arrangements agreed upon before beginning treatment.

Daily visits for DOT offer many opportunities to provide information and support, and answer any questions the patient might have about prevention, diagnosis and treatment. At some visits, you may want to explain the need and schedule for follow-up sputum examinations. At all visits, you need to check for new factors affecting the quality of life of the patient and anything which might make it difficult for the patient to attend for their treatment. At every visit, show a welcoming and supportive attitude so that patients will be willing to return for their next

treatment. If the patient has side-effects or questions or concerns, it is imperative that you take the time to discuss the problem and offer appropriate care, information and encouragement.

At very busy times, health-care workers may feel unable to provide the supportive, friendly attitude needed; however, under no circumstance should the patient be treated to a hostile, humiliating or judgemental attitude or language. Encourage regular attendance by making DOT as quick and easy for the patient as possible: try to avoid making a patient with DR-TB stand in line and, when that is unavoidable, try to ensure that some entertainment or education material is available for the waiting patients. You may need to give repeated encouragement to patients who feel that daily treatment is too time-consuming and inconvenient. Whenever possible, liaise with properly trained community-based health-care workers to provide additional support, especially if you do not have the time or resources needed.

The physician at the DR-TB management centre will also provide information and motivation to the patient during monthly monitoring visits. Remember that providing verbal motivation without listening to and enabling the patient to solve the major barriers they may be facing, such as problems with work, breakdown of relationships, addiction or other health problem may be useless.

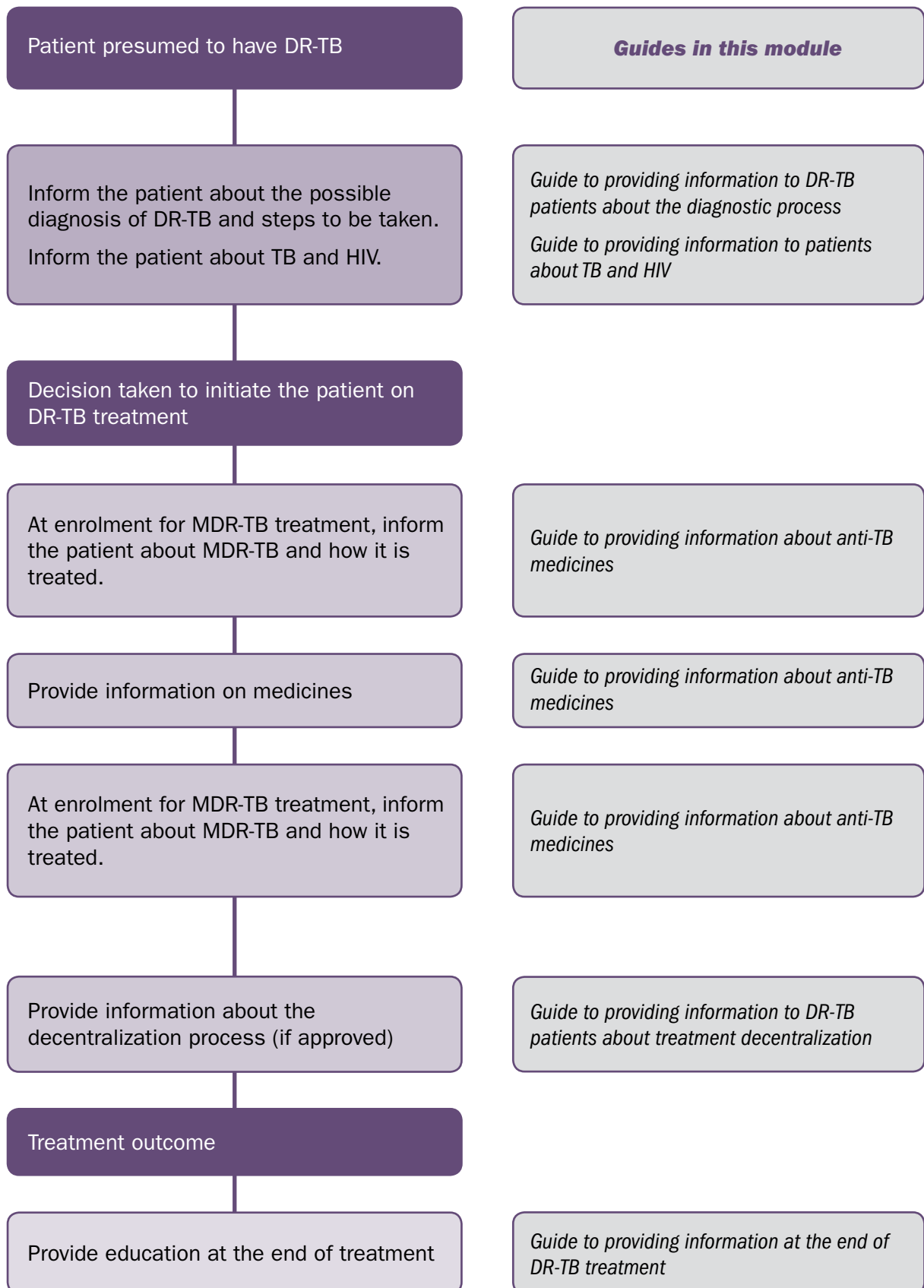
Objectives of this module

After completing this module participants will be able to do the following: Section:

- ▶ Use good communication skills. 1
- ▶ Ensure that the patient understands the possible diagnosis of DR-TB and the treatment2
- ▶ Inform DR-TB patients, their family and contacts about HIV and TB. 3
- ▶ At enrolment for DR-TB treatment, inform the patient about the disease and how it is treated..... 4
- ▶ Provide information about the medicines used to treat DR-TB..... 5
- ▶ Continue to provide information and support to the patient as needed about side-effects, the need to continue treatment, and monthly sputum examinations and monitoring visits..... 6
- ▶ Provide information about the decentralization process. 7
- ▶ Provide information at the end of treatment..... 8

If you need to look up an unfamiliar word, refer to the Glossary at the end of Module A.

Figure 1 **Flowchart for informing patients about drug-resistant tuberculosis (DR-TB)**



1. Use good communication skills

Good communication begins when the health worker sees the patient promptly, addresses the patient by name, and offers a comfortable place to sit. It continues as the health worker makes eye contact, speaks in a respectful tone of voice, and encourages the patient to ask questions. Good communication is more than just talking or giving advice. It involves asking questions, listening carefully, trying to understand a patient's worries or needs, demonstrating a caring attitude and helping to solve problems.

Good communication is needed not only to inform patients of important messages about DR-TB and its treatment but **good communication is also critical to encouraging patients to return for the next treatment visit, day after day and month after month.** One of the main reasons that patients are lost to follow up is the attitude of the health worker. Patients who are lost to follow up often report that the health worker was rude, impatient or seemed too busy to care. For patients with DR-TB, the relationship with their health worker will last 20 months or more. It is vital to the success of treatment to maintain a harmonious relationship. **Every patient deserves to be treated with respect.**

Table 1 summarizes the important communication skills. The right side of the table defines the purpose of each skill in the context of providing treatment and information to patients. This module focuses on using these communication skills when informing patients about DR-TB and its treatment.

Table 1 **Summary of communication skills**

USE THESE SKILLS	IN ORDER TO
1.1 Ask questions and listen.	Understand the patient's medical history. Understand how much the patient knows about DR-TB. Identify and help solve any problems that the patient may have with treatment.
1.2 Demonstrate a caring, respectful and friendly attitude.	Make the patient feel at home and welcome.
1.3 Praise and encourage the patient.	Motivate the patient to continue treatment. Help the patient feel good about the treatment so far.
1.4 Speak clearly and simply.	Inform patients (and their family) about DR-TB and its treatment
1.5 Encourage the patient to ask questions.	Ensure that the patient understands and remembers important messages about DR-TB and its treatment.
1.6 Ask checking questions.	Ensure that the patient knows exactly what to do next.

1.1 Ask questions and listen

Asking questions and listening carefully to the patient's responses are important in communicating effectively with the patient. Different patients may need different information. Rather than giving everyone exactly the same messages, first ask questions to determine what each patient already knows or believes about DR-TB.

As much as possible, ask questions that are **open-ended**. These are questions that cannot simply be answered "Yes" or "No." You will usually obtain more information if you ask questions that begin with such words as, "What, why, how and when". These types of questions require the patient to think about the answer and elaborate. Nonetheless, sometimes it may be necessary to ask a question that requires a direct response of "Yes" or "No".

Listen carefully to each answer. If the patient is slow to respond, do not be tempted to suggest an answer. Let the patient have time to think.

Examples of questions to ask to understand the patient's current knowledge about DR-TB

- What do you know about DR-TB?
- What do you think causes DR-TB? How is it spread?
- Have you ever known anyone who had DR-TB? What happened to that person?
- What have you heard about curing DR-TB?

Asking these types of questions will help you tailor messages to the needs of each particular patient. You can build on accurate information that the patient already knows and believes. You can concentrate on giving new information and correcting mistaken beliefs.

For example, a patient may believe that DR-TB is inherited or it comes from exposure to paints and fumes, etc. Your initial messages to this patient should focus on the causes of TB and DR-TB, and the fact that it can be cured with medicines.

Another patient may know a lot about DR-TB but may demand a chest X-ray or a blood test instead of sputum examinations. The messages for this patient should focus on the need for examining sputum.

1.2 Demonstrate a caring, respectful and friendly attitude

The purpose of DOT is not simply to ensure that the patient takes the medicines, but also to support the patient throughout treatment. The patient is likely to be worried and need a friend. If you have a caring attitude, the patient will be more likely to return each day for treatment. You can demonstrate a caring attitude through your choice of actions, words, tone of voice, and by making eye contact.

Demonstrate a caring attitude from the time that the patient enters the health facility by offering a place to sit and addressing the patient by name. Attend to the patient as soon as possible, without making the patient wait. You can show respect by remembering that the patient's time is as valuable as your own.

When providing treatment or advice, look directly at the patient. This will help you see signs of concern, fear or confusion. Speak slowly enough to be understood. Do not rush through instructions. Use a kind tone of voice, and choose words that are caring rather than accusing. Scolding the patient does not help. For example, if a patient misses a day:

Do NOT say: You missed yesterday. Do you want your whole family to catch TB?

Instead, say: I did not see you yesterday. What happened that kept you away? Is there any way I might be able to help?

Ask about and sympathize with the patient's problems. Help find solutions. Solutions may involve talking with the patient's family or employer, dealing with a side-effect from the medicines or finding an alternative treatment site closer to the patient's home.

1.3 Praise and encourage the patient

Treatment for DR-TB is a long process that may last 20 months or more. In order to motivate patients to continue treatment, praise and encourage them at every visit. Begin by saying, "I'm glad to see you. You are doing the right thing by coming for treatment every day." Include positive remarks and friendly questions, such as those in the list below.

- I'm happy that you have been taking your medications every day. Keep it up.
- You may start looking for a job when you get well.
- How is your family?

Reassure patients frequently that **DR-TB is curable** and that as long as they come for treatment, they will receive highly effective care. Point out signs of progress such as how much weight they have gained, how much less they are coughing, and how well they look. Encourage patients by telling them how much of the treatment they have finished.

1.4 Speak clearly and simply

Speak clearly, using words that the patient can understand. For example, many patients would NOT understand the following statement:

- Your drug-susceptibility pattern shows resistance to first-line agents. The treatment for DR-TB requires daily combination therapy including a fluoroquinolone and second-line anti-TB agents.

Instead, say something like the following:

- The tests of your sputum show that the TB germs you have are not killed by the medicines usually used to treat TB. To treat the kind of TB that you have, which is called "drug-resistant" TB, you will have to take a number of different medicines every day for at least 20 months. During this treatment, you will also have an injection every day for at least 8 months.

1.5 Encourage the patient to ask questions

Make sure that the patient feels comfortable enough to ask questions. After giving instructions or an explanation, pause and ask, “Do you have any questions? I know this is a lot of information at once.”

Patients may be timid and concerned about appearing ignorant. Or they may be nervous or in a panic and simply want to leave the health facility in a hurry. It may take courage for them to ask questions. Praise patients for asking questions, and answer them thoughtfully and carefully. For example, say something like:

- I’m glad you asked that question, or
- Good question!

1.6 Ask checking questions

Checking questions are questions intended to find out what a person has learnt, so that you can provide more information or clarify your instructions if needed. **After providing information**, ask checking questions to ensure that the patient understands the information. **At the end of a visit**, ask checking questions to ensure that the patient understands what to do next.

For example, suppose that you have explained to the patient the necessity of DOT for DR-TB and what can happen when someone does not take their medicines. To check the patient’s understanding, you might ask:

- Why is it important to take all of the medicines and come for all appointments?

Suppose that you have instructed the patient to return with an early morning sputum sample for a follow-up examination. To make sure that the patient knows what to do and understands the importance, you might ask such checking questions as:

- When will you cough up the sputum?
- What container will you use?
- Why is this so important?

When you ask a checking question, try to phrase it so that the answer must be more than simply “Yes” or “No.” For example, do **not** ask:

- Do you know what to do next?

The patient might answer “Yes” to avoid seeming forgetful. Better questions would be:

- Where will you go for your next follow-up sputum and culture exams? or
- When will you go?

Asking checking questions requires patience. Give the patient time to think and answer. If the patient is silent, your impulse may be to answer the question yourself or quickly ask a different question.

The patient may know the answer but be slow to respond for several reasons. The patient may be timid, may be surprised that you really expect an answer, or may be afraid of answering incorrectly. Wait for an answer and give encouragement.

Sometimes you may get an incomplete or unclear answer to a checking question. Then you will need to ask a follow-up question to see if the patient really understands. For example, after explaining which household members should be examined or tested for DR-TB, you might ask:

- Who among your household needs to be examined or tested for DR-TB?

The patient might answer:

- The children who are under 5.

As it is not clear that the patient knows that older children and adults who have a cough should be tested, you could follow up by saying:

- You are right that all children who are younger than 5 should be examined for TB symptoms. What about others in the household? What is the main sign to look for in others?

If the patient answers incorrectly or cannot remember, be careful not to make the patient feel uncomfortable. Clarify what you mean or give more information. Then ask a checking question again.



Now do Exercise A – written exercise

When you have reached this point in the module, you are ready to do Exercise A, a written exercise about how to ask checking questions. Turn to the exercise section in the module and follow the instructions. Do this exercise by yourself. Then discuss your answers with a facilitator.

2. Inform the patient about the possible diagnosis of DR-TB and its treatment

The DR-TB management centre's staff should carry out the following tasks when they first meet with a patient presumed to have DR-TB:

1. Collect and send sputum samples for smear examination, culture and drug-susceptibility testing (DST) if this has not already been done.
2. Complete and return the bottom part of the presumptive *DR-TB case referral form* if the presumptive case was referred from another facility.
3. Complete the *DR-TB screening form* (this requires that the physician perform a clinical assessment and evaluate the patient's condition).
4. **Inform the patient about the possible diagnosis of DR-TB and the treatment.**
5. **Assess the patient's understanding of drug resistance and attitude.**

Most of these tasks are taught in Module B. This section of this module focuses on the fourth task, informing the patient about the possible diagnosis of DR-TB and the next steps in the diagnostic and treatment processes.

Remember that the patient presumed to have DR-TB may be scared or nervous, especially if they have known someone else who has been diagnosed with DR-TB and struggled on treatment or even died. Think about how you might feel if you were the patient. All communication must be kind and supportive, and all information must be medically correct. It is most important for the patient presumed to have DR-TB to understand the following points.

Possible diagnosis of DR-TB

You may want to say something like the following:

- You have been identified as possibly having drug-resistant TB, or DR-TB. DR-TB is presumed in patients who continue to have symptoms while being treated for TB, or who have been treated for TB before, or who have had close contact with someone who has DR-TB. It is possible that the medicines you are taking or took earlier did not kill the TB germs. DR-TB can be cured as long as the medicines are taken regularly for about 20 months.
- Do you know anyone who has been in this situation? What happened?
- What questions do you have about this?

Diagnostic or baseline tests to be done (sputum-smear microscopy, molecular tests, culture, DST)

Several sputum tests may need to be done to diagnose DR-TB. Inform the patient about the tests by explaining in the following manner:

- Diagnosing DR-TB is similar to diagnosing TB: we will ask you to provide sputum samples.
- These samples will be sent for a couple of tests to see if you have TB germs in your lungs which cannot be killed by the usual drugs. First, we will do a rapid test to see if you have TB, and if the TB you have is resistant to the usual drugs. This test takes just a day. If found positive for resistance to a key first-line drug, a culture test will be done followed by a drug-susceptibility test or DST. The process takes a long time but if initial tests indicate resistance, we will discuss and initiate appropriate treatment for drug-resistant TB as soon as possible without waiting for the other test results just to save time for you and prevent the disease from getting worse.
- The results of DST tell us which medicines may kill the TB germs and which will not. Once we have the results from DST, we will know which medicines will work best to treat the disease that you have.

Timelines for receiving test results

The patient needs to know when to expect the test results. Inform the patient about the timelines for receiving the test results (substitute the actual time that it takes at your facility):

- Smear results should be ready (*1–2 days*) after you submitted the second sample.

- Rapid test result will be available within (*a few hours/ a day*). This is the first point where the need for treatment with second-line drugs may be determined.
- The results of the culture test will be ready (**inform duration according to local setting – whether a liquid or solid culture medium is being used*) after we have collected your sputum sample.
- DST test results will be ready (*a few weeks*) later.

Next steps

As described in Module C, most patients who are presumed to have DR-TB will either receive a standardized regimen with second-line drugs while waiting for the DST results or will receive a regimen with first-line drugs depending upon results of molecular tests. Which regimen they receive depends on their risk factors, the guidelines of your national TB programme, and the recommendations of the physician and the review panel. Discuss with the patient about the treatment that he or she will receive until the DST results are available.

- For patients who will continue the present treatment/treatment with first-line drugs, explain that the patient should continue taking the medicines regularly until the results of DST are available, which should be in a few weeks/months.
- For patients who will begin a regimen with second-line drugs, explain that the previous medicines have not worked, or that the disease will probably not respond to the most common medicines. Beginning a new treatment with different medicines lasting around 20 months is the only chance for cure. (*See section 4 for information to give at the time of enrolment for second-line drug treatment.*)

Tell all patients presumed to have DR-TB who are already on TB treatment that their progress will be monitored closely with smear examinations and monthly visits. Let them know that they will be informed about their DST results as soon as the results are available. Discuss any problems they foresee with regard to being able to attend for these visits.

Information about treatment for DR-TB

- Ask if the patient knows what treatment for DR-TB is like. Briefly provide information on DR-TB treatment by saying something like the following:
- If you are diagnosed with DR-TB (RR-TB/MDR-TB), you will be prescribed medicines for about 20 months without interruption. The medicines you will be taking are different from the medicines that you used to take earlier for TB. During the initial part of the treatment, you may need to stay in hospital to ensure that you are comfortable with the medicines and that they do not cause you any problems.
- DR-TB can be cured, but it takes dedication to complete the many months of treatment. Treatment is provided free of charge.
- You will have medicines 6 (or 7) days each week, and will need a health worker on each of these days to receive the correct dose of medicines and to have the injections. When you do not need injections any longer, somebody other than a health worker may act as your treatment supporter. The health worker will support you throughout your treatment and help you with any problems even if you also have another treatment supporter.

- Ask how the patient feels about the treatment you have described and discuss any questions. What about the hospital stay, do they have children or other responsibilities that need to be taken care of while they are away? Who can help?

Information on how to avoid spreading TB to close contacts

Patients presumed to have DR-TB are likely to be infectious. They need to know how to keep from spreading the disease to people in their family and community without getting stigmatized or emotionally isolated. It is relevant to know first how patients think TB is transmitted before telling them something like the following:

- To avoid spreading TB to people in your family and community, you need to cover your mouth and nose when you cough or sneeze. If possible, use a face mask.
- If the weather permits, you also need to open the windows and doors in your home to allow fresh air to flow through it. You may use an electric fan to direct air from inside your house to the outside.
- Avoid meeting new people inside your home. It is better to meet new people outside your house instead.
- You do not need to eat a special diet or to sterilize dishes or any household items.
- Having sexual relations, kissing, sharing cutlery and clothes, etc. do not spread TB.

The next pages present a brief *Guide to providing information to DR-TB patients about the diagnostic process*. The guide summarizes how to use the communication skills, questions and messages discussed so far during the initial meeting when a patient is informed that he or she may have DR-TB.

Guide to providing information to DR-TB patients about the diagnostic process

Use this guide to remind you of what to ask and say during an initial information session with a patient presumed to have DR-TB. The column on the left includes examples of questions to ask these patients. The column on the right describes messages related to the questions on the left, which you may want to convey to the patient.

Throughout the visit: demonstrate a caring, respectful and friendly attitude. Praise and encourage the patient. Speak clearly and simply. Encourage the patient to ask questions.

ASK THE PATIENT QUESTIONS SUCH AS

THEN GIVE RELEVANT MESSAGES ON

Why do you think you have been referred here today?
 How do you think people get this illness?
 Do you know anyone who has been in this situation? What happened?

Possible diagnosis of DR-TB (RR/MDR-TB)

You may want to say something like the following:

You have been asked to visit the DR-TB management centre because you may have a type of tuberculosis known as drug-resistant TB, or DR-TB. DR-TB is presumed in patients who continue to have symptoms while being treated for TB or if they have been treated for TB before and the treatment was not completed or if they have been in close contact with someone who has the disease. It is possible that the medicines you are taking now or took before did not kill the TB germs. DR-TB can be cured, but the treatment requires you to take medicines regularly for around 20 months.

What do you know about how this disease is diagnosed?

Diagnostic and baseline tests to be done (smear, molecular tests like Xpert MTB/RIF and line-probe assay [LPA], culture, DST)

You may want to say something like the following:

Diagnosing DR-TB is similar to diagnosing TB. We will ask you to provide sputum samples. The samples will be sent to the lab for a couple of tests to see if you have TB germs in your lungs.

An Xpert MTB/RIF or LPA^a test will tell us quickly if you have TB and whether or not it is DR-TB (RR/MDR-TB, depending on the tests). After this test, culture and DST may be done to confirm the quick diagnosis. However, you do not have to wait for these test results; you can start treatment immediately.

A culture test will tell us if there are live TB germs in your sputum. If the result of the test shows that you have live TB germs in your sample, then another test will be done next. This is called drug-susceptibility testing or DST.

DST tells us which medicines may kill the TB germs and which medicines will not. Once we have the results from DST, we will know which medicines will work best to treat the disease you have.

^a Depending on country policy. However, a positive sputum test result would be required before performing the LPA test.

ASK THE PATIENT QUESTIONS SUCH AS

THEN GIVE RELEVANT MESSAGES ON

What do you know about how long it takes to get results from the tests for this disease?

Timelines for receiving test results (substitute the actual time that it takes at your facility)

Say something like the following:

Smear results should be ready (*a few days*) after you submit the second sample.

An Xpert MTB/RIF test result is available within a day and LPA in 2–4 days.

Culture test and DST results will be ready (*4–16 weeks*) after your sample was collected (depending on country policy of using liquid or solid culture techniques).

What do you know about the treatment?

Next steps

How do you feel about this change in your treatment?

For patients who will continue their present treatment: You should continue taking your medicines regularly until the results of DST are available.

For patients who will begin another regimen with first-line drugs: You should take the new treatment regularly until the results of DST are available.

For patients who will begin a regimen with second-line drugs: The medicines that you took previously have not worked (or the medicines most commonly used to treat the disease will probably not work for the type of TB that you have). You will start a new treatment plan using different medicines; this new plan will last 20 months. (*See section 4 for information to give to patients at the time they enrol for second-line drug treatment.*)

For all patients: Your treatment will be monitored and supported closely with sputum examinations and monthly monitoring visits with a doctor. We will let you know your laboratory results as soon as they are available.

What do you know about treatment for DR-TB?

Directly observed treatment for 20 months

What about the hospital stay; do you have children or other responsibilities that need to be taken care of while you are away? Who can help?

Say something like the following:

What do you think you will find most difficult?

If you are diagnosed as having RR/MDR-TB, you will need treatment for around 20 months. During this time, you will be provided medicine 6 (or 7) days per week with what are known as “second-line” medicines. These are the medicines that work best for treating the type of TB that you have. You may need to stay in hospital during the first few weeks/months of treatment until we are sure that the medicines do not cause you any problems.

DR-TB can be cured, but it takes dedication to complete the many months of treatment. Treatment is provided free of charge.

You will have treatment 6 (or 7) days each week, and will see a health worker on each of these days initially to receive the correct dose of medicines and injections. Once the need for injections is over, we can discuss using a mutually convenient treatment supporter. The health worker will support you throughout your treatment and help you with any problems.

ASK THE PATIENT QUESTIONS SUCH AS

THEN GIVE RELEVANT MESSAGES ON

What do you know about ways to prevent spreading the infection?
 How do you think you will be able to manage this?
 What is your home like – are you able to open windows or greet people outside?
 Who are you most worried about?

How to stop transmission of TB to family and community
Say something like the following:
 To keep from spreading TB to people in your family and community:
 • To avoid spreading TB to people in your family and community, you need to cover your mouth and nose when you cough or sneeze. If possible, use a face mask.
 • If the weather permits, you also need to open windows and doors in your home to allow fresh air to flow through it. You may use an electric fan to direct air from inside your house to the outside.
 • Avoid meeting new people inside your home. It is better to meet new people outside your house instead.
 • You do not need to eat a special diet or to sterilize dishes or any household items.
 • Having sexual relations, kissing, sharing cutlery and clothes, etc. do not spread TB.

Review: ask checking questions to ensure that the patient remembers the important messages and knows what to do next. Reinforce earlier messages, or give more information as needed.

DR-TB, drug-resistant tuberculosis; DST, drug-susceptibility testing, LPA, line-probe assay; RR/MDR-TB; rifampicin/multidrug-resistant tuberculosis

3. Inform DR-TB patients, their family and contacts about TB and HIV

Inform DR-TB patients, people presumed to have DR-TB, their families and contacts about HIV and its relationship to TB, and DR-TB in particular. Patients with both HIV and DR-TB are particularly vulnerable and must be followed closely to quickly address any deterioration in the patient’s condition. HIV counselling and testing should be offered to all patients with TB or DR-TB.

Women of childbearing age who are presumed to have DR-TB should be encouraged to seek counselling about birth control because the disease poses a risk to the life of the mother and the fetus. However, pregnancy is not a contraindication for treatment.

Some guidance on talking about HIV is given below.

What is HIV? (if the patient does not know)

You may want to say something like the following:

- HIV is the abbreviation for human immunodeficiency virus. HIV causes a viral infection that you get mainly through having unprotected sex with an HIV-infected partner, or by coming in contact with HIV-infected blood – for example, if you have a blood transfusion or use infected needles – and from an HIV-infected mother to her child during pregnancy

and/or delivery. The best way to protect yourself from sexual transmission is to always use condoms when you have sex. When you have HIV, your immune system is not able to resist other infections such as tuberculosis. Although some of the infections that you get when you are HIV positive can be treated and cured, there is no cure for the HIV infection itself. The medicines used to treat HIV improve a patient's resistance to infections, but they must be taken for life, are expensive and often have side-effects; people who have HIV need specialized medical care.

- People with HIV often get TB. The treatment for DR-TB is the same for HIV-positive patients as it is for patients who do not have HIV. The treatment cures most cases of DR-TB if the patient takes the medicines regularly. TB can be cured in people who are HIV positive, but the chance of the disease coming back (which is called a relapse) or dying during treatment is greater. A therapy called co-trimoxazole preventive therapy (or CPT) can be taken in addition to the anti-TB medicines to reduce the risk of other infections. You will also need antiretroviral therapy (ART) for your HIV infection and we may have to adjust the anti-TB medicines accordingly.

Why is HIV testing useful?

Say something like the following:

- There are benefits to knowing your HIV status.
 - It is important to know whether you are HIV positive to help the doctors make decisions about treatment, such as whether you need ART and CPT.
 - It is important so that health workers can offer you appropriate advice on TB and HIV, about your prognosis (prospect for recovery) and the side-effects of medicines.
 - If you are HIV positive with TB and do not take the ART, your disease could progress rapidly or you may develop even greater resistance to the usual TB drugs. However, knowing the HIV status would help us know if we need to start ART and therefore prevent this situation.
- If you are pregnant, an additional benefit of knowing whether you are HIV positive is that it may be possible to provide therapy to keep you from passing HIV infection to your child. The chances that children born to HIV-positive mothers will be infected with HIV and continue to be HIV positive can be greatly reduced if you have ART during pregnancy.
- If you want to find out about your HIV status, these are the options (*Explain options available locally for testing*).

In areas where there is a high prevalence of HIV, DR-TB patients should be retested for HIV after several months in case a test conducted at the beginning of treatment did not accurately reflect the patient's HIV status – that is, it was done during the window period – or they became infected after the first test was done.

What if the test is negative?

Say something like the following:

- Congratulations, your HIV test was negative. You should keep in mind that there is still a risk of being infected. Infection occurs mainly through unprotected sex with an HIV-infected

partner, so if you are sexually active you should always use condoms. Never share needles or syringes that may be infected or have been used by another person.

- There is a small possibility that you might have been infected recently and the test did not identify the infection. Because of this, you should consider repeating the test in 3 months.

What if the test is positive?^c

Say something like the following:

- The laboratory reported that your HIV test was positive. This indicates that you are infected with HIV. The infection will gradually interfere with your body's ability to defend itself against many infections, including TB.
- A person who is HIV positive is much more likely to develop TB. TB can be cured in people who are HIV positive, but the likelihood of the disease coming back (which is known as a relapse) or dying during treatment is greater.
- Knowing that you have HIV will help health workers
 - prevent complications, and diagnose and treat any other diseases that you may develop;
 - make decisions about treatment to help you stay healthier, such as giving you CPT (to prevent other infections) and ART (to improve the functioning of your immune system);
 - give you better information about your prognosis (prospect for recovery) and the side-effects of treatment.
- If you are receiving care for HIV to help you stay healthy, your TB is more likely to be cured and less likely to come back.
- Taking co-trimoxazole daily (as CPT) can prevent other infections. ART can help you feel better and live longer. You can be assessed for eligibility for ART at (*explain options available locally for HIV treatment*).
- If you are pregnant, you should receive treatment to keep you from passing HIV to your child. All children born to a mother infected with HIV test positive for the first 7 months of life because infants receive protection from their mother. The chances that children born to HIV-positive mothers will be infected with HIV and continue to be HIV positive are 1 in 3. However, if the mother takes ART during pregnancy, the chances may be reduced to 1 in 50.

The next page presents a brief *Guide to providing information to patients about TB and HIV*. This guide summarizes how to use the communication skills, questions and messages discussed in section 1.

^c Depending on the national policy, a person may need to be tested twice before being declared HIV positive.

Guide to providing information to patients about TB and HIV

Use this guide for patients with DR-TB in areas where HIV is common. Note the special messages for pregnant women.

Throughout the visit: demonstrate a caring, respectful and friendly attitude. Praise and encourage the patient. Speak clearly and simply. Encourage the patient to ask questions.

ASK PATIENTS THEN GIVE RELEVANT MESSAGES

<p>What do you know about HIV?</p>	<p><i>You might want to say:</i></p> <ul style="list-style-type: none"> • HIV is the abbreviation for human immunodeficiency virus. HIV is a viral infection that you get mainly through sex or by blood – for example, if you have a transfusion with infected blood or use infected needles – and may be passed from an HIV-infected mother to her child during pregnancy and/or delivery. The most common way that people become infected is by having unprotected sex with someone who is HIV positive. The best way to protect yourself is to always use condoms when you have sex. When you have HIV, your immune system is not able to resist other infections, such as TB. Although some of the infections that you get when you are HIV positive can be treated and cured, there is no cure for the HIV infection itself. The medicines used to treat HIV improve a patient’s resistance to infections, but they must be taken for life, are expensive and often have side-effects; people who have HIV need specialized medical care. • People with HIV often get TB. The treatment for DR-TB is the same for HIV-positive patients as it is for patients who do not have HIV. The treatment cures most cases of DR-TB if the patient takes the medicines regularly. TB can be cured in people who are HIV positive, but the likelihood of the disease coming back (which is called a relapse) or dying during treatment is greater. A therapy called co-trimoxazole preventive therapy (or CPT) can be taken in addition to anti-TB medicines to reduce the risk of other infections. However, if you need treatment for HIV, we may have to adjust the anti-TB medicines that we give you.
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<p>Do you know your HIV status? <i>If status is unknown (or undocumented) or if a test was done more than 3 months ago was negative, recommend HIV testing</i></p>	<p>Recommend that all TB patients be tested for HIV</p> <p><i>Say something like the following:</i></p> <p>There are benefits to knowing your HIV status. <i>If testing shows that you are HIV positive</i>, it is helpful</p> <ul style="list-style-type: none"> in diagnosing TB, because people who are HIV positive and who also have TB may have different symptoms than people who are not infected with HIV; in making decisions about treatment, such as whether you need antiretroviral therapy (ART) and CPT; in making decisions about advice, so that health workers can offer you appropriate information on TB and HIV, your prognosis (prospect for recovery) and the side-effects of medicines; in providing ART to pregnant women, in whom it is especially important, because taking it during pregnancy makes it much less likely that HIV will be passed on to your child. <p><i>If you are HIV negative</i>, you will receive counselling on safer sex and other practices that will help you remain HIV negative.</p>
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<p>What do you think about being tested?</p>	<p>Explain options available for HIV testing.</p>
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Information to give after test results are received

ASK PATIENTS THEN GIVE RELEVANT MESSAGES

If patient is HIV negative

Say something like the following:

- Congratulations, your HIV test was negative. You should keep in mind that there is still a risk of being infected. Infection occurs mainly through unprotected sex with an HIV-infected partner, so if you are sexually active you should always use condoms. Never share needles or syringes that may be infected or have been used by another person.
- There is a small possibility that you might have been infected recently and the test did not identify the infection. Because of this, you should consider repeating the test in 3 months.

To prevent HIV transmission, all sexually active people should use condoms, no matter what their HIV status.

If a TB patient is HIV positive²

Say something like the following:

- The laboratory reported that your HIV test was positive. This indicates that you are infected with HIV. The infection will gradually interfere with your body's ability to defend itself against many infections, including TB.
- A person who is HIV positive is much more likely to develop TB. TB can be cured in people who are HIV positive, but the likelihood of the disease coming back (which is known as a relapse) or dying during treatment is greater.

–Knowing that you have HIV will help the health services:

- to prevent complications, and diagnose and treat any other disease that you may develop;
- to make decisions about treatment to help you stay healthier, such as giving you CPT (to prevent other infections) and ART (to improve your immune system);
- to give you better information about your prognosis (prospect for recovery), the side-effects of treatment and associated diseases.

–If you are receiving care for HIV to help you stay healthy, your TB is more likely to be cured and less likely to come back.

–Taking co-trimoxazole daily (as CPT) can prevent other infections. ART can help you feel better and live longer. You can be assessed for eligibility for ART at (*explain options available for HIV treatment*).

–If you are pregnant, you should receive ART to keep you from passing HIV to your child.

Review: ask checking questions to ensure that the patient remembers important messages and knows what to do next. Reinforce earlier messages, or give more information as needed.

^d Depending on the national policy, a person may need to be tested twice before being declared HIV positive.

4. At enrolment for second-line treatment, inform the patient about the disease and how it is treated

Once treatment with second-line treatment regimen has been discussed and decided, and the patient has come to the treatment centre for enrolment, the health worker does the following:

1. prepares the patient's *Second-line TB treatment card*;
2. **informs the patient about DR-TB and how it is treated. Confirms the patient's willingness to undertake treatment for DR-TB as per the country policy, which may require DOT 6 (or 7) days per week for at least 20 months, follow-up sputum examinations, and monthly monitoring visits with the physician at the DR-TB management centre;**
3. enters the name of the patient and relevant details in the *Second-line TB treatment register*, and reports the approval of second-line treatment to the District TB Officer;
4. makes a home visit.

Most of these tasks are explained in Module C. This section of this module focuses on the second task, informing the patient about DR-TB and the enrolment procedures. Remember to ask questions about the patient's knowledge of DR-TB in order to determine what information to provide.

TB is more than just a medical problem. Some DR-TB patients have gone through a lot of emotional stress from having a chronic illness. They may have felt isolated, rejected and frustrated as a result of repeated unsuccessful treatments, and they may feel a lack of self-worth. For many of them, drug resistance is a result of previous inadequate treatment, and the reasons they received irregular treatment may continue during their treatment for DR-TB. Patients may continue to undergo stress because they are responsible for supporting their families or raising their children. Many will need to make major changes in their lifestyle when they relocate to undertake treatment or while they cope with the side-effects from second-line anti-TB medicines. It is essential to understand and address these feelings, stresses and lifestyle changes to help the patient complete the treatment regimen.

It is most important for DR-TB patients (and their family, if present) to understand the following.

What DR-TB is

Most patients do not know about DR-TB. Make sure that you inform the patient about the disease using simple language. You may want to say something like the following:

- When you have TB that is called "drug resistant" it means that the TB bacteria are not killed by the medicines used to treat ordinary TB, so we have to use other medicines. TB germs that are drug resistant are more difficult to treat than ordinary TB germs. Even so, most forms of this type of TB can be cured if they are treated early, and if all of the medicines are taken regularly and for as long as necessary.

The difference between treatment for TB and for DR-TB

To further clarify to the patient the nature of DR-TB and differentiate it from TB, explain that:

- the germ causing TB and DR-TB is the same, but the DR-TB germ is more difficult to kill and this means that treatment for DR-TB (RR/MDR-TB) takes much longer (usually 20 months, or possibly longer);
- DR-TB cannot be cured with the medicines used to treat ordinary TB, so other medicines are used; these are called second-line anti-TB medicines;
- these second-line medicines can cause more side-effects, but these medicines are the best option for treating DR-TB;
- DR-TB is more difficult to treat than TB that can be treated in the usual way, and if DR-TB is not treated correctly, the germs causing it will develop resistance to more medicines. The disease can then become incurable and you could die.
- **patients with DR-TB can be cured by taking the prescribed medicines regularly and for the complete duration.**

Why the patient has DR-TB

Patients may already have their own ideas about why they have DR-TB. Take time to find out about these beliefs and consider them when you offer explanations.

There are two main reasons why a person could have DR-TB.

1. The germ became resistant to some medicines during a previous treatment (known as acquired resistance):
 - because the medicines were not used correctly or were not of good quality; or
 - because treatment was interrupted or did not last long enough (do not blame the patient, simply explain the possible reasons); or
 - because the intake of the medicines was not directly observed to ensure uninterrupted treatment. (It is the health worker's job to ensure patients take their medicines.)
2. The patient may have caught DR-TB from another person.

The DR-TB regimen

Inform the patient what treatment is like for RR/MDR-TB. You may want to say something like the following:

- Just like the treatment for ordinary TB, you will receive at least five kinds of medicines,^c and one of them will be a daily injection. The number of tablets or capsules you take depends on how much you weigh. The treatment will last for approximately 20 months. Your physician will decide which medicines will work best for you, and will tell you when the treatment will end. You will take medicines 6 (or 7) days a week. **A health worker will always support you in taking your medicines.** You may need to stay in hospital to begin treatment; this is because we need to ensure that the medicines do not cause you any problems.
- The medicines used to treat DR-TB are expensive but will be provided to you free of charge.

^c As discussed in Module C, this includes four second-line drugs and pyrazinamide.

See the guide to anti-TB medicines in section 5 for messages about the specific medicines used in the patient's regimen.

Necessity for directly observed treatment

DOT is one of the most essential aspects of treatment for DR-TB. Describe the process to the patient. Emphasize why this approach is useful and the benefits that can be derived from it. You may want to say something like the following:

- A hospital nurse, a trained health worker or a treatment supporter must observe you swallowing all the medicines every time. This ensures that you take the correct medicines regularly for the required time. By seeing you regularly, the health worker will also be able to tell whether you are getting better or having problems with treatment, such as side-effects.
- If you do not take all of the medicines regularly, DR-TB will not be cured and you will continue to spread the disease to your family and your community. It is dangerous to stop or interrupt treatment because then we may not be able to cure your disease. If you have DOT, your health worker will be able to help quickly if you miss a dose.
- We all want treatment to be successful and this is one way to help ensure that it works.

This discussion should be conducted with utmost respect for the patient, emphasizing the fact that the ultimate concern is for the disease to be cured.

- Sometimes you may not be able to come for treatment because you have a conflict – for example, you may need to travel or attend a wedding or a funeral. It is important that you try to come every day that you are scheduled to. If you miss a dose, you will need to make it up at the end of treatment, so your treatment may last slightly longer.
- If you have to travel for an emergency, it is important to let the health worker or your treatment supporter know as soon as possible so that arrangements can be made with another trained health worker or volunteer to continue treatment without interruption.

Hospitalization (if needed)

Depending on the guidelines of the national TB programme, patients may need to be hospitalized during the first few weeks/months of treatment. You may want to explain it to the patient like this:

- You will have to be hospitalized to begin the treatment with second-line drugs. This is so that if you have any problems with the medicines we will know right away and we can take care of them. Treating you in the hospital also allows us to be sure that you are treated on time and with the correct medicines. If you live far away, it will make your treatment easier. When it is no longer likely that you will spread the disease, a local facility can be identified or a treatment supporter can be trained to provide your treatment.

Hospitalization may also be necessary to manage other diseases or conditions that the patient might have, such as HIV, diabetes or renal insufficiency. It is important to explore any problems the patient might face if hospitalized; for instance, if they have a job or family responsibilities to take care of.

Preventing the spread of DR-TB

Although most DR-TB patients have undergone more than one treatment course, they may still have incorrect notions about how TB is transmitted. Listen carefully to the patient's ideas about how they think the disease is transmitted, and provide correct information by saying something like the following:

- DR-TB, just like ordinary TB, spreads when a person with TB coughs or sneezes, and sprays TB germs into the air; these germs are inhaled by others who then become infected.
- You may pass on the germs to household members, especially when someone who is infected lives with many other people. Anyone can become infected with TB or DR-TB. However, not everyone who is infected will become sick. Starting appropriate treatment quickly reduces the risk of this transmission.

Emphasize prevention measures. You may want to say something like the following:

- Take all of your medicine every day so that your treatment will kill the germs and you will be less likely to infect others.
- Cover your mouth and nose when coughing or sneezing.
- Do not spit anywhere. If you need to, spit directly into a can or handkerchief and dispose of it appropriately.
- Open windows and doors to allow fresh air to flow through your home. You can use an electric fan to blow the air from inside your house to the outside.
- Avoid meeting new people inside your home; meet them outside.
- You do not need to eat a special diet or use separate eating utensils or household items, such as cooking pots.
- Having sexual relations, kissing, sharing cutlery and clothes, etc. do not spread TB.

How do you think this will work for you at home? Who are the people you are most concerned about?

Patients' rights and responsibilities

The patients' charter for tuberculosis care was initiated and developed by patients and affected communities from around the world, and outlines the rights and responsibilities of people with TB; the charter attempts to make the relationship between patients and health workers mutually beneficial. For more information, see "The patients' charter for tuberculosis care" in the "International standards for tuberculosis care".¹

Explain that all patients have rights and responsibilities. You may want to say:

- The rights of patients include receiving information, and being diagnosed and treated with respect; patients' responsibilities are mainly to take the treatment regularly, attend follow-up examinations and keep from spreading DR-TB in the community.

A copy of the charter can be found in Annex A.

Support services that are available at the DR-TB management centre during and after treatment to help patients cope with their situation

Support services are essential in ensuring that patients adhere to the treatment regimen and that it is completed successfully. Ask about what the patient foresees might be an issue and inform them about the services or support options (if any) in your DR-TB management centre, such as group therapy sessions, one-on-one counselling, meetings where patients receive education and support from peer counsellors and health workers, livelihood or skills training, and other group activities.

Social support in managing MDR-TB

Social support refers to the person's perception and confirmation that he/she is part of a social network that cares for him/her. A large body of evidence has confirmed that social support is a predictor of health status and mortality. Social support is determined by access to four resources:

- a. Informational support refers to any useful information that helps a person to solve problems and address sources of stress; it includes training and education.
- b. Emotional support refers to all expressions of care that contribute to strengthening self-esteem through empathy, trust, encouragement and care, among others, and that helps to deal with the psychological challenges in life.
- c. Companionship support refers to the help that makes a person feel that he or she belongs to the social network, and that he or she can rely on it for certain needs.
- d. Material support refers to all commodities, including financial products that a person receives through the social network as assistance to deal with daily hurdles.

Information support on MDR-TB treatment

There should be a well-formulated plan for preparing the patient for treatment. This includes educating the patient and caregiver on the use of drugs, length of treatment, possible side-effects, and mechanisms to access the support that will be available to the patient. Patient information and education takes place over several visits with different health-care providers (from the DOT provider to the physician). Information and educational pamphlets with reminders of the main points, in the local language, are helpful.

Emotional support

Having MDR-TB can be an emotionally devastating experience for patients and their social networks. Considerable stigma is attached to the disease, and this may interfere with adherence to therapy, and may badly affect the quality of life of patients in view of the discrimination that follows stigma. The provision of emotional support services to patients may increase the likelihood of adherence to therapy, and the acquisition of skills to deal with stigma and discrimination. This support may be organized in the form of support groups or in one-to-one counselling sessions by trained providers.

Material support

Poverty, depression, stigmatization, discrimination and perceived isolation are common among drug-resistant TB patients. Socioeconomic problems, not only hunger, homelessness and unemployment but also family responsibilities, should be addressed to enable patients and their families adhere to MDR-TB treatment and reduce the impact that the disease and treatment have on their quality of life. These challenges can be successfully tackled through socioeconomic interventions that enable patients to adhere to treatment, such as food baskets or transportation vouchers, which usually work best in combinations tailored to specific needs.

Companionship support

On-site social support for patients and their support networks through peer counselling can help to contribute to the effectiveness of TB programmes. TB programmes can develop a comprehensive component that identifies a cured patient (“community champion/expert patient”), and provides them with training to function as a peer supporter. This worker engages in support, treatment literacy and communicating with peers under treatment. These “community champions/expert patients” would follow each patient from diagnosis through to cure, and they would act as both “friend” and educator. From the patient’s perspective, having this companion available greatly reduces the psychological burden of the long duration of treatment and provides them with skills to cope with stigma and discrimination.

Tracing close contacts

Tracing contacts of the patient allows early detection and treatment of DR-TB in others. Inform the patient about contact tracing by saying something like the following:

- Everyone who lives in the same place as you and people with whom you work closely will be interviewed to see if they have any symptoms of TB. All those who are younger than 5 years, and anyone who has had a cough lasting for more than 2 weeks must be examined for TB and DR-TB. This examination may include a physical examination, sputum collection and possibly a chest X-ray and a type of skin test called testing with purified protein derivative (PPD, tuberculin testing) for children.
- It is especially important that we see any children who live in your household or with whom you have regular contact.

What to expect; what to do next

Treatment will begin when the patient has completed the requirements for enrolment, including being approved by the review panel. You may say something like the following:

- Once you have completed the requirements for enrolment, you will be ready to begin treatment. You may need to stay in hospital for a time or limit your activities and contacts with other people while there are TB germs in your sputum.

If the patient is not admitted on the day you see him or her, or if the patient is starting ambulatory second-line drug treatment, make sure that the patient knows exactly where and when to go for the next treatment; say something like, “Come back here (or local health centre) tomorrow before the

(referral or health) centre closes at (insert time) in the afternoon.” Ask questions to ensure that this will be possible and that the patient is committed to returning.

Remind the patient to bring close contacts aged 5 years and younger and all close contacts who have had a cough for DR-TB screening.

Confirm that the patient agrees to undertake treatment for DR-TB, which requires DOT 6 (or 7) days per week for at least 20 months (or longer), monthly follow-up sputum examinations, and monthly monitoring visits with the physician at the DR-TB management centre.

The next pages present a brief *Guide to providing information to DR-TB patients being enrolled for treatment*. It summarizes how to use the communication skills, questions and messages discussed in this module during the meeting held to inform the patient that treatment will begin. Feel free to take out the pages and use them as an aid.

Guide to providing information to DR-TB patients being enrolled for treatment

Use this guide to remind yourself what to ask and say during the information session with an MDR-TB patient who is about to begin treatment. The column on the left includes examples of the questions that you need to ask. The column on the right describes messages related to the questions on the left; these are the messages that you may want to convey to the patient. Emphasize different messages with different patients, depending on their knowledge about TB and DR-TB.

Throughout the visit: demonstrate a caring, respectful attitude. Praise and encourage the patient. Speak clearly and simply. Encourage the patient to ask questions.

ASK THE PATIENT QUESTIONS SUCH AS

THEN GIVE RELEVANT MESSAGES

What do you understand about drug-resistant tuberculosis (also called DR-TB)?

DR-TB

Say something like the following:

- Having DR-TB means that the TB bacteria causing your illness are not killed by the medicines normally used to treat TB, so we have to use other medicines.
- This DR-TB germ is more difficult to treat than the ordinary TB germ. Even so, most forms of DR-TB can be cured if they are treated early and if all of the medicines are taken regularly for as long as necessary, usually at least 20 months.

What do you know about the differences between treating TB and DR-TB?

The differences between treatment for TB and for DR-TB

Say something like the following:

The germ causing TB and DR-TB is the same, but DR-TB germ is more difficult to kill and this means that:

- treatment for DR-TB takes longer (usually 20 months or possibly longer);
- DR-TB cannot be cured with the medicines used to treat ordinary TB, so other medicines are used; these are called second-line anti-TB medicines;
- these second-line medicines are not as effective as the medicines used for ordinary TB and hence need to be taken for longer and can cause more side-effects, but these medicines are the best options for treating DR-TB;
- DR-TB is more difficult to treat than TB that can be treated in the usual way, and if DR-TB is not treated correctly, the germs causing it will develop resistance to more medicines. The disease can then become incurable and you could die.

DR-TB can be cured by always taking your medicines.

**ASK THE PATIENT
QUESTIONS SUCH AS**

THEN GIVE RELEVANT MESSAGES

Why do you think you have DR-TB?

Why the patient has DR-TB

There are two main reasons why a person could have DR-TB.

1. The germ became resistant to some medicines during a previous treatment (known as acquired resistance) because:
 - the medicines were not used correctly or were not of good quality; or
 - treatment was interrupted or did not last long enough. (Do not blame the patient, simply explain the possible reasons); or
 - the intake of the medicines was not directly observed to ensure uninterrupted treatment. (It is the health worker's job to ensure that patients take their medicines.)
 2. The patient may have caught DR-TB from another person.
-

What do you know about the treatment for DR-TB?

The DR-TB regimen

Say something like the following:

- Just like the treatment for ordinary TB, you will receive at least four kinds of medicines and one of them will be a daily injection. The number of tablets or capsules you take depends on how much you weigh. The treatment will last approximately 20 months. Your physician will decide which medicines will work best for you and will tell you when the treatment will end. You will take medicines 6 days a week. A health worker will always support you in taking your medicines. You may need to stay in hospital to begin treatment; this is because we need to ensure that the medicines do not cause you any problems.
- The medicines used to treat DR-TB are expensive but will be provided to you free of charge.

(See the guide to anti-TB medicines in section 5 for messages about the specific medicines used in the patient's regimen.)

Confirm that the patient is willing to undergo at least 20 months of treatment with second-line drugs.

ASK THE PATIENT QUESTIONS SUCH AS

THEN GIVE RELEVANT MESSAGES

Why do you think patients have directly observed treatment (DOT)?

Necessity for DOT

Say something like the following:

- A hospital nurse, a trained health worker or a treatment supporter must observe you swallowing all the medicines every time and give you injections. This ensures that you take the correct medicines regularly for the required time. By seeing you regularly, the health worker will also be able to tell whether you are getting better or having problems with treatment, such as side-effects.
- If you do not take all of the medicines regularly, DR-TB will not be cured and you will continue to spread DR-TB to your family and your community. It is dangerous to stop or interrupt treatment because then we may not be able to cure your disease. With DOT, your health worker will be able to help quickly if you miss a dose.
- Treatment for DR-TB is expensive, lasts long and may be your last chance of being cured. We all want treatment to be successful and this is one way to help ensure that it works.
- Sometimes you may not be able to come for treatment because you have a conflict – for example, you may need to travel or attend a wedding. It is important that you try to come every day that you are scheduled to. If you miss a dose, you will need to make it up at the end of treatment, so your treatment may last slightly longer.
- If you have to travel for an emergency, it is important to let the health worker or your treatment supporter know as soon as possible so that arrangements can be made with another trained health worker or volunteer to continue treatment without interruption.
- If you are given a scheduled time to come for treatment, come at that time. That way you will not have to wait too long for treatment.

Confirm that the patient agrees to come for DOT 6 (or 7) days per week.

Why do you think you need to stay in hospital? *(Ask only if relevant to national guidelines)*
How will you cope with being away from home?

Patients may need to be hospitalized initially

Say something like the following:

- You will have to be hospitalized to begin the treatment for DR-TB. This is so that if you have any problems with the medicines we will know right away and we can take care of them. Treating you in the hospital also allows us to be sure that you are treated on time and with the correct medicines. If you live far away, it will make your treatment easier. As soon as possible, a local facility can be identified or a treatment supporter can be trained to provide your treatment.

ASK THE PATIENT QUESTIONS SUCH AS

THEN GIVE RELEVANT MESSAGES

How do you think DR-TB spreads?
How can you avoid spreading DR-TB?

Preventing the spread of DR-TB

Say something like the following:

- DR-TB, just like ordinary TB, spreads when a person with TB coughs or sneezes, and sprays TB germs into the air; these germs are inhaled by others, who then become infected.
- It is easy to pass on the germs to household members, especially when someone who is infected lives with many people. Anyone can become infected with TB or DR-TB. However, not everyone who is infected with TB will become sick.

Emphasize prevention measures

You may want to say something like the following:

- Take all of your medicine every day so that your treatment will kill the germs and you will be less likely to infect others.
- Cover your mouth and nose when coughing or sneezing.
- Do not spit anywhere. If you need to, spit directly into a can or handkerchief.
- Open windows and doors to allow fresh air to flow through your home. You can use an electric fan to blow the air from inside your house to the outside.
- Avoid meeting new people inside your home; meet them outside.
- You do not need to eat a special diet or use separate eating utensils or household items, such as cooking pots.
- Having sexual relations, kissing, sharing cutlery and clothes, etc. do not spread TB.

What are the rights of DR-TB patients and what are their responsibilities?

The patients' charter for tuberculosis care

- The rights of patients include receiving information, and being diagnosed and treated with respect; patients' responsibilities are mainly to take the treatment regularly, attend follow-up examinations and keep from spreading DR-TB to others in the community.

Do you know what support services are available during and after treatment to help you cope with your illness and treatment?

Support services are essential for ensuring that patients adhere to the treatment regimen and that it is completed successfully. Inform patients about the services or support options (if any) in your DR-TB management centre, such as:

- social support for MDR-TB management
- information support for MDR-TB treatment
- emotional support
- material support
- companionship support.

ASK THE PATIENT QUESTIONS SUCH AS

THEN GIVE RELEVANT MESSAGES

How many people live with you? What are their ages?
Does anyone else in your household have a cough?

Tracing close contacts

Say something like the following:

- Everyone who lives in the same place as you and people with whom you work closely will be interviewed to see if they have any symptoms of TB. All those who are younger than 5 years, and anyone who has a cough must be examined for TB and DR-TB. This examination may include a physical exam, sputum collection and possibly a chest X-ray and a type of skin testing called PPD (tuberculin testing) for children.

What are the next steps?

What to expect; what to do next

Say something like the following:

- You are ready to begin treatment. You may need to stay in hospital for a time or limit your activities and contacts with other people while your laboratory tests show that you are still likely to spread the disease.

If the patient is not admitted on the day you see him or her, make sure that the patient knows exactly where and when to go for the next treatment; say for example, "Come back here tomorrow before the DR-TB management centre closes at (insert time)." Ask questions to ensure that this will be possible and that the patient is committed to returning.

Remind the patient to bring close contacts aged 5 years and younger and all close contacts who have had a cough lasting more than 2 weeks for DR-TB screening.

Confirm that the patient agrees to undertake treatment for DR-TB, which requires DOT 6 (or 7) days per week for 20 months (or possibly longer), monthly follow-up examinations, and monthly monitoring visits with the physician at the DR-TB management centre.

Review: ask checking questions to ensure that the patient remembers important messages and knows what to do next. Reinforce earlier messages, or give more information as needed.



Now do Exercise B – role-play

When you have reached this point in the module, you are ready to do Exercise B, a role-play. Turn to the relevant pages in the exercise section of this module and follow the instructions; wait for additional instructions from your facilitator.

5. Provide information about the medicines used to treat DR-TB

Once the patient's treatment regimen has been discussed and decided, and the initial information about DR-TB has been given to the patient, inform the patient about the specific medicines that he or she will be taking.

A flipchart or other patient education tool may be used during this meeting if one is available. A flipchart has information for the patient on one side; on the other side are important messages that the health worker should communicate, such as information about side-effects. Flipcharts can help both the patient and the health worker. Ideally, they should contain drawings or photographs so that the patient not only listens but also sees images to help him or her remember the messages. It is useful for patients to know what to expect and to be told which of the side-effects warrant medical consultation.

Provide information only on the medicines that the patient will be taking. Providing too much information will not be helpful, and may confuse the patient.

The next pages present a brief *Guide to providing information about anti-TB medicines*. Your programme may already have educational tools on anti-TB medicines; if not, you can use this guide as a basis for developing your own tools.

Guide to providing information about anti-TB medicines

This guide presents basic information on the different medicines used to treat DR-TB. You can use it as a reference to remind you of the important messages to deliver to each patient. As isoniazid and rifampicin will not be used in confirmed DR-TB patients, they are excluded from this section.

Throughout the meeting: demonstrate a caring, respectful attitude. Praise and encourage the patient. Speak clearly and simply. Encourage the patient to ask questions.

MEDICINE (GROUPS 1–4)	IMPORTANT INFORMATION
Z: pyrazinamide (group 1)	<ul style="list-style-type: none"> • Common side-effects are mild; they include nausea and vomiting, abdominal pain, body ache, joint pain, and having big pimples on the face and the body; these effects usually occur only during the first few weeks of treatment; if they persist, the patient should consult the doctor immediately. • Advise patients to consult the doctor right away if their skin turns yellow.
E: ethambutol (group 1)	<ul style="list-style-type: none"> • Common side-effects are mild; they include abdominal pain, nausea, vomiting and headache; they sometimes occur during the first few weeks of treatment. • Advise patients to consult the doctor right away if there is blurring of vision and signs of colour blindness, especially to red and green.
Am: amikacin Cm: capreomycin Km: kanamycin S: streptomycin (group 2)	<ul style="list-style-type: none"> • These medicines are given as injections. • The injection is given daily for at least 8 months and is a very important part of treatment. • Rotation of injection sites is advised to avoid local discomfort; if patients have pain, they should place a warm compress on the area. • if there is bleeding after injection (this does not happen often), apply pressure to the injection site. • Advise patients to inform the doctor immediately if any of the following symptoms occur: swelling, pain and redness in the injection area, ringing in the ears, dizziness, vertigo, deafness, skin rash, problems in urinating or muscle weakness.

MEDICINE	IMPORTANT INFORMATION
<p>Lfx: levofloxacin Mfx: moxifloxacin Ofx: ofloxacin Gfx: gatifloxacin (group 3)</p>	<ul style="list-style-type: none"> • Common side-effects include difficulty in sleeping, abdominal pain, decreased appetite, headache and dizziness. • Special precaution: advise patients to avoid taking medicines or food containing milk, aluminium, magnesium or zinc within 2–3 hours of any of these medicines. • Advise patients to drink lots of water and limit exposure to sunlight by using an umbrella, sunglasses and wearing long-sleeved clothing. • Although gatifloxacin is similar to moxifloxacin in its efficacy against TB, it is associated with serious hypo/hyperglycaemia and new-onset diabetes, and its use is not recommended.
<p>Eto: ethionamide Pto: prothionamide (group 4)</p>	<ul style="list-style-type: none"> • Common side-effects include dizziness, vomiting, abdominal pain, diarrhoea, sensitivity to light, hypersalivation and metallic taste in the mouth. • Eating candy may help to decrease the unpleasant taste. • Patients may become sensitive to sunlight and other sources of ultraviolet light; patients should limit exposure to sunlight; if this cannot be avoided, patients should wear sunglasses, and use an umbrella. • Because this medicine may cause dizziness, patients should avoid driving a vehicle or operating machinery that requires alertness and attention.
<p>Cs: cycloserine (group 4)</p>	<ul style="list-style-type: none"> • Patients should inform the doctor immediately if they experience any of the following symptoms: dizziness, headache, chills, a decrease in mental ability or ability to speak, numbness of the feet and hands, nervousness, confusion, hearing voices that others cannot hear, difficulty in sleeping or feeling depressed. • Recommend that patients inform the doctor of any side-effects. • Because this medicine may cause dizziness, patients should avoid driving a vehicle or operating machinery that requires alertness and attention. • Patients may be given vitamin B6 to lessen the side-effects.
<p>PAS: para-amino salicylic acid (group 4)</p>	<ul style="list-style-type: none"> • To increase absorption, mix PAS granules with an acidic juice, such as orange, pineapple or mango; do not use water, soft drinks or iced tea. • Common side-effects include vomiting, abdominal pain and diarrhoea. • If a patient's symptoms persist, he or she should consult the doctor immediately. • If the patient has signs of dehydration, he or she may need oral rehydration or the doctor may administer fluids intravenously. • It is normal for patients to see granules in their faeces.

6. Continue to provide information throughout treatment at subsequent meetings

After the initial meetings with the DR-TB patient, continue to give appropriate information about the disease during daily treatment. Physicians will also answer the patient's questions and give information during the monthly monitoring visits. Remember to use good communication skills by asking questions, showing a caring attitude, praising and encouraging the patient, and using simple language.

Choose a few appropriate messages to reinforce. Do not provide too much information at one visit. During the first several weeks of treatment, you may need to reinforce messages about the disease and how it spreads. You may need to remind the patient to bring family members, close friends or people with whom they work closely for testing. It is also important to provide information about side-effects early in the treatment process. In order to convince the patient to continue with treatment, you may need to reassure him or her that side-effects usually go away in a few weeks.

As treatment continues, you will need to explain the reasons for follow-up sputum examinations and, after some months, the process of decentralization. As the patient feels better, you may need to emphasize the importance of continuing treatment and the dangers of stopping. If a patient misses a day of treatment, or appears discouraged, ask questions to find out why. Offer encouragement and help to solve problems as needed.

Give the following information as needed throughout treatment.

Side-effects of medicines (if reported or observed)

Patients should be informed about the possible side-effects they might experience, and what they should do if they have them.

Ask the patient, "How are you feeling?" or another general question, such as, "Have you had any problems after taking the medicines?" Then listen to the patient's answers, and look carefully at the patient to see whether you observe any signs of side-effects. Screen patients regularly for symptoms of common side-effects: rashes, gastrointestinal symptoms (nausea, vomiting, diarrhoea), psychiatric symptoms (psychosis, depression, anxiety, suicidal thoughts), jaundice, ototoxicity, peripheral neuropathy and symptoms of electrolyte wasting (muscle cramping, palpitations).

Patients who experience side-effects may be scared, may feel physically worse (for example, nauseated) and may want to discontinue the anti-TB treatment. Patients are more likely to be fearful or anxious about a side-effect if they do not understand why it is happening. Discuss the possible reasons for the side-effects and what steps can be taken to try to alleviate them. In general, treat the side-effects to the extent possible (with ancillary medicines or other measures to relieve symptoms), and encourage the patient to tolerate these effects until they resolve. (See section 6 in Module C for additional information.)

Informing patients that side-effects occur most frequently during the early months of treatment and then diminish with time may reassure them. Educate the patient about the side-effects, and encourage the patient to continue treatment. Explain to the patient that although the side-effects of the medicines may be difficult to tolerate, they are generally less severe than stopping treatment and continuing to be sick. Also explain that although most patients experience some kind of side-effects, these generally do not last more than a few weeks and will probably lessen in intensity or go away.

Changes in regimen

Describe the type and colour of the medicine(s), and the number of pills that will be added to the patient's treatment, and explain which medicine(s) will be stopped. Tell the patient how long the medicines must be taken.

Importance of continuing treatment and danger of irregular treatment

Emphasize the importance of continuing treatment. You may want to say the following:

- To be cured, you must take all of the medicines for the length of time that your doctor recommends. Even after you begin to feel better, you must continue taking the medicine for the entire length of time. DR-TB takes much longer to cure than ordinary TB, and although you may feel fine, stopping the treatment now could make it more difficult to be cured later because the TB germs will not be killed by the medicines that you have already been treated with. Taking only some of the medicines, or not taking them on the proper schedule is dangerous and will make it harder to cure you. If the TB germs are not killed by the medicines, you may not be cured and you may die. Also, if you do not take all of the medicines, you will continue to spread DR-TB to your friends and family.

If the patient complains that there are “too many pills” or that “treatment is too long”, explain that as TB is caused by a strong germ, many medicines are needed to get rid of it completely.

Very important

Patients should be strongly discouraged from travelling to avoid interrupting treatment. If travel cannot be avoided, the patient should inform the staff so treatment can be arranged at another facility or through a trained community supporter. If this is not possible, any days of treatment missed will be considered missed doses, and the patient will have to take treatment for longer.

Frequency and importance of required sputum examinations and monthly monitoring visits with the physician

As the time for each monthly sputum examination approaches, explain the need for the examination. You may want to say the following:

- Every month during DR-TB treatment, you will be required to cough up sputum and collect it for testing. As TB germs cannot be seen with the naked eye, a laboratory technician must examine the sample using a microscope. The technician will see if there are TB germs. The sample will then be sent for another test called a culture. The culture allows the laboratory technician to see if the TB germs are alive and growing. The best way to tell if treatment is helping you improve as expected is if the culture is negative – that is, if the germs are not growing.
- Every month a sample will be examined. There should be no TB germs growing in the culture, or fewer TB germs than in the last test. If after the first 4 months there are still TB germs growing in the culture, we will need to do further testing to make sure that the medicines you are taking are the ones that are most effective in killing the TB germs. If TB germs are still seen by the fourth month of treatment, your treatment may be changed.
- Once there are no more TB germs in your sputum and the medicine is not causing you any problems, you will be ready to continue treatment at a local health facility that is more convenient for you. This is called decentralization. As long as there are no problems with the treatment, and you continue to come in for treatment, you will be able to continue to receive the medicines at your local health facility.

The next pages are a guide to *Providing information to patients continuing treatment for DR-TB*. Remember to practise good communication skills at every visit, to be alert to any side-effects reported and to respond appropriately.

Guide to providing information to patients continuing treatment for DR-TB

Use good communication skills at every visit. At different points during treatment, discuss the messages that are most relevant at the time. Choose a few appropriate messages to reinforce or to teach. Do not try to teach too much at one visit.

At every visit: demonstrate a caring, respectful attitude. Praise and encourage the patient. Speak clearly and simply. Encourage the patient to ask questions.

BE ALERT TO SIDE-EFFECTS

Ask general questions to identify side-effects:

- How are you feeling?
- Have you had any problems?

Listen and look for common adverse effects:

- anorexia
- nausea or vomiting
- diarrhoea
- joint pain
- dizziness or vertigo
- hearing disturbances
- headache
- sleep disturbance
- dehydration
- abdominal pain.

RESPOND AS NECESSARY

For mild side-effects, give reassurance and advice

- If the patient has loss of appetite, nausea or abdominal pain, advise the patient to take the medicines with food.
- If the patient is anorexic, provide an appetite stimulant.
- If the patient has arthralgia, flu-like syndrome, headache or musculoskeletal pain, advise the patient to take (or provide the patient with) pain reliever (paracetamol, non-steroidal anti-inflammatory drugs [NSAIDs]).
- If the patient has cutaneous reactions or insomnia, advise the patient to take (or provide the patient with) antihistamines..
- If you notice a change in behaviour (for example, talkativeness or irritability) or peripheral neuropathy, advise the patient to take (or provide the patient with) pyridoxine.
- If the patient has pain at the injection site, massage the site with a warm cloth and switch sites.

(See Annex B for a list of mild side-effects and their suggested management.)

For moderate or severe side-effects, refer the patient immediately to the physician at the DR-TB management centre. *(See Annex C for a list of moderate-to-severe side-effects).*

As needed, remind the patient of one or more relevant messages

If patient is unfamiliar with the medicines or a change occurs in the regimen

- Describe the type and colour of the medicine, and the number of pills that will be added to the patient's regimen.
- Describe how for long the medicines should be taken.

(See the guide to anti-TB medicines in section 5 of this module.)

If the patient feels better and complains about continuing treatment

You may say something like the following:

- To be cured, you must take all of the medicines for the length of time that your doctor recommends. Even after you begin to feel better, you must continue taking the medicines for the entire length of time. DR-TB takes much longer to cure than ordinary TB, and although you may feel fine, stopping the treatment now could make it more difficult to be cured later because the TB germs will not be killed by the medicines that you have already been treated with. Taking only some of the medicines, or not taking them on the proper schedule is dangerous and will make it harder to cure you. If the TB germs are not killed by the medicines, you may not be cured and you may die. Also, if you do not take all of the medicines, you will continue to spread DR-TB to your friends and family.

If the patient is be planning to travel or move

You may want to say the following:

- During treatment, it would be helpful if you would avoid travelling, and I would encourage you to avoid interrupting your treatment. However, if you have to travel, please let us know, so that we can try to help you continue treatment while you are away. If we cannot make other arrangements for treatment then any doses that you miss will need to be added at the end of your treatment. It is important that you take every dose.

Absences of more than 2 weeks may require reconsideration of treatment and other special measures.

If the patient must be referred or hospitalized, explain that it is necessary to continue DR-TB treatment while receiving referral care. If admission is necessary, confine patients in hospitals that have links to a DR-TB management centre and health staff trained to provide DOT. When the patient is discharged from the hospital, the patient should return to the DR-TB management centre to continue treatment.

Every month during treatment

Explain the need for the sputum examination and monthly monitoring visit

At the beginning of treatment

You may say something like the following:

- Every month during DR-TB treatment, you will be required to cough up sputum and collect it for testing. As TB germs cannot be seen with the naked eye, a laboratory technician must examine the sample using a microscope. The technician will see if there are TB germs. The sample will then be sent for another test called a culture. The culture allows the laboratory technician to see if the TB germs are growing and reproducing. The best way to tell if treatment is helping you improve as expected is if the culture is negative – that is, if the germs are not growing.
- Every month the sample will be examined. There should be no TB germs growing in the culture, or fewer TB germs than in the last test. If after the first 4 months, there are still TB germs growing in the culture, we will need to do further testing to make sure that the medicines you are taking are the ones that are most effective in killing the TB germs that are causing your illness. If TB germs are still seen by the fourth month of treatment, your treatment may be changed.
- Once there are no more TB germs in your sputum and the medicines are not causing you any problems, you will be ready to continue treatment at a local facility that is more convenient for you. This is called decentralization. As long as there are no problems with the treatment, and you continue to come in for treatment, you will be able to continue receiving the medicines at your local health facility.
- At a minimum, you will come to the DR-TB management centre each month to see a physician for an examination so that the physician can monitor your progress.

Review: ask checking questions to ensure that the patient remembers important messages and knows what to do next. Reinforce earlier messages, or give more information as needed.



Now do Exercise C – written exercise

When you have reached this point in the module, you are ready to do Exercise C. Turn to relevant pages in the exercise section of this module and follow the instructions.

7. Provide information about the decentralization process

All DR-TB patients are generally diagnosed and enrolled in treatment at DR-TB management centres or at local health centres (depending on country policies). For patients starting

treatment at a DR-TB management centre, once they have been on treatment, they may be eligible to be decentralized. **Decentralization** means that a patient will be referred to a local facility nearer to home to continue treatment. When a patient is eligible for decentralization, the following points should be discussed.

What decentralization means

Explain to the patient briefly what decentralization means by saying:

- Congratulations! This is the first step along the road to being cured. You will continue to receive treatment for DR-TB but the treatment can be given closer to your home, so you can live at home.

The value and benefits of receiving DR-TB services at the local facility

Describe to the patient how the DR-TB management centre and the local health facility will coordinate to ensure that treatment will be convenient by saying something like the following:

- The local facility will be easier for you to get to than the DR-TB management centre because it is nearer to your home. A local facility is a smaller facility with staff that has been trained to continue your treatment. Although you will be treated at the local facility, you will still have monthly sputum examinations. You will come back to this DR-TB management centre for monthly visits with the physician. If you have any problems or need specialized services, the local facility can send you back to this DR-TB management centre at any time so that we can help care for you.

The different responsibilities of the local facility and the patient

Describe the responsibilities of the local facility and the patient by saying something like the following:

- Staff at the local facility will be responsible for providing treatment to you as well as maintaining good records of your treatment. If you have side-effects from the medicines you are taking, or you do not feel well, you must tell the staff at the local facility so that they can help you quickly and send you for specialized care if necessary.
- You must keep your copy of the *Second-line TB treatment card* and take it with you every day that you have treatment; the staff at the local facility will record when you receive treatment. Bring your card to the DR-TB management centre when you return for your monthly visit with the physician at the DR-TB management centre.
- You must continue to collect sputum for monthly examinations. You must come back to this DR-TB management centre every month to have a visit with the physician; the physician will give you a physical examination and check that your treatment is going well.

The patient's feelings and thoughts about the decentralization plan

Many patients prefer to receive treatment in facilities near their place of residence. However, there are patients who may feel attached and comfortable going to the DR-TB management centre for treatment. If it is easy for them to get to the DR-TB management centre, they may

continue treatment there as outpatients. Take time to listen to the patient's thoughts and feelings, and try to respond to all queries and solve the patient's problems.

If necessary, identify a community-based treatment supporter

DOT will continue 6 days a week once treatment has been decentralized. If the local health facility cannot supervise the patient for all 6 days during the week, the patient will need a community-based DR-TB treatment supporter to give DOT on the days that the facility cannot. Plans must be worked out before the patient's treatment is decentralized. Talk to the patient about getting to the facility 6 days a week for treatment. Explain:

- When your treatment is decentralized to (*provide the name of the facility*), someone must observe you taking your medicines 6 days a week, as has happened here.

Discuss with the patient:

- where the patient lives and where they work, whom the patient sees each day, whether transport is available, and whether the family is supportive of treatment;
- possible community-based treatment supporters who would be convenient and acceptable, taking into account the supporter's proximity to the patient, relationship to the patient (if any) and whether the supporter is already supervising treatment for other patients; where and when the patient could meet regularly with a treatment supporter. During the intensive phase when a patient needs to receive an injectable drug, the patient may be required to visit a local health facility at least for the injections. In some countries, a community nurse trained to provide injections may also do so at a location convenient for the patient.

On the next page is a *Guide to providing information to DR-TB patients about treatment decentralization*. The process of treatment decentralization is also discussed in Module E.

Guide to providing information to DR-TB patients about treatment decentralization

When treatment is to be decentralized, patients may feel hesitant about leaving the DR-TB management centre as they have been attending for so long, or they may be pleased to be leaving. Congratulate the patient; explain the situation and the next steps in the treatment process. Use good communication skills. Make sure you congratulate the patient who has successfully completed the first few months of treatment. The patient should feel pleased that treatment is progressing well and that the treatment can be taken closer to home.

At every visit: demonstrate a caring, respectful attitude. Praise and encourage the patient. Speak clearly and simply. Encourage the patient to ask questions.

ASK THE PATIENT QUESTIONS SUCH AS

THEN GIVE RELEVANT MESSAGES

How do you feel now that your tests show that you are unlikely to spread the disease?

Say something like the following:

Congratulations!

This is the first step along the road to being cured. You will continue to receive treatment for DR-TB but the treatment can be given closer to your home, so you can live at home.

Do you have any ideas about how decentralization may help you and your treatment?

Say something like the following:

The local facility will be easier for you to get to than the DR-TB management centre because it is nearer to your home. A local facility is a smaller facility with staff who have been trained to continue your treatment. Although you will be treated at the local facility, you will still have monthly sputum examinations. You will come back to this DR-TB management centre for monthly visits with the physician. If you have any problems or need specialized services, the local facility can send you back to this DR-TB management centre at any time so that we can help care for you.

What about the local facility's responsibilities to you?

Say something like the following:

Staff at the local facility will be responsible for providing treatment to you as well as maintaining good records of your treatment. If you have any side-effects from the medicines you are taking, or if you do not feel well, you must tell the staff at the local facility so that they can help you quickly and send you for specialized care if necessary.

You must keep your copy of the *Second-line TB treatment card* and take it with you every day that you have treatment; the staff at the local facility will record when you receive treatment. Bring your card to the DR-TB management centre when you return for your monthly visit with the physician at the DR-TB management centre.

You must continue to collect sputum for monthly examinations. You must come back to this DR-TB management centre every month to have a visit with the physician; the physician will give you a physical examination and check that your treatment is going well.

Do you have any questions? Is there anything that is not clear?

Say something like the following:

Do you have any questions or concerns about this process?

ASK THE PATIENT QUESTIONS SUCH AS

THEN GIVE RELEVANT MESSAGES

Will you have difficulty getting to the local health facility every day for treatment?
Do you know anyone who might be able to give you treatment on the days that you cannot make it to the facility?

Say something like the following:
When your treatment is decentralized to (*provide the name of the facility*) someone must observe you taking your medicines 6 days a week as has happened here.
If necessary, we can train someone in your community to provide treatment, and you can help us choose who to train. We will provide the medicines and supervise this person.
Discuss with the patient:

- where the patient lives and works, whom the patient sees each day, whether transport is available, and whether the family is supportive of treatment;
- possible community-based treatment supporters who would be convenient and acceptable, taking into account the supporter's proximity to the patient, relationship to the patient (if any) and whether the supporter is already supervising treatment for other patients;
- where and when the patient could meet regularly with a treatment supporter.

Review: ask checking questions to ensure that the patient remembers important messages and knows what to do next. Reinforce earlier messages or give more information as needed.

8. Provide information at the end of treatment

Before the last dose of treatment is given, you should applaud the patient's efforts and comfort him or her if the treatment has failed. In some centres, patients who have completed treatment successfully receive a certificate or are offered the opportunity to help other DR-TB patients who are having treatment. At the end of treatment, provide information about the following issues.

Provide information to patients whose outcome is cured or treatment completed

You may want to say something like the following:

- Congratulations! You have just finished a long and difficult treatment. I am very proud of the commitment and dedication you have shown over the past 20 months. You no longer have to take any medications. However, it is possible that the disease may come back. If you develop any symptoms of TB, such as a cough, back or chest pain, blood in your phlegm, or unexplained fever or weight loss, let us know immediately so that we can conduct the proper tests to see what the problem is. If anyone close to you, such as family members or other people in your community, has symptoms of TB, bring that person in; let the staff know that you had DR-TB so that they are aware that the person was in close contact with you while you had the disease.

Discuss the importance of a healthy lifestyle

Say something like the following:

- Leading a healthy lifestyle is always good but it is especially important after you have had a long treatment, such as the one for DR-TB. Exercising, eating healthy food, not smoking or

drinking, and getting enough rest will help you recover, combat other illnesses and reduce the risk of TB coming back. People with weak defences get sick from TB more often than healthy people. Now that you are cured, try to maintain a healthy lifestyle.

Give support to patients whose treatment has failed

Patients whose treatment with a standardized regimen has failed may have the opportunity to be treated with an individualized regimen. The review panel should assess the patient's case; the panel will know what is feasible and determine whether an individualized regimen is appropriate. If there is no possibility of adding additional medicines to the regimen, the review panel may decide to terminate the patient's treatment.

If this happens, initiate counselling and provide moral support from a psychologist or psychosocial services team before the treatment ends. Failing treatment can be devastating to a patient and must be handled with utmost caution. The patient may be left with a debilitating chronic disease and respiratory insufficiency, or may die. Medical care and supportive measures must continue so that the patient does not feel abandoned. Also, provide information about preventing further transmission.

Say something like the following:

- You have been through so many difficulties with your medicines. Unfortunately, they do not seem to be helping you. It is time that you take a break from your treatment. We will continue to provide medical care and support. You are still infectious, so it is best that you avoid crowded, enclosed areas, and avoid sleeping in the same room with other people, if possible. Cover your mouth and nose when you cough or sneeze. Open the windows in your room to allow air to flow out. If possible, use an electric fan to direct the air outside.

The guide on [page D-48](#) summarizes how to provide the information discussed in this section when the DR-TB patient has completed treatment.

9. Palliative and end-of-life care for patients in whom all the possibilities of treatment have failed

WHO defines palliative care as an “approach that improves the quality of life of patients and their families facing problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual”.² While high MDR-TB cure rates are reported by some programmes, in many others, MDR-TB remains a life-threatening condition with high mortality and poor cure rates. There is also considerable suffering associated with MDR-TB illness and its treatment. These burdens add to the possibility that TB patients will not be able to adhere to treatment and, as a result, treatment fails to cure them. Thus, the need for palliative and end-of-life care is increasingly being recognized as an important part of the continuum of care for all MDR-TB patients.

All measures to relieve the patient of suffering caused by the disease and its treatment begins at the time of diagnosis, and continues regardless of whether or not the patient is expected to be cured or fail treatment. Thus, all the measures mentioned in this chapter are appropriate for

patients in all stages of MDR-TB disease, especially those who are less likely to be cured as well as those who are nearing the end of life. Nonetheless, in patients with DR-TB who have no anti-TB regimen options, the only realistic choice is support in the form of palliative/end-of-life care and putting in place proper infection control measures.

There is a moral obligation to continue providing care through to the end of life to those in whom treatment alternatives have been exhausted. Effective support at the end of life requires a broad multidisciplinary approach that includes the family and makes use of available community resources. It can be successfully implemented even if resources are limited. It can be provided in tertiary care facilities, in hospices, in community health centres and even in the patient's home. Proper collaboration and coordination of the national TB control programme (NTP) with other units in the health ministry responsible for cancer or HIV care, and with nongovernmental organizations working in palliative care can facilitate access to services for MDR-TB patients that otherwise the NTP is not set up to provide. However, the primary responsibility for the care of the patient should remain with the NTP, especially when the patient remains a source of infection.

Guide to providing information at the end of DR-TB treatment

This is the last time you will be providing information to the patient. Use good communication skills. Make sure you congratulate the patient who has been cured or successfully completed treatment. These patients should feel happy.

Demonstrate a caring, respectful attitude. Praise and encourage the patient. Speak clearly and simply. Encourage the patient to ask questions.

ASK THE PATIENT QUESTIONS THEN GIVE RELEVANT MESSAGES OR DISCUSS THE FOLLOWING

How do you feel about finishing treatment?

Congratulate patients who have been cured or have completed treatment.

Say something like the following:

Congratulations! You have just finished a long and difficult course of treatment. I am very proud of the commitment and dedication you have shown over the past 20 months. You no longer have to take any medications.

However, it is possible that the disease may come back. If you develop any symptoms of TB, such as a cough, back or chest pain, blood in the phlegm, or unexplained fever or weight loss, let us know immediately so we can conduct the proper tests to see what the problem is.

If anyone close to you, such as family members or other people in your community, has symptoms, bring that person in; let the staff know that you had DR-TB so that they are aware that the person was in close contact with you when you had the disease.

ASK THE PATIENT QUESTIONS THEN GIVE RELEVANT MESSAGES OR DISCUSS THE FOLLOWING

How will you keep your body healthy?

Say something like the following:

Leading a healthy lifestyle is always good but it is especially important after you have had a long treatment, such as the treatment for DR-TB. Exercising regularly, eating healthy food, not smoking or drinking, and getting enough rest will help you recover, combat other illnesses and reduce the risk of TB coming back. People with weak defences get sick from TB more often than healthy people. Now that you are cured, try to maintain a healthy lifestyle.

Give support to patients whose outcome is treatment failure.

Say something like the following:

You have been through so many difficulties with your medicines. Unfortunately, they do not seem to be helping you. It is time that you take a break from your treatment. We will continue to provide medical care and support.

Because you may still spread the disease, it would be best if you avoid crowded, enclosed areas, and avoid sleeping in the same room with other people, if possible. Cover your mouth and nose when you cough or sneeze. Open the windows in your room to allow the air to flow out. If possible, use an electric fan to direct the air outside.



Now do Exercise D – written exercise

When you have reached this point in the module, you are ready to do Exercise D. Turn to relevant pages in the exercise section of this module and follow the instructions.

Summary

- Good communication is needed to provide information about DR-TB and its treatment, and to encourage patients to continue treatment without interruption. Use the following communication skills when informing patients about DR-TB:
 - Ask questions and listen.
 - Demonstrate a caring, respectful attitude.
 - Praise and encourage the patient.
 - Speak clearly and simply.
 - Encourage the patient to ask questions.
 - Ask checking questions (that is, use open-ended questions to check understanding).
- Asking questions and listening carefully to the patient's responses are important in communicating effectively with the patient. Different patients may need different information. Rather than giving everyone exactly the same messages, first ask questions to determine what each patient already knows or believes about MDR-TB.
- During the first meeting with patients presumed to have DR-TB, inform them about the possible diagnosis and the next steps in the diagnostic process, and discuss the following important topics (*see* section 2):
 - the possible diagnosis of DR-TB;
 - the diagnostic or baseline tests to be done (sputum-smear microscopy, Xpert MTB/RIF, culture, DST);
 - timelines for receiving the test results;
 - next steps in the process;
 - what treatment for DR-TB is like;
 - how to stop spreading TB or DR-TB to family and friends while waiting for test results.
- Discuss HIV and TB with all cases (*see* section 3).
- Once the review panel has authorized a DR-TB regimen for the patient, discuss the following topics when the patient is enrolled for treatment (*see* section 4):
 - what DR-TB is
 - the difference between treatment for drug-susceptible TB and DR-TB
 - why the patient has DR-TB
 - the DR-TB regimen
 - the necessity of DOT
 - hospitalization (if needed)
 - preventing the spread of DR-TB
 - patients' rights and responsibilities
 - support services available at the DR-TB management centre
 - tracing close contacts
 - what to expect and what to do next.
- Before starting treatment, confirm that the patient agrees to undertake treatment for DR-TB, which requires DOT 6 (or 7) days per week for at least 20 months, monthly

follow-up sputum examinations, and monthly monitoring visits with the physician at the DR-TB management centre.

- Provide information about the specific medicines that the patient will be taking (*see* section 5).
- At subsequent meetings with the patient, reinforce previous messages and continue to provide relevant information on the following topics (*see* section 6):
 - side-effects of the medicines (if reported or observed);
 - changes in regimen;
 - importance of continuing treatment and danger of irregular treatment;
 - frequency and importance of required sputum examinations and monthly monitoring visits to the physician.
- When a patient is eligible for decentralization, the following points should be discussed (*see* section 7):
 - what decentralization means;
 - the value and benefits of receiving DR-TB services at a local facility;
 - the responsibilities of the local facility and of the patient;
 - the patient's feelings and thoughts about the decentralization plan;
 - if necessary, the identification of a community-based treatment supporter.
- Before the last dose of treatment is given, you should congratulate the patient for his or her efforts, and provide support if the treatment failed. Be sure to congratulate the patient who is cured or who has completed treatment, and offer support to patients whose treatment has failed. Also provide information about the following (*see* section 8):
 - what to do if TB symptoms return
 - the importance of maintaining a healthy lifestyle.

Self-assessment questions

Answer the self-assessment questions below to check what you have learned. Then compare your answers to those on pages D-54–D-55.

1. List six communication skills to use when informing patients about DR-TB:
–
–
–
–
–
–

2. Write two questions that could be asked in order to determine a patient’s knowledge about DR-TB:
–
–

3. A health worker has just explained the following to Mrs Saras, a DR-TB patient who will begin treatment as an outpatient at the Balboa DR-TB management centre:
“You will need to come to the DR-TB management centre to take these anti-TB medicines every day except Sundays. You must continue this until the intensive phase is over (this will last at least 8 months) to make sure that the treatment is working well. The centre is open from 09:00 a.m. until 17:00 p.m. Monday to Saturday.”

Write two checking questions that the health worker might ask this patient:

–
–

4. When you are talking with a patient who is presumed to have DR-TB about the diagnostic process, she interrupts and exclaims, “I don’t want my children to get this disease! Do I have to send them away? I don’t have anywhere to send them.”

Write your response to her here:

5. A health worker has recommended to Mr Pakas, a patient with DR-TB, that he should be tested for HIV today. Mr Pakas is hesitating. What are some of the benefits of knowing one’s HIV status that the health worker could explain? (List two or three benefits.)

–
–

6. Tick the information that should be discussed with the patient once the review panel has approved DR-TB treatment and the patient is enrolling in treatment: (*You may tick more than one.*)

- | | |
|---|--|
| <input type="checkbox"/> why the patient has DR-TB | <input type="checkbox"/> the DR-TB regimen |
| <input type="checkbox"/> preventing the spread of DR-TB | <input type="checkbox"/> what decentralization means |
| <input type="checkbox"/> necessity of directly observed treatment | <input type="checkbox"/> how the patient can keep his or her body healthy |
| <input type="checkbox"/> timelines for receiving test results | <input type="checkbox"/> frequency of required follow-up sputum examinations |
| <input type="checkbox"/> tracing close contacts | |

7. When a patient is decentralized, it means that treatment has been progressing _____ and the patient is no longer _____. The patient will continue to receive treatment for DR-TB _____ days a week but the treatment can be given closer to the patient's _____. Even after decentralization, the patient will return to the DR-TB management centre every _____ for a monitoring visit with a physician.

8. List two things you would say to a patient who feels better and does not want to continue treatment for DR-TB:

-
-

Now compare your answers with those on the next page.

Answers to self-assessment questions

If you had difficulty in answering any question, turn back and study the section indicated. If you do not understand something, discuss it with a facilitator.

1. *Six communication skills taught in this module are:*
 - *ask questions and listen*
 - *demonstrate a respectful, caring attitude*
 - *praise and encourage the patient*
 - *speak clearly and simply*
 - *encourage the patient to ask questions*
 - *ask checking questions.*

(See section 1.)

2. *You should have written two questions similar to the following:*
 - *What do you understand about your illness (drug-resistant tuberculosis, or DR-TB)?*
 - *How do you think it is different from TB?*
 - *What do you think causes DR-TB? How is it spread?*
 - *Have you ever known anyone who had DR-TB? What happened to that person?*
 - *What have you heard about DR-TB being cured?*

(See section 1.1.)

3. *There are many checking questions that could be asked. Questions should be open-ended, beginning with words like “who, what, when, where, why”. Examples of appropriate checking questions are:*
 - *How often will you return to take your anti-TB medicines?*
 - *What time will you come?*
 - *How long will you need to continue treatment?*

(See section 1.6.)

4. *Your answer may be worded differently but should include most of the same points as the following:*

“There are several important things that you can do to keep from spreading the germs to your children and other family members and friends. TB can spread easily if you spend time in crowded conditions with others.”

“Always cover your mouth and nose when you sneeze or cough. If possible, use a mask till you are declared non-infectious. Open windows and doors to allow fresh air to flow through your home. Put an electric fan at a window to pull the air from indoors to the outdoors. Avoid meeting people inside your home; meet them outdoors. Whenever you wish to be with your children, spend time outdoors as much as possible.”

“When you have started treatment for TB or DR-TB, take all your treatment every day (6 days a week) so that you will no longer be likely to infect others; this is the first step towards being cured.”

“There is no need to separate your eating utensils or household items from the rest of your family.”

(See sections 2 and 4.)

5. *Benefits of knowing the HIV status include:*

- it helps during diagnosis because HIV-positive people who have TB may have different symptoms from people who are not HIV-positive;*
- it guides decisions on treatment, such as whether ART and CPT are necessary;*
- it is important for offering appropriate counselling and advice on TB and HIV in terms of prognosis and side-effects.*

(See section 3.)

6. *The following items should have been ticked:*

- why the patient has DR-TB*
- preventing the spread of DR-TB*
- the DR-TB regimen*
- necessity of directly observed treatment*
- tracing close contacts*

(See section 4.)

7. *When a patient is decentralized, it means that treatment has been progressing **well** and the patient is no longer **contagious** . The patient will continue to receive treatment for MDR-TB **6** days a week but the treatment can be given closer to the patient’s **home or work**. Even after decentralization the patient will always come to the DR-TB management centre every **_ month_** for a monitoring visit with a physician.*

(See section 7.)

8. *The answers may include some of the following information:*

- To be cured, you must take all of the recommended medicines together, for the recommended duration of treatment.*
- Even after you begin to feel better, you must continue taking the medicines for the entire duration of treatment or the TB will become worse.*
- DR-TB takes much longer to cure than ordinary TB.*
- Although you may feel fine, stopping treatment could result in increased drug resistance, and that means you are at risk of spreading the disease to friends and family members, and possibly dying.*

(See section 6.)

If you had difficulty answering any question, turn back and study the section indicated. If you do not understand something, discuss it with a facilitator.

References

1. TB CARE I. International standards for tuberculosis care, third edition. The Hague: TB CARE I; 2014. (http://www.who.int/tb/publications/ISTC_3rdEd.pdf?ua=1, accessed 15 October 2014).
2. Palliative care. Geneva: World Health Organization; 2012 (<http://www.who.int/cancer/palliative/en/>, accessed 28 March 2014).
3. The patients' charter for tuberculosis care: patients' rights and responsibilities. World Care Council; 2006. (<http://www.istcweb.org/documents/istccharter.pdf>, accessed 16 October 2014).



The End

Congratulations on finishing this module!

Exercises for Module D: Inform patients about DR-TB

Exercise A

Written exercise: Checking questions

For this exercise, you will practise using checking questions to make sure that patients understand the information being provided. For each of the following situations, read the case information and then provide two checking questions to ensure that the patient has understood the message.

1. During an initial interview with a patient who has just been diagnosed with DR-TB, the health worker gives the following information:

“Just like the treatment for ordinary TB, you will receive five kinds of medicine and one of them will be a daily injection. The number of tablets or capsules you take depends on how much you weigh. The treatment will last for approximately 20 months. Your physician will decide which medicines will work best for you and will tell you when the treatment will end. You will take medicines every day, except Sundays. A health worker will always watch as you take your medicines. You will need to be admitted to a hospital to begin treatment so that we can be sure that the medicines you are taking do not cause serious side-effects and you are getting better.”

Write two checking questions that the health worker might ask at the end of the visit to ensure that the patient understands:

—

—

2. A patient presumed to have DR-TB is talking with a health worker about preventing transmission to others in the household. The health worker emphasizes the following:

“During the initial phase of treatment, you may infect other people, so you need to limit how much contact you have with others, especially in enclosed areas such as your house. However, after a few weeks of regular treatment, you start to get better and may be able to go back to your usual activities. Most importantly, you must take all of your treatment every day so that you are less likely to infect other people; this is the first step to towards being cured. TB and DR-TB are transmitted in the same way: through the air. You should cover your mouth and nose when you cough or sneeze; use a mask or handkerchief. Do not spit anywhere. If you need to, spit directly into a can and dispose of it in a safe manner. In your home, open the windows and doors to allow fresh air to flow through. You can use an electric fan to blow the air from inside your house to the outside. If possible, sleep in a room by yourself until your doctor says that you are no longer likely to infect other people. There is no need to eat a special diet or to separate eating utensils or household items, such as cooking pots, clothes, etc. TB is not spread through sexual relations and kisses because DR-TB, just like TB, is transmitted only through the air.”

Write two checking questions that the health worker might ask at the end of the visit to ensure that the patient understands:

—

—

When you have finished this exercise, review your answers with a facilitator.



Then **GO BACK** to section 2 and work to the next stop sign.

Exercise B

Role-play: Initial patient information about DR-TB

For this exercise, your facilitator will divide you into groups to enact a role-play.

In the role-play, one person will act as the health worker, one as the patient and one as an observer. Then you will change roles and repeat the role-play. The role-play will be done three times so that each participant practises the role of the health worker.

Background

In this role-play, a 36-year-old patient, Mr Singh, has just been informed that he has been diagnosed with MDR-TB. His DST results show resistance to R and H. He can begin treatment at once.

Instructions for the health worker

In this role-play, your goal is to use good communication skills to provide relevant information on **treatment with second-line drugs and what it entails**. Mr Singh has been taking a retreatment regimen for 4 months and is still sputum positive. To ensure that you include all of the necessary information, use the *Guide to providing information to DR-TB patients being enrolled for treatment*.

Instructions for the patient

As the patient, you should respond realistically to the health worker. You may make up additional information that is consistent with the role, as needed. When the health worker explains to you what to do, ask questions if the instructions are not clear.

Instructions for the observer

Your task is to watch carefully during the role-play so that you can comment on what was done well and what could be improved. Refer to the *Guide to providing information to DR-TB patients being enrolled for treatment* as you observe. Mark the *Checklist for the observer* as the health worker asks questions and gives information. After the role-play, comment on what was done well and what could be improved.

At the end of the role-play, tell the health worker whether any steps were omitted. Comment on the steps done well and possible improvements. Your comments should be brief.

After the observer has commented, change roles and repeat the role-play described above. Repeating the role-play will help you become more familiar and comfortable with the steps. When all participants have practised the role of the health worker, the facilitator will lead a brief discussion.

Checklist for the observer

Patient information at enrolment for DR-TB treatment

USE OF GOOD COMMUNICATION SKILLS	OBSERVATION		REMARKS
	DONE	NOT DONE	
1. Ask questions and listen			
2. Demonstrate a caring, respectful and friendly attitude			
3. Praise and encourage the patient			
4. Speak clearly and simply			
5. Encourage the patient to ask questions			
6. Ask checking questions			
Messages			
1. Difference in treatment between DR-TB and TB			
2. Why the patient has DR-TB			
3. What the DR-TB regimen is			
4. Necessity of DOT			
5. Need for hospitalization			
6. Preventing the spread of DR-TB			
7. Rights and responsibilities of DR-TB patients			
8. Tracing close contacts			
9. What to expect and what to do next			

Tell a facilitator when you are ready for the group discussion.



When the group has finished this exercise, **GO BACK** to section 5, and continue reading until the next stop sign.

Exercise C

Written exercise: Problem-solving

In this exercise, you will suggest information that can be provided during some difficult situations. For each situation listed in the column on the left, briefly describe what you would say or do. Remember to demonstrate a caring attitude and provide only information that is relevant for the patient's problem or concern.

WHAT WOULD YOU SAY OR DO IF...?

BRIEFLY WRITE YOUR IDEAS BELOW

A patient wants to take the medicine unsupervised at home.

The patient has missed 1 day of treatment but reported the following day.

A patient says her husband, who has a cough, does not have time to be tested for TB.

A patient has DR-TB and HIV. He is resisting admission to hospital to start treatment because he says he does not feel that bad and must work.

A patient who has completed 5 months of DR-TB treatment seems angrier each day.

A patient has been on treatment for 3 weeks and has nausea and vomiting. She says she cannot stand it any more and wants to stop treatment.

When you have finished this exercise, review your answers with a facilitator.



When the group has finished this exercise, **GO BACK** to section 7, and continue reading until the next stop sign.

Exercise D

Written exercise: Preparing for decentralization

You have to make a decision on whether or not patients can be decentralized to a local health centre closer to their homes where they can continue their treatment.

List the indicators for treatment decentralization:

Write what you would tell a patient when she/he is ready for decentralization:

Exercise E

Group discussion: At the end of treatment

In this exercise, the group will discuss how the procedures described in this module can be carried out at your DR-TB management centre. Write answers to the questions below in preparation for the discussion.

In your country:

1. Do you have a conversation with patients at the end of their treatment?
2. If there is no conversation with patients, do you think it is important that this should be started?
3. What do you tell patients when their treatment outcome is either cured or treatment completed?
4. What do you tell patients whose treatment has failed?

When everyone is ready, there will be a group discussion on these questions.



GO BACK and read the *Summary* and work until the end of the module.

Annexes

Annex A: *The patients' charter for tuberculosis care* _____ D-68

Annex B: Mild side-effects of drugs used to treat DR-TB _____ D-71

Annex C: Moderate-to-severe side-effects of drugs used to treat DR-TB _____ D-72

Annex A: The patients' charter for tuberculosis care³

The patients' charter for tuberculosis care (The Charter) outlines the rights and responsibilities of people with tuberculosis. It empowers people with the disease and their communities through this knowledge. Initiated and developed by patients from around the world, *The Charter* makes the relationship with health-care providers a mutually beneficial one.

Patients' rights

You have the right to:

Care

The right to free and equitable access to tuberculosis care, from diagnosis through treatment completion, regardless of resources, race, gender, age, language, legal status, religious beliefs, sexual orientation, culture, or having another illness

The right to receive medical advice and treatment which fully meets the new *International Standards for Tuberculosis Care*, centering on patient needs, including those with multidrug-resistant tuberculosis (MDR-TB) or tuberculosis-human immunodeficiency virus (HIV) coinfections and preventative treatment for young children and others considered to be at high risk

The right to benefit from proactive health sector community outreach, education, and prevention campaigns as part of comprehensive care programs

Dignity

The right to be treated with respect and dignity, including the delivery of services without stigma, prejudice, or discrimination by health providers and authorities

The right to quality healthcare in a dignified environment, with moral support from family, friends, and the community

Information

The right to information about what healthcare services are available for tuberculosis and what responsibilities, engagements, and direct or indirect costs are involved

The right to receive a timely, concise, and clear description of the medical condition, with diagnosis, prognosis (an opinion as to the likely future course of the illness), and treatment proposed, with communication of common risks and appropriate alternatives

The right to know the names and dosages of any medication or intervention to be prescribed, its normal actions and potential side-effects, and its possible impact on other conditions or treatments

The right of access to medical information which relates to the patient's condition and treatment and to a copy of the medical record if requested by the patient or a person authorized by the patient

The right to meet, share experiences with peers and other patients and to voluntary counseling at any time from diagnosis through treatment completion

Choice

The right to a second medical opinion, with access to previous medical records

The right to accept or refuse surgical interventions if chemotherapy is possible and to be informed of the likely medical and statutory consequences within the context of a communicable disease

The right to choose whether or not to take part in research programs without compromising care

Confidence

The right to have personal privacy, dignity, religious beliefs, and culture respected

The right to have information relating to the medical condition kept confidential and released to other authorities contingent upon the patient's consent

Justice

The right to make a complaint through channels provided for this purpose by the health authority and to have any complaint dealt with promptly and fairly

The right to appeal to a higher authority if the above is not respected and to be informed in writing of the outcome

Organization

The right to join, or to establish, organizations of people with or affected by tuberculosis and to seek support for the development of these clubs and community-based associations through the health providers, authorities, and civil society

The right to participate as "stakeholders" in the development, implementation, monitoring, and evaluation of tuberculosis policies and programs with local, national, and international health authorities

Security

The right to job security after diagnosis or appropriate rehabilitation upon completion of treatment

The right to nutritional security or food supplements if needed to meet treatment requirements

Patients' Responsibilities

You have the responsibility to:

Share Information

The responsibility to provide the healthcare giver as much information as possible about present health, past illnesses, any allergies, and any other relevant details

The responsibility to provide information to the health provider about contacts with immediate family, friends, and others who may be vulnerable to tuberculosis or may have been infected by contact

Follow Treatment

The responsibility to follow the prescribed and agreed treatment plan and to conscientiously comply with the instructions given to protect the patient's health, and that of others

The responsibility to inform the health provider of any difficulties or problems with following treatment or if any part of the treatment is not clearly understood

Contribute to Community Health

The responsibility to contribute to community well-being by encouraging others to seek medical advice if they exhibit the symptoms of tuberculosis

The responsibility to show consideration for the rights of other patients and healthcare providers, understanding that this is the dignified basis and respectful foundation of the tuberculosis community

Show Solidarity

The moral responsibility of showing solidarity with other patients, marching together towards cure

The moral responsibility to share information and knowledge gained during treatment and to pass this expertise to others in the community, making empowerment contagious

The moral responsibility to join in efforts to make the community tuberculosis free

Annex B: Mild side-effects of drugs used to treat DR-TB

Medicines listed in **bold** type are more strongly associated with the side-effect.

SIDE EFFECT	SUSPECTED AGENTS	SUGGESTED MANAGEMENT
Anorexia	Z, Pto, Eto	Appetite stimulant (for example, pizotifen)
Arthralgia	Z	Non-steroidal anti-inflammatory drugs (NSAIDs); paracetamol; exercise
Change in behaviour (talkativeness, irritability)	Cs , Ofx	Haloperidol; pyridoxine 50 mg/250 mg of Cs, up to 200 mg/day maximum
Cutaneous reaction	H, Z, E, Pto, Eto, Cs, PAS, and other aminoglycosides	Antihistamines; hydrocortisone creams
Depression	Cs , H, Pto, Eto	Selective serotonin reuptake inhibitors (fluoxetine, sertraline); tricyclic antidepressants (amitriptyline)
Diarrhoea	PAS	Rehydration; loperamide
Excessive salivation	Eto, Pto	Ice chips; metoclopramide
Gastritis	PAS, Pto, Eto	Antacids (for example, calcium carbonate); H2 blockers; proton pump inhibitors
Gynaecomastia	Pto, Eto	Reassurance; surveillance
Headache	Pto, Eto	Non-steroidal anti-inflammatory drugs (NSAIDs); paracetamol; exercise
Insomnia	Ofx, Lfx, Mfx	Antihistamine; zolpidem
Metallic taste	Pto, Eto	Reassurance
Musculoskeletal pain	No specific medicine	Non-steroidal anti-inflammatory drugs (NSAIDs); paracetamol
Nausea and vomiting	Pto, Eto, PAS , H, Z, E	Rehydration; metoclopramide; divide dose (morning and afternoon) of medicine only if both doses can be supervised
Olfactory hallucination	Pto, Eto	Reassurance
Peripheral neuropathy	H, Cs , S, Km, Pto, Eto	Increase pyridoxine to maximum daily dose (200 mg/day); tricyclic antidepressants (for example, amitriptyline)
Pain at injection site	S, Km, Am , Cm	Cold compress
Photophobia	Pto, Eto	Reassurance
Vertigo or dizziness	S, Km , Cm, Pto, Eto	Betahistine; cinnarizine

Am, amikacin; Cm, capreomycin; Cs, cycloserine; E, ethambutol; Eto, ethionamide; H, isoniazid; Km, kanamycin; Lfx, levofloxacin; Mfx, moxifloxacin; Ofx, ofloxacin; PAS, para-aminosalicylic acid; Pto, prothionamide;; S, streptomycin; Z, pyrazinamide

Annex C: Moderate-to-severe side-effects of drugs used to treat DR-TB

Medicines listed in **bold** type are more strongly associated with the side-effect.

SIDE-EFFECT	SUSPECTED AGENTS	SUGGESTED MANAGEMENT
Acute renal failure	Km, Am, Cm	Discontinue medicine suspected of causing the effect; consider using Cm if an aminoglycoside had been the prior injectable agent in the regimen; consider dosing 2–3 times/ week if agent is essential to regimen and patient can tolerate (closely monitor creatinine concentrations); adjust doses of all anti-TB agents according to creatinine clearance.
Electrolyte abnormalities (decreased blood concentrations of potassium, magnesium and calcium)	Cm, Km, Am	Check electrolytes (K, Mg, Ca); replace electrolytes as needed.
Generalized hypersensitivity (Stevens–Johnson syndrome)	Any medicine	Withdraw the medicines and refer to specialist.
Hearing loss	Km, Am, Cm, Clr	Document hearing loss and compare with baseline audiometry if available; change parenteral treatment to Cm if appropriate (that is, no resistance is confirmed or suspected); increase frequency and lower dose, or both, of suspected agent if it can be done without compromising regimen; discontinue agent suspected of causing the effect if this can be done without compromising the regimen.
Haemolysis	R	Discontinue medicine and refer to specialist.
Hepatitis or jaundice	Z, Pto, Eto, PAS, E	Discontinue therapy pending resolution of hepatitis; eliminate other potential causes of hepatitis; consider suspending agent most likely to have caused side-effect permanently; reintroduce remaining agents, one at a time, using the most hepatotoxic agents first and monitoring liver function.
Hypothyroidism	PAS, Pto, Eto	Initiate thyroxine therapy.

SIDE-EFFECT	SUSPECTED AGENTS	SUGGESTED MANAGEMENT
Intractable vomiting	Pto, Eto, PAS, E, Z	Assess for dehydration and initiate rehydration if indicated Divide the dose (morning and evening) only if both can be directly observed; discontinue agent suspected of causing side-effect if this can be done without compromising the regimen.
Optic neuritis	E	Discontinue medicine and refer to ophthalmologist.
Psychosis or psychotic symptoms (violent or suicidal tendencies)	Cs	Discontinue agent suspected of causing the side-effect for a short time (1–4 weeks) while psychotic symptoms are brought under control; initiate antipsychotic treatment and refer to psychiatrist. Lower the dose of the agent suspected of causing the side-effect if this can be done without compromising the regimen.
Seizures	Cs	Discontinue agent suspected of causing side-effect pending resolution of seizures; initiate anticonvulsant therapy (phenytoin, valproic acid). Permanently discontinue agent suspected of causing side-effect if this can be done without compromising regimen.

Am, amikacin; Clr, clarithromycin; Cm, capreomycin; Cs, cycloserine; E, ethambutol; Eto, ethionamide; Km, kanamycin;; PAS, para-aminosalicylic acid; Pto, prothionamide; Z, pyrazinamide

Management of drug-resistant tuberculosis

Training for staff working at DR-TB management centres

Module E: A patient-centred approach to
ensuring continuation of DR-TB treatment



**World Health
Organization**

MODULE E

A patient-centred approach to ensuring continuation of DR-TB^a treatment

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^a Although in these modules drug resistance refers to *M. tuberculosis* that is resistant to the first-line anti-TB drugs, the modules focus on the management of rifampicin- and/or isoniazid-resistant TB, i.e. RR- or MDR-TB (RR/MDR-TB) because of its clinical significance and the need to use second-line drugs in such cases.

Introduction

This module describes the basis of a patient-centred approach to supporting patients with drug-resistant tuberculosis (DR-TB) to adhere to treatment through a directly observed treatment (DOT) modality, and how to prevent interruptions in treatment. It also describes how to decentralize services to DR-TB patients (that is, transfer their care) from DR-TB management centres to local health facilities, and how to coordinate medical referrals and transfers. Improving the support offered to patients and coordinating the transfer of their care should improve the likelihood of patients continuing their treatment and eventually being cured.

A patient-centred approach to TB care and, more specifically, to DOT, consists of assessing the patient's needs and values that influence adherence to treatment. This would mean coordinating with relatives and community members, and other health-care workers, to mount an effective response that removes the barriers to adherence that have been identified (from material needs to discrimination due to stigma). In addition, it includes promoting access to the services that prevent and relieve all suffering associated with the disease and its treatment, including effective management of adverse drug reactions (*see* chapter 12 of the Companion Handbook to the WHO Guidelines for the management of DR-TB).¹

The risk of treatment interruption leading to failure or death is much higher for patients being treated for DR-TB than for TB patients treated with the first-line anti-TB medicines because of the frequent side-effects of the medicines. The DR-TB treatment regimen may be less effective; there are a limited number of anti-TB medicines (second-line drugs) to which the patient's strain of DR-TB may be susceptible; and the anti-TB medicines used for DR-TB may be less well tolerated. Treatment for rifampicin-resistant/multidrug-resistant (RR/MDR)-TB lasts for at least 20 months. The duration of treatment greatly increases the probability that the treatment will be interrupted or the patient will be lost to follow up. Additionally, the stigma and discrimination attached to the disease makes it very difficult for patients to adhere to treatment. As many patients would have already incurred high expenses on previous failed treatment courses, the indirect costs are often so high for patients that treatment interruptions are unavoidable while they look for options to improve income. In addition, partial or irregular treatment greatly increases the probability that the patient's strain of *Mycobacterium tuberculosis* will develop further drug resistance, putting the patient at risk of even greater difficulty with treatment and a higher likelihood of dying.

Given the complicated process of treating DR-TB, it is critical to maintain contact with patients and relatives or other caregivers to ensure that patients have regular, uninterrupted treatment and a good chance of achieving a successful outcome. Depending on the country policy, the patient may start treatment as an inpatient or outpatient in the DR-TB management centre, where comprehensive services are offered. DR-TB patients who begin treatment as inpatients are subsequently discharged from the DR-TB management centre to continue their treatment as outpatients at the DR-TB management centre. Alternatively, the patient's care may be decentralized to a local health facility. The decentralization process is designed to help patients receive ambulatory treatment at a convenient location, closer to their home, thereby reducing costs for both patients and the health-care system.

1. Support DR-TB patients when giving them directly observed treatment at the DR-TB management centre

Treatment for RR/MDR-TB is long; it usually takes at least 20 months or more for a patient to finish treatment and be cured. The process of supporting DR-TB patients begins even before the first dose of medicine is administered. During discussions at the time of enrolment into DR-TB treatment, the health worker describes exactly how treatment must be completed, and obtains the patient's agreement to undertake the regimen. You carefully explain the requirement for daily DOT and the duration of the treatment. You discuss the need for adherence, the consequences of missing doses and the responsibilities of both the patient and the provider. (See Module D for additional information.)

Each day a patient is scheduled for treatment, he or she must be directly observed while taking the medicines: first as an inpatient or outpatient at the DR-TB management centre for several months and later at a local health facility or by a community-based treatment supporter. Taking the medicines every day, especially those that cause side-effects, is tedious and uncomfortable, and the patient may become discouraged. DOT should be delivered as quickly as possible, and you should support patients by providing friendly, personal attention to help them overcome possible barriers to treatment. However, if the patient wants to swallow medicines slowly, the patient should be made comfortable and allowed sufficient time.

During treatment, emphasize the need for DOT and completing the full course of treatment. There are many reasons why a patient may miss doses. It is important that you understand the patient's situation and identify any issues that may cause him or her to miss doses; this will enable you to deliver appropriate information and support. Without sustained efforts being made by the patient, his or her family and the health worker, it will be difficult for DR-TB treatment to be successful.

1.1 Provide support for the DR-TB patient each time treatment is given

Each time you see a patient for treatment, whether as an inpatient or an outpatient, ask how the patient is feeling and if there have been any problems. Give the patient your complete attention as you listen to his or her answers. Give DOT as described in Module C and record the administration of the medicines on the patient's *Second-line TB treatment card*. Remind the patient when the next dose should be taken. **Show interest in the patient's condition and progress.** This daily interaction with DR-TB patients is very important and offers an opportunity to provide constant support and encouragement. The daily interaction is important for both inpatients and outpatients, and is especially important for a patient who is experiencing side-effects or other frustrating factors, such as social exclusion.

1.2 Identify problems that may hinder directly observed treatment and help solve them

In conversation with the patient, identify any concerns or problems about treatment or other issues, and try to address them before they become obstacles to treatment. Some patients will attend regularly for treatment, but others will miss their appointments and require more

support. Although it is impossible to know which patients will interrupt treatment, there are some important signs to look for in all DR-TB patients. One indicator of whether a patient will require additional encouragement is if the patient was lost to follow up in the past. Other possible obstacles to completing treatment are a lack of economic resources for transportation or food, constraints at home or work, or substance abuse; these may be identified during the home visit made before treatment starts (described in Module B). Patients may become tired or discouraged; or stop treatment because of side-effects, the inconvenience of attending for treatment or standing in line every day; because they have a poor relationship with the health worker; or because they are depressed or feel that treatment does not matter.

Explain that this type of treatment ensures that they receive all of the doses necessary to cure them, and that if all the doses are not taken they may lose their last chance to be cured. Emphasize that experience has shown that patients have a much better chance of being cured if they are treated in this way. Patients who have DOT can be certain that no doses are forgotten, and no medications are omitted because they are lost or ruined.

You may also reassure the patient that DOT offers the benefit that the health worker or treatment supporter will know right away if the patient experiences any side-effect and will be able to help the patient with the side-effect. You should encourage the patient to continue treatment and provide supportive measures – for example, antihistamines for itching or anti-inflammatories for joint pain. Reassure the patient that side-effects usually diminish with time. As the treatment of DR-TB is expensive and takes a long time to complete, every measure must be taken to ensure that treatment is a success. When you discuss treatment, its completion and possible obstacles to completion, be certain that you show the utmost respect for the patient, and emphasize that your ultimate concern is that he or she should be cured.

There are times when a patient will not be able to attend the DR-TB management centre for DOT because he or she needs to travel or attend an event, such as a wedding or a funeral. If a patient cannot attend, then the missed doses are counted as absences; however, absences should be avoided if at all possible. Do not give medicines to DR-TB patients for self-administered treatment. Rather, missed doses must be made up and treatment time will be extended to cover these.

When problems arise during treatment, discuss them with the patient. Try to discover why the patient missed a dose or why the patient wants to stop treatment. When the cause of the problem has been identified, try to help the patient solve it. Some examples of possible causes and solutions are given in *Table 1* (note: the list is illustrative and not exhaustive).

Sometimes patients simply need to be reminded of the reasons why it is important not to interrupt treatment. Remind the patient why it is important to take all of the recommended medicines together for the full duration of treatment. Remind the patient that taking only some of the medicines, or taking them irregularly, is dangerous and may make the disease more difficult, or impossible, to cure.

DR-TB patients may start to feel better as they continue to take their treatment. This is an indication that treatment is working. Nonetheless, it is important to emphasize that treatment must be continued and completed as prescribed to ensure that a patient is cured.

Table 1 Causes of missed doses and possible solutions

CAUSE OF MISSED DOSE	POSSIBLE SOLUTION
Patient feels better and does not understand or accept the need to continue treatment.	<ul style="list-style-type: none"> • Explain that although the patient may feel better now, if the medicines are not taken for the prescribed time, the disease will return and may be more difficult to treat. • Explain that the patient may die if DR-TB treatment is stopped. • If acceptable to the patient, discuss the situation with the family and ensure that they also understand and can encourage the patient to continue.
Patient has a side-effect.	<ul style="list-style-type: none"> • Identify the side-effect early through pro-active discussions. • Reassure the patient that side-effects occur mainly during the first few months of treatment and diminish with time. Sometimes medicines can be used to alleviate the symptoms of side-effects. Treat the side-effects if possible, and encourage the patient to tolerate these effects until they resolve. • Give appropriate advice or remedies for the side-effect free of charge, such as ancillary medicine. Refer to a specialist if necessary. See the tables listing side-effects and how to manage them in Module C. • Educate the patient about the side-effect and encourage the patient to continue treatment. Explain that although the side-effects of medicines may be difficult to bear, they are generally less severe than stopping treatment and continuing to be sick.
Attending the DR-TB management centre is inconvenient.	<ul style="list-style-type: none"> • Find an alternative facility closer to patient's home where the treatment can be delivered under the desired conditions. Admit the patient to the DR-TB management centre. • Help the patient find housing closer to the DR-TB management centre – for example, find the patient temporary shelter in a housing facility or in a home rented specifically for DR-TB patients.
Patient dislikes waiting in a long queue.	<ul style="list-style-type: none"> • Make arrangements in the clinic so that DR-TB patients receive DOT promptly.
Health-care staff are rude or have no time for the patient.	<ul style="list-style-type: none"> • Ensure that the workload is manageable by using appointment times. • If this is not possible, relieve the workload by transferring care to local health facilities. • Discuss the situation with health-care workers and assess what their concerns are and find out what ideas they have for improvement. • Recognize the important and difficult role health-care workers play. • If this is a common complaint, provide training in communication skills to health-care workers.

CAUSE OF MISSED DOSE POSSIBLE SOLUTION

Patient is dependent on alcohol or drugs.

- Explain the dangers of alcohol interacting with anti-TB medicines and other drugs.
- Refer the patient to a specialist or self-help group.
- Speak with the family and, if possible, explain the situation and ask them to intervene and support the patient.
- Find a local treatment supporter who is acceptable to the patient, able to cope with the patient's dependence, willing to assist the patient on a daily basis, and able to be a link between the patient and the treatment facility.

Patient feels alone or depressed or lacks support.

- Refer the patient to a support group, group therapy or one-on-one counselling.
- Talk to the patient's family, if possible, to try to gain support.
- Identify another patient who may be able to encourage the patient to continue treatment.
- Explore other social support schemes available within the country and try to link the patient to these schemes.

Patient cannot leave the children at home.

- Suggest that a family member or neighbour watch over the children when the patient attends for treatment.
- Remind family members that the patient must continue treatment to protect the family's health, particularly the health of children.
- If the patient is already in the continuation phase, explore the possibility of DOT through a community member close to the patient's home.

Patient is homeless.

- Put the patient in contact with an organization that can assist with housing.

Patient has lost his or her job and needs to find work or is not being given time off to attend appointments.

- Work with employers directly to help them understand the fact that DR-TB is curable and uninterrupted treatment will give the patient the best chance of recovery and keep fellow workers safe.
- Give the patient information to pass on to their employer.
- Work with partner agencies to run campaigns addressing stigma in the workplace.
- Put the patient in contact with an organization that can help him or her find work.
- Offer financial support so that the patient can cope while he or she is receiving no income.

1.3 Provide enablers and/or incentives to help the patient continue treatment

Enablers such as financial support to cover the cost of transport or food, or compensation for lost wages, may be used to encourage and reward adherence to treatment. Depending on your situation, there will be different ways to provide enablers.

When you make a home visit before treatment starts, you will be able to observe the family's situation and identify what type of help may be needed. The family may need additional support, especially if the family's breadwinner needs to relocate or attend the DR-TB management centre regularly to start treatment.

Depending on the provisions in your programme, patients and family members may be eligible to receive some enablers or incentives to participate, such as the following:

- food parcels/coupons for patients and their dependents;
- temporary shelter in a housing facility or a rented home for DR-TB patients close to the treatment centre;
- school fees for dependent children;
- transportation vouchers;
- advice on and assistance in resolving administrative matters relating to the treatment;
- assistance in defending the rights of or reinforcing the responsibilities of patients; and
- skills training to help patients obtain work during treatment or after completing treatment, or both.

1.4 Use the *DR-TB daily attendance sheet* to track a patient's attendance for treatment

For those who are seen as outpatients, use the *DR-TB daily attendance sheet* to keep track of their attendance in the outpatient department of the DR-TB management centre. Check the sheet at the end of the clinic: there should be a tick (✓) next to the names of those patients who received DOT that day. Place a "0" or "Ø" next to the names of patients who were absent; then make sure that those patients are traced and the proper actions are taken (*See* section 3 of this module). Any action taken should be recorded on that patient's *Second-line TB treatment card*.

An example of a *DR-TB daily attendance sheet* appears on the next page.

If your facility treats only a small number of patients (less than five or six), it is not necessary to use this form. You can use the patients' *Second-line TB treatment cards* to determine quickly which patients did not attend treatment.

The same *DR-TB daily attendance sheet* can be used in an inpatient setting to verify that all patients receive treatment each day as prescribed.

Example

DR-TB daily attendance sheet

Facility: Blue Acorn		DR-TB daily attendance sheet																																				
Month: JULY	Year: 2010	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	Remarks					
DR-Registration #	Name																																					
BA-08-10	Mary Musowe	○	✓			✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓							
BA-35-10	Josiak Kacere	✓	✓	✓	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	○	✓	○	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			Working outside city on 16-17th		
BA-38-10	Kamruai Nyathi	✓	✓	✓	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓					
BA-43-10	Sarah Nyathi	✓	✓	✓	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓				
BA-46-10	Mohammed Fazal				-						-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			Began treatment on 13th		
BA-47-10	Mansour Osman	✓	✓	✓	-	✓	✓	✓	✓	✓	✓	○	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓				
BA-52-10	Nesa Farah	✓	✓	✓	-	✓	✓	✓	○	✓	○	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			Side effect - nausea on 9 & 10	
BA-54-10	Bhaghen Dutta	✓	✓	✓	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓				
BA-57-10	A.K. Prakash	✓	✓	✓	-	✓	✓	✓	✓	✓	○	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			Home visit on 13th - dose given
BA-58-10	K. Misra	✓	✓	✓	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓				
BA-59-10	Grace Msiska				-						-							-																			Began treatment on 26th	

Register the days on which patients did not take their medicines and also provide explanations.

2. Decentralize treatment of DR-TB patients from the DR-TB management centre to a local health facility

Many patients will begin DR-TB treatment at a DR-TB management centre, though some of these patients will come from areas that are far from the centre. During the initial period at the centre, the patient will start treatment, any side-effects will be managed and the patient will be closely monitored. If the regimen is not working, it will be adjusted. However, a patient who must travel far each day to obtain treatment is less likely to complete the regimen, which lasts 20 months or longer. Therefore, following the initial period of hospitalization or temporary residence near the DR-TB management centre, it is recommended that a patient's treatment be decentralized to a local health facility nearer to the patient's home. When the patient is stable on the regimen, a local health facility can be selected to administer the rest of the regimen; this allows the patient to complete treatment without the hardship of travel or relocation.

2.1 Identify DR-TB patients who are eligible for treatment decentralization

Determine whether any patient meets the following criteria for treatment decentralization:

- the patient does not have any uncontrolled or severe side-effects or a condition that prevents moving his or her care to a local health facility (for example, the patient does not have renal failure or need oxygen); and
- the patient can attend a local health facility for daily treatment or will have access to a trained community-based supporter; if the patient is still receiving daily injections, local arrangements must be able to support this.

Occasionally, there may be patients who do not meet the criteria for decentralization but whose treatment needs to be decentralized. For example, if patients have financial or health problems that make it difficult for them to attend the DR-TB management centre to receive DOT and they cannot be hospitalized, special arrangements may be made with the local health facility to receive these patients earlier in the treatment process.

2.2 Coordinate with local health authorities about training for staff at the local facility

Each month, list the DR-TB patients who are eligible for decentralization. On the list include:

- a. each patient's complete address; and
- b. the relevant local health facilities, with their addresses.

Discuss this list with the appropriate District TB Officer (or the officer in charge of TB control in the relevant administrative unit). Ask the officer to match the local facilities with each patient's address to ensure that there is a facility close to each patient's residence that can accept the patient. The District TB Officer should coordinate arrangements to ensure that facilities **are ready to receive the DR-TB patients.**

Once the treatment of a patient is decentralized, staff at the local health facility is responsible for the following:

- administering directly observed DR-TB treatment, including daily injections if necessary, and documenting when treatment is directly observed;
- selecting with the patient a community-based treatment supporter, if necessary, and training and supervising the supporter; providing information regularly to the patient and family members during treatment (*see* Module D for additional information);^b
- ensuring that the patient continues to take treatment, and tracing the patient promptly if he or she does not attend for treatment. If the facility loses contact with the patient, the DR-TB management centre must be informed right away;
- promptly recognizing, documenting and managing minor side-effects, and sending the patient to the DR-TB management centre for management of moderate and severe side-effects;
- ensuring that the patient continues collecting sputum for follow-up examinations as scheduled, and goes to the DR-TB management centre for monitoring visits with a physician (the patient should attend at least monthly, or more frequently if requested by the physician);
- managing second-line and first-line anti-TB medicines and other medical supplies for DR-TB (*see* Module F for additional information).

Staff at the local health facility must be appropriately trained to carry out all the tasks listed above. If a community-based TB treatment supporter will be providing treatment for a DR-TB patient, the supporter must be specifically trained in DR-TB activities. The supporter will need to have regular contact with the health facility to obtain the medicines and be supervised. The local health facility **must assign someone to supervise each community-based DR-TB treatment supporter**.

The District TB Officer will inform the DR-TB management centre and staff at the local health facility of the exact date and time a patient will be decentralized.

2.3 Discuss the decentralization process with the DR-TB patient

Discuss the treatment decentralization process with the DR-TB patient before treatment is formally decentralized to a local health facility. During the meeting, explain the following to the patient and, if possible, the patient's family:

- what decentralization is and the eligibility criteria for decentralization;
- the benefits of receiving DR-TB services at the local health facility;
- the responsibilities of the local health facility and the patient;
- that the patient must keep his or her copy of the *Second-line TB treatment card* and have it available each day when receiving treatment;

^b How to identify, train and supervise a community treatment supporter is taught in Module E: identify and supervise community TB treatment supporters. In: Management of tuberculosis: training for health facility staff. Geneva: World Health Organization; 2009 [WHO/HTM/TB/2009.423e]. Treatment supporters for DR-TB patients must be specially trained

- the schedule for monthly monitoring visits with the physician and required follow-up sputum examinations, which will continue at the DR-TB management centre;
- the possibility that the local health facility will identify, train and supervise a community-based treatment supporter for the patient.

Ensure that the patient and his or her family are able to ask any questions they have and that they have understood the information they have been given. More detail about the points that should be discussed with the patient whose treatment is about to be decentralized may be found in Module D.

Discuss the date that the patient will begin reporting to the local health facility. Also provide the patient with the name and address of the local health facility, and directions to it, as well as the name of a contact person at the facility.

2.4 Prepare the medicines, supplies and forms to be sent to the local health facility

Coordinate with the pharmacist at the DR-TB management centre to prepare a supply of anti-TB medicines for the local health facility. The process of preparing medicines for DR-TB patients is described in Module F. Prepare other medical supplies, such as syringes, needles and water for injection, if necessary.

In addition, prepare the following documents and forms:

- Tuberculosis referral/transfer form* (see section 5 for instructions on preparing this form for a transfer);
- two copies of the patient's *Second-line TB treatment card* (one for the local facility and one for the patient);
- the *Medicine delivery form* listing the medicines sent, so that the local facility can confirm that all were received.

Prepare two copies of the *Second-line TB treatment card*. Send one to the local health facility and give the other to the patient. The patient's copy can be used to update the original card kept at the DR-TB management centre when the patient returns for monthly monitoring visits.

Ideally, when a patient's care is decentralized, a staff member from the DR-TB management centre should accompany the patient during the first visit to the local health facility to deliver the patient's medicines, ensure that all arrangements have been made correctly and discuss any issues with the facility's staff.

When the patient returns to the DR-TB management centre for monthly monitoring visits, you will be able to review the patient's copy of the *Second-line TB treatment card* to learn about the patient's adherence and discuss any problems encountered during his or her visits to the local facility. Transfer significant information from the patient's *Second-line TB treatment card*

to the copy of the card at the DR-TB management centre. If a patient has been attending irregularly, talk with the patient to reinforce the importance of adherence to treatment and the consequences of missing doses. Information added to the card by the DR-TB management centre, such as observations, physician's recommendations or laboratory results, will be copied by the local health facility onto their version of the card.

3. Take action to trace a DR-TB patient who has missed treatment

Take immediate action when a DR-TB patient misses any dose. If the patient does not attend an appointment, put a "0" or "Ø" under that date on the *Second-line TB treatment card* to indicate that a dose was missed. Separate the *Second-line TB treatment card* of the patient who did not receive the daily dose from other patients' cards so that you can give it special attention. If the patient does not come for treatment within the next 24 hours, take action to contact the patient immediately.

3.1 Call or make a home visit after the first missed dose

If a patient unexpectedly misses a dose, locate and contact the patient by telephoning or visiting within 24 hours of the missed appointment.

If a patient who is receiving outpatient treatment at the DR-TB management centre does not have a telephone or cannot be reached, someone must make a home visit to try to contact the patient at the address on the *Second-line TB treatment card*. If staff from the DR-TB management centre cannot make the visit, seek immediate assistance from staff at the local health facility or community treatment supporters near the patient's home to locate and visit the patient.

Use the patient's *Second-line TB treatment card* to find the patient's address and the address of the patient's contact person. When making the home visit, take the day's medicines with you so that the patient can take them in your presence. If the patient is not at home, ask the family or neighbours where the patient is and try to learn why the patient missed treatment (do not leave the medicines with the family or neighbours). Be sensitive about the patient's privacy when talking with neighbours.

Making home visits may be more feasible for staff at the local health facility than for staff at the DR-TB management centre.

If necessary, visit the contact person. The contact person is usually a family member, a close friend, co-worker or a neighbour. Again, be sensitive about the patient's right to confidentiality. The contact person may not know about the extent of the patient's illness.

When you find the patient, give the patient one dose of treatment and watch the patient take it. Do not give an extra dose on any day. If a patient misses doses, treatment will be extended until all of the medicines have been taken as prescribed.

Check that the date of the missed dose is marked on the *Second-line TB treatment card* with a “0” or “Ø” and tick the date that you located the patient and gave a dose. Note that you made a home visit, and the result of the visit, in the “Comments” section of the patient’s *Second-line TB treatment card*.

Document every attempt made by the DR-TB management centre or local health facility to address treatment interruptions, such as by telephoning, sending text messages by mobile, making home visits, and talking with the patient and family. Document these attempts on the patient’s *Second-line TB treatment card*.

3.2 Take steps to prevent future absences

Talk to the patient and, if necessary, the family about the problem that caused the absence from treatment. Make sure that you talk with the patient and the family in a private area, preferably in their home. Once privacy is ensured, you may want to say something like the following:

“We missed you yesterday. What happened?”

“Do you have any problems? Can you share them with me?”

Find out why the patient missed a dose, and discuss solutions if the patient’s reason for missing treatment will pose a problem for subsequent doses. In a respectful manner remind the patient to avoid missing further treatment because this may make it harder to treat the patient’s illness, the patient may spread the disease, or may die.

You can take these steps to try to diminish the problem of missed doses and treatment interruption.

- During the discussion at the time of enrolment into treatment with second-line drugs, describe exactly how treatment must be taken, including the requirement for having DOT 6 (or 7) days each week, and the duration of treatment; obtain the patient’s agreement to undertake the regimen. Discuss the reasons why it is important to adhere to the treatment schedule, the consequences of missing doses and the responsibilities of both the patient and the provider. (*See Module D for more detailed information on how to discuss these issues.*)
- Seek assistance from the patient’s family, friends or others if the patient continues to miss treatment.
- Use a “buddy” system in which a patient who is having adherence problems is paired with a patient who has gone through the difficult period of treatment and can act as a positive role model.
- Always positively reinforce good adherence. Recognize the patient’s efforts to complete treatment during a specified period of time. You may want to say something like, “Let’s get through this month together.” This may help to strengthen adherence.
- Appeal to the patient’s sense of care for friends and family by explaining how the best way to protect loved ones is to adhere to treatment: by adhering to treatment, the patient will become non-contagious and will eventually be cured.

Patients who are habitually absent (once or twice a week) put themselves at risk for treatment failure or loss to follow up. A patient whose care has been decentralized and who has poor adherence that cannot be resolved should be sent back to the DR-TB management centre for treatment (and readmitted if at risk of treatment failure; *see* section 4.2). Staff at the DR-TB management centre should evaluate the patient's treatment history and, if necessary, ask the review panel for recommendations on how to proceed.

3.3 Place a patient who interrupted treatment for more than 2 weeks but less than 2 months back on treatment

If a DR-TB patient is traced, and the treatment regimen was interrupted for more than 2 weeks but less than 2 months, the patient will need to undergo a clinical examination by the physician at the DR-TB management centre, and sputum will be collected for smear and culture. Treatment with the same regimen should be resumed and continued as long as smear results and culture results are negative. However, if either result is positive, drug-susceptibility testing (DST) must be performed. Once the results of culture and DST are available, the case should be presented to the review panel for re-evaluation.

3.4 Place a patient who interrupted treatment for 2 months or longer back on treatment as a new presumptive case

Continue to look for the patient until the patient is found or for as long as specified in your local guidelines. For example, if a DR-TB patient has moved to another province and did not leave any contact information, it may be fruitless to continue to search for him or her; or if despite several sessions of counselling, a patient has decided to discontinue DR-TB treatment, it may be hopeless to try to find and convince him or her.

If treatment is interrupted for 2 consecutive months or longer, the patient is given a final outcome of "lost to follow up". This is entered on the copies of the *Second-line TB treatment card* at the DR-TB management centre (and at the local health facility if the patient had been decentralized) and in the *Second-line TB treatment register* at the DR-TB management centre. If the patient returns, the patient must undergo screening as a new presumptive case of DR-TB. The case will need to be presented to the review panel again, which will decide whether treatment should be restarted right away or wait until after the results from the new DST become available. If treatment is restarted, a new registration number will be assigned, a new *Second-line TB treatment card* will be opened, and the patient will be entered into the *Second-line TB treatment register* as a case of "treatment after loss to follow up".



Now do Exercise A – written exercise and group discussion

When you have reached this point in the module, you are ready to do Exercise A, a written exercise followed by a group discussion. Turn to the relevant pages in the exercise section of this module, complete the exercise and let your facilitator know when you are ready for the discussion.

4. Coordinate medical referrals of DR-TB patients

4.1 Refer the DR-TB patient to a specialist or hospital for additional care

Some patients may need to be referred to a specialist or to a hospital for care for an acute or chronic problem (for example, diabetes). When a medical referral is necessary, discuss the referral with the patient. Inform the patient and the family of the need to return to the DR-TB management centre (or local health facility, if the patient has been decentralized) to continue DR-TB treatment after the patient is discharged by the clinician or hospital. Also ensure that the patient continues to take treatment for DR-TB while receiving special care at another facility. (If the local health facility makes an emergency referral for medical care, the DR-TB management centre should be informed of this within 24 hours.)

A *Tuberculosis referral/transfer form* should be used when making a medical referral. Tick the middle option at the top of the form (as shown in the example below). Complete the rest of the form and send it with the patient. When the patient attends the hospital, the hospital should complete the bottom of the form, cut it off and send it back to you to confirm that the patient arrived.

When a DR-TB patient is discharged from hospital, there is a risk that the patient will be lost to follow up. Sometimes the patient may think that all of his or her health problems have been treated and believe that there is no need to return to the DR-TB management centre or local health facility for DR-TB treatment. To prevent this misconception, you should discuss the need to resume treatment after discharge with the patient and the family before the patient is admitted or transferred to the care of a specialist. Also, it is helpful to establish a relationship with the hospital where patients are usually referred for specialist treatment and ask staff at the hospital to instruct the DR-TB patient to return to the DR-TB management centre to complete treatment.

Example

Tuberculosis referral/transfer form

Tick and comment to indicate the reason for this referral or transfer:

Referral to register and begin TB treatment

Referral for _____

Transfer (registered patient is moving)

Tick and explain when a patient is moving to another area or being decentralized.

Name/address of referring/transferring facility _____

Name/address of facility to which patient is referred/transferred _____

Tick and describe the reason for referral – for example, diagnosis, side-effects, another illness, need for hospitalization.

Name of patient _____ Age _____ Sex: M F

Address (if moving, future address) _____

Tick this when referring a patient to another DR-TB management centre to begin treatment after a diagnosis of DR-TB.

Name and address of contact person for patient _____

Diagnosis* _____

This address may be helpful later if the patient does not return for treatment.

District TB no.* _____ Date treatment started* _____

Treatment regimen:* New patient
 Retreatment
 RR/MDR-TB

Medicines patient is receiving _____

Remarks (e.g. side-effects observed) _____

Signature _____ Position _____ Date of referral/transfer _____

**Complete if known. If this is a referral for diagnosis, these items may be unknown.*

For use by facility to which patient has been referred or transferred:

Name of facility _____

District _____ Date _____

Name of patient _____ District TB no. _____

The above patient reported at this facility on _____ (date)

Signature _____ Position _____

Send this part back to referring/transferring facility as soon as patient has reported.

4.2 Receive a DR-TB patient who returns to the DR-TB management centre after experiencing difficulties in receiving care at a local health facility

The majority of patients who start DR-TB treatment at DR-TB management centres are expected to complete treatment at a local health facility. However, some patients may have difficulties that cause the local health facility or the physician at the DR-TB management centre to refer the patient back to the original DR-TB management centre to continue treatment. Some of the reasons for sending a patient back to the DR-TB management centre include poor treatment progress and difficulties with adherence.

Poor treatment progress

Signs that the patient's treatment is not progressing well include the following:

- The patient's tests revert to culture positive after being culture negative.
- The patient's symptoms worsen or reappear after having disappeared earlier.

A patient whose treatment is not progressing well is at high risk of treatment failure and should be transferred back to the DR-TB management centre for evaluation and possibly a change of regimen. Under no circumstances should the regimen be changed at the local health facility.

Difficulties with adherence

Signs that the patient is having difficulties with adherence include the following:

- The patient misses treatment more frequently while at the local health facility.
- The patient is experiencing financial constraints – for example, the patient can no longer afford travel, and does not have housing or food.
- The patient develops moderate-to-severe side-effects from treatment.
- The patient has moved and the local facility has become inconvenient.

Any factor that causes a patient to miss treatment should be addressed by the DR-TB management centre. When a patient is sent back to the DR-TB management centre, contact the local health facility to confirm that the patient has arrived.

5. Coordinate the DR-TB patient's transfers between treatment facilities

A DR-TB patient may need to be transferred to a different DR-TB management centre or health facility to continue treatment. A patient may need to be transferred because of the following reasons:

- a. The patient is moving (changing residence) to the catchment area of a different DR-TB management centre.
- b. The patient is ready for their care to be decentralized (described in section 2).

- c. The patient is having difficulties with transportation or access to the present place of treatment; in this case, the patient should be transferred to a different DR-TB management centre or local health facility.

Transfers of DR-TB patients are carried out by the DR-TB management centre where the patient is registered, *not* by a local health facility. The District TB Officer must be notified of every transfer.

5.1 Decide if the *Tuberculosis referral/transfer form* should be used

When a DR-TB patient is transferred, it is essential to ensure that treatment will continue after the move.

- a. If a patient is moving outside the catchment area of the DR-TB management centre, a *Tuberculosis referral/transfer form* should be completed and sent to the receiving DR-TB management centre. Find out when and where the patient is moving. Discuss the move with the patient and the need to continue treatment. Emphasize the importance of reporting to the new facility. Explain that to be cured the patient must continue taking all of the required medicines for the entire time prescribed.
- b. When a DR-TB patient's treatment is to be decentralized, the procedures described in section 2 should be followed, including completing a *Tuberculosis referral/transfer form* as described in section 5.2.
- c. If after decentralization a patient needs to move from one local health facility to another within the catchment area of the DR-TB management centre, the patient's *Second-line TB treatment card* should also be transferred from one local health facility to another. There is no need for a transfer form. However, the DR-TB management centre, not the local health facility, should organize the transfer and ensure that the receiving facility has appropriately trained staff and appropriate medicines to continue the patient's treatment.

5.2 Complete the *Tuberculosis referral/transfer form*

The *Tuberculosis referral/transfer form* is used when a patient **is transferred** from one DR-TB management centre to another, or the treatment is decentralized. Three copies of the transfer form are prepared. One copy stays at the first DR-TB management centre. One will be received and remain at the receiving DR-TB management centre; and one will be sent to the District TB Officer in the patient's new residential district. The purpose of using this form (or one similar to it) is to keep track of the patient to ensure that treatment continues after the transfer.

At the top of the form, tick the box on the right to indicate that this patient is transferring because of a move. Fill out the date of the transfer; the DR-TB registration number; the patient's name, age, sex and complete new address; the name of the transferring facility, including the city and region; and the name of the receiving facility, including the city and region. Describe the reason for the transfer, and sign and date the form.

management centre does not receive a report of the treatment outcome within a reasonable period, it is your responsibility to follow up. The possible treatment outcomes for the transferred patient are the same as for other patients: cured, treatment completed, died, treatment failure, or lost to follow up. The outcome “not evaluated” is used only if the patient was transferred and another outcome cannot be determined. Although the loss of a small minority of patients is unavoidable, the aim should always be to have the fewest possible cases that were not evaluated.

When your DR-TB management centre receives a patient from another DR-TB management centre, make a note on the patient’s *Second-line TB treatment card* that the patient has transferred in to remind yourself to report the treatment outcome to the originating DR-TB management centre. When any patient completes treatment, check to see whether the patient had transferred in. If so, contact the originating DR-TB management centre and report the treatment outcome.



Now do Exercise B – written exercise

When you reach this point, turn to Exercise B in the exercise section of this module, read the instructions and complete the exercise. Discuss your answers with a facilitator after you have finished.

Summary

- Taking medicines for DR-TB for 20 months or more, especially those that cause side-effects, is tedious, costly and uncomfortable for patients. A patient-centred approach to DOT that ensures adherence to treatment should be given each day. The patient should be supported with friendly, personal attention from staff. Not all patients are able to swallow all tablets quickly. They should feel comfortable about taking their time and not feel rushed.
- Although it is practically impossible to know which patients will interrupt treatment, if a patient was lost to follow up in the past you should consider that there may be a risk of treatment interruption again. Some possible causes of interruption include a lack of economic resources for transportation or food, work constraints, or substance abuse, or a combination of these factors.
- Depending on the provisions in your DR-TB programme, patients and family members may be eligible to receive some enablers and/or incentives to assist with adherence to treatment, such as the following:
 - food parcels/coupons for patients and their dependents;
 - temporary shelter in a housing facility or a rented home for DR-TB patients;
 - school fees for dependent children;
 - transportation vouchers;
 - advice on and assistance in resolving administrative matters relating to the treatment;
 - assistance in defending the rights of or reinforcing the responsibilities of patients;
 - skills training to help patients obtain work during treatment or after completing treatment, or both.
- Mark attendance for treatment of DR-TB patients on the *DR-TB daily attendance sheet*. At the end of each day, review the sheet and mark the DR-TB patients who were absent during the day. Make sure that they are contacted and proper actions are taken.
- When a DR-TB patient is stable on the regimen, a local health facility can be selected to administer the rest of the regimen; this allows the patient to complete treatment without the hardship of travel or relocation.
- When a patient is eligible for their care to be decentralized, coordinate with the District TB Officer to match the DR-TB patient's address with a local facility close to the patient's residence. The District TB Officer should coordinate arrangements to ensure that staff at the local health facility have been trained to manage DR-TB patients and that the facility is ready to receive such patients.
- Ideally, when the patient's care is decentralized, a staff member from the DR-TB management centre should accompany the patient during the first visit to the local health facility to deliver the patient's medicines, ensure that all arrangements have been made correctly and discuss any issues with the facility's staff.
- If a patient unexpectedly misses a dose of treatment, locate and contact the patient by telephoning or visiting within 24 hours of the missed appointment. If the patient cannot be reached, visit the home address entered on the patient's *Second-line TB treatment card* and, if necessary, visit the patient's contact person.

- When you find the patient, give the patient one dose of treatment and watch the patient take the dose. Talk with the patient and find out why the patient missed the appointment. Discuss possible solutions if the patient’s reason for missing treatment will continue to pose a problem for subsequent doses.
- Take steps such as these to prevent missed doses and treatment interruption:
 - At the start of treatment, describe exactly how treatment must be taken (for example, 6 days a week under direct observation, and the duration of treatment) and obtain the patient’s agreement. Also discuss reasons why it is important to adhere to the treatment schedule, the consequences of missing treatment and the responsibilities of both the patient and the provider.
 - Show genuine interest in the patient’s concerns and answer any questions kindly and clearly.
 - Seek assistance from the patient’s family, friends or others if the patient continues to miss treatment.
 - Use a “buddy” system.
 - Always provide positive feedback for adherence.
 - Appeal to the patient’s sense of care for loved ones by explaining that the best way to protect others is to adhere to treatment and become non-contagious.
- Manage patients whose treatment is interrupted as follows:
 - A patient who has interrupted treatment for more than 2 weeks but less than 2 months should resume treatment after having a clinical examination and providing sputum for smear and culture.
 - A patient who has interrupted treatment for 2 months or longer is given a final outcome of “lost to follow up”.
 - A patient who returns to treatment after an interruption of 2 months or longer must undergo screening as a new presumptive case of DR-TB; this should include DST, and the case should be presented to the review panel.
- When a DR-TB patient needs to be referred to a specialist or to a hospital for care of an acute or chronic problem, use a *Tuberculosis referral/transfer form*; the hospital should return the bottom part of the form to confirm that the patient has attended. Ensure that the patient will continue DR-TB treatment while in the hospital and will return to continue DR-TB treatment after discharge.
- If a DR-TB patient who was decentralized has difficulties with adherence or shows signs of poor treatment progress (for example, test results revert to culture positive, the patient’s symptoms worsen, or symptoms disappear and then reappear), the local health facility or the physician at the DR-TB management centre may decide to move the patient’s treatment back to the DR-TB management centre so that the problems can be addressed.
- Use the *Tuberculosis referral/transfer form* when a DR-TB patient’s care is decentralized or transferred from one DR-TB management centre to another. The form helps to keep track of the patient. Prepare three copies: one copy for the originating DR-TB management centre, one for the receiving facility, and one for the District TB Officer.

Self-assessment questions

Answer the self-assessment questions below to check what you have learnt. Then compare your answers to those on pages E-26–E-30.

1. List five things that a health worker could do to support DR-TB patients when DOT is given.

-
-
-
-
-

2. Write “T” for true or “F” for false for the following statements:

_____ While DR-TB patients are being treated as inpatients at the DR-TB management centre, support is not usually required every day.

_____ When a patient’s care is decentralized, the District TB Coordinator should ensure that staff at the local health facility are trained to treat DR-TB patients.

_____ When a patient is transferred to a different DR-TB management centre, the receiving DR-TB management centre should notify the health centre from which the patient was transferred that the patient has reported for treatment.

_____ If a patient is moving from the catchment area of the original DR-TB management centre to the catchment area of a different DR-TB management centre, complete a *Tuberculosis referral/transfer form* to transfer all records and responsibility for reporting on the patient to the receiving DR-TB management centre.

_____ If a DR-TB patient misses several doses, you should try to telephone the patient or make a home visit within a few days.

3. A patient whose care has been decentralized may be asked to return to the DR-TB management centre for daily treatment because of difficulties with treatment adherence or signs of poor treatment progress. Two signs of poor treatment progress are:
4. What is the main purpose of the *Tuberculosis referral/transfer form*?
5. Read the following case history and answer the questions.

Ursula, a 47-year-old woman, has missed 2 days of her first week of treatment after her care was decentralized to her hometown. The health worker makes a home visit. The child who comes to the door says that Ursula has moved, and she does not know where. A neighbour says that Ursula has gone to stay with her son, who lives 10 minutes away by foot. The

health worker goes to the son's house, where she finds Ursula. Ursula says that she missed treatment because she was moving. She moved because her former household was afraid of catching DR-TB. She does not want to go for treatment because she does not want anyone to know that she has DR-TB.

Tick all of the actions that would be appropriate to take.

- Try to find an alternative method to give treatment so that Ursula's privacy is not compromised.
- Educate Ursula's former household members and her son about DR-TB and how it spreads.
- Insist that Ursula's former household members allow her to live with them.
- Remind Ursula that she is not infectious as her sputum and culture are negative, and that she will probably remain non-infectious if she continues to take all of her medicines.
- Ask more questions to find out whether there are any other problems that are keeping Ursula from coming for treatment.
- Hand to Ursula the doses for a few days, until she has time to talk with her family and resolve her problems about coming for treatment.
- Have Ursula agree to come to the local health facility the next day for treatment.

Suggest one motivating statement that the health worker could make to Ursula:

6. List two steps that you might take to try to diminish a patient's frequent absences from treatment:

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Now compare your answers with those on the next page.

Answers to self-assessment questions

If you had difficulty in answering any question, turn back and study the section indicated. If you do not understand something, discuss it with a facilitator.

1. List five things that a health worker could do to support DR-TB patients when DOT is given.

Some possible answers are as follows:

- Ask how the patient is feeling and listen carefully to the answer.*
- Show interest in the patient's condition and progress.*
- Identify problems that may cause the patient to miss doses and try to solve them.*
- Provide enablers or incentives to help the patient adhere to treatment, such as food parcels, temporary housing close to the DR-TB management centre or transportation vouchers.*
- Before the patient begins treatment, describe exactly how treatment must be completed, and get the patient's agreement to undertake DR-TB treatment.*
- If the patient experiences side-effects, explain why they are occurring, provide supportive measures as appropriate, and reassure the patient that the side-effects should diminish over time.*
- Remind the patient of the need to take all of the recommended medicines together and for the full duration of treatment in order to be cured.*

(See section 1.)

2. F While DR-TB patients are being treated as inpatients at the DR-TB management centre, support is not usually required every day. *(See section 1.)*

 T When a patient's care is decentralized, the District TB Coordinator should ensure that staff at the local health facility is trained to treat DR-TB patients. *(See section 2.)*

 T When a patient is transferred to a different DR-TB management centre, the receiving DR-TB management centre should notify the health centre from which the patient transferred that the patient has reported for treatment. *(See sections 2 and 5.)*

 F If a patient is moving from the catchment area of the original DR-TB management centre to the catchment area of a different DR-TB management centre, complete a Tuberculosis referral/transfer form to transfer all records and responsibility for reporting on the patient to the receiving DR-TB management centre.^c *(See section 5.)*

 T If a DR-TB patient misses several doses, you should try to telephone the patient or make a home visit within a few days. *(See section 3.)*

3. Two signs of poor treatment progress are as follows:

- The patient's test results revert to culture positive after being culture negative.*

^c The responsibility for reporting treatment outcome is still with the centre where the patient was originally registered for DR-TB treatment.

- *The patient’s symptoms worsen, or the symptoms disappear and then reappear.*

(See section 4.2.)

4. What is the main purpose of the *Tuberculosis referral/transfer form*?

To keep track of the patient and to ensure that treatment will continue after the patient is transferred.

(See section 5.2.)

5. *The following answers should be ticked.*

Try to find an alternative method to give treatment so that Ursula’s privacy is not compromised.

Educate Ursula’s former household members and her son about DR-TB and how it spreads.

Insist that Ursula’s former household members allow her to live with them.

Remind Ursula that she is not infectious as her sputum and culture are negative, and she will probably remain non-infectious if she continues to take all of her medicines.

Ask more questions to find out whether there are any other problems that are keeping Ursula from coming for treatment.

Hand to Ursula the doses for a few days, until she has time to talk with her family and resolve her problems about coming for treatment.

Have Ursula agree to come to the local health facility the next day for treatment.

Suggest one motivating statement that the health worker could make to Ursula:

Examples of motivating statements:

- *You have done so much already, it is important that you continue the treatment until you are cured. If you stop the treatment, you will probably become sick and infectious again.*
- *Your illness can be cured if you keep coming for treatment.*
- *You will remain non-infectious to your family and friends if you continue taking your medicines as recommended.*
- *I look forward to seeing you tomorrow.*
- *If you have a problem in the future, please tell me about it. Maybe I can help.*

(See sections 1, 2 and 3.)

6. List two steps that you might take to try to diminish a patient's frequent absences from treatment.

You may have listed two of the following:

- Discuss the reasons why it is important for patients to adhere to treatment, the consequences of missing treatment and the responsibilities of both the patient and the provider.*
- Seek assistance from the family, friends or others if the patient continues to miss treatment.*
- Use a “buddy” system so that a patient who is having adherence problems is paired with a patient who has gone through the difficult period of treatment and can be a positive role model.*
- Always provide positive reinforcement for adherence. Recognize patients' efforts to complete treatment for a specified period of time. Say something like, “Let's get through this month together.” This will help strengthen adherence.*
- Appeal to the patient's sense of care for friends and family by explaining that the best way to protect loved ones is to adhere to treatment, to become non-infectious and eventually to be cured.*

(See section 3.)



The End

Congratulations on finishing this module!

Reference

1. Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. Geneva: World Health Organization; 2014 (WHO/HTM/TB/2014.11).

Exercises for Module E: Ensure continuation of DR-TB treatment

Exercise A:

Written exercise and group discussion: Supporting DR-TB patients and ensuring continued treatment

In this exercise, you will reflect on how patients are supported at your DR-TB management centre, and you may identify ways to improve the services that your facility offers.

Read the following questions and write answers that describe the situation at your DR-TB management centre. Your facilitator will lead a discussion on the responses to these questions.

1. a) At your DR-TB management centre, how frequently are patients **not able to adhere** to the treatment schedule?
 - b) What are the most common reasons that DR-TB patients miss doses or interrupt their treatment?
 - c) Does your DR-TB management centre offer any enablers or incentives to help and encourage patients to adhere to treatment? If so, what are they?

2. a) Do you feel that DR-TB patients receive good support at your DR-TB management centre when they are inpatients? Outpatients?
 - b) List some ways that good support is provided at your DR-TB management centre:

 - c) Describe any improvements that could be made to the way your centre provides support:

3. a) What is the procedure for decentralizing the treatment of patients at your DR-TB management centre? Please mention the ways in which the procedure is similar to and the ways in which is it different from the procedures described in this module.
 - b) Do you ever lose DR-TB patients after treatment decentralization? How often?

- c) Could the procedures for treatment decentralization at your DR-TB management centre be improved? If so, how?
4. a) How soon after a patient misses treatment does the staff take action to contact the patient? What is the first action? Whose responsibility is it to take this action?
- b) Does staff from the DR-TB management centre make home visits to trace patients who have interrupted treatment? If yes, when are these visits warranted? Who makes the home visit?
- c) Are efforts to bring patients back to treatment always successful? Usually successful?
- d) How do you think the procedures to trace patients could be improved at your DR-TB management centre?

When you have written answers to these questions, tell your facilitator that you are ready for the discussion.



When the group has finished the discussion,
GO BACK to section 4 and work till the next stop sign.

Exercise B

Written exercise: Decentralizing a DR-TB patient's treatment

In this exercise, you will fill out a *Tuberculosis referral/transfer form* for a DR-TB patient. Read the case below and use the information to complete the form on the following page. Then answer the questions about this transfer.

Case information

Mrs Paula Musunga is a 60-year-old retired teacher who lives at 34, Eighteenth Way, Darma. On 2 December 2009, she was diagnosed with DR-TB, and she began treatment at the Blue Acorn DR-TB management centre on 18 December. Her treatment regimen is Z-Km-Ofx-Eto-Cs. Her district TB registration number is 0996-09.

Mrs Musunga has been receiving treatment at the Blue Acorn DR-TB management centre located at 100 Tsinga Way, Semma. She has been attending treatment for 4 months but the DR-TB management centre is a long way from her home. She is eager to move back home because she lives with her daughter, and before she relocated for treatment, she helped care for her two grandchildren. Her daughter, Eva Thida, is her contact person.

After her second month of treatment, Mrs Musunga's culture result was negative, and her smear results have been negative for 3 months. The DR-TB management centre decided to decentralize her treatment to Silbe Health Centre, 1 Talle Street, Darma, which is near her home. Silbe Health Centre has staff who are prepared to continue her treatment. It was agreed that the patient's treatment would be decentralized on 7 May 2010.

Based on the information provided, fill out a *Tuberculosis referral/transfer form* on the next page so that Mrs Musunga can be transferred to the Silbe Health Centre.

Now write your answers to these questions about decentralization:

1. What documents should the staff at the Blue Acorn DR-TB management centre send with the patient to the Silbe Health Centre?
2. What information should be discussed with Mrs Musunga prior to the decentralization of her treatment?
3. How will the staff know whether Mrs Musunga arrived at the Silbe Health Centre to continue her treatment?
4. What should be the next contact that staff at the Blue Acorn DR-TB management centre have with Mrs Musunga?

When you have finished this exercise, review your work with a facilitator.



Then **GO BACK** to the summary section and work until the end of the module.

Management of drug-resistant tuberculosis

Training for staff working at DR-TB management centres

Module F: Manage medicines and
supplies for DR-TB



**World Health
Organization**

MODULE F

Manage medicines and supplies for DR-TB

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Introduction

Essential medicines and other supplies for detecting drug-resistant tuberculosis (DR-TB) and treating patients with the disease at DR-TB management centres and local health facilities include the following:

- Second-line drugs (sufficient quantities of oral medicines for various regimens plus injectable agents);
- Ancillary medicines, such as antiemetics, analgesics and co-trimoxazole;
- Medical supplies, such as syringes, gloves, surgical masks, needles and sterile water for injections;
- Sputum containers;
- Forms and registers;
- Personal protective equipment (PPE) for health workers.

Some DR-TB management centres have a diagnostic centre or laboratory located within the centre. If this is the case, adequate supplies of laboratory consumables also need to be ensured. These include stains, reagents, cartridges, gels, equipment, etc.

The DR-TB management centre must keep sufficient quantities of medicines and supplies in stock and store them carefully so that they will be available and effective when needed. Medicines for treating DR-TB are more costly and difficult to procure than medicines used to treat TB that is susceptible to first-line agents.

Although WHO recommends using fixed-dose combinations (FDCs) to facilitate correct medicine intake, these are not available for DR-TB regimens. Additionally, the use of boxes that contain a full regimen is also not feasible because of the long duration of treatment, the possibility that a patient will receive an individualized regimen, and the large number of medicines that must be used. However, some countries have tried to use innovative boxes containing medicines for a shorter duration for patients. To ensure that treatment is administered correctly and to avoid interruptions in the supply during treatment, health-care workers who treat DR-TB patients must always be alert to the quantity of medicines and supplies available and the amount needed, and be able to quickly resolve any discrepancies.

You should always be aware of the quantities that should be in stock. Then if stocks are low, you can react in time to request a resupply. Good management and storage procedures will keep medicines and supplies safe from stock-out and losses due to theft, misuse, spoiling and expiration.

Objectives of this module

After completing this module participants will be able to do the following: Section:

- ▶ Ensure adequate supplies of DR-TB medicines for your DR-TB management centre 4
- ▶ Order medicines and supplies for DR-TB patients..... 4
- ▶ Plan for other necessary supplies..... 5
- ▶ Prepare medicines for DR-TB patients 6
- ▶ Use good storage and management procedures for anti-TB medicines and supplies 7

If you need to look up an unfamiliar word, refer to the Glossary at the end of Module A.

1. Presentation and packaging of medicines used in second-line regimen

There are a number of different anti-TB medicines used to treat patients with DR-TB. These medicines (and their standard abbreviations and presentations) are shown in *Table 1*. (See Module C for additional information.)

Table 1 WHO pre-qualified anti-tuberculosis medicines available for treating tuberculosis^a

FIRST LINE ANTI-TUBERCULOSIS MEDICINES

Oral solid dosage forms: fixed-dose combinations for adults

Product	Description	Packaging
4FDC/RHZE 150/75/400/275 (blister)	Rifampicin 150 mg/isoniazid 75 mg/ pyrazinamide 400 mg/ethambutol 275 mg film-coated tablets	28 tablets * 24 blisters
4FDC/RHZE 150/75/400/275 (loose)	Rifampicin 150 mg/isoniazid 75 mg/ pyrazinamide 400 mg/ethambutol 275 mg film-coated tablets	HDPE container of 1000 loose tablets
3FDC/RHE 150/75/275 (blister)	Rifampicin 150 mg/isoniazid 75 mg/ ethambutol 275 mg film-coated tablets	28 tablets * 24 blisters
3FDC/RHE 150/75/275 (loose)	Rifampicin 150 mg/isoniazid 75 mg/ ethambutol 275 mg film-coated tablets	HDPE container of 1000 loose tablets
2 FDC/RH 150/75 (blister)	Rifampicin 150 mg/isoniazid 75 mg film- coated tablets	28 tablets * 24 blisters
2 FDC/RH 150/150 (blister)	Rifampicin 150 mg/isoniazid 150 mg film-coated tablets	28 tablets * 24 blisters
2 FDC/EH 400/150 (blister)	Ethambutol 400 mg /isoniazid 150 mg film-coated tablets	28 tablets * 24 blisters

Continues...

Continued from previous page

Oral solid dosage forms: single-dose formulations for adults

Product	Description	Packaging
Ethambutol 400 mg	Ethambutol 400 mg film-coated tablets	28 tablets * 24 blisters
Isoniazid 300 mg	Isoniazid 300 mg film-uncoated tablets	28 tablets * 24 blisters
Pyrazinamide 400 mg	Pyrazinamide 400 mg film-uncoated tablets	28 tablets * 24 blisters
Pyrazinamide 500 mg	Pyrazinamide 500 mg film-uncoated tablets	28 tablets * 24 blisters
Pyrazinamide 750 mg**	Pyrazinamide 750 mg film-uncoated tablets	28 tablets * 24 blisters
Rifabutin 150 mg	Rifabutin 150 mg hard capsules	30 capsules * 1 blister

**India-specific product

Oral solid dosage forms: fixed-dose combination for children

Product	Description	Packaging
2FDC/RH 60/30	Rifampicin 60 mg/isoniazid 30 mg dispersible, film-uncoated tablets	28 tablets * 3 blisters
2FDC/RH 60/60	Rifampicin 60 mg/isoniazid 60 mg dispersible, film-uncoated tablets	28 tablets * 3 blisters
3 FDC/RHZ 60/30/150	Rifampicin 60 mg/isoniazid 30 mg/pyrazinamide 150 mg dispersible, film-uncoated tablets	28 tablets * 3 blisters

Oral solid dosage forms: single-dose formulations for children

Product	Description	Packaging
Ethambutol 100 mg	Ethambutol 100 mg film-coated tablets	10 tablets * 10 blisters
Isoniazid 100 mg	Isoniazid 100 mg dispersible tablets	10 tablets * 10 blisters

Parenteral injectables

Product	Description	Packaging
Streptomycin 1 g inj.	Streptomycin 1 g powder for injection	100 vials

SECOND LINE ANTI-TUBERCULOSIS MEDICINES

Group 2: Parenteral injectables

Product	Description	Packaging
Amikacin 500 mg inj	Amikacin 500 mg solution for injection (2 ml)	1 ampoule in a carton box
Amikacin 500 mg inj	Amikacin 500 mg solution for injection (2 ml)	10 ampoules in a carton box
Amikacin 500 mg inj.	Amikacin 500 mg solution for injection (2 ml)	5 vials in a carton box

Product	Description	Packaging
Capreomycin 0.5 g inj.	Capreomycin 0.5 g powder for injection	1 vial in a carton box
Capreomycin 0.75 g inj.	Capreomycin 0.75 g powder for injection	1 vial in a carton box
Capreomycin 1 g inj.	Capreomycin 1 g powder for injection	1 vial in a carton box
Kanamycin 1 g inj.	Kanamycin 1 g solution for injection (4 ml)	10 ampoules in a carton box
Kanamycin 1 g inj.	Kanamycin 1 g powder for injection	50 vials in a carton box

Group 3: Fluoroquinolones

Product	Description	Packaging
Levofloxacin 250 mg	Levofloxacin 250 mg film-coated tablets	Blister pack of 100 tablets
Levofloxacin 500 mg	Levofloxacin 500 mg film-coated tablets	Blister pack of 100 tablets
Levofloxacin 500 mg	Levofloxacin 500 mg film-coated tablets	Blister pack of 80 tablets
Moxifloxacin 400 mg	Moxifloxacin 400 mg film-coated tablets	5 tablets * 20 blisters
Moxifloxacin 400 mg	Moxifloxacin 400 mg film-coated tablets	10 tablets * 10 blisters
Moxifloxacin 400 mg	Moxifloxacin 400 mg film-coated tablets	Blister pack of 5 tablets
Ofloxacin 200 mg	Ofloxacin 200 mg film-coated tablets	Blister pack of 100 tablets
Ofloxacin 400 mg	Ofloxacin 400 mg film-coated tablets	Blister pack of 100 tablets

Group 4: Bacteriostatics

Product	Description	Packaging
Cycloserine 250 mg	Cycloserine 250 mg hard capsules	Blister pack of 100 capsules
Cycloserine 250 mg	Cycloserine 250 mg hard capsules	HDPE container of 100 capsules
Ethionamide 125 mg	Ethionamide 125 mg film-coated tablets	Blister pack of 90 tablets
Ethionamide 250 mg	Ethionamide 250 mg film-coated tablets	Blister pack of 100 tablets
Ethionamide 250 mg	Ethionamide 250 mg film-coated tablets	Blister pack of 90 tablets
PAS acid	P-aminosalicylic acid (PAS) sachet 4 g enteric-coated delayed-release granules in sachets	30 sachets in a carton box
PAS sodium	100 g of PAS sodium granules 60% w/w	100 g in HDPE container
PAS sodium	PAS sodium salt powder for oral solution 5.52 g sachet	25 sachets in a carton box
PAS sodium	9.2 g of PAS sodium granules 60% w/w	30 sachets in a carton box
Prothionamide 250 mg	Prothionamide 250 mg film-coated tablets	Blister pack of 100 tablets
Prothionamide 250 mg	Prothionamide 250 mg film-coated tablets	Blister pack of 140 tablets
Terizidone 250 mg	Terizidone 250 mg capsules	Blister pack of 50 capsules

Continues...

Continued from previous page

Group 5: Anti-TB drugs with limited data on efficacy and/or long-term safety

Product	Description	Packaging
Amoxicillin clavunate 250 mg	Amoxicillin clavunate 250/62.5 mg powder for oral suspension	1 bottle
Amoxicillin clavunate 250+125 mg	Amoxicillin 250 mg and clavulanic acid 125 mg film-coated tablet	Blister pack of 14 tablets
Amoxicillin clavunate 250+125 mg	Amoxicillin 250 mg and clavulanic acid 125 mg film-coated tablet	Blister pack of 20 tablets
Amoxicillin clavunate 500+125 mg	Amoxicillin 500 mg and clavulanic acid 125 mg film-coated tablet	Blister pack of 100 tablets
Amoxicillin clavunate 500+125 mg	Amoxicillin 500 mg and clavulanic acid 125 mg film-coated tablet	Blister pack of 15 tablets
Amoxicillin clavunate 500+125 mg	Amoxicillin 500 mg and clavulanic acid 125 mg film-coated tablet	Blister pack of 20 tablets
Amoxicillin clavunate 875+125 mg	Amoxicillin 875 mg and clavulanic acid 125 mg film-coated tablet	Blister pack of 100 tablets
Amoxicillin clavunate 875+125 mg	Amoxicillin 875 mg and clavulanic acid 125 mg film-coated tablet	Blister pack of 12 tablets
Amoxicillin clavunate 875+125 mg	Amoxicillin 875 mg and clavulanic acid 125 mg film-coated tablet	Blister pack of 14 tablets
Clofazimine 100 mg	Clofazimine 100 mg capsules	HDPE container(s) of 100
Clofazimine 50 mg	Clofazimine 50 mg capsules	HDPE container(s) of 100
Clarithromycin 250 mg	Clarithromycin 250 mg film-coated tablets	Blister pack of 14 tablets
Clarithromycin 500 mg	Clarithromycin 500 mg film-coated tablets	Blister pack of 14 tablets
Imipenem /cilastatin 500+500 mg	Imipenem 500 mg /cilastatin 500 mg powder for solution for IV infusion	1 vial
Linezolid 600 mg	Linezolid 600 mg film-coated tablets	10 tablets * 2 blisters

New anti-TB medicine

Product	Description	Packaging
Bedaquiline 100mg	Bedaquiline 100 mg film-uncoated tablets	Blister pack of 188 tablets

FDC fixed-dose combination; HDPE high-density polyethylene

^a Source: Global Drug Facility (GDF) product catalogue 2014. (www.stoptb.org/gdf/drugsupply/drugs_available.asp, accessed 17 October 2014).

Medicines are manufactured as different preparations in different countries. You will use the preparations that are provided to you but you should be aware that other preparations may exist. Unlike the medicines used for new-patient regimens and retreatment regimens, **fixed-dose combinations** (FDCs) are **not** available to treat DR-TB yet. Instead, formulations of single medicines are used to treat DR-TB. This means that patients need to take a large number of pills, and increases the importance of direct observation to ensure that the patient takes the full dose of all medicines.

Manufacturers package anti-TB medicines used to treat DR-TB in different ways. Some examples are shown below.



Oral medicines may be packaged in strips and blister packs of tablets.



Oral medicines may be delivered in a canister.



Sterile powders may be delivered in sealed vials for intramuscular injections.

Second-line drug regimens include injectable agents during the intensive phase of treatment. In addition to the injectable agents, sterile water, sterile needles and syringes should also be available for each patient.

Para-aminosalicylic acid (PAS) used in some countries comes in granules in individual sachets requiring refrigeration (temperatures below 15 °C). However, PAS sodium does not need refrigeration. Pay attention to which PAS is used in your programme.

Monitor the stock on-hand at the DR-TB management centre so that every DR-TB patient is assured of having uninterrupted daily treatment.

2. Procurement, forecasting and storage of second-line drugs

Your national TB control programme or your specific project will procure medicines for second-line regimens. If the medicines are procured with support from the Global Fund to Fight AIDS, Tuberculosis and Malaria, the procurement should follow the Global Drug Facility (GDF) mechanisms to ensure that high-quality medicines are available at lower prices. If the government procures the medicines out of the national budget, it is still possible to

procure through GDF; however, if the government chooses its preferred manufacturers, it is essential to ensure that the drugs are of the highest possible quality.

Several factors should be considered when forecasting the schedule and quantity of medicines to be procured. Lead time in delivery and the short shelf-life of second-line drugs play an important role in deciding the timing, frequency and volume of the procurement. Generally, there is a central-level annual procurement of drugs in countries, while requisition for drugs from subnational units to the central stores could be 6-monthly or quarterly. Local health facility requests are sent on a monthly or quarterly basis, depending on the established systems. Forecasting could be done quarterly at the central level, and a review of the medicine status could be done monthly at DR-TB management centres and at local health facilities to ensure an uninterrupted supply of medicines.

When medicines are needed to treat only a small number of patients, stock is kept in a storage area. When more patients are treated and more medicines are needed, a bigger space for storage is needed, as well as more complex procedures to ensure a continuous supply and to preserve the quality of medicines from the point of delivery to the point of use. The specifics of the processes described below will depend on your programme's patient load, and procurement and distribution arrangements.

3. Medicine distribution system

Medicines used in second-line regimens will be delivered by their manufacturers to a central medical warehouse. They will be used at DR-TB management centres and distributed quarterly to the local health facilities to which DR-TB patients have been decentralized. Some local facilities may not have adequate capacity for storing certain medicines – for example, they may not have enough secure space, or air conditioning or refrigeration. In these cases, the national TB programme must coordinate with them to guarantee adequate storage before patients can be decentralized to these facilities.

The DR-TB management centre makes quarterly or 6-monthly requests for medicine using the *TB medicine requisition form*. The DR-TB management centre then supplies the local health facilities in its area monthly or quarterly, based on the number of patients decentralized to each facility.

In all instances, proper and safe storage conditions of the medicines must be implemented, even during transport from one point to another.

4. Ensure adequate supplies of second-line drugs for your DR-TB management centre

It is absolutely essential that enough medicines are always in stock for all DR-TB patients being treated at your DR-TB management centre and at the local health facilities to which patients have been decentralized. Running out of any medicine used for treatment is disastrous for a patient who will miss doses and perhaps become sicker or whose strain of *Mycobacterium tuberculosis* may show additional resistance.

There are some key considerations when requesting medicines for the DR-TB management centre:

1. Determine the total amount of each medicine consumed daily, monthly and quarterly.
2. Determine the quantity to order by completing the *TB medicine requisition form* based on quarterly consumption.
3. Factor in the lead time, any expected change in the number of patients due to expansion of services and existing versus anticipated stocks.

4.1 Determine the quantity of second-line drugs used each quarter

Two weeks before the beginning of each quarter, inventory the medicines that DR-TB patients are receiving. Each patient may have a different regimen so the quantity of each anti-TB medicine must be calculated. Look at the second-line regimen section on each patient's *Second-line TB treatment card* and record the medicines that should be taken each day, row by row in a table. In larger programmes, these steps are usually performed by a pharmacist at the DR-TB management centre, but you should understand how they are done.

To determine the total amount of each medicine consumed daily, monthly and quarterly, complete the following steps in the worksheet on the next page.

1. Using the *Second-line TB treatment card* for each patient being treated at the DR-TB management centre, record the medicines to be taken each day by each patient.
2. Using the *Second-line TB treatment card* for each decentralized patient being treated at a local health facility in the DR-TB management centre's area, record the medicines to be taken each day by each patient.
3. Calculate the DAILY consumption of each medicine for all patients receiving it.
4. Calculate the MONTHLY consumption by multiplying the daily consumption by 26 days.^a
5. Calculate the QUARTERLY consumption by multiplying the monthly consumption by 3.

^a The number of days per month used to calculate drug requirement may vary between countries from 26 to 31 days. Here, 26 working days are being assumed, to account for a 30-day month with four Sundays.

Example:

Worksheet: Calculate the current consumption of second-line drugs

Patients	DRUGS USED TO TREAT RR/ MDR-TB PATIENTS									
	Z 500 mg	E 400 mg	Km 1 g	Cm 1 g	Lfx 250 mg	Mfx 400 mg	Pto 250 mg	Cs 250 mg	PAS 4 g	B6
1							3			
2							3			
3							3			
4							3			
5							2			
6							3			
7							3			
8							2			
9							3			
10							2			
11							2			
12							3			
13							3			
14							3			
15							3			
16										
17										
18										
19										
20										
Daily total (sum)							41			
Monthly (daily x 26)							1066			
Quarterly (monthly x 3)							3198			

For example, imagine that you want to know the total consumption of prothionamide (Pto) in your DR-TB management centre. Using the example in the worksheet above, you can see that 11 patients take 3 tablets of 250 mg Pto each day, and 4 patients take 2 tablets of Pto each day. The worksheet shows the daily need for each patient; the sum for all of these patients is 41 tablets of Pto per day.

By multiplying the daily total by 26, you can calculate the monthly consumption (1066 tablets). By multiplying the monthly total by 3, you can calculate the quarterly consumption (3198 tablets).

4.2 Determine the quantities of second-line drugs to be ordered for your DR-TB management centre

Use the quarterly consumption of each medicine to complete the *TB medicine requisition form*. This form guides the calculation of the amount to order, including buffer stock. In general, the quantities to order will depend on the following:

1. Consumption pattern
2. Expected increase or decrease in the number of patients
3. Available stocks at the facility
4. Expected delay in delivery
5. Order cycle (quarterly in most cases).

To fill out the *TB medicine requisition form*, follow the steps below. Refer to the form on the next page as you read the steps.

1. Write the name of your DR-TB management centre and the quarter for which the request is being made.
2. In the first column of the *TB medicine requisition form*, write the names of the medicines you will request.
3. Enter the quarterly consumption, then the amount for a 1-month buffer^b (which is the same amount as the quantity in the “Monthly” row of the worksheet that is completed to calculate consumption).
4. Follow the formula shown on the form to complete each of the remaining columns (C, D and E).
5. Always double-check your calculations.

One month’s supply is added to the need calculated for the quarter as buffer stock to have on hand in case of emergencies. Then the stock on-hand (the quantity of each medicine presently in the facility) is subtracted from this number. The pharmacist should be able to tell you how much of each medicine is in stock.

Although ordering is done quarterly, it is vital to check the stock monthly. The quantity in stock will factor into the actual quantity that needs to be ordered. Assessing stock monthly allows you to identify sudden increases or decreases in consumption caused by unexpected changes in enrolment and outcomes. You should be aware of the usual quantities needed for patients so that you will know whether your supply of second-line drugs is too large or too small.

Given below is a partially completed *TB medicine requisition form* that shows the amount that needs to be ordered for the next quarter for patients being treated at a DR-TB management centre and its affiliated local health facilities. The last two columns in the form will be completed by the warehouse when the order is filled and sent.

^b The quantity of buffer stock may vary with country policy.

Example: TB medicine requisition form

Requesting facility: Blue Cross Hospital Date requested: 15 March 2013

For the month/s of: April-June 2013

#	Description (Please specify preparation of drug)	Unit	Quarterly use (a)	Buffer (1 month) (b)	Quantity needed (c=a+b)	On-hand (d)	Quantity requested (e=c-d)	Units per container	# Containers sent
1	Pyrazinamide 500mg	Tab	4095	1365	5460	1210	4250		
2	Syringe 5cc	Syringe	390	130	520	110	410		
3	Kanamycin 1g	Vial	390	130	520	110	410		
4	Levofloxacin 250mg	Tab							
5	Prothionamide 250mg	Tab	3444	1148	4592	950	3642		
6	Cycloserine 250mg	Cap							
7									
8									
9									

Follow the formulas to calculate the amount you need to request for the quarter.

The buffer is 1 month's supply.

Requested by: Joel Asunga 15-3-13
(Signature and printed name/date)

4.3 Check the medicines when they are received

When you receive a delivery, undertake a physical inspection to check that the correct medicines have been received in the correct quantities and that their expiry dates will allow all medicines to be used in a timely fashion. If incorrect medicines have been delivered or if there are other problems with the order, address the problem by requesting the missing medicines and returning any extra or expired medicines that were sent in error. If there are no discrepancies, sign the receipt; if there are problems with the order, ensure that these are noted on the receipt before you sign it.

When you receive a delivery of medicines, complete the following steps.

- Sort through the medicines:
 - inspect packages for damaged medicines, discoloured tablets, distorted boxes or canisters;
 - check expiry dates;
 - confirm the number of tablets received and the doses of the medicines by inspecting all containers, both full and partially full;
 - compare the quantities of each medicine received with the quantities stated on the invoice.
- Note discrepancies (for example, note whether an insufficient quantity of a medicine was received or in the incorrect strength, or whether the medicines have expired). Initial any discrepancies noted on the invoice. Inform your pharmacist about any discrepancies.

3. Sign the receipt.
4. Stock the medicines, placing them behind medicines that have earlier expiry dates.

Accept only those medicines that can be utilized before their expiry date. It is normal to receive second-line anti-TB medicines that will expire in the near future because the procurement process is long and the shelf-life of the medicines is relatively short. For this reason, it is important to make sure that medicines are monitored regularly and used according to the **first expiry, first out (FEFO) rule** so that medicines expiring soonest are used first.

All expired medicines should be documented by following your local guidelines, stored separately from unexpired medicines and returned to the central medical warehouse.

When medicines sent from the DR-TB management centre are received at a local health facility, staff there should check the medicines upon delivery and report any discrepancies directly to the DR-TB management centre that sent the medicines.

4.4 Determine the quantity of medicines to be sent to the local health facility when the treatment of a patient is first decentralized

When treatment of a patient is decentralized from the DR-TB management centre, send the local health facility enough anti-TB medicines to treat that patient **for one quarter**.

The quantity of medicines sent to the local facility by the DR-TB management centre during the initial stages of decentralization depends on the timing of the decentralization. As patients may not be decentralized on the first day of the first month of a quarter, a table such as the one below can serve as a guide for determining the quantity of medicines to be prepared and delivered. If decentralization happens during the first month or second month of the quarter, prepare medicines for the remaining days of the quarter. **Count the actual remaining doses for the month, and count 26 doses for a full month.** If decentralization happens during the third month of the quarter, send medicine for the remaining days of the quarter plus the entire coming quarter. Also include a buffer stock as shown.

Table 2 Calculating the amount of medicines to send to a local health facility when treatment of a patient is decentralized

Month of decentralization	Quantity to send
First month of the quarter	Remaining days of the quarter + 1 month buffer ^c
Second month of the quarter	Remaining days of the quarter + 1 month buffer
Third month of the quarter	Remaining days of the quarter + next quarter + 1 month buffer

^c The quantity of buffer stock may vary as per country policy.

For example, a DR-TB patient, Mrs Bird York, will be decentralized to a local health facility on 15 January (first month of the quarter). The DR-TB management centre will need to prepare the following quantities of medicines for delivery to the local facility:

- enough medicines for the number of days remaining in January (count the actual remaining doses; 15– 31 January = 15 doses, excluding Sundays);
- plus days in February and March (2 months x 26 days = 52 doses);
- plus 1 month buffer (26 doses).

The quantity of medicines that should be sent to the local facility will cover 93 days (15 days + 52 days + 26 days). You will send medicines again in March for the next quarter (April–June).

Always double-check your calculations.

4.5 Each month, count the medicines in stock and return the expired medicines

Each month, you should count all medicines. With experience, you will be aware of the number of DR-TB patients being treated each quarter or month (not only at the DR-TB management centre but also those at the local facilities that you supply) and the quantities of medicines needed to treat them. If you think that your facility does not have sufficient quantities for the period, you may need to place a special order. Take action or inform the person responsible for the supplies of anti-TB medicines.

There are a number of instances when anti-TB medicines should be sent back to the central medical warehouse, or from local facilities back to your DR-TB management centre. Medicines will need to be returned when the following situations occur:

- a patient’s regimen is changed;
- a patient is lost to follow up;
- a patient dies;
- a patient finishes treatment;
- medicines expire;
- medicines are damaged.

When returning medicines to the central medical warehouse, use a *TB medicine return form*. On the form, indicate to where the medicines should be returned, the medicine and quantity returned, and the reason for return. If you need to request more medicines (because some of them have been spoiled, for example) follow the steps described in section 4.2. In the “Comments” section you can write specific instructions, such as those shown in the example.

Example: TB medicine return form

Facility: Blue Acorn Centre Date Sent: 21 June 2013

#	Description (Please specify preparation of drug)	Unit	Number of units	Reason	Comments
1	<i>Pyrazinamide 500mg</i>	<i>Tab</i>	<i>1800</i>	<i>Drugs spoiled because of flooding</i>	<i>Please replace with equal quantity, need by 31 July</i>
2					
3					
4					
5					

List the medicine being returned, the number of units and the reason for the return (for example, expired, spoiled, no longer needed).

Sent by: _____
(Signature and printed name/date)



Now do Exercise A – written exercise

When you reach this point in the module, turn to Exercise A and read the instructions. When you have finished the exercise, discuss your answers with a facilitator.

5. Plan for other necessary supplies

Make sure that your health facility maintains an adequate supply of disposable needles and syringes, sterile water for injections, and sufficient containers for sputum collection. It should also have adequate supplies of the ancillary medicines used to counter the side-effects of anti-TB treatment. Remember that side-effects that are not addressed may lead to irregular attendance and default; therefore, patients should not need to purchase ancillary medicines; these should be readily available at the DR-TB management centre for patients who need them.

Estimate the quantities needed for each of these supplies, and periodically check the quantities in the storeroom. If supplies are not likely to meet the centre’s projected needs, request more using the usual procedures.

5.1 Estimate the quantity of ancillary medicines needed

It is not easy to estimate the quantity of ancillary medicines that should be kept in a DR-TB management centre or local health facility. Some medicines are used frequently, such as

vitamin B6 (pyridoxine), and some are used only when specific side-effects occur. In addition, you may need a supply of co-trimoxazole for patients who are HIV positive for providing co-trimoxazole preventive treatment (CPT).

As DR-TB management centres handle a considerable number of patients who are in the intensive phase of treatment, and these patients frequently encounter side-effects, the centre should stock most of the necessary ancillary medicines. Local health facilities will keep only a limited stock of ancillary medicines.

The HIV programme will manage medicines for antiretroviral therapy and their supply. The health facility caring for the HIV-positive patient should coordinate the administration.

5.2 Estimate the required quantity of sputum containers

DR-TB management centres need to ensure that enough sputum containers are available. A large number of sputum containers are needed to identify and investigate patients suspected of having DR-TB and to follow up with patients. A shortage of sputum containers is a serious problem.

Estimate the quarterly need for sputum containers based on the number of sputum examinations expected to be performed for diagnosis plus the number expected to be performed for follow up. Base these estimates on the number of DR-TB patients treated during the previous quarter. When estimating and ordering sputum containers, it is recommended to round up the numbers.

Example: Method for calculating the number of sputum containers needed at a DR-TB management centre

- **The number of sputum containers needed for diagnosis** may be calculated as follows:

- number of new patients tested for drug resistance during the previous quarter
- multiplied by 2 (because 2 sputum samples are needed from each patient who needs to be tested for DR-TB^d)

For example

22 patients tested for drug resistance
 $\times 2$
 44 sputum containers for diagnosis

- The number of sputum containers needed **for follow up** during treatment is calculated as follows:

- number of DR-TB patients treated during the previous quarter
- multiplied by 3 (3 follow-up examinations per patient on treatment during the quarter, providing 1 sputum sample each time) – assuming all patients need a monthly sputum test in the intensive phase of treatment.

For example

102 DR-TB cases on treatment
 $\times 3$
 306 containers
 306 + 44 = 350 containers for diagnosis and follow up

^d Two samples should be collected if performing AFB microscopy and culture and DST or a single sample for Xpert/MTB RIF.

- The **total** number of **sputum containers** that need to be ordered is calculated as follows:
 - number needed for diagnosis
 - plus the number needed for follow-up examinations
 - plus 10% for additional investigations
 - plus 20% for reserve stock
 - minus the number of sputum containers in stock at the end of the previous quarter
 - round up the result.

For example

44 for diagnosis
<u>+ 306</u> for follow-up
350
<u>+ 35</u> for additional
385
<u>+ 77</u> for reserve stock
462 TOTAL needed
<u>- 150</u> in stock
312 to order
Order 320 containers (rounded up)

5.3 Estimate the quantity of needles, syringes and sterile water needed for injections

All DR-TB patients will receive an injectable agent 6 days a week during the intensive phase of treatment. Injections must be given with **sterile needles and syringes**. Needles and syringes must not be reused to avoid transmission of bloodborne diseases (especially HIV infection). The number of **syringes and needles** needed is the same as the number of doses of the injectable agent.

Example: Method for calculating the quantity of needles, syringes and vials of sterile water for injection needed at a DR-TB management centre

The number of needles, and syringes and vials of sterile water for injection needed for DR-TB patients may be calculated as follows:

- number of DR-TB patients currently being treated whose regimen includes an injectable agent
- multiplied by doses per patient (26 doses per month)
- multiplied by 4 for a buffer supply to cover 3 months plus 1 month
- minus the number of syringes in stock at the facility at the end of the previous quarter.

For example

8 patients receiving an injectable agent
<u>× 26</u>
208 doses (and syringes) needed
per month
<u>× 4</u> (3 months + 1 month buffer)
832 syringes needed per quarter when
fully stocked
<u>- 80</u> in stock
752 syringes (and needles) to order

It is also important to keep a sufficient number of vials of sterile water in stock reserved for DR-TB patients. For example: for kanamycin, 4 ml of sterile water; and for capreomycin, 2 ml

of sterile water; these amounts may vary by manufacturer. Amikacin may come in solution form and hence may not require additional sterile water. Sterile water may be available in a 5 cc vial or in another quantity in your country. Assuming that a vial of sterile water is used only once, irrespective of the total quantity in the vial, calculate the quantities of sterile water that need to be ordered as one vial for every one dose of an injectable anti-TB medicine.

5.4 Ensure that DR-TB forms and registers are available

A yearly allocation of forms will be provided to DR-TB management centres. See *Table 3* for the list of forms that should always be available in your DR-TB management centre.

Table 3 Forms^e that may be used at DR-TB management centres treating patients with drug-resistant tuberculosis (DR-TB)

Forms for detection	Forms for treatment
<i>DR-TB screening form</i>	<i>Second-line TB treatment card</i>
<i>Request for examination of biological specimen for TB</i>	<i>MDR-TB daily attendance sheet</i>
<i>DR-TB treatment waitlist</i>	<i>Second-line TB treatment register</i>
Forms for managing medicines	Forms for decentralization
<i>TB medicine requisition form</i>	<i>Tuberculosis referral/transfer form</i>
<i>TB medicine return form</i>	

At the local facility, only a few forms are needed. The DR-TB management centre should send the following forms:

- *Presumptive DR-TB referral form*
- *Request for examination of biological specimen for TB*
- *Second-line TB treatment card*
- *TB medicines return form.*

5.5 Each month, check stocks of supplies

Just as all medicines in stock should be counted each month, supplies should also be counted monthly. Check the stocks of ancillary medicines used to treat side-effects and associated diseases, sputum containers, needles, syringes, gloves, alcohol, cotton swabs, water for injections, masks, forms and registers. If supplies of any of these items are not likely to meet the centre's expected needs for the quarter, alert the person responsible or request for more according to your centre's usual procedures.

^e The list and titles of forms may vary as per the country programme guidelines.

6. Prepare medicines for DR-TB patients

Unlike WHO's new-patient regimen and retreatment regimen, second-line regimens can change during the course of treatment and the duration of treatment is long (at least 20 months). In addition, there are no FDCs for second-line drugs, so each patient takes a large number of pills every day. Therefore, it is not feasible to place the entire supply of medicines for each patient for the duration of treatment in one box. You must prepare 1 week's supply of daily doses for each DR-TB patient.

6.1 Prepare enough oral medicines for DR-TB patients for 1 week

As soon as it is decided to initiate a patient on second-line drugs, complete the *Second-line TB treatment card*, specifying the approved regimen and the corresponding doses of each medicine. The TB nurse or pharmacist will prepare the patient's oral medicines according to what is written on the *Second-line TB treatment card*. This is done for all patients. There are several ways of doing this. Countries have their own preferred way of preparing supplies for DR-TB patients. Below is an example of how it can be done.

On a designated day of the week, a nurse or pharmacist will prepare **1 week's supply of daily doses for every patient being treated at the facility**.

1. For every patient who has been newly approved for treatment and for every patient who receives treatment at the DR-TB management centre, the pharmacist prepares the daily regimen using the patient's *Second-line TB treatment card* as a guide; the daily dose of all medicines is placed in a small packet or envelope.
2. The pharmacist prepares six packets, enough for a week.
3. The pharmacist places the individual packets inside a pouch. The pouch is labelled with the patient's name and his or her district TB registration number. The pouches for all patients being treated at the DR-TB management centre are arranged on a tray or in a box. This tray or box should be kept out of direct sunlight; other good storage practices should also be followed.

The procedure described here **excludes granules of** para-aminosalicylic acid, which must be kept cold. It also excludes the injectable agent, which is too bulky to include in the daily packet or weekly pouch. *See* section 6.2 and section 6.3 for more information on how to prepare these medicines.

Note: When pyridoxine or vitamin B6 is routinely given, it should be included in the medicine packet.

6.2 Prepare para-aminosalicylic (PAS) acid granules each day

There are two types of para-aminosalicylic acid (PAS).

1. PAS acid – acid form, in granules. This type of PAS requires refrigeration.
2. PAS sodium – salt form, which does not require refrigeration. PAS sodium – salt form comes in two formulations: granules and powder.

Para-aminosalicylic acid sachets must be prepared daily because they must be kept refrigerated before being used. If patients in your DR-TB management centre receive para-aminosalicylic acid, take the following steps every morning before the patients arrive:

1. Take from the refrigerator the number of sachets expected to be used for that morning or afternoon, one box at a time.
2. Ensure that when the box containing the sachets is removed from the refrigerator it is kept in a cool place.
3. When a patient comes in for directly observed treatment (DOT) –
 - a. pour the patient a glass of acidic fruit juice, such as pineapple, orange or similar juice. *Note: water, iced tea and other non-acidic juices are not appropriate for para-aminosalicylic acid;*
 - b. open the sachet and pour the granules into the juice. The granules will not dissolve;
 - c. swirl the glass and watch the patient sip the mixture, ensuring that all granules are ingested.

Note: If the sachet appears bloated, or if the granules are discoloured (have turned purple or dark brown, do not administer the granules to the patient. Document the problem and return the sachets to the pharmacist for appropriate disposal. Open a new sachet and check whether it can be used.

If your country uses PAS sodium – salt form, refrigeration is not needed, and PAS can be prepared weekly like the other drugs.

6.3 Prepare and give injections

Prepare the injectable agent each day that the patient arrives for treatment. The injectable agent is given after all of the oral anti-TB agents. Always use the *Second-line TB treatment card* as a guide when preparing the injectable agent.

After watching the patient swallow all the oral anti-TB medicines, prepare the injection as follows:

1. Make sure that you have all the materials needed to prepare the injection, such as the agent, water for injection, needle, syringe, alcohol and cotton swabs.
2. Prepare the dose exactly as it is written on the patient's *Second-line TB treatment card*.
3. Before administering it, check the injection you have prepared against the dose prescribed on the *Second-line TB treatment card*.
4. When the patient is ready, administer the injection intramuscularly.

It is assumed that participants in this training course know how to prepare and give a sterile injection; therefore, the preparation of injections will not be described in this module. However, there are a number of different injectable agents that can be used to treat DR-TB, and you should note the different instructions for diluting each agent.

Reconstituted injectable agents should be refrigerated and used within 24 hours and any unused amount should be discarded after this time-period.



Now do Exercise B – practical exercise

You are ready to do Exercise B. Tell your facilitator when you have reached this point. Turn to the relevant pages in the exercise section of this module to complete the exercise. When you have finished the exercise, discuss your answers with a facilitator.

7. Use good storage and management procedures for anti-TB medicines and supplies

Proper storage and management procedures are important for all medicines and supplies; second-line drugs require special attention because of the absolute need to ensure an uninterrupted supply and their high cost. If you handle medicines and supplies for TB treatment, do your part to ensure that good storage procedures are followed. If there are problems that you are not able to correct, talk to the person responsible in the DR-TB management centre.

7.1 Keep medicines safe and secure

Keep stocks of anti-TB medicines safe in the main storeroom; this should be locked when not in use. Access to this storeroom should be limited to the one or two people who are responsible for managing it. These people will be the pharmacist at the DR-TB management centre or another authorized person, or both.

Keep medicines safe:

- from theft – always keep the storeroom locked; restrict access only to authorized people;
- from fire – keep a fire extinguisher handy;
- from moisture, leaks and other forms of water exposure – stock should be placed on shelves or pallets, raised off the floor and not stacked against the wall;
- from pests – fumigate periodically and ensure that pests are controlled.

7.2 Organize medicines and supplies

Place anti-TB medicines in the storeroom on shelves organized by type of medicine. Arrange each type of medicine by expiry date: medicines that will expire soonest should be placed in front of those that will expire later. When you take stock from the shelves, use those medicines

that will expire first. These procedures follow the FEFO rule, and if medicines that will expire sooner are placed in front, they are easier to identify.

It is important to have bin cards in the storage area, which indicate the stock levels of drugs in a particular section. The bin card needs to be updated as soon as a drug is added/removed from the shelf where it is stored.

7.3 Monitor storeroom conditions

Keep the temperature, light and humidity in the main storeroom moderate. Although anti-TB medicines are stable, a storeroom should not be excessively hot or humid, or be exposed to direct sunlight because extremes may cause some medicines to spoil before their expiry date. For instance, some tablets, such as ethambutol, absorb humidity and deteriorate.

No one should eat, drink or smoke where medicines are stored. Do not keep food or drink in the storeroom. This will help keep the storeroom clean and free of pests. For some examples of storage recommendations, please see *Table 4* below.

The recommendations for cycloserine are fairly strict with regard to the maximum temperature under which it is stored.

7.4 Recognize and correct storage problems

Every box and vial must have a label with the expiry date of the medicine. If you identify expired medicines at the DR-TB management centre, notify the centre's pharmacist. Expired medicines should be stored separately from medicines that have not expired, and should be returned promptly to the central medical warehouse.

Periodically check the condition of anti-TB medicines (those kept in the storeroom and those on hand for patients) to identify any problems. When a problem is identified, correct it without delay. Collaborate with other staff, if necessary, to improve storage conditions.

8. Other supplies

There are several other items that have to be managed at a DR-TB management centre and a list has to be prepared and approved by the concerned authorities. A practice session on calculating the need for such supplies can be held separately but the principles of quantification remain the same as those for drugs. The following suggested steps need to be followed:

1. Calculate the daily/weekly need based on consumption pattern.
2. Project for needs for three months (quarterly need).
3. Add the requirement of buffer stocks to account for possible delays in delivery for the next quarter or unforeseen increase in consumption.
4. Subtract the available stocks.

Some of the supplies that are essential for a DR-TB management centre include the following:

1. Ancillary medicines, such as antiemetics, analgesics and co-trimoxazole;
2. Medical supplies, such as syringes, gloves, surgical masks, needles and sterile water for injections;
3. Forms and registers;
4. PPE for the health workers, including N95 respirators;
5. Surgical masks for patients;
6. Disinfectants.

Table 4 Storage recommendations for medicines used to treat drug-resistant tuberculosis^a

Medicine	Storage recommendation^f
First-line medicines	
Ethambutol (E)	Store in original blister packs at room temperature (below 30 °C).
Pyrazinamide (Z)	Store in original blister packs at room temperature (below 30 °C).
Second-line medicines	
Amikacin (Am)	Store vials at room temperature (below 30 °C); once reconstituted, vials should be kept refrigerated and used within 24 hours.
Amoxicillin/clavulanate (Amx/Clv)	Store in original blister packs at room temperature (below 25 °C).
Capreomycin (Cm)	Store vials at room temperature (below 30 °C); once reconstituted, vials should be kept refrigerated and used within 24 hours.
Clarithromycin (Clr)	Store in original blister packs at room temperature (below 25 °C).
Cycloserine (Cs)	Store in airtight containers at room temperature (below 25 °C).
Ethionamide (Eto)	Do not store with other medicines (this medicine has a strong odour). Store at room temperature (below 25 °C).
Kanamycin (Km)	Store vials at room temperature (below 25 °C); once reconstituted, vials should be kept refrigerated and used within 24 hours.
Levofloxacin (Lfx)	Store in airtight containers protected from light at room temperature (below 25 °C).

Continues...

^f The storage temperatures here are indicative only. Depending on the stability data of the product, some manufacturers may recommend a storage temperature of less than 30 °C.

Continued from previous page

Medicine	Storage recommendation
Moxifloxacin (Mfx)	Store in airtight containers protected from light at room temperature (below 25 °C).
Ofloxacin (Ofx)	Store in airtight containers protected from light at room temperature (below 25° C).
Para-aminosalicylic acid (PAS)	Store in the refrigerator or freezer; do not use if granules turn purple or dark brown.
Para-aminosalicylic sodium (PAS Na)	Store at room temperature (below 25 °C); do not use when sachets are bloated or granules turn purple or dark brown.
Prothionamide	Store in airtight containers at room temperature (below 25 °C).

^a The list does not include Group 5 drugs.



Now do Exercise C – pair exercise and group discussion

You are ready to do Exercise C. Tell your facilitator when you have reached this point. Turn to the relevant pages in the exercise section of this module to complete the exercise with your neighbour. When you have finished the exercise, the facilitator will start a group discussion on storage conditions.

Summary

- Essential medicines and other supplies for detecting and treating DR-TB patients at DR-TB management centres include the following:
 - second-line drugs for treatment (sufficient quantities of oral medicines for regimens plus injectable agents);
 - ancillary medicines, such as antiemetics, analgesics and co-trimoxazole;
 - medical supplies, such as syringes, gloves, surgical masks, needles and sterile water for injection;
 - sputum containers;
 - DR-TB forms and registers;
 - PPE for health workers.
- When the treatment of DR-TB patients is decentralized to local health facilities, those facilities should be prepared for continued treatment of the patient and provided with the medicines used in each patient's regimen and a copy of the patient's *Second-line TB treatment card*.
- A number of different medicines are used to treat patients with DR-TB, including first-line and second-line anti-TB medicines. Unlike the medicines used for new-patient regimens and retreatment regimens, **fixed-dose combination** (FDC) tablets are **not** available to treat DR-TB. Instead, formulations of single medicines are used in DR-TB treatment. This

means that patients take a large number of pills, which increases the importance of direct observation to ensure that the patient takes the full dose of all medicines.

- Be sure that enough medicines are in stock each **quarter** for all DR-TB patients being treated at your DR-TB management centre and in the local health facilities to which patients have been decentralized.
- There are two steps that have to be taken when requesting second-line drugs for the DR-TB management centre.
 1. Determine the quantity of second-line drugs used each quarter:
 - calculate the DAILY quantity of each medicine consumed by all patients receiving it;
 - calculate the MONTHLY quantity consumed by multiplying daily consumption by 26 days;
 - calculate the QUARTERLY consumption by multiplying the monthly consumption by 3.
 2. Determine the quantity of second-line drugs to order for the DR-TB management centre by completing the TB medicine requisition form:
 - list the medicines to be ordered and the quantity consumed QUARTERLY for each medicine;
 - add the quantity of each medicine consumed in 1 month to provide buffer stock;
 - subtract the quantity of each medicine that you have in stock;
 - the result is the quantity you need to order.
- When you receive a delivery, check that the correct medicines have been received in the correct quantities and that their expiry dates will allow all medicines to be used in a timely fashion. If incorrect medicines have been delivered or if there are other problems with the order, address the problems by requesting the missing medicines and returning any extra or expired medicines that were sent in error. If there are no discrepancies, sign the receipt; if there are problems with the order, ensure that these are noted on the receipt before you sign it.
- When the treatment of a patient is decentralized, the DR-TB management centre sends the local health facility enough anti-TB medicines to treat the patient **for the days remaining in the quarter plus 1 month's buffer stock**. Thereafter, the DR-TB management centre will send one quarter's supply each quarter.
- There are a number of instances when the pharmacy at the local health facility may have more than the expected quantities of drugs at hand, as in the following instances:
 - a patient's regimen is changed;
 - a patient is lost to follow up;
 - a patient dies;
 - a patient finishes treatment;
 - medicines expire;
 - medicines are damaged.
- A large number of sputum containers are needed for diagnosing and following up on DR-TB patients. Calculate the total number of sputum containers you need to order for the quarter as follows:
 - use the number needed for diagnosis or baseline investigation;
 - add the number needed for follow-up examinations;
 - add 10% for additional investigations;

- add 20% for reserve stock;
- subtract the number of sputum containers in stock at the end of the previous quarter.
- On a designated day of the week, a nurse or pharmacist will prepare **1 week's supply** (6 days) of daily doses of medicine for every DR-TB patient being treated by the facility.
- Prepare the injectable agent each day that the patient arrives for treatment. Always use the *Second-line TB treatment card* as a guide when preparing the injectable agent.
- Place anti-TB medicines in the storeroom on shelves organized by type of medicine. Arrange each type of medicine by expiration date: medicines that will expire soonest should be placed in front of those that will expire later. When you take stock from the shelf, use those medicines that will expire first. These procedures follow the FEFO rule, and if medicines that will expire sooner are placed in front, they are easier to identify.

Self-assessment questions

Answer the self-assessment questions below to check what you have learnt. Then compare your answers to those on pages F-31–F-33.

1. Fill in the blanks.

As a first step towards calculating the number of medicines to order each quarter, determine the total consumption for each medicine daily, monthly and quarterly.

- 1) Using the _____ for each patient being treated at the DR-TB management centre, record the medicines taken each day by each patient.
- 2) Using the _____ for each decentralized patient being treated at a local health facility in the DR-TB management centre’s catchment area, record the medicines taken each day by each patient.
- 3) Calculate the DAILY consumption of each medicine by all patients receiving it by:
 - 4) Calculate the MONTHLY consumption by multiplying the daily consumption by _____ days.
 - 5) Calculate the QUARTERLY consumption by multiplying the monthly consumption by _____.
2. The quantity of second-line drugs that should be ordered each quarter depends on the quarterly consumption of the patients enrolled at your facility and another piece of information. What is that information?
3. Look at the following patient’s *Second-line TB treatment card* and list the medicines that the patient should have in each daily medicine packet.

Date	Z	E	Km	Am	Cm	Lfx	Mfx	Pto/Eto	Cs	PAS
15/05/10	3		1			4		3		2
12/02/11			X			4		3		2

Is this patient in the intensive or continuation phase of treatment? _____

4. List the supplies critical to managing DR-TB (other than medicines) that should be stocked at a DR-TB management centre and at local health facilities that care for decentralized patients with DR-TB.
 - For sputum examination: (1 item)

 - For injections: (3 items)

 - Forms and registers: (4 items for DR-TB management centres and 3 for local health facilities that care for decentralized patients)

5. Write “T” for true or “F” for false by the following statements:
 - _____ Every time the treatment of a patient is decentralized from the DR-TB management centre, enough medicines for 1 month of treatment should be sent to the local facility.
 - _____ DR-TB patients will take their medicines 6 days a week throughout treatment.
 - _____ PAS acid, if used, needs to be refrigerated, and cannot be stored with other medicines at room temperature.
 - _____ Second-line drugs need to be returned by the local health facility to the DR-TB management centre when the medicines have expired or are damaged.
 - _____ DR-TB patients are allocated an entire supply of medicines for the intensive phase of treatment until the injectable agent is discontinued.

6. When taking medicines off the shelf, use those that will expire _____.

Now compare your answers with those on the next page.

Answers to self-assessment questions

If you had difficulty in answering any question, turn back and study the section indicated. If you do not understand something, discuss it with a facilitator.

1. Fill in the blanks.

As a first step towards calculating the number of medicines to order each quarter, determine the total consumption for each medicine daily, monthly and quarterly.

- 1) Using the Second-line TB treatment card for each patient being treated at the DR-TB management centre, record the medicines taken each day by each patient.
- 2) Using the Second-line TB treatment card for each decentralized patient being treated at a local health facility in the DR-TB management centre's catchment area, record the medicines taken each day by each patient.
- 3) Calculate the DAILY consumption of each medicine by all patients receiving it by: *adding the total number of pills of the particular medicine being consumed by all patients each day.*
- 4) Calculate the MONTHLY consumption by multiplying the daily consumption by 26 days.
- 5) Calculate the QUARTERLY consumption by multiplying the monthly consumption by 3. (See section 4.1.)

2. The quantity of second-line drugs that should be ordered each quarter depends on the quarterly consumption of the patients enrolled at your facility and another piece of information. What is that information?

The stock on hand (See section 4.2.)

3. Look at the following patient's *Second-line TB treatment card* and list the medicines that the patient should have in each daily medicine packet.

Date	Z	E	Km	Am	Cm	Lfx	Mfx	Pto/Eto	Cs	PAS
15/05/10	3		1			4		3		2
12/02/11			X			4		3		2

Each packet should contain: 3 tablets of Z, 4 tablets of Lfx, and 3 tablets of Pto. PAS (2 sachets) are not put into the daily packet because they must remain refrigerated.

Is this patient in the intensive or continuation phase of treatment? _____

This patient is in the continuation phase. You can see this because the injectable agent was stopped and the patient has been on treatment for 9 months. (See Module C.)

(See section 6.)

4. List the supplies critical to managing DR-TB (other than medicines) that should be stocked at a DR-TB management centre and at local health facilities that care for decentralized patients with DR-TB.

- For sputum examination: (1 item) *sputum containers*
- For injections: (3 items)
needles, syringes and sterile water for injection
- Forms and registers: (4 items for DR-TB management centres and 3 for local health facilities that care for decentralized patients)

At a DR-TB management centre:

- *DR-TB screening form*
- *Request for examination of biological specimen for TB*
- *Second-line TB treatment card*
- *DR-TB daily attendance sheet*
- *Second-line TB treatment register*
- *TB medicine requisition form*
- *TB medicine return form*
- *Tuberculosis referral/transfer form*

At a local health facility:

- *Presumptive DR-TB referral form*
- *Request for sputum examination for smear, culture and DST*
- *Second-line TB treatment card*
- *TB medicine return form*

(See section 5.)

5. Write “T” for true or “F” for false by the following statements:

 F Every time the treatment of a patient is decentralized from the DR-TB management centre, enough medicines for 1 month of treatment should be sent to the local facility.

(Medicines for the rest of the quarter should be sent – that is, the remaining doses for the current month, plus 26 doses for each full month remaining in the quarter, plus 1 month’s buffer stock.)

 T DR-TB patients will take their medicines 6 days a week throughout treatment.

 T PAS acid, if used, needs to be refrigerated, and cannot be stored with other medicines at room temperature.

 T Second-line drugs need to be returned by the local health facility to the DR-TB management centre when the medicines have expired or are damaged.

(However, in certain countries, the policy may be to destroy the medicine at the facility after notifying the DR-TB management centre about the expiry or damage.)

 F DR-TB patients are allocated an entire supply of medicines for the intensive phase of treatment until the injectable agent is discontinued.

(Because of the large number of medicines needed, it is not feasible to prepare medicine boxes for DR-TB patients which hold all the medicines needed for the intensive phase. Instead, the nurse or pharmacist prepares a 1-week supply in daily packets and places the packets in a pouch with the patient's name on it.)

6. When taking medicines off the shelf, use those that will expire first (See section 7.2.).



The End

Congratulations on finishing this module!

Exercises for Module F: Manage medicines and supplies for DR-TB

Exercise A

Written exercise: Determine the quantity of second-line drugs to order

In this exercise, you will determine the quantity of medicines that need to be ordered for the DR-TB patients being treated at your DR-TB management centre.

- Three DR-TB patients are currently being treated at your DR-TB management centre. Excerpts from their *Second-line TB treatment cards* are shown on the next page. Review each patient's treatment regimen and use the worksheet to calculate the current consumption of second-line drugs at your DR-TB management centre.

Worksheet: Calculate current consumption of second-line drugs

Patients	Drugs used to treat RR/ MDR-TB patients									
	Z 500 mg	E 400 mg	Km 1 g	Cm 1 g	Lfx 250 mg	Mfx 400 mg	Pto 250 mg	Cs 250 mg	PAS 4 g	B6 50 mg
1- CC										
2- JB										
3- JV										
4										
5										
6										
Daily total (sum)										
Monthly (daily x 26)										
Quarterly (monthly x 3)										

Patient CC

Second-line Treatment Regimen (Date treatment started and dosage (mg), change of dosage and cessation of drugs):															
Date	H	R	E	S	Z (500mg)	Amik (vial - 1 g)	Km (vial - 1 g)	Cm	FQ (250 mg)	Pto/Eto (250 mg)	CS (250 mg)	PAS	Other	Other	Comments
4/12/2013					3 tab		1 vial		Lfx 4 tab	Pto -3 tab	3 cap				

Patient JB

Second-line Treatment Regimen (Date treatment started and dosage (mg), change of dosage and cessation of drugs):															
Date	H	R	E	S	Z (500mg)	Amik (vial - 1 g)	Km (vial - 1 g)	Cm	FQ (250 mg)	Pto/Eto (250 mg)	CS (250 mg)	PAS	Other	Other	Comments
8/07/2012			3		4 tab		1 vial		Lfx 4 tab	Pto -3 tab	3 cap				
10/03/2013			3		4 tab				Lfx 4 tab	Pto -3 tab	3 cap		2		Continuation phase

Patient JV

Second-line Treatment Regimen (Date treatment started and dosage (mg), change of dosage and cessation of drugs):															
Date	H	R	E	S	Z (500mg)	Amik (vial - 1 g)	Km (vial - 1 g)	Cm	FQ (250 mg)	Pto/Eto (250 mg)	CS (250 mg)	PAS	Other	Other	Comments
12/01/2013			3		4 tab		1 vial		Lfx 4 tab	Pto -3 tab	3 cap				
4/03/2013			3		4 tab		1 vial		Lfx 4 tab	Pto -3 tab		2 sac			Adv effect to Cs

2. Complete the *TB medicine requisition form* below based on the current consumption. Today's date is 1 June 2013. You are preparing a request for the medicines only for these three patients. The stock on-hand at your DR-TB management centre is shown below.

- | | |
|--------------------------|--------------------------|
| Z 500 mg – 107 tablets | Pto 250 mg – 126 tablets |
| E 400 mg – 110 tablets | Cs 250 mg – 102 capsules |
| Km 1 g – 46 vials | PAS 4 g – 55 sachets |
| Lfx 250 mg – 132 tablets | B6 50 mg – 0 tablets |
| Mfx 400 mg – 113 tablets | |

TB medicine requisition form

Requesting facility: Rose DR-TB management centre Date requested: _____

For the month/s of: _____

#	Description (Please specify preparation of drug)	Unit	Quarterly use	Buffer (1 month)	Quantity needed	On-hand	Quantity requested	Units per container	# Containers sent
			(a)	(b)	(c=a+b)	(d)	(e=c-d)		
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									
11									
12									

Requested by: _____
(Signature and printed name/date)

When you have finished this exercise, review your answers with a facilitator.
There will be a group discussion when everyone has finished.



GO BACK to section 5, and read until the next stop sign.

Exercise B

Practical exercise: Prepare daily medicine packets

In this exercise, you will practise preparing a week's supply of medicines using a patient's *Second-line TB treatment card*.

Patient's name: Jose Delgado. Second-line drugs registration number: kk-08-13

Your facilitator will tell you which medicines Mr Delgado takes.

Your facilitator will distribute second-line drugs to your group. Refer to Mr Delgado's *Second-line TB treatment card* below so that your group can prepare 6 individual packets. Each participant should make at least one packet.

Place the packets in a medicine pouch. Label the medicine pouch.

Excerpt from page 2 of the *Second-line TB treatment card* of Jose Delgado

Second-line Treatment Regimen (Date treatment started and dosage (mg), change of dosage and cessation of drugs):															
Date	H	R	E	S	Z (500mg)	Amik	Km (vial – 1 g)	Cm	FQ (250 mg)	Pto/Eto (250 mg)	CS (250 mg)	PAS	Other	Other	Comments
12/01/2013					3 tab		750 mg		Lfx 3 tab	Pto -3 tab	3 cap				
4/03/2013					3 tab		750 mg		Lfx 3 tab	Pto -3 tab		2 sac			Adv effect to Cs
15/09/2013									Lfx 3 tab	Pto -3 tab		2 sac			Cont phase

Show your prepared pouch with the packets to your facilitator when your group has finished.



GO BACK to section 7, and read until the end of the module.

Exercise C

Pair exercise and group discussion: Assess your own storage room and recommend improvements

For TB drugs to be safe and well kept, it is important to assess the storage room at your facility and, if necessary, discuss improvements.

Pair exercise:

Discuss the storage room(s) at your facility.

1. What does it look like?
2. Does it take into consideration any of the requirements that you have just learnt?
3. If yes, what is done appropriately?
4. If no, what could be improved?

Group discussion:

1. What are the main findings while discussing your storage rooms?
2. What needs improvement?



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