Programmatic Uptake of Novel Treatments for Multidrug-Resistant TB: A Failure of Innovation?

Jennifer Furin, MD., PhD.
Harvard Medical School
Department of Global Health and Social Medicine

Objectives

- To review the global uptake of novel drugs and regimens for the treatment of DR-TB.
- To describe barriers to the use of these therapeutic innovations.
- To discuss strategies for overcoming these barriers and providing optimal treatment for all.

Exciting Time in the Treatment of DR-TB

- The past 6 years have seen the introduction of 2 new drugs (bedaquline and delamanid) and one new shorter regimen for the treatment of DR-TB.
- Increasing use of re-purposed agents—including linezolid, clofazimine and the carbapenems.
- Multiple planned and ongoing clinical trials for optimal treatment of DR-TB.

Are innovations reaching those in need?

Asia & Pacific

Indian teen's court battle for a new tuberculosis drug draws global support

By Rama Lakshmi January 15, 2017 Email the author

NEW DELHI — A woman's court battle to gain urgent access to a new, government-controlled tuberculosis drug has become a rallying point for

The National

Indian girl dying of TB sues to get

Government restricts access to bedaquiline in a bid to retain effectiveness of th drug-resistant TB.

Politics and protocol leave Indian teen's life in the balance pending TB drug ruling

After five years of battling tuberculosis, Shreya Tripathi faces a new struggle: to overcome India's strict controls on bedaquiline, a drug that could save her life

Methodology

- Drug-Resistant TB Scale-Up Treatment Action Team (DR-TB STAT) established in 2015 to monitor and support the use of the novel agents bedaquiline and delamanid (and later shorter regimen).
- Collect monthly/quarterly data on the programmatic use of new drugs from >40 countries participating on a voluntary basis.
- Cumulative data presented and reviewed on monthly calls. Data valid through Feb 1, 2018
- Close collaboration to also monitor orders placed with the Global Drug Facility.
- Other collaborating groups include KNCV, MSF, PIH, IRD, multiple NTPs, Stop TB Partnership, Global Drug Resistance Initiative

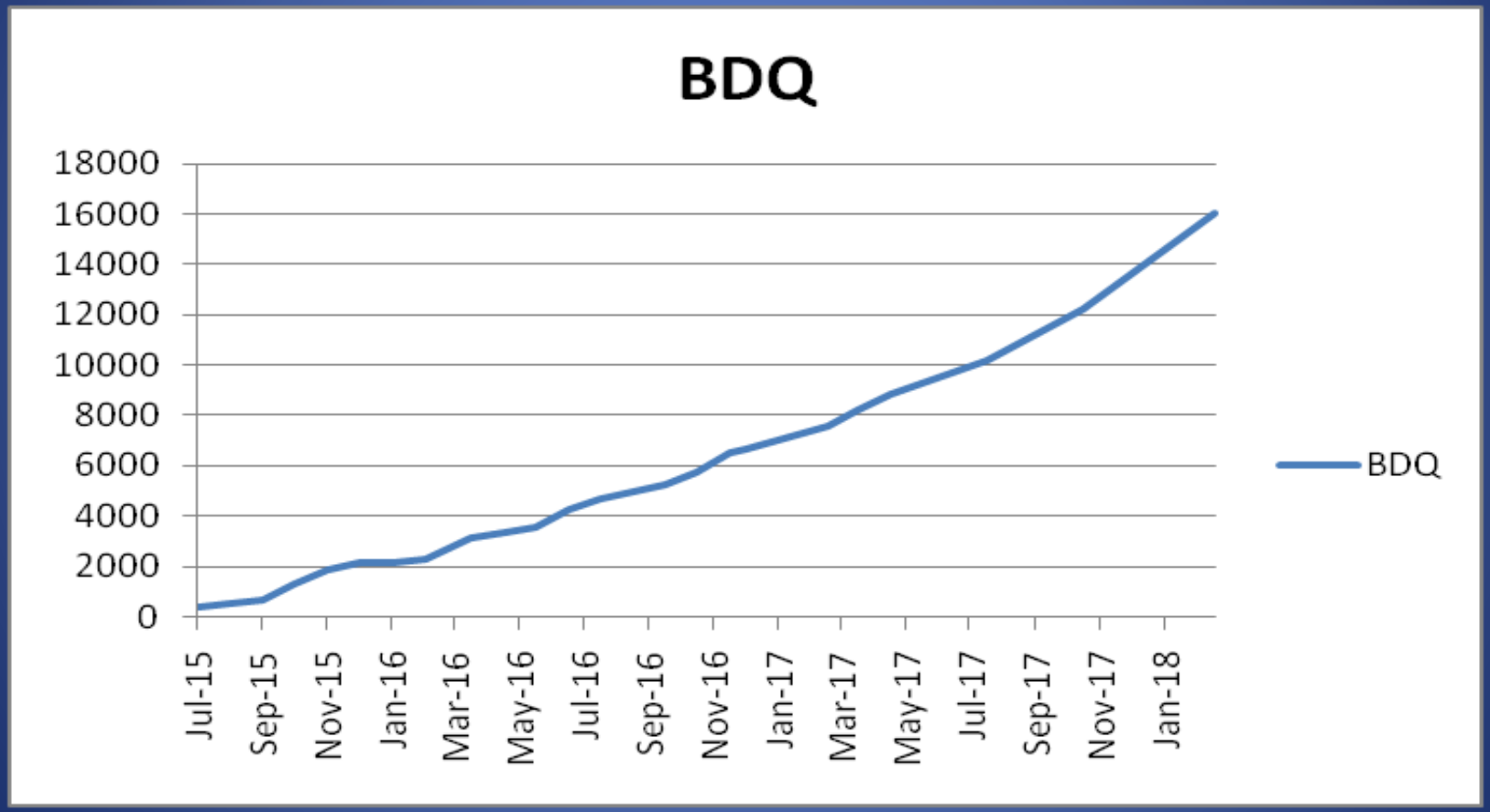
Bedaquiline

- Blocks synthesis of ATP, approved by US FDA in July 2012
- Recommended by WHO in 2013 and 2017 for persons with resistance or intolerance to second-line drugs provided country met certain criteria.
- Phase III trial currently ongoing as part of the STREAM study
- Available via donation program for some countries; otherwise costs between USD 900 and USD 33,000 for a six month treatment course

Current Global Programmatic Use

- Used under program conditions in 38 countries
- A total of 16,038 persons treated with BDQ under program conditions since April, 2015
- 65% (10,429) of these persons are in South Africa.
- 21,404 orders placed with GDF
- India using but low numbers, China to start in March 2018
- Concerning lack of use in PAHO region.

BDQ Uptake Graph



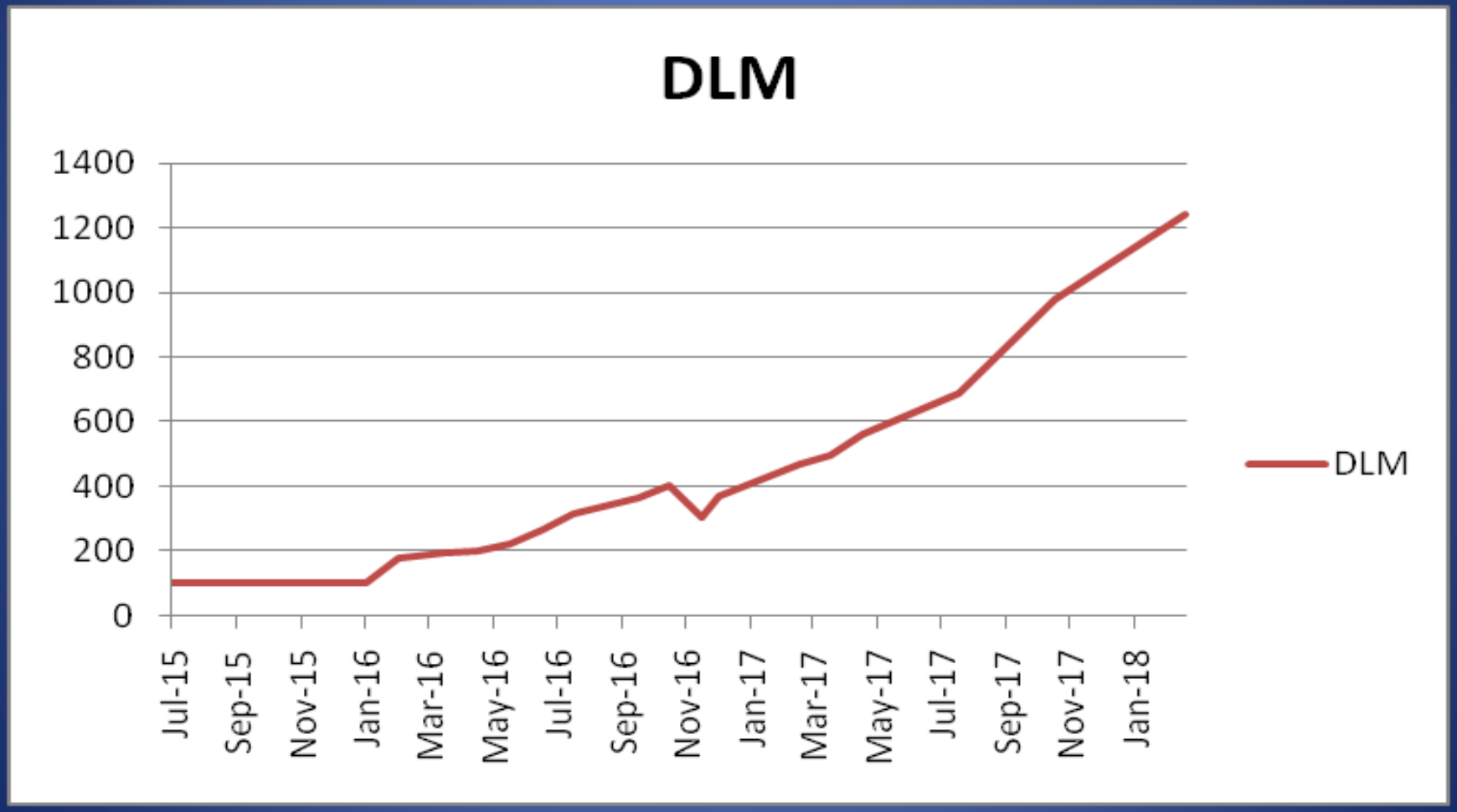
Delamanid

- Nitroimidazole agent, interferes with cell wall synthesis, conditionally approved by EMA in 2014
- Recommended by the WHO in 2014 for persons with resistance or intolerance to SLDs or high risk of treatment failure provided country meets certain conditions
- WHO recommendations extended to children ages 6-17 years in 2016.
- Phase III trial completed in 2017, results show NS faster time to culture conversion.
- WHO recommendations continued without changes in 2018 but advice from WHO suggested countries may need to change their forecasting and procurement plans.
- Available via the GDF for GF-eligible countries for USD 1700 for 6 months course: other pricing ?

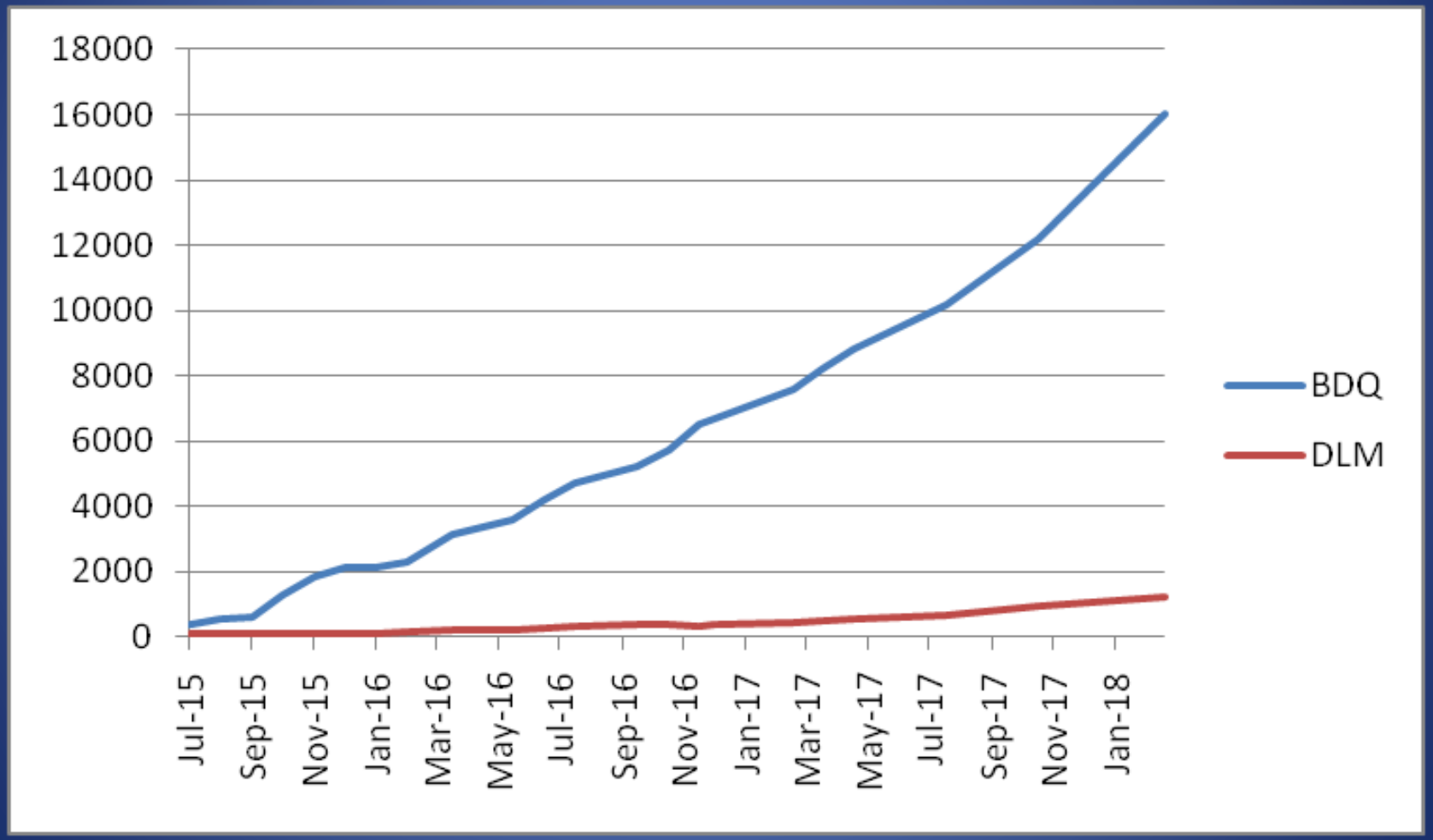
Current Global Programmatic Use

- Use under program conditions in 27 countries
- A total of 1240 persons treated with DLM under program conditions since April, 2015
- 4920 orders placed with GDF
- Majority of these individuals treated as part of the UNITAID endTB Project (MSF, IRD, PIH).
- Case reports in children
- Increasing use in combination with BDQ

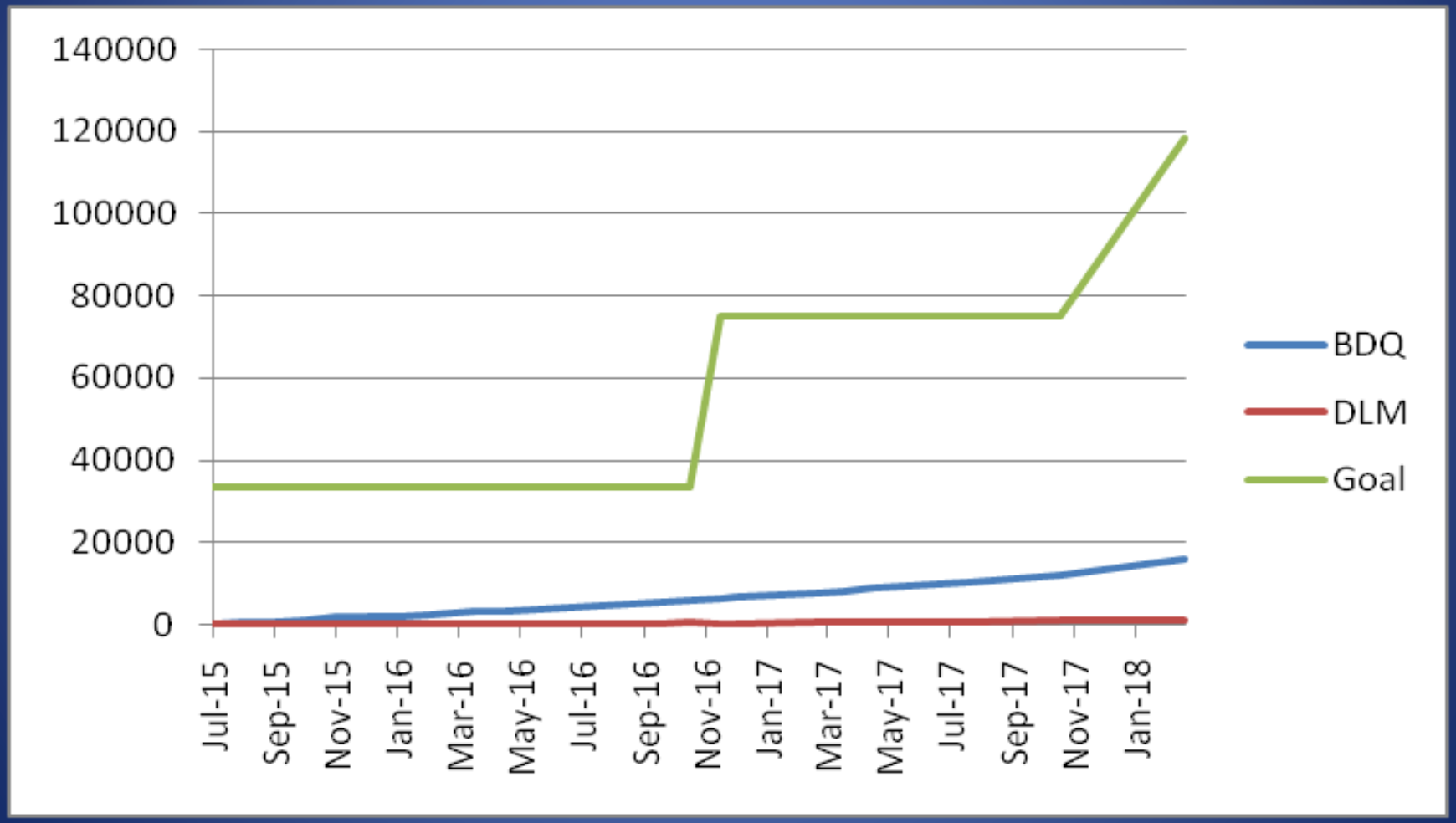
DLM Uptake Graph



BDQ compared with DLM



BDQ/DLM compared with estimated global need

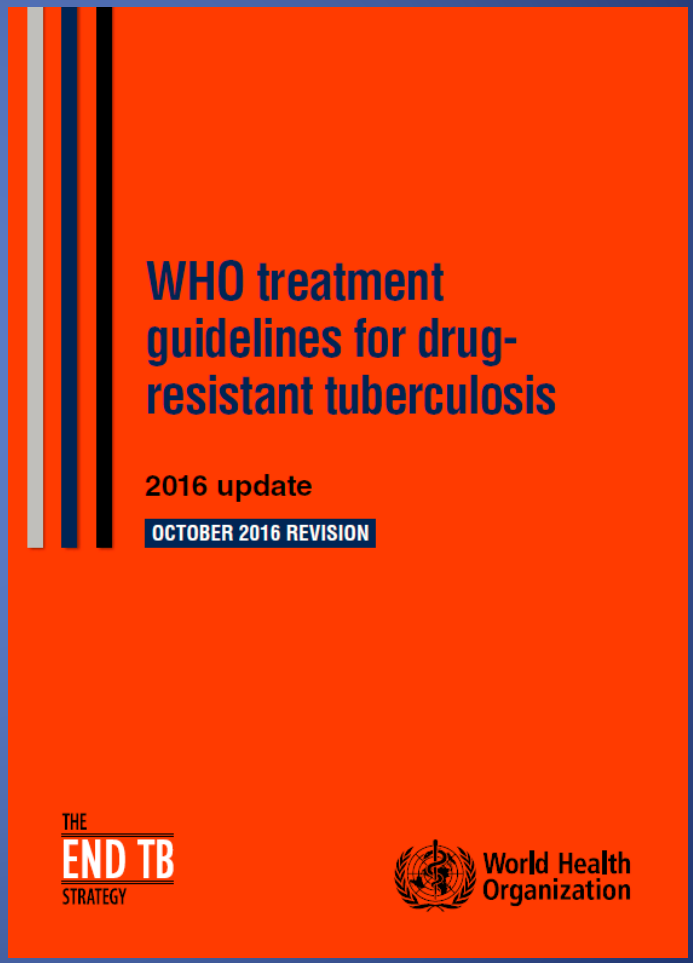


Shorter Regimen

- Recommended by WHO in 2016 for the treatment of DR-TB in persons without resistance (known or suspected) to FQ or SLI
- Observational cohorts from multiple countries (Trebucq, Francophone Africa, 2018 *IJTLD*; Khan, Bangladesh, Niger, Cameroon, Uzbekistan, Swaziland, 2017, *ERJ*)
- Phase III trial showed high rates of treatment success (78%), but failed to establish non-inferiority with conventional regimen
- Cheaper in the short term than conventional regimen for patients and programs.

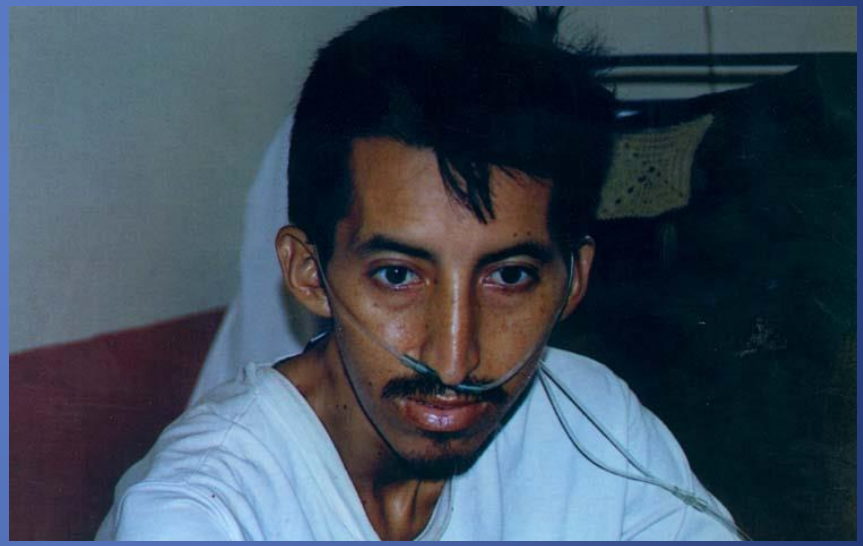
Shorter Regimen Uptake

- DR-TB STAT data limited on shorter regimen
- As of Feb 1, 2018, there were at least 13,072 persons on the shorter regimen.
- Majority of these in Bangladesh, Philippines Francophone Africa, and South Africa (25% in South Africa)



Roll Out of Innovation ***NOT*** Keeping Pace with Need

- People living with DR-TB suffering and dying unnecessarily in era of novel therapeutic approaches ("protecting drugs instead of people" phenomenon).
- Lack of uptake of innovation threatens development of new treatments and drugs for DR-TB ("you can't even give it away" phenomenon).
- Anemic use of new drugs and regimens violates human rights of persons living with DR-TB (right to health and right to benefit from scientific progress).
- Slow uptake raises doubts about global community's ability to "End TB".



Barriers to Uptake of Therapeutic Innovation

- Non-published qualitative study of barriers reported in monthly DR-TB STAT call
- 16 hours of call recordings analyzed for theme and content using standard qualitative methods
- Barriers in multiple categories identified

Reported Barriers

- **1) perceived need for new drugs;**
- **2) interpretation of WHO “recommendations”;**
- **3) issues of cost, registration, and importation;**
- **4) implementation concerns;**
- **5) active TB drug-safety monitoring and management (aDSM) requirements;**
- **6) perceived goal of RR-TB management**

Conclusions

- For the first time in 20 years, multiple novel therapeutic approaches for the treatment of DR-TB.
- Roll out of innovation has NOT keep pace with desperate need.
- New drugs and trials welcomed, but must ensure they can reach people most in need, including those that participated in the trials.
- Approach to DR-TB still conservative and punitive, violates human rights of people living with the disease.
- High-level meetings unlikely to solve field implementation barriers.
- South African model could be an excellent place to start.

Thank you!