Lessons from the endTB Project

5th KATRD TB & NTM International Symposium

TB & NTM: New Perspectives, New Solutions (Meet the professor)

18 October 2025

Seoul, Republic of Korea

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Tuberculosis, Poverty, and "Compliance": Lessons From Rural Haiti

Paul Farmer, Simon Robin, St. Luc Ramilus, and Jim Yong Kim

Seminars in Respiratory Infections, Vol 6, No 4 (December), 1991: pp 254-260

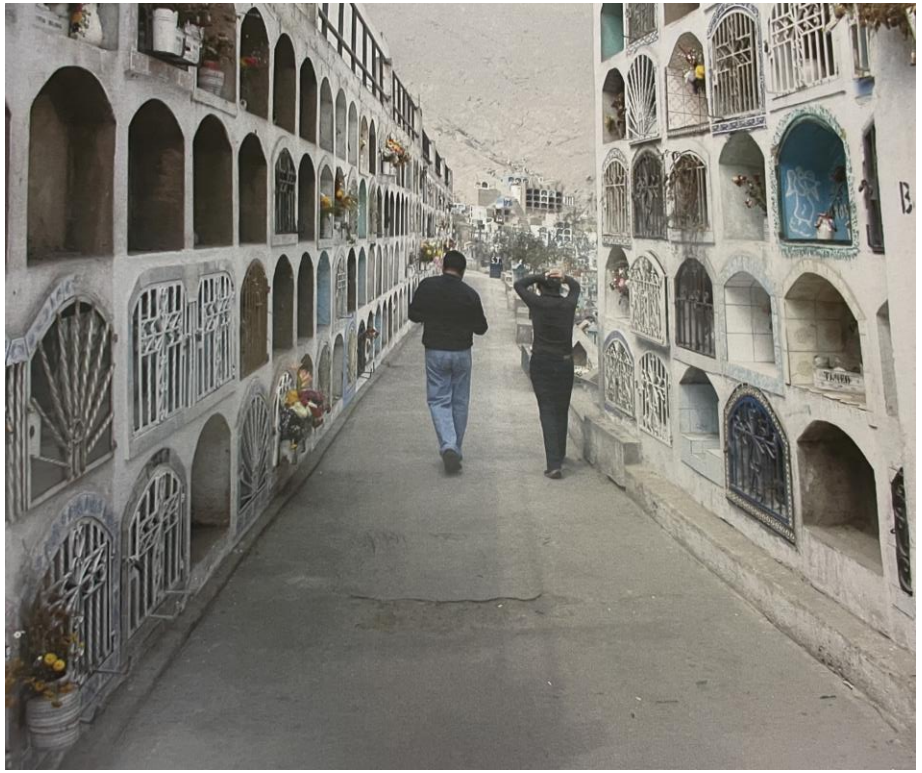
Table 1. Characteristics of TB in Sector 1 Versus Sector 2 Patients

	Sector 1	Sector 2
Mortality from TB during 18 mo after diagnosis	0 (0%)	3 (10%)
Sputum positivity for acid-fast bacilli 6 mo after diagnosis	0 (0%)	4 (13.3%)
Peristent pulmonary symptoms after 1 yr of treatment	2 (6.7%)	13 (43.3%)
Average weight gained/patient/yr (lb)	10.4	1.7
Return to work after 1 yr of treatment	28 (93.3%)	14 (46.7%)
Average no. of clinic visits per patient per yr	11.4	5.8
Average no. of home visits per patient per yr	37.9	1.4
Seropositivity to HIV	1 (3.3%)	2 (6.7%)
No. of patients who denied possible role of sorcery in illness	5 (16.7%)	4 (13.3%)
Cure rate	30 (100%)	17 (56.7%)

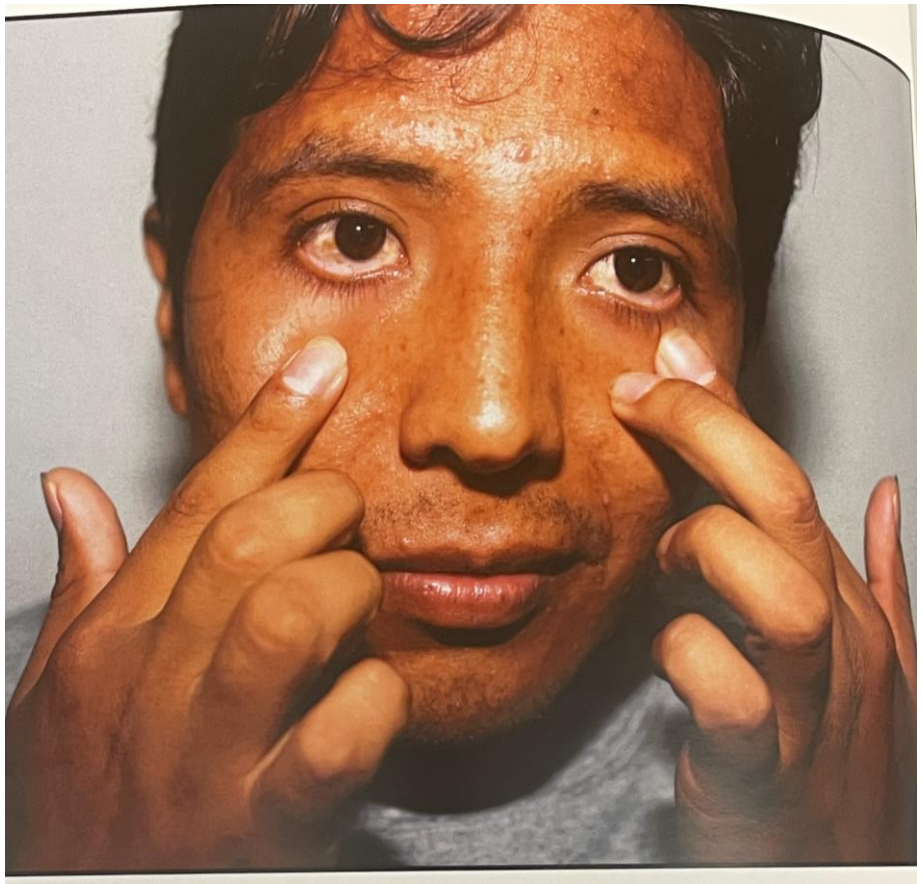
(Brief) Historical context for the endTB project

Joel—A Photodocumentary

Joel's Mother: "My first son died in the year 2000, on October 21, and he was 17. My other son, who was 29 years old, also died in the year 2000, on November 21. And, the third one, 34 years old, died almost a year after the first two, on October 1, 2001. My daughter (28 years old) died on November 1, 2002. "



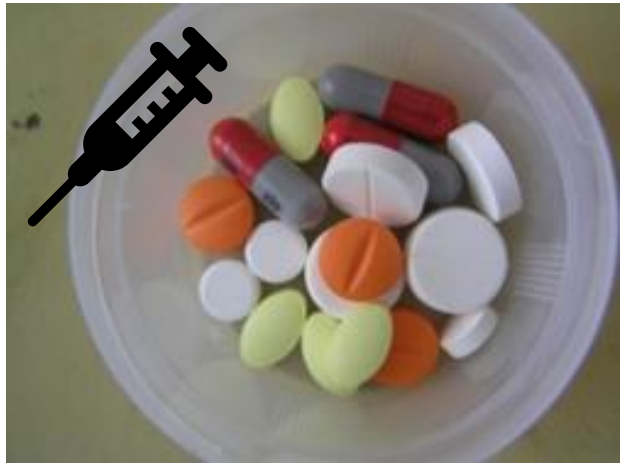
Credit: Mark Rosenberg

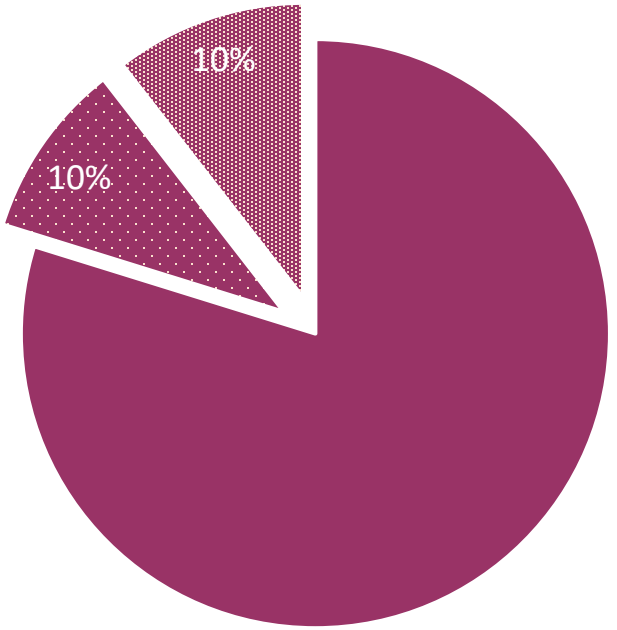


Joel: "I take 16 pills—10 in the morning and at night 6—in total 16 pills daily. I feel tempted to not take cycloserine because I get in my head that it's going to my head. It makes you feel upset, like your eyes are going in different directions from each other. I feel a lack of concentration, and I feel accelerated when I walk, when I talk, and it's difficult. I think this will damage me permanently so in the future I won't be able to do anything else. "

State of treatment for multidrug/rifampin-resistant TB c. 2013[1]

18-24 month treatment





500K new cases/year[2]

[1] Brigden et al. Bull WHO, 2013; [2] WHO. Global TB report, 2014; [3]WHO. Global TB report, 2016.

Background c. 2013

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The Diarylquinoline TMC207 for Multidrug-Resistant Tuberculosis

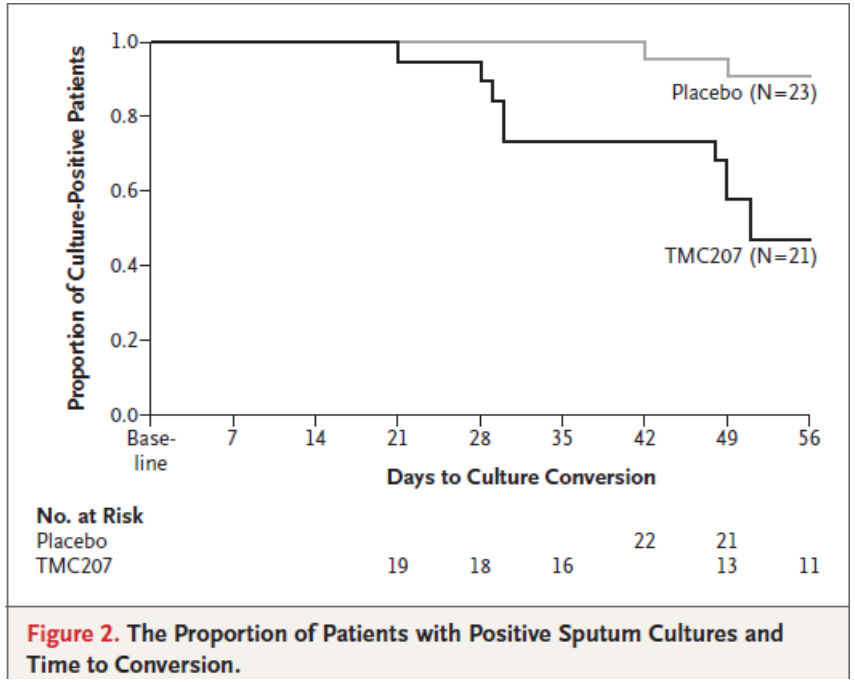
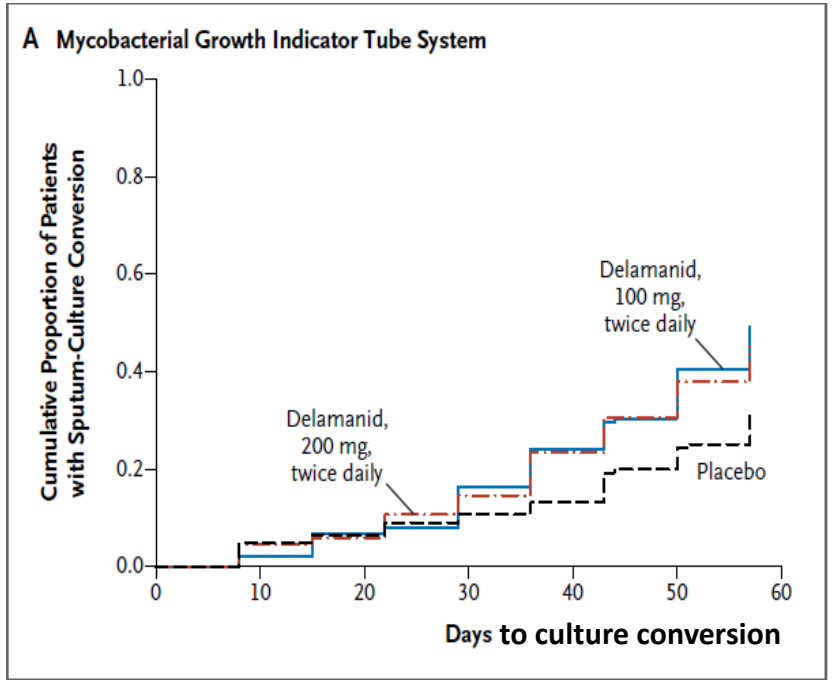


Figure 2. The Proportion of Patients with Positive Sputum Cultures and Time to Conversion.

Bedaquiline (US FDA Dec 2012)

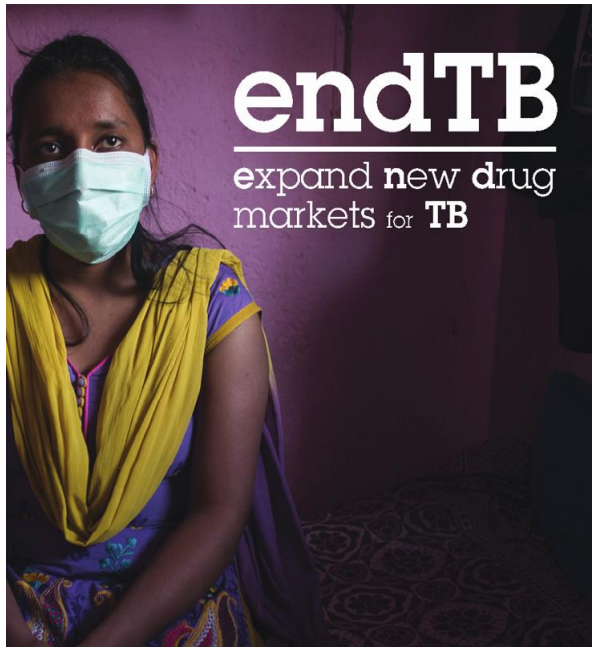
The NEW ENGLAND JOURNAL of MEDICINE

Delamanid for Multidrug-Resistant Pulmonary Tuberculosis

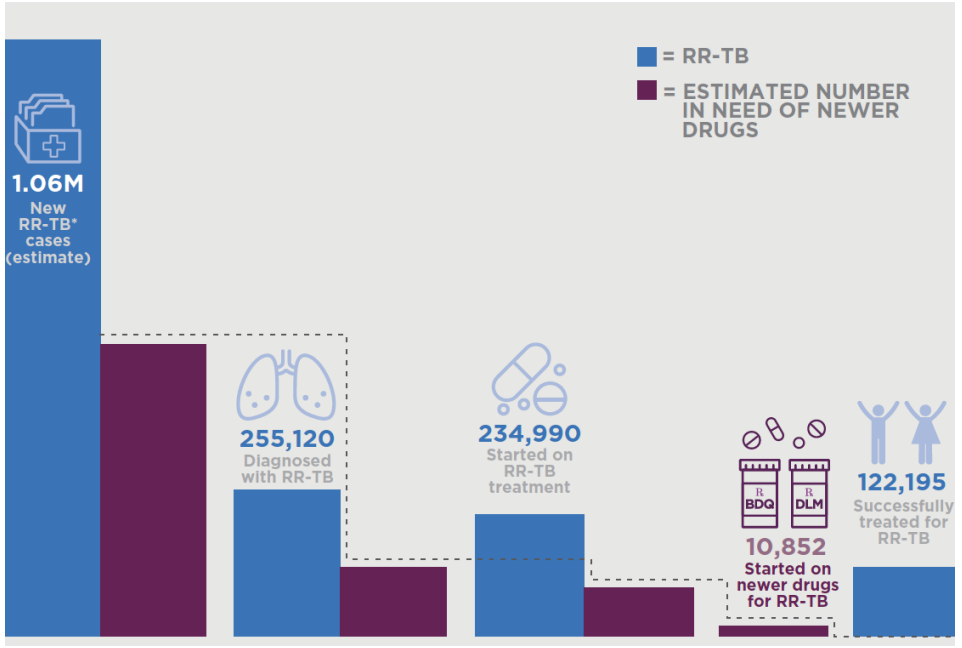


Delamanid (EMA Nov 2013)

The endTB project



endTB Project overview:



Goals

- Expand access to new/repurposed TB drugs
- Find better, shorter, less toxic regimens
- Generate & disseminate evidence

Funding

- $81.2 M over 9 years **from Unitaid**
- Cofunding: >$9M co-funding (MSF, PIH)

Studies

endTB observational study 17 Countries > 2800 patients
Long regimens for all forms of rifampin-resistant (RR-) TB

endTB clinical trial 8 Countries 754 participants
Short regimens RR- & FQ-susceptible (FQ-S) pulmonary TB

endTB-Q trial 5 Countries 324 participants
Short regimens for RR- and FQ-R pulmonary TB (FQ-R)

Partners In Health · Medecins Sans Frontieres · IRD Interactive Research & Development · Unitaid · Institute of Tropical Medicine Antwerp · Harvard Medical School · epicentre Épidémiologie • Epidemiology · UCSF University of California San Francisco

endTB Observational Study (Mar 2015-Dec 2019)

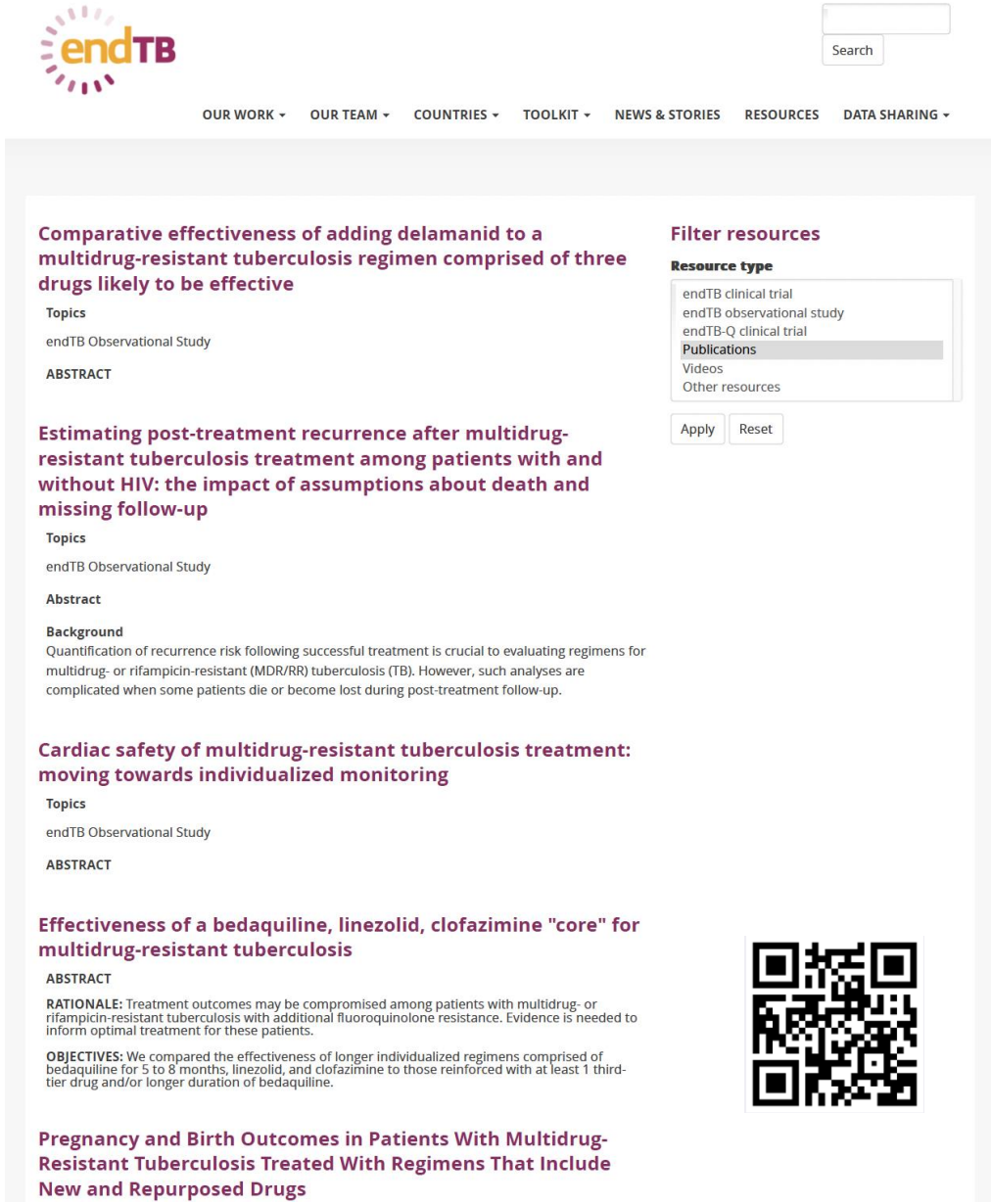
Largest multi-centre observational study of regimens containing bedaquiline or delamanid

17 Countries

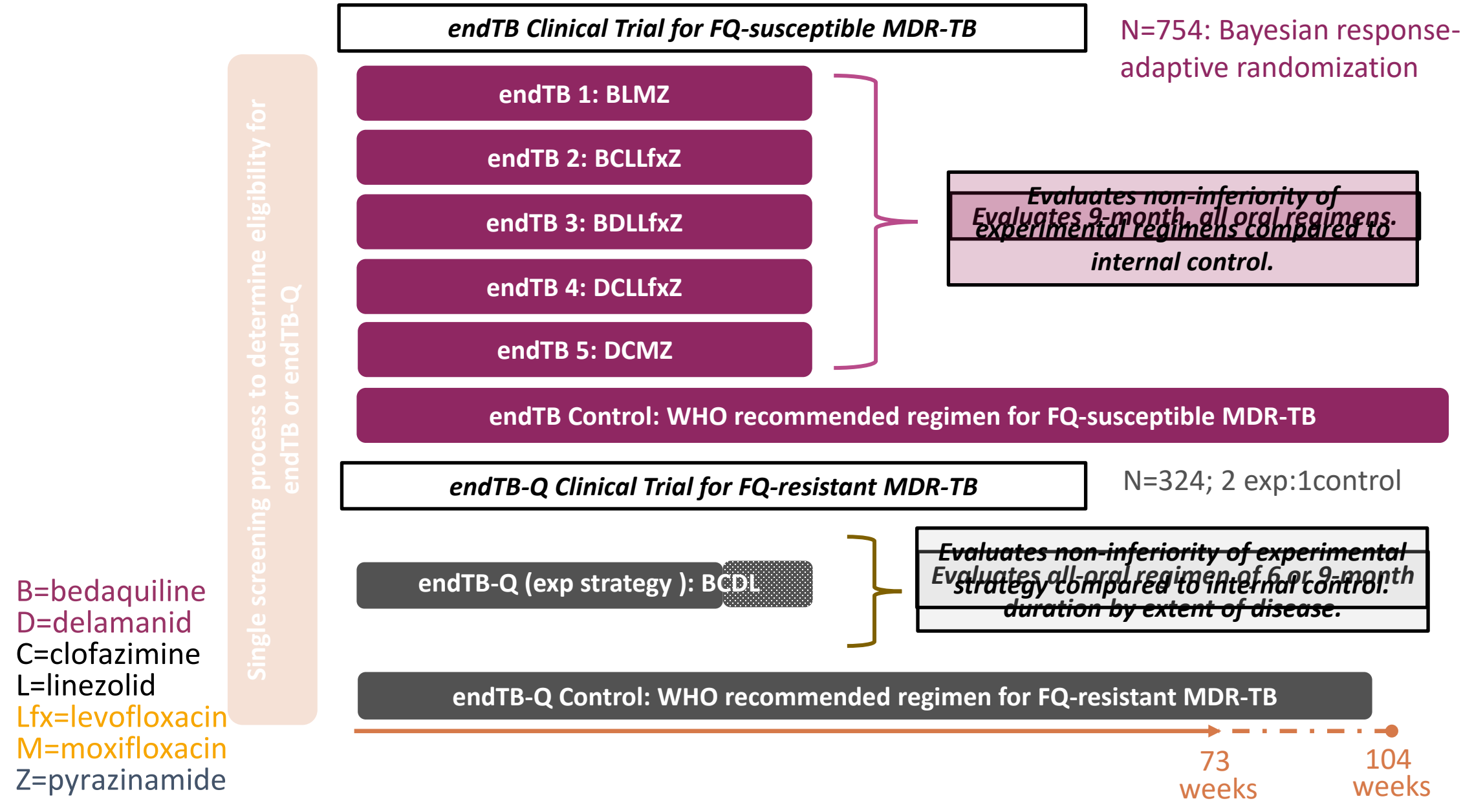
> 2800 Patients

Main results:

- 80% effectiveness of long regimens
- Good safety of bedaquiline & delamanid
  - Alone
  - In combination
  - For prolonged duration
- Data shared for WHO guideline revisions (2018, 2019, 2022)



endTB/endTB-Q trial designs



endTB trial: Ph 3 Bayesian response-adaptive non-inferiority trial of 5 short, experimental regimens for FQ-S MDR/RR-TB

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endTB trial (N=754)

Evaluates non-inferiority of experimental regimens compared to internal control.

Screening for eligibility for endTB

endTB 1: BLMZ	**Post-treatment follow-up**	
endTB 2: BCLLfxZ	**Post-treatment follow-up**	
endTB 3: BDLLfxZ	**Post-treatment follow-up**	
endTB 4: DCLLfxZ	**Post-treatment follow-up**	
endTB 5: DCMZ	**Post-treatment follow-up**	
endTB Control: WHO recommended regimen for FQ-susceptible MDR-TB		

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

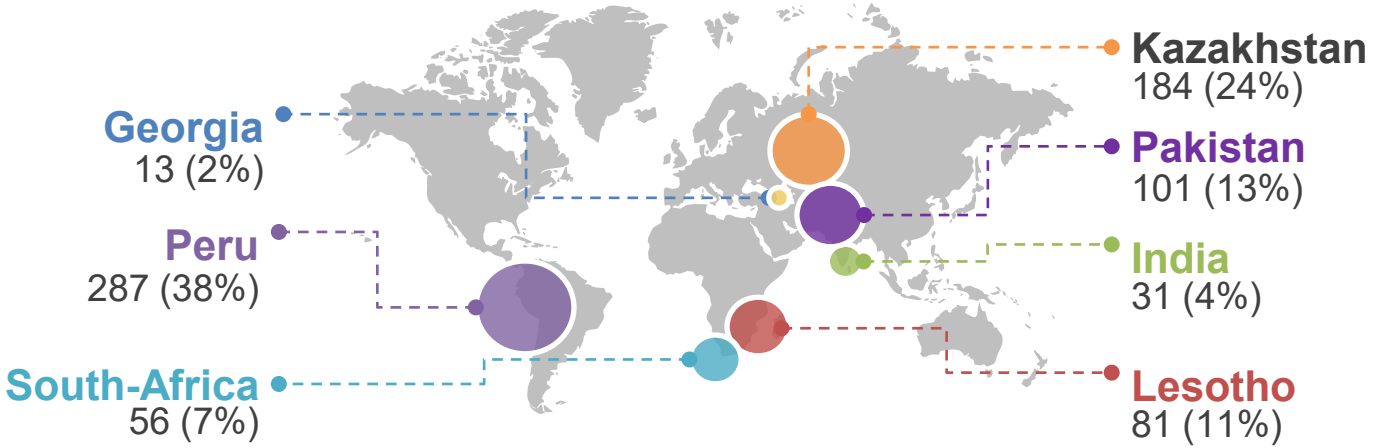
Month (study visit frequency)

1 2 3	4 5 6 7 8 9 10 11 12	13 14 15 16 17 18 19 20 21 22 23 24
Weekly	Every 4 Weeks	Every 6-8 weeks
Clinical, biochemical, hematologic, bacteriologic, adherence, neurologic, optic, audiometric, radiographic, cardiac monitoring + daily treatment support		

73 weeks

104 weeks

The endTB clinical trial



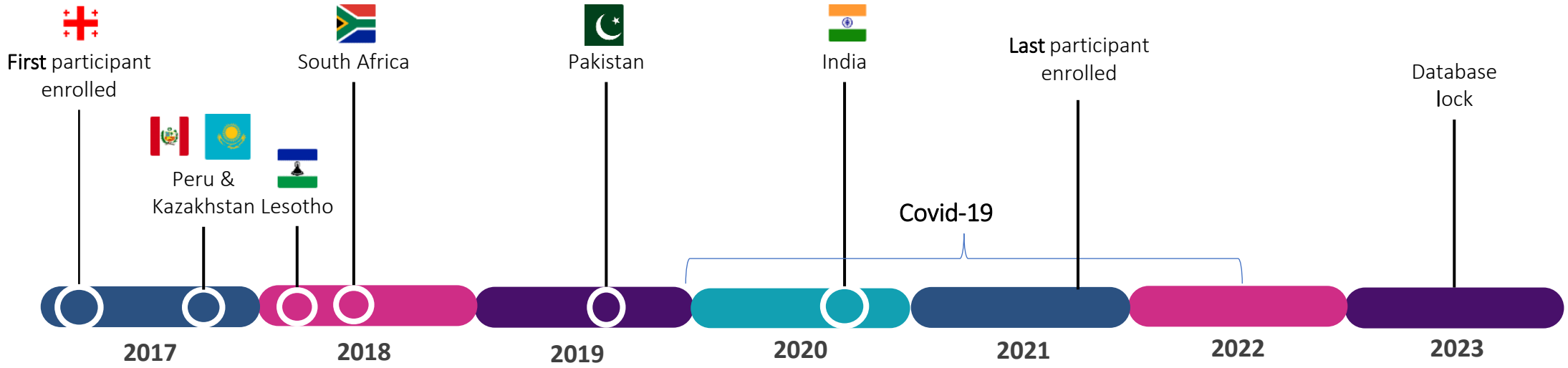
7 countries

12 sites

1539 screened

754 randomized

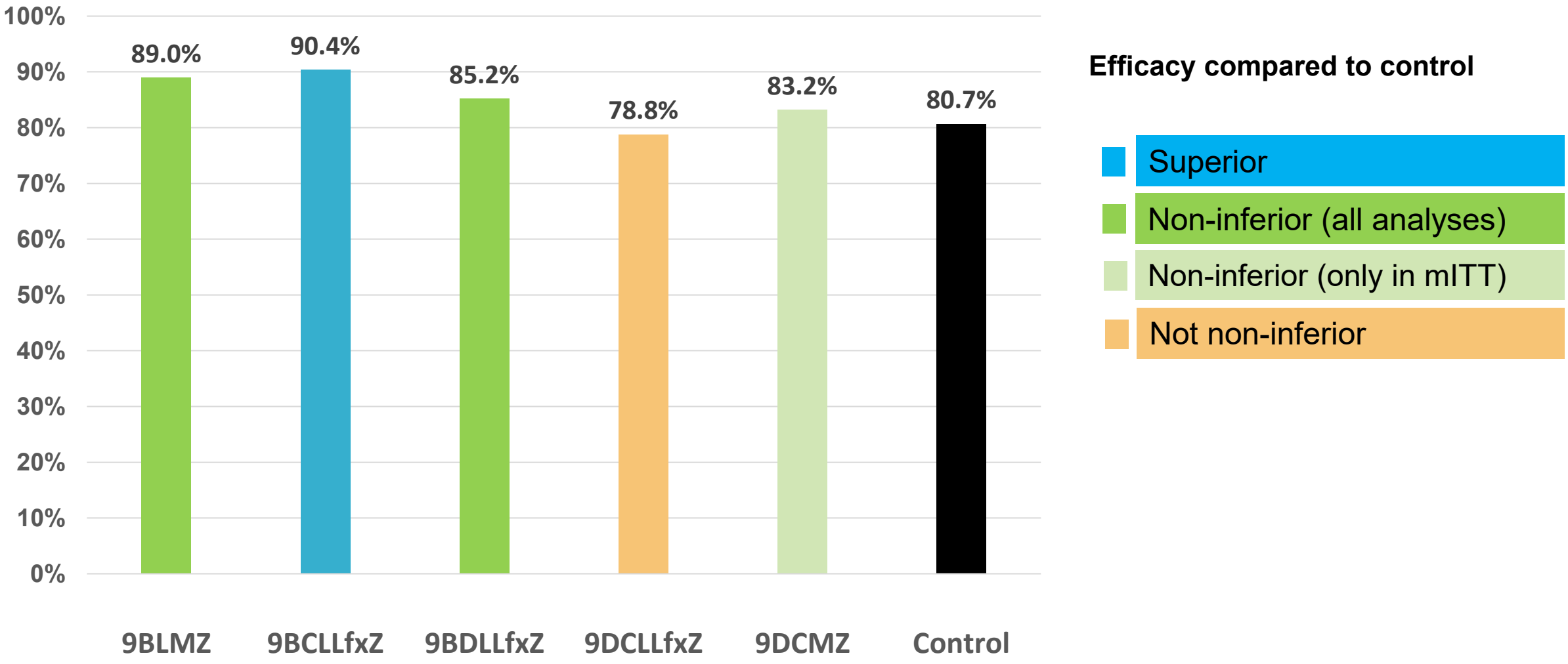
> 18,000 study visits



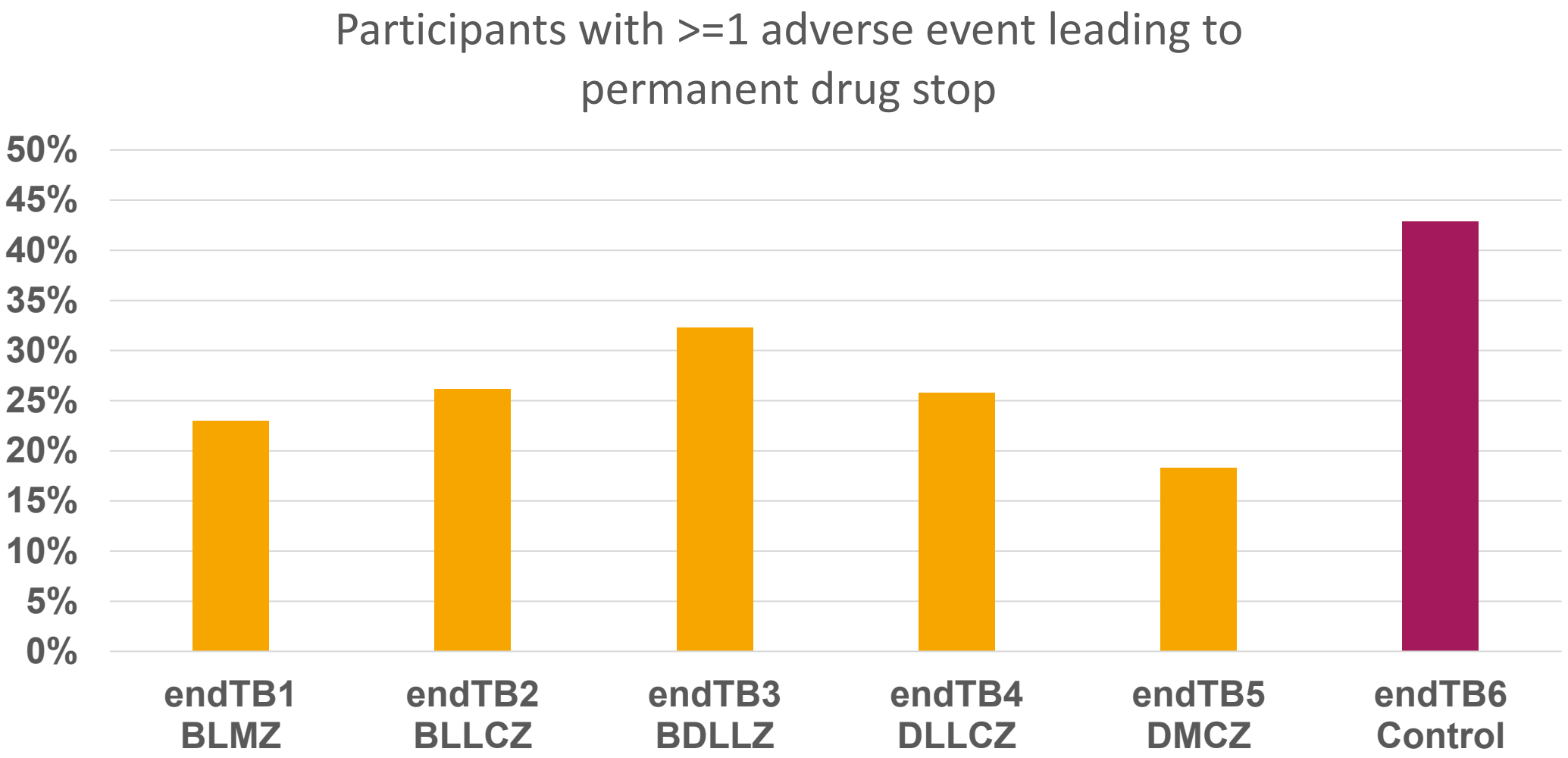
endTB trial | Selected baseline characteristics

Baseline characteristic	**Total (N = 699)**
Age (years), median (range)	32.0 [15.0;71.0]
Sex, female	264 (37.8%)
BMI (kg/m^2), median (IQR)	20.4 [18.0;22.8]
HIV positive	98 (**14.0%**)
Hepatitis B	17 (2.4%)
Hepatitis C	26 (3.7%)
Diabetes	105 (**15.0%**)
Sputum smear positive	568 (**81.3%**)
Lung cavitation	399 (**57.1%**)
Pyrazinamide resistance	377 (**53.9%**)
Prior exposure to other 2nd line drugs	78 (11.2%)

endTB trial | Efficacy results, mITT population (N=699)



endTB trial: Safety at Week 73



endTB trial – conclusions

- 3 nine-month regimens (BLMZ, BCLLfxZ, BDLLfxZ) are **non-inferior (1 superior)** to current, well-performing 18-month standard of care
- Low mortality
- Good results in people with severe disease, comorbidities
- Similar, high rates of important AEs, except liver toxicity (pyrazinamide, bedaquiline, moxifloxacin, linezolid)
- All 3 regimens can be used to treat MDR-TB in adults, adolescents, children & pregnant people

July 28 - August 3 2024 Sunday Express

10 News

Mathatisi Sebusi

Hope for TB patients

THERE is finally hope for multi-drug resistant tuberculosis (TB) and rifampicin-resistant tuberculosis (MDR/RR-TB) patients as newly discovered treatments promise to be more effective, shorter, and have more manageable side effects.

Compared to the current 24 months treatment, which has proved to be ineffective in some cases, this new endTB programme is expected to reduce the treatment period to nine months.

The new treatment includes endTB1 [BLMZ], endTBC [BLLCZ], endTB3 [BDLLZ], endTB4 [DLLCZ] and alternatively enTB5 [DMCZ] for MDR/RR-TB patients "who cannot take bedaquiline and/or linezolid" which constitute part of the new regimen.

The endTB treatments are yet to be recommended by the World Health Organisation (WHO) for them to be rolled out in health facilities.

A team led by Médecins Sans Frontières (MSF), Partners In Health (PIH), and Interactive Research and Development (IRD) formed the endTB consortium and began a Phase III randomized controlled trial in 2017.

With financial assistance from Unitaid, they evaluated the efficiency and safety of five new oral, shortened regimens for MDR-TB.

Unitaid is a global health initiative that works with partners to bring about innovations to prevent, diagnose and treat major diseases in low- and middle-income countries, with an emphasis on tuberculosis, malaria, and HIV/AIDS and its deadly co-infections. It was founded in 2006, jointly by France, United Kingdom, Brazil, Norway and Chile.

This development was announced during a press conference by the MDR-TB Senior Medical Officer and Lesotho Site Principal Investigator for the endTB trial, Kunda Kwabisha Mikanda, this past week. He explained that the current regimens, which they sought to replace, required patients to take around 14,000 pills over 24 months.

Dr Mikanda said, if recommended by WHO, these new patient-centred treatment regimens would allow clinicians to offer shortened MDR-TB treatment regardless of age, pregnancy, and common comorbidities among MDR-TB patients.

He highlighted that current MDR-TB regimens, which require up to 24 months of treatment, were only 59 percent effective and often caused severe side effects.

"The regimens which are now in use often cause terrible side including acute psychosis and permanent deafness. While the newly found regimens provides for nine months treatment with manageable side effects," Dr Mikanda said.

The endTB trials involved 754 patients from seven countries: Lesotho, South Africa, Georgia, India, Kazakhstan, Pakistan, and Peru.

"We stand on the cusp of a significant breakthrough in the battle against MDR-TB, a disease that disproportionately affects impoverished populations worldwide. Our results offer hope to those in dire need and underscore the urgency of continued research and innovation.

"For far too long, MDR-TB has been a formidable threat with limited, poorly tolerated treatment options.

Today, we unveil evidence for multiple innovative all-oral, short-ened regimens that will allow patient-centred, individualized treatment of MDR-TB.

This marks a pivotal moment in the fight against a disease that has plagued vulnerable populations worldwide. The new regimens would provide nine months of treatment with manageable side effects."

Dr Mikanda said the new regimens were expected to complement the other treatment, BPaLM which was recommended by WHO in 2022.

He also noted that trial results could address major barriers to care and that the endTB consortium will continue to advocate for improved access and affordability of quality TB care.

According to WHO, an estimated 410,000 people globally developed multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) in 2022. While the treatment success rate for people diagnosed with MDR/RR-TB has steadily improved, it remains alarmingly low.

In 2020, the global treatment success rate was 63 percent, up from 60 percent in 2019 and 50 percent in 2012. WHO identified mismanagement of TB treatment and person-to-person transmission as key reasons for the emergence and spread of MDR/RR-TB. Most people with TB were cured by a 6-month treatment regimen (BPaLM) provided with adequate support.

WHO further stated that inappropriate or incorrect use of TB drugs, ineffective drug formulations, poor quality medicines, bad storage conditions, and premature treatment interruption could cause drug resistance, which could then be transmitted, especially in crowded settings such as prisons and hospitals.

Based on current WHO policy, several regimens could be used for patients with MDR/RR-TB. Key factors defining treatment regimen choice include the patient's drug-resistance profile, prior exposure to TB medicines, patient history, the drug-resistance profile of close contacts, the patient's age, the extent of pulmonary TB disease, and the localisation of extrapulmonary TB lesions.

concerns among citizens, particularly those

endTB-Q trial

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UCSF University of California San Francisco

endTB-Q trial (N=324)

Evaluates non-inferiority of experimental strategy (6 or 9 months per disease extent) compared to internal control.

Screening for eligibility for endTB-Q

Randomized 2:1 experimental to control

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

endTB-Q (exp strategy): BCDL | **Post-treatment follow-up**

endTB-Q Control: WHO recommended regimen for FQ-resistant MDR-TB

Month (study visit frequency)

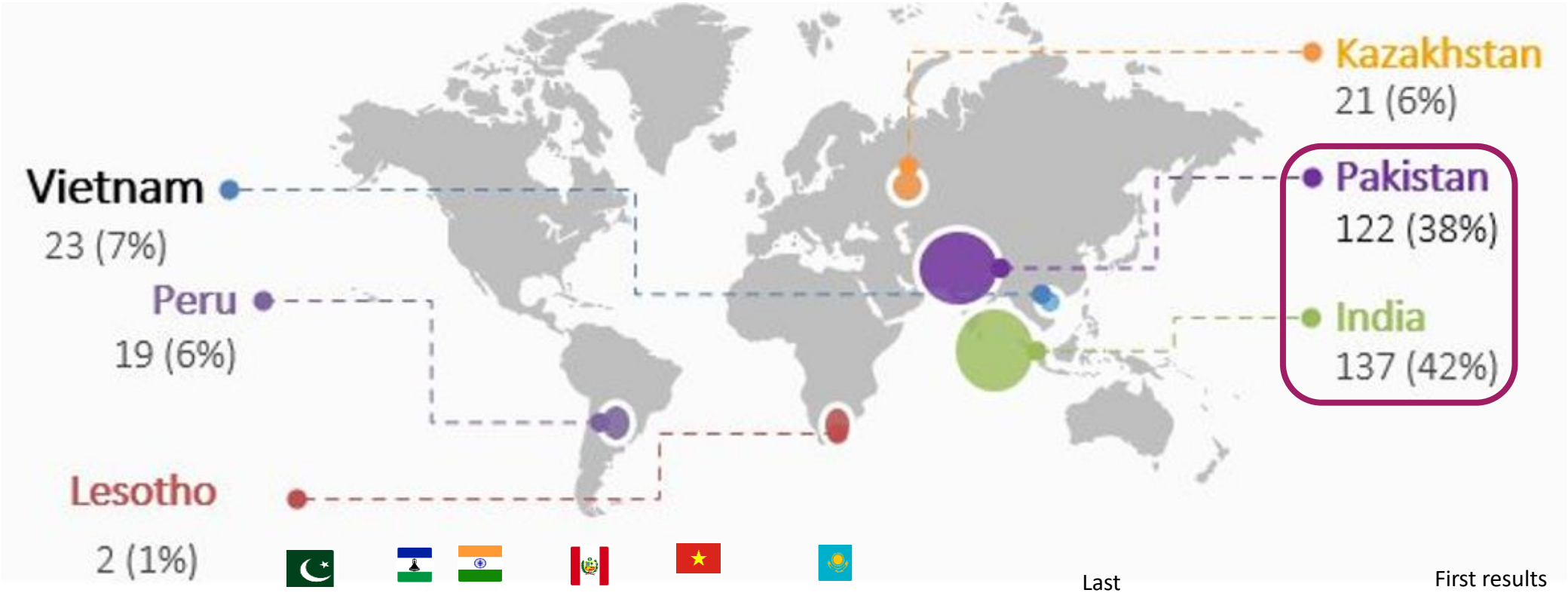
1 2 3	4 5 6 7 8 9 10 11 12	13 14 15 16 17 18 19 20 21 22 23 24
Weekly	Every 4 Weeks	Every 6-8 weeks
Clinical, biochemical, hematologic, bacteriologic, adherence, neurologic, optic, audiometric, radiographic, cardiac monitoring + daily treatment support		

73 weeks

104 weeks

endTB-Q| Timeline and enrollment

Patients screened: 1030 -> **Randomized: 324 (31.5%) in endTB-Q** + 138 (19.5%) in endTB trial



Select Baseline Characteristics (mITT)

	Experimental	Control	Total
N (%)	**163 (66.0%)**	**84 (33.9%)**	**247 (100.0%)**
Female	71 (43.6%)	43 (51.2%)	114 (46.2%)
Age*	31 [21.0; 42.0]	28.5[20.0; 44.0]	30 [21.0; 42.5]
<18	11 (6.7%)	7 (8.3%)	18 (7.3%)
BMI*	17.5 [15.6; 20.0]	17.9 [15.3; 20.1]	17.6 [15.4; 20.1]
HIV+	1 (0.6%)	3 (3.6%)	4 (1.6%)
Hepatitis C+	7 (4.3%)	5 (6.0%)	12 (4.9%)
Diabetes	37 (22.7%)	18 (21.4%)	55 (22.3%)
Cavitation	108 (66.3%)	57 (67.9%)	165 (66.8%)
Smear result			
Negative/Scanty	45 (27.6%)	23 (27.4%)	68 (27.6%)
1-2+	80 (49.0%)	39 (46.5%)	119 (48.1%)
3+	38 (23.3%)	22 (26.2%)	60 (24.3%)

* Median [IQR]

endTB-Q| Control arm composition

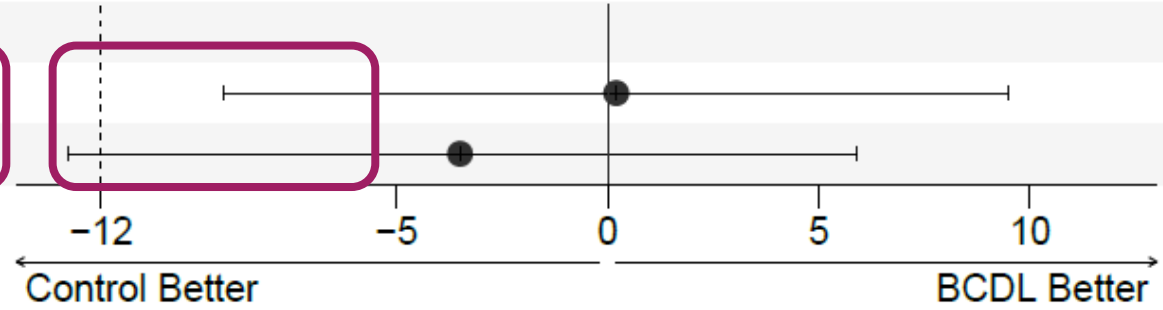
≈90% received BCDL + 1 or more drugs

Regimens	n (%)
BCDL+Cs	59 (70.2%)
BCDL+Cs+E	5 (6.0%)
BCDL+Z	5 (6.0%)
BCDL other	7 (8.4%)
BCL+Cs+Z	8 (9.5%)

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

Relative efficacy*: mITT & PP efficacy at Week 73

Analysis population	BCDL	Control	Risk Difference with 95% Confidence Interval
	n with favorable outcome/N (%)		
W73			
mITT	141/163 (86.5%)	75/84 (89.3%)	0.2% [−9.1%;9.5%]
PP	138/157 (87.9%)	71/76 (93.4%)	−3.5% [−12.8%;5.9%]

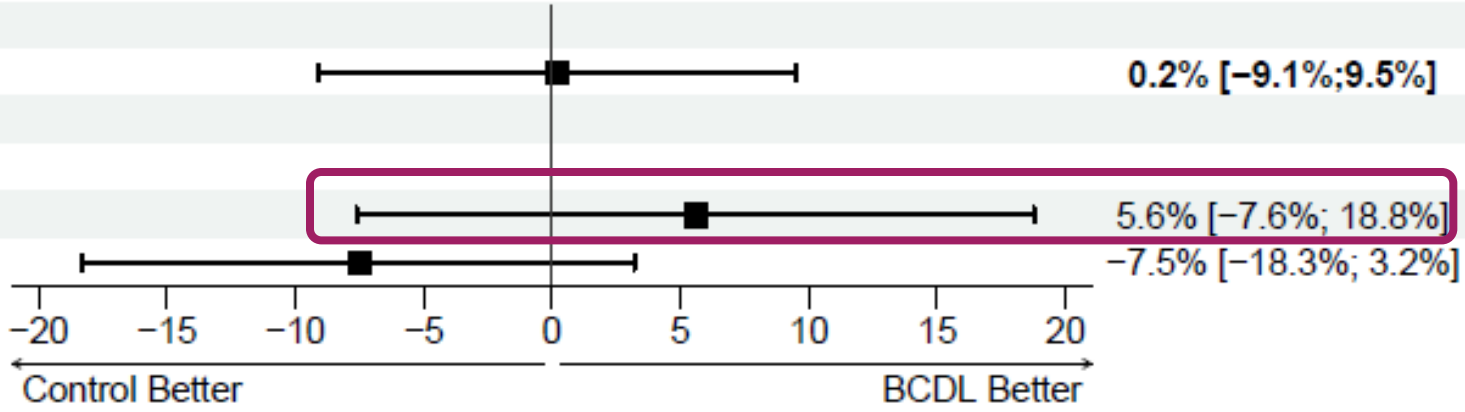


Recurrence	8 (8.4%)	0 (0.0%)

*adjusted for randomization stratification variables: country & baseline extent of disease

Relative efficacy*: Efficacy at Week 73, stratified by baseline disease extent (mITT & PP populations)

Analysis population	BCDL	Control	Risk Difference with 95% Confidence Interval
	no. with favorable outcome/total no. (%)		
mITT	**141/163 (86.5%)**	**75/84 (89.3%)**	**0.2% [−9.1%;9.5%]**
Baseline disease extent			
Limited	54/58 (93.1)	28/32 (87.5)	5.6% [−7.6%; 18.8%]
Extensive	87/105 (82.9)	47/52 (90.4)	−7.5% [−18.3%; 3.2%]



Recurrence	
Limited	1 (1.7%)
Extensive	7 (6.7%)

*adjusted for randomization stratification variables: country & baseline extent of disease

endTB-Q|

Adverse Events: Total, Grade ≥3 & SAE at treatment end + 4 weeks[#] (Safety population)

	Experimental N=213	Control N=105	Total N=318
Participants with **any Grade ≥3 AE**[*]	136 (63.8%)	80 (76.2%)	216 (67.9%)
Participants with **any SAE**[**]	31 (14.5%)	23 (21.9%)	54 (17.0%)
Permanent discontinuation of ≥1 drug(s) for AEs	30 (14.1%)	57 (54.3%)	87 (27.4%)
Death[#]	9 (4.2%)	2 (1.9%)	11 (3.5%)

Post hoc analysis; primary safety analysis is at Week 73; * Graded according to MSF Severity Scale; ** Serious adverse event = leading to death or life threatening; or leading to hospitalization, permanent disability or congenital defect; or medically important.

Conclusions

- The endTB-Q strategy is an excellent option for patients with limited FQ-R, MDR/RR-TB disease. In extensive disease, it may not be sufficient to prevent relapse.
- **endTB-Q reinforces the importance of FQ** in RR/MDR-TB treatment:
  - Relapse may be more likely when treating FQ-R-TB with the current, recommended short regimens (6BCDL, 2.0-5.0% & 6/9 BPaL, 2.7-4.4%)
  - FQ resistance testing is critical in patients with RR-TB
- **Future research** is required to optimize regimen composition, duration:
  - Trials should be designed specifically for pre-XDR-TB population to glean effects in that population
  - Trials require an internal control to correctly interpret well-performing experimental arm

”Be careful about a race to the bottom…” Paul Farmer, March 2017

???

”Be careful about a race to the bottom…” Paul Farmer, March 2017

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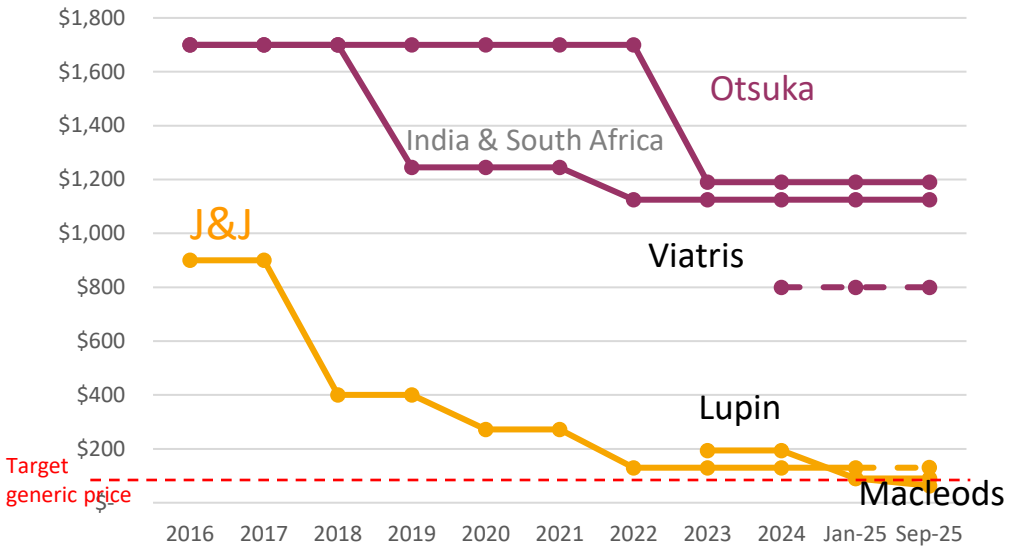
After the endTB project studies:

Dissemination, activism, advocacy, & more science

Price and pill burden considerations

Price of bedaquiline & delamanid over time



Delamanid –

Bedaquiline –

Regimen price in USD & pill burden#

Regimen	Current regimen price*	Current: Lowest possible**	Average daily pill burden
9BLMZ	**$173**	0.9	6.5
9BCLLfxZ	**$282**	1.1	8.5
9BDLLfxZ	$1,464	8.0	11.5
6BPaLM	**$284**	1.5	4
6BCDL	$956	~4.9	6
18-month B_6LLfxLC	$428	~0.5	8

#For people weighing 35-50kg

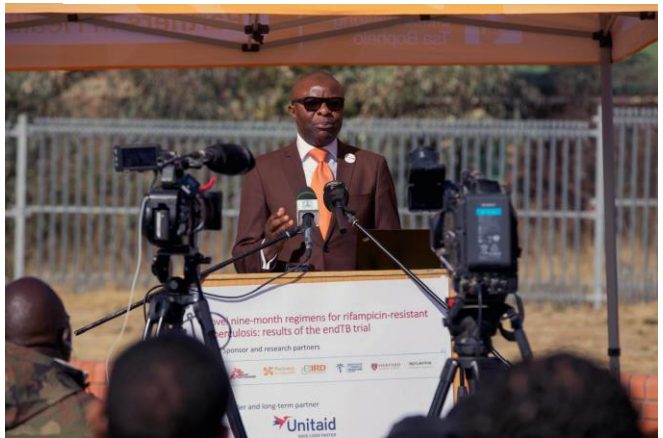
*Using lowest GDF prices (Sep 2025)

** Using lowest GDF prices (Sep 2025), except estimated cost-based generic prices for Bdq, Dlm & Pa

Courtesy of Christophe Perrin, MSF Access Campaign; GDF, Sep 2025

Articles

Bedaquiline, delamanid, linezolid, and clofazimine for rifampicin-resistant and fluoroquinolone-resistant tuberculosis (endTB-Q): an open-label, multicentre, stratified, non-inferiority, randomised, controlled, phase 3 trial



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What Will It Take to End Tuberculosis?

A boundary-pushing global collaboration is betting on the power of science

By JAKE MILLER | February 15, 2024 | Research, Education, Care Delivery

The NEW ENGLAND JOURNAL of MEDICINE

WHO consolidated guidelines on tuberculosis

Module 4: Treatment and care

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Q&A: Why New WHO-Approved Tuberculosis Treatments Matter

PIH researcher discusses major advancement, its impact in vulnerable communities, and what's next in the fight against TB

Posted on Sep 24, 2024

84 Shares

1.2 The 6-month bedaquiline, delamanid, linezolid, levofloxacin and clofazimine (BDLLfxC) regimen (a)

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)

2. Treatment of drug-resistant TB using 9-month regimens

2.1 The 9-month all-oral regimen for MDR/RR-TB (b)

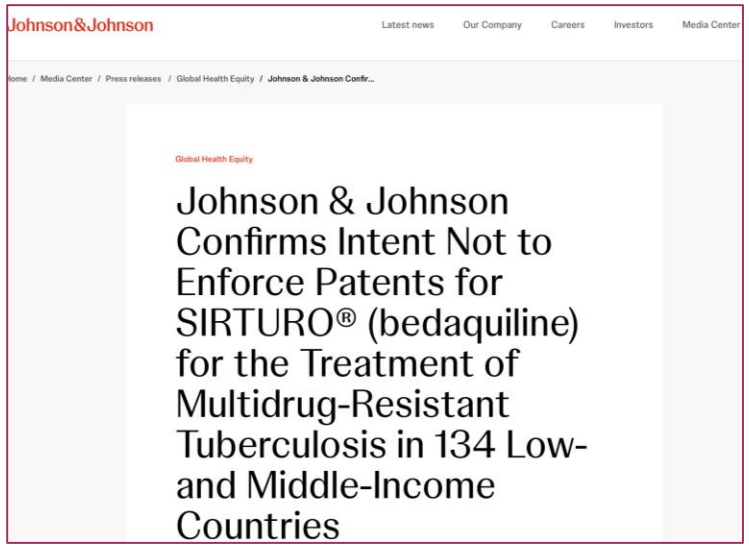
WHO suggests the use of the 9-month all-oral regimen rather than longer (18-month) regimens in patients with MDR/RR-TB and in whom resistance to fluoroquinolones has been excluded.

(Conditional recommendation, very low certainty of evidence)

2.2 The modified 9-month all-oral regimens for MDR/RR-TB (a)

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. Amongst these regimens, using BLMZ is suggested over using BLLfxCZ, and BLLfxCZ is suggested over BDLLfxZ.

(Conditional recommendation, very low certainty of evidence)



Partner to learn more from the endTB project data?

The **endTB Data Sharing Initiative (eDSI)** affords ethical, equitable and transparent access to endTB data for a range of users who share the common goal of increasing information to improve care for MDR-TB patients. It is a unique set of data on more than 3,700 participants spread across 4 continents.

Scan this QR code to learn more about eDSI

Billions in Global Health and Development Assistance Funding is at Risk

Open Scientific Questions

Comparison across range of shorter regimens-MELD DR-TB

- Patient preference/improved safety & tolerability
- Shorter regimens for people with extensive disease?
- Improved treatment for XDR-TB
- Prevention of acquisition of drug resistance
- Prevention & management of PTLD

Special thanks to the people and organizations who made the endTB Project a reality…

The nearly 4000 participants and the other patients screened

All the team members, investigators and sites which implemented the project over 9 years.
The National TB Programs and all local partners in 18 countries

The Sponsor and research partners:

MEDECINS SANS FRONTIERES
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UCSF University of California San Francisco

The PIs, the central endTB team, all contributing expert teams (Protocol Writing Committee, Scientific Advisory Committee, MSF Logistique, unblinded statisticians, the Clinical Advisory Committee, the Pharmacovigilance unit, Data and Safety Monitoring Board, MSF Access Campaign, Global Tuberculosis Community Advisory Board, WHO) and all other support teams

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We are grateful to all endTB Project participants and teams!