





62ND ANNUAL

Denver TB Course

MARCH 25-27, 2026



Management of MDR-TB





2006 2008 2011 2013 2014 2016 2018 2019 2019 2020 2022

2024

2025

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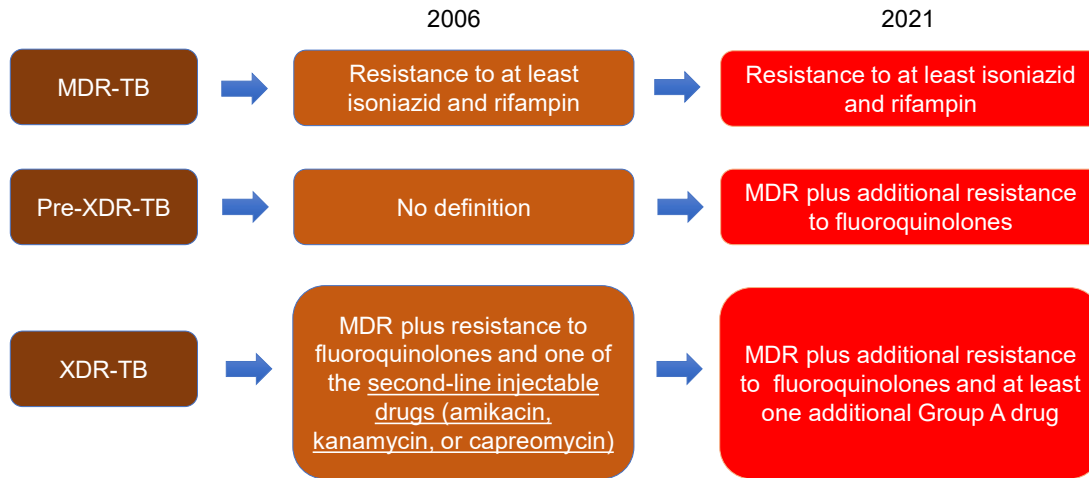
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Management of MDR-TB

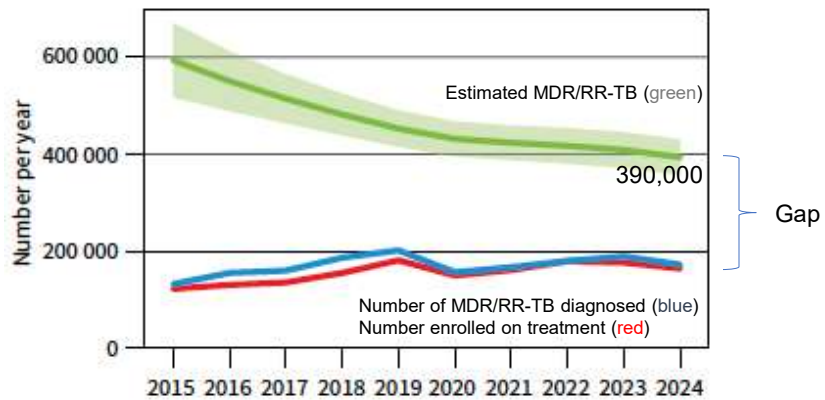
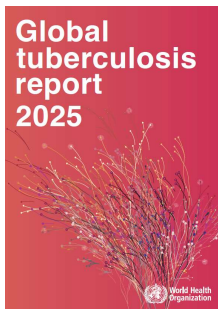


- Brief epidemiology of MDR-TB
- Choosing a "longer" vs. "shorter" regimen
 - Building a "longer" regimen
 - Evidence for effective "shorter" regimens
- Evidence for all oral regimens
- Updated US and WHO recommendations for all oral regimens

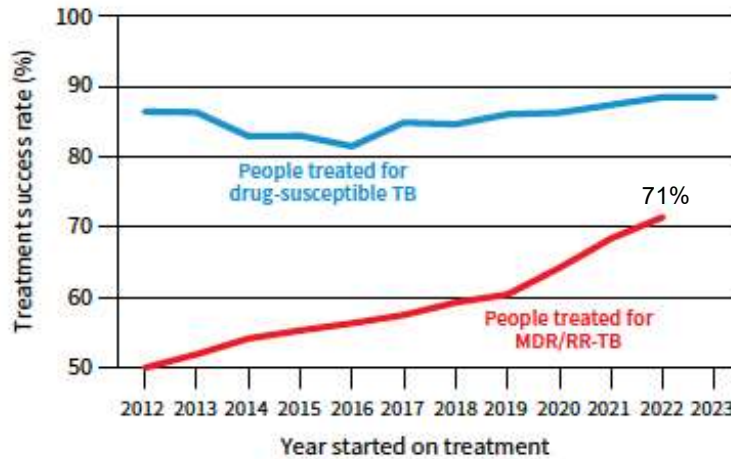
Definitions for Pre-XDR and XDR-TB



Number of Estimated and Notified MDR/RR-TB Globally, 2015-2024



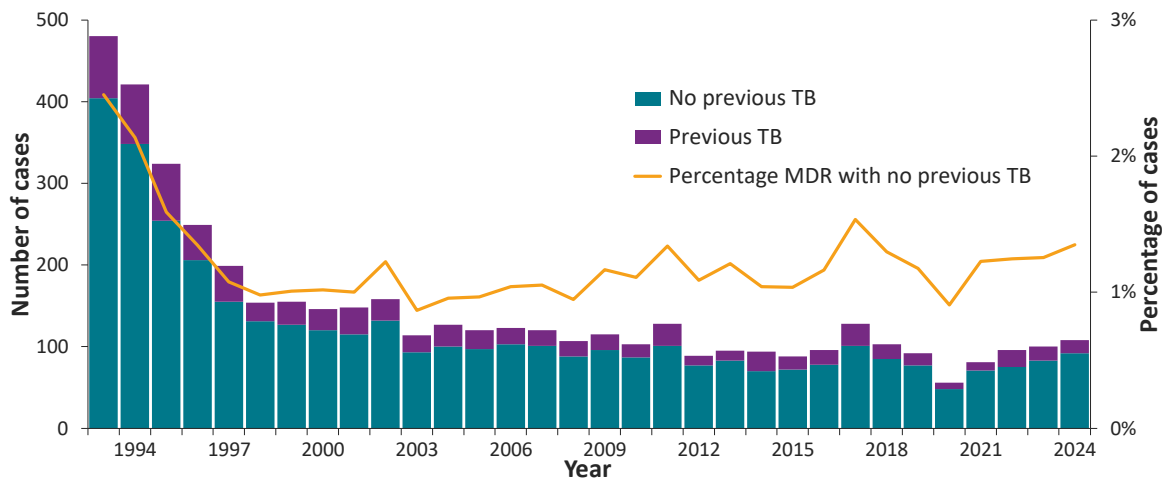
Global Treatment Success Rates for DS TB and MDR/RR-TB, 2012-2023



WHO Global TB Report, 2025



Number and Percentage of MDR-TB Cases in the US, 1993-2024



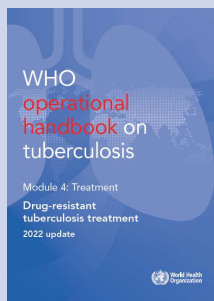
*Starting in 2023, information on drug resistance included results of molecular drug susceptibility testing in addition to growth-based susceptibility testing for isoniazid and rifampin. An isolate is considered resistant to isoniazid or rifampin if either the growth-based test or molecular test detects resistance. CDC Slide Set 2024.



WHO Guidelines For Treatment of MDR-TB



Regimen	Drugs and Duration																														
✓ BPaLM	6 Bdq – Pa – Lzd - Mfx																														
9-month all oral	4–6 Bdq(6 m)-Lfx/Mfx-Cfz-Z-E-Hh-Eto or Lzd(2 m) / 5 Lfx/Mfx-Cfz-Z-E)																														
Longer individualized	<table border="1"> <thead> <tr> <th>Groups and steps</th> <th>Medicine</th> <th>Abbreviation</th> </tr> </thead> <tbody> <tr> <td rowspan="3">Group A: Include all three medicines</td> <td>Levofloxacin or moxifloxacin</td> <td>Lfx Mfx</td> </tr> <tr> <td>Bedaquiline[®]</td> <td>Bdq</td> </tr> <tr> <td>Linezolid[®]</td> <td>Lzd</td> </tr> <tr> <td rowspan="2">Group B: Add one or both medicines</td> <td>Clotazimine</td> <td>Cfz</td> </tr> <tr> <td>Cyloserine or terizidone</td> <td>Cs Tdz</td> </tr> <tr> <td rowspan="7">Group C: Add to complete the regimen and when medicines from Groups A and B cannot be used</td> <td>Ethambutol</td> <td>E</td> </tr> <tr> <td>Delamanid[®]</td> <td>Dim</td> </tr> <tr> <td>Pyrazinamide[®]</td> <td>Z</td> </tr> <tr> <td>Imipenem–cilastatin or meropenem[®]</td> <td>Imp–Cin Mpm</td> </tr> <tr> <td>Amikacin (or streptomycin)[®]</td> <td>Am (S)</td> </tr> <tr> <td>Ethionamide or prothionamide[®]</td> <td>Eto Pto</td> </tr> <tr> <td><i>P</i>-aminosalicylic acid</td> <td>PAS</td> </tr> </tbody> </table>	Groups and steps	Medicine	Abbreviation	Group A: Include all three medicines	Levofloxacin or moxifloxacin	Lfx Mfx	Bedaquiline [®]	Bdq	Linezolid [®]	Lzd	Group B: Add one or both medicines	Clotazimine	Cfz	Cyloserine or terizidone	Cs Tdz	Group C: Add to complete the regimen and when medicines from Groups A and B cannot be used	Ethambutol	E	Delamanid [®]	Dim	Pyrazinamide [®]	Z	Imipenem–cilastatin or meropenem [®]	Imp–Cin Mpm	Amikacin (or streptomycin) [®]	Am (S)	Ethionamide or prothionamide [®]	Eto Pto	<i>P</i> -aminosalicylic acid	PAS
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Longer or Shorter MDR-TB Regimen?

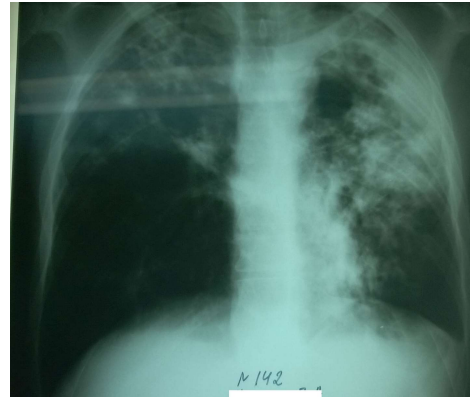


- Regimen choice depends on:
 - Fluoroquinolone susceptibility
 - History of second-line drugs received (for > 1 month)
 - Drugs available
 - Drug susceptibility testing available
 - Site of disease
 - Severity of disease
 - Patient preference

Clinical Case



- 36 year old male from former Soviet Republic previously treated for drug-susceptible TB in 2015
- Represented in 2018 with dyspnea, cough
- Sputum was AFB smear positive and Xpert MTB/RIF demonstrated likely rifampin resistance
- Treated for MDR-TB with Cm-Mfx-Pto-Cs-Lzd-Imp/Cln (amox-clav) pending DST results
- Had anaphylactic reaction to Imp/Cln, all drugs stopped

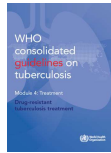


Longer MDR-TB Treatment Regimen Intensive and Continuation Phases



	Intensive Phase (injectable)	Continuation Phase
	Provide greater bactericidal activity early when bacillary load is highest	<ul style="list-style-type: none"> • Fixed duration? • Timing of culture conversion?
WHO	6-7 months	18-20 months <i>or</i> 15-17 months after culture conversion
ATS/CDC/ERS/IDSA	5-7 months after culture conversion	15-21 months after culture conversion for MDR-TB 15-24 months after culture conversion for pre-XDR/XDR-TB

Grouping of MDR-TB Drugs



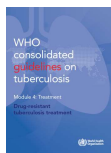
Build Regimen

WHO	Drugs
Group A	Levofloxacin or moxifloxacin Bedaquiline
	Linezolid
Group B	Clofazimine Cycloserine or terizidone
Group C	Ethambutol Delamanid Pyrazinamide Carbapenems with clavulanic acid Amikacin or streptomycin
	Ethionamide or prothionamide P-aminosalicylic acid
Do not use	Kanamycin Capreomycin Macrolides Amox/Clavulanate

WHO Consolidated Guidelines on Tuberculosis, 2020



Grouping of MDR-TB Drugs



Build Regimen

WHO	Drugs	ATS/CDC/ERS/IDSA
Group A	Levofloxacin or moxifloxacin Bedaquiline	Strong recommendation for
	Linezolid	
Group B	Clofazimine Cycloserine or terizidone	Conditional recommendation for
Group C	Ethambutol Delamanid Pyrazinamide Carbapenems with clavulanic acid Amikacin or streptomycin	
	Ethionamide or prothionamide P-aminosalicylic acid	
Do not use	Kanamycin Capreomycin	Conditional recommendation against
	Macrolides	
	Amox/Clavulanate	

WHO Consolidated Guidelines on Tuberculosis, 2020

Nahid P, et al. AJRRCM 2019;200:e93-142



Treatment Success and Adverse Reactions in MDR-TB: individual patient data meta-analysis



50 studies (12,030 patients) from 25 countries

58 studies (9178 patients) from 35 countries

Treatment Failure/relapse vs Treatment Success		Absolute Risk of Serious AE	
Drug	Adj. OR (95% CI)	Drug	Median (%) (95% CI)
Levofloxacin or moxifloxacin	0.3 (0.1, 0.5)	Bedaquiline	2.4 (0.7, 7.6)
Bedaquiline	0.3 (0.2, 0.4)	Moxifloxacin	2.9 (1.4, 5.6)
Linezolid	0.3 (0.2, 0.5)	Clofazimine	3.6 (1.3, 8.6)
Clofazimine	0.3 (0.2, 0.5)	Levofloxacin	4.1 (1.9, 8.8)
Cycloserine or terizidone	0.6 (0.4, 0.9)	Linezolid	17.2 (10.1, 27.0)

WHO Consolidated Guidelines on Tuberculosis, 2020



Building a "Longer" Treatment Regimen For Our Patient



	Drugs	ATS	
		Taken Before	Susceptibility
Build Regimen ↓	Levofloxacin or moxifloxacin	Y	R
	Bedaquiline	N	S
	Linezolid	Y	S
	Clofazimine	N	S
	Cycloserine or terizidone	Y	S
	Ethambutol	Y	R
	Delamanid	N	S
	Pyrazinamide	Y	R
	Carbapenems + clavulanic acid	Y	?
	Amikacin or streptomycin	Y	R
	Ethionamide or prothionamide	Y	S
	P-aminosalicylic acid	N	S

Nahid P, et al. AJRRCM 2019;200:e93-142

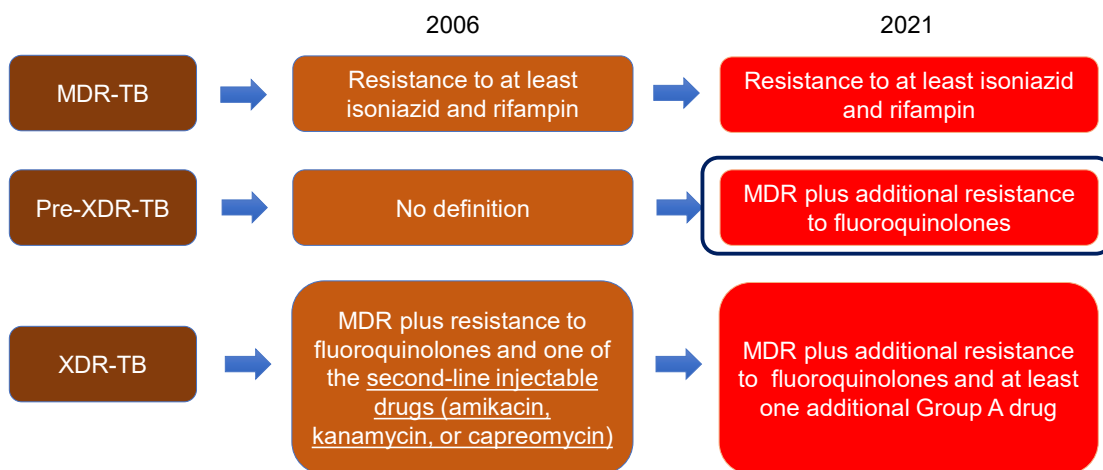


Our patient has..



1. MDR-TB
- 2. Pre-XDR-TB**
3. XDR-TB
4. None of the above

Definitions for Pre-XDR and XDR-TB



Building a "Longer" Treatment Regimen For Our Patient



	Drugs	ATS		
		Taken Before	Susceptibility	Use Drug?
Build Regimen	Levofloxacin or moxifloxacin	Y	R	
	Bedaquiline	N	S	✓
	Linezolid	Y	S	✓
	Clofazimine	N	S	✓
	Cycloserine or terizidone	Y	S	?
	Ethambutol	Y	R	
	Delamanid	N	S	✓
	Pyrazinamide	Y	R	
	Carbapenems + clavulanic acid	Y	?	
	Amikacin or streptomycin	Y	R	
	Ethionamide or prothionamide	Y	S	✓
	P-aminosalicylic acid	N	S	✓

Goal: ≥ 5 likely effective drugs in intensive phase and ≥ 4 in continuation phase

Possible Regimens

1. Bdq-Lzd-Cfz-Dlm-Cs
2. Bdq-Lzd-Cfz-Eto-Cs
3. Bdq-Lzd-Cfz-PAS-Cs

Nahid P, et al. AJRRCM 2019;200:e93-142



Randomized Trials of Shorter Course MDR/RR-TB Regimens – STREAM Trials



Study	Design	Control Regimen	Study Regimens	Duration (wks)	Treatment Success
Stream, Stage 1	Randomized, open label	WHO longer regimen (20 m)	Km+INH+Pto+Mfx+Cfz+E+Z X 16 wks then Mfx+Cfz+E+Z X 24 wks	40	79% v 80% with WHO long regimen

Bdq-bedaquiline, Cfz-clofazimine, E-ethambutol, INH-isoniazid, Km-kanamycin, Lfx-levofloxacin, Mfx-moxifloxacin, Pto-prothionamide, Z-pyrazinamide

Nunn AJ, et al. NEJM 2019;380:1201-1213
 Goodall RL, et al. Lancet, 2022;400:1858-1868
 WHO. Module 4. 2020



Randomized Trials of Shorter Course MDR/RR-TB Regimens – STREAM Trials



Study	Design	Control Regimen	Study Regimens	Duration (wks)	Treatment Success
Stream, Stage 1	Randomized, open label	WHO longer regimen (20 m)	Km+INH+Pto+Mfx+Cfz+E+Z X 16 wks then Mfx+Cfz+E+Z X 24 wks	40	79% v 80% with WHO long regimen
Stream, Stage 2	Randomized, open label	Stage 1 regimen	Stage 1 regimen vs	40	71%
			Bdq for Km and Lvx for Mfx	40	83%
			Km plus above	28	91%

Bdq-bedaquiline, Cfz-clofazimine, E-ethambutol, INH-isoniazid, Km-kanamycin, Lfx-levofloxacin, Mfx-moxifloxacin, Pto-prothionamide, Z-pyrazinamide

Nunn AJ, et al. NEJM 2019;380:1201-1213
 Goodall RL, et al. Lancet, 2022;400:1858-1868
 WHO. Module 4. 2020



Randomized Trials of Shorter Course MDR/RR-TB Regimens – Nix and ZeNix



Randomized trials of PBaL administered for 26 weeks

Study	Design	Control Regimen	Study Regimens	Lzd duration (wks)	Treatment Success	Neuropathy
Nix*	Open label	–	Bdq, Pa, Lzd (1200 mg/d)	26	90%	81%

Bdq-bedaquiline, Pa-prothionamide, Lzd-linezolid

*In the Nix trial, only 15% (16/109) of patients completed the starting 1200 mg/day dosing with no interruptions or dose reductions. All completed 4 weeks of the full dose.

Conradie F, et al. NEJM 2020;382:893-902
 Conradie F, et al. NEJM 2022;387:810-23
 WHO. Module 4. 2020



Randomized Trials of Shorter Course MDR/RR-TB Regimens – Nix and ZeNix



Randomized trials of BPaL administered for 26 weeks

Study	Design	Control Regimen	Study Regimens	Lzd duration (wks)	Treatment Success	Neuropathy
Nix*	Open label	–	Bdq, Pa, Lzd (1200 mg/d)	26	90%	81%
ZeNix	Randomized, open label	Nix regimen	Bdq, Pa, Lzd (1200 mg/d)	26	93%	38%
			Bdq, Pa, Lzd (1200 mg/d)	9	89%	24%
			Bdq, Pa, Lzd (600 mg/d)	26	91%	24%
			Bdq, Pa, Lzd (600 mg/d)	9	84%	13%

Bdq-bedaquiline, Pa-prothionamide, Lzd-linezolid

BPaL (600 mg/day) administered for 26 weeks was considered to provide the best risks/benefits balance

Conradie F, et al. NEJM 2020;382:893-902
 Conradie F, et al. NEJM 2022;387:810-23
 WHO. Module 4. 2020



CDC BPaL Recommendation



- **August 2019** - FDA approved the use of pretomanid 200mg in combination with bedaquiline and linezolid (BPaL) in adults with pulmonary extensively drug resistant (XDR), treatment-intolerant, or nonresponsive multidrug-resistant (MDR) tuberculosis (TB).
- **February 2022** – CDC provides provisional guidance for the use of BPaL
 - The CDC recommendation for initial linezolid dose within BPaL regimen of 1200 mg
- **February 2024** – CDC updates guidance
 - The CDC recommendation for initial linezolid dose within BPaL regimen changed from 1200 mg to 600 mg, based on results of the ZeNix trial.

<https://archive.cdc.gov/#/details?url=https://www.cdc.gov/tb/hcp/treatment/bpal.html>



Demographics and TB Characteristics of First 70 Patients Treated with BPaL in US



Demographics

- 70 patients in 12 states
- Median age: 37 yrs (range 14-83)
- Median weight: 58.0 kg (40-132.7 kg)
- Male: 65.7%
- Non US born: 90%
- Nonwhite: 77.9%
- Not Hispanic: 84.3%

Haley CA, et al. Clin Infect Dis 2023;77:1053-62



Demographics and TB Characteristics of First 70 Patients Treated with BPaL in US



Demographics

- 70 patients in 12 states
- Median age: 37 yrs (range 14-83)
- Median weight: 58.0 kg (40-132.7 kg)
- Male: 65.7%
- Non US born: 90%
- Nonwhite: 77.9%
- Not Hispanic: 84.3%

TB Characteristics

- Pulmonary TB: 75.6%
- Extrapulmonary TB: 10.0%
- Both: 14.2%
- AFB smear: 54.0%
- Cavitory: 46%
- Drug resistance:
 - Rifampin monoresistance: 12.9%
 - MDR-TB: 61.4%
 - Pre-XDR-TB: 14.3%
 - XDR-TB: 1.4%

Haley CA, et al. Clin Infect Dis 2023;77:1053-62



BPaL Treatment Effectiveness/Adverse Reactions



Effectiveness

Treatment Outcomes	Patient No. (%)
Completed treatment	68 (100%)
Completed 26 wks	55 (80.9%)
Treatment interruption	18 (26.5)
Time to culture conversion	37 days (1-90)
Lost to follow-up	0
Died	0
TB "relapsed"*	2 (2.9%)

Adverse Reactions

Adverse reaction	Patient No. (%)
Hematologic/neurologic events (n=68)	
Linezolid discontinued	3 (4.4)
Linezolid dose change/discontinuation	7 (10.3)
No dose change or discontinuation	5 (7.4)
Gastrointestinal	14 (20.6)
QTc > 500 ms or increase of > 60 ms	0

*Duration of follow-up \geq 6 months in 80.9% and \geq 12 months in 52.9%

BPaL Treatment and Linezolid Dosing



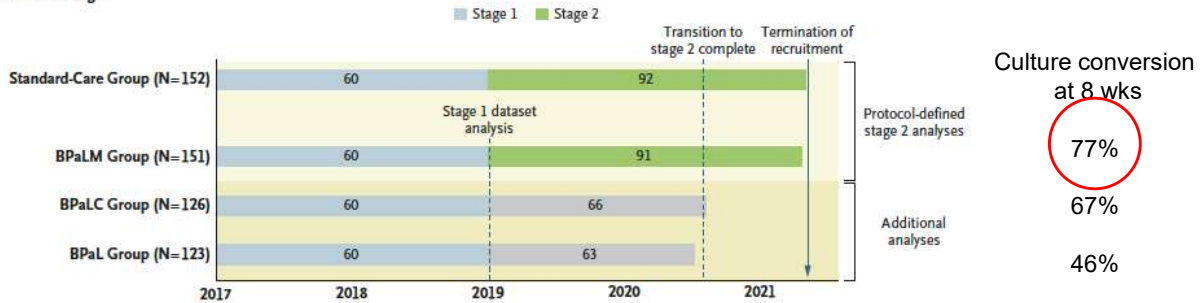
Characteristic	Patient No. (%)
Initial BPaL regimen (n=70)	
Initial linezolid dose 600 mg daily	66 (94.3)
Given other TB drugs with PBaL	0
BPaL stopped after rifampin-resistance excluded	2 (2.9)
Linezolid Dose Adjustment (n=68)	
TDM performed*	66 (97.1%)
Dose or frequency adjusted	42 (61.8)
Adjusted based on TDM	36 (52.9)
Finished on 600 mg daily	27 (39.7)
Finished on 600 mg tiw	21 (30.9%)

*TDM – therapeutic drug monitoring, aiming for trough of < 2

TB PRACTECAL: Open-label, phase 2b-3, adaptive multicenter, randomized, controlled noninferiority trial



B Trial Design

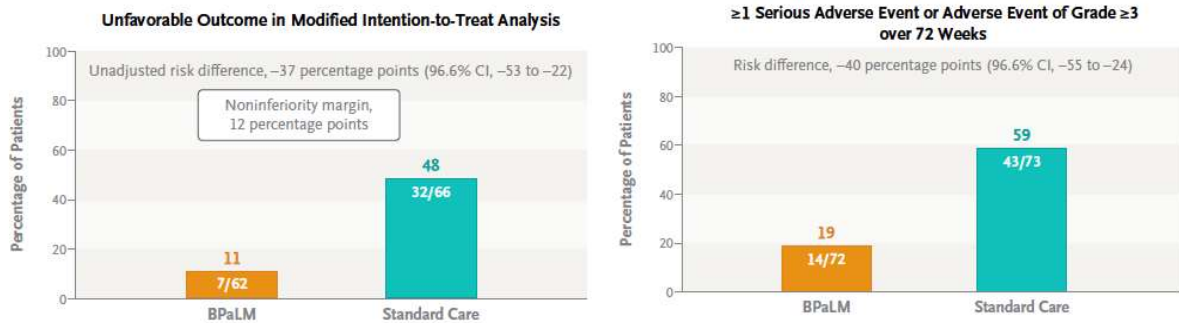


SCG – WHO recommended 9-12 month regimen
 BPaLM - bedaquiline, linezolid, pretomanid, moxifloxacin
 BPaLC - bedaquiline, linezolid, pretomanid, clofazimine
 BPaL - bedaquiline, linezolid, pretomanid

Nyang'wa BT, et al. NEJM 2022;387:25



Stage 2 Treatment Outcomes and Safety Analysis



- BPaLM was noninferior and superior to standard of care and safer
- WHO preferred regimen for fluoroquinolone susceptible MDR-TB

Nyang'wa BT, et al. NEJM 2022;387:2331-43
 WHO. Module 4. 2022



Could Our Patient Receive BPaL or BPaLM?



	Drugs	ATS		
		Taken Before	Susceptibility	
Build Regimen	Levofloxacin or moxifloxacin	Y	R	X
	Bedaquiline	N	S	✓
	Linezolid	Y	S	✓
	Clofazimine	N	S	✓
	Cycloserine or terizidone	Y	S	✓
	Ethambutol	Y	R	X
	Delamanid	N	S	✓
	Pyrazinamide	Y	R	X
	Carbapenems with clavulanic acid	Y	?	X
	Amikacin or streptomycin	Y	S	✓
	Ethionamide or prothionamide	N	S	✓
	P-aminosalicylic acid			

+ Pa = BPaL

Nahid P, et al. AJRCCM 2019;200:e93-142

Clinical Case




- After several attempts to start a longer MDR-TB regimen he was started on BPaL at the following doses:
 - Bdq 400 mg once daily for two weeks then 200 mg three times a week
 - Pa 200 mg once daily
 - Lzd 600 mg twice daily
- After 2 months, he noticed tingling and numbness in his feet
- What would you do now?

Friday, March 27


Visual settings Edit

When poll is active respond at [PollEv.com /professionaleducationnationaljewishhealth910](https://poll.ev.com/professionaleducationnationaljewishhealth910) Send [professionaleducationnationaljewishhealth910](https://poll.ev.com/professionaleducationnationaljewishhealth910) to 22333



Which of the following would be an appropriate next step?

A Hold the BPaL regimen and restart when symptoms improve	0%
B Reduce the pretomanid dose	0%
C Hold linezolid and restart at reduced dose or frequency	0%
D Continue the BPaL regimen and add pyridoxine	0%

Powered by  Poll Everywhere

Which of the following would be an appropriate next step?



- a) Hold the BPaL regimen and restart when symptoms improve
- b) Reduce the pretomanid dose
- c) **Hold linezolid and restart at reduced dose or frequency**
- d) Continue the BPaL regimen and add pyridoxine

Adverse Reactions Associated with Drugs in BPaL/BPaLM



Drug	Adverse effects
Bedaquiline	<ul style="list-style-type: none"> • QTc prolongation • Hepatitis • Nausea • Joint pain • Headache • Elevated amylase
Pretomanid	<ul style="list-style-type: none"> • ? • Testicular toxicity was observed in mice and rats but not in non-human primates or in humans to date.
Linezolid*	<ul style="list-style-type: none"> • Myelosuppression; thrombocytopenia, anemia, and leukopenia • Diarrhea and nausea, including <i>C. difficile</i> colitis • Optic and peripheral neuropathy – most resolve, but can be irreversible • Serotonin syndrome



*Mitochondrial toxicity is less common when the serum trough level is < 2 µg/mL

Pharmacokinetic Considerations



Drug	Metabolism	DDI with ARVs	PK notes
Bedaquiline	CYP3A4/5 substrate Long-terminal half-life	EFV reduces Bdq concentration Bdq exposure increased by boosted PI	Strong PK-PD correlation Black race associated with 30-50% decrease in Bdq exposure QT prolongation driven by M2 metabolite
Pretomanid	CYP3A substrate	EFV reduces Pa concentration	PK studies in children not yet completed
Linezolid	No P450 metabolism	None	Use with caution in renal dysfunction, advanced age Very narrow therapeutic margin Inhibitor of MAO A and B
Moxifloxacin	Glucuronide and sulfate conjugation in liver	None	Do not co-administer with iron, magnesium or calcium

Updated TB Guidelines



AMERICAN THORACIC SOCIETY DOCUMENTS

Updates on the Treatment of Drug-Susceptible and Drug-Resistant Tuberculosis

An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline

Jussi J. Saukkonen*, Raquel Duarte*, Sonal S. Munsiff*, Carla A. Winston*, Manoj J. Mammen, Ibrahim Abubakar, Carlos Acuña-Villaorduña, Pennan M. Barry, Mayara L. Bastos, Wendy Carr, Hassan Chami, Lisa L. Chen, Terence Chorba, Charles L. Daley, Anthony J. Garcia-Prats, Kelly Holland, Ioannis Konstantinidis, Marc Lipman, Giovanni Battista Migliori, Farah M. Parvez, Adrienne E. Shapiro, Giovanni Sotgiu, Jeffrey R. Starke, Angela M. Starks, Sanket Thakore, Shu-Hua Wang, Jonathan M. Wortham, and Payam Nahid; on behalf of the American Thoracic Society, U.S. Centers for Disease Control and Prevention, European Respiratory Society, and Infectious Diseases Society of America

THIS OFFICIAL CLINICAL PRACTICE GUIDELINE WAS APPROVED BY THE AMERICAN THORACIC SOCIETY (ATS) AND THE INFECTIOUS DISEASES SOCIETY OF AMERICA (IDSA) SEPTEMBER 2024, WAS CLEARED BY THE U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC) SEPTEMBER 2024, AND WAS APPROVED BY THE EUROPEAN RESPIRATORY SOCIETY (ERS) OCTOBER 2024

Saukkonen JJ, et al. A J Resp Crit Care Med 2025 in press



ATS/CDC/ERS/IDSA Updated Recommendations



Recommendation #3: In adolescents aged 14 and older and adults with rifampin-resistant pulmonary TB with **resistance or patient intolerance to fluoroquinolones**, who either have had no previous exposure to bedaquiline and linezolid or have been exposed for less than one month, **we recommended the use of the 6-month treatment BPaL regimen rather than more than 15-month regimens** (*strong recommendation, very low certainty of evidence*)

Recommendation #4: In adolescents aged 14 and older and adults with rifampin-resistant, fluoroquinolone susceptible pulmonary TB **we recommended the use of the 6-month treatment BPaLM regimen rather than the 15-month or longer regimens in persons with MDR/RR-TB** (*strong recommendation, very low certainty of evidence*).

Saukkonen JJ, et al. A J Resp Crit Care Med 2025 in press

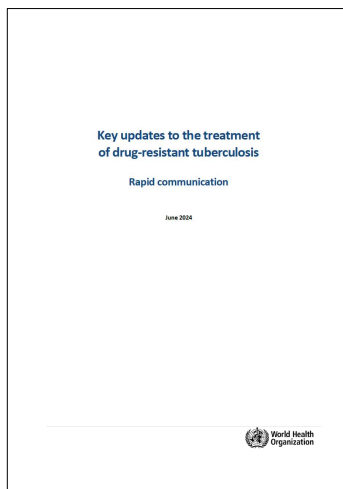


Sub-group Analysis and Challenges



- Subgroup Analyses
 - Age – in low incidence settings a greater proportion of patients will be older (more medications and co-morbidities)
 - Children – Longer regimens are recommended for those < 14 yrs as well as pregnant and lactating women
 - People living with HIV – recommended regardless of HIV status or CD4 count
 - Extrapulmonary disease – recommended for non-severe forms
- Availability of rapid drug susceptibility testing
- Availability of therapeutic drug monitoring
- Drug-drug interactions

Key Updates in MDR-TB Treatment from the WHO

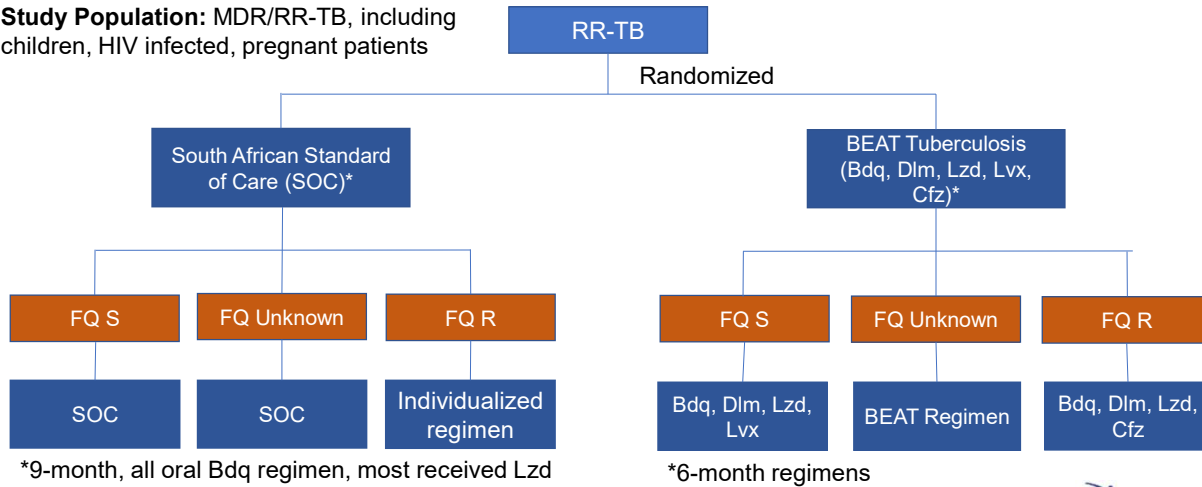


- BEAT TB Trial
- endTB Trial

BEAT-Tuberculosis Trial



Study Population: MDR/RR-TB, including children, HIV infected, pregnant patients



WHO. Rapid Comm 6/2024d; ; Conradie F, et al. medRxiv. <https://doi.org/10.1101/2025.05.04.25326549>



BEAT-Tuberculosis Trial



- **Treatment success:** 86% in both arms
- WHO suggests the use of a 6-month regimen composed of **bedaquiline, delamanid, linezolid (600 mg), levofloxacin, and clofazimine (BDLLfxC)** in MDR/RR-TB patients **with or without FQN resistance** (conditional recommendation, very low certainty of evidence)

WHO. Rapid Comm 6/2024d; ; Conradie F, et al. medRxiv. <https://doi.org/10.1101/2025.05.04.25326549>



endTB Trial



- Study Population: 754 adults and adolescents with MDR/RR-TB, including adolescents, HIV infected, and pregnant patients
- Regimens: five different 9-month

Trial Regimens	Bedaquiline	Delamanid	Clofazimine	Linezolid	Quinolone	Pyrazinamide	Duration (months)
endTB 1	Bdq			Lzd	Mfx	Z	9
endTB 2	Bdq		Cfz	Lzd	Lfx	Z	
endTB 3	Bdq	Dlm		Lzd	Lfx	Z	
endTB 4		Dlm	Cfz	Lzd	Lfx	Z	
endTB 5		Dlm	Cfz		Mfx	Z	
Control Arm	Local SOC*						18-24

*Standard of care (SOC) control, composed according to WHO Guidelines, may include Bdq and/or Dlm

Guglielmetti L, et al. NEJM 2025;392:468-482



endTB Trial



- WHO suggests using the **9-month** all-oral regimens (BLMZ, BLLfxCZ, BDLLFxZ*) over the WHO long regimen in patients with MDR/RR-TB in whom resistance to FQNs has been excluded;
 - BLMZ is suggested over using BLLfxCZ
 - BLLfxCZ is suggested over BDLLfxZ
 - CDLLfxZ and CDMZ regimens **are not** recommended due to high rates of treatment failure/relapse and acquired resistance

*BLMZ (Bdq,Lzd,Mfx,Z)

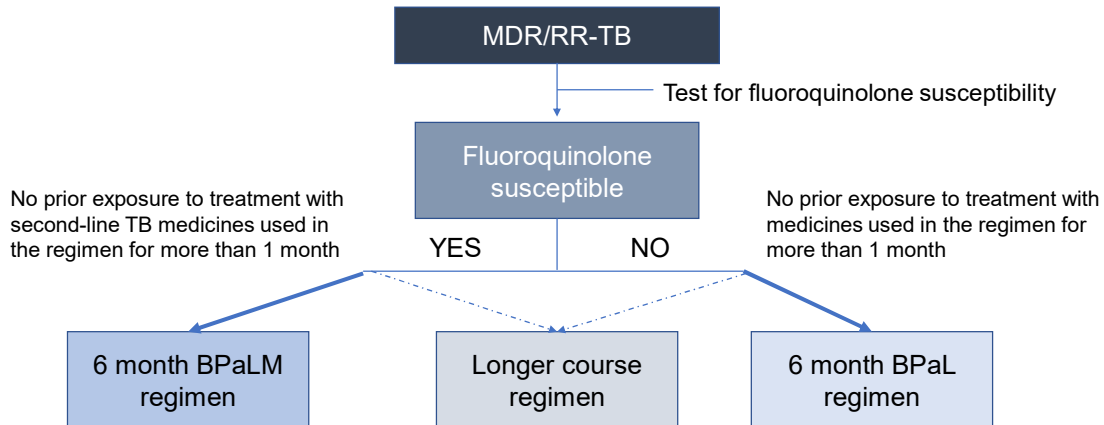
BLLfxCZ (Bdq,Lzd,Lfx,C,Z)

BDLLFxZ (Bdq,Dlm,Lzd,Lfx,Z)

WHO. Rapid Comm 6/2024



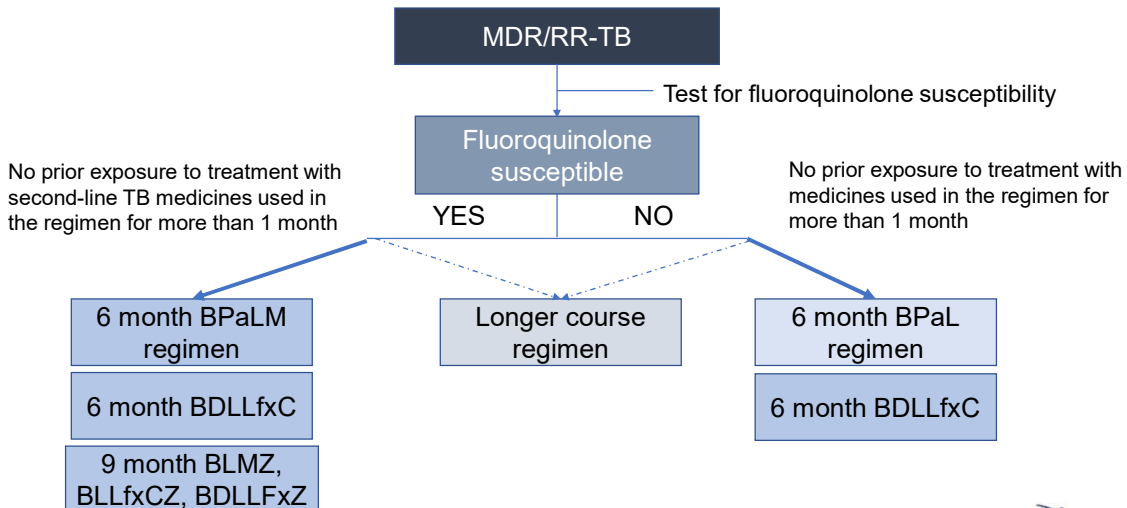
Treatment of MDR-TB: US Regimens



Saukkonen JJ, et al. A J Resp Crit Care Med 2025 in press
 Daley CL. Pulmonary TB and its Prevention, 2022



Treatment of MDR-TB: WHO Regimens



Adapted from Daley CL. Pulmonary TB and its Prevention, 2022 WHO. Module 4. 2020



Relapse and Emergent Resistance with BPaL/M in the US

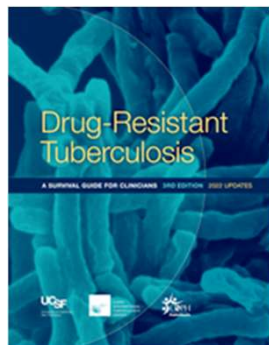


- Case series of 8 relapse patients in the US treated with BPaL/M
 - Treatment completed in 6-10 months
 - Relapse occurred within 5-8 months
- Outcome of treatment of recurrence: 2 deaths
- Development of resistance:
 - Bedaquiline - 5
 - Pretomanid - 1
 - Linezolid - 1
 - Fluoroquinolone - 2

Liang R, et al. OFID 2025;1-10



Drug Resistant Tuberculosis: A survival guide for clinicians



Treatment

Contributors to 2021 updates: CHARLES L. DALRY, MD, LISA CHEN, MD

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<https://www.currytbcenter.ucsf.edu/products/cover-pages/drug-resistant-tuberculosis-survival-guide-clinicians-3rd-edition>

