

Standardised regimen for adult XDR-TB treatment

Injectable Phase: Treatment taken daily for at least 6 months		
Patient weight	Drug	Dosage
< 33 kg	Capreomycin	15-20 mg/kg
	Moxifloxacin	400 mg
	Ethionamide	15-20 mg/kg
	Ethambutol or Terizidone or Cycloserine	25 mg/kg 15-20 mg/kg 15-20 mg/kg
	Pyrazinamide	30-40 mg/kg
	PAS	150 mg/kg
	33–50 kg	Capreomycin
Moxifloxacin		400 mg
Ethionamide		500 mg
Ethambutol or Terizidone or Cycloserine		800-1200 mg 750 mg 500 mg
Pyrazinamide		1000-1750 mg
PAS		8000 mg
51–70 kg		Capreomycin
	Moxifloxacin	400 mg
	Ethionamide	750 mg
	Ethambutol or Terizidone or Cycloserine	1200-1600 mg 750 mg 750 mg
	Pyrazinamide	1750-2000 mg
	PAS	8000 mg
	> 70 kg	Capreomycin
Moxifloxacin		400 mg
Ethionamide		750-1000 mg
Ethambutol or Terizidone or Cycloserine		1600-2000 mg 1000 mg 750-1000 mg
Pyrazinamide		2000-2500 mg
PAS		8000 mg

Continuation Phase: Treatment taken daily for at least 18 months		
Patient weight	Drug	Dosage
< 33 kg	Moxifloxacin	400 mg
	Ethionamide	15-20 mg/kg
	Ethambutol or Terizidone or Cycloserine	25 mg/kg 15-20 mg/kg 15-20 mg/kg
	Pyrazinamide	30-40 mg/kg
	PAS	150 mg/kg
	Moxifloxacin	400 mg
	33–50 kg	Ethionamide
Ethambutol or Terizidone or Cycloserine		800-1200 mg 750 mg 500 mg
Pyrazinamide		1000-1750 mg
PAS		8000 mg
Moxifloxacin		400 mg
Ethionamide		750 mg
Ethambutol or Terizidone or Cycloserine		1200-1600 mg 750 mg 750 mg
51–70 kg	Pyrazinamide	1750-2000 mg
	PAS	8000 mg
	Moxifloxacin	400 mg
	Ethionamide	750-1000 mg
	Ethambutol or Terizidone or Cycloserine	1600-2000 mg 1000 mg 750-1000 mg
	Pyrazinamide	2000-2500 mg
	PAS	8000 mg



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Monitoring during treatment of drug-resistant TB

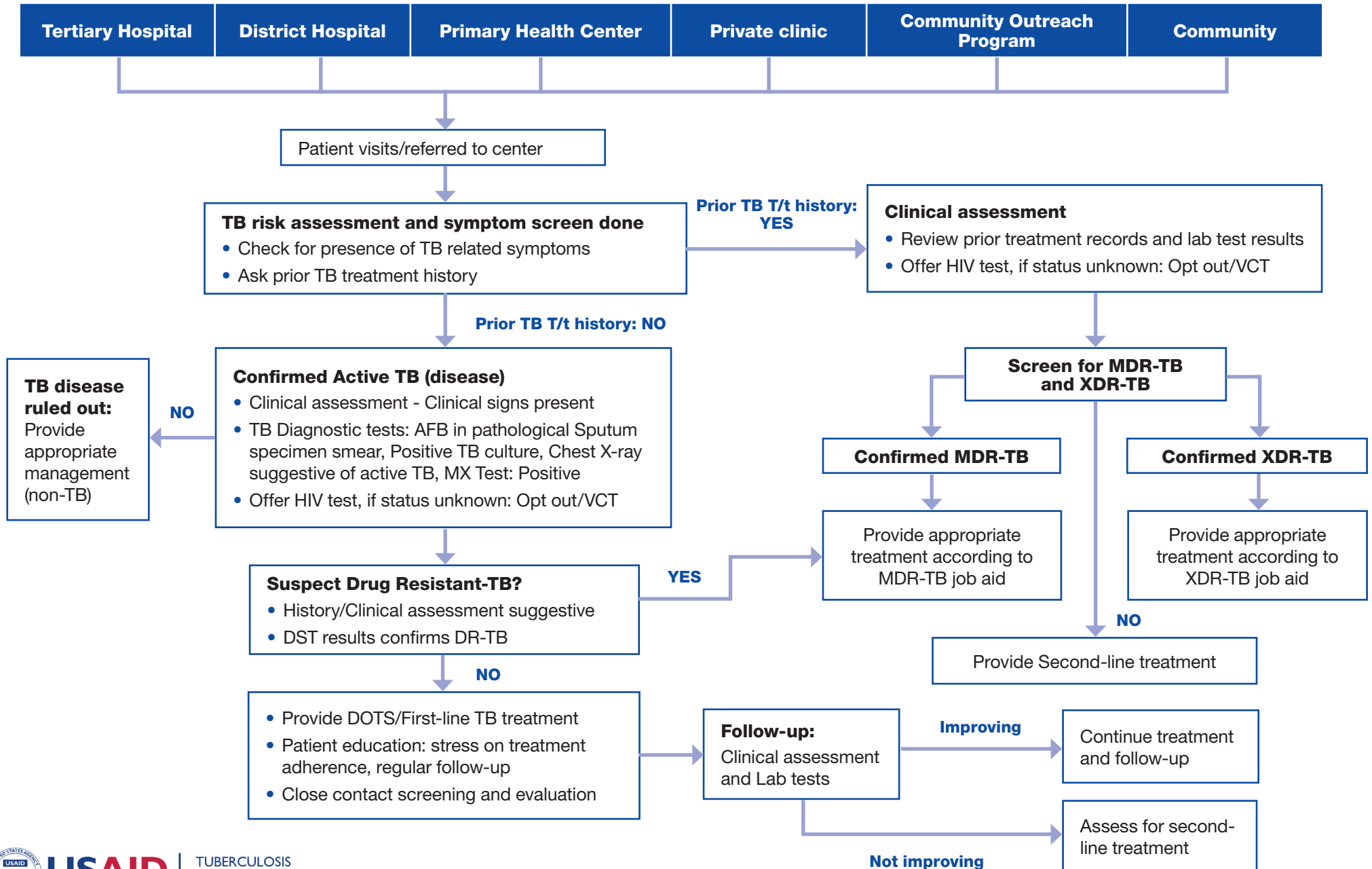
Monitoring Evaluation	Recommended Frequency
Evaluation by Clinician	At baseline, and at least monthly until conversion, then Every 2-3 months
Screening by DOT worker	At every DOT encounter
Sputum smear and cultures	Monthly Bi-monthly cultures acceptable during continuation phase
Weight	At baseline and weekly during intensive phase Monthly during continuation phase
Height	At baseline in adults
Body mass index	At baseline and then monthly
Drug Susceptibility Testing (DST)	At baseline For patients who remain culture-positive, it is not necessary to repeat DST within less than 3 months of treatment
Chest radiograph	At baseline, and then every six months Also when indicated by clinician
Serum creatinine	At baseline, then monthly during injectable phase
Serum potassium	Monthly during injectable phase
Thyroid stimulating hormone	Every six months if receiving ethionamide and/or PAS Monitor monthly for signs of hypothyroidism
Liver serum enzymes	Periodic monitoring (every 1-3 months) in patients receiving pyrazinamide for extended periods or for patients at risk for or with symptoms of hepatitis
HIV screening	At baseline, and repeat if clinically indicated
Pregnancy tests	At baseline for women of childbearing age, and repeat if indicated
Audiometry	At baseline and when indicated
Eye test	At baseline and when necessary
Lung CT-scan	When indicated



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Management of a Suspected TB Case



TB Screening Questions

Ask about presence of TB related symptoms

- Cough for more than 2 weeks
- Blood in sputum
- Fever with night sweats
- Chest pain/ breathlessness
- Weight Loss
- Loss of appetite
- Malaise, tiredness

Any current or past history of long-term illness (TB, HIV)?

Any history of TB in family members or close contacts?

Is any one in family/friends on TB treatment?

Pointers to suspect DR-TB

- HIV positive
- Family member/ close contact under treatment for DR-TB

TB Diagnostic tests

Adult

- Sputum smear for AFB
- Sputum culture for AFB
- DST (when indicated)
- Chest X-ray
- If Miliary/Extrapulmonary TB suspected: CSF exam, Biopsy of LN, X-ray spine, Abdominal USG

Child

- Gastric aspirate for AFB
- Gastric aspirate culture for AFB
- DST (when indicated)
- Chest X-ray-
- Mantoux Test
- Miliary/Extrapulmonary TB suspected: CSF exam, Biopsy or FNA of LN
- X-ray spine, Abdominal USG

DST should be reserved for the following individuals

- Patients who remain sputum smear positive after 2-3 months' of intensive therapy;
- Treatment failure and interruption cases;
- Close contacts of MDR tuberculosis cases who have S/s of TB;
- High risk individuals who have S/s of TB, e.g. health care workers.
- Newly diagnosed TB patients with previous history of TB treatment.



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Review of Prior TB Treatment History

Ask

- Did you ever receive treatment for TB for more than 1 month/ any illness?
- Did you complete the full-course of treatment?
- If not completed the treatment, ask reasons
- How was the response of earlier treatment? Improved/worsened

Review records

- Review diagnosis, diagnostic/lab test results, any DST result
- Any treatment regimen provided, Duration of treatment, number of episodes of treatment taken, duration of non-compliance, any adverse reactions
- Any follow-up notes
- Previous long term hospitalization
- Exposure to mining industry
- History of incarceration

Pointers to suspect DR-TB

- Incomplete treatment
- Multiple episodes of non-compliance
- Worsening of symptoms/ No improvement
- Prior DST suggestive of DR

First-line TB Treatment

New adult patient

Intensive Phase (2 months): Start INH, Rifampicin, Pyrazinamide, Ethambutol daily 7 days per week

Continuation Phase (4 months): continue INH and Rifampicin daily, 7 days a week

Retreatment adult patient

Intensive Phase: For initial 2 months: Start INH, Rifampicin, Pyrazinamide, Ethambutol and Streptomycin; All drugs given 7 days a week except Streptomycin can be given 5 times a week.
For 3rd month: RHZE

Continuation Phase (5 months): continue INH, Rifampicin & Ethambutol daily for 7 days a week

Children

Intensive Phase (2 months): Start INH, Rifampicin, Pyrazinamide, daily

Continuation Phase (4 months): continue INH and Rifampicin

Dosages of treatment: 7 times per week in the intensive phase AND for continuation phase treatment

Patient education: treatment adherence, cough etiquette, regular follow-up

Close contacts monitoring

Pointers to suspect DR-TB

- Multiple episodes of treatment non-compliance
- No clinical improvement or worsening of symptoms/signs
- Follow-up lab tests and X-ray shows worsening
- Follow-up DST results suggestive of drug resistance



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Management of MDR-TB Case

Pointers to Suspect MDR-TB

- Category II failures (chronic TB cases)
- Close contact of known MDR-TB case
- Prior DST results confirmed MDR-TB
- MDR-TB endemic region
- HIV patients in highly endemic regions for M(X)DR-TB
- High risk individuals with Symptoms of TB
- Newly diagnosed patients with history of TB
- Patients who remain smear positive after 2-3 months of intensive phase of TB treatment
- Symptomatic patients with history of incarceration
- Symptomatic patients with history of prolonged hospitalization

YES

Confirm MDR-TB suspicion

- Clinical assessment
- Review prior treatment history and DST results
- TB Diagnostics tests
- HIV screening, if status unknown: VCT/opt-out
- Infection control triage

- Provide DOTS/First-line TB treatment according to guidelines
- Patient education: focus on treatment adherence
- Assess TB risk in close contacts/ family members

Provide appropriate treatment according to XDR-TB job aid

YES

- Suspected XDR-TB?
- Close contact of XDR TB case
- DST results confirms XDR-TB

Active MDR-TB confirmed

- DST results confirms resistance to INH and Rifampicin
- Clinical signs of active TB present
- AFB in pathological specimen/ culture

NO

YES

INJECTABLE PHASE
(At least 6 months depending on culture conversion, 6-7 times a week)

- Provide MDR-TB treatment regimen
- Treatment adherence counseling
- Close contact screening and evaluation

CONTINUATION PHASE
(12 - 18 months, depending on culture conversion)

PERIODIC MONTHLY FOLLOW UP

JOB AID on Monitoring During Treatment



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Guidelines for standardized drug treatment regimen for MDR-TB

Provide directly observed therapy throughout the treatment course.

Drugs should be administered seven times per week in clinics and seven times per week in hospitals.

Duration of Treatment

Aim for 18-24 months of treatment, always with an initial 6 months of intensive therapy. The recommended duration is guided by culture conversion. Treatment should be continued for at least 18 months after culture conversion as demonstrated by 2 consecutive negative monthly cultures, taken 30 days apart.

- Injection/Intensive Phase (initial 6 months): Start 5 drugs: Kanamycin, Ofloxacin, Pyrazinamide, Ethionamide, and Ethambutol or Terizidone or Cycloserine
- Continuation Phase (12 -18 months): continue 4 drugs: Ofloxacin, Pyrazinamide, Ethionamide, and Ethambutol or Terizidone or Cycloserine

When side-effects occur that are not potentially life threatening, every effort should be made to coach patients through palliation and psychological support. Drugs with known severe side effects may be given in divided doses to improve tolerance. Patients with severe side effects should be hospitalized.

Treatment should never be changed without laboratory support. However, laboratory errors do occur. If a single discrepant result is received and it does not accord with the clinical assessment, the test should be repeated and treatment should not be changed while awaiting laboratory results.

The Management of Nausea and Vomiting as the most common side effect of drugs

- try to get patient to identify the drug
- ethionamide often implicated but also ethambutol, ofloxacin and isoniazid
- give antiemetics ie metaclopramide 10 mg tid (beware long term use can induce extrapyramidal signs)
- if continues, stop ethionamide
- when settles, restart with 250 mg/day
- if tolerated, build up to 250 mg bid and then 250 mg tid at 3 or 4 day intervals.
- Retry 750mg/day
- If the patient is very intolerant despite all of these measures, stop the offending drug; continuation will often lead to treatment interruption.

Patient education: treatment adherence, cough etiquettes, regular follow-up

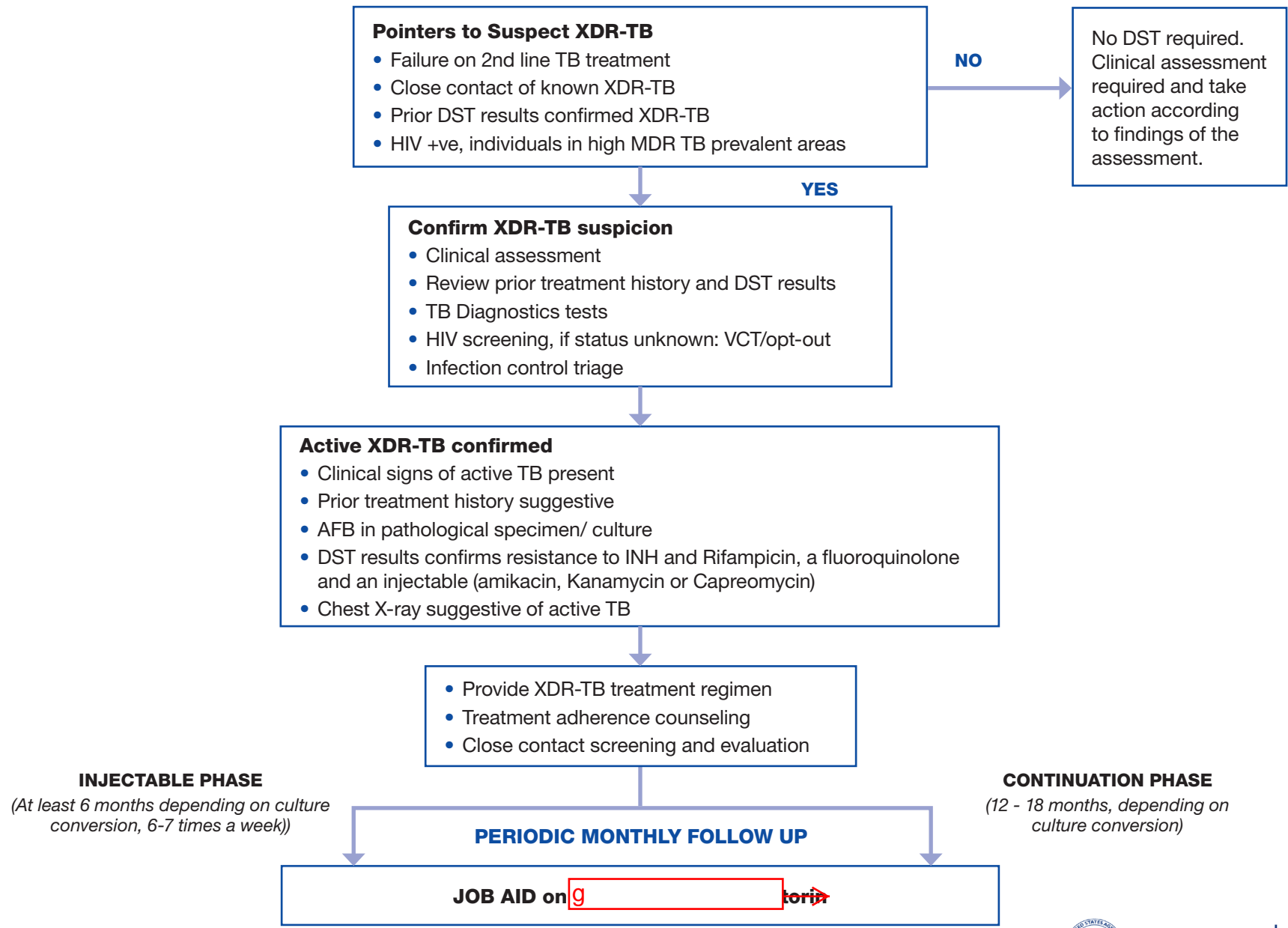
Close contacts monitoring



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Management of a Suspected TB XDR



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Classification	Name of Drug	Daily Dosage		Side-effects	
Group	Drugs	Adult and child (mg/kg)	Adult dosage	Common	Uncommon
Group 1: First –line oral anti-TB agents	Isoniazid (H)	4-6	300 mg	Hepatitis, Cutaneous hypersensitivity, Peripheral neuropathy	Giddiness, Convulsion, Optic neuritis, Mental symptoms, Haemolytic anaemia, Aplastic anaemia, Lupoid reactions, Arthralgia, Gynaecomastia
	Rifampicin (R)	10-20	450 mg (<50 kg) 600 mg (≥ 50 kg)	Hepatitis, Cutaneous hypersensitivity, Gastrointestinal reactions, Thrombocytopenic purpura, Febrile reactions, "Flu syndrome"	Shortness of breath, Shock, Haemolytic anaemia, Acute renal failure
	Ethambutol (E)	25	800 mg-1.2 g (<50 kg) 1.2-1.6 g (≥ 50 kg)	Retrolbulbar neuritis, Arthralgia	Cutaneous reaction, Peripheral neuropathy
	Pyrazinamide (Z)	30-40	1.0-1.5 g (<50 kg) 1.5-2.0 g (≥ 50 kg)	Hepatitis, Nausea, Vomiting, Arthralgia, Cutaneous reaction	Sideroblastic anaemia
Group 2: Injectable anti-TB agents	Streptomycin (S)	15-20 (adult) 20-40 (child)	500-750 mg (<50 kg) 1g (≥ 50 kg)	Cutaneous hypersensitivity, Giddiness, Numbness, Tinnitus, Vertigo, Ataxia, Deafness	Renal damage, Aplastic anaemia
	Kanamycin (Km)	15-30 (child)	500-750 mg (<50 kg) 1g (≥ 50 kg)	Ototoxicity: hearing damage, vestibular disturbance, Nephrotoxicity: deranged renal function test	Clinical renal failure
	Amikacin (Am)	15-22.5 (child)	500-750 mg (<50 kg) 1g (≥ 50 kg)	Ototoxicity: hearing damage, vestibular disturbance, Nephrotoxicity: deranged renal function test	Clinical renal failure
	Capreomycin (Cm)	15-30 (child)	500-750 mg (<50 kg) 1g (≥ 50 kg)	Ototoxicity: hearing damage, vestibular disturbance, Nephrotoxicity: deranged renal function test	Clinical renal failure
Group 3: Fluoroquinolones	Ofloxacin (Ofx)	15-20 (child)	800 mg	Gastrointestinal reactions, Insomnia	Anxiety, Dizziness, Headache, Tremor, Convulsion
	Levofloxacin (Lfx)	7.5-10 (child)	750 mg	Gastrointestinal reactions, Insomnia	Anxiety, Dizziness, Headache, Tremor, Convulsion
	Moxifloxacin (Mfx)	7.5-10 (child)	400 mg	Gastrointestinal reactions, Insomnia	Dizziness, Restlessness, Diarrhea
Group 4: Oral Bacteriostatic 2nd line anti-TB agents	Ethionamide (Eto)	15-20	500 mg (<50 kg) 750 mg (≥ 50 kg)	Gastrointestinal reactions	Hepatitis, Cutaneous reactions, Peripheral neuropathy
	Protonamide (Pto)	15-20	500 mg (<50 kg) 750 mg (≥ 50 kg)	Gastrointestinal reactions	Hepatitis, Cutaneous reactions, Peripheral neuropathy
	Cycloserine (Cs)	10-20	500 mg (<50 kg) 750 mg (≥ 50 kg)	Dizziness, Headache, Depression, Memory loss	Psychosis, Convulsion
	P-aminosalicylic acid (PAS)	150	8 g	Gastrointestinal reactions	Hepatitis, Drug fever, Hypothyroidism, Haematological reactions
	Terizidone	15-20	500 mg (<50 kg) 750 mg (≥ 50 kg)	Dizziness, Headache, Depression, Memory loss	Psychosis, Convulsion

**Group 5:
Anti-TB agents with unclear efficacy**
(not recommended for routine use in MDR-TB patients by WHO): Clofazimine, High-dose INH, Thioacetazone, Amoxicillin/Clavulanate, Azithromycin, Linezolid, Clarithromycin, Imipenem.

Infection Control Measures

Preventing Transmission of TB

Follow cough etiquette

- Cover the nose and mouth when coughing or sneezing
- Avoid coughing directly into hands — use tissue or other cloth
- Use sleeve if no tissue or cloth available
- Dispose of tissues in the nearest waste container immediately after use
- Wash hands with soap & water or antiseptic hand-rub after contact with respiratory secretions and contaminated objects/materials.

Adherence to treatment regimen

Regular treatment follow-up

What can communities do to prevent transmission of TB?

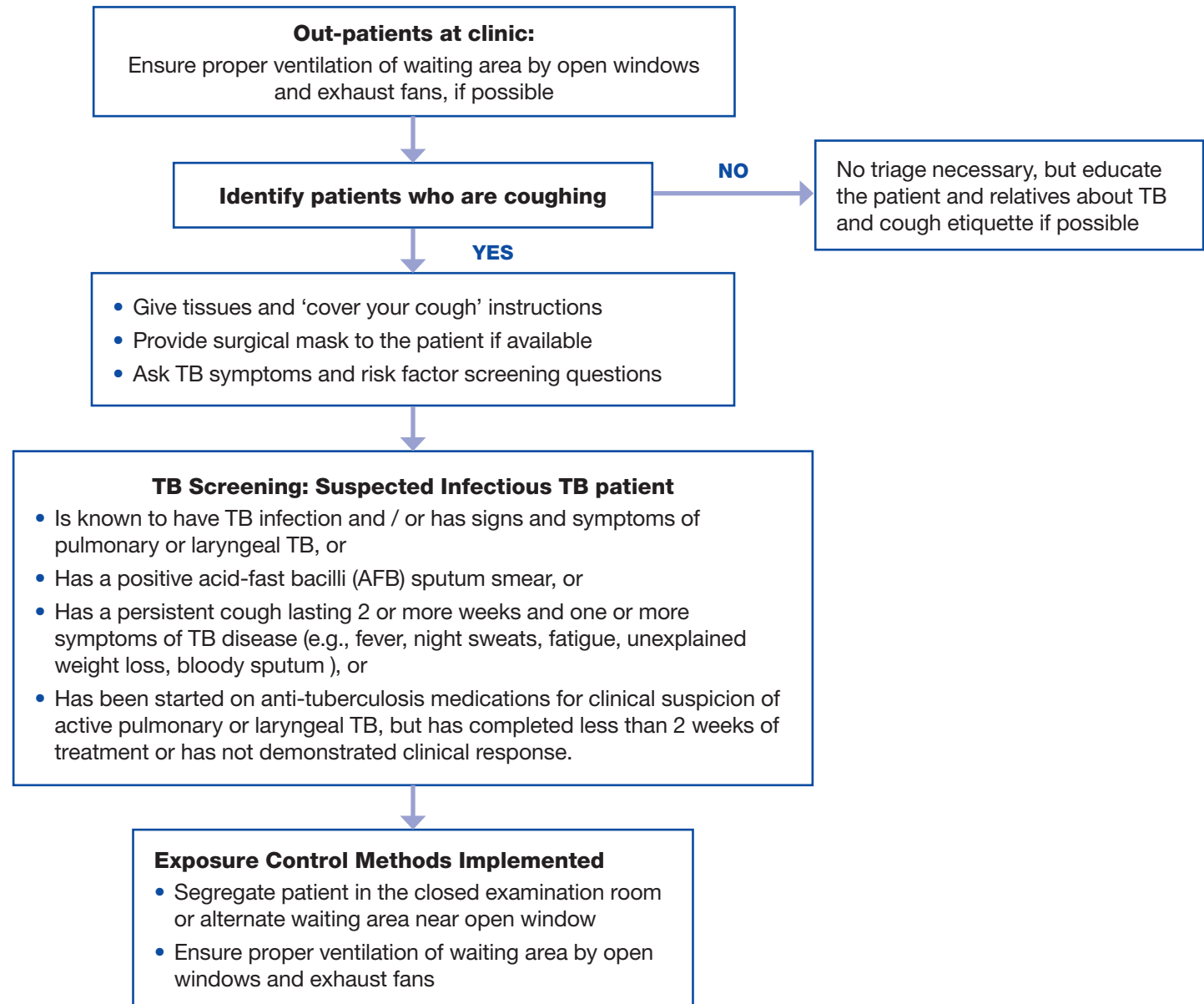
- Community outreach, contact tracing, provider-initiated screening: Focus on high risk groups
- Targeted MDR/XDR advocacy and awareness programs for communities
- Support social mobilization activities to increase awareness about TB as a curable disease
- Regular cases — strengthening home/community level support



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Infection Control Triage and Environmental Control



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