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Monitoring & Case Managment

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SUMMARY OF KEY UPDATES (2022)

- Case management and monitoring components for newer regimens such as bedaquiline, pretomanid, and linezolid (BPaL) and BPaL plus moxifloxacin (BPaLM)
- New BPaL/BPaLM TB Care Plan (Tool 7)
- Updated tools: MDR-TB Checklist (Tool 2) and Lab Flow Sheet (Tool 4)
- Updated patient assistance program table

Careful monitoring of patients with drug-resistant tuberculosis (DR-TB), using a case management approach, is a critical component of effective TB care.

Case management of DR-TB

Case management is:

> "A professional and collaborative process that assesses, plans, implements, coordinates, monitors, and evaluates the options and services required to meet an individual's health needs. It uses communication and available resources to promote health, quality, and cost-effective outcomes in support of the 'Triple Aim' of improving the experience of care, improving the health of populations, and reducing per capita costs of health care."
>
> — *Commission for Case Manager Certification*

The goal of TB case management is to provide person-centered care for completion of treatment, and to ensure completion of all public health activities related to stopping transmission.

Public health departments (i.e., under TB or communicable disease control programs) are encouraged to assign a specific health department employee (case manager) the primary responsibility for ensuring the person receiving care is educated about DR-TB, that treatment is completed and interruptions minimized, and that contacts are examined. Some specific responsibilities may be assigned to other persons.

Roles and responsibilities

Providing care for persons with DR-TB is a team effort and a variety of staff and community members may be involved. It is very important that roles and responsibilities are clearly delineated and understood and that effective lines of communications are maintained. Duties and responsibilities may change throughout care as the person's needs change.

Case manager

The case manager coordinates the care provided by the treating clinician(s), specialists, and other caregivers such as outreach workers, directly observed therapy (DOT) providers, social workers, correctional facility nurses, school nurses, and contact investigators. The case manager has primary responsibility for:

- Establishing a trusting relationship with the person engaged in care.
- Identifying the patient's primary language and providing medically trained interpreters to ensure accurate communication, to build trust, and to support an effective contact investigation.
- Educating the person engaged in care and significant others about DR-TB and its treatment.
- Developing an individualized case management plan in collaboration with the patient and family.
- Ensuring the person being treated adheres to and completes treatment.
- Ensuring referral to appropriate supportive services.
- Ensuring individuals exposed during the infectious period are identified, located, prioritized, evaluated, and treated as needed.
- Ensuring response to therapy is evaluated regularly. If response is not in accordance with expected outcomes, ensures the treating clinician is informed.
- Monitoring for adverse effects of treatment and notifying the treating clinician if they occur.

Depending on the expertise, resources, and infrastructure of the clinic or medical provider managing the actual care of the patient, the case manager may have other roles and responsibilities. When primary clinical care is obtained through a private provider or when patients are hospitalized or incarcerated, the case manager may take on the role of liaison or coordinator-of-care. In addition to the previously listed responsibilities, the case manager:

- Facilitates exchanges of information among the family, medical providers, laboratories, pharmacies, insurance companies, and the public health infrastructure.
- Builds relationships within all these systems to achieve the best results for the patient.
- Ensures expert consultation has been sought and provides referral for consultation as needed.
- Ensures patient remains linked to primary care and continues management of co-morbidities (such as diabetes) throughout TB treatment.
- Offers training, education, and resources to staff who will be providing patient care.

Treating clinician

The treating clinician provides the direct medical care of the patient. Given the toxicities of second-line drugs and the importance of ensuring response to treatment, it is recommended that the treating clinician regularly evaluate the person with multidrug-resistant (MDR)-TB. See section: ***Monitoring treatment response.***

It is also important for the treating clinician to engage the patient's primary care provider during TB treatment. The primary care provider can support maintenance of chronic conditions, assist with changes to maintenance medications if there are drug-drug interactions with TB treatment, provide insight into the patient's cultural and social contexts, and facilitate collaboration between the patient and treating clinician and TB care team.

When the treating clinician is not part of the public health team (e.g., private or community practice), it is essential to establish linkage with the public health department for case reporting, case management, and provision of adherence verification (e.g., DOT).

DOT provider

The role of the DOT provider for patients with DR-TB is similar to that for patients with drug-susceptible TB. However, because of the large number of pills needed and toxicity of second-line drugs, the DOT provider may need additional training to become familiar with expected side effects and strategies to support the person in taking medications. In general, the DOT provider is responsible for:

- Watching the patient take pills
- Checking for side effects
- Protecting confidentiality
- Documenting the visit
- Communicating regularly with the case manager and prescribing clinician regarding the status of TB symptoms (e.g., improvement, resolution, or new onset) and immediately about symptoms of serious side effects
- Other duties, including helping persons keep appointments, providing information about TB, and offering relevant incentives and enablers

The DOT provider may be the first person to identify a change in a patient's condition or development of an adverse reaction. DOT providers often develop strong relationships with persons undergoing care because they see them daily and provide ongoing encouragement and support. Ideally a DOT provider will speak the patient's language or have ready access to in-person or virtual interpreters.

This role is evolving in many programs with the implementation of adherence verification, e.g., video (v)DOT, electronic (e)DOT, and these responsibilities may be assumed by other case management staff.

Clinic staff

Nurses and other personnel at the TB or outpatient clinic may be involved with providing DOT, injections, and assessments, as well as alerting the case manager and treating clinician about signs or symptoms of serious side effects.

Other staff

Other health department staff such as contact investigators, social workers, and community health workers may have important roles in the management and support of persons with DR-TB; this would include alerting the case manager and/or treating clinician about signs or symptoms of side effects. Staff in other organizations or outside the health department may also have a role in supporting and/or treating the patient.

Initiating treatment

Initial evaluation

The important task of case managing and monitoring the person with DR-TB begins with a thorough and organized initial evaluation. The objective of the initial evaluation is to identify those persons at greater risk of adverse effects and to establish a baseline for essential monitoring.

Medical history and physical evaluation

- Demographic information (name, address, date of birth, etc.)
- Past medical history (including allergies, HIV status or other immunocompromising conditions, diabetes mellitus, hypertension, acute or chronic renal insufficiency, acute or chronic liver disease, psychiatric history, thyroid disease, drug or alcohol dependence, pregnancy, chronic epilepsy or seizure disorder, and other complicating conditions as well as all medications and supplements)
- Contact information for primary care and specialty providers
- Full TB history including previous treatment for latent TB infection (LTBI) or active TB (anti-TB medications, duration and dates taken, as well as location where treatment was given), TB symptoms and date of onset, surgeries, and complications; prior drug treatment can be documented in **Tool 1: *Drug-O-Gram***
- Social history, including country of birth, local family and social support network, food insecurity, employment, insurance status, housing history, travel, as well as history of substance use, immigration, and incarceration
- Review of systems
- Focused physical exam
- Weight and height to assess nutritional status and calculate body mass index (BMI) and lean body weight
- Source case and contact information including incarceration history, previous residences, household contacts, and visitors

Baseline examinations

- **Laboratory exams** should include an HIV test, complete blood count (CBC), and a comprehensive metabolic panel plus magnesium for all persons starting treatment for DR-TB. Additional baseline examinations to consider include:
  - Hgb A1C for patients with risk factors or history of diabetes
  - Viral hepatitis panel for persons with risk factors for viral hepatitis
  - Pregnancy test for women of childbearing age
  - Thyroid stimulating hormone (TSH) if regimen will include ethionamide (ETA) or para-aminosalicylate (PAS), or if there is concern about prolonged QT interval on ECG screening while on a QT-prolonging medication.
  - Baseline bicarbonate, lipase, and amylase are recommended by the Centers for Disease Control and Prevention (CDC) for those persons treated using the BPaL regimen.
  - Baseline creatinine clearance in persons with serum creatinine greater than expected, or if any concerns arise. (**See Chapter 7, *Co-morbidities and Special Situations***, **Table 1** for a formula to calculate creatinine clearance).

  Tool 4: *Laboratory Flow Sheet* may be helpful in summarizing bloodwork results that will be assessed at baseline and throughout treatment.

- Obtain **radiography** prior to treatment initiation. Posteroanterior (PA) views (and lateral in children or patients with immunocompromising conditions) of the chest for pulmonary disease are recommended. Additional views and/or other imaging may be helpful in some instances.
- **Sputum for nucleic acid amplification testing (NAAT), acid-fast bacilli (AFB) smear microscopy, culture, and drug-susceptibility testing (DST):** At the start of treatment, obtain 3 sputa for AFB smear and culture. Note: In a patient started on a standard 4-drug TB regimen for pan-susceptible disease for 4 weeks or more prior to starting a DR-TB regimen and for whom the initial isolate was not known to be resistant to all first-line drugs at baseline, request a repeat DST from a subsequent positive TB culture obtained near the time of DR-TB regimen initiation. This will help to ensure that no additional resistance developed during the initial period of therapy. Sputum should generally be collected even in patients thought to have extrapulmonary TB only. Other specimens from sites of extrapulmonary disease may also need to be collected. **Tool 3: *Bacteriology Flow Sheet*** may be helpful for summarizing the important microbacteriology, molecular tests, and DST results.
- **Rapid molecular assays for identification of drug resistance.** If not already obtained (and conventional DST results are still pending), all patients in whom a clinical suspicion for drug-resistant active pulmonary TB exists should have a sputum specimen submitted for a NAAT with rapid molecular DST for at least rifampin (RIF) and ideally, also for isoniazid (INH) and fluoroquinolones. If resistance to either of these key first-line agents is identified, more extensive rapid molecular DST is indicated, particularly for early identification of fluoroquinolone resistance.

- **ECG:** For patients who will be taking a drug with known risk for QT interval prolongation (bedaquiline [BDQ], moxifloxacin [MFX], clofazimine [CFZ], delamanid [DLM]), a baseline ECG is recommended. If such patients have known QT prolongation, hypokalemia, bradycardia, or known structural heart disease, consider cardiology consultation.
- **Psychosocial assessment:** Assess for existing mental health and social conditions that may impact treatment. See section: ***Psychosocial Support.***
- **Vision:** For patients who will be taking linezolid (LZD), ethambutol (EMB), or rifabutin (RFB) baseline vision screening (visual acuity and color discrimination) is recommended. **Tool 5: *Vision Screening Flow Sheet*** may be helpful for tracking results of vision monitoring.
- **Hearing and vestibular function:** If an injectable agent (amikacin [AK] or streptomycin [SM]) will be used in the regimen, assess hearing and vestibular function at baseline and document results. **Tool 6: *Hearing and Vestibular Flow Sheet*** may be helpful for tracking these serial monitoring results.

Initial patient education

Many people will only be able to process a small amount of information during the diagnosis and early treatment period. Ongoing education and support will help patients and families understand what to expect so they are better able to anticipate toxicities, tolerate inconveniences, and participate in their own care and decisions during the long course of treatment. (See section: ***Patient Education***).

Help persons receiving care to understand:

- They may feel worse before they feel better.
- The toxicity **symptoms will diminish over time** as the body adjusts to the treatment.
- **Steps can be taken to minimize the side effects** if and when they occur.
- In the long run, the **treatment will cure the disease,** save the patient's life, and prevent transmission to loved ones.

Use of case management tools

Drug-O-Gram, MDR-TB Monitoring Checklist, and *BPaL/BPaLM TB Care Plan*

The case manager should develop an individualized case management plan based on the patient's treatment regimen, co-morbidities, adherence barriers and facilitators, and psychosocial assessment. The plan format may vary among health departments depending on their record-keeping processes. Specialized tools such as the ***Drug-O-Gram***, the ***MDR-TB Monitoring Checklist***, and the ***BPaL/BPaLM TB Care Plan*** can be part of the case management plan to summarize recommended clinical monitoring, treatment, and key findings from evaluations.

The ***Drug-O-Gram*** is an important case management tool for following the patient's progress through TB treatment:

- Documents previous and current drug treatment, weights, microbiology including molecular results, radiology, DST results, and other important information in an easy-to-read, summary format.
- See **Tool 1: *Drug-O-Gram.***

DR-TB, particularly MDR-TB, requires close attention to the patient's response to treatment as well as prompt remediation of adverse events that may arise. A monitoring checklist can help the case manager keep track of the various required examinations as the person moves through treatment. The individualized ***MDR-TB Monitoring Checklist:***

- Delineates the important monitoring events that should occur throughout treatment to assess for clinical response to treatment as well as toxicity, based on the person's drug regimen and underlying comorbidities.
- Ensures that elements of care are not neglected and can be reviewed with patients so they can anticipate upcoming events.
- See **Tool 2: *MDR-TB Monitoring Checklist,*** for a sample of how this checklist can be customized for persons receiving care.

Tool 7: *BPaL/BPaLM TB Care Plan* summarizes the clinical response and toxicity monitoring activities that should occur at baseline and throughout treatment for persons taking the BPaL or BPaLM regimen.

Use a systematic approach to monitoring.

Monitoring throughout treatment

Persons with DR-TB will require regular monitoring throughout treatment to document sputum culture conversion and to watch for the development of toxicities. Patients should also be monitored closely for signs of treatment failure. The case manager is responsible for ensuring that all necessary monitoring for both toxicity and clinical response occurs and that abnormal results are brought to the attention of the treating clinician. See **Chapter 9, *Adverse Reactions.***

Monitoring treatment response

Monitoring response to treatment is done through regular evaluation of microbiology results, symptoms, weight, radiography, and other imaging.

TABLE 1. **Activities for monitoring treatment response**

Monitoring evaluation	Recommended frequency
Evaluation by clinician	First few months of treatment: Every day during the first weeks if hospitalized and at least every 1-2 weeks if treated as outpatient until the treatment is well tolerated. Once stable, once or twice a month based on medical complexity, response to treatment, and assessed need. Month 3 to end of treatment: Monthly assessments unless there is a medical necessity to see the patient more often. The DOT provider sees the patient daily between consultations and signals any concerns to the case manager and clinician.
Treatment adherence and tolerance	Daily at every DOT encounter whether in-person or virtual.
Sputum smears and culture	Obtain 3 sputa at the start of treatment and then at least 1 sample every 1-2 weeks until smear conversion, followed by 1-2 sputa every month until culture conversion, and then 1 sputum monthly throughout treatment.
Weight	At start of treatment, weekly until stable, and then monthly throughout treatment.
Height	At start of treatment for all patients (to be able to assess lean body weight or BMI); monthly for children (to assess growth).
Drug-susceptibility testing	At baseline for first- and second-line anti-TB drugs. Repeat DST for patients who remain culture-positive at month 3 or revert after month 4 (see **Chapter 2, *Diagnosis*** for more information on DST).
Chest radiograph	At baseline, every 3 months during initial treatment (then every 6 months if treatment extends beyond 12 months), and at the end of treatment.

Monitoring microbiologic response to TB treatment is essential in adults with pulmonary disease.

Even for drug-susceptible disease, the prompt conversion to culture-negative sputum is very reassuring and allows for the use of short-course TB therapy. For DR-TB, monitoring of sputum for smear and culture positivity is even more important.

Microbiology

- Patients who are on and adherent to an effective regimen will usually achieve **culture conversion** (from positive to negative x 2, collected at least 1 week apart) within 3 months. Patients with fewer effective drugs in their treatment regimens (e.g., extensively-drug-resistant [XDR-]TB patients) may convert more slowly.
- At the start of treatment, obtain 3 sputa for AFB smear and culture. Sputum specimens should be collected at least 8 hours apart. At least 1 specimen should be an early morning specimen. Some patients will be able to produce higher quality specimens if all of them are collected first thing in the morning. Instruct the patient on how to collect a good quality specimen or arrange for sputum induction if a good quality sample is difficult to obtain.
- Obtain at least 1 sputum sample every 1 to 2 weeks until smear becomes negative (as early assessment of response to treatment).
- Once smear conversion is achieved, continue to collect 1 to 2 sputum samples monthly until TB cultures become consistently negative (e.g., 1 sample every 2 weeks).
- Once the culture has converted to negative, most experts and guidelines recommend obtaining at least 1 specimen of sputum for AFB smear and culture monthly throughout the remaining course of treatment, and more frequently if indicated. Keep track of these smear and culture results using tools such as **Tool 1: *Drug-O-Gram*** and **Tool 3: *Bacteriology Flow Sheet.***
- Whenever sputum is being collected, pay attention to infection control. Collect sputum in a secure isolation area or an outdoor environment. **If the patient cannot spontaneously expectorate sputum, perform sputum induction with hypertonic saline in an appropriately engineered environment.**
- Serial culture collection in children can be difficult. For information on the best methods for collecting specimens for smear and culture in children, see **Chapter 6, *Pediatrics.***
- An important activity of the case manager is coordination of microbiologic evaluation for the patient's cultures. Specimens should be of good quality and at least 5 to 10 mL in volume. Route specimens to the appropriate reference laboratories, request tests for specific detection of drug resistance, and communicate results as quickly as possible to the treating clinician.
- When sputa remain culture-positive after 3 months of treatment, conduct a full reevaluation, including repeat DST (molecular and phenotypic) for the possibility of further development of resistance. Patients are considered to have failed therapy when their sputum cultures are still positive after 4 months of treatment. See section: ***Assessment for treatment failure.***

Extrapulmonary TB

- Microbiologic monitoring of **extrapulmonary** disease is more difficult, and serial biopsies or aspirates are rarely indicated. However, if the patient is not responding to treatment, or if there is any reason to suspect that the treatment is failing, strongly consider repeat specimen collection.

Symptoms

> "The classic symptoms of TB — cough, sputum production, fever and weight loss — generally improve within the first few weeks of treatment."
>
> — *WHO Companion Handbook*

- Assess for symptoms of TB weekly in the first month or two of treatment, and then monthly throughout treatment thereafter.
- **Document resolution of symptoms** that were present at diagnosis.
- Patients with chronic, progressive symptoms such as cough, fever, chest pain, and weight loss will often notice improvement or resolution of these symptoms within weeks of starting effective treatment.

Systemic symptoms

- Assess and monitor improvement of the following symptoms commonly reported in persons with TB: **fever, loss of appetite, pain,** and **fatigue.**
- Monitor TB site-specific symptoms, and document changes from baseline findings; for example, headache, vomiting, and neurologic changes may be present with central nervous system (CNS) disease.
- Screen for symptoms of co-morbid conditions, especially diabetes and HIV.
  - While initial immune reconstitution may exacerbate TB disease, the long-term health of the patient and ability to cure TB disease relies on the successful treatment of HIV.
  - HIV, diabetes mellitus, and other diarrheal and malabsorption syndromes affect drug absorption and may undermine TB treatment, resulting in treatment failure, amplification of drug resistance, or increased risk for relapse. If a patient is at risk for poor absorption, monitor for diarrhea and other symptom changes. Consider checking serum drug levels in patients with these comorbid conditions (see section: ***Therapeutic Drug Monitoring***). For more information, see **Chapter 7, *Co-morbidities and Special Situations.***

Respiratory symptoms

Routinely monitor the patient's cough, respiratory status, and sputum production. Most respiratory symptoms should begin to improve within weeks of starting on appropriate DR-TB treatment.

Investigate failure to improve or return of respiratory symptoms after initial improvement.

Consider all the following possibilities:

- **Other respiratory infection or process** (e.g., malignancy)
- **Non-adherence to therapy or not achieving therapeutic concentrations**
- **TB treatment failure? If failure is suspected:**
  - Repeat cultures and DST, including rapid molecular DST to assess for acquired resistance
  - Consider a regimen change **(never add a single drug to a failing regimen)**
- **Interpret respiratory symptoms in the context of the entire clinical picture:** fever curve, weight gain, other systemic symptoms, co-morbidities, and microbiologic response to treatment

Weight

Many patients with TB are poorly nourished. This is especially pronounced in patients who have developed drug-resistant disease over years of failed treatments or have had long delays in diagnosis. Weight and nutritional status are important markers for disease status; addressing them is an important aspect of therapy.

- Check weight weekly until weight gain stabilizes, and then monthly throughout the course of treatment and follow-up.
- Lean body or ideal body weight (drug-specific, see **Chapter 5, *Medication Fact Sheets***) may be calculated for obese individuals to adjust medication dosage. Calculate BMI for underweight patients to assess nutritional status.
- Occasionally, patients will lose weight while on treatment due to side effects; monitor patients closely to investigate the likely cause and to ensure there are no other signs of treatment failure.
- Very young children with DR-TB may need more frequent weight monitoring as well as monitoring of other indices of growth and development.

Note: Drug dosages may need to be adjusted as weight changes, particularly in young children and persons who have sustained significant weight loss prior to diagnosis.

Nutritional support and use of supplements

- Maximize the nutrition of persons who are undernourished.
  - Offer persons who are hospitalized flexible meals of their choice, solicit dietary consultation, and offer dietary supplementation.
  - Some persons with TB will feel best and gain the most nutritional benefit from small, frequent meals (mini-meals) throughout the day.
  - Occasionally, tube feedings for supplementation are required, and rarely, parenteral nutrition is used (especially prior to surgery to improve post-operative healing).
- Assess and address food insecurity.
- Ensure sufficient nutrition is available for people in respiratory isolation.
- Customize outpatient management based on the nutritional status of the patient. Some persons undergoing care will only need to have their weights monitored, and others will require food diaries, regular nutritional labs, and ongoing nutrition consultation.
- Consider food preferences and cultural differences. Arrange for foods to which the person is accustomed and finds appetizing.
- Some food supplements (such as Ensure and multi-vitamins) interfere with absorption of fluoroquinolones and should be offered at least 2 hours before or after the drug.
- Refer persons with co-morbidities affected by nutritional intake (such as diabetes) for dietary consultation.

Radiography

Radiographic response to TB treatment lags behind clinical and microbiologic response.

Obtain routine chest radiographs in patients with pulmonary TB:

- Every 3 months during treatment
- Every 6 months in year 2 when treatment extends beyond 12 months
- At the end of therapy primarily to establish a new baseline against which future imaging can be compared.
- 6, 12, and 24 months after treatment is completed or as clinically indicated. In patients completing newer regimens (e.g., BPaL), some clinicians suggest more frequent post-treatment assessment (e.g., 3, 6, 12, 18, and 24 months).

Additional imaging is sometimes obtained when the patient has a clinical decompensation or co-morbidities. CT scans and special views (lordotic or bilateral obliques) may be useful for individual cases.

In particular, CT scans should be obtained to assist in evaluating the differential diagnosis or when a more accurate assessment of the extent of disease is needed for surgery, duration of treatment, or unexplained changes on the chest radiograph.

CT scans may be particularly useful for following lymph node and mediastinal disease, as well as extensive pleural and parenchymal changes. In very complex cases, an end-of-treatment CT is often useful as a baseline for future follow-up. Radiographs (plain films, CT, or MRI) are particularly useful in monitoring response to treatment for patients whose disease cannot be followed microbiologically:

- **Intracranial lesions**
- **Abscesses**
- **Bone disease**
- **Pleural disease**
- **Deep lymph nodes**

Assessment for treatment failure

Patients are considered to have failed therapy when their sputum cultures are still positive after 4 months of treatment.

When AFB smear or culture positivity persists or recurs, consider and address:

- Adherence to therapy
- Accurate dose calculation and administration
- Drug absorption
- Adequacy of the drug regimen
- Development of acquired resistance
- Respiratory and constitutional symptoms
- Radiographic findings
- Possible poor penetration of drugs into a localized area (e.g., empyema, thick-walled cavity in poorly vascularized lung)
- Presence of conditions that may delay culture conversion (e.g., uncontrolled diabetes, malabsorption, extensive disease)

Monitoring for drug toxicity

Screening for drug toxicity and adverse effects is an important part of DR-TB treatment. Close monitoring is needed to ensure a prompt response to side effects, particularly when treatment is initiated in an outpatient setting.

General principles

- **Counsel every patient beginning any TB therapy to anticipate side effects.**
  - Even patients taking INH monotherapy frequently feel poorly in the first few weeks of therapy. If patients do not anticipate this reaction and are not reassured that it will improve, they may stop the therapy.
  - Monitor patients for general toxicities and drug-specific toxicity at every healthcare visit (including during DOT encounters). See **Tool 2: *MDR-TB Monitoring Checklist.*** A sample side effect monitoring checklist can be found in the ***Nursing Guide for Managing Side Effects to Drug-resistant TB Treatment*** (see section: ***Resources***).
  - Many of the second-line TB drugs are associated with significant potential toxicities. Patients on these medications may experience more toxicity than patients treated with first-line medications.
- Take measures to minimize toxicity and to help patients tolerate minor side effects through counseling and use of adjuvant therapies rather than losing the drug in the regimen. In many cases, there are no alternative drugs for replacement.
  - **Supplemental ancillary medication** can be helpful in addressing some common side effects.
  - Also consider **non-pharmaceutical approaches.** Examples include:
    - **Change the timing of the dose** to minimize toxicity (e.g., dose at bedtime).
    - **Dose some medicines with food** (have patient try different foods to find something palatable).
    - **Relaxation techniques** may be helpful.
- See **Chapter 9, *Adverse Reactions,*** for approaches to address common adverse events.
- The ***Nursing Guide for Managing Side Effects to Drug-resistant TB Treatment*** (see section: ***Resources***) offers additional guidance on nursing assessment and suggested interventions to address side effects that arise during treatment.

Routine toxicity monitoring

Screening is necessary to detect adverse effects that are not apparent through physical exam or observed by the patient. For patients with MDR-, pre-XDR-, or XDR-TB, routine monitoring for drug toxicity frequently includes the following:

- **Screening for bone marrow suppression:** Complete blood counts intermittently as clinically indicated; every 1-2 weeks for the first 6-8 weeks, then monthly thereafter for patients on **LZD**.
- **Monitoring renal function:** Serum creatinine at least monthly for patients receiving **aminoglycosides or BPaL regimen.**
  - Calculate creatinine clearance especially for persons with small body weight, older age, or with diabetes. See **Chapter 7, *Co-morbidities and Special Situations,* Table 1** for formula to calculate creatinine clearance.
- **Monitoring liver function:** Liver function tests (LFTs) monthly (AST, ALT, total bilirubin, alkaline phosphatase) for patients taking **BDQ, pretomanid (Pa), pyrazinamide (PZA), ETA,** or **PAS.**
- **Monitoring serum electrolytes and bicarbonate:** Potassium, calcium, and magnesium monthly for patients on **BDQ** and **aminoglycosides.**
- **Screening for hypothyroidism:** When hypothyroidism is identified at treatment initiation or during treatment, thyroid replacement therapy should be considered. Thyroid disease may increase risks for QTc prolongation and should be taken into consideration when using medications that also effect the QTc. TSH function should be checked during treatment when:
  - Baseline thyroid testing shows abnormalities
  - Symptoms of hypothyroidism develop during treatment
  - Regimen contains **ETA** or **PAS** (check every 3 months)
- **Screening for visual changes:** Screen monthly for visual acuity and red-green color discrimination for persons taking **EMB** or **LZD**. Watch for evidence of uveitis for patients on **RFB**. Refer a patient for further evaluation if changes in vision (acuity, visual field, or color discrimination) or complaint of eye pain are noted. Rarely, ETA and INH have also been reported as causes of optic nerve toxicity. Patients taking **CFZ** over many months may develop red-brown corneal or conjunctiva discoloration, usually not associated with ocular symptoms; however, there are a few case reports of "bull's-eye" retinopathy with long-term use of CFZ. See **Tool 5: *Vision Screening Flow Sheet*** for tracking of monthly visual acuity and color vision screening results.
- **ECG** at least 2, 12 and 24 weeks after initiating treatment when regimen contains **BDQ or DLM** (some providers may check at 2 and 4 weeks, then monthly if multiple QT-prolonging drugs are used).
  - The corrected QT interval should ideally be calculated to assess for QT prolongation using the Fridericia formula (QTcF). See section: ***Resources*** for QTc measurement guidance, online calculator tools to convert to Fridericia, and online resource site to identify QT-prolonging medications.

- Note that automatic QTc calculations within ECG machines often use the Bazett formula and should be recalculated to QTcF. Bazett works well for heart rates from 60-100 bpm but may over-correct at slower heart rates and under-correct if faster. Fridericia has the same limitation at slow heart rates but is reportedly better at correcting at higher heart rates.
- Target QTcF is below 450ms for men or 470ms for women. If QTcF appears prolonged, confirm on a repeat ECG performed 30 minutes later. If QTcF is prolonged, increase monitoring to weekly and address other reversible causes of prolonged QTcF (such as abnormal electrolytes, non-TB medications, hypothyroidism, etc.).
- Consider discontinuation of **BDQ** and all other QT-prolonging medications if QTcF exceeds 500ms or if clinically significant ventricular arrhythmia develops.

- **Screening for peripheral neuropathy:** Monitor for peripheral neuropathy monthly while patient is on **LZD** and as clinically indicated for patients on fluoroquinolones (or high-dose INH). See Appendix C of the ***Nursing Guide for Managing Side Effects to Drug-resistant TB Treatment*** (see section: ***Resources***) for a sample assessment tool for peripheral neuropathy.
- **Screening for depression, agitation, and psychosis:** Monitor at least monthly for depression and mood changes (including agitation) for patients taking **cycloserine (CS)**. The most common toxicities associated with CS are depression, psychosis, and suicidal thoughts. Standardized tools for assessing and documenting mental health symptoms are very helpful. It is also important to educate family members and DOT workers to notify the case manager or clinician if they notice any changes in the patient's mood or behavior since the patient may not be aware of these adverse effects. Sometimes patients may report more subtle symptoms such as difficulty concentrating. See section: ***Resources*** for examples of screening tools.
- **Screening for hearing loss and vestibulopathy.** Assess audiometry and vestibular function monthly for patients receiving **aminoglycosides**, noting toxicity is related to the total dose and cumulative. See **Tool 6: *Hearing and Vestibular Screening Flow Sheet*** for a sample tool that can assess vestibular function and track monthly vestibular and audiogram screening results. If a change in hearing or vestibular function from baseline occurs, promptly inform the treating clinician, and refer the patient for further evaluation. Some sequelae resulting from ototoxicity can be permanent (hearing loss, vertigo, and tinnitus). Early identification and referral are important to enable appropriate modification to the drug regimen to limit or prevent these outcomes. See **Chapter 9, *Adverse Reactions,*** for information on the management of ototoxicity.

See **Tool 2: *MDR-TB Monitoring Checklist*** and **Chapter 5, *Medication Fact Sheets.***

Drug interactions

Many drugs interfere with TB therapy or contribute to toxicity. Monitor patients when any new medication is started. This should include all newly prescribed medications and over-the-counter therapies such as:

- Vitamin/mineral supplements
- Antacids
- Traditional medicine, home remedies, and "alternative" or herbal supplements

See **Chapter 5, *Medication Fact Sheets*** for more information on drug interactions.

Therapeutic drug monitoring (TDM)

The case manager also frequently coordinates collection and transport of blood samples for TDM as a part of drug toxicity monitoring and prevention.

- Few reference laboratories perform these levels, so it is important ensure that the correct test has been ordered (e.g., cycloserine not cyclosporin) and is sent to a laboratory with the capacity to perform the specific drug level.
- Factors such as cost, and a patient's insurance status require the expert evaluation of the case manager.

For details about timing of blood draws, processing, and shipping of samples, see **Chapter 3, *Laboratory***, section on ***Therapeutic drug monitoring.***

For information on how to interpret the results of therapeutic drug monitoring, see **Chapter 4, *Treatment,*** section on ***Timing and interpretation of TDM.***

Monitoring tools and strategies

As previously noted, the use of monitoring tools will help track the many details of case management, enabling the case manager and treating clinician to keep results organized, to anticipate problems and to manage them as they occur. Additional helpful strategies include:

- **Scheduling regular visits** with the patient either in-person or via telemedicine, initially weekly and then monthly, to perform a thorough assessment until treatment is completed.
- **Setting real-time reminders** on the computer or mobile phone, a tickler system, etc.
- Seeking **expert consultation** from resources such as state TB control programs and regional TB Centers of Excellence for Training, Education, and Medical Consultation (TB COEs). The learning curve is very steep during case management of the first case or two of DR-TB; use of the resources included in this *Guide* and discussions with experts will help. See **Appendix 1: *Expert Resources for Drug-Resistant TB.***

Post-treatment monitoring

At the end of treatment, obtain a sputum culture and chest radiograph (CXR). The patient should undergo post-treatment monitoring for a minimum of 2 years to monitor for relapse. At **6-, 12- and 24-months post-treatment (or as clinically indicated), monitor the patient with:**

- Symptom review
- Medical evaluation
- Sputum for AFB smear and culture
- CXR

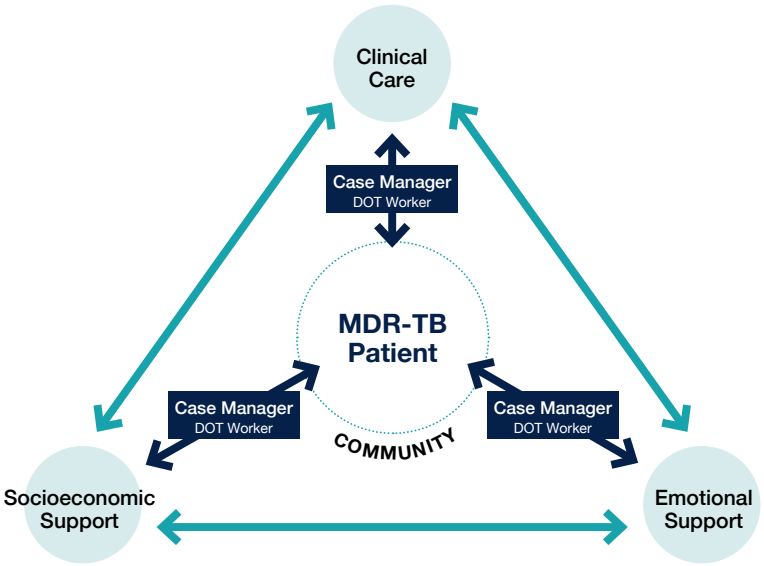
In patients completing newer regimens (e.g., BPaL), some experts suggest more frequent post-treatment assessment (e.g., 3, 6, 12, 18 and 24 months).

Patient-centered care and ensuring adherence

> "Patient-centered approach to treatment should be developed for all patients in order to promote adherence, improve quality of life, and relieve suffering. This approach should be based on the patient's needs and mutual respect between the patient and the provider."
>
> — Standard 9 of the *International Standards for TB Care*

Model programs utilizing a case management and patient-centered care approach in community-based care of patients with DR-TB (**Figure 1**) demonstrate high levels of treatment success.

FIGURE 1. **Community-Based Model of DR-TB Treatment**



Adapted with permission from *The Community Based Model of Multidrug-Resistant Tuberculosis Treatment,* Jaime Bayona, MD, MPH, Socios En Salud Sucursal, Peru

Adherence to DR-TB treatment is essential to prevent the amplification of resistance, to increase the chances of treatment cure, and to prevent ongoing transmission in the community. Even in high-resource settings, adherence to DR-TB treatment can be challenging due to the long duration of treatment, the frequent and serious side effects, and the social and economic burdens to patients and their families.

A variety of factors influence adherence to treatment, including: the individual's knowledge and beliefs; social and emotional support available to the patient; and economic support to cover the cost of treatment, associated monitoring and potential loss of income to the patient and family while the patient is unable to work or attend school. To promote adherence and support the patient, the case manager will be providing or coordinating the following activities:

- **Adherence verification support** (e.g., DOT [in-person, video or electronic] or other medication monitoring strategies)
- **Information support** (education to the patient and family with medically trained interpreters as needed)
- **Psychological/social support** (including use of culturally appropriate resources)
- **Material support** (including use of incentives and enablers, and linkage to health care coverage or other support services/resources)
- **Use of legal orders** when indicated

Adherence verification

The consequences of treatment failure and further acquired drug resistance make **DOT a high-priority strategy for adherence verification when treating DR-TB.** DOT is an important case management strategy for ensuring patients take their medications correctly and is recognized as a standard of care worldwide when treating DR-TB. Achieving this standard of care, however, requires far greater time and commitment in the setting of DR-TB than of drug-susceptible disease. Weekend doses, drugs given more than once a day, and drugs tolerated only at bedtime will present programmatic challenges; therefore, a variety of options for DOT may be needed (e.g., vDOT, eDOT, etc.).

DOT is recognized around the world as an essential treatment adherence strategy for DR-TB

DOT entails a health care worker or other designated individual asking the patient about the presence of potential treatment side effects and watching the patient swallow every dose of the prescribed regimen. Regardless of the adherence verification method, it is important to communicate in the patient's preferred language. This could be through a trained interpreter or interpretation service or via the language capabilities of electronic adherence verification platforms. See section: ***Roles and responsibilities—DOT provider.***

Case managers must keep open lines of communication with DOT providers and ensure that they can assess for signs and symptoms that may indicate potential toxicities.

- When the case manager is not the individual providing the DOT, **regular contact with the DOT provider and weekly contact with the patient will be important during the initial phase** to ensure that the patient is tolerating the medication and that side effects are quickly addressed.
- While many patients will experience mild effects that can be managed without a change in the drug regimen (e.g., initiating adjuvant therapy, changing dosing time), some side effects warrant at least temporary discontinuation of the associated drug. Any toxicity must be quickly identified, reported, and acted upon (see **Chapter 9, *Adverse Reactions***). Address all complaints, even if no change can be made.
- It is very important to use standardized forms to record DOT doses and toxicities for persons with complicated disease.
- Some programs have patients complete a DOT acknowledgement or contract so that expectations are clearly explained and agreed upon.
- Other methods of adherence verification may include eDOT, vDOT, electronic pills boxes, calendars, or other developing technologies. Each of these methods offers different levels of certainty of adherence.

No detail regarding medication administration should be assumed or left to chance.

Routinely ask:

- "How did you take your medication?" (when medications are taken over the weekend or when the dose is self-administered)
- "Have you eaten any milk-based products, antacids, or vitamin products within 2 hours of taking medications?" (these inhibit the absorption of fluoroquinolones)
- "Did you throw up after taking your medicine?" (important to ask even if medications are given by DOT in case the patient is vomiting after the DOT provider leaves)

Providing an injectable agent

With newer drug options, the use of injectable agents has become highly infrequent, often only for temporary circumstances (e.g., bridging regimens while awaiting other drug procurement or for hospitalized persons). Arranging for or administering an injectable agent for patients with DR-TB can be challenging as many local health departments are not staffed to provide either infusions or daily injections. Although providing an injectable agent may be daunting, when there are few drug options, an injectable agent may be needed.

If there is the choice of either intramuscular (IM) or intravenous (IV) administration, strongly consider patient preference in addition to safety concerns, ability to provide DOT of the injectable agent, and logistics.

Injectable Agents	
Why:	Bactericidal
When:	5-7 times per week at start of treatment, often drops to 3 times per week after culture conversion to minimize toxicity
Where:	Hospital, home, clinic, infusion center
How:	Intramuscular or intravenous
How long:	Usually 6 months post culture conversion unless toxicity develops

IM injections

Some programs provide the IM injection in the patient's home, which can be more comfortable and convenient for the patient, especially while the patient remains infectious and on home isolation. Public health and/or clinic nursing staff may require additional in-service training if they have not had recent experience in providing IM injections. Good injection technique can make the experience less painful for the patient. Lidocaine can be added to the injection to lessen the pain. See ***Resources*** at the end of this chapter for additional information.

IV infusions

Patients may prefer to receive infusions versus IM injections. A major challenge in providing infusions is finding staff to perform the infusion. Typically, public health nurses are not trained to provide infusions—or it falls outside of their scope of practice—and a home health agency may be needed to provide home-based infusions. Often, home health agencies train family members to administer medications; agency staff may visit once a week to assess the insertion site of the peripherally inserted central catheter (PICC) line (or other intravenous catheter) and provide the supply of medications. It is important that the case manager communicate closely

with the home health agency regarding the assessment of whether the patient or family member can safely administer the infusion using proper clean technique.

Even if case managers are not directly administering infusions, it is important that they be aware of and assess for **signs of infection or venous thrombosis.** Additionally, when the patient or family member administers the infusion, arrangements for DOT of both parenteral and oral medications are needed. Some programs coordinate the DOT of the oral medications with the timing of the infusion. For example, the DOT provider arrives as the infusion is finishing. Programs should establish protocols and procedures for the DOT provider to document administration of the infusion. Once a patient is no longer considered infectious, another option is to use an infusion center.

Patient education

All patients and their family members should receive education about DR-TB, its treatment, and the need for adherence to therapy. Education may be provided by physicians, nurses, community health workers, and other health care providers. The case manager will have a key role in providing TB information, health coaching, and support to the patient throughout treatment. If the patient's primary language is not English, identify and secure a trained interpreter or interpretation service to assist with the delivery of the information.

Tips for delivering patient health information

- Always use a venue that guarantees confidentiality in communication. Ensure sufficient time is available for patients to ask questions and raise concerns.
- Use language that promotes mutual respect and esteem among the patient, caregivers, and healthcare providers.
- Do not make promises that the healthcare service cannot keep.
- Build upon what the patient already knows about TB, responding to questions, concerns, or fears that may be expressed.
- Talk with patients about their experiences as clinical assessments and treatment are underway. Address any experience of stigma and/or discrimination.
- Provide reassurance and link to patient support services and resources (e.g., We are TB). See section: ***Resources***.

Adapted from: *Companion Handbook to the WHO Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis,* 2014

The following phases may not fit the treatment course for all individuals with DR-TB but will provide a context for case managers to anticipate their patients' information needs throughout the course of treatment. The analogy of preparing for a marathon has been suggested to emphasize the key role the case manager can play in coaching the patient through the various phases of treatment and setting achievable interim goals.

1. First phase

The first phase spans from diagnosis through the time the patient may require airborne infection isolation. During this time, the patient is facing multi-drug treatment with the potential for many side effects and may have already been feeling very ill for some time. If the patient's medical needs are not given careful attention during this phase, the person may become discouraged. Involve the family and/or significant others in provision of initial patient education. Information to share and discuss includes:

- **Patient's understanding** of the diagnosis and plan for treatment
- **Major concepts:** TB of the lungs is often contagious, which means it can be spread from person to person. TB generally affects the lungs, but it can also infect other parts of the body. Left untreated, it can be fatal. DR-TB can be cured with the right medicine.
- **Clarify how DR-TB can be transmitted and how it cannot be transmitted** (i.e., not through sharing food, shaking hands, etc.).
- **Simple infection control practices,** such as wearing a well-fitted mask when indoors with other people, covering the mouth when coughing, and opening windows to improve air-circulation in the home when feasible.
- **Airborne infection isolation plans,** discussing best option available for safe isolation and the importance of adhering to visitor restrictions if isolated at home.
- **Counsel around management of side effects** that may be anticipated early during treatment for DR-TB. Inform on what to do should side effects occur, including how to connect with the healthcare team and/or clinician in case of an urgent issue when the health department is closed.
- **Criteria for non-infectiousness** (i.e., when home isolation can be discontinued per program protocols and the person with TB will be allowed to return to work or school or be able to travel).
- **Recognize and address the person's fears and concerns.** People with TB are less likely to retain treatment information and instructions if they are fearful or preoccupied with worries about their jobs or family members. Identify potential barriers to adherence and initiate use of incentives and enablers to support persons while they are unable to work.

Help patients to understand:

- They may feel worse before they feel better.
- The toxicity **symptoms will diminish over time** as the body adjusts to the treatment.
- **Steps can be taken to minimize the side effects** if and when they occur.
- In the long run, the **treatment will cure the disease,** save lives, and prevent transmission to loved ones.

2. Second phase

Once the person is stabilized on treatment, the emphasis of education will shift. During this phase, **focus on helping the patient manage any side effects, maximizing nutrition** and continuing to reassess **potential barriers to adherence.** Drug toxicity can occur at any phase in treatment and should continue to be closely monitored. If surgical intervention is indicated, it might occur during this phase. Information to share and discuss may include:

- **Person's knowledge and understanding of the disease, treatment plan** and potential serious side effects of treatment
- **Management of side effects** (see **Chapter 9, *Adverse Reactions*** and ***Nursing Guide for Managing Side Effects to Drug-resistant TB Treatment*** [see section: ***Resources***])
- **Signs of clinical improvement** and the importance of regular monitoring tests to document clinical improvement
- **Arrangements for DOT and required toxicity monitoring**
- **Incentives and enablers** that might aid adherence to treatment (see section: ***Use of incentives and enablers***)
- **Management and care for co-morbid conditions**
- Appetite, **nutritional status,** and **physical activity** as tolerated
- **Available educational and social support resources** in the community and online as appropriate. See section: ***Resources***
- **Management of injection site(s)** (care of IM/IV sites if person is receiving an injectable)
- Patient's **plans concerning work, travel, or moving**

3. Third phase

If continued clinical response is achieved, the third phase begins when the person has achieved culture-conversion, is tolerating their DR-TB regimen, and continues until the end of treatment. The patient may have many months more of daily oral medication to complete before reaching the finish line. Information to revisit and discuss includes:

- Patient's plans concerning **work, travel, or moving**
- **Management of side effects** (different side effects may develop later into therapy requiring additional management and sometimes a change of medication)
- **Arrangements for DOT and clinical response monitoring**
  - As circumstances change (e.g., return to work), make necessary adjustments in collaboration with the patient
  - Continually reassess the person's belief in and understanding of the importance of uninterrupted treatment to prevent treatment failure and relapse
- **Acceptable interventions and strategies for addressing potential barriers** as needed

4. Final phase

The final phase begins once treatment is completed. The marathon is over, yet the person will require clinical monitoring for the next 2 years to ensure that if a relapse occurs, it will quickly be identified and acted upon. Information to share and discuss:

- Ensure patients are **knowledgeable about signs and symptoms of TB and what to do** should they experience them.
- **Schedule and inform about follow-up appointments.** Arrange for reminder notification that is suitable to the patient.
- Revisit the patient's **plans concerning work, travel, or moving.** Provide appropriate referral and contact information as indicated.

Psychosocial support

Persons with DR-TB face many stressors, including the diagnosis of a potentially life-threatening disease, stigma, serious side effects, and economic hardships. A 2006 report by Chalco and colleagues found that many patients with MDR-TB experience strong feelings of guilt and in some cases, the stigma may not come from the social surrounding, but rather from the patient's own family; relatives may react in accordance with past experiences and cultural beliefs. **Most patients will need ongoing social and emotional support** to cope with these challenges. The case manager often plays a key role in providing emotional and social support by listening to the patient, and talking with patient and family to reduce stigma, fear, and misunderstandings about the disease.

Engage family members in the patient's care to the extent desired by the patient; encourage and praise their support. Do everything possible to maintain the involvement of family members and their support of the treatment plan. An initial investment of time is well worth the benefits it often reaps. Offer to evaluate family members for TB disease or LTBI and answer their questions using an interpreter or interpretation services as needed.

Assess the patient's social support network and the strengths and barriers to adherence. Ensure that plans are in place for addressing issues such as mental illness, substance use disorder, and homelessness. **Partnering with the patient's primary care provider,** especially if they have an established rapport with the patient, can help with linking to supportive services, encouraging the patient's collaboration with the TB care team, and providing the TB care team with insight into the patient's cultural and social contexts.

Avoid using potentially stigmatizing language in TB programs, clinics, and with people with TB. See section: ***Resources.***

Consider **community services** that can assist in addressing challenges:

- Social services and programs for the medically indigent
- Community-based organizations
- Legal counsel regarding immigration or housing
- Substance use counseling
- Mental health programs

The keys to successfully assisting patients with these challenges are to develop a trusting relationship with the person undergoing care and to be familiar with local community resources. Ideally, case managers will be familiar with — and connected to — community resources prior to their first cases of DR-TB.

Substance use and mental illness

Some persons with TB are at higher risk of substance use disorder and mental health issues. Treatment programs for persons experiencing substance use disorders are important partners with TB clinics and providers. Similarly, treatment of mental health disease is paramount in keeping a patient adherent to TB therapy.

- Closely monitor success and/or relapse with substance use during TB treatment in order to anticipate toxicity and to avoid adherence complications.
- Facilitate referral to programs and services that can work with the person on harm reduction.

Even persons without an underlying mental health disorder will need significant mental health support and monitoring during treatment for DR-TB. Situational depression is not uncommon in patients undergoing treatment for DR-TB and it can be quite debilitating. Some medications used to treat DR-TB carry the potential side effect of depression and sometimes psychosis (e.g., CS, fluoroquinolones). See section: ***Resources*** for tools to monitor for depression and psychosis.

There are important drug interactions to consider for persons who use substances or have mental illness:

- Some drugs used to treat depression such as **selective serotonin reuptake inhibitors (SSRIs)** are not recommended for patients on **LZD** because of an increased risk of serotonin syndrome. Nonpharmaceutical interventions for depression (e.g., counseling, cognitive behavioral therapy) are potential initial alternatives.
- In patients treated with **LZD**, use of drugs such as amphetamines, MDMA (ecstasy), cocaine, or others that increase serotonin production can cause serotonin syndrome.
- Methadone can prolong the QT interval.

Cultural and religious backgrounds

The proportion of patients with MDR-TB in the United States (U.S.) who are non-U.S.-born is substantial (approximately 72% in 2020). **Cultural background, spiritual traditions, prior experiences of treating illness, and history of access to care may impact how a patient views the path towards health.** Assessing patients' understanding of and beliefs about their diagnoses and treatment plans can provide case managers and other care providers with important information to negotiate mutually acceptable approaches to treatment.

TABLE 2. **Leveraging cultural- and religious-related resources during DR-TB diagnosis and treatment**

Examples of potential barriers	Strategies to build on cultural strengths

• Cultural stigma about TB
• Concern that the illness might interfere with immigration process and/or result in deportation
• Hindered access to health care because of:
  • Lack of health insurance coverage and/or eligibility
  • Language or cultural barriers combined with the general difficulty of navigating complex healthcare systems in the U.S.
• Patients' preference to:
  • Seek traditional medicine and healing modalities when ill
  • Seek out physicians from their own cultures, who may not be familiar with diagnosis and treatment of DR-TB
• Loss of importance to family if patient cannot continue usual activities or, especially for women, if partner expresses disapproval
• Fear of the diagnosis itself if the individual has lost a friend or family member due to DR-TB
• Psychological or other symptoms may be described in culturally-specific ways
	Explore local resources to help bridge the barriers and develop partnerships with the patient to facilitate communication and understanding:
	• Trained medical interpreters
	• Trained patient navigators
	• Bilingual health department staff
	• Cultural health brokers
	• Healthcare professionals from the patient's culture
	• Community leaders, community organizations
	• Church-based services
	• Traditional healers
	• Other local health departments with experience working with specific ethnic groups
	• Court interpreters, telephone-accessed interpreters, university language departments
	• Refugee health and social service programs
	Connect patients to supportive services and care:
	• Legal resources, especially immigration
	• Counseling services and/or peer support groups
	• Access to spiritual or religious counsel, particularly during the isolation period

Few translated patient materials that pertain specifically to DR-TB exist; however, there are several websites offering general TB patient education material in various languages. Additional sites contain cultural information that may be helpful to the case manager in anticipating the patient's cultural practices and needs. See section: ***Resources*** for translated patient education on TB-related topics, TB-specific cultural information, and other health-related cultural resources.

Economic support

Persons with DR-TB may face **economic hardship** due to the cost of treatment, loss of work, interruption in schooling, and stigma. Costs associated with the treatment and management of patients with DR-TB may vary widely and are influenced by the amount and type of drug resistance as well as the extent of disease. For patients with limited or no health insurance coverage, charges associated with the cost of drugs, diagnostic exams, and surgery may pose an extreme financial burden on individuals and families.

Health care coverage

- In states that have expanded Medicaid access under the Patient Protection and Affordable Care Act (PPACA or ACA), inpatient and outpatient TB care can be provided to adults who meet income and immigration eligibility criteria through **full-scope Medicaid.** In states where Medicaid access was not expanded under the ACA, TB Medicaid provides coverage for outpatient TB care for adults who do not qualify for full-scope Medicaid.
- In some jurisdictions, all TB care may be provided free of charge in the public health setting.
- Persons who are **undocumented immigrants** may also be able to enroll in full-scope Medicaid under the Permanently Residing in the United States Under Color of Law (PRUCOL) immigration eligibility criteria. See section: ***Resources*** for more information.
- **Organizations that provide pro bono immigration legal services** can be very helpful in exploring options available to undocumented persons or low-income immigrants. These organizations can also provide clarification about the effect of receiving public medical benefits on immigration status (e.g., "public charge" questions).

Many patients experience periods of **prolonged unemployment** associated with the period of infectiousness or due to illegal employment discrimination. The case manager may intervene and educate employers to help protect a patient's job during the period the patient must remain in isolation. The case manager may also be instrumental in assisting to find alternative sources of income and/or other assistance (i.e., obtaining disability benefits) for the patient and family while the patient cannot work (see sections: ***Patient assistance programs*** and ***Incentives and enablers***).

Addressing any financial challenges early and throughout treatment will go a long way in establishing a foundation of confidence and trust.

Patient assistance programs (PAPs)

The distribution of drugs used to treat DR-TB varies throughout the U.S., with some states maintaining central purchasing and distribution. The cost of these drugs is also variable, but in general, they are expensive, particularly when the length of treatment is factored. PAPs may be helpful in offsetting costs. **Table 3** displays some drugs used to treat DR-TB that are known to be included in PAPs. Please note that PAP information changes periodically and some offers are time-limited.

The National AIDS Drug Assistance Program (ADAP) is available as a payer of last resort, to help people with HIV/AIDS pay for the cost of some prescription drugs. The ADAP formulary includes antituberculosis agents. To inquire about a patient's eligibility for this program, contact the local ADAP coordinator at the state health department.

TABLE 3. **TB medications and patient assistance programs (PAPs)***

Brand name	Generic name	Manufacturer / assistance program	Eligibility criteria	PAP telephone / contact information
Sirturo	**Bedaquiline**	Janssen Pharmaceuticals/ Johnson & Johnson Patient Assistance Foundation	Resident of U.S. or U.S. territory, uninsured, and meets income requirements	800-652-6227 https://www.jjpaf.org/ NTCA Bedaquiline Access Guide https://www.tbcontrollers.org/docs/bedaquiline/Bedaquiline_Access_Guide_v1.1_23July2019.pdf
Pretomanid	**Pretomanid**	Viatris/ Viatris Patient Assistance Program	Resident of U.S. or U.S. territory, uninsured, and meets income requirements (will also review applicants that fall outside these criteria on a case-by-case basis)	800-796-9526 Email: ViatrisPAP@Viatris.com Patient Assistance Program website: https://www.viatris.com/en-us/lm/united-states/patient-assistance-program
Zyvox	**Linezolid**	Pfizer/ Pfizer RxPathways	Resident of U.S. or U.S. territory without prescription coverage or insufficient coverage, and meets income requirements	866-706-2400 Pfizer RxPathways www.pfizerrxpathways.com
Lamprene	**Clofazimine**	Novartis	MDR-TB	301-796-3400 FDA Division of Drug Information
Trecator	**Ethionamide**	Pfizer/ Pfizer RxPathways	Resident of U.S. or U.S. territory without prescription coverage or insufficient coverage, and meets income requirements	866-706-2400 Pfizer RxPathways www.pfizerrxpathways.com

***Please note:** PAP information changes periodically. Information in this table is current as of August 16, 2022.

Use of incentives and enablers

The use of **incentives and enablers** is another effective strategy to assist treatment adherence. Enablers such as transportation and food vouchers can address some of the economic hardships experienced during treatment. Additionally, motivation commonly wanes once the patient begins to feel better and may affect the patient's commitment to the treatment plan. Simple interventions that ease the patient's experience, as well as that of the family, can go a long way towards gaining commitment to treatment.

For more information about incentives and enablers, see section: ***Resources***.

Patients experiencing homelessness

When DR-TB is diagnosed in someone who is experiencing homelessness or at risk of becoming unhoused, additional support is necessary to ensure stable housing can be procured and co-morbidities addressed and managed early on.

- A 2014 study by Marks, et al., indicated that patients with TB who were recently unhoused were 5 times more likely to acquire drug resistance during treatment than were patients without a recent history of experiencing homelessness.
- It may be necessary to conduct closer monitoring of patients with DR-TB who have recently experienced homelessness to ensure they are showing response to treatment.
- See section: ***Resources***.

Use of legal orders

Legal measures are sometimes required when patients with infectious DR-TB remain nonadherent despite interventions to overcome barriers and to enlist cooperation. The case manager should be knowledgeable about the process for referring such patients and must **ensure that less restrictive measures have been employed and documented.** Legal orders can be especially threatening to immigrants or to people with prior experience with the justice system. Programs should understand legal orders' potential effect on an individual's legal status. When nonadherence persists, local, regional, and/or state TB programs can provide additional information on the state laws and regulations pertaining to TB.

Continuity of care

The role of the case manager becomes increasingly important when the person with DR-TB is being treated in the private sector and/or changes providers during treatment. When a person moves between facilities (such as a hospital or jail) and the community during treatment, or moves to a different jurisdiction, the case manager must ensure that appropriate treatment, monitoring, and education continue. This may require:

- Establishing relationships with a new group of staff
- Providing training and/or information on DR-TB to staff caring for the patient
- Establishing processes or utilizing standardized tools for sharing information

Hospitalization and discharge planning

Some patients may require inpatient admission to enable prompt management of drug side effects and adverse reactions.

- **If the patient is hospitalized, the case manager will need to provide support to the patient as well as to the hospital staff.** Hospital staff who do not care for TB patients routinely will need to be reminded to observe each dose of medicine (not to leave the medicine at the bedside) and may need to be educated about many aspects of DR-TB care.
- Encourage hospital staff to seek expert consultation when necessary.

Frequent and timely communication with the patient's hospital-based treatment team regarding **discharge planning** should include:

- Procurement of medications prior to discharge
- Plan for DOT (adherence verification method)
- Coordination of infusion therapy services when indicated
- Plan for home isolation if the patient will be discharged while still considered infectious (see **Table 4** and section: ***Infection control—Home isolation*** for further guidance when a patient is still considered infectious)
- Plan for addressing psychosocial issues (such as mental illness, housing, substance use disorders)
- Scheduling of follow-up clinic appointments and monitoring tests (e.g., ECGs), and providing a contact number to call should problems arise
- Ensuring the hospital is working with the patient to address **ongoing care of co-morbid conditions,** such as HIV, diabetes mellitus, and renal disease.

Interjurisdictional transfers

If the patient moves out of the case manager's jurisdiction, **concrete plans for transfer of care need to be in place before the move.** Even if the patient moves out of country, identify an accepting provider and responsible jurisdiction to apprise them of the patient's disease and treatment history. Provide the patient with enough medications to last through the travel period until they can re-establish TB care and DOT in the new jurisdiction. Contact information for family and friends, both in the current location and at the destination site, may be helpful if the patient does not arrive at the destination in a timely manner.

For persons with active or suspected TB disease or TB contacts moving domestically, either within the state or country, an **Interjurisdictional Notification (IJN)** form supports communication to the receiving jurisdiction and continuity of care.

- The National Tuberculosis Controllers Association (NTCA) has developed a standardized referral form for use with domestic transfers and maintains a list of points of contact for IJN referrals at state, large city, and U.S. territories. See section: ***Resources***.

For patients moving abroad prior to completion of therapy, a **referral to CureTB** as soon as the potential move is known will facilitate a smooth transition of care to the receiving TB program and provider. CureTB is an international referral program and a collaboration between CDC's Division of Global Migration and Quarantine (DGMQ) and the County of San Diego's Tuberculosis Control Program. CureTB works with health authorities throughout the U.S. and around the world to link people with TB to care at their destinations. Enrollment with CureTB is available for all patients with TB and is strongly recommended for any patient with MDR-TB with potential for international movement. This program also provides a treatment outcome report to the enrolling site upon case closure. This program is available at no cost to clinicians and persons under care for TB. Note: Availability of second-line medications, TB cultures, and DOT may be limited in some countries. The lead time required to obtain second-line medications may be considerable, so the earlier a referral is made, the better. See section: ***Resources***.

Co-management between private providers and public health

If the person with TB is managed by a private provider, public health staff might consider the following outreach steps:

- Make an appointment to meet the provider and the office staff as soon as possible.
- Explain the health department's role and legal responsibility to monitor the patient throughout the course of treatment and **explain the regulations** in the state or jurisdiction regarding the provider's responsibility to report information to the health department.
- Convey through actions and words the specific areas, such as DOT, that the health department team can assist in the co-management of the patient.

- Explain the **importance of treatment adherence verification** and options for DOT available through the health department. Emphasize to the provider the benefit of DOT to the person with TB. Daily contact with patients through the provision of DOT (e.g., through home or clinic visits, or video-assisted/ virtual check-ins) will ensure that any problems the patient may experience are identified and addressed quickly. Patients frequently take their cues from their clinicians; enlist the provider's support to encourage DOT and the close case management that supports a path towards successful cure.
- Explain the **infection control** practices required to keep office staff and other patients safe.
- Point the provider to resources to help manage **co-morbid conditions,** such as diabetes, malnutrition, and HIV.
- **Share this *Survival Guide* and a list of consulting resources** with the provider. Stress the importance of a DR-TB expert being involved throughout the course of treatment. In some areas, ongoing consultation with regional experts is routine. See **Appendix 1, *Expert Resources for Drug-Resistant TB.***
- If the provider and staff have the infrastructure and resourcefulness to problem-solve with the person undergoing care for TB (i.e., interfacing with insurance companies; seeking supplies of hard-to-get medications; ensuring that patients follow through on all monitoring; ordering and monitoring results of drug-resistance testing, serum drug levels, etc.), public health staff should stay actively involved to ensure that **everything** gets done and is followed up appropriately.
- Touch base with the office staff regularly. Ensure essential monitoring tests are performed as indicated. Continue to help as a problem-solver and advocate. Anticipate staff needs, such as an audiologist who takes the patient's insurance or an interpreter whom the patient trusts.
- Ensure that the office staff has been appropriately evaluated if unprotected exposure to the patient has occurred.

Reach an agreement about how and when important information (sputum and other laboratory results and radiographic results) will be shared between the private provider and public health agency.

Patients who are incarcerated or detained

Special coordination of care is necessary when a patient with DR-TB is incarcerated at the time of diagnosis or during the course of treatment. Areas for special attention include:

- **Airborne infection isolation (AII):** Persons with TB disease will require isolation and may not be returned to the general population until they are considered non-infectious (see section: ***Infection control*** for suggested criteria). The need for respiratory isolation may require movement to a hospital or different facility and additional coordination to ensure all providers involved know the treatment plan. Occasionally, persons with TB are isolated for prolonged periods and may require physical, mental and/or occupational therapy to pre-

vent physical deconditioning and situational depression due to lack of movement and stimulation. Consider allowing them out of AII for recreation daily. The need for medical isolation should not result in undue restrictions that block access to family and legal communications.

- **Adherence and DOT:** Educate facility staff regarding DOT; do not assume that medications are always observed when given in a correctional facility. Persons with TB cannot be forced to take medications while incarcerated, and staff will need to work closely to address side effects and potential barriers to adherence.
- **Coordination of care:** The local TB program should be closely involved with the management of DR-TB treatment and may also enlist a DR-TB expert to provide consultation. The case manager should maintain regular communication with the facility's nursing and clinical staff to review whether all recommended clinical monitoring and assessments for medication side effects are occurring. Other key members to involve in the coordination of care include the facility pharmacist, state or federal correctional medical officers (as applicable), and the facility administrator.
- **Transfer or release:** Persons undergoing care for TB may move to different facilities or be paroled to the community while still receiving treatment. To ensure a person with TB is not moved without the awareness of medical staff, an alert or notation can be placed in the person's record indicating the need to ensure continuity of TB care. For a person with TB who is likely to be transferred or released, coordination between medical, custody, and the local health department is critical to minimize interruption and to ensure appropriate follow-up and transfer of care and reporting of outcomes. The case manager can assist with sending an IJN to the receiving jurisdiction and coordinating a warm hand-off (e.g., scheduling a teleconference with staff from both facilities and/or health departments to review the care plan) as needed.
- **Federal custody:** Give special consideration to persons with DR-TB who are in federal custody or who may transfer to the custody of a federal law enforcement agency. For persons who are diagnosed with DR-TB while incarcerated or detained, health department staff should verify which agency has legal custody. Health department staff should communicate with the respective law enforcement agency's health service staff to coordinate continuity of care and prepare and plan for possible transfer, release, or deportation. Transfers may occur to another jurisdiction and/or to the custody of a different law enforcement agency for reasons unrelated to health status. Keep in mind that the law enforcement agency having legal custody may differ from the correctional or detention facility providing housing, security, and care for the patient.
- **Deportation:** Persons with DR-TB may be at risk for deportation if they are ordered removed by a federal immigration judge. Health department staff should ascertain whether the patient is in the custody of U.S. Immigration and Customs Enforcement (ICE), or if they have an ICE detainer and are scheduled to transfer to ICE custody upon completion of the sentence or resolution of

criminal charges. Health department staff should promptly communicate with the ICE Health Service Corps, Public Health, Safety, and Preparedness Unit to coordinate case management and prepare for any possible outcome to the legal proceedings. ICE has a partnership with and reports all patients with TB in their custody to CureTB for referral management upon deportation or bonding into the U.S. Verify **referral to CureTB** to ensure continuity of care. See section: ***Resources*** for contact information.

Infection control

DR-TB is similar in transmissibility to drug-susceptible TB and requires similar infection control strategies. Stopping TB transmission requires that the correct diagnosis be made, appropriate treatment initiated, and appropriate infection control measures instituted. Infectious or potentially infectious patients with DR-TB should be housed within a **negative pressure room** in the hospital setting, or if they are outpatients, should be **separated from medically vulnerable family or friends.**

When dealing with patients with suspected or confirmed infectious DR-TB, even greater emphasis should be placed on strict adherence to infection control standards as there is limited data on the efficacy of treatment of latent DR-TB in exposed contacts. Unfortunately, infection control practices, including isolation, are a significant hardship for many patients and their family members and may unnecessarily perpetuate and exaggerate stigmatization of the patient with DR-TB. When determining the duration of isolation, the safety of the public and the patient's family and contacts must be weighed against the mental health and morale of the patient as well as the resources required to isolate a patient.

- See section: ***Resources*** for publications that reflect current standard practices regarding TB and infection control. Local health jurisdictions are an important resource and may have specific guidelines.

Assessing infectiousness and criteria for release from airborne infection isolation

Consider the following information to guide decisions in assessing infectiousness and determining when isolation may be discontinued:

- Studies have shown that most transmission of TB occurs before drug treatment has been initiated and that smear-positive cases transmit more efficiently than smear-negative cases. However, a 1999 molecular epidemiology study in San Francisco documented TB transmission following exposure to AFB smear-negative, culture-positive TB cases accounting for 17% of secondary cases. Subsequent studies in the Netherlands and China substantiated this finding. See **Chapter 10, *Contacts*** for additional considerations regarding transmission and assessment for infectiousness.
- For drug-susceptible TB, a patient receiving TB treatment is deemed to be non-infectious when: they have taken and tolerated 2 weeks of an appropriate treatment regimen; are clinically improving; and AFB smears have shown

improvement if initially smear-positive. If initially AFB smear-negative, the patient can be deemed non-infectious after 5 days of effective treatment with clinical response. In a 2014 report from South Africa, MDR-TB patients became non-infectious once they were AFB smear-negative, started an effective regimen, and had evidence of clinical improvement.

- Because the transmission of MDR-TB has more serious potential consequences for contacts, **it is appropriate to be more cautious about returning patients with DR-TB back to their homes, schools, work sites, and congregate settings. *All settings should be assessed by the local health department before determining whether a patient may safely return.***
- **Take particular care when considering if patients can return to settings where there are young children, immunocompromised individuals, and people who have not previously been exposed to the person with TB.**
- Some experts would consider DR-TB patients **potentially** infectious as long as their sputum cultures remain positive. These experts recommend isolation while hospitalized and would not release a person with DR-TB to a high-risk setting until sputum cultures are negative. See **Table 4 for an example of criteria used to determine when a patient with MDR-TB or suspected MDR-TB may be released from isolation to either a high-risk or low-risk setting.**
- Newer data suggest risk of infection drops rapidly once effective treatment is started; however, results of second-line drug susceptibilities that inform what will be an effective regimen can take time to receive. This is an evolving area of research that may result in changes in practice for release from isolation, but at this time there are no updates to guidelines.

TABLE 4. **Criteria for release from isolation to high and lower risk settings***

Patient category	Setting	Criteria
Patient with known MDR-TB	**High risk**	• Three consecutive respiratory specimens, including at least one early AM or induced sputum, or bronchoalveolar lavage (BAL), collected at least 8 hours apart, are AFB smear negative, and no subsequent sputum specimen is AFB smear positive; **and** • At least 2 consecutive negative sputum cultures without a subsequent positive culture; OR if subsequent AFB smear positive after 3 negative AFB smears, a clinical assessment has been performed and determined to most likely NOT represent viable *M. tuberculosis*; **and** • At least 14 daily doses of appropriate† treatment for MDR-TB taken and tolerated, preferably by DOT; **and** • Clinical improvement
	Lower risk**	• Three consecutive sputum specimens, including at least one early AM or induced sputum, or BAL, collected at least 8 hours apart are AFB smear negative; **and** • At least 14 daily doses of appropriate† treatment for MDR-TB taken and tolerated, preferably by DOT; **and** • Clinical improvement

†For definition of "appropriate" treatment refer to the most recent CDC TB treatment guidelines.

Definitions:

High risk setting

- A residential or work setting in which others will share air with the TB patient and which is characterized by 1 or more of the following factors:
  - A large number or high density of persons
  - The presence of persons at high risk of progression to active TB disease (e.g., children under age of 5, persons with medical conditions associated with increased risk of progression to active TB)
  - The presence of persons who have not been previously exposed to the TB patient

Lower risk setting

- A residential setting not characterized as high risk, and:
  - No other persons will share the air with the TB patient, OR
  - All persons at increased risk of progression to TB disease if infected, including all children under the age of 5 years, who will share the air with the TB patient, have been previously exposed to the TB patient, have had a complete medical evaluation and have been started on therapy, including window period treatment for presumed LTBI (TB1), as appropriate
- A work setting not characterized as high risk, and in which no contacts are known or reasonably expected to be at increased risk of progression to TB disease if infected

*Adapted from *CDPH/CTCA Joint Guidelines for the Assessment of Tuberculosis Patient Infectiousness and Placement into High and Lower Risk Settings*, 2017

A patient may be considered for placement in a lower risk setting without meeting these criteria if no previously unexposed persons will be present (see section: ***Home isolation*)

Home isolation

Many patients with DR-TB do not require hospitalization and may be on home isolation at the start of treatment. Some patients may be hospitalized to initiate treatment and become ready for discharge prior to becoming non-infectious. Consider the following factors when deciding whether home isolation is appropriate:

- **Physical environment** (is the home very small and crowded with little air flow?)
- **Medical risks of household members** (young children, immunocompromised?)
- **Stability of household** (relative likelihood that no new members will enter)
- **Safety and protection of service providers** in the home

While TB patients cannot be isolated from their families and homes indefinitely, every effort should be made to ensure the safety of contacts.

When caring for persons with DR-TB who are considered potentially infectious, healthcare and other service providers entering the home to deliver DOT and/or other healthcare services (e.g., patient interviews, home infusions) must comply with current infection control measures to prevent occupational exposure. For information that is essential to consider when preparing for the care of patients with infectious TB in the home setting, consult with national (National Institute for Occupational Safety and Health [NIOSH]) and state occupational health and safety programs, your state TB program, or your TB Center of Excellence.

Decisions about home isolation should be made in consultation with the local health officer/ TB controller and experts in the care of DR-TB.

In some cases, home isolation will not be possible. In these cases, if resources permit, consider:

- Patients can sometimes be housed in a motel room which has an air supply that vents to the outdoors.
- A mobile home or trailer may be rented or purchased and used to house the patient until they are non-infectious.

Transportation

Considerations for transporting the patient with infectious DR-TB:

- **Private car:** Have windows open, mask patient, if possible, eat outdoors at stops.
- **Ambulance:** Identify an ambulance company that has vehicles with negative pressure and high efficiency particulate air (HEPA) filtration. Patients should wear surgical masks, and providers and drivers should wear N-95 respirators.
- **Commercial airline flights:** WHO guidelines consider patients with MDR-TB to be infectious until there is evidence of clinical response to treatment and two consecutive sputum culture-negative results (see ***Resources***).

- **Air ambulance:** Contact the patient's insurance company, the hospital social worker or case manager, or expert resources to identify an air ambulance company or private flight arrangements to safely transport the patient. WHO has published guidelines regarding transporting potentially infectious TB patients by airline (see ***Resources***).

Drug supply management

Drug availability

Many second-line TB medications are not regularly in stock at local pharmacies or wholesalers. If the local pharmacy does not carry the drug, ask the pharmacist to order it and ask how long it will take to get it. If a pharmacy or wholesaler states a drug is not available or "in stock," additional steps can help determine if the drug is truly unavailable.

1. Check the U.S. Food and Drug Administration (FDA) Drug Shortage website, or the American Society of Health-System Pharmacists Drug Shortage website to see if a drug shortage has been reported (see ***Resources***).
2. Ask the pharmacy or wholesaler to check with other distribution centers.
3. Call (or ask the pharmacy to call) the drug manufacturer directly and ask:
    - If there is stock
    - How the drug can be obtained (e.g., through wholesalers and/or directly from the manufacturer)
    - If the drug is on allocation that requires a special request (as has been the case for AK)
    - If the drug is short-dated (expiration date is imminent and wholesalers will not keep in stock and may require special agreement to release the drug)
    - If out of stock, anticipated date of availability

If **not available** from the pharmacy or manufacturer:

- Contact the TB nurse consultant at the state health department or the state TB controller; if your state TB program supplies TB medications, its central pharmacy may carry or have access to second-line drugs.
- Contact local hospitals to see if they have a supply to share.
- Try to identify a patient in the area who has recently been taking the drug and see how that patient's case manager obtained the drug.

Additionally, if the local pharmacy cannot obtain the drug in a timely fashion, call your local hospital or a neighboring TB clinic and ask if you can borrow a quantity of the drug.

Drug shortages

Drug shortages have become increasingly common in the U.S. and most TB programs have been impacted by shortages of first- and second-line TB drugs. CDC has received reports of difficulty obtaining INH, RIF, CS, ETA, and rifapentine.

Suggestions for managing drug supply and addressing drug shortages:

- If your state does not have a central pharmacy that stocks and distributes drugs used to treat DR-TB, order and keep on hand a several-month supply of drugs to prevent treatment interruption due to supply shortages.
- If you are told a required drug is on **back order, unavailable,** or **out of stock,** report this immediately to your state TB program and complete the *TB Drugs & Diagnostics Shortages Reporting Form* at the National TB Controllers Association website. The FDA is also a potential resource. See ***Resources***.

TB drug supply can also be impacted by insurance company policies. Some insurance companies will limit the number of days or weeks a pharmacy can supply certain medications. Fluoroquinolones, and macrolides in particular, may require special treatment authorization from the insurance company. To address this issue:

- Ask the pharmacy to help anticipate any such restrictions on the patient's prescription plan.
- Write a letter to the insurer explaining the medical condition, duration of anticipated use of the drug, and need for that particular drug over another formulary drug to request authorization for prescription coverage. For most efficient processing, include the patient's name, date of birth, insurance ID and policy numbers, as well as the subscriber information.

See **Chapter 5, *Medication Fact Sheets,*** for more details about each drug.

Tools for monitoring and case management

Tool 1: Drug-o-Gram

Tool 2: MDR Monitoring Checklist

Tool 3: Bacteriology Flow Sheet

Tool 4: Lab Flow Sheet

Tool 5: Vision Screening Flow Sheet

Tool 6: Hearing and Vestibular Screening Flow Sheet

Tool: 7 BPaL/BPaLM TB Care Plan

SUMMARY DATE:	NAME:	DOB:	HEALTH DEPARTMENT:	TREATING PHYSICIAN:	FILE NO:

Treatment Regimen

Bacteriology

Date	Wt.	INH	RIF	PZA	EMB	LFX	MFX	BDQ	Pa	LZD	CFZ	CS			Date	Spec	Sm/Cult	Comments

Susceptibility Results

Date	Spec.	Lab	INH	RIF	EMB	PZA	SM	KM	AK	OFX	MFX	RFB	CS	CFZ	ETA	PAS	BDQ	LZD		Reported

Treatment Key: ● = DOT ▲ = SAT

PATIENT NAME: _____ TREATMENT START DATE: _____ TREATMENT REGIMEN: _____

Activity	Baseline	Month of Treatment 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Date																			
CLINICAL MONITORING																			
Sputum smear and culture[1]	☐☐☐	☐☐	☐☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Imaging[2] (CXR, CT, other)	☐			☐			☐			☐			☐						☐
Weight[3] and baseline BMI	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Symptom review[4]	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Clinician evaluation	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
DST[5]	☐																		
LAB MONITORING FOR TOXICITY / CO-MORBIDITIES																			
CBC[6]	☐	☐☐	☐☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Creatinine[7]	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
LFTs[8]	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
K, Ca, Mg, bicarbonate[9]	☐	☐	☐	☐	☐	☐	☐	☐	☐										
Lipase/amylase[10]	☐																		
Drug level[11]		☐																	
TSH[12]	☐			☐			☐			☐			☐			☐			☐
HIV (± viral hep serology)[13]	☐																		
Pregnancy	☐																		
MONITORING PROCEDURES																			
Audiogram & vestibular exam[14]	☐	☐	☐	☐	☐	☐	☐	☐	☐										
Vision exam[15]	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Peripheral neuropathy[16]	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Arthralgias[17]	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Depression[18]	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
ECG[19]	☐	☐		☐			☐												

*Important: Monitoring recommendations may change if treatment regimen or patient status changes. A box indicates monitoring activity is recommended. Check box when activity is completed. **Updated 6/22/2022**

1. Collect 3 sputum specimens for AFB smear and culture at baseline and at least 1 sample every 1-2 wks, then 1-2 specimens monthly until culture conversion, then at least 1 sample monthly until end of treatment.
2. Obtain baseline imaging and monitor every 3 mos during treatment (every 6 mos in year 2 when treating beyond 1 year). Consider obtaining end of treatment imaging to serve as new baseline going forward.
3. Monitor weight monthly and adjust medications as needed.
4. Monitor for symptoms monthly documenting when symptoms resolve.
5. Obtain 1st and 2nd-line DST results at baseline. Repeat if patient on RIPE and remains culture positive prior to MDR-TB treatment start, and again if patient fails to convert culture after 3 mos on treatment.
6. Obtain CBC with diff every 1-2 wks for first 6-8 wks, then monthly thereafter while taking LZD.
7. Obtain serum creatinine at baseline and monthly when taking BPaL or an injectable agent.
8. LFTs (ALT, AST, T.bili, Alk phos) at baseline then monthly while on BDQ, Pa, PZA, ETA or PAS; consider checking at week 2 of treatment in patients with increased risk for hepatotoxicity.
9. K, Ca, Mg, and bicarbonate at baseline and monthly while taking BDQ or an injectable agent.
10. Consider checking lipase (+/- amylase) if underlying concerns for pancreatitis or if symptoms develop.
11. Therapeutic drug monitoring (TDM) should be obtained for patients receiving CS or LZD after 1-2 weeks on target dose. TDM may be obtained for other drugs as clinically indicated.
12. Obtain TSH at baseline and every 3 mos when initiating ETA or PAS. Consider more frequent monitoring if symptoms or abnormalities. Consider baseline TSH if concerns for prolonged QT interval on baseline ECG.
13. Obtain baseline HIV test for all. Consider viral hep serology testing for those with risk factor for Hep B or C.
14. Perform audiogram and vestibular exam at baseline then monthly while taking an injectable agent.
15. Perform visual acuity + color discrimination exams at baseline and monthly while taking EMB or LZD.
16. Monitor for peripheral neuropathy at baseline and monthly when taking LZD and as clinically indicated for patients on fluoroquinolones (MFX/LFX).
17. Monitor for arthralgias at baseline and monthly while taking PZA or fluoroquinolone (MFX/LFX).
18. Monitor for depression at baseline and monthly while taking CS.
19. Obtain ECG and check QTcF at baseline and at least 2, 12, and 24 weeks when taking BDQ. Consider checking monthly if taking additional QT prolonging agents (e.g., MFX, CFZ, other).

TOOL 3: **Bacteriology Flow Sheet**

File # _____

Bacteriology

Date/time collected	Report date	Spec #	Source	Laboratory	Smear	NAAT/PCR	Culture	Susceptibilities & Comments

TOOL 4: **Lab Flow Sheet**

	DATE:								
HEME	WBC								
	Hemoglobin								
	Hematocrit								
	Platelets								
Chemistry	Na								
	K								
	Cl								
	CO_2								
	Ca								
	Mg								
	Glucose								
	BUN								
	Creatinine								
	CrCl								
	Total Bili								
	Alk Phos								
	AST (SGOT)								
	ALT (SGPT)								
	T. Protein								
	Albumin								
	Amylase								
	Lipase								
	Uric Acid								
Urine	Spec. gravity								
	pH								
	Ketone								
	Glucose								
	Protein								
	Heme								
Other	TSH								
	PT / PTT								
	HgbA1C								
	CD4								
	Viral Load								
	Pregnancy								
	HIV								
	IGRA								
Drug Levels									

TOOL 5: **Vision Screening Flow Sheet**

Visual acuity chart used (type and distance; e.g., 10 or 20 foot): ____________________________________

Color discrimination tool used (type and number of plates if applicable):______________________________

BASELINE RESULT

Date	Visual acuity		Color vision		Performed by (signature)	Comment or action
	Right eye	Left eye	Right eye	Left eye		
	___ /___	___ /___				

MONTHLY RESULT

Date	Visual acuity		Color vision		Performed by (signature)	Comment or action
	Right eye	Left eye	Right eye	Left eye		
	___ /___	___ /___				
	___ /___	___ /___				
	___ /___	___ /___				
	___ /___	___ /___				
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	___ /___	___ /___				
	___ /___	___ /___				

Note: If changes from baseline noted during monthly screening, inform treating clinician and refer for further evaluation.

Adapted from the Oregon Health Authority TB Program Visual Acuity and Test for Color Discrimination form

TOOL 6: **Hearing and Vestibular Screening Flow Sheet**

Date	Change in hearing, ringing or fullness in ears?	Dizzy, weak or unsteady?	Romberg	Walking	Heel-to-Toe Walk	Audiogram		Signature	Comment/Action
Baseline	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of Balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		
	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of Balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		
	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of Balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		
	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of Balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		
	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of Balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		
	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of Balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		
	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of Balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		
	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of Balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		

Note: If changes from baseline noted during monthly screening, inform treating clinician and refer for further evaluation.

Adapted from the Texas Center for Infectious Disease Hearing/Vision/Vestibular Report

Activity	Baseline	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7-9
Request and review medical records	Medical/social history, physical exam	Physician assessment every 1-2 weeks	Physician assessment minimum monthly	→	→	→	→	⋯▸
Drug susceptibility testing (DST)	Review DST results; request 2nd-line DST/MDDR	N/A	N/A	Repeat DST **if culture remains (+)** after 2M	Repeat as indicated	Repeat as indicated	Repeat as indicated	
Imaging	**PA chest** [other view(s) if indicated]	N/A	N/A	Consider repeat imaging	N/A	N/A	End of treatment imaging	
Height and weight	**Calculate BMI**/LBW. Obtain weight monthly	→	→	→	→	→	→	⋯▸
Vision screening	Assess **visual acuity and color vision** monthly	Monthly while taking Linezolid	→	→	→	→	→	⋯▸
Peripheral neuropathy screening	Assess at baseline and monthly	→	→	→	→	→	→	⋯▸
CBC with differential	Obtain at baseline	Obtain every 1-2 weeks	Obtain every 1-2 weeks	Monthly (or more frequently as indicated while on Linezolid)	→	→	→	⋯▸
Metabolic panel (CMP)	**CMP to include:** K, Ca, Mg, creatinine, bicarbonate, (amylase and lipase)*	Listed components of CMP monthly	→	→	→	→	→	⋯▸
Liver function (LFTs)	**LFTs to include:** ALT, AST, total bilirubin, and alkaline phosphatase	**LFTs** (at week 2)*, **monthly** (if symptomatic, consider more frequent monitoring)	→	→	→	→	→	⋯▸
Other lab testing	**Obtain HIV test;** consider hep serology, A1C when risk factor(s) present; TSH* when indicated	Repeat only if indicated ⋯▸	⋯▸	⋯▸	⋯▸	⋯▸	⋯▸	
Electrocardiogram (ECG)	Obtain baseline ECG **(check QTcF)**	**Week 2 following treatment start** (check QTcF)	Repeat as indicated	**Week 12 ECG** (check QTcF)	Repeat as indicated	Repeat as indicated	**Week 24 ECG** (check QTcF)	
Sputum monitoring (pulmonary TB)	Sputum x 3 (one early morning) for AFB smear & TB culture	Consider at least 1 sputum 1x/wk until Sm(-) then one every 2 wk until culture conversion	Monthly sputum for TB culture following culture conversion	→	→	→	Extend 3 months **if sputum remains culture (+) after M2**	⋯▸
Airborne isolation precautions	Continue until deemed non-infectious per local/state guidelines	⋯▸	⋯▸	⋯▸				
Therapeutic drug monitoring	Not performed at baseline	Obtain **Linezolid peak** (2hr & 6hr) **and trough 1-2wks following treatment start**	Repeat peak/trough drug levels if needed until targets achieved	⋯▸				
Treatment monitoring	Directly observed therapy (DOT)/patient education	→	→	→	→	→	→	⋯▸
Nutritional assessment	→	→	→	→	→	→	→	⋯▸
Assess overall health, mental, emotional needs	→	→	→	→	→	→	→	⋯▸

* These are laboratory examinations recommended in the *Provisional CDC Guidance for the Use of Pretomanid as part of a Regimen [Bedaquiline, Pretomanid, and Linezolid (BPaL)] to Treat Drug-Resistant Tuberculosis Disease* (2021) but may not be necessary for all patients. Consider performing amylase/lipase when there are underlying concerns for pancreatitis, TSH if prolonged QT interval on baseline ECG or concern for hypothyroidism, and LFTs at week 2 if elevated risk for hepatotoxicity.

Post-treatment monitoring: Complete a symptom review, medical evaluation, sputa for AFB smear and cultures, and chest x-ray every 6 months for at least 2 years.

Resources

MONITORING THROUGHOUT TREATMENT

Assessing for and addressing potential side effects

Nursing Guide for Managing Side Effects to Drug-resistant TB Treatment
International Council of Nurses and Curry International Tuberculosis Center
https://www.currytbcenter.ucsf.edu/products/view/nursing-guide-managing-side-effects-drug-resistant-tb-treatment guidebook and tools

Guidance on requirements for QTc measurement in ECG monitoring when introducing new drugs and shorter regimens for the treatment of Drug-resistant Tuberculosis
USAID/KNCV Challenge TB, 2018
https://www.challengetb.org/publications/tools/pmdt/Guidance_on_ECG_monitoring_in_NDR_v2.pdf

Examples of online QTc calculators include:

- MD+CALC: https://www.mdcalc.com/calc/48/corrected-qt-interval-qtc
- Mayo Clinic QT Interval/QTc Calculator: https://www.mayoclinic.org/medical-professionals/cardiovascular-diseases/calculators/corrected-qt-interval-qtc-calculator/itt-20487211

Screening for depression and psychosis

Beck Depression Inventory (BDI)
https://www.apa.org/pi/about/publications/caregivers/practice-settings/assessment/tools/beck-depression

Personal Health Questionnaire Depression Scale (PHQ-9)
PHQ-9 in multiple languages available through Multicultural Mental Health Resource Centre
https://multiculturalmentalhealth.ca/clinical-tools/screening-for-common-mental-disorders/

Mental Health Assessment Tool
Heartland National Tuberculosis Center (2013)
https://www.heartlandntbc.org/wp-content/uploads/2021/12/mental_health_screening_tool.pdf

PATIENT-CENTERED CARE AND ENSURING ADHERENCE TO TREATMENT

Providing the injectable agent

Administration of Amikacin Injection
Heartland National TB Center
https://www.heartlandntbc.org/wp-content/uploads/2021/12/administration_of_amikacin_injection.pdf

***Outpatient infusion therapy for MDR-TB: A practical guide* (2004)**
New Jersey Medical School National Tuberculosis Center.
https://globaltb.njms.rutgers.edu/downloads/products/InfusionTherapy.pdf

Patient education

For patient information sheets in multiple languages on some of the second-line anti-TB medications (CFZ, ETA, PAS, LZD, levofloxacin, MFX) see British Columbia Centre for Disease Control website:
http://www.bccdc.ca/health-info/diseases-conditions/tuberculosis/translated-content

We are TB
Tuberculosis survivors and advocates network in the U.S.A.
https://www.wearetb.com/

Preferred Terms for Select Population Groups and Communities
Centers for Disease Control and Prevention
https://www.cdc.gov/healthcommunication/Preferred_Terms.html

Patient disclosure/consent examples

Disclosure and consent for drug therapy for treatment of TB disease
Texas Department of State Health Services (2021)
https://www.dshs.texas.gov/sites/default/files/IDCU/disease/tb/forms/DOCS/TB-411.doc

Economic support
(health care coverage, incentives and enablers, housing)

National Immigration Law Center
https://www.nilc.org/

CDC's *Self-Study Module 6: Managing Tuberculosis Patients and Improving Adherence* has a section on incentives and enablers.
Centers for Disease Control and Prevention
https://www.cdc.gov/tb/education/ssmodules/pdfs/Modules6-508.pdf

Office of Equal Employment Opportunity and Workplace Equity
Centers for Disease Control and Prevention
https://www.cdc.gov/eeo/faqs/rehabact.htm#5

Introduction to Persons Residing Under Color of Law (PRUCOL) Factsheet
Health Law Advocates
https://hcfama.org/wp-content/uploads/2020/11/itl-ma_prucol_fact_sheet.pdf

Homelessness and TB Toolkit
Curry International Tuberculosis Center
https://www.currytbcenter.ucsf.edu/products/view/homelessness-and-tb-toolkit

MULTICULTURAL RESOURCES

Translated TB-specific patient education

British Columbia Centre for Disease Control
http://www.bccdc.ca/health-info/diseases-conditions/tuberculosis/translated-content

Georgia Department of Public Health
https://dph.georgia.gov/health-topics/tuberculosis-tb-prevention-and-control/tb-public-health-clinic-forms

Massachusetts Health and Human Services Department
https://www.mass.gov/lists/tb-information-for-your-patients-in-english-and-other-languages

Minnesota Department of Health
https://www.health.state.mn.us/diseases/tb/basics/index.html

National Library of Medicine, National Institutes of Health
www.nlm.nih.gov/medlineplus/languages/tuberculosis.html

New South Wales Health
https://www.mhcs.health.nsw.gov.au/

Oregon Health Authority
https://www.oregon.gov/oha/PH/DISEASESCONDITIONS/COMMUNICABLEDISEASE/TUBERCULOSIS/Pages/factsheets.aspx

TB Education and Training Resources (CDC)
https://findtbresources.cdc.gov/

TB-specific cultural information

Country Guides
Cambodia, Colombia, Dominican Republic, Ecuador, El Salvador, Honduras, Indonesia, Myanmar (Burma), Peru, Philippines, Somalia, South Korea, Vietnam

Cultural Quick Reference Guides
Philippines, Afghanistan, China, Guatemala, Haiti, India, Mexico, Ukraine
Produced by Southeastern National Tuberculosis Center
https://sntc.medicine.ufl.edu/home/index#/products

Cultural Competency and Tuberculosis Care:
A guide for self-study and self-assessment (2008)
Produced by Rutgers Global Tuberculosis Institute
https://globaltb.njms.rutgers.edu/educationalmaterials/productfolder/culturalcompetency.php

Ethnographic Guides
Burma, China, Laos, Mexico, Somalia, Vietnam
Produced by Centers for Disease Control and Prevention — Division of TB Elimination
www.cdc.gov/tb/publications/guidestoolkits/EthnographicGuides/default.htm

Health-related cultural information and cross-cultural training

Culture, Language, and Health Literacy | HRSA
https://www.hrsa.gov/about/organization/bureaus/ohe/health-literacy/culture-language-and-health-literacy

EthnoMed
https://ethnomed.org/

Think Cultural Health: Bridging the Health Care Gap through Cultural Competency Continuing Education Programs.
U.S. HHS, Office of Minority Health. Online nurse training with CEUs.
https://thinkculturalhealth.hhs.gov/education/nurses

A Physician's Practical Guide to Culturally Competent Care and Culturally Competent Nursing Care: A Cornerstone of Caring.
U.S. Health Human Services, Office of Minority Health. Online courses with CMEs.
https://thinkculturalhealth.hhs.gov/education/physicians

CONTINUITY OF CARE

Interjurisdictional transfers

Process for international notification of TB cases
National TB Controller's Association
https://www.tbcontrollers.org/resources/interjurisdictional-transfers/

CureTB
619-542-4013
https://www.sandiegocounty.gov/hhsa/programs/phs/cure_tb/
E-mail: CureTB@cdc.gov

Incarcerated patients

ICE Health Service Corps
202-809-8798; 202-660-2463; 202-321-0829
Contact updated: September 1, 2022.

Tuberculosis Case Management for Undocumented and Deportable Inmates/Prisoners/ Detainees in Federal Custody (2014)
https://www.tbcontrollers.org/docs/corrections/Federal_TBCaseMgmt_for_Undoc-Deport_Corrections_v3_08-12-2014.pdf

INFECTION CONTROL

CDC's Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings
MMWR 2005; 54 (No. RR-17)
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm

Tuberculosis Infection Control: A Practical Manual for Preventing TB, Second Edition, 2022/2023 Updates
Curry International Tuberculosis Center
https://www.currytbcenter.ucsf.edu/products/view/tuberculosis-infection-control-practical-manual-preventing-tb

Transportation — commercial airline flights

Tuberculosis and air travel: guidelines for prevention and control; 3rd edition, 2008
World Health Organization
https://www.who.int/publications/i/item/9789241547505

DRUG SUPPLY MANAGEMENT

U.S. Food and Drug Administration Drug Shortage website:
https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages

American Society of Health-System Pharmacists Drug Shortage website:
https://www.ashp.org/drug-shortages

TB Drugs & Diagnostics Shortages Reporting Form
at the National TB Controllers Association website:
https://www.tbcontrollers.org/

Accessibility of all websites verified February 22, 2023.

References

Case management of MDR-TB—Roles and responsibilities

- Commission for Case Manager Certification: Definition of Case Management, 2022. Available at: https://ccmcertification.org/about-ccmc/about-case-management/definition-and-philosophy-case-management#. Accessed December 15, 2022.
- Global Tuberculosis Institute. Tuberculosis Case Management: A Guide for Nurses. 2017:1-116. Available at: https://globaltb.njms.rutgers.edu/educationalmaterials/productfolder/tbcasenurse.php. Accessed December 15, 2022.
- Mitnick C, Bayona J, Palacios E, et al. Community-based therapy for multidrug-resistant tuberculosis in Lima, Peru. *N Engl J Med.* 2003;348(2):119-128. doi:10.1056/NEJMoa022928.
- Nahid P, Mase SR, Migliori GB, et al. Treatment of drug-resistant tuberculosis. An official ATS/CDC/ERS/IDSA clinical practice guideline [published correction appears in *Am J Respir Crit Care Med*. 2020 Feb 15;201(4):500-501]. *Am J Respir Crit Care Med.* 2019;200(10):e93-e142. doi:10.1164/rccm.201909-1874ST.
- Palacios E, Guerra D, Llaro K, Chalco K, Sapag R, Furin J. The role of the nurse in the community-based treatment of multidrug-resistant tuberculosis (MDR-TB). *Int J Tuberc Lung Dis.* 2003;7(4):343-346.

Initiating and monitoring treatment

- Centers for Disease Control and Prevention. Provisional CDC guidance for the use of Pretomanid as part of a regimen [Bedaquiline, Pretomanid, and Linezolid (BPaL)] to treat drug-resistant tuberculosis disease. https://www.cdc.gov/tb/topic/drtb/bpal/default.htm. Accessed December 15, 2022.
- Centers for Disease Control and Prevention. Provisional CDC guidelines for the use and safety monitoring of bedaquiline fumarate (Sirturo) for the treatment of multidrug-resistant tuberculosis. *MMWR Recomm Rep.* 2013 Oct 25;62(RR-09):1-12. Erratum in: *MMWR Recomm Rep.* 2013 Nov 15;62(45):906.
- Jahnavi G, Sudha CH. Randomised controlled trial of food supplements in patients with newly diagnosed tuberculosis and wasting. *Singapore Med J.* 2010;51(12):957-962.
- Holland DP, Hamilton CD, Weintrob AC, et al. Therapeutic drug monitoring of antimycobacterial drugs in patients with both tuberculosis and advanced human immunodeficiency virus infection. *Pharmacotherapy*. 2009;29(5):503-510. doi:10.1592/phco.29.5.503.
- International Council of Nurses and Curry International Tuberculosis Center. Nursing Guide for Managing Side Effects to Drug-resistant TB Treatment. Available at: https://www.currytbcenter.ucsf.edu/products/nursing-guide-managing-side-effects-drug-resistant-tb-treatment. Accessed December 15, 2022.
- Partners in Health. The PIH guide to the medical management of multidrug-resistant tuberculosis, 2nd Edition. Boston, MA. USAID TB CARE II. 2013. Available at: https://www.pih.org/article/download-the-pih-guide-to-medical-management-of-multidrug-resistant-tubercu. Accessed December 15, 2022.
- Postema PG, Wilde AA. The measurement of the QT interval. *Curr Cardiol Rev.* 2014;10(3):287-294. doi:10.2174/1573403x10666140514103612.
- Seaworth BJ. Multidrug-resistant tuberculosis. *Infect Dis Clin North Am.* 2002;16(1):73-105.
- Seaworth BJ. Multidrug-resistant tuberculosis. *Infect Dis Clin North Am.* 2002;16(1):73-105. doi:10.1016/s0891-5520(03)00047-3.
- Toczek A, Cox H, du Cros P, Cooke G, Ford N. Strategies for reducing treatment default in drug-resistant tuberculosis: systematic review and meta-analysis. *Int J Tuberc Lung Dis.* 2013;17(3):299-307. doi:10.5588/ijtld.12.0537.
- Vandenberk B, Vandael E, Robyns T, et al. Which QT correction formulae to use for QT monitoring? [published correction appears in *J Am Heart Assoc.* 2018 Aug 21;7(16):e004252]. *J Am Heart Assoc.* 2016;5(6):e003264. Published 2016 Jun 17. doi:10.1161/JAHA.116.003264.
- World Health Organization. WHO consolidated guidelines on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment, 2022 update https://www.who.int/publications/i/item/9789240065116. Accessed December 15, 2022.
- World Health Organization. WHO operational handbook on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment, 2022 update. https://www.who.int/publications/i/item/9789240065116. Accessed February 20, 2023.
- Wu S, Zhang Y, Sun F, et al. Adverse events associated with the treatment of multidrug-resistant tuberculosis: a systematic review and meta-analysis. *Am J Ther.* 2016;23(2):e521-e530. doi:10. 1097/01.mjt.0000433951.09030.5a.

Patient-centered care and ensuring adherence to treatment

- Baral SC, Aryal Y, Bhattrai R, King R, Newell JN. The importance of providing counselling and financial support to patients receiving treatment for multi-drug resistant TB: mixed method qualitative and pilot intervention studies. *BMC Public Health.* 2014;14:46. Published 2014 Jan 17. doi:10.1186/1471-2458-14-46.
- Centers for Disease Control and Prevention, 2022. *Preferred terms for select population groups & communities.* Available at: https://www.cdc.gov/healthcommunication/Preferred_Terms.html. Accessed March 16, 2023.
- Chalco K, Wu DY, Mestanza L, et al. Nurses as providers of emotional support to patients with MDR-TB. *Int Nurs Rev.* 2006;53(4):253-260. doi:10.1111/j.1466-7657.2006.00490.x.
- Farmer P, Kim JY. Community based approaches to the control of multidrug resistant tuberculosis: introducing "DOTS-plus". *BMJ*. 1998;317(7159):671-674. doi:10.1136/bmj.317.7159.671.
- Lutge EE, Wiysonge CS, Knight SE, Sinclair D, Volmink J. Incentives and enablers to improve adherence in tuberculosis. *Cochrane Database Syst Rev.* 2015;2015(9):CD007952. Published 2015 Sep 3. doi:10.1002/14651858.CD007952.pub3.
- Marks SM, Flood J, Seaworth B, et al. Treatment practices, outcomes, and costs of multidrug-resistant and extensively drug-resistant tuberculosis, United States, 2005-2007. *Emerg Infect Dis.* 2014;20(5):812-821. doi:10.3201/eid2005.131037.
- M'Imunya JM, Kredo T, Volmink J. Patient education and counseling for promoting adherence to treatment for tuberculosis. *Cochrane Database of Syst Rev.* 2012 (5): CD006591. Doi:10.1002/14651858.CD006591.pub2.
- Munro SA, Lewin SA, Smith HJ, Engel ME, Fretheim A, Volmink J. Patient adherence to tuberculosis treatment: a systematic review of qualitative research. *PLoS Med.* 2007;4(7):e238. doi:10.1371/journal.pmed.0040238.
- Toczek A, Cox H, du Cros P, Cooke G, Ford N. Strategies for reducing treatment default in drug-resistant tuberculosis: systematic review and meta-analysis. *Int J Tuberc Lung Dis.* 2013;17(3):299-307. doi:10.5588/ijtld.12.0537.
- TB CARE 1. *International Standards for Tuberculosis Care.* Edition 3. TB CARE 1. The Hague. 2014. Available at: https://theunion.org/technical-publications/international-standards-for-tuberculosis-care. Accessed March 17, 2023.
- Peloquin CA, Auclair B. Pharmacology of the second-line antituberculosis drugs. In: Bastian I, Portaels F, eds. Multidrug-resistant tuberculosis. AA Dordrecht, The Netherlands: Kluwer Academic Publishers, 2000:163-174. DOI: 10.1007/978-94-011-4084-3_10
- World Health Organization. WHO operational handbook on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment, 2022 update. Available at: https://www.who.int/publications/i/item/9789240065116. Accessed February 20, 2023

Continuity of care

- Centers for Disease Control and Prevention. Tuberculosis - United States, 2021. *MMWR*. 2022 March 25;71(12):441–446.
- Mitruka K, Winston CA, Navin TR. Predictors of failure in timely tuberculosis treatment completion, United States. *Int J Tuberc Lung Dis.* 2012;16(8):1075–1082. doi:10.5588/ijtld.11.0814.

Infection control

- California Department of Public Health and California Tuberculosis Controllers Association. Guidelines for the assessment of tuberculosis patient infectiousness and placement into high and lower risk setting. 2017. Available at: https://ctca.org/wp-content/uploads/2018/11/InfectiousnessOctober2017.pdf. Accessed December 15, 2022.
- Centers for Disease Control and Prevention. Guidelines for preventing the transmission of Mycobacterium tuberculosis in health-care settings. *MMWR Recomm Rep.* 2005 March 25;54(No. RR-17) :1-141.
- Sosa LE, Njie GJ, Lobato MN, et al. Tuberculosis screening, testing, and treatment of US health care personnel: recommendations from the National Tuberculosis Controllers Association and CDC, 2019. *MMWR*. 2019 May 17;68(19):439–443.
- Curry International Tuberculosis Center, 2011. *Tuberculosis Infection Control: A Practical Manual for Preventing TB.* Available at: https://www.currytbcenter.ucsf.edu/products/view/tuberculosis-infection-control-practical-manual-preventing-tb. Accessed December 15, 2022.
- Martinez L, Blanc L, Nunn P, Raviglione M. tuberculosis and air travel: WHO guidance in the era of drug-resistant TB. *Travel Med Infect Dis.* 2008;6(4):177-181. doi:10.1016/j.tmaid.2007.10.004.

- Dharmadhikari AS, Mphahlele M, Venter K, et al. Rapid impact of effective treatment on transmission of multidrug-resistant tuberculosis. *Int J Tuberc Lung Dis.* 2014:18(9):1019–1025. doi:10.5588/ijtld.13.0834.
- Tostmann A, Kik SV, Kalisvaart NA, et al. Tuberculosis transmission by patients with smear-negative pulmonary tuberculosis in a large cohort in the Netherlands. *Clin Infect Dis.* 2008;47 (9):1135–1142. doi:10.1086/591974.
- World Health Organization, 2008. Tuberculosis and Airline Travel: Guidelines for Prevention and Control, 3rd Edition. Available at: https://www.who.int/publications/i/item/9789241547505. Accessed December 15, 2022.

Drug supply management

- Centers for Disease Control and Prevention. Interruptions in supplies of second-line antituberculosis drugs—United States, 2005–2012. *MMWR*. 2013 Jan 18;62(02);23-26.