27es JNI 2026 PARIS
et la région Île-de-France Palais des Congrès
Journées Nationales d'infectiologie
du jeudi 18 juin au samedi 20 juin 2026
Journée Nationale de Formation des Paramédicaux en Infectiologie
Vendredi 19 juin 2026

Les traitements courts sont-ils applicables chez nous/chez tous ?

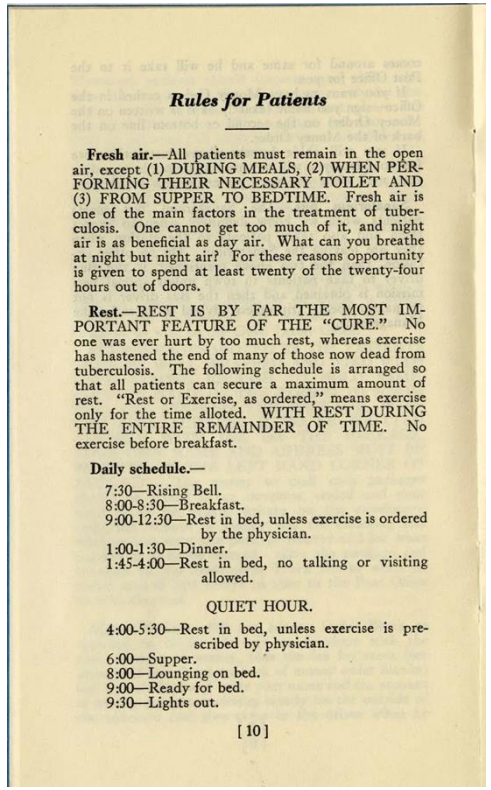
Lorenzo Guglielmetti

Déclaration de liens d'intérêt avec les industriels de santé en rapport avec le thème de la présentation (loi du 04/03/2002) :

- Consultant ou membre d'un conseil scientifique ☐ OUI ☑ NON
- Conférencier ou auteur/rédacteur rémunéré d'articles ou documents ☐ OUI ☑ NON
- Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations ☐ OUI ☑ NON
- Investigateur principal d'une recherche ou d'une étude clinique ☑ OUI ☐ NON
  - Investigateur Coordonnateur de l'essai FAST-MDR, étude indépendante soutenu par Viatris par le don du médicament (prétomanide)

Agenda – traitements courts

- Tuberculose sensible (DS-TB)
- Tuberculose résistante (DR-TB)
- Accès aux traitements
- Recherche clinique & Innovation



Rules for Patients

Fresh air.—All patients must remain in the open air, except (1) DURING MEALS, (2) WHEN PERFORMING THEIR NECESSARY TOILET AND (3) FROM SUPPER TO BEDTIME. Fresh air is one of the main factors in the treatment of tuberculosis. One cannot get too much of it, and night air is as beneficial as day air. What can you breathe at night but night air? For these reasons opportunity is given to spend at least twenty of the twenty-four hours out of doors.

Rest.—REST IS BY FAR THE MOST IMPORTANT FEATURE OF THE "CURE." No one was ever hurt by too much rest, whereas exercise has hastened the end of many of those now dead from tuberculosis. The following schedule is arranged so that all patients can secure a maximum amount of rest. "Rest or Exercise, as ordered," means exercise only for the time alloted. WITH REST DURING THE ENTIRE REMAINDER OF TIME. No exercise before breakfast.

Daily schedule.—

7:30—Rising Bell.
8:00-8:30—Breakfast.
9:00-12:30—Rest in bed, unless exercise is ordered by the physician.
1:00-1:30—Dinner.
1:45-4:00—Rest in bed, no talking or visiting allowed.

QUIET HOUR.

4:00-5:30—Rest in bed, unless exercise is prescribed by physician.
6:00—Supper.
8:00—Lounging on bed.
9:00—Ready for bed.
9:30—Lights out.

[10]

Patient Pamphlet for Piedmont TB Sanatorium, VA, 1940

DS-TB & short treatments

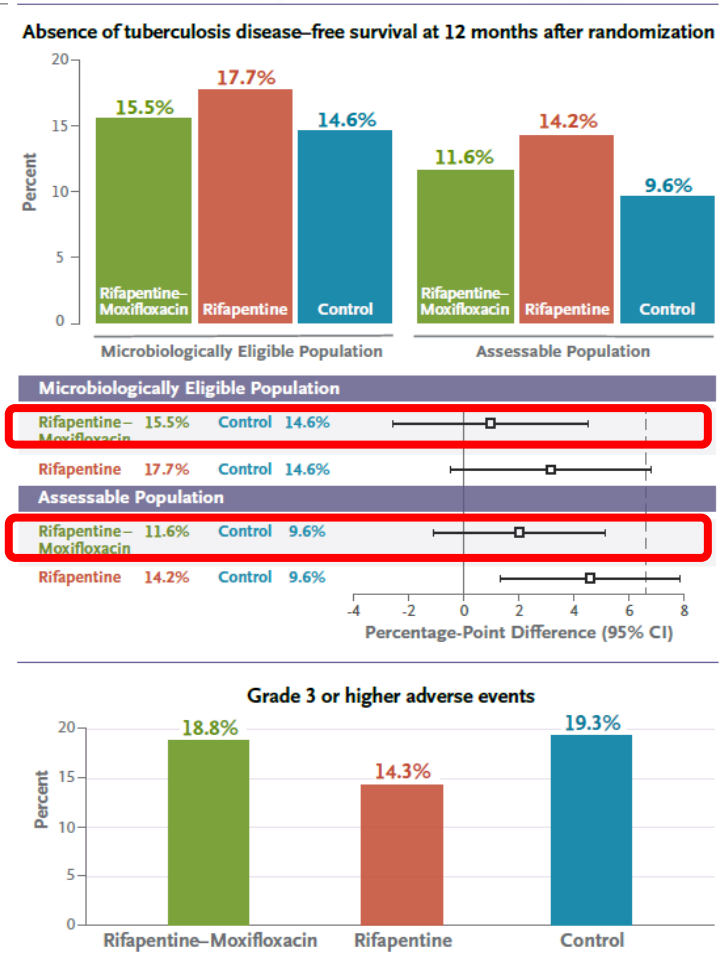
Shorter treatment for all DS-TB: TBTC Study 31

4-month treatment with moxifloxacin and high-dose rifapentine (2HPMZ/2HPM)

- Non-inferior to control (2HRZE/4HR)
- Similar safety

Implementation challenges:

- High pill burden
- Eligibility and tolerability issues
- Access challenges



Dorman et al, NEJM 2021

Louie et al, Open Forum Inf Dis 2024; Galvis et al, IJTLD 2025

Shorter treatment for children with non-severe TB: SHINE

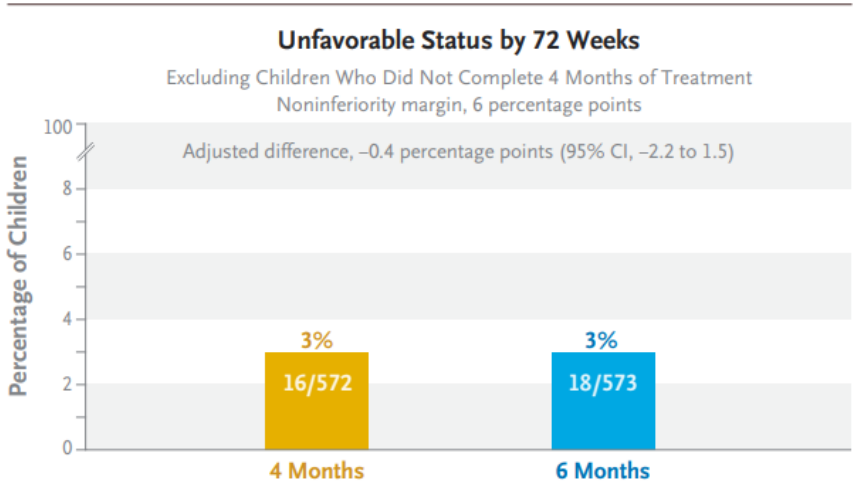
4-month HRZE treatment for children with:

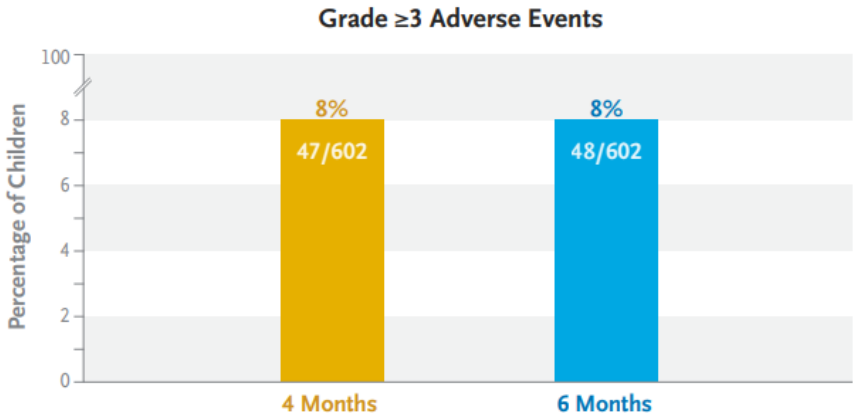
- Non-severe TB*
- Smear-negative
- Drug-susceptible

Implementation challenges:

- Availability of chest X-ray
- Treatment algorithm: clinical predictors alone sub-optimal to determine severity

*Non-severe = one lobe, no cavities, no miliary TB, no complex pleural effusion, no significant airway obstruction





Turkova et al, NEJM 2022

Gupta et al, SOA01-506-18, Union Conference 2025.

High-dose rifampicin is not enough: RIFASHORT trial

- Open-label, Phase 3 RCT
- 672 DS-TB patients:
  - **HRZE 6**
  - **HRZE 4** with **R 1200** mg/d
  - **HRZE 4** with **R 1800** mg/d

Table 2. Primary and Key Secondary Outcome Analyses.*

mITT-M Primary Analysis Assessable Outcomes	Control (n=187)	Study Regimen 1 (n=186)	Study Regimen 2 (n=186)
Favorable			
Participants with outcome — no. (%)	174 (93.0)	167 (89.8)	161 (86.6)
Unfavorable			
Participants with outcome — no. (%)	13 (7.0)	19 (10.2)	25 (13.4)
Adjusted percentage point difference from control (90% CI)		3.1 (–1.6 to 7.9)	6.3 (1.1 to 11.5)
Change in treatment because of adverse event‡	1 (0.5)	2 (1.1)	7 (3.8)
Two consecutive positive cultures after completing treatment	2 (1.1)	9 (4.8)	9 (4.8)

Table 3. Laboratory-Defined and Clinical Adverse Events According to Treatment Group.*

Participants Experiencing	Control (n=224)	Study Regimen 1 (n=223)	Study Regimen 2 (n=225)
Primary safety outcome			
Grade 3 or 4 adverse event — no. (%)	9 (4.0)	10 (4.5)	10 (4.4)
Percentage point difference from control (95% CI)		0.5 (–3.3 to 4.2)	0.4 (–3.3 to 4.2)
Secondary safety outcome			
Grade 1–4 adverse event — no. (%)	120 (53.6)	109 (48.9)	115 (51.1)
Percentage point difference from control (95% CI)		–4.7 (–13.9 to 4.6)	–2.5 (–11.7 to 6.8)

- NOT non-inferior to HRZE 6 (due to ↑ relapse)
- R1200: well tolerated; R1800: similar Grade ≥3 but lower tolerability

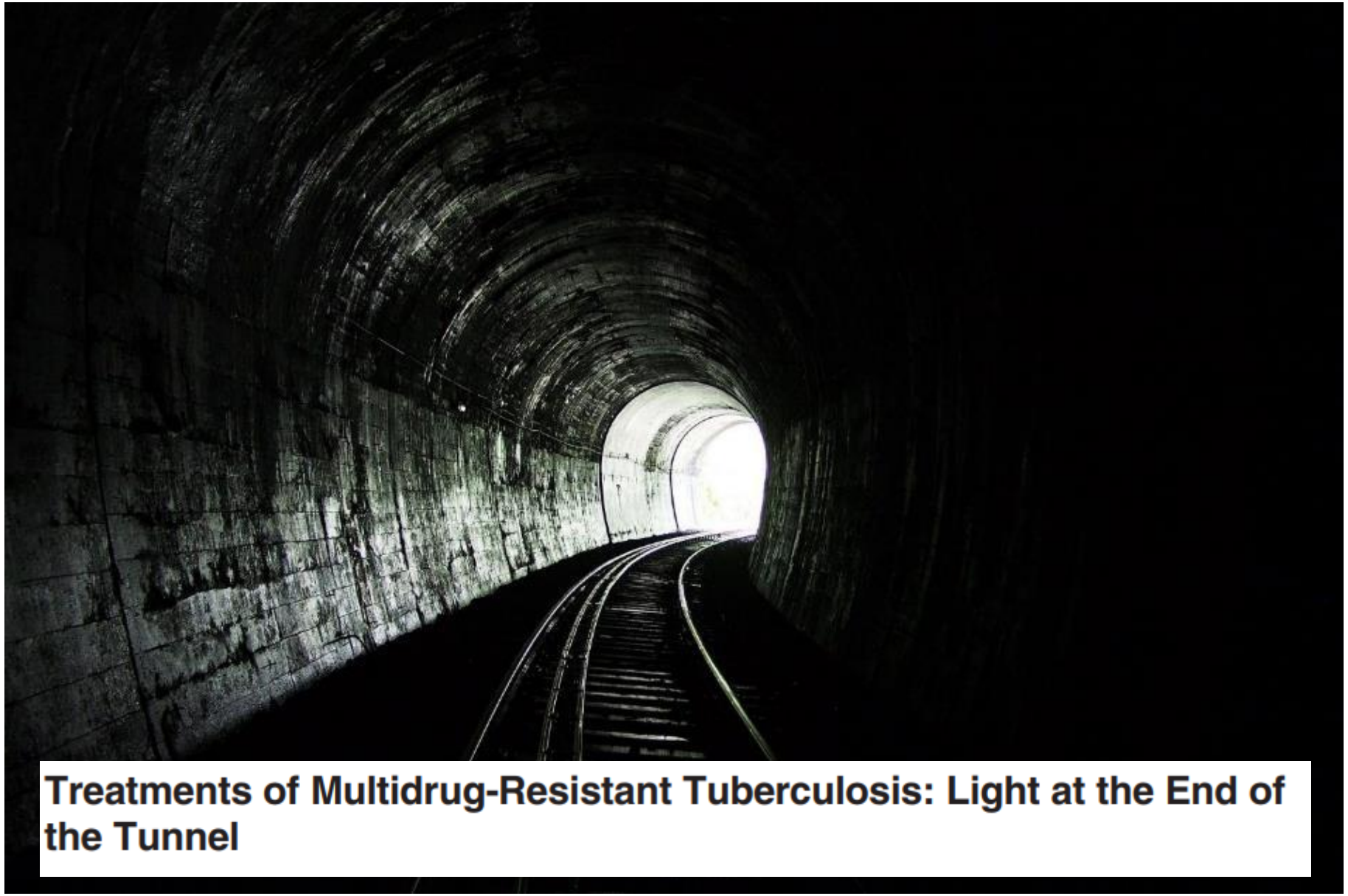
Jindani et al, NEJM Evid 2023

High dose R + FQ = ?

Trial	Population	Exp regimen(s)	Phase	Status
STEP2C	Pulmonary	**High-dose R and Z + Mfx**, 3 or 4 mts	2c	Completed
OptiRiMox	Pulmonary	**High-dose R** in 4HRZE and 4HRZM	3	Completed
Hi-DoRi-3	Pulmonary	**High-dose R** until 3 mts post-culture conversion	3	?
ORIENT	Pulmonary	**High dose Rpt** in 4HPZM (=Study31 in China)	2	?
(PORT & RIALTA)	Pulmonary	**High-dose R** for 6 mts (primary objective: safety)	3 & 2b/c	Enrolling

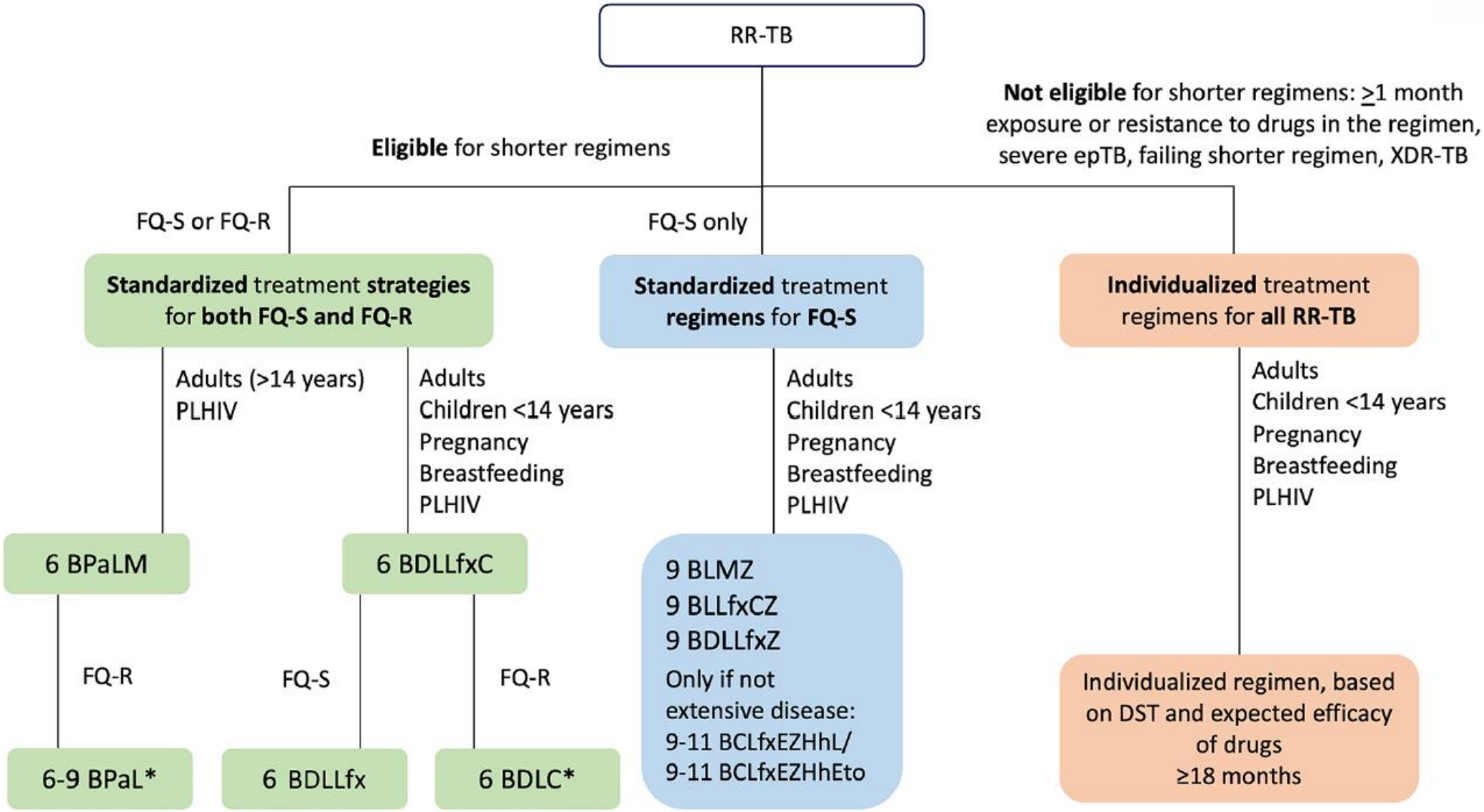
Modified from Motta et al, CMI 2023

DR-TB & short treatments



Lange et al, AJRCCM 2022

RR-TB: 2025 treatment algorithm

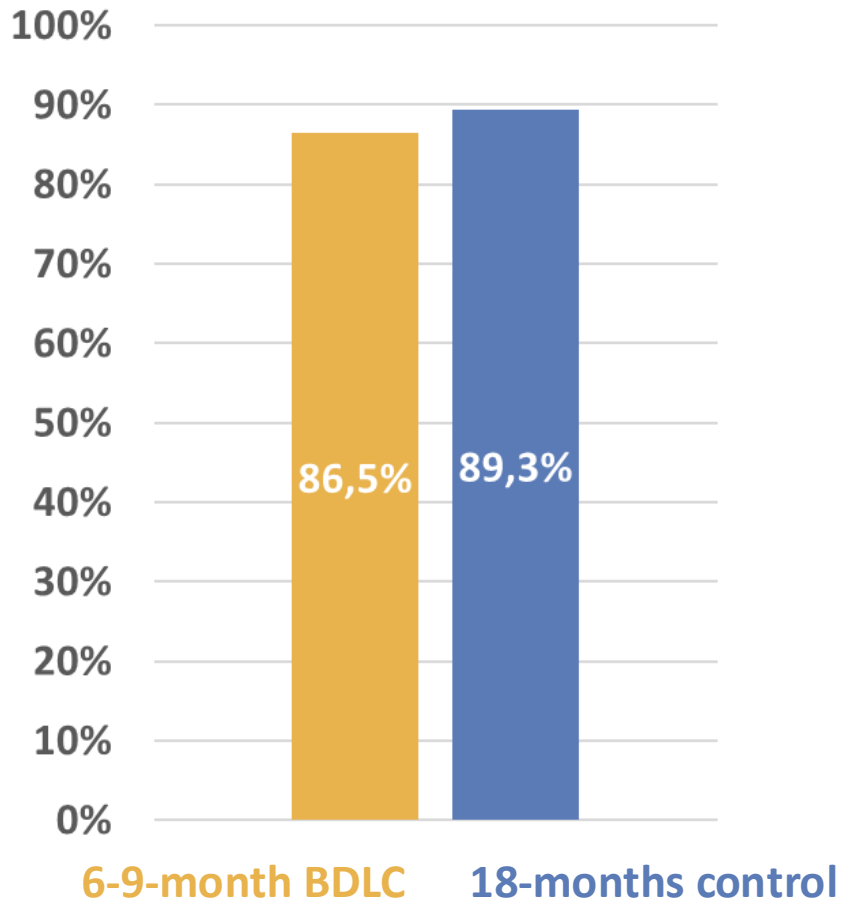


Lange et al, Pathogens and Immunity 2025

*pre-XDR treatment based on low-quality evidence

endTB-Q:
Phase 3 stratified RCT for pre-XDR-TB

- **6/9-month BDLC** *vs* 18-month control
- BDLC duration stratified by extent of disease (sputum smear + cavity) and culture conversion
- NOT non-inferior due to ↑ relapses, more in extensive disease -> **7/9 relapses acquired drug resistance** (all B resistance)
- **6/9-month BDLC** may be **inadequate to prevent relapses in patients with extensive TB**
- **Upcoming WHO guideline update** will provide recommendations based on stronger evidence

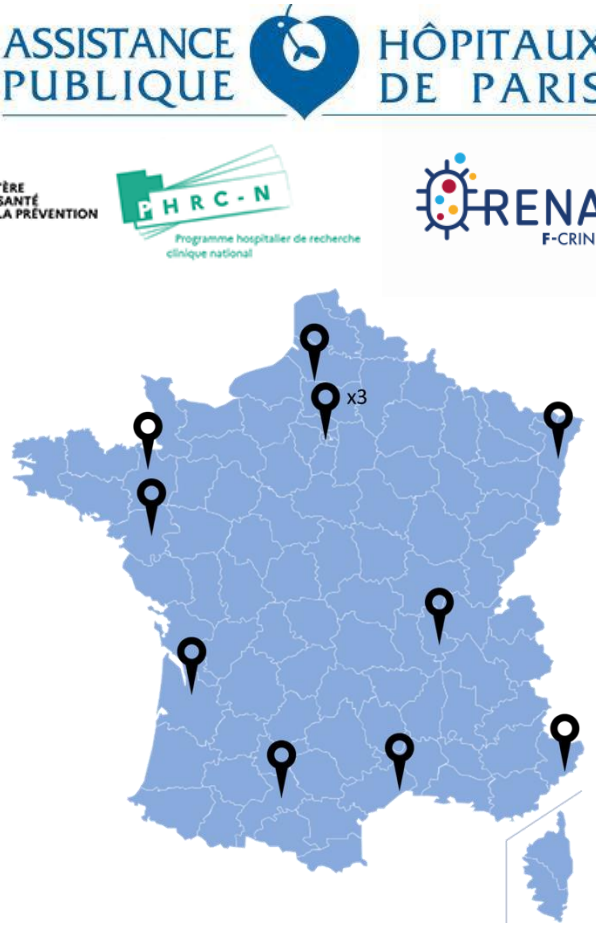


Guglielmetti et al, Lancet Resp Med 2025

B=bedaquiline, D= delamanid, L=linezolid, C=clofazimine

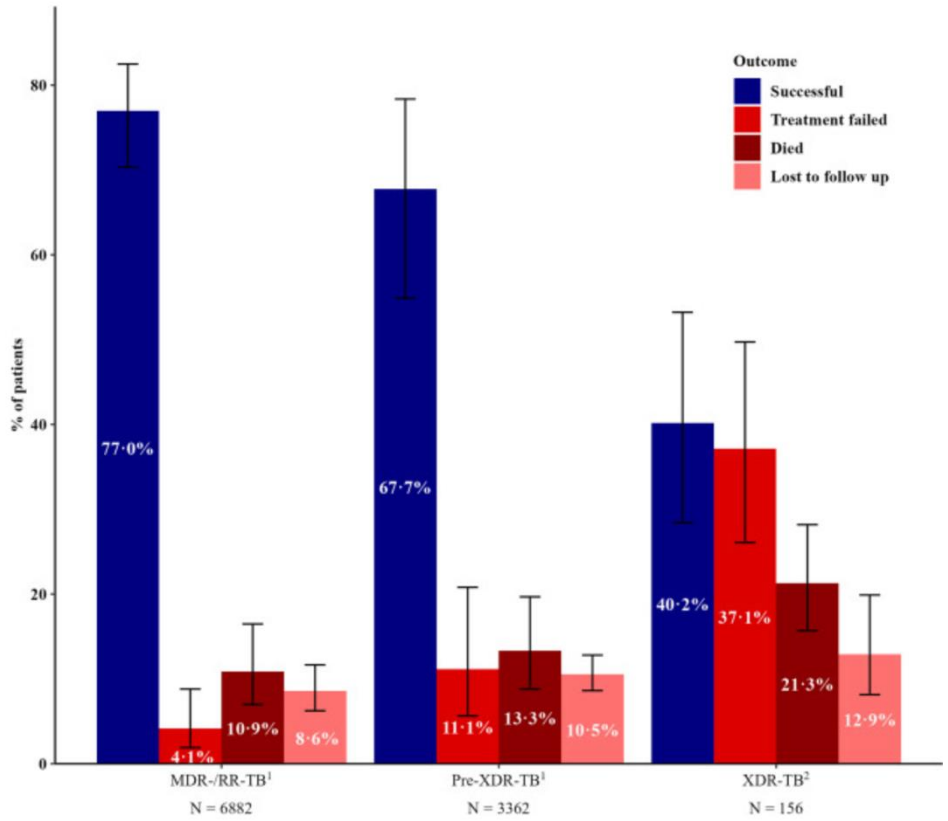
FAST-MDR trial

- Non-inferiority, multicentre Phase 3 RCT for adult MDR/RR-TB
- **6-month BPaLM-based strategy** vs **French National MDR-TB cohort** (2006-2022)
- PK/PD & MIC testing for second-line drugs
- B dose randomization (daily vs thrice weekly)
- 55 patients, 12 sites in 12 hospitals
- **Inclusions starting Q3 2026**



TBnet/ESGMYC XDR-TB retrospective study

- **16 countries, 188 XDR-TB* patients**
- Treatment success rates **similar to pre-antibiotic era (40%)**
- **Each additional effective drug** in regimens significantly **reduced the odds of unsuccessful outcomes**

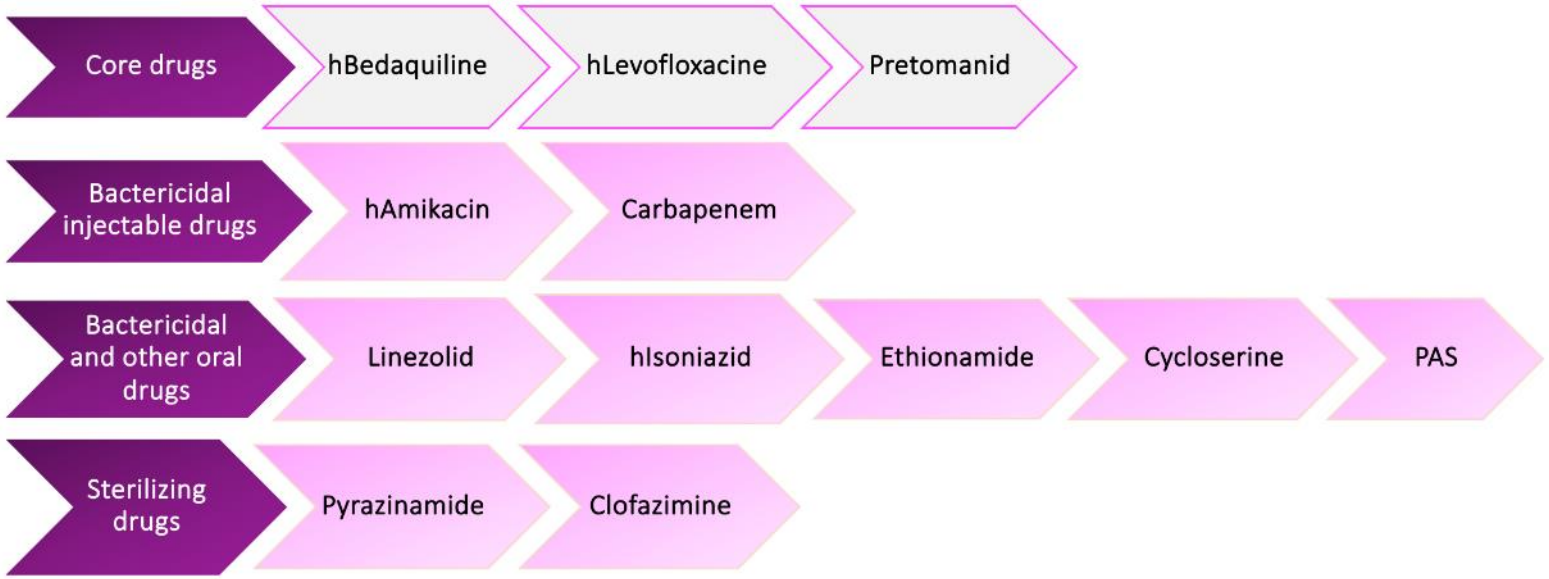


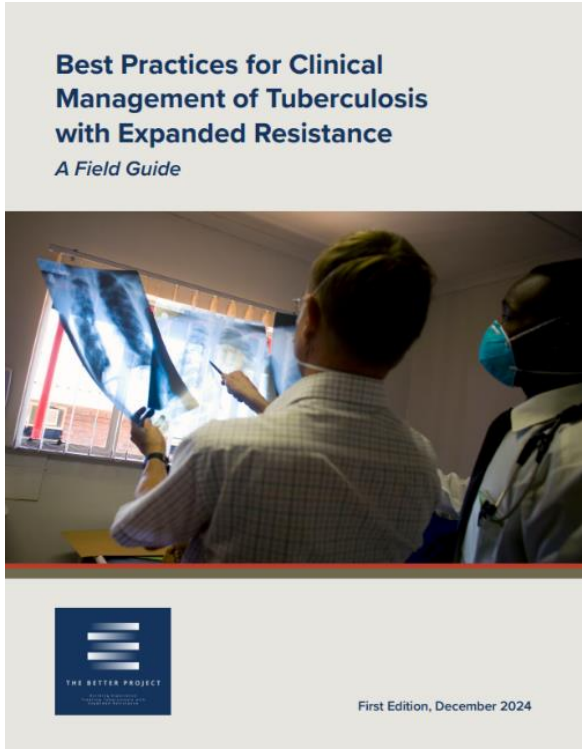
Kherabi et al, Lancet Reg Health Europe 2025

* XDR-TB = RR-TB with resistance to any FQ and Bdq/Lzd

XDR-TB treatment

STEPS

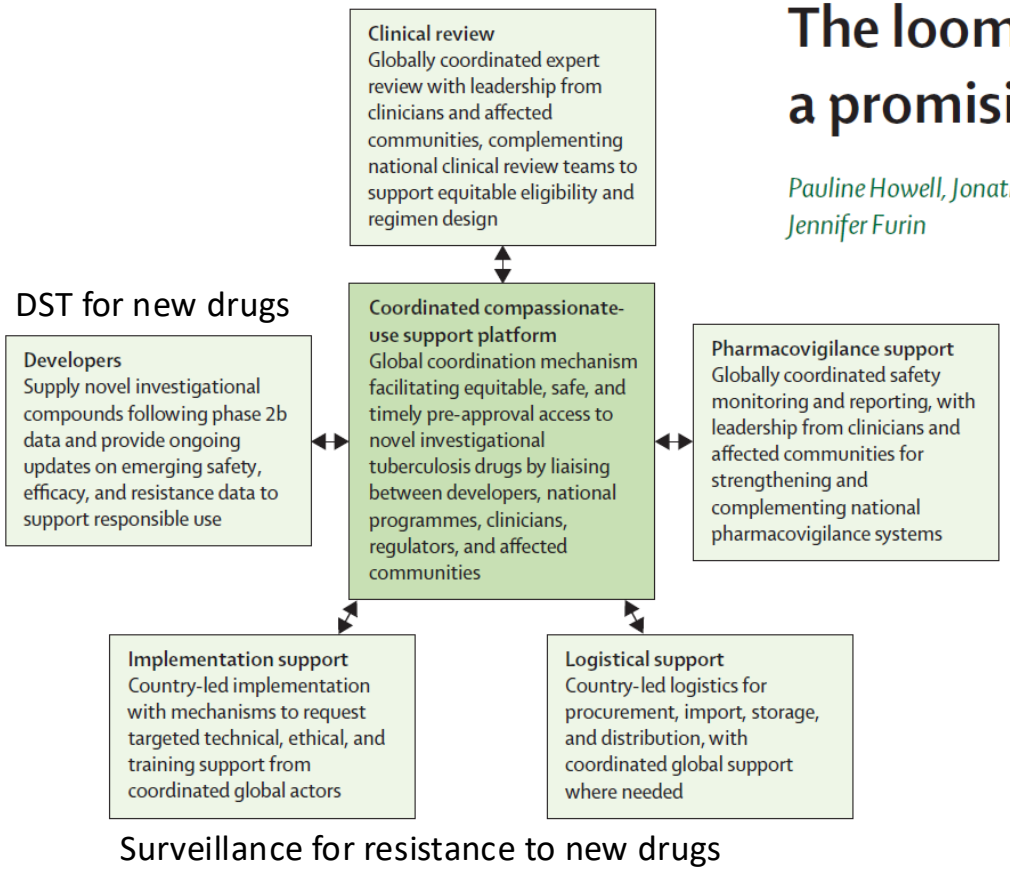




https://tbcenter.jhu.edu/wp-content/uploads/2024/12/BETTER-Field-Guide-December-2024.pdf

Nkomo et al, IJTLD Open 2025

XDR-TB & Compassionate use

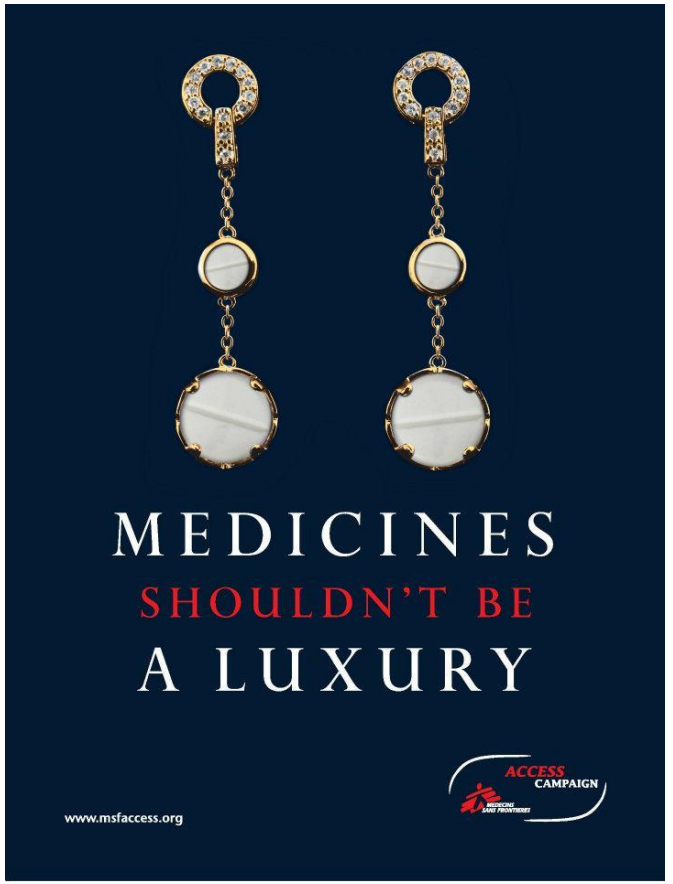


The looming crisis of bedaquiline-resistant tuberculosis and a promising way forward

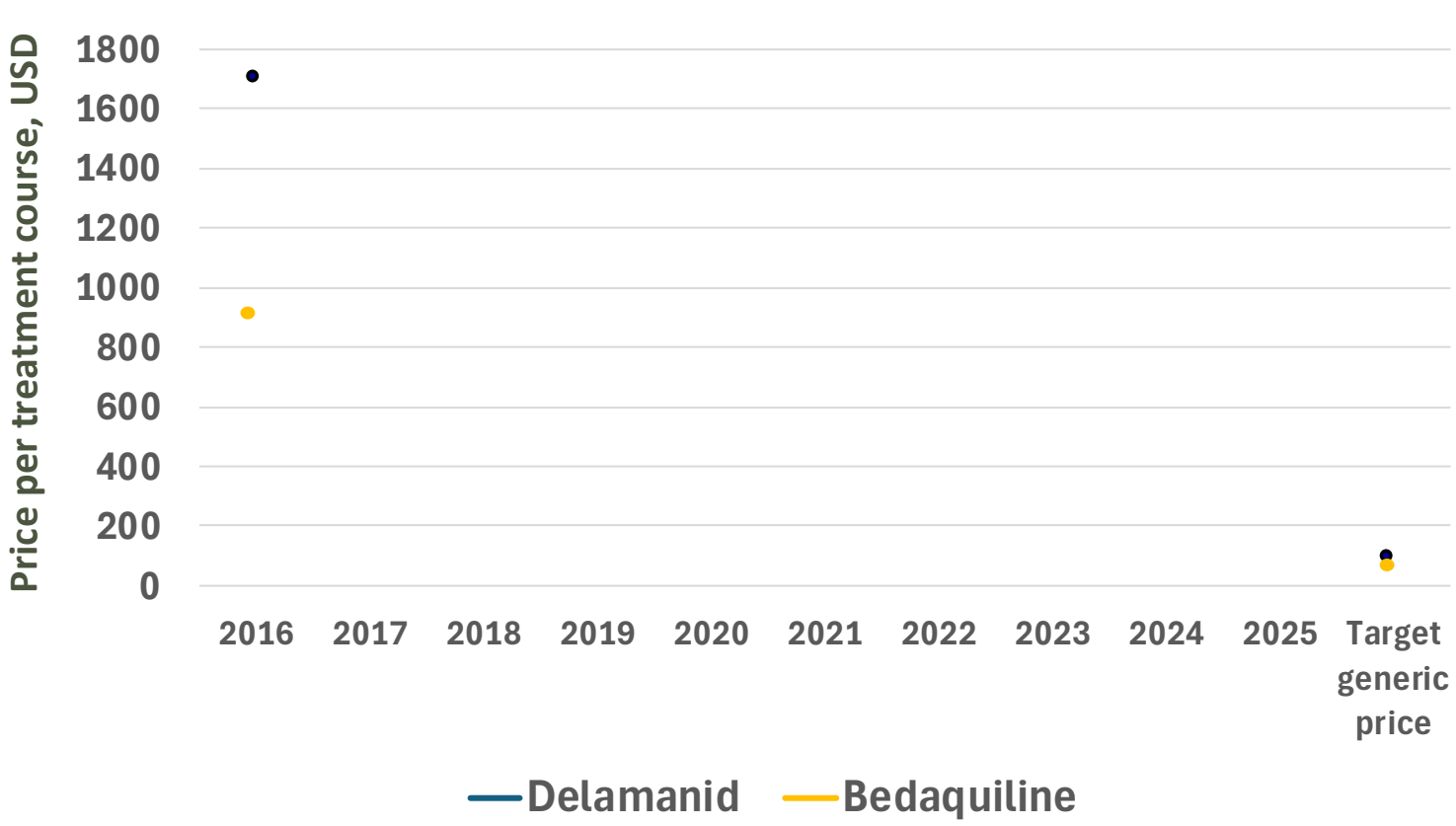
Pauline Howell, Jonathan Stillo, Anja Reuter, Tendai Nkomo, Carole D Mitnick, Lorenzo Guglielmetti, Kelly Curran, Richard E Chaisson, Jennifer Furin

Howell et al, Lancet ID 2026

Access

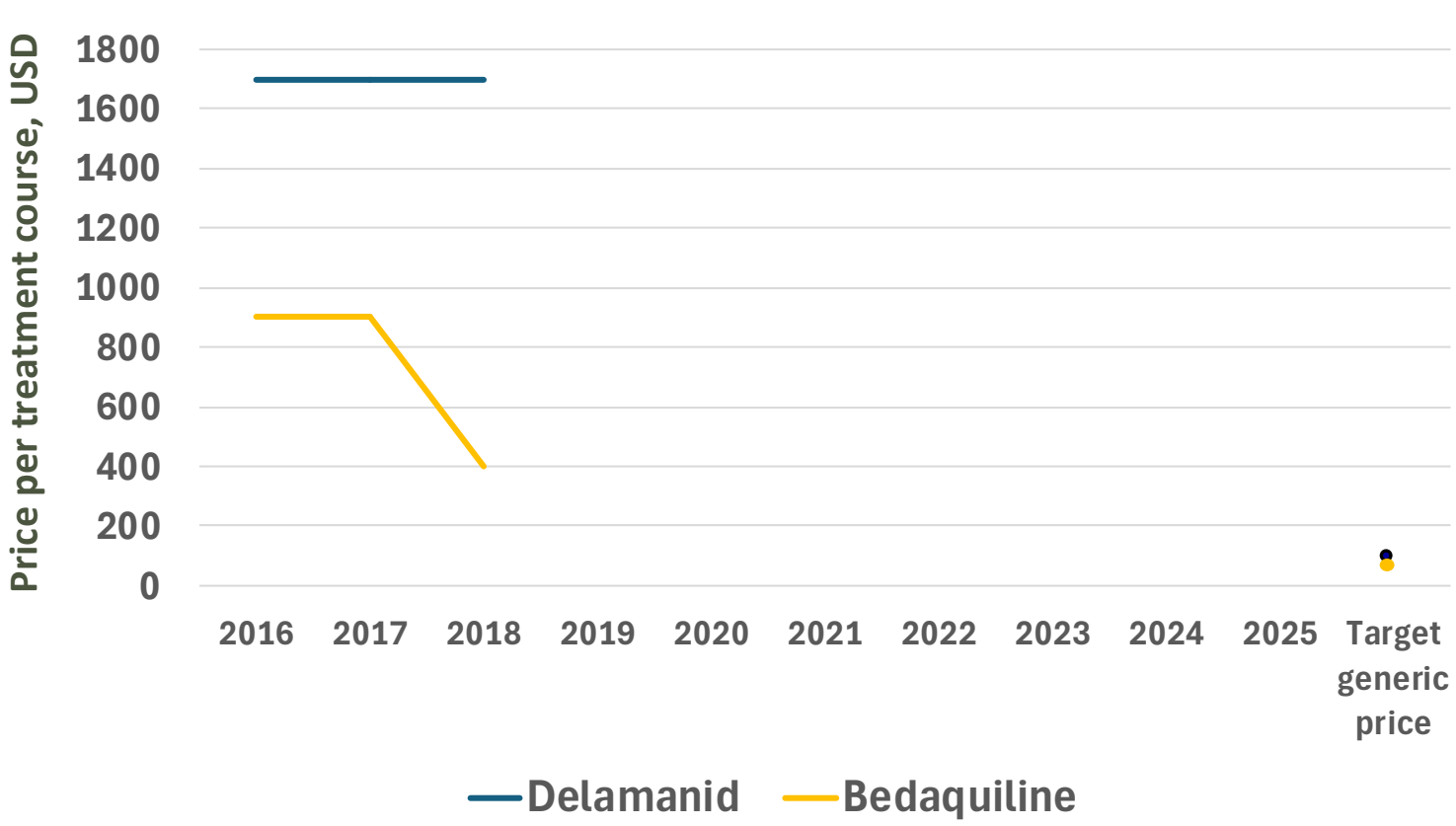

MEDICINES
SHOULDN'T BE
A LUXURY
ACCESS
CAMPAIGN
www.msfaccess.org

Access to life-saving drugs



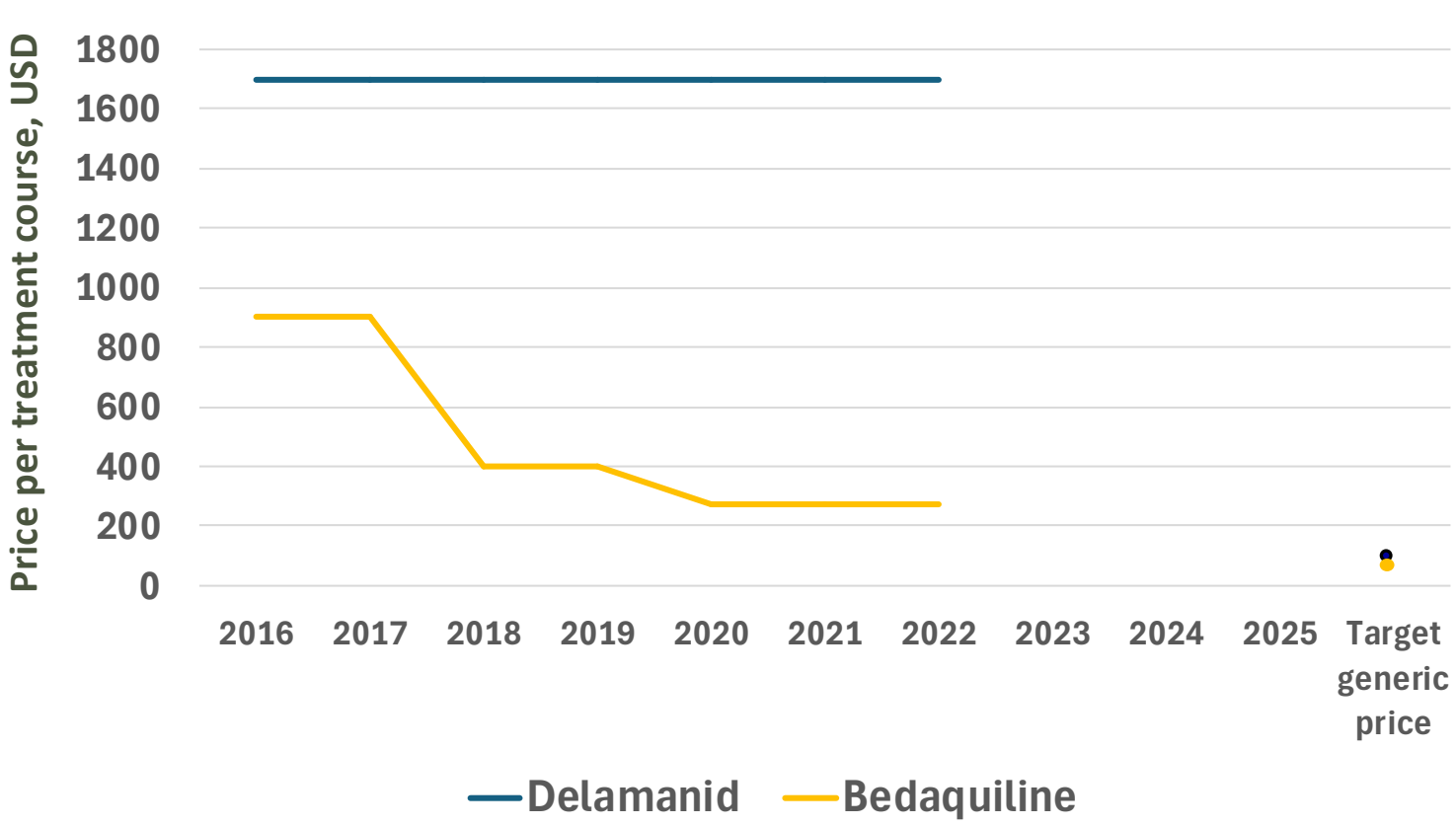
Global Drug Facility prices

Access to life-saving drugs



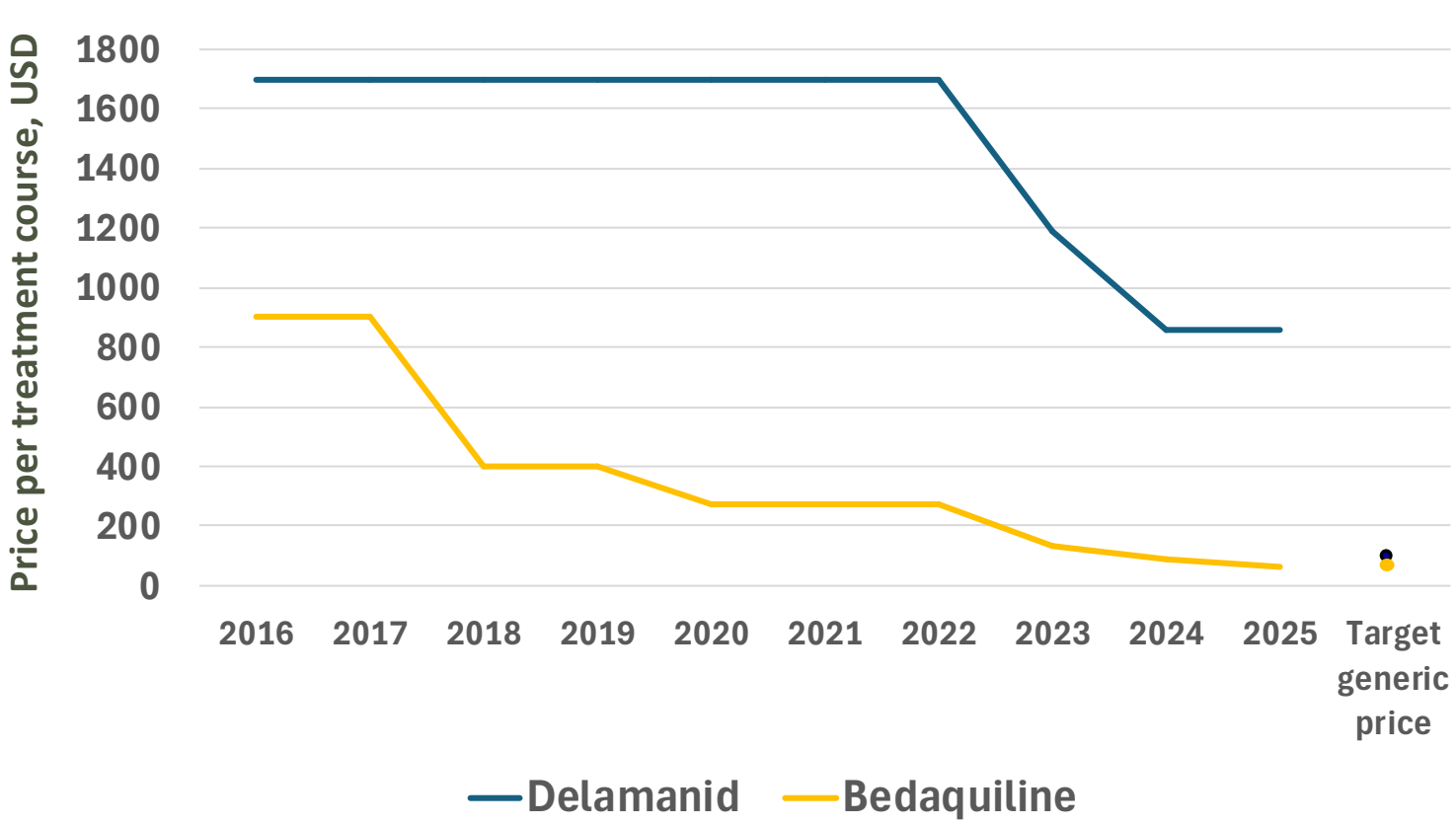
Global Drug Facility prices

Access to life-saving drugs



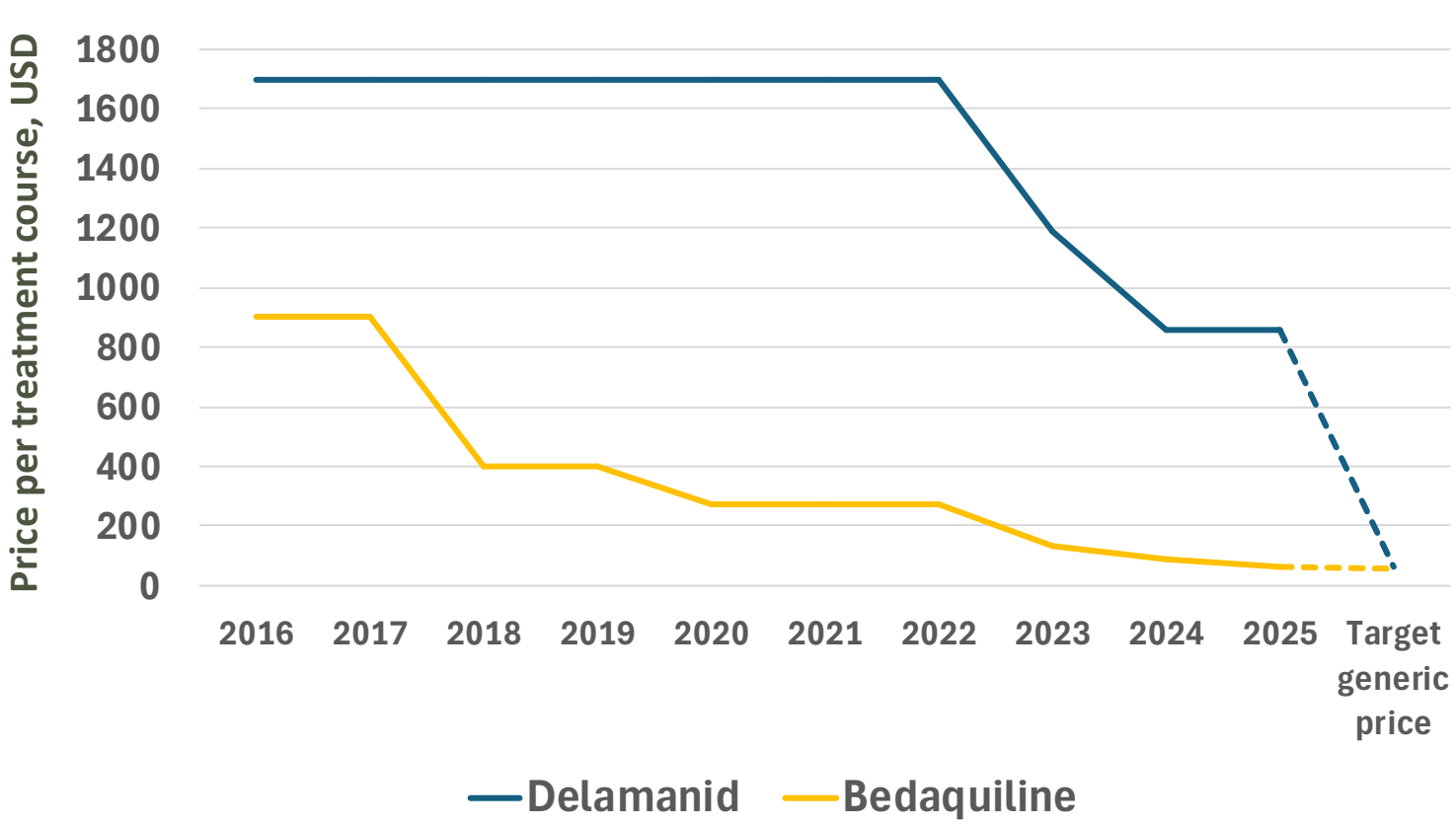
Global Drug Facility prices

Access to life-saving drugs



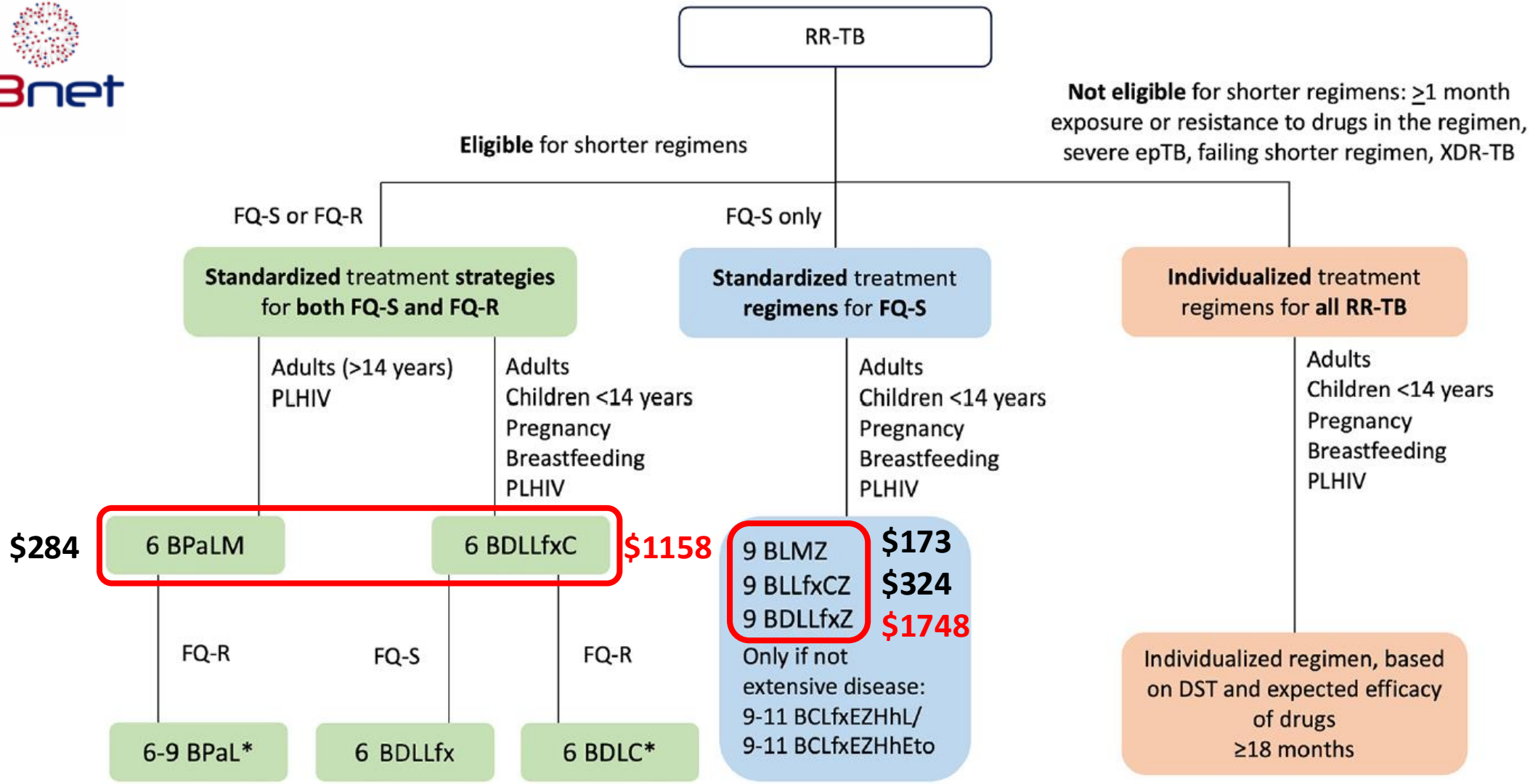
Global Drug Facility prices

Access to life-saving drugs



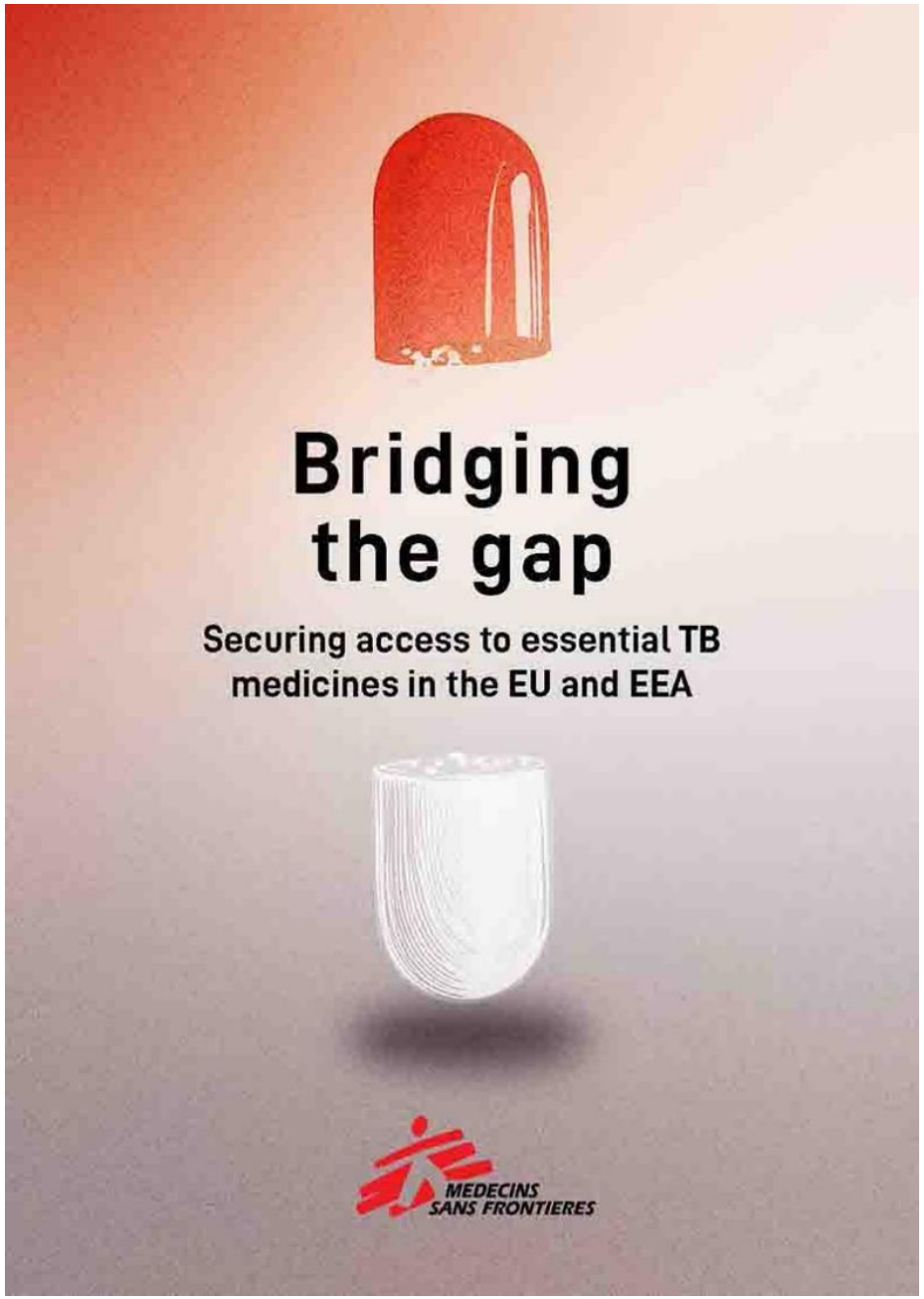
Global Drug Facility prices

RR-TB treatment: affordable?

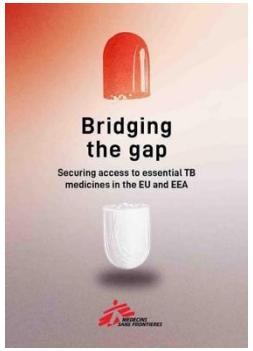


Lange et al, Pathogens and Immunity 2025

Global Drug Facility prices, Jan 2026


Bridging
the gap
Securing access to essential TB
medicines in the EU and EEA
MEDECINS
SANS FRONTIERES

MEDECINS SANS FRONTIERES
DOCTORS WITHOUT BORDERS



PRICE COMPARISON OF KEY DR-TB MEDICINES IN THE EU/EEA VS. GDF (APRIL 2025)

MEDICINE	Prices in EU for six-month course	GDF prices for six-month course
Bedaquiline	€20,000 - €25,000	~€86
Pretomanid	€15,000 - €35,000	~€151
Delamanid	€30,000 - €35,000	~€764
Linezolid	€5,000 - €10,000	~€23

Full BPaL regimen : € 45,000 vs € 275 (150 * more expensive)

MSF, Bridging the Gap. 2025.

Editorial

The Empty Medicine Cabinet: Urgent Action Needed to Resolve TB Drug Shortages in Europe

Lack of **drug registration** + lack of **regulatory approval** + excessive **costs** + drug **shortages**

"…far from being just a supply chain issue…the **lack of a coordinated, Europe-wide mechanism** to ensure an uninterrupted drug supply highlights **systemic neglect**."

TBnet

ESCMID Study Group for Mycobacterial Infections ESGMYC

ERS EUROPEAN RESPIRATORY SOCIETY

The Union
International Union Against Tuberculosis and Lung Disease
Health solutions for the poor

Guenther et al, CMI 2024; Goletti et al, IJID 2025

Innovation in clinical TB research

Towards personalised medicine?

Equitable, personalised medicine for tuberculosis: treating patients, not diseases

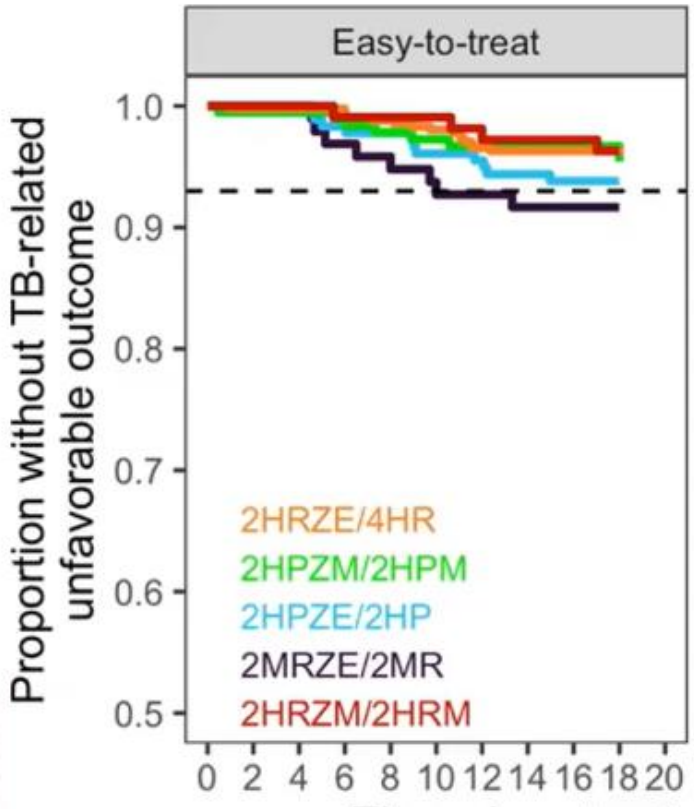
*Lorenzo Guglielmetti, Samiran Panda, Amanzhan Abubakirov, Naseem Salahuddin, Christophe Perrin, Carole D Mitnick

Lancet Respir Med 2025

Published Online March 21, 2025

https://doi.org/10.1016/S2213-2600(25)00080-3

Phase 3 DS-TB trials meta-analysis (TBReFLECT + Study31, N=6,959)

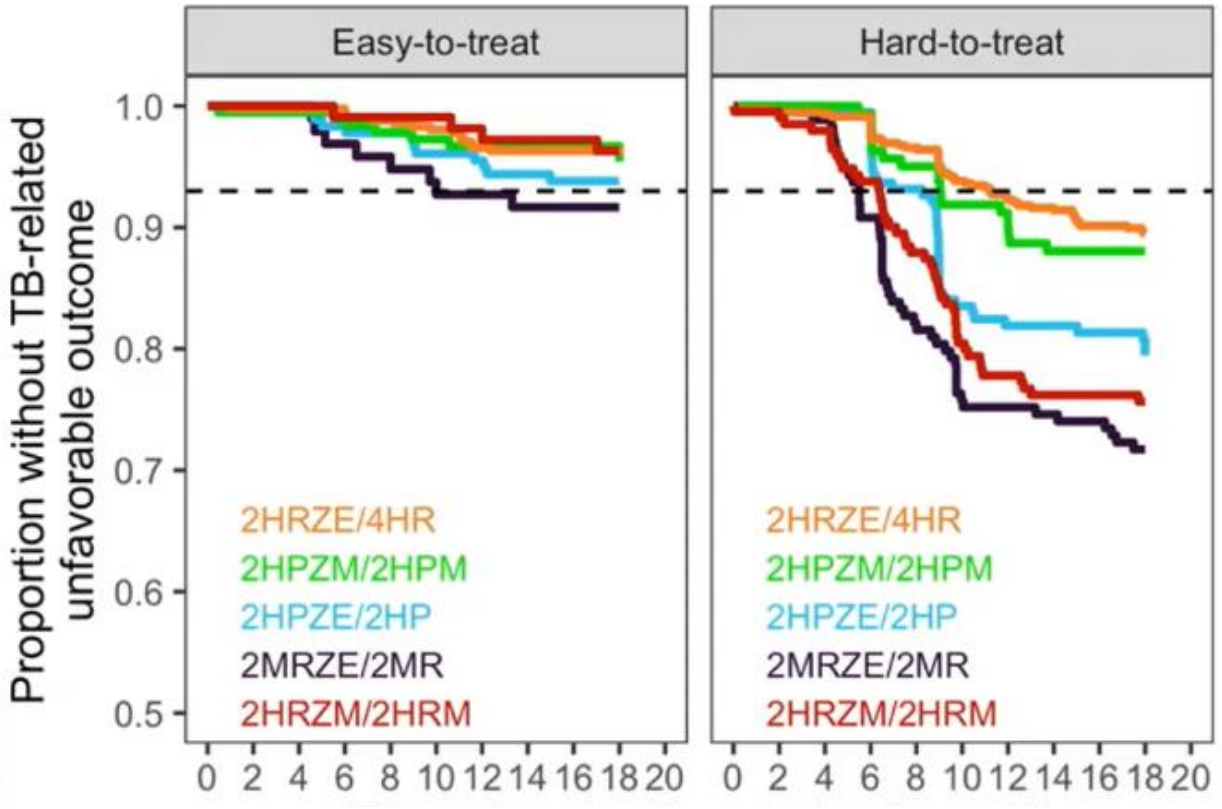


Easy to treat:
Smear <2+ or No Cavity+ (TB-Reflect, Imperial et al 2018)

Control (standard of care)
Study 31 - successful arm
Study 31 - inferior arm
RIFAQUIN - inferior
REMoxTB - inferior

Imperial et al, Nature Med 2018; Savic R, Union World Conference 2024

Phase 3 DS-TB trials meta-analysis (TBReFLECT + Study31, N=6,959)



Hard to treat:
Smear ≥2+ & Cavity+ (TB-Reflect, Imperial et al 2018)

Control (standard of care)
Study 31 - successful arm
Study 31 - inferior arm
RIFAQUIN - inferior
REMoxTB - inferior

Imperial et al, Nature Med 2018; Savic R, Union World Conference 2024

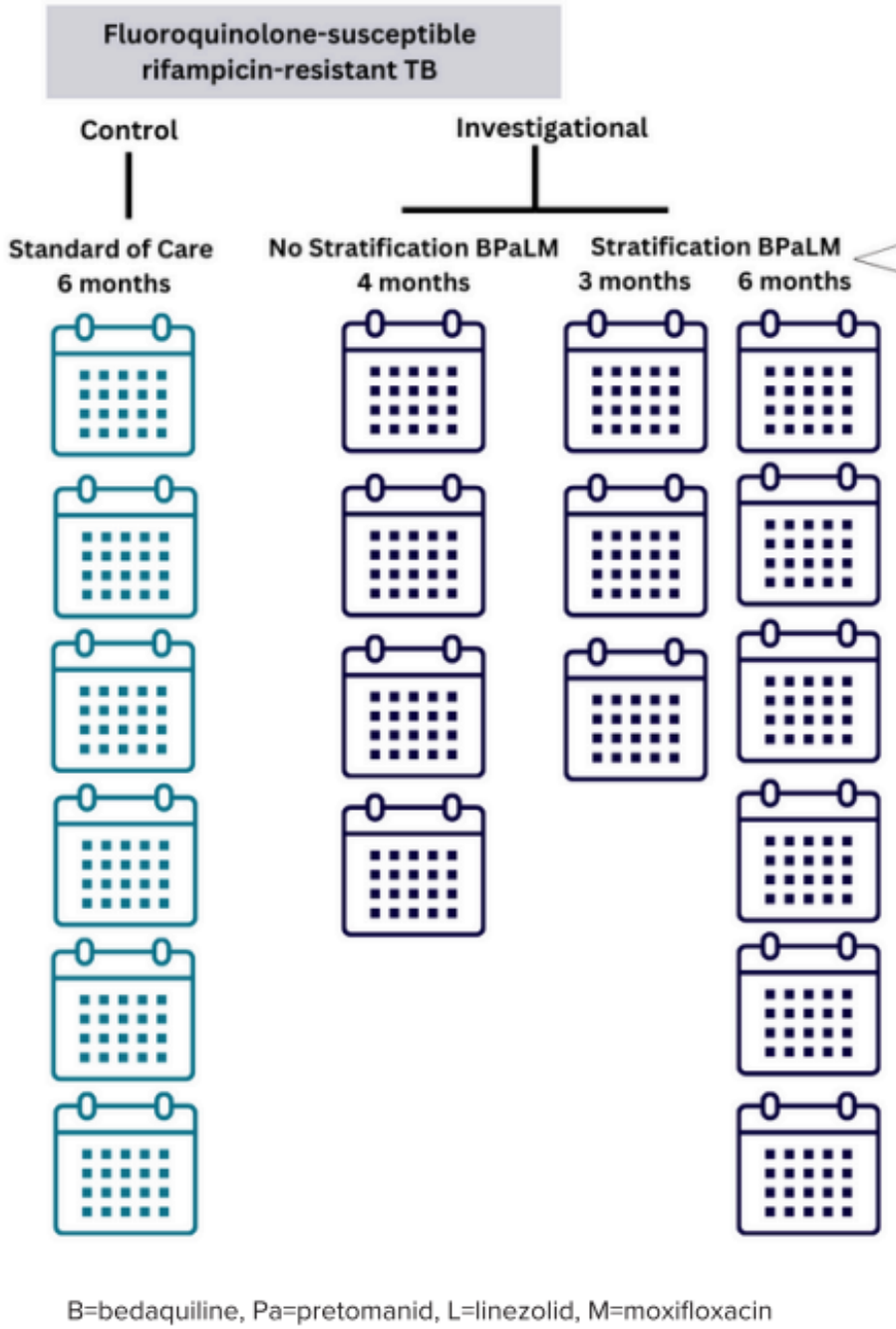
PRISM-TB

Phase 2c, stratified RCT

FQ-S, RR-TB

Goal: identify optimal BPaLM duration

https://clinicaltrials.gov/study/NCT06441006



Stratification algorithm:

- Sputum smear
- % affected lung
- Age
- Sex
- BMI
- HIV

Testing what matters: Patient-centered **objectives**

Shorter TB treatment regimens should be safer as well

O. Rucsineanu,[1,2] P. Agbassi,[2] R. Herrera,[2] M. Low,[3] L. McKenna,[2,4] J. Stillo,[2,5] P. Winarni,[2] A. Acharya,[6] A. H. Sari[2]

« …with a **myopic focus on treatment duration**, researchers and clinicians are missing opportunities to address other (challenging) aspects of treatment… »

« …most TB treatment shortening trials **overlook the subjective experience of adverse events**—(…)the amount of **time** people spend feeling unwell, the required toxicity **monitoring schedules** and the relative **impact (…) on the quality of life** »

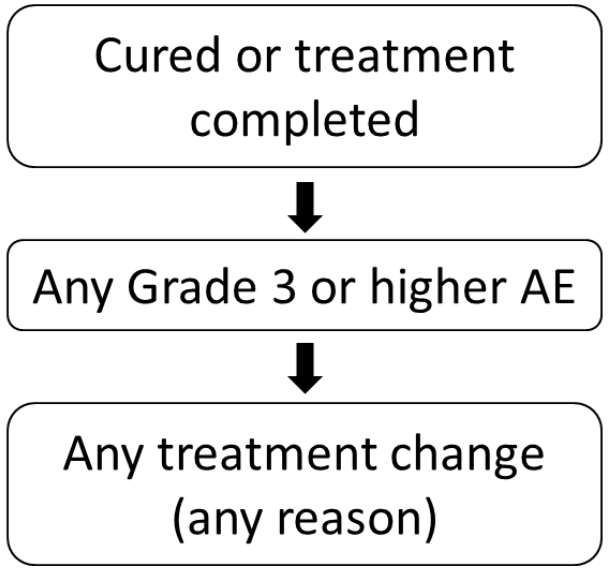
« High rates of **linezolid toxicity** are a cause for concern among impacted communities, given its (…) inclusion in DS-TB treatment-shortening trials »

Ruscineanu et al, Pub Health Act 2023

Measuring what matters: patient-centered **outcomes**

PRISM-TB, Phase 2c (Superiority)

Primary outcome: **Desirability of Outcome Ranking (DOOR)**



Conclusions

✓ 4-month regimens for **DS-TB**
yes, implementation challenging

⚠ 6/9-month regimens for **pre-XDR-TB**
yes, with caution (evidence needed)

✓ 6/9-month regimens for **RR-TB**
yes, multiple choices

✗ Short regimens for **XDR-TB**
No

Major drug **access challenges**
in Europe

Conclusions

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yes, multiple choices

✕ Short regimens for **XDR-TB**
No

Major drug **access challenges** in Europe

Need to **innovate the clinical research approach** in TB

SACRO CUORE DON CALABRIA
I R C C S

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

SANTÉ SORBONNE UNIVERSITÉ

MEDECINS SANS FRONTIERES
DOCTORS WITHOUT BORDERS

MEDECINS SANS FRONTIERES
DOCTORS WITHOUT BORDERS

10 years since the first UN resolution calling on protection of medical personnel

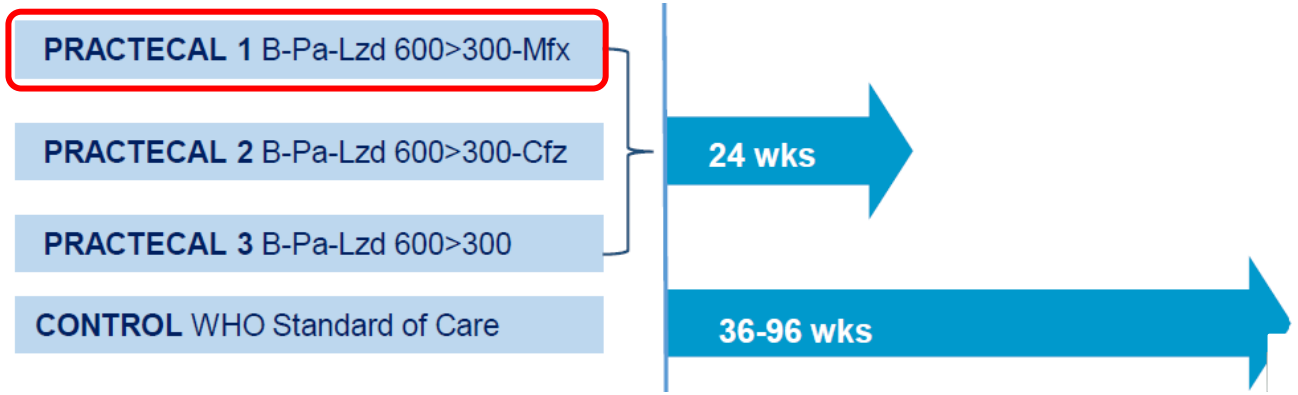
Healthcare is @notatarget

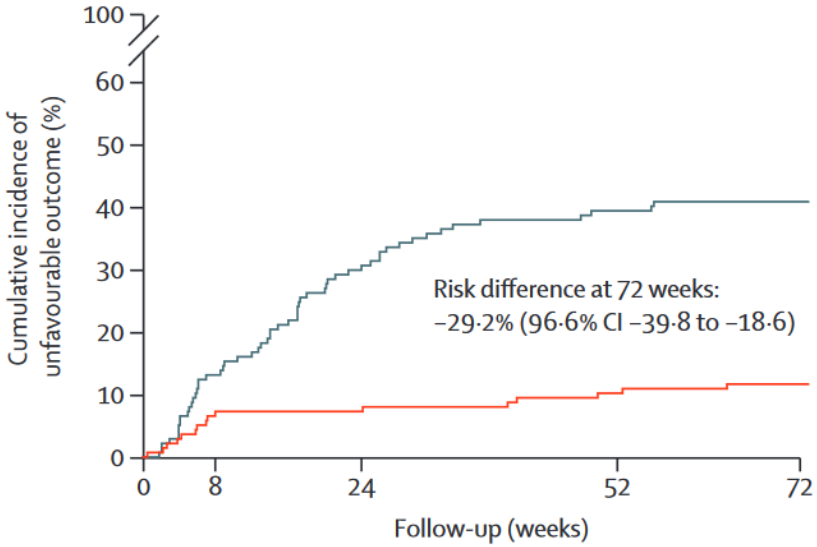
EXTRA

TB Practecal
Innovating MDR-TB Treatment

MEDECINS SANS FRONTIERES
DOCTORS WITHOUT BORDERS

Phase 2/3, MAMS RCT for RR-TB



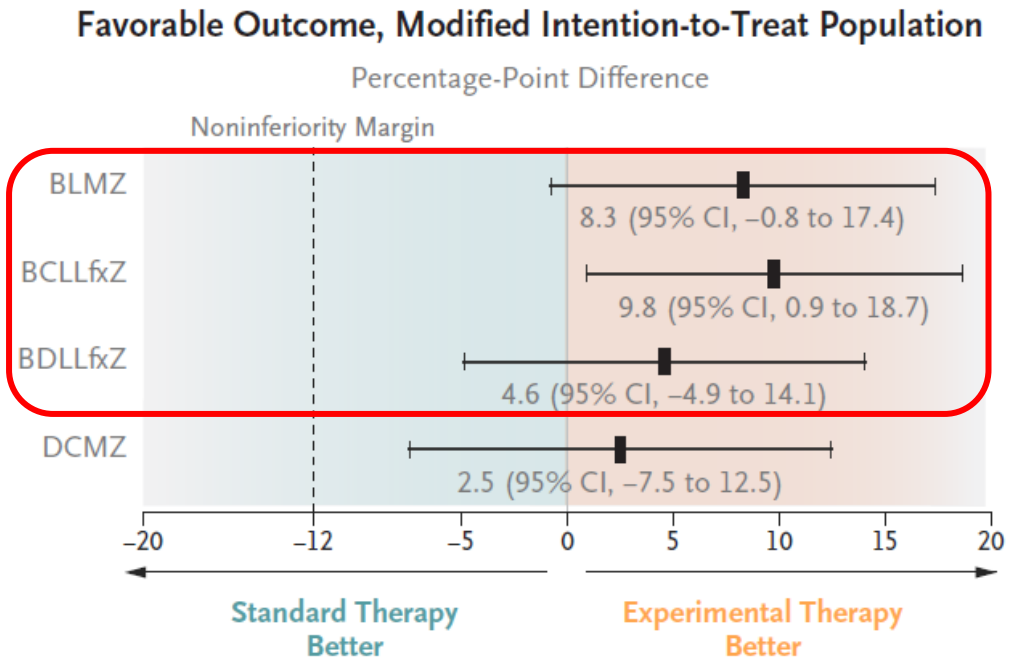


6 Bdq-Ptm-Lzd-Mfx (BPaLM) vs control:

- Efficacy: non inferiority (PP) / superiority (mITT)
- Better safety and adherence
- **Not suitable for children <14 or pregnant/breastfeeding women**
- (not powered for pre-XDR-TB)

Nyang'wa et al, NEJM 2022 & Lancet Resp Med 2024

Phase 3, outcome-adaptive RCT for FQ-S, RR-TB



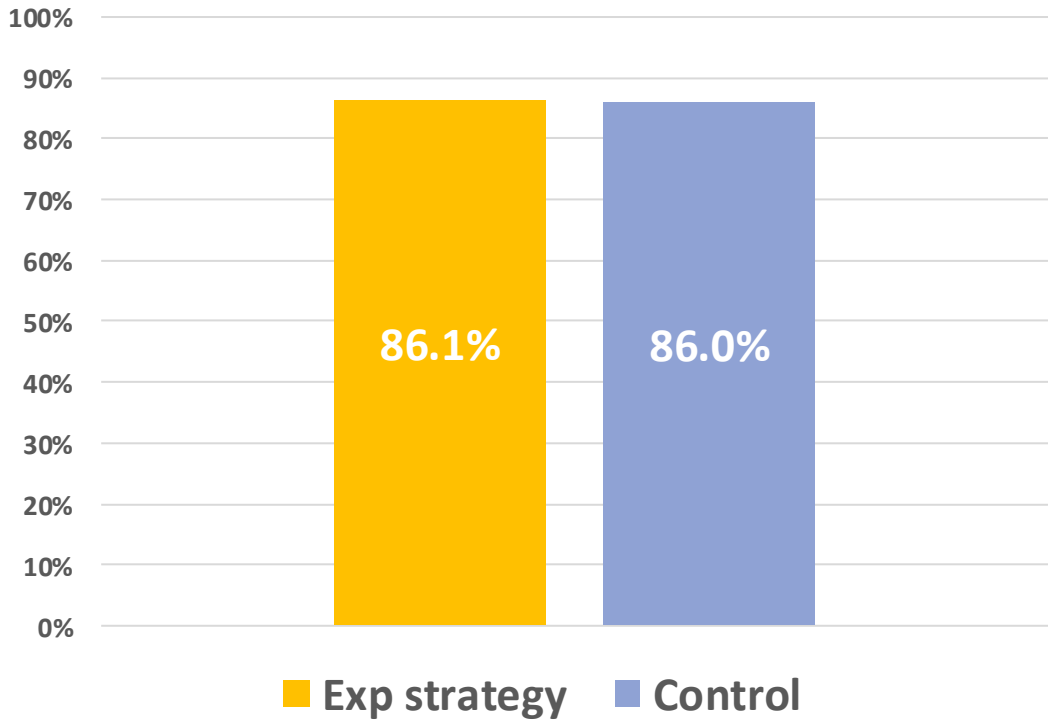
- **Three 9-month regimens** for **adults, children & pregnant women** (**9BLMZ, 9BCLLfxZ, 9BDLLfxZ**)*
- **Increased hepatotoxicity** with 9BLMZ & 9BCLLfxZ (no liver-related deaths)

Guglielmetti et al, NEJM 2025

B=bedaquiline, L=linezolid, M=moxifloxacin, Z=pyrazinamide, C=clofazimine, Lfx=levofloxacin, D= delamanid

BEAT Tuberculosis

Phase 3 pragmatic RCT **for RR-TB**



- Initial treatment: 6 **BDLLfxC**
- FQ-susceptible: 6 **BDLLfx**
- FQ-resistant: 6 **BDLC**

Strategy non-inferior to control, similar safety (not powered for pre-XDR-TB); suitable for **children & pregnant women**

Unpublished; pre-print available here

B=bedaquiline, D= delamanid, L=linezolid, Lfx=levofloxacin, C=clofazimine

MEDECINS SANS FRONTIERES
DOCTORS WITHOUT BORDERS

A decade ago, on May 3, 2016, **the UN Security Council adopted Resolution 2286, calling for the protection of medical personnel and facilities in armed conflicts**.

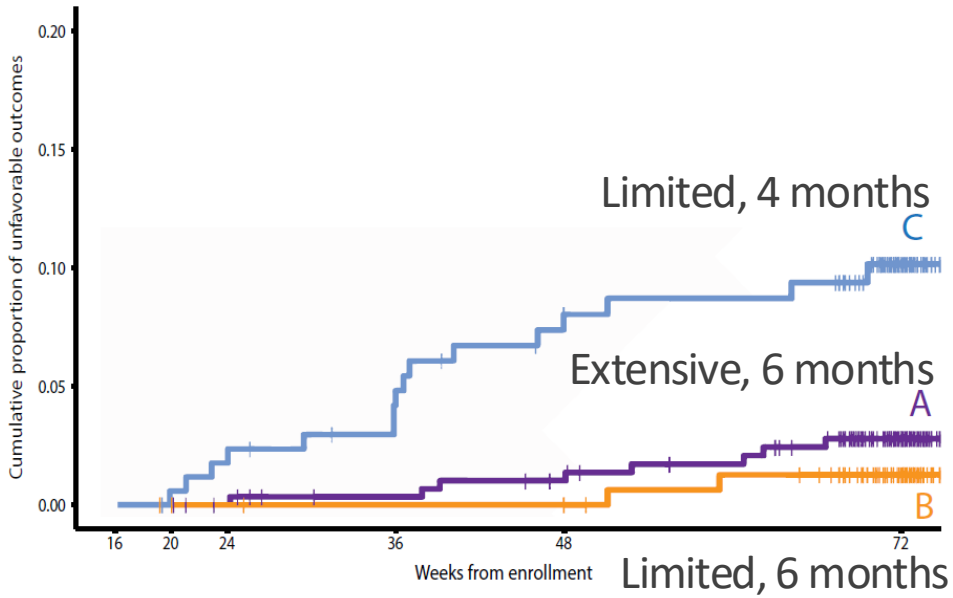
Ten years on, **that promise lies in ruins**.

Over the last 10 years, attacks on healthcare have been various and have included airstrikes on hospitals in Syria, Yemen, Ukraine and Palestine, drone strikes on a hospital in Myanmar, and attacks on clearly marked ambulances in Cameroon, Haiti and Lebanon.

Healthcare is @notatarget

PET-CT imaging & treatment shortening: PredictTB

- Randomised, controlled, Phase 3 clinical trial
- 704 DS-TB participants, stratified into limited (n=273) and extensive disease (n=250) according to FDG PET/CT imaging at baseline and 4 wks + Xpert at 16 wks
- Less extensive disease group: randomized to 4- (n=132) or 6-month HRZE (n=141); extensive disease group: 6-month HRZE
- **The 4-month group had significantly more TB-specific unfavorable outcomes** (12.1%, mostly relapses) **than those in the 6-month groups** (1.5% for limited & 3.2% for extensive disease)
- **PET/CT imaging failed to predict post-treatment relapse**



Malherbe et al, Science Transl Med 2026

ESCMID | Study Group for Mycobacterial Infections ESGMYC

A 2-month regimen? TRUNCATE-TB

2-month regimens for uncomplicated DS-TB*

- Primary outcome: TB-free status at 96 wks
- Ok to extend treatment, retreat, close FU
- 2 regimens to Phase 3: HZE+R^{35}+L & HZE+B+L
- HZE+B+L non-inferior

	24 weeks Standard Rx (N=181)	8 weeks BDQ/LZD (N=189)
Unfavourable outcome – no (%)	7 (3.9%)	26 (13.8%)
Treatment failure at switch to standard Rx	0 (0.0)	1 (0.5)
Treatment failure at end of treatment	0 (0.0)	1 (0.5)
Confirmed relapse	4 (2.2)	20 (10.6)

*Exclusion: severe TB disease, HIV, uncontrolled diabetes

	HRZE	HZE+R35+L
	Grade ≥3 AE	**Grade ≥3 AE**
Dizziness	0	1%
Headache	0	0
Abdominal pain	0	0
Nausea	0	0
Vomiting	1%	2%

Paton et al, NEJM 2023

Paton et al, Lancet Inf Dis 2025

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	HRZE		HZE+R35+L	
	Any AE	**Grade ≥3 AE**	**Any AE**	**Grade ≥3 AE**
Dizziness	3%	0	**14%**	1%
Headache	2%	0	**16%**	0
Abdominal pain	12%	0	**28%**	0
Nausea	14%	0	**33%**	0
Vomiting	16%	1%	**45%**	2%

Paton et al, NEJM 2023

Paton et al, Lancet Inf Dis 2025

ESCMID | Study Group for Mycobacterial Infections ESGMYC

RR-TB: reducing linezolid-related toxicity

- **Structured linezolid dose reduction**
  - endTB/Q: no difference in efficacy or safety between 16W reduction to 600 tiw & 300 qd[1]
  - A5356 (BDLC): 1200 qd for 4 wks then 1200 tiw -> more discontinuations, worse outcomes than 600 mg qd[2]
- **Replacing linezolid** in new MDR-TB regimens
  - New oxazolidinones: delpazolid, sutezolid, tedizolid, contezolid
  - New drugs -> quabodepistat

1. Velasquez et al, Union Conference 2025, unpublished; 2. Presented at CROI 2026

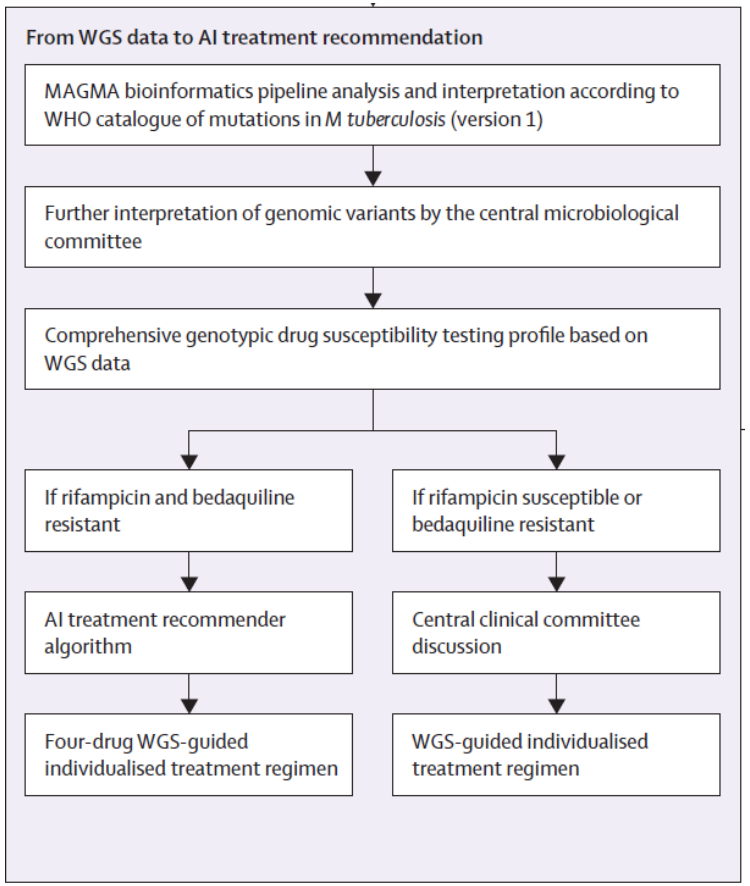
WGS-guided precision medicine (SMARTT trial)

Pragmatic randomized, single-blind **Phase IV trial**

South Africa (13 hospitals, 35 clinics)

Pulmonary RR-TB adults 1:1 to SOC (all-oral 9 mts or 18 mts regimen) **vs WGS + AI algorithm-guided 4-drug regimen (6 mo)***

	Standard of care group	Whole genome sequencing group
Clinical effectiveness		
Number of participants*	77	82
Favourable treatment outcomes	45 (58%)	62 (76%)
Cure	44/45 (98%)	62/62 (100%)
Treatment completed	1/45 (2%)	0/62 (0%)
Unfavourable treatment outcome	32 (42%)	20 (24%)
Death	16/32 (50%)	11/20 (55%)
Loss-to-follow-up	15/32 (47%)	7/20 (35%)
Bacteriological failure	1/32 (3%)	2/20 (10%)



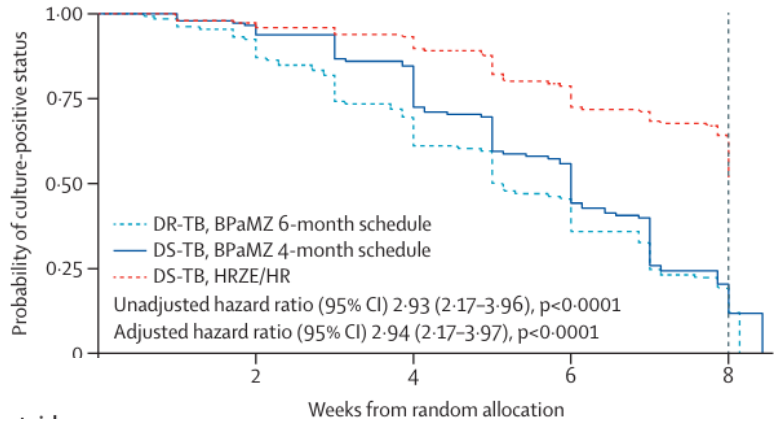
*started in 65 (79%) pts after a median of 48 days after empiric treatment

Van Rie et al, Lancet Respir Med 2026

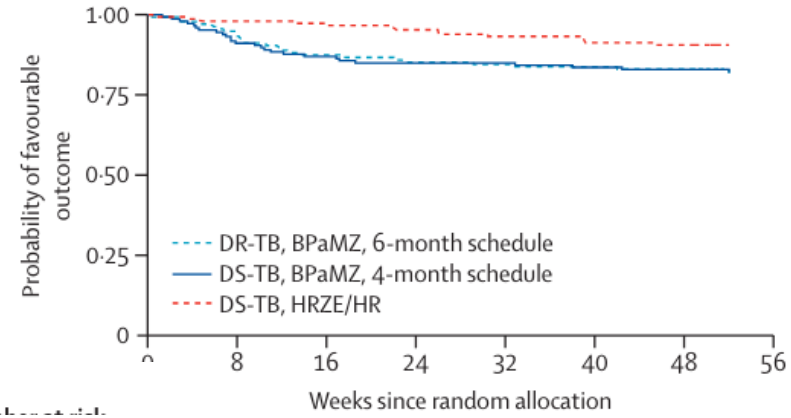
Hepatic toxicity & treatment shortening: SimpliciTB

- Partially-randomised, controlled, Phase 2c, open-label clinical trial
- 455 participants, including 303 DS-TB: **4** months of **BPaMZ** (n=150) or **6** months of **HRZE** (n=153)
- **BPaMZ did not meet the key efficacy endpoint** due to adverse events resulting in treatment withdrawal
- These results **confirm the liver toxicity of** the combination of **PaZ+M** (STAND) & **PaZ+B** (NC-005)

Primary efficacy analysis in the mITT population—time to culture-negative status by 8 weeks



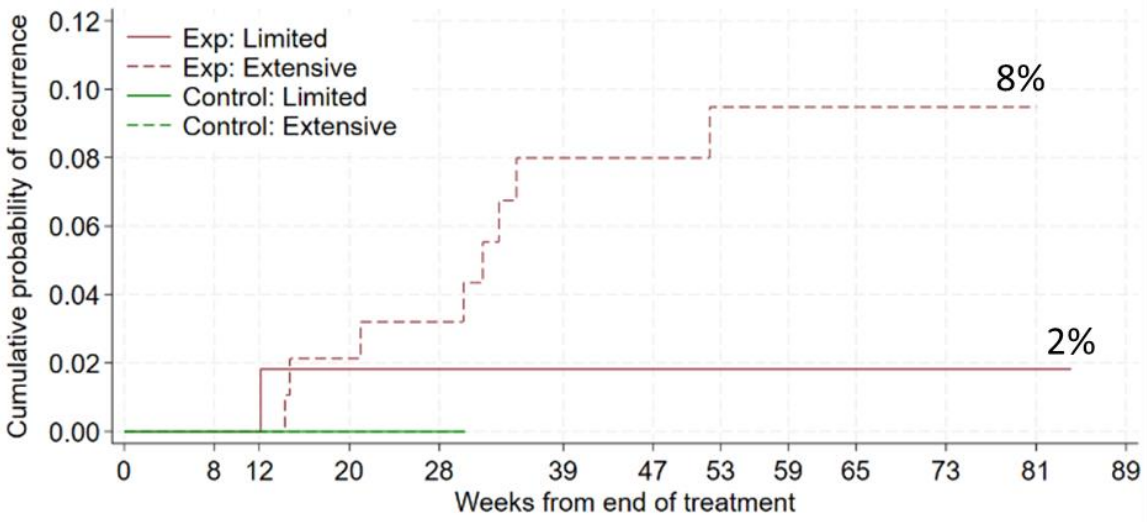
Time to unfavourable status at week 52 (mITT)



Cevik et al, Lancet Inf Dis 2024

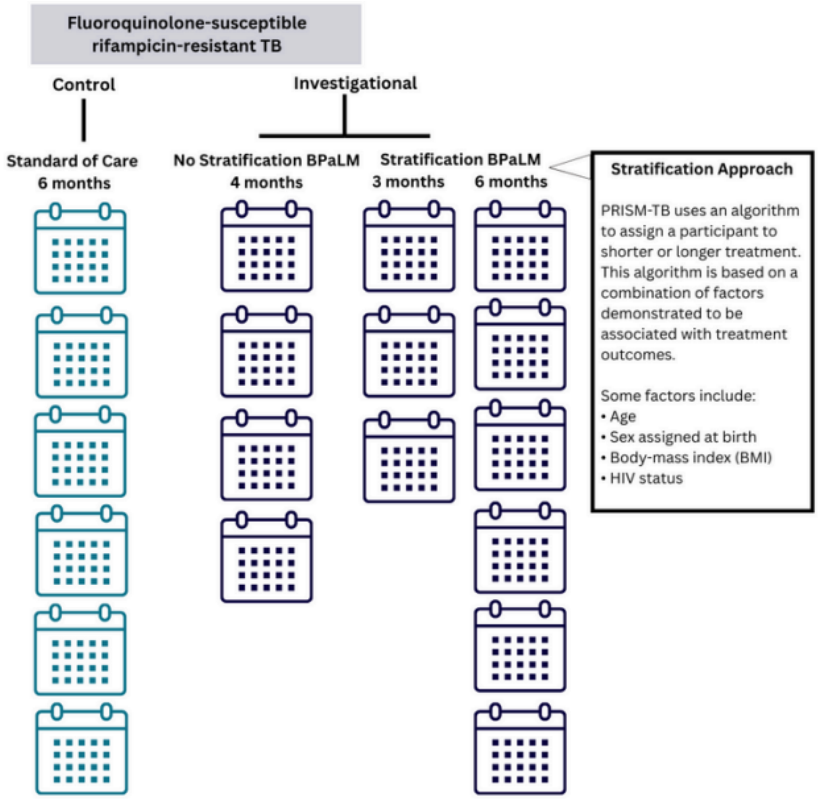
BPaMZ = bedaquiline, pretomanid, moxifloxacin, pyrazinamide.

endTB-Q & **relapses**



Guglielmetti et al, Lancet Resp Med 2025

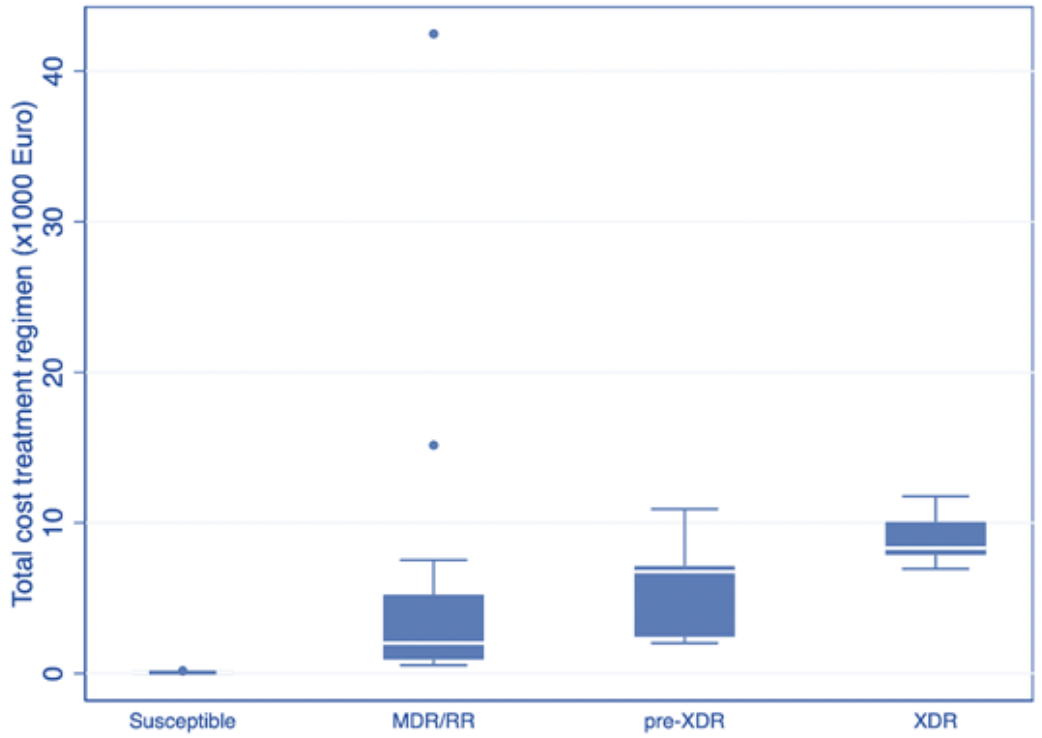
Phase 3 DS-TB trials meta-analysis (TBReFLECT + Study31, N=6,959)



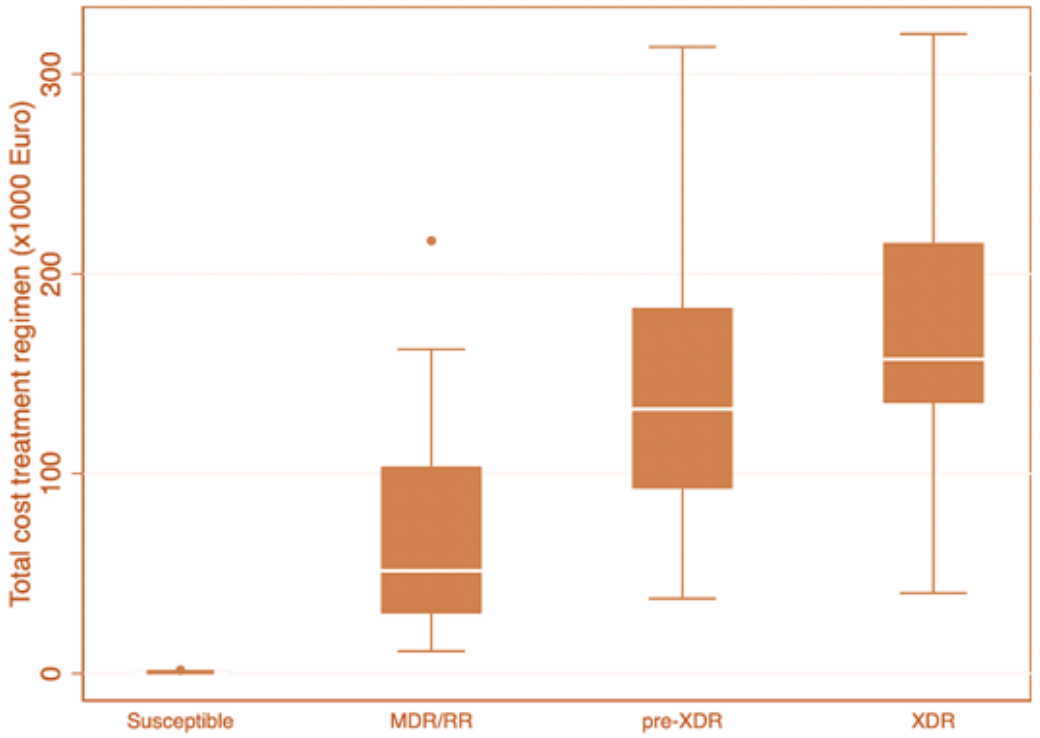
Imperial et al, Nature Med 2018; Savic R, Union World Conference 2024

Cost of TB drugs in WHO Europe region

Middle income countries



High income countries

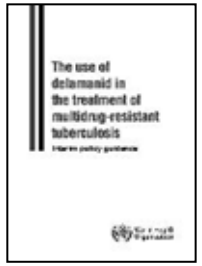


Guenther et al, CMI 2022

WHO RR-TB guidelines

2011
DR-TB Guidelines

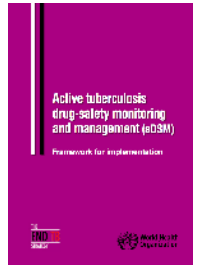
June 2013
WHO BDQ Guidance



October 2014
WHO DLM Guidance

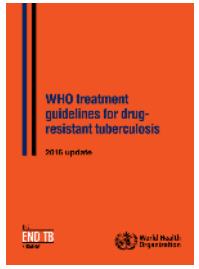
2014
Policy Implementation Package

Jan 2015
Companion Handbook, w/ BDQ and DLM



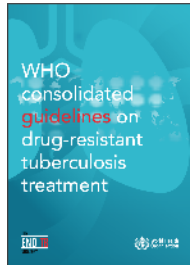
Nov 2015
aDSM Guide

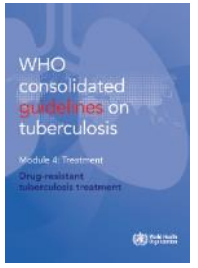
Nov 2015
Bdq Country Implementation



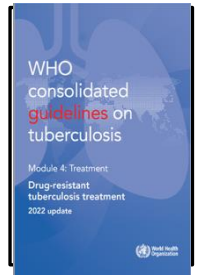
April 2016
New DR-TB guidelines

March 2017
Updated Bdq guidance

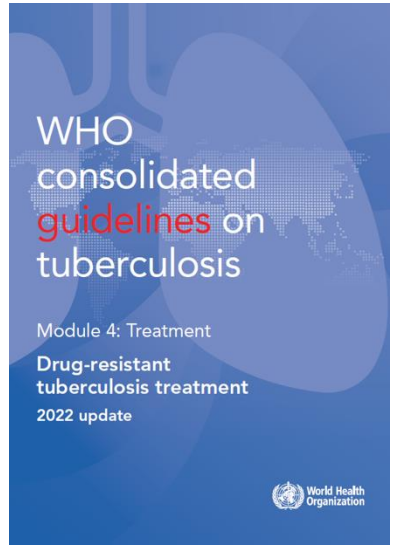




2019/2020
Consolidated DR-TB guidelines



2022
New DR-TB guidelines



2025
update