

Facilitator Guide

Management of Drug-resistant Tuberculosis and DOTS-Plus

2007

**Lesotho Ministry of Health and Social Welfare
Partners In Health**



Each participant should receive:

- 1 training **module** (*Chronic Care for MDR-TB*)
- 1 **Case Book** contains cases used for discussion throughout the course
- 1 **national MDR-TB guidelines**
- 1 **PIH Guide to the Medical Management of MDR-TB**

The following lectures will require an LCD projector and PowerPoint slide set:

- Day 1/Session 1: TB-HIV Epidemiology
- Day 1/Session 2: TB-HIV Co-management
- Day 1/Session 3: Introduction to MDR-TB
- Day 2/Session 2: Community-based Care for MDR-TB
- Day 2/Session 3: Second-line Anti-tuberculosis Drugs
- Day 2/Session 3: Constructing a Regimen
- Day 3/Session 2: MDR-TB in Pregnancy
- Day 3/Session 2: MDR-TB in Children
- Day 4/Session 1: Infection Control

Additional materials:

- **TB-HIV Co-management wallcharts.** This is a teaching aid and job aid. Post one up on the wall to use in Day 1/Session 2. and hand out the rest to be posted on the wall of the ART corner and TB corner at each hospital.
- **TB drug cards** (laminated): 5 sets per class
- **Side effect cards** (laminated): 10 sets per class
- National TB Programme **Category 4 Treatment Card** (card stock): one copy for each participant
- National TB Programme **Category 4 Follow-up Form** (paper): one copy for each participant
- **Dosing Job Aid** (laminated)

Maximum class size should be less than 15 participants. Two or more facilitators are recommended to provide enough supervision during the group sessions and case work.

We recommend separate classes for nurses and doctors, as we have found that nurses are find it difficult to discuss freely, particularly when doctors they work with daily are in the same classroom. Nurses and doctors may go into their separate classrooms after the first session on Day 1. We do not have separate classes for nurses and nurse assistants, even though the knowledge level may be quite different.

Schedule (for doctors)

Time	Day 1	Day 2	Day 3	Day 4
8:30 – 10:45	Day 1/Session 1: Introduction <ul style="list-style-type: none"> • Inauguration of Workshop • Introduction: TB and MDR-TB in Lesotho 	Day 2/Session 1: Initiation of MDR-TB therapy <ul style="list-style-type: none"> • High-risk and medium-risk patients • Standardized Cat 4 regimen 	Day 3/Session 1: Management of MDR-TB/HIV <ul style="list-style-type: none"> • Adverse effects • Common problems • IRIS 	Day 4/Session 1: Administration <ul style="list-style-type: none"> • Infection control • Roles and relationships
10:45 – 11:15	TEA BREAK	TEA BREAK	TEA BREAK	TEA BREAK
11:15 – 1:15	Pre-test Day 1/Session 2: TB-HIV co-management <ul style="list-style-type: none"> • Diagnosis of TB in high HIV settings • TB-HIV co-management 	Day 2/Session 2: Chronic care for MDR-TB <ul style="list-style-type: none"> • Community-based care for MDR-TB • Triage • Assess • Contacts 	Day 3/Session 2: Management of MDR-TB in special cases <ul style="list-style-type: none"> • Interpreting DST results • MDR-TB in pregnancy and children 	Day 4/Session 2: Recording and reporting <ul style="list-style-type: none"> • Category 4 Treatment Card • Category 4 Follow-up Form • Category 4 Register
1:15 – 2:30	LUNCH	LUNCH	LUNCH	LUNCH
2:30 – 4:30	Day 1/Session 3: Diagnosis of MDR-TB <ul style="list-style-type: none"> • Introduction to MDR-TB • Diagnosis of drug resistance 	Day 2/Session 3: Second-line anti-tuberculosis drugs <ul style="list-style-type: none"> • Classes of drugs • Constructing a regimen 	Day 3/Session 3: Adherence and social support <ul style="list-style-type: none"> • Adherence • DOTS-Plus treatment supporter • Incentives and enablers 	Day 4/Session 3: Closing <ul style="list-style-type: none"> • Post Test • Evaluation and certification
4:30 – 5:30	Question and answer session	Question and answer session	Question and answer session	Question and answer session / Departure

Schedule (for nurses)

Time	Day 1	Day 2	Day 3	Day 4
8:30 – 10:45	Day 1/Session 1: Introduction <ul style="list-style-type: none"> • Inauguration of Workshop • Introduction: TB and MDR-TB in Lesotho 	Day 2/Session 1: Diagnosis of MDR-TB: <ul style="list-style-type: none"> • Introduction to MDR-TB • Diagnosis of drug resistance 	Day 3/Session 1: Second-line anti-tuberculosis drugs <ul style="list-style-type: none"> • Classes of drugs • Constructing a regimen 	Day 4/Session 1: Administration <ul style="list-style-type: none"> • Infection control • Roles and relationships
10:45 – 11:15	TEA BREAK	TEA BREAK	TEA BREAK	TEA BREAK
11:15 – 1:15	Pre-test Day 1/Session 2: <ul style="list-style-type: none"> • Diagnosis of TB in high HIV settings 	Day 2/Session 2: Initiation of MDR-TB therapy <ul style="list-style-type: none"> • High-risk and medium-risk patients • Standardized Cat 4 regimen 	Day 3/Session 2: Management of MDR-TB/HIV <ul style="list-style-type: none"> • Adverse effects • Common problems • IRIS 	Day 4/Session 2: Recording and reporting <ul style="list-style-type: none"> • Category 4 Treatment Card • Category 4 Follow-up Form • Category 4 Register
1:15 – 2:30	LUNCH	LUNCH	LUNCH	LUNCH
2:30 – 4:30	Day 1/Session 3: TB-HIV co-management (cont.) <ul style="list-style-type: none"> • TB-HIV co-management 	Day 2/Session 3: Chronic care for MDR-TB <ul style="list-style-type: none"> • Community-based care for MDR-TB • Triage • Assess • Contacts 	Day 3/Session 3: Adherence and social support <ul style="list-style-type: none"> • Adherence • DOTS-Plus treatment supporter • Incentives and enablers 	Day 4/Session 3: Closing <ul style="list-style-type: none"> • Post Test • Evaluation and certification
4:30 – 5:30	Question and answer session	Question and answer session	Question and answer session	Question and answer session / Departure

Day 1/Session 1: Introduction

1. Make welcoming comments.
2. Give **lecture** "TB-HIV Epidemiology".

Day 1/Session 2: Review of TB-HIV Co-management

[Note: doctors and nurses may be separated at this point]

1. Give **Pre-test**.
2. Give **lecture** "TB-HIV Co-management".

Diagnosis of TB in high HIV settings

3. Ask a volunteer to pretend they are coaching a patient to give a sputum sample. Ask the others if there is anything else they would add to the coaching. Discussion points:
 - a. How do you know if a sputum sample is "good" or not?
4. Read and discuss **Annex A.5** (*How to collect sputum samples*). Discussion points:
 - a. What do you do if the patient says he cannot make sputum?
 - b. Who should coach patients? [all health workers, not just lab technicians]
 - c. How many sputum samples are needed? [For diagnosis, three samples: preferably "spot-morning-spot". For monitoring, two samples.]
 - d. What should we do if the patient lives far away and is unlikely to return? [We may keep the patient in the clinic for several hours and try a "spot-spot-morning" sampling. Then if the first two samples are positive, the morning sample will not even be necessary to start treatment.]
5. What is "smear-negative TB"? ["Smear-negative" means that the sputum smear is negative, but the patient still has pulmonary TB. The sputum smear is not always positive; the laboratory technician can see TB mycobacteria only when there is a high concentration in the sputum. The sputum can be smear-negative but culture-positive.]
6. Review again the statistics from the presentation about the percentage of smear-negative TB patients in HIV-negative (25%) and HIV-positive (45%). Why is it higher in HIV-positive patients? [bacillary load is lower; less cavities where bacilli reside]

7. Discuss the diagnosis of TB:
 - a. Write "TB suspect" on the flipchart and ask, "What is a TB suspect"? [cough more than 2 weeks].
 - b. Ask, "What should we do with a TB suspect?" [send 3 sputum samples for smear microscopy—spot-morning-spot; offer HIV testing; and treat with broad-spectrum antibiotics.]
 - c. Ask, "What do we do if all three sputum samples are negative?" [If the patient is HIV-positive, and has not responded to antibiotics, and request x-ray. If the patient is HIV-negative, send three more sputum samples.]

TB-HIV Co-management

For this part, have the class stand up and go over to where the **TB-HIV Co-management wallchart** is posted. You can read and discuss the points while standing. This reinforces the use of the wallchart as a job aid. Each clinical team should receive a copy to post on the clinic wall.

8. Have a volunteer read point 1 of **TB-HIV Co-management wallchart** (*Offer HIV testing and counseling to all TB suspects*) aloud to the class. Discussion points:
 - a. Why is HIV testing important for TB patients?
 - b. What percentage of TB patients are HIV positive?
 - c. How many TB patients do you have each quarter? How many of them are tested for HIV? [Keep brief the discussion about why TB patients are not tested for HIV, but explain that community counselors can be very helpful in this regard.]
 - d. When should TB patients tested for HIV? [HIV testing needs to happen immediately, since otherwise co-infected patients will not get CTX or ART in time. The national guidelines say that all TB suspects should be tested for HIV, which means that TB patients should already be tested, even before they start TB treatment.]
 - e. Ask someone to show the class how to offer a patient an HIV test. If review is needed, have the class turn to **Annex A.1** (*Offer HIV counseling and testing*). The three parts of HIV pre-test education are: (1) HIV information, (2) explain that the results will be confidential, (3) obtain consent. In Lesotho, the last requires a written consent form.
9. Have a volunteer read point 2 of **TB-HIV Co-management wallchart** (*Start TB treatment immediately*) aloud to the class. Discussion points:
 - a. Why is it important not to wait to start TB treatment?
 - b. Why should you change the ART regimen to EFV?

10. Have a volunteer read point 3 of **TB-HIV Co-management wallchart** (*Give cotrimoxazole prophylaxis to all TB-HIV co-infected patients*) aloud to the class. Discussion points:
- Why is this important? [Prevention of opportunistic infections.]
 - Which patients should receive CTX? [Answer: all patients, irrespective of CD4]
 - What is the correct dosing of CTX?
 - Have a volunteer read **section 5.1** of *Chronic Care for MDR-TB*. Discuss the management of side effects of CTX.
11. Have a volunteer read point 4 of **TB-HIV Co-management wallchart** (*Start ART when appropriate*) aloud to the class. Discussion points:
- What is the correct ART regimen for a patient receiving Category 1? [Patients receiving NVP should not receive R, because of interactions—make sure they all understand this point]
12. Have a volunteer read point 5 of **TB-HIV Co-management wallchart** (*Prevention for PLHIV*). Explain that health care workers can play an important role in prevention for positives. Ask a volunteer to explain why different interventions are important.
13. Have three different volunteers explain what is going on in each of the three options in **TB-HIV Co-management wallchart**. Have them explain the reason for the timing in each option. [Make sure to mention that EFZ is not needed in option 3 because there is no interaction with R].
14. Discuss the following exercises (all these exercises are at the end of the lecture entitled, "TB-HIV Co-management"). Read the description and ask what should be done next. In the first set of exercises, CD4 is not available. In the second set of exercises, CD4 is available. [CD4 may not be available sometimes even at the district hospital.]

Exercise (CD4 not available)	Plan
1. A patient in HIV Care, clinical stage 2, on co-trimoxazole prophylaxis then develops positive sputums. No previous TB or ART treatment and no other signs clinical stage 3 or 4.	Start Category 1. Do not start ART now. Reassess patient at end of intensive phase whether to start ART after intensive phase or after finishing TB treatment.
2. A patient comes to the clinic with cough and fever. Sputum smears are positive. He was previously treated for TB at your health center last year. He also started on ART at that time, but	Start Category 2. Adherence counseling. Reassess patient at end of intensive phase. (Could also start after 2 weeks, since presumably

stopped taking it. He has no other symptoms.	CD4 was probably < 200 before)
3. A patient was diagnosed with pulmonary TB and HIV at the same time. She has oral thrush. She says she has persistent diarrhea and has lost weight.	Start Category 1. Start ART as soon as patient tolerates TB treatment.
4. A patient comes to the clinic saying he was diagnosed and treated for TB meningitis in the hospital for 2 months, and was discharged yesterday with instructions to continue TB treatment at the health center. He has never had an HIV test in his life. You offer him one and it is positive.	Continue Category 1. Start ART as soon as patient tolerates TB treatment.

Exercise (CD4 is available)	Plan
1. An HIV-positive patient is currently in month 2 of Category 1 treatment and doing well. Her CD4 is 75.	Start ART as soon as patient tolerates TB treatment.
2. A patient in HIV Care, clinical stage 2 and CD4 250. Now diagnosed with smear negative pulmonary TB and started on Category 1.	Start ART as soon as patient finishes intensive phase.
3. A patient in HIV Care, CD4 400. Has just started Category 1 treatment.	Start ART after finishing TB treatment.
4. A patient is diagnosed with TB and HIV at the same time and is currently on Category 1 treatment. He has oral thrush and persistent diarrhea. CD4 is 300.	Start ART after intensive phase of TB treatment. (Stage 3 unless HIV wasting syndrome)

15. Have the class break up into pairs. Hand out the case description, allows several minutes for discussion, then ask for a volunteer group to present their treatment plan to the whole group. Discuss. Repeat with another case as time allows. Use Cases 1-4 in the **Case Book**.

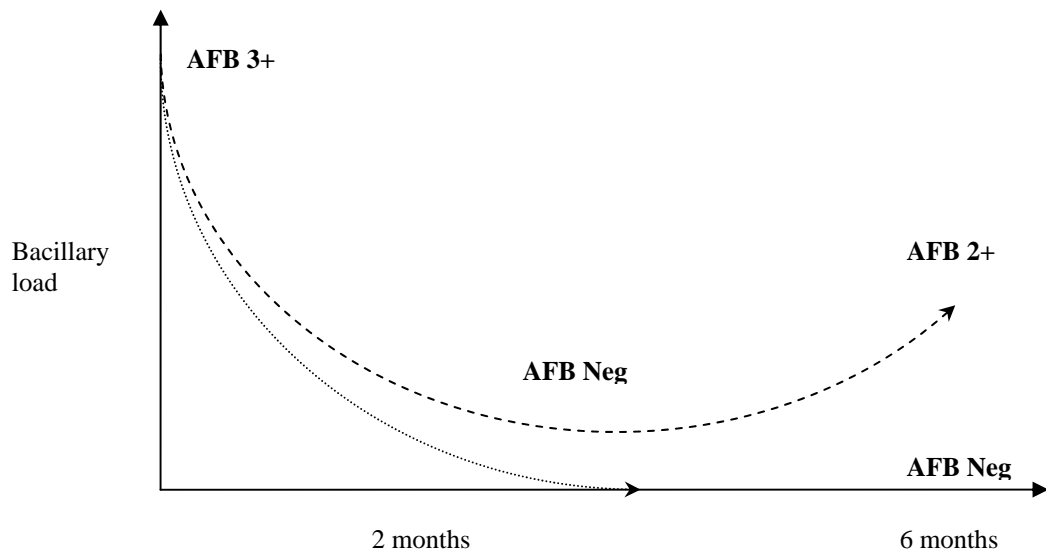
Discussion points
Case 1: Category 1 (ART after intensive phase, or when CD4 is back)
Case 2: CTX, 2 sputum smears (for monitoring, not for diagnosis)
Case 3: Category 1, CTX, ART co-treatment Option 1 (as soon as TB treatment tolerated), pregnancy test
Case 4: Category 2, ART co-treatment Option 3 or 2 (after completion or after intensive phase), treatment supporter/intensive adherence counseling

Day 1/Session 3: Diagnosis of Drug Resistance

1. Give **lecture** "Introduction to MDR-TB".
2. What is TB culture?
 - a. What is DST?
 - Drug
 - Susceptibility (or Sensitivity)
 - Testing
 - b. What is the difference between culture and smear? [In sputum smear microscopy, the laboratory technician looks for mycobacteria, so if there are very few, it may be impossible to see. In the culture, the mycobacteria grow over several weeks, so the number of mycobacteria increases and can be easily seen.]
 - c. Can the smear be negative but culture positive? [Yes. Culture is more sensitive than smear.]
3. For culture and DST, two sputum samples are needed, but do not keep for more than 72 hours. [We are currently sending samples on Wednesday to Pretoria, so sample collection should be timed. When culture and DST are done in Maseru, this will not be a problem.]
 - a. Who can request culture and DST? [Every clinician (including nurses and nurse assistants) can request culture and DST. The important thing is that the cases meet clinical criteria—will be discussed later.]
 - b. When will we be able to do culture and DST in Maseru? [We will be doing culture in QE2 by August 2007. DST will take longer, but hopefully by the end of the year.]
4. Pass out smear/culture/DST form and discuss.
5. Have a volunteer read **section 5.2** of *Chronic Care for MDR-TB (Start empiric regimen in patients at risk for drug resistance)*. Discuss the different cases in this table, and why each needs culture and DST.
6. Read and discuss **section 5.1** (*Treatment categories*). [Major change in NTP guidelines for 2007: Cat 4 for failures of Cat 1.]
 - a. Can patient be failure of Category 1 and have drug-sensitive TB? This is very unlikely IF the patient has been taking medications regularly. If the medical officer thinks that the patient has not been taking medications regularly, the

medical officer may send culture and DST and start Category 2 treatment, which reinforced measures to ensure adherence.

- b. [Optional: discuss the following diagram. These are two patients taking Category 1 treatment. The dotted line is a patient who being cured; the dashed line is a patient who is failing. In each patient, the second month smear is negative. The bacillary load falls and then rises by the end of treatment, which is how a patient can become smear negative and then smear positive at the end of treatment. There are two common reasons why this happens: non-adherence and drug resistance. If the DOTS programme is weak, the former is probably more likely than the latter—but the former can create the latter. Re-infection in this short a period is unlikely. (In reality, patients on Category 1 become smear negative more quickly than in this diagram, but it is drawn this way for clarity.)]



7. Read the following case descriptions and ask the class if culture and DST should be sent for the patient.

Exercise	Culture and DST?
1. 22 year old man, HIV-positive, with smear-positive TB. Has never received treatment for TB.	No. [Cat 1]
2. 35 year old nurse at a health centre near the hospital. HIV-negative. No previous treatment for TB.	Yes. [Cat 1]
3. 18 year old woman with productive cough for 2 months. Smear-negative and diagnosed with TB by chest x-ray. HIV-positive. No previous treatment	No. [Cat 1]

TB.	
4. 5 year old daughter of a patient currently in treatment for MDR-TB. Sputum smear positive. HIV-negative.	Yes. [Cat 4]

8. Have the class break up into pairs. Hand out the case description, allow several minutes for discussion, then ask for a volunteer group to present its treatment plan to the whole group. Discuss. Repeat with another case as time allows. Use Cases 5-8 in the **Case Book**.

Discussion Points

Case 5: 18 year old woman just released from the hospital with TB meningitis.

Start ARV now (option 1); HIV testing for husband and children; TB screening of children. Needs reliable contraceptive method in addition to condoms because will be on EFZ.

Case 6: 32 year old HIV+ man in 3rd month.

CD4 is more important than in other cases because he may be failing treatment; start ART now if no CD4; continue current treatment regimen; look for other causes of night sweats and dry cough; no need for culture and DST according to guidelines (but ok to send if you think the patient is worse).

Case 7: 40 year old nurse with smear negative TB

Start Category 1; send culture/DST; offer HIV testing.

Case 8: 19 year old woman who has just finished Category 1 treatment.

Start Category 2; send culture/DST; strongly recommend HIV testing.

Day 2/Session 1: Initiation of MDR-TB therapy

1. Read **Section 5.3** of the *Chronic Care for MDR-TB*. Discussion points:
 - a. What is the difference between high-risk and medium risk? [High-risk patients should be started on a standardized Category 4 regimen.]
 - b. What is the difference between a standardized Category 4 regimen and an individualized Category 4 regimen? [An individualized Category 4 regimen is any regimen different from the standardized regimen. Doctors may prescribe an individualized regimen based on DST results, or based on the past TB treatment history for patients who have taken strange regimens including second-line drugs (chronic patients). Standardized regimens are for patients who have just received Category 1 or 2 and who do not have DST results yet—they are based on surveys of drug resistance. Patients who are started on a standardized Category 4 regimen are changed to an individualized Category 4 regimen when the DST results are available.]
 - c. What is the difference between first-line and second-line drugs? [First-line drugs are used in Category 1 and 2.]
2. Read the table in **Section 5.2** again, this time focusing on which types of patients should receive an standardized Category 4 regimen, and which a Category 1 or 2 regimen.
3. Read the criteria for use of a standardized Category 4 regimen (**Section 5.4**). Ask participants why these patients should not receive the standardized regimen.
 - a. Pregnancy: certain second-line drugs cause birth defects; injectable drugs can affect the foetal ear; ofloxacin is probably fine.
 - b. Chronic liver disease: second-line drugs can be toxic to the liver (even though Z is probably more hepatotoxic than the second-line drugs); will probably use the same regimen, but with very close follow-up.
 - c. Chronic illness: particularly those with kidney disease or diabetes may need to have special renal dosing of second-line TB drugs.
 - d. Household contacts: regimen should be based on DST of index case.
 - e. Chronic cases who have received second-line drugs before: very difficult; recommend they call Botsabelo.
4. Who will be able to start Category 4 regimens?
 - a. What is the role of Botsabelo Hospital and which patients should be started there? [inpatient ward for sick patients, attachments for district doctors and nurses, supervision of district hospital clinical teams]
 - b. What type of patients should be referred to Botsabelo Hospital? [seriously ill patients. Even patients who need individualized treatment can be managed at district level.]

c. [The roles and responsibilities of the different levels of the health system will be discussed in more detail later in the course.]

5. Read the following descriptions to the class. Should the patient receive a standardized or individualized regimen?

Exercise	What regimen?
18 year old failure of Category 1.	Standardized Cat 4
45 year old man with history of multiple defaults, currently receiving Category 2. DST shows MDR-TB.	Individualized Cat 4
12 year old son of a patient with documented MDR-TB.	Individualized Cat 4
22 year old pregnant woman who is sputum smear positive in 5 th month of Category 1.	Individualized Cat 4

6. Have the class break up into pairs. Hand out the case description, allow several minutes for discussion, then ask for a volunteer group to present their treatment plan to the whole group. Discuss. Repeat with another case as time allows. Use Cases 9-11 in the **Case Book**.

Discussion Points

Case 9: Individualized Category 4 regimen based on DST of husband. Continue same ARV regimen for both, since MDR-TB treatment does not include Rifampicin. Send two sputum samples for culture/DST.

Case 10: Standardized Category 4 regimen because this is a treatment failure. Send two sputum samples for culture/DST.

Case 11: (based on a patient from Leribe Hospital) Standardized Category 4 regimen, then change to individualized when DST comes back. If we follow strict national guidelines, this patient is not a failure of Category 2 yet. However, if the medical officer has excluded all other possible causes of respiratory failure, he can call this patient a clinical failure and start a Category 4 regimen.

Day 2/Session 2: Chronic care for MDR-TB

1. Give **lecture**: “Community-based Care for MDR-TB”

2. Read **page 8-9** of *Chronic Care for MDR-TB*. Explain that this diagram explains what should happen on every visit to the health facility. Read the bold headings on each step, then have a volunteer read the bullet points under each step.
 - a. What can be done by a nurse, and what can be done by a doctor? [Look at the symbols on the left side of the page.]
 - b. This describes the facility follow-up visits. Where is community support indicated on this diagram? [In the middle]
 - c. The treatment supporter is very much involved during the facility follow-up visits. In which steps? [1, 2, 8]

3. Read **Section 1** (*Triage*). Key points (will discuss the infection control issues later, so don't spend too much time on those):
 - a. Patient comes with the treatment supporter to all clinical consultations.
 - b. Smear-positive patients should be seen first.
 - c. Smear-positive patients should not be seen in ART corner.
 - d. Separate MDR-TB treatment card kept by the facility, so need to fetch it when the patient comes for the monthly consultation.

4. Read **Section 3** (*Assess*).
 - a. Discuss the questions in **section 3.1** and the reasons for asking them. [looking for side effects of second-line drugs and ART.]
 - b. Why is asking about alcohol abuse important? [can be related to non-adherence, or depression]
 - c. Discuss the exam in **section 3.2** and the reasons for looking for these things. [Looking for major side effects. This lists what nurses should do, but doctors may do more.]
 - d. Why is it important to weigh the patient on every visit?
 - e. Discuss the clinical and lab follow-up in **section 3.3**.

5. Read **Section 4** (*Assess Family Status*). If participants do not understand family planning methods, have the class turn to **Annex A.4** (*Family Planning*) and review the various methods. Discussion point:
 - a. Female patients should be asked about family planning on every visit. Why is it important that women do not become pregnant on second-line TB drugs? [Birth defects, but more importantly, the stress of pregnancy can lead to respiratory distress and death, particularly in severely ill patients.]
 - b. Most of the methods in Annex A.4 are available in Lesotho. Injectable contraceptives are preferred. [For hospitals where pregnancy tests and injectable contraceptives are not readily available, will try to package them into the drug packages for each patient.]

6. Read and discuss the part of Section 4 that concerns screening of household contacts.
 - a. What is the difference between TB infection and TB disease? [Most people infected with TB are asymptomatic (and non-infectious). Only 10% of HIV-negative people infected with TB will develop active TB disease (cough, fever, night sweats, etc.) in their lifetimes. It is much higher for people living with HIV who are infected with TB—about 50% of developing active TB during their lifetimes.]
 - b. What is a "household contact"?
 - c. How should we screen household contacts for MDR-TB?
 - i. Screen for respiratory symptoms
 - ii. Symptomatic household contacts should receive smear, culture and DST.
 - iii. Asymptomatic household contacts should still get a chest x-ray, particularly if they are HIV+. Keep these in the patient's file for the future, in case the contact becomes sick and you need a baseline x-ray to compare.
 - d. Don't forget screening household contacts for HIV as well as TB

Day 2/Session 3: Second-line anti-tuberculosis drugs

1. Give **lecture** "Second-line anti-tuberculosis drugs". [may skip this lecture for nurses]
2. Do the **Second-line Drug Game**: Divide into groups of 3. Each group should get one of each card. There are 16 total.
 - a. Hold up the first-line drugs. [5 including streptomycin]
 - b. Hold up the injectable drugs. How can you identify them? [have a surname "-mycin" (not really because of amikacin, but they'll get the point).]
 - c. Hold up the fluoroquinolones. How can you identify them? [have a surname "-floxacin".]
 - d. Which drugs are "identical"; same dose, same side effects, same resistance? These are like identical twins. [Eto-Pto; Am-Km; Cs-Trd]
 - e. Which drugs have cross-resistance? [In addition to the identical pairs, the quinolone class and injectable class each have cross-resistance within the class. These are like brothers in a family: similar mode of action, but dose, side effects and resistance may be slightly different.]
 - f. Repeat until the drugs are memorized.
3. Read **Section 5.6** of *Chronic Care for MDR-TB (Anti-TB drug dosing)*. Make sure the class understands how this table works.
4. Read **Section 5.9** of *Chronic Care for MDR-TB (Second-line standardized regimen instructions)*. Make sure the class understands the dosing of the standardized regimen. Discussion points:

- a. Many pills for co-infected patients; very difficult to be adherent
- b. Ethionamide, cycloserine and PAS are given in divided doses for better tolerance.
- c. Ofloxacin (and all fluoroquinolones) may be given in a single daily dose for TB, even if they are given BD for bacterial infections. [This is because TB replicates slowly compared to other bacteria.]

5. Give **lecture**, "Constructing a Regimen".

6. Have the class break up into pairs. Hand out the case description, allows several minutes for discussion, then ask for a volunteer group to present their treatment plan to the whole group. Discuss. Repeat with another case as time allows. Use Cases 12-15 in the **Case Book**.

Discussion Points

For all of these cases, the groups should give the doses of all drugs, including ARV drugs.

Case 12: Standardized Cat 4 regimen. Start ART when tolerating Cat 4 regimen.

Case 13: Standardized Category 4 regimen. Would not continue Category 2 because DST shows MDR-TB (might continue it if there was only H monoresistance). Would continue 6 drugs because the DST was done before Category 2 (with Z) was started. because Clinical response probably due to streptomycin monotherapy. Start ART when tolerating Cat 4 regimen.

Case 14: Individualized Cat 4—same as the index case.

Case 15: Very difficult case because this patient was previously treated with second-line drugs. Will need an individualized Category 4 regimen—nurses should refer to doctor for an individualized regimen based on previous TB treatment.

- Need to try to get information about previous treatment from South Africa—patients often have problems remembering accurately past TB treatment history.
- A good individualized empiric regimen would be: Cm-Ofx-Eto-Cs-PAS.
- Very important to educate the patient about adherence. By his past TB history, he is likely to default from MDR-TB.

Day 3/Session 1: MDR-TB/HIV Co-management

1. Quick review of TB-HIV co-management:
 - a. What is the CD4 criteria for ART in a TB-HIV co-infected patient [the CD4 is only used to determine the timing of ART—all co-infected patients need ART.]
 - b. When do you start ART in a TB co-infected patient? [CD4 of <200, 200-350, >350]
 - c. When do you start ART in an MDR-TB co-infected patient? [Start as soon as treatment is tolerated. CD4 is not necessary to decide on the timing of ART.]

2. Have a volunteer explain **Section 6.2** of *Chronic Care for MDR-TB (ART co-treatment)*. Discuss dosing of both MDR-TB drugs and ART in detail. Discussion point: since many patients are co-infected, they are taking a large number of pills of different types, and it can be difficult to know which ones are causing side effects.

3. Read **Section 7.9** of *Chronic Care for MDR-TB (Adverse effects of MDR-TB/ART co-treatment)*. Make sure that the class understands the cross-toxicities of ARVs and second-line anti-TB medications.

4. Do the **Side Effect Matching Game**.
 - Each sheet should be divided into 4 quarters. Drugs: Z, Km, Eto, Cs, PAS, AZT/3TC, EFZ, CTX.

Z	Km
Jaundice	Ringing of ears Tingling of feet
Eto	Cs
Nausea and Vomiting Fatigue	Psychosis Depression and Anxiety Tingling of Feet

PAS	AZT/3TC
Nausea and Vomiting Diarrhea Fatigue	Nausea and Vomiting Fatigue
EFZ	CTX
Psychosis Depression and Anxiety Jaundice Rash	Rash

[If there is any confusion about side effects of Category 1 drugs, review them:

- Isoniazid: hepatotoxicity (rare), neuropathy

- Rifampicin: hepatotoxicity, orange urine
 - Ethambutol: blindness (optic neuritis)
 - Pyrazinamide: hepatotoxicity, arthralgias
 - Streptomycin: (same as kanamycin) ototoxicity, nephrotoxicity]
5. Read **Section 7.1-8** of *Chronic Care for MDR-TB* on how to deal with common problems that arise during treatment. Make sure that participants know the principles of aggressive side-effect management.
 6. Read **Section 5.3** of *Chronic Care for MDR-TB (Manage Immune Reconstitution Syndrome)*.
 7. Have the class break up into pairs. Hand out the case description, allows several minutes for discussion, then ask for a volunteer group to present their treatment plan to the whole group. Discuss. Repeat with another case as time allows. Use Cases 17-23 in the **Case Book**.

Discussion Points

Case 16:

- This is severe neuropathy that is unlikely to resolve even after stopping the offending agents. It is probably due to Cs or injectable. Start pyridoxine and amitryptiline 25 mg at night. All MDR-TB patients should be taking pyridoxine (150 mg daily in this case). MO should consider stopping injectable now and decreasing the dose of Cs to 500 mg daily if no improvement.

Case 17:

- Check pregnancy test. Patient should be using condoms AND injectable contraceptives.
- Give ethionamide and PAS in divided doses. Metoclopramide 1 hour before morning/evening doses.
- Patient needs ART but cannot start now because she is not tolerating MDR-TB treatment. Start CTX, and give at night to reduce pill burden in the morning.
- Cat 4 dosing: Z 3, Km 750, Ofx 4, Eto 1/1, Cs 1/1, PAS 1/1, pyridoxine 0/4 (of 25 mg tabs)

Case 18:

- There are three possible explanations of the depression. In order of probability, they are: socioeconomic problems; cycloserine, efavirenz. Efavirenz is very unlikely to be the cause.
- Patients can be depressed for many reasons besides cycloserine.
- With psychosis (hearing voices is common), can give antipsychotic such as haloperidol. Need to stop cycloserine immediately, and will resolve slowly.

Symptoms start slowly and disappear slowly, as the drug slowly works its way out of the patient's body/brain. Then cycloserine can be started at a lower dose.

- Patients rarely become psychotic quickly. Usually depression/anxiety is missed by the health workers.
- Cat 4 dosing: Km 1, Ofx 4, Eto 1/2, Cs 1/2, PAS 1/1, CTX 1, AZT-3TC 1/1, EFZ 0/1, pyridoxine 0/6 (of 25 mg tablets), amitriptyline 0/1

Case 19:

- Family planning even though she is not sexually active
- HIV testing
- Reassurance and support for nausea
- TSH is not high enough to be clinically relevant—but could be subclinical hypothyroidism
- Needs urgent potassium supplements (Slow-K 600 mEq daily); check in one week
- Cat 4 dosing: Cm 1, Ofx 4, Cs 2/1, Eto 2/1, PAS 1/1, pyridoxine 0/6 (25 mg tabs)

Case 20:

- Look for other causes of cough and fever—unlikely to be PCP by clinical symptoms
- Most likely IRIS; not likely to be treatment failure.
- Supportive care for side effects: warm fluids, cough syrup, panadol, tepid sponging
- Cat 4 dosing: 1 gm, Ofx 4, Eto 1/2, Cs 1/2, PAS 1/1, pyridoxine 0/6 (25 mg tabs)
- Family planning: injectable contraceptives

Case 21:

- Stop all drugs, including ART, TB drugs, CTX, pyridoxine, metoclopramide.
- Check LFT's: AST, ALT, bilirubin. This is just for monitoring since we already know that the patient has hepatotoxicity. But we need to monitor the LFT's and can rechallenge the patient when the LFT's are 2-3x normal.
- Most likely offending drugs: Z, EFZ, Eto, PAS

Case 22:

- This case of XDR-TB is very difficult. The capreomycin is causing significant side effect of ototoxicity and the patient is going deaf. It is important to discuss what is happening to the patient and the risks of stopping the capreomycin. In this case, it would be medically indicated to continue capreomycin despite the side effects.

Day 3/Session 2: Management of MDR-TB in special cases

[Nurse class may skip these cases and go to the next section.]

1. Have the class break up into pairs. Hand out the case description, allows several minutes for discussion, then ask for a volunteer group to present their treatment plan to the whole group. Discuss. Repeat with another case as time allows. Use Peru Cases.

Discussion Points

Peru Case 1: Km-Ofx-Eto-Cs-PAS

Should be registered as a "New" patient on the Category 4 Treatment Card.

Peru Case 2: E-Z-Km-Ofx-Eto-Cs-PAS

Cannot be sure about E or Z because has been taking them after DST was sent.

Peru Case 3: Z-Cm-Ofx-Eto-Cs-PAS

Still give Cm because patient has never received it; however could have primary resistance.

Peru Case 4: This is the reason why contacts shouldn't get Category 1.

Peru Case 5: Z-S-Ofx-Cs-PAS or Z-Cm-Ofx-Cs-PAS.

S because of "partial" resistance. The QE2 lab will probably call this resistant.

Peru Case 6: Z-Km-Ofx-Eto-Cs-PAS

Might use Eto because of "partial" resistance. Some might use moxifloxacin, but cross-resistance is close to 100%

Peru Case 7: Standardized Cat 4.

Peru Case 8: Z-Cm-Ofx-Eto-Cs-PAS or Z-Cm-Ofx-Cs-PAS.

2. Give **lecture:** "MDR-TB in pregnancy".
3. Give **lecture:** "MDR-TB in children".

Day 3/Session 3: Adherence and social support

1. Have a volunteer read **Section 2.1** of *Chronic Care for MDR-TB (Directly observed therapy)*. Discussion points:

- a. Is this any different from Category 1 or 2? [No, except maybe the part about the treatment supporter accompanying the patient to the facility each month. This is done by some health centres for DOTS patients.]
- a. Have a volunteer read **Section 2.2** of *Chronic Care for MDR-TB (MDR-TB treatment supporters)*. Discussion points:
 - a. What are acceptable DOTS treatment supporters? What is the difference with MDR-TB treatment supporters. Why are we excluding family members or friends? [MDR-TB treatment is very complicated and the MDR-TB treatment supporter needs additional training to supervise it. Family members easily become burned out.]
 - b. What is a "trained community or workplace volunteer"? [Has received specific training on how to supervise MDR-TB treatment.]
 - c. Why do patients do not accept community health workers? Write these on the flipchart. Some reasons:
 - i. Do not want to disclose outside the family
 - ii. Fear of bewitchment
 - iii. Lack of trust in CHW's
 - iv. Frequent neighborhood conflict/Political differences
 - v. Stigmatization and discrimination
 - vi. Superiority complex
 - vii. Lack of confidentiality
 - viii. Why are we looking outside of the VHW pool?
 - ix. Why do we limit the number of patients to less than 5?
4. Have a volunteer read **Section 2.3** of *Chronic Care for MDR-TB (Adherence support)*. Make sure that everyone understands this page very well. This page also explains how a patient is enrolled in Category 4 treatment.
5. Briefly discuss the 5 A's: Assess, Advise, Agree, Assist, Arrange (those who have received IMAI training in the past will know these concepts well). What is the step most commonly skipped by health workers? [Agree]
6. Have a volunteer read **Section 2.4** of *Chronic Care for MDR-TB (Adherence preparation)*. In case there is any confusion about the different types of adherence support, the reasons for each are below.
 - Food packages—monthly food stipend of beans and rice or other sources of protein; should be given to the patient at the monthly visit at the health facility.
 - Transportation costs for health facility visits—monthly visits to the health facility can be a financial burden. Both patients and treatment supporters should receive financial support to defray transportation costs.

- Additional education—about MDR-TB, HIV and the importance of taking medications regularly and having monthly clinic visits. Treatment supporters should also have monthly educational meetings.
 - Peer support groups—People facing similar life situations, especially adverse or unpleasant situations, often find comfort, support and strength in being together with others who are in the same or similar situations. These may be peer-led groups or therapeutic groups led by a professional or paraprofessional.
 - Treatment supporter meetings can also be a forum for discussion: burn out, patient not adherent, barriers to treatment and adherence, etc.).
7. Have a volunteer read **Section 2.5** of *Chronic Care for MDR-TB (Adherence monitoring)*
 8. Read and discuss **Section 2.6** of *Chronic Care for MDR-TB (Education)*
 9. Discuss how to use the job aid: **Check understanding of doses.**
 10. **Post-test:** Participants may use their modules, books, notes, etc. (keep doctors and nurses separate)

Day 4/Session 1: Administration

[Note: doctors and nurses may be re-combined at this point]

1. Give **lecture** "Infection Control". Discussion points:
 - a. Administrative controls are the cheapest and most effective. Personal protective equipment is the least effective because they cannot work unless there are administrative controls and infrastructure improvements to identify and separate TB suspects. It's not possible to wear N95 masks 8 hours a day.
 - b. Immunosuppressed health workers should not be required to work on TB wards or TB outpatient services. This has to be a private discussion between the worker and supervisor, because of confidentiality issues.
 - c. N95 masks will be provided by Disease Control now, but needs to be budgeted by the hospital next year.

2. Discuss **pages 4-5** of *Chronic Care for MDR-TB (Roles and responsibilities)*. Discussion points:
 - a. The health centre has to provide injections. It will manage minor side effects, but not be responsible for the clinical management of the patient.
 - b. Training and supervision of the treatment supporter will be done by the district hospital clinical team.
 - c. Certain health centres will be accredited to provide MDR-TB care, particularly in areas of high MDR-TB prevalence.

Day 4/Session 2: Recording and Reporting

1. Pass out the **Category 4 Treatment Card** and have the class look at it for a few minutes.
 - a. Discuss the "Registration Group" table. For an explanation, read the first page of **Section 8** of *Chronic Care for MDR-TB (Arrange follow-up and record)*.
 - a. Discuss the "Previous TB Treatment Episodes" table in the upper right. How should this be recorded?
 - b. Where should weight be recorded?
 - c. How should regimens be recorded?
 - d. How should doses be marked on the MDR-TB treatment card? How is this different from the regular TB treatment card?

2. Exercise: Ask the class to fill in the "Registration Group" table and the "Previous TB Treatment Episodes" table for each of the Cases 9-15. For each case, ask a volunteer to come up to the flipchart and write their answers.
3. Pass out the **Category 4 Follow-up Form** and have the class look at it for a few minutes.
 - e. The "Symptoms and Signs" section may include a physical examination and vital signs.
 - f. In the "Adherence Assessment" what do the two suggestions on the right mean?
 - g. Discuss the side effect box: For Cases 16-22, ask which side effect would be ticked.
4. Read and discuss the second page of **Section 8** of *Chronic Care for MDR-TB*.
 - a. Treatment supporter fills out the DOT section, not the patient.
 - b. This needs to be copied to the facility-based card at the monthly consultation.
5. Pass out the **Category 4 Register** and discuss briefly.

Day 4/Session 3: Closing

1. Closing remarks
2. Certification