DEVELOPMENT OF A GENERIC DR-TB PROTOCOL FOR ALL-ORAL STRS

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TDR For research on diseases of poverty

UNICEF • UNDP • World Bank • WHO

Outline

- Why developing generic research tools
- Key elements of the research package
- Plan & timelines

WHAT IS TDR?

THE SPECIAL PROGRAMME FOR RESEARCH AND TRAINING IN TROPICAL DISEASES:
Building the Science of Solutions

Established in 1975 and hosted by the World Health Organization.

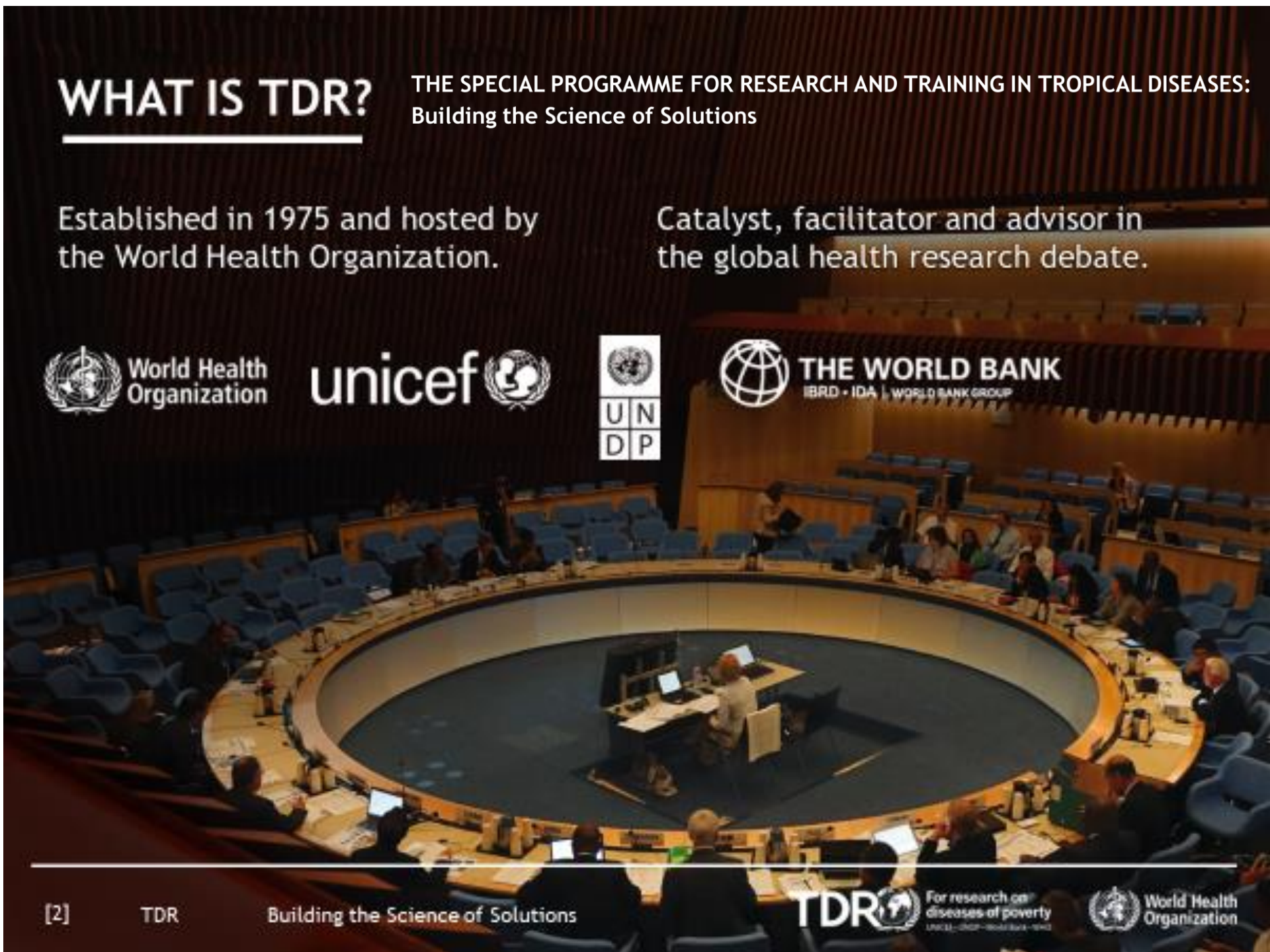
Catalyst, facilitator and advisor in the global health research debate.

World Health Organization

unicef

UNDP

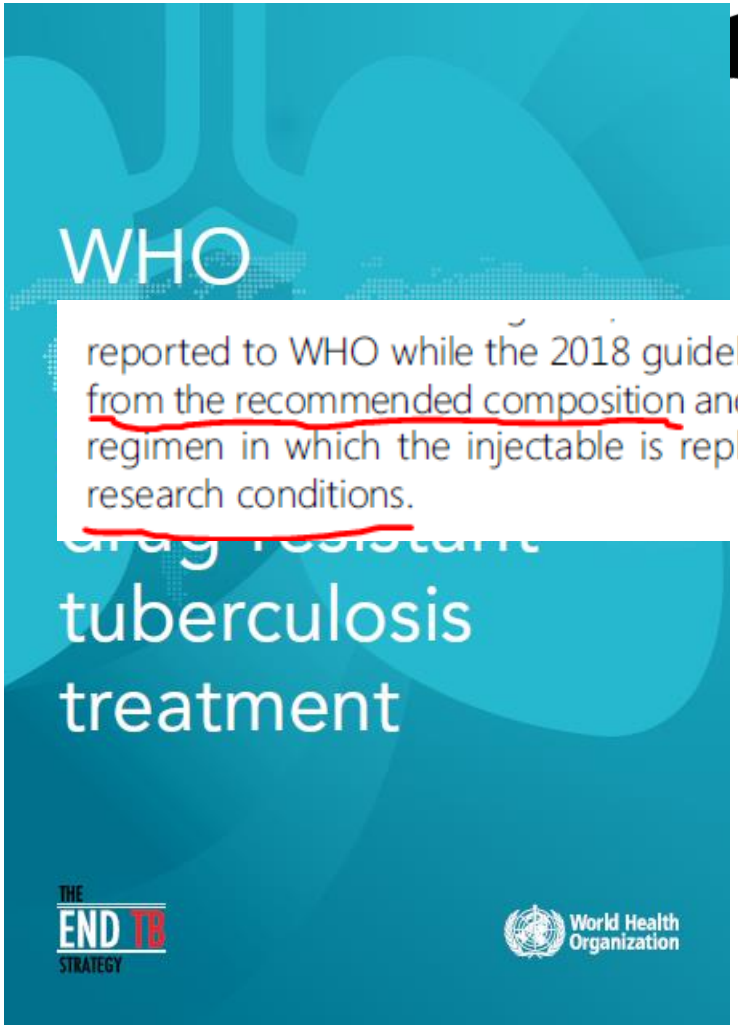
THE WORLD BANK
IBRD • IDA | WORLD BANK GROUP



TDR For research on diseases of poverty

World Health Organization

Rationale



reported to WHO while the 2018 guideline update was in process. Regimens that vary substantially from the recommended composition and duration (e.g. a standardized 9–12-month shorter MDR-TB regimen in which the injectable is replaced by bedaquiline) can be explored under operational research conditions.

How to support NTPs for conducting these OR studies ?

Other aspects to consider

If choosing to implement the use of all oral shorten regimen under OR:

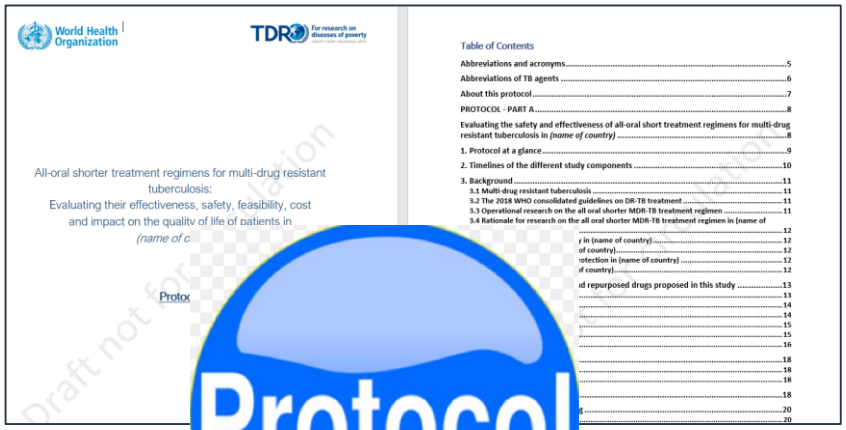
- should look at **national solutions** but also **global needs**

- Data generated by operational research should **complement Randomised Controlled Trial experiences** to better inform MDR/RR-TB guidelines

- **The conduct of operational research** should not slow down the implementation of shorten treatment regimen for the patients

- **Gives the responsibility to the NTPs to fully contribute to the generation of evidences**

Development of a research package for all-oral STRs



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a) **Master protocol**

b) Generic **electronic data collection tools** and guidance for using them (Data toolkit)

c) **set of key study procedures** for the conduct of the studies

d) **Training material** for initiating the study

Development of a research package for all-oral STRs

Objectives

- **To facilitate the conduct** of OR studies for the use of all oral shorten MDR/RR-TB regimen
- **To harmonize data collection** in order to better inform MDR/DR-TB guidelines

Methods

A Collaborative approach

led by TDR

- NTPs

Initiative conducted in concertation with WHO GTB team and WHO regional offices

Master research protocol

Development of an **“à la carte” protocol** to collect data on:

- **Effectiveness** (taking into consideration recurrences),
- **Safety** (strengthening of aDSM),
- impact on **health Quality of Life**
- the **feasibility** (process indicators),
- **the acceptability** (by the patients, by the HCW)
- **the cost** (of implementation)

of the use of all-oral shorten drug regimens for patients with MDR/RR-TB

Master research protocol : 2 Parts

PART 1

For evaluating the **SAFETY and EFFECTIVENESS** of all-oral short treatment regimens for MDR/RR-TB

- **GDI protocol** and other already developed protocols used as a base for the development of this core element

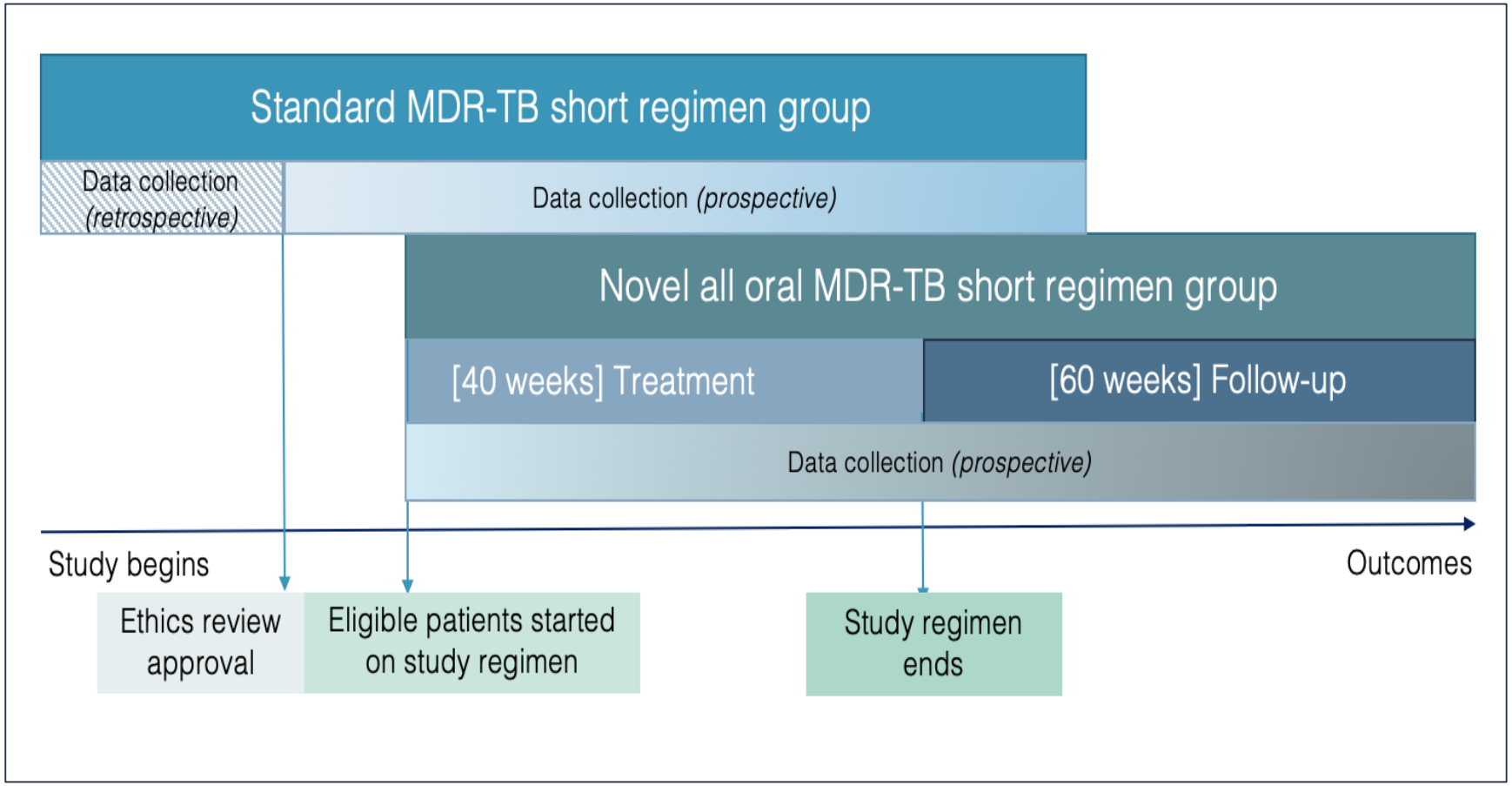
PART 2

Sub studies that can be added to the core study to evaluate other outcomes

- **Impact on HQoL**
- **Stigma**
- **Feasibility & acceptability**
- **Implementation cost & cost-effectiveness**

Differences with the GDI protocol

Study design: Longitudinal design with two almost concurrent cohorts (oral MDR/RR-TB regimen and standard short treatment)



Differences with the GDI protocol

Study Population

The study population includes TB patients with evidence of resistance to rifampicin by conventional DST (culture-based) or rapid DST (Xpert MTB/RIF or LPA) or in the case of children, close contacts of confirmed MDR patients

Pregnant women & children > 3 years are proposed to be eligible

Differences with the GDI protocol

Study outcomes

Primary outcome: the proportion of MDR-TB patients who have **a favourable treatment outcome**.

This is defined as **“cured” without recurrence during 12 months after successful treatment**

Key differences with the GDI protocol

Treatment regimens: 3 regimens highlighted in the master protocol but countries can decide to use other modified treatment regimen

<u>For FQ sensitive patients:</u>

Treatment regimen 1:

6 Bdq-MfX- Pto-Cfz-Z- Hhigh dose-E/3-6 MfX-Cfz-Z-E

Treatment regimen 2:

2 Lzd-Bdq-Lfx-Cfz-Z/4Bdq-Lfx-Cfz-Z/3 Lfx-Cfz-Z

<u>For FQ resistant patients:</u>

Treatment regimen: 9 Bdq+Cfz+Dlm+Lz(600 mg)

Master research protocol

PROTOCOL - PART B

Evaluating the acceptability, feasibility and the impact on health-related quality of life of all-oral short treatment regimens for multi-drug resistant tuberculosis in *(name of country)*

- Sub-study for evaluating the impact on HRQoL: **Section 2**
- Sub-study for measuring stigma: **Section 3**
- Sub-study for assessing feasibility and acceptability: **Section 4** & **Section 5**
- Sub-study for evaluating cost-effectiveness: **Section 6**

Data collection tool

Harmonized data collection at least for the core variables

- In coherence with McGill DB
- Effort to agree on key outcomes definitions
- The tool will facilitate data collection and datasharing

Timelines

- 1st meeting of the protocol writing committee in April 2019
- July 2019: 1st draft of the protocol
- Protocol and data collection tools should be made available by the **end of the summer 2019**
- Open access and freely available
- Support to NTPs for using this research package can be provided through partners
- The package could be used in full or in part

Conclusion

- Research package available for OR implementation **Q4 2019**
- Other research packages/tools are also underdevelopment
- Common goal looking for **national solutions** but also considering **global needs**
- **Harmonized data collection** in order to better inform MDR/DR-TB guidelines
- **Contribution of NTPs is essential**

Aknowledgements

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Thank You