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What you need to know about multidrug-resistant tuberculosis (MDR-TB): A clinical and public health overview

September 16, 2025

PHO Rounds

Disclosures – Liane Macdonald

Relationships with commercial interests:

- No relationships with commercial interests

Other:

- Employed at Public Health Ontario
- Co-applicant on CIHR-funded research projects (tuberculosis and COVID-19 / respiratory virus related)

By the end of today's session, participants should be able to:

1. Describe recent MDR-TB epidemiologic trends in Ontario.
2. Define MDR-, pre-extensively drug-resistant (XDR)TB and XDR-TB, as per the Canadian Tuberculosis Standards, 8th Edition.
3. Discuss a key current challenge and/or opportunity for public health management of individuals with MDR-TB, in the Ontario context.
4. Discuss a key current challenge and/or opportunity for clinical management of individuals with MDR-TB, in the Ontario context.

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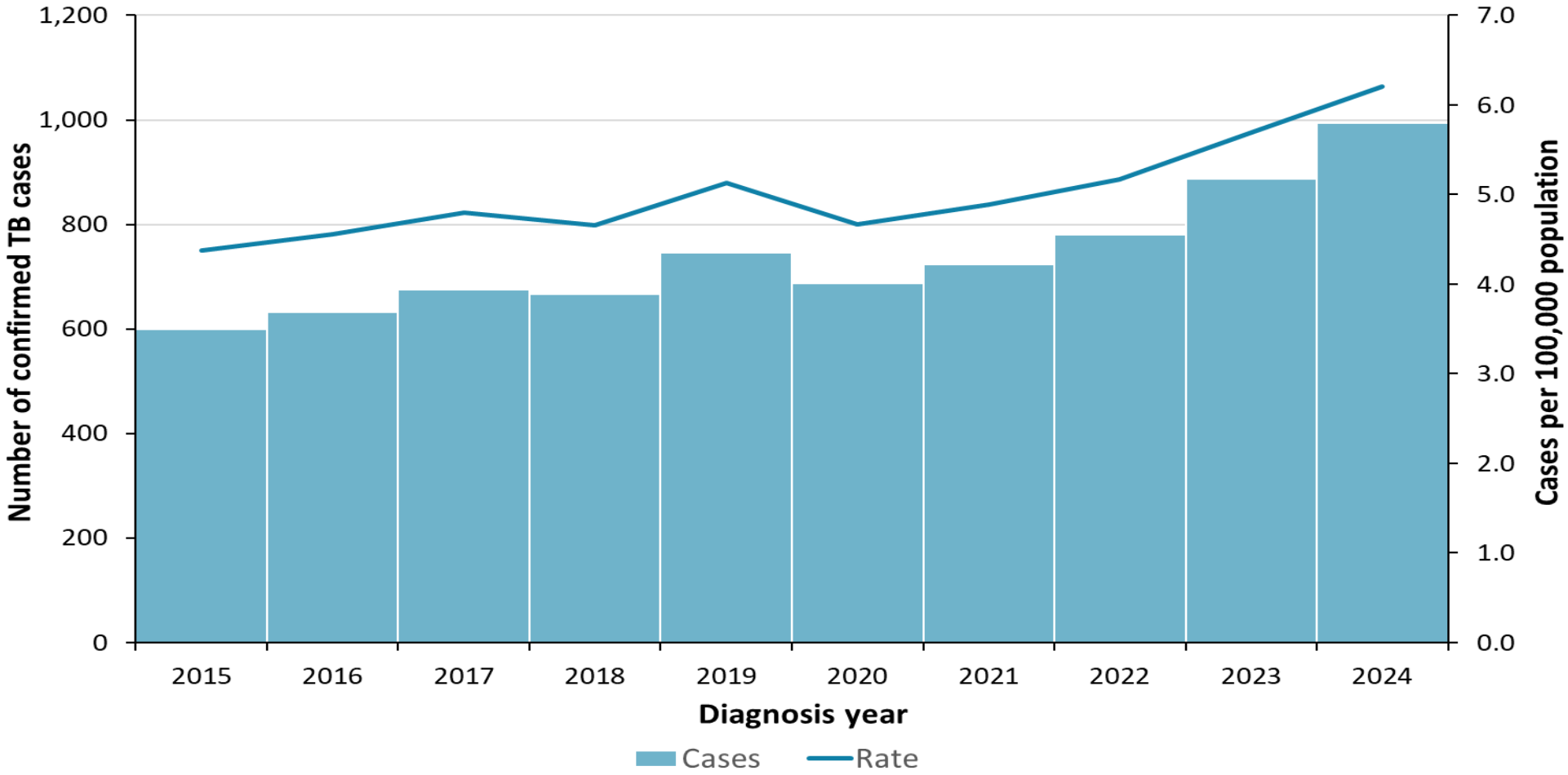
Epidemiologic trends in drug-resistant tuberculosis (TB) in Ontario

Presented by: Dr. Liane Macdonald

September 16, 2025

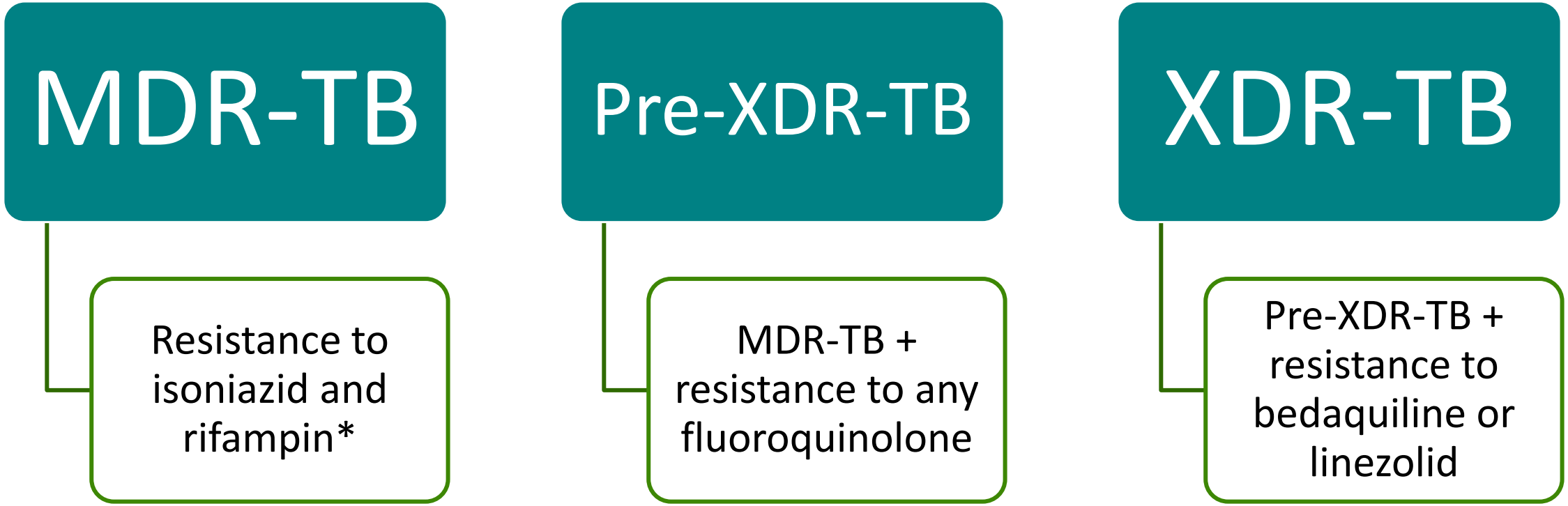
PHO Rounds

Confirmed TB cases and rates per 100,000 population by diagnosis year, Ontario: 2015 to 2024



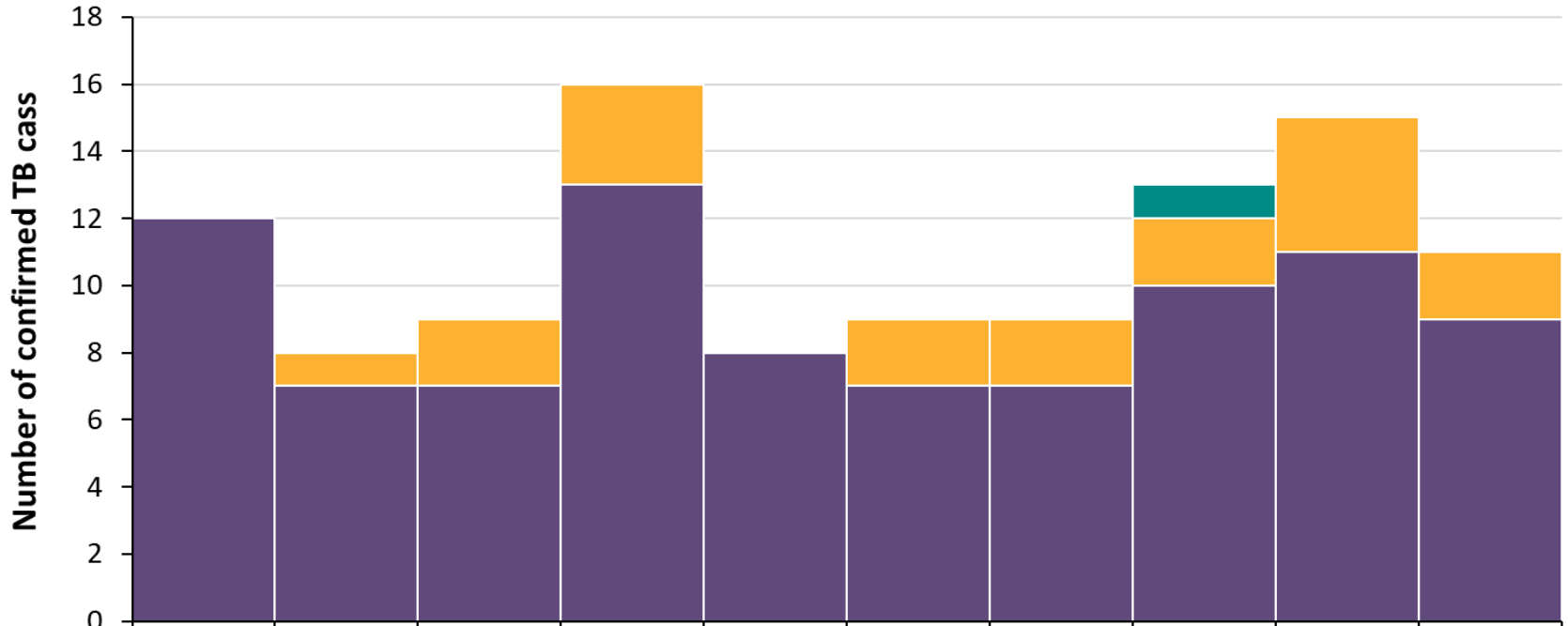
Data sources: Cases: integrated Public Health Information System (iPHIS) [Database; extracted Aug 28 2025]. Population denominators: Statistics Canada Table 17-10-0157-01: Population estimates, July 1, by health region and peer group, 2023 boundaries [extracted Feb 21 2025].

Definitions of multidrug-resistant TB (MDR-TB), pre-extensively drug-resistant TB (pre-XDR-TB), and XDR-TB



Source: Brode SK, Dwilow R, Kunimoto D, Menzies D, Khan FA. Chapter 8: Drug-resistant Tuberculosis. Canadian Journal of Respiratory, Critical Care, and Sleep Medicine. 2022;6(sup 1): 109-128. [cited 2025 Sep 16].

Drug-resistant TB cases by diagnosis year, Ontario: 2015 to 2024



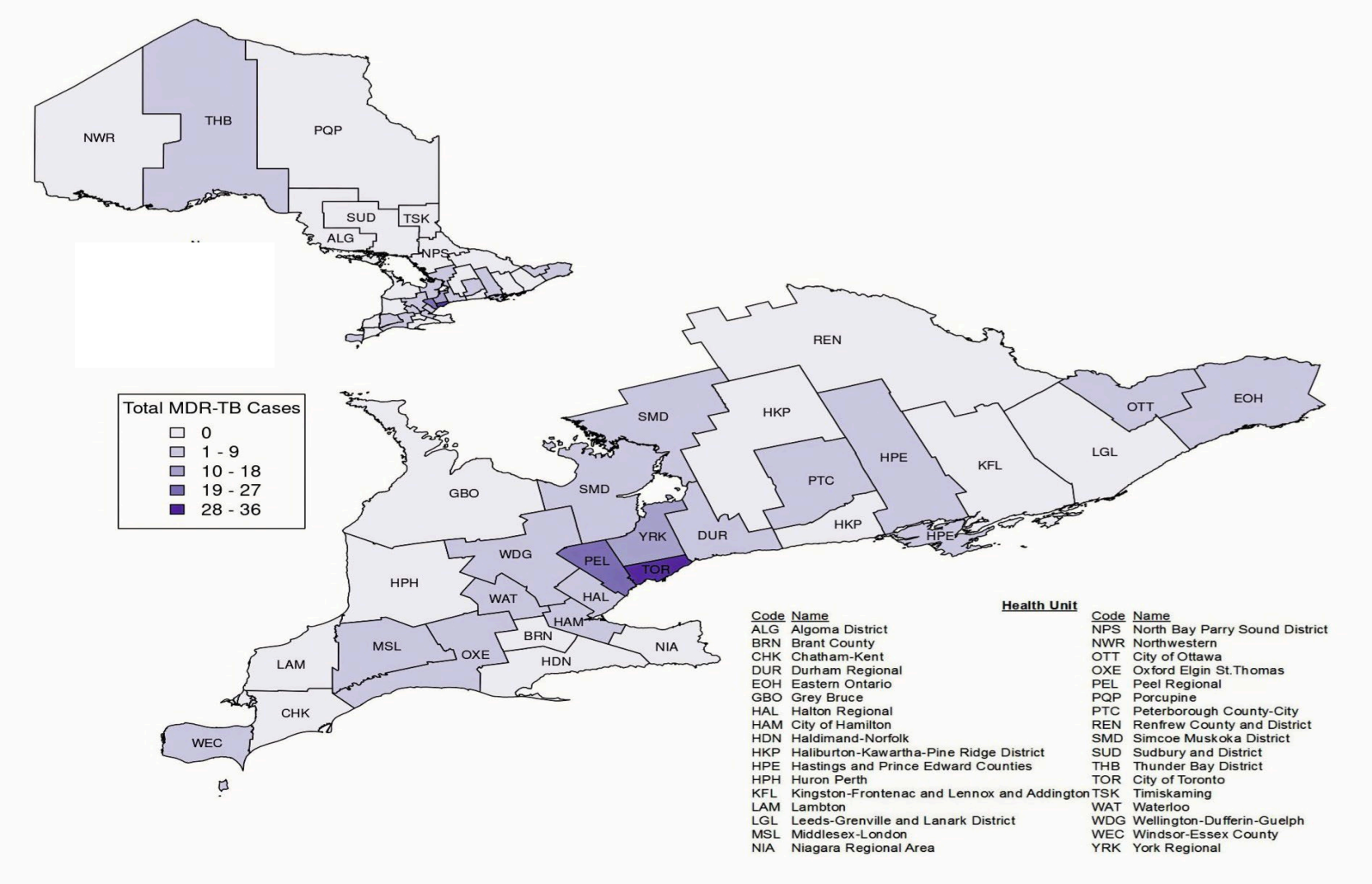
	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	TOTALS
XDR-TB*	0	0	0	0	0	0	0	1	0	0	1
Pre-XDR TB	0	1	2	3	0	2	2	2	4	2	18
MDR-TB	12	7	7	13	8	7	7	10	11	9	91

Diagnosis year

***Note:** Based on WHO-recommended critical concentrations and minimum inhibitory concentration of isolate. Clinical and Laboratory Standards Institute (CLSI) breakpoints for interpretation have not yet been established for bedaquiline.

Data sources: MDR-TB cases: iPHIS [Database; extracted 2025 Aug 28]. Pre-XDR- and XDR-TB cases: Ontario Universal Typing of Tuberculosis by Whole Genome Sequencing (OUT-TB by WGS); extracted 2025 Aug 25.

Total number of confirmed MDR-TB cases by PHU: 2015 - 2024



Data source: iPHIS [Database; extracted 28 Aug 2025].

Characteristics of MDR-TB cases, Ontario: 2015 to 2024

Characteristic		MDR-TB cases n (%)
Place of birth	Outside of Canada In Canada Unknown/missing	83 (91.2) 7 (7.7) 1 (1.1)
Sex	Female Male Unknown	48 (52.7) 43 (47.3) 0 (0.0)
Age group (years)	0 – 19 20 – 39 40 – 59 60 – 79 80+	9 (9.9) 43 (47.3) 21 (23.1) 15 (16.5) 3 (3.3)
Total		**91 (100)**

Data source: iPHIS [Database; extracted 28 Aug 2025].

Summary

- The annual provincial incidence of TB disease has increased in recent years

- 91 cases of MDR-TB were reported in Ontario from 2015 to 2024; the annual median was 8.5 MDR-TB cases/year over this period
  - Range: 7-13 cases/year; varied year-to-year
  - MDR-TB case counts varied considerably between PHUs
  - > 90% of MDR-TB cases reported being born outside of Canada
  - Pre-XDR-TB and XDR-TB cases were infrequently reported

- Continuing to monitor the epidemiology of drug-resistant TB in Ontario is key to informing prevention and care

Acknowledgements:

Ana Cecilia Ulloa, Andrea Saunders, Karen Johnson, Emily Karas (CDC, PHO)
Angela Ma (PHO Laboratory); Public health units, and clinical and provincial partners

For more information:

PHO tuberculosis resources: https://www.publichealthontario.ca/en/Diseases-and-Conditions/Infectious-Diseases/Respiratory-Diseases/Tuberculosis

Contact: Communicable.diseasecontrol@oahpp.ca

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What You Need to Know About Multidrug-Resistant TB:

A clinical and public health overview

PHO Rounds

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September 16, 2025

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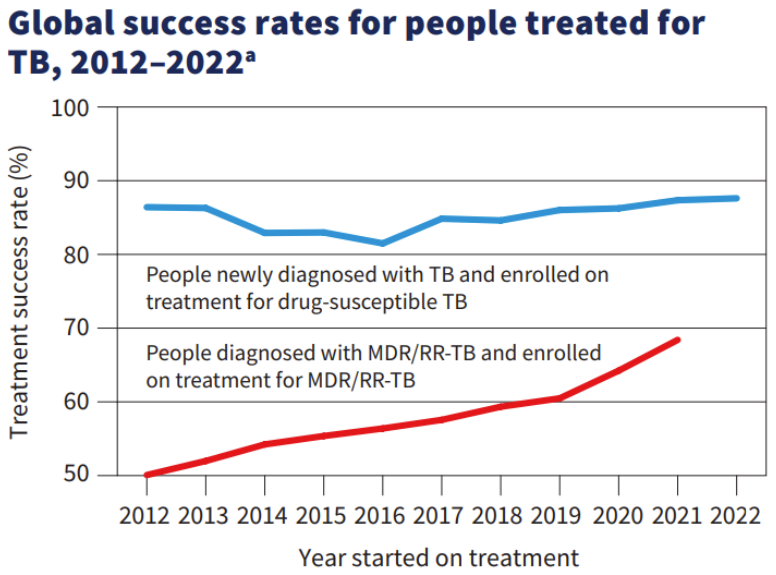
Conflicts of Interest

- AstraZeneca: Speaking honorarium (fees paid to my institution)
- Intend to make therapeutic recommendations for medications that have not received regulatory approval

MDR-TB: Why is it important?

- Globally, MDR-TB treatment outcomes lag far behind those for drug susceptible TB
  - Higher mortality
  - Lower rates of cure/treatment completion, higher rates of relapse
  - Higher rates of drug related adverse effects
- Costs of treating MDR-TB are substantially higher than costs of treating drug susceptible TB



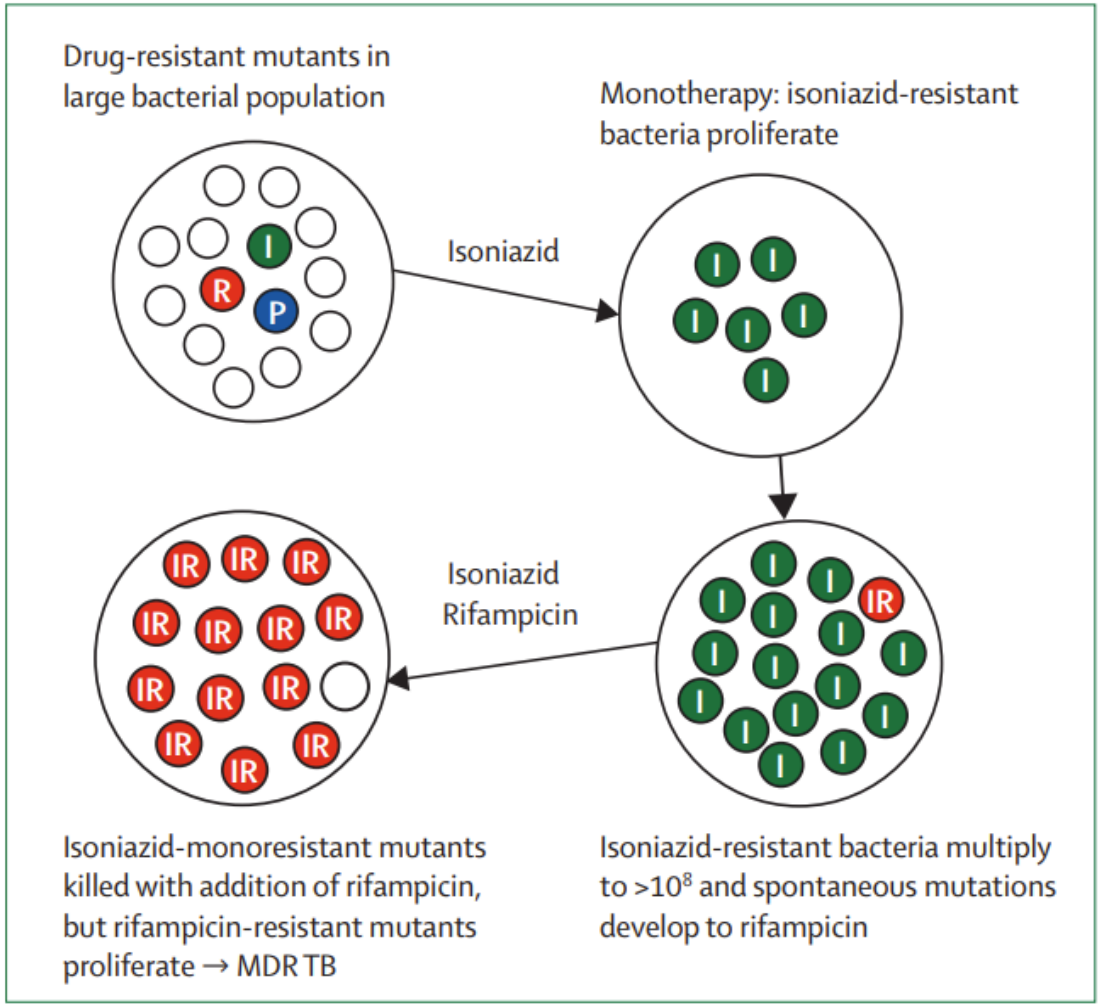
Global tuberculosis report 2024. Geneva: World Health Organization; 2024.
Campbell et al. EID 2022; 9:1814-1823.

Pathogenesis of drug resistance

- Primary (transmitted) drug resistance: previously untreated patients are found to have drug-resistant organisms, presumably because they have been infected from an outside source of resistant bacteria
- Secondary (acquired) drug resistance: patients who initially have drug-susceptible TB bacteria that later become drug-resistant during treatment

Canadian TB Standards, 8th Ed. Chapter 8. *Canadian Journal of Respiratory, Critical Care, and Sleep Medicine* 2022, Vol. 6, No. s1

Acquisition of drug resistance



Gandhi NR et al.
Lancet 2010; 375: 1830–43

Acquisition of drug resistance: Clinical causes

- Treatment regimen is inadequate
- Intermittent or erratic ingestion of the prescribed anti-TB drugs
- Low drug concentration exposures at site of infection
  - suboptimal drug doses
  - poor-quality drugs
  - drug malabsorption
  - cavitary pulmonary TB – drugs differentially penetrate into cavities, which contain large numbers of bacteria with large numbers of drug-resistant mutants

1. Canadian TB Standards, 8th Ed. Chapter 8. *Canadian Journal of Respiratory, Critical Care, and Sleep Medicine* 2022, Vol. 6, No. s1
2. Dheda K et al. *Lancet Respir Med* 2017; 5: 291–360

Global burden of MDR/RR-TB 2023

- Approx. 400,000 new cases of MDR/RR-TB
- 3.2% of new cases and 16% of previously treated cases

Estimated number of people who developed MDR/RR-TB (incident cases) in 2023, for countries with at least 1000 incident cases[a]

[a] The labels show the five countries that accounted for more than half of the global number of people estimated to have developed MDR/RR-TB in 2023.

Global tuberculosis report 2024

Risk factors for drug-resistant TB

1) Previously treated for TB disease

2) Originated from, resided in or travelled to a country with higher rates of drug resistance

3) Exposed to a person with confirmed (or highly suspected) infectious drug-resistant TB

4) HIV infection

5) Foreign born: Younger age, more recent arrival to Canada

Canadian TB Standards, 8th Ed. Chapter 8. *Canadian Journal of Respiratory, Critical Care, and Sleep Medicine* 2022, Vol. 6, No. s1

INH and RIF-resistance: Diagnosis

- Diagnosis can be made by several methods
  - genotypic: nucleic acid amplification testing, sequencing
  - phenotypic: culture-based testing

- INH-R: ~90% due to known mutations in 2 genes (*katG* and *InhA)*
- RIF-R: ~95% due to known mutations *rpoB* gene

Canadian TB Standards, 8th Ed. Chapter 3. *Canadian Journal of Respiratory, Critical Care, and Sleep Medicine* 2022, Vol. 6, No. s1

Drug resistant TB diagnosis

Mycobacteria Smear, Concentrate

AFB Quantitation (x200)

Few 3-9/smear, 1+ 1-9/10 fields, 2+ 1-9/field, 3+ 10-90/field, 4+ >90/field

Copy of results sent to MOH. (Public Health Laboratory - Toronto) (Lab 4269)

Name	Result	Flag	Ref Range	Units
Microscopic Examination		A		
Result: Acid Fast Bacilli seen: 1+				

Mycobacterium tuberculosis Multi-drug Resistance Detection PCR

Results should be interpreted in the context of patient clinical history and other findings.

Copy of results sent to MOH.

Molecular detection of determinants of drug resistance is presumptive; results must be confirmed by phenotypic drug susceptibility testing. (Public Health Laboratory - Toronto) (Lab 4269)

Name	Result	Flag	Ref Range	Units
Mycobacterium tuberculosis Complex DNA; PCR/NAAT		A		
Result: MTBC DNA Detected				
Mycobacterium tuberculosis Rifampin Resistance (rpoB) Gene; Probe, Target Amplification	Detected	A		
Mycobacterium tuberculosis Isoniazid Resistance (katG + inhA) Genes; PCR/NAAT	Not Detected	N		

AFB; Superficial; Culture

Mycobacterial culture results are only final when all culture media has been completed.

Copy of results sent to MOH. (Public Health Laboratory - Toronto) (Lab 4269)

Name	Result	Flag	Ref Range	Units
Culture Findings		A		

Result: Mycobacterium tuberculosis complex

Isoniazid Susceptibility

Copy of results sent to MOH.(Public Health Laboratory - Toronto)(Lab 4269)

Name	Result	Susceptibility
Isoniazid 0.1 mg/L	Susceptible	S

I=Intermediate, MS=Moderately Susceptible, NI=No Interpretation, NS=Non Susceptible

R=Resistant, S=Susceptible, S-DD=Susceptible Dose Dependant, VS=Very Susceptible

Rifampin Susceptibility

Copy of results sent to MOH.(Public Health Laboratory - Toronto)(Lab 4269)

Name	Result	Susceptibility
Rifampin 1.0 mg/L	Resistant	R

I=Intermediate, MS=Moderately Susceptible, NI=No Interpretation, NS=Non Susceptible

R=Resistant, S=Susceptible, S-DD=Susceptible Dose Dependant, VS=Very Susceptible

Ethambutol Susceptibility

Copy of results sent to MOH.(Public Health Laboratory - Toronto)(Lab 4269)

Name	Result	Susceptibility
Ethambutol 5.0 mg/L	Susceptible	S

I=Intermediate, MS=Moderately Susceptible, NI=No Interpretation, NS=Non Susceptible

R=Resistant, S=Susceptible, S-DD=Susceptible Dose Dependant, VS=Very Susceptible

Pyrazinamide Susceptibility

Name	Result	Susceptibility
Pyrazinamide 100.0 mg/L	Susceptible	S

I=Intermediate, MS=Moderately Susceptible, NI=No Interpretation, NS=Non Susceptible

R=Resistant, S=Susceptible, S-DD=Susceptible Dose Dependant, VS=Very Susceptible

Mycobacterium tuberculosis Whole Genome Sequencing

MTB complex whole genome sequencing pipeline: BCC Genomics (TB) Pipeline v1.1.0
Reference genome: Mycobacterium tuberculosis H37Rv
Antimicrobial resistance prediction TB-Profiler version and database: v6.2.1 and 82777ea
Kraken version and database: 2.1.2 and kraken2-expanded 2020-01-01
MTB complex genomic antimicrobial resistance prediction was developed with its performance characteristics determined by Public Health Ontario for clinical testing. It has not been cleared or approved by Health Canada. The absence of mutations does not exclude the possibility of other

Name	Result	Flag	Ref Range	Units
Mycobacterium sp identified; Sequencing		A		
Result: M. tuberculosis var. tuberculosis				
Mycobacterium tuberculosis Complex Lineage; Sequencing				
Result: 4-Euro-American				
Isoniazid; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				
Rifampin; Sequencing		A		
Result: Resistance predicted in gene(s) analyzed (rpoB)				
Ethambutol; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				
Pyrazinamide; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				
Moxifloxacin; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				
Amikacin; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				
Capreomycin; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				
Ethionamide; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				
Kanamycin; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				
Linezolid; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				
Levofloxacin; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				
Streptomycin; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				
Clofazimine; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				
Bedaquiline; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				
Delamanid; Sequencing		N		
Result: No high confidence resistance mutations detected. Cannot rule out resistance.				

Management of MDR TB

Canadian TB Standards: Good practice statement

Providers should have access to

- Drug susceptibility testing for all drugs that will be used
- An uninterrupted supply of quality assured drugs
- A patient centred comprehensive management program
- A team experienced in the management of drug-resistant TB

Canadian TB Standards, 8th Ed. Chapter 8. *Canadian Journal of Respiratory, Critical Care, and Sleep Medicine* 2022, Vol. 6, No. s1

New treatment recommendations for MDR/RR-TB since publication of the Canadian TB Standards

- Treatment recommendations for MDR/RR-TB in Canadian TB Standards, 8th edition, are not current
- Since 2022, multiple clinical trials of new treatment regimens have been published
- Best references:
  - WHO Consolidated Guidelines on Tuberculosis (2025) – most current
  - ATS/CDC/ERS/IDSA Clinical Practice Guideline: Updates on the Treatment of Drug-Susceptible and Drug-Resistant Tuberculosis (2025) – does not incorporate some of the newest regimens

BPaLM: 6 months

- WHO suggests, ATS/CDC/ERS/IDSA recommends, the use of a 6-month regimen of bedaquiline, pretomanid, linezolid, and moxifloxacin (BPaLM) in patients MDR/RR-TB, rather than longer regimens. *(WHO conditional recommendation, ATS strong recommendation, very low certainty of evidence)*
  - *Include moxifloxacin if fluoroquinolone susceptible; do not include/stop moxifloxacin if fluoroquinolone resistant*
- *Evidence: TB-PRACTECAL and ZeNix trials*

1. WHO consolidated guidelines on tuberculosis. Module 4: treatment and care, 2025. Geneva: World Health Organization; 2025.
2. Saukkonen JJ et al. Updates on the Treatment of Drug-Susceptible and Drug-Resistant Tuberculosis: An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline. Am J Respir Crit Care Med. 2025 Jan;211(1):15-33.
3. Nwyang'wa B-T et al. A 24-Week, All-Oral Regimen for Rifampin-Resistant Tuberculosis. NEJM 2022 Dec; 387:2331-2343.
4. Conradie F et al. Bedaquiline–pretomanid–linezolid regimens for drug-resistant tuberculosis. *N Engl J Med* 2022;387:810-823.

TB PRACTECAL: modified Intention to treat

	SOC N=137	BPaLM N=138	BPaLC N=115	BPaL N=111
Favorable outcome	81 (59%)	121 (88%)	88 (77%)	96 (86%)
Unfavorable outcome	56 (41%)	16 (12%)	27 (23%)	15 (14%)
-Death	5 (4%)	0	1 (1%)	1 (1%)
-Early discontinuation	50 (37%)	11 (8%)	11 (10%)	11 (10%)
-Failure	0	0	1 (1%)	0
-Loss to follow up	2 (3%)	2 (3%)	3 (5%)	3 (5%)
-Recurrence	0	1 (1%)	5 (4%)	3 (3%)

SOC = standard of care; B = bedaquiline; Pa = pretomanid; L = linezolid; M = moxifloxacin; C = clofazimine

Nyang'wa, B.-T., et al. (2024). Lancet Respir Med 12: 117-28.

BPaLM

- Bedaquiline 400 mg daily x 2 weeks then 200 mg TIW
- Pretomanid 200 mg daily
- Linezolid 600 mg daily
- +/- Moxifloxacin 400 mg daily

- 26 weeks

- ATS/IDSA/CDC/ERS: Consider extension to 9 months (39 weeks) if evidence for delayed response (e.g. culture conversion > 8 weeks with clinical condition slow to improve)

1. WHO consolidated guidelines on tuberculosis. Module 4: treatment and care, 2025. Geneva: World Health Organization; 2025.
2. Saukkonen JJ et al. Updates on the Treatment of Drug-Susceptible and Drug-Resistant Tuberculosis: An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline. Am J Respir Crit Care Med. 2025 Jan;211(1):15-33.

BPaLM Implementation

- BPaLM not advised for CNS TB, bone/joint TB, disseminated/miliary, pregnant/breastfeeding, <14 yo
  - No clinical trial data, but limited programmatic experience has been published
- Should have <1 month prior exposure to components, or resistance ruled out

1. WHO consolidated guidelines on tuberculosis. Module 4: treatment and care, 2025. Geneva: World Health Organization; 2025.
2. Saukkonen JJ et al. Updates on the Treatment of Drug-Susceptible and Drug-Resistant Tuberculosis: An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline. Am J Respir Crit Care Med. 2025 Jan;211(1):15-33.

BPaLM Implementation

- Bedaquiline and pretomanid drug susceptibility testing is not performed at PHOL… *bedaquiline pDST done at NML, and we now have WGS for the bedaquiline and delamanid*
- Bedaquiline and pretomanid are not licensed in Canada
  - Health Canada Special Access Program and manufacturer approval required
  - Delay of a couple of weeks between when drugs needed and when available
  - ‘Bridging regimen’ for sick or infectious patients
- Linezolid therapeutic drug monitoring may be useful[2]
- How to handle side effects and treatment interruptions?
  - Linezolid is recommended for at least 9 weeks[1,2]

1. WHO consolidated guidelines on tuberculosis. Module 4: treatment and care, 2025. Geneva: World Health Organization; 2025.
2. Saukkonen JJ et al. Updates on the Treatment of Drug-Susceptible and Drug-Resistant Tuberculosis: An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline. Am J Respir Crit Care Med. 2025 Jan;211(1):15-33.

BPaLM patient monitoring

Table 8. Monitoring Plan for Patients Treated with BPaL or BPaLM*

Activity	Month of Treatment										Post-Treatment†				
	0 (Baseline)	1‡	2	3	4	5	6	7	8	9	3	6	12	18	24
Sputum smear and culture§	●	● ● ●	●	●	●	●	●	○	○	○	●	●	●	●	●
Imaging (CXR, CT, other)‖	●			●			●			○	○	○	○	○	○
Weight¶	●	●	●	●	●	●	●	○	○	○	●	●	●	●	●
Symptom review**	●	●	●	●	●	●	●	○	○	○	●	●	●	●	●
DST††	●			○											
CBC‡‡	●	● ● ● ●	● ●	●	●	●	●	○	○	○					
Creatinine§§	●	●	●	●	●	●	●	○	○	○					
ALT/AST, alkaline phosphatase, bilirubin‖‖	●	●	●	●	●	●	●	○	○	○					
K^+, Ca^{2+}, Mg^{2+}, bicarbonate¶¶	●	●	●	●	●	●	●	○	○	○					
Serum drug concentration***		○													
HIV†††	●														
Pregnancy‡‡‡	○	○	○	○	○	○	○	○	○	○					
EKG§§§	●	● ○	○	●	○	○	●	○	○	○					
Vision exam‖‖‖	●	●	●	●	●	●	●	○	○	○					
Peripheral neuropathy¶¶¶	●	●	●	●	●	●	●	○	○	○					
Arthralgias****	●	○	○	○	○	○	○	○	○	○					
Amylase, lipase, TSH††††	○														

Saukkonen JJ et al. Updates on the Treatment of Drug-Susceptible and Drug-Resistant Tuberculosis: An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline. Am J Respir Crit Care Med. 2025 Jan;211(1):15-33.

Alternative 6-month regimen (WHO)

- WHO suggests the use of a 6-month treatment regimen composed of bedaquiline, delamanid, linezolid (600 mg), levofloxacin, and clofazimine (BDLLfxC) in MDR/RR-TB patients with or without fluoroquinolone resistance *(Conditional recommendation, very low certainty of evidence)*
- Note: Can be given to people of all ages, including children, adolescents, PLHIV, and pregnant and breastfeeding women
- *Evidence: BEAT Tuberculosis trial (data not yet published outside of WHO guidelines)*

WHO consolidated guidelines on tuberculosis. Module 4: treatment and care, 2025. Geneva: World Health Organization; 2025.

9 month all oral regimens (WHO)

- WHO suggests using the 9-month all-oral regimens (BLMZ, BLLfxCZ and BDLLfxZ) over currently recommended longer (>18 months) regimens in patients with MDR/ RR-TB and in whom resistance to fluoroquinolones has been excluded
- BLMZ > BLLfxCZ > BDLLfxZ

  (Conditional recommendation, very low certainty of evidence)
- Note: Fluoroquinolone resistance must be excluded. Can be given to people of all ages, including children, adolescents, PLHIV, and pregnant and breastfeeding women
- *Evidence: endTB trial*

B=Bedaquiline
L=Linezolid
M=Moxifloxacin
Z=Pyrazinamide
Lfx=Levofloxacin
C=Clofazimine
D=Delamanid

1. WHO consolidated guidelines on tuberculosis. Module 4: treatment and care, 2025. Geneva: World Health Organization; 2025.
2. Guglielmetti et al. Oral Regimens for Rifampin-Resistant, Fluoroquinolone-Susceptible Tuberculosis. NEJM 2025;392:468-482

9 month all oral regimens (WHO)

- WHO suggests the use of the 9-month all-oral regimen rather than longer (18-month) regimens in patients with MDR/RR-TB and in whom resistance to fluoroquinolones has been excluded *(Conditional recommendation, very low certainty of evidence)*
- 7 drugs (bedaquiline, levofloxacin/moxifloxacin, ethionamide, high dose INH, pyrazinamide, clofazimine) x 4-6 months, then 4 drugs (levofloxacin/moxifloxacin, clofazimine, ethambutol, pyrazinamide) x 5 months
  - Ethionamide can be replaced with 2 months linezolid
- **Limited applicability in high resource settings**
  - Experts would not recommend use if TB resistant to any component medications (with the exception of INH)

- *Evidence: South Africa Programmatic data*

WHO consolidated guidelines on tuberculosis. Module 4: treatment and care, 2025. Geneva: World Health Organization; 2025.

Longer, individualized regimen (if 6 or 9 months regimens cannot be used)

Initially five drugs:

- Levofloxacin or moxifloxacin
- Bedaquiline
- Linezolid
- Clofazimine
- Cycloserine

Less extensive disease: 4 drugs initially

- One of the drugs can be stopped 5-to-7 months after culture conversion
- Total treatment duration of 18 to 20 months (15-17 months post culture conversion)

(*Conditional recommendations, poor evidence)*

Canadian TB Standards, 8th Ed. Chapter 8. *Canadian Journal of Respiratory, Critical Care, and Sleep Medicine* 2022, Vol. 6, No. s1

MDR-TB Drugs: Longer regimen

Table 5. Grouping and doses for anti-TB drugs used for the treatment of MDR-TB.

GROUP[a]	MEDICINE		Adults	Children (<15 years old)[99–102]
Group A	Levofloxacin OR Moxifloxacin	LFX MFX	750-1000 mg PO or IV daily 400 mg PO or IV daily	15–20 mg/kg/day (max 750 mg) PO or IV 10-15 mg/kg/day (max 400 mg) PO or IV
	Bedaquiline	BDQ	400 mg PO daily x 14 days then 200 mg PO 3 times/ week	Use only in patients > 6 years AND > 15 kg; 6-month duration Weight Band: 16-30 kg: 200 mg PO daily x 14 days, 100 mg PO thrice weekly >30 kg: 400 mg PO daily x 14 days, 100 mg PO thrice weekly; 6 mg/kg PO x 14 days followed by 3-4 mg/kg/day PO thrice weekly (max 400 mg)
	Linezolid	LZD	600 mg PO or IV daily	<16kg: 15mg/kg/day PO or IV ≥16kg: 10-12mg/kg/day PO or IV (max 600mg)
Group B	Clofazimine	CFZ	100 mg PO daily	2-5 mg/kg/day PO (max 100 mg) Often given on alternate days or thrice weekly due to formulation (see references for specific weight banded dosing)
	Cycloserine OR Terizidone	CS TRD	250–750 mg PO daily to achieve serum levels of 20-35 mg/L	15-20 mg/kg/day PO divided BID (max 1 gram)
Group C	Ethambutol	EMB	15 mg/kg PO daily	15-25 mg/kg/day PO (max 800 mg)
	Pyrazinamide	PZA	25-40 mg/kg PO daily	30-40 mg/kg/day PO (max 2000 mg)
	Delamanid	DLM	100 mg PO twice daily	Use only in patients >2 years; use with caution if splitting dose or crushing; use up to 6 months Weight-band: 7-23 kg: 25 mg PO BID 23-34 kg: 50 mg PO BID >34 kg: 100 mg PO BID; 3-4 mg/kg/day PO (max 200 mg)
	Amikacin (OR Streptomycin)	AM S	15mg/kg IV daily or 25mg/kg IV three times weekly[b]	15-20 mg/kg/day IV or IM (max 1 gram) [b] 20-40 mg/kg/day IV or IM (max 1 gram) [b]
	Imipenem-cilastatin OR Meropenem[c]	IPM-CLN MPM	1,000 mg IV BID – QID 1,000 mg IV 3 times daily	IPM-CLN not used in <15 years old MPM: 20-40 mg/kg IV q8h (max 6 grams)
	Ethionamide	ETO	15–20 mg/kg PO daily divided BID (usually 250–500 mg PO once or twice daily)	15-20 mg/kg/day PO (max 1 gram)
	p-aminosalicylic acid	PAS	4 g PO 2–3 times daily (total 8 to 12 grams per day)	200 mg/kg/day PO once daily OR divided BID (see references for weight-banded dosing)

Canadian TB Standards, 8th Ed. Chapter 8. *Canadian Journal of Respiratory, Critical Care, and Sleep Medicine* 2022, Vol. 6, No. s1

De-isolation for pulmonary MDR/RR-TB

Confirmed or suspected rifampin-resistant pulmonary TB:

- "We conditionally recommend that airborne precautions may be discontinued once there is clinical improvement, second-line drug susceptibility results are available, and a minimum of 4 weeks of effective therapy has been completed. In addition, for those initially smear positive, 3 consecutive sputum smears must be negative (*poor evidence*)."
  - Effective therapy = at least 3 drugs to which the isolate is confirmed or highly likely to be susceptible to

Canadian TB Standards, 8th Ed. Appendix B. *Canadian Journal of Respiratory, Critical Care, and Sleep Medicine* 2022, Vol. 6, No. s1

Current (evolving!) challenges in MDR-TB care

Universal challenges

- Treatment outcomes, medication side effects
- Costs
- Rapidly evolving treatment recommendations

Canada-specific challenges

- Access to diagnostics
  - Ontario diagnostics access significantly improved!
- Access to drugs
- Small numbers of patients, geographically spread, limited experience

Summary

- MDR-TB is TB resistant to isoniazid + rifampin, +/- other drugs
- Diagnosis is made by genotypic and/or phenotypic methods
- BPaLM x 6 months is now the WHO/ATS/IDSA/CDC/ERS recommended treatment for MDR/RR-TB
- There are several other new 6-9 months regimens recommended by WHO
- MDR-TB care continues to pose some unique challenges not encountered with DS-TB, but major improvements have occurred in the past few years

End: Questions?