

MDR-TB Current status

Stellah Mpagama

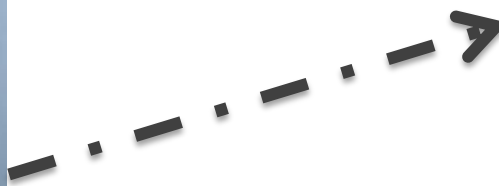
Background

Tanzania stated MDR-TB case management in Nov 2009

KNTH



**Scaling up to
Regional referral hospital**



Capacity building UCSF



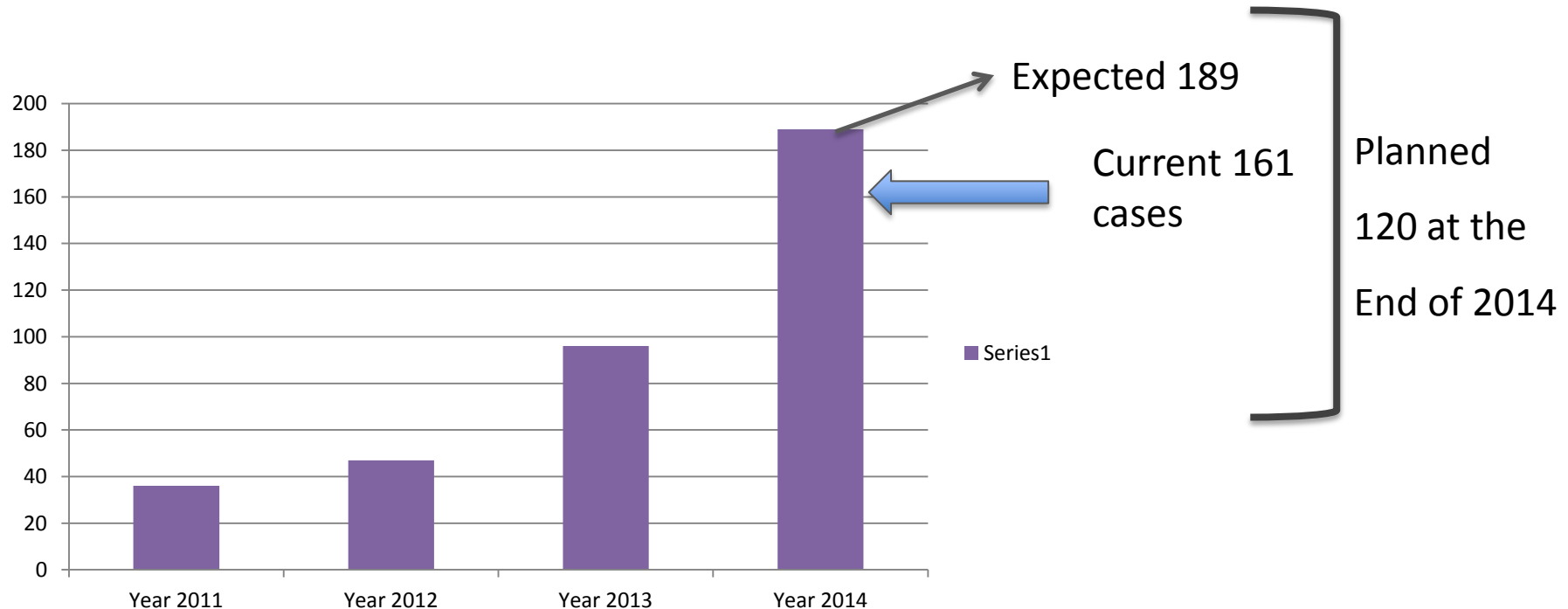
**2015 at least 6
Regional Hospitals
HSSP III 2009 - 2015**

Background

From Nov 2009 until yesterday

– admitted 339 MDR-TB patients

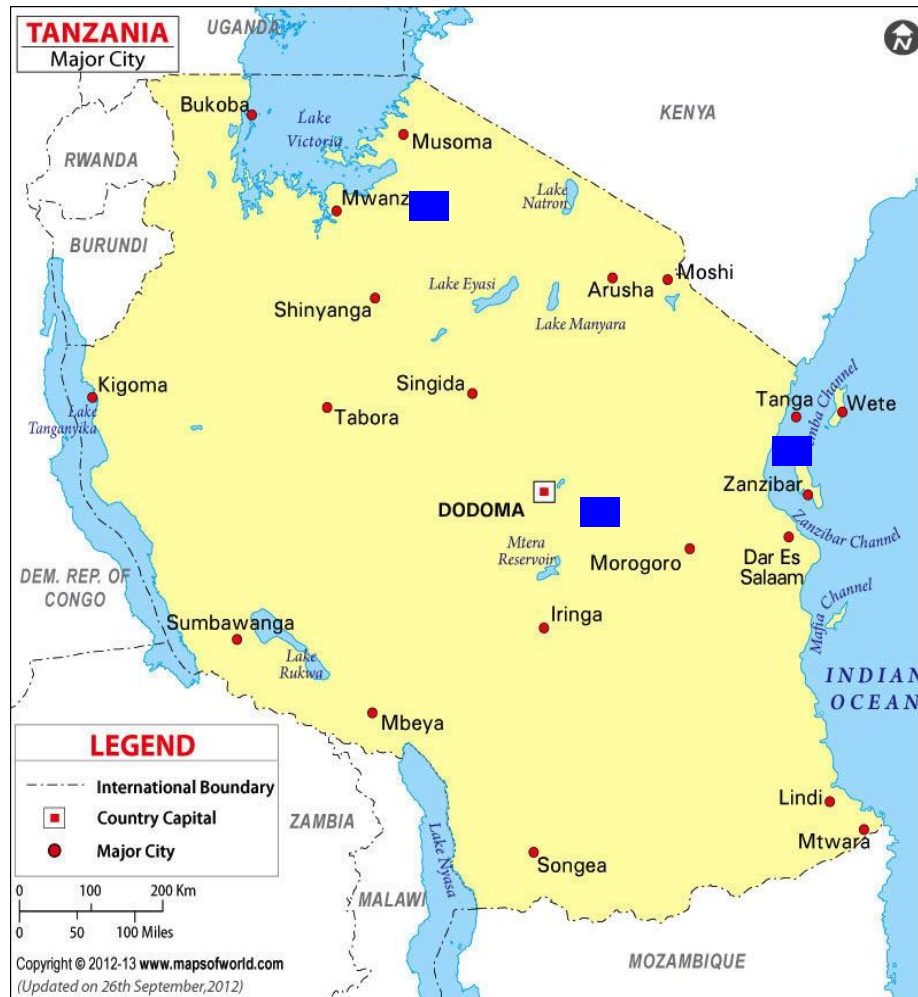
MDR-TB cases reported for treatment at Kibong'oto hospital



Scaling of MDR-TB Centers

HSSP 2009 – 2015

Scale MDR-TB to the regional referral hospitals



Scale depends
On the # of cases
diagnosed

Background

MDR-TB case management

Group 1	First line oral anti-tuberculosis medicines: Isoniazid, rifampicin, pyrazinamide , ethambutol
Group 2	Flouroquinolones: ofloxacin, levofloxacin , moxifloxacin
Group 3	Injectable anti-tuberculosis medicines: streptomycin, kanamycin , amikacin, capreomycin
Group 4	Less effective second-line anti-tuberculosis medicines: Ethionamide /prothionamide, cycloserine /terizidone, P-aminosalicylic acid (acid/salt)
Group 5	Less effective medicines or medicines for which clinical data are sparse: clofazimine, amoxicillin with clavulanate, linezolid, imipenem, clarithromycin, high dose isoniazid, thiacetazone

Intensive phase = 8months

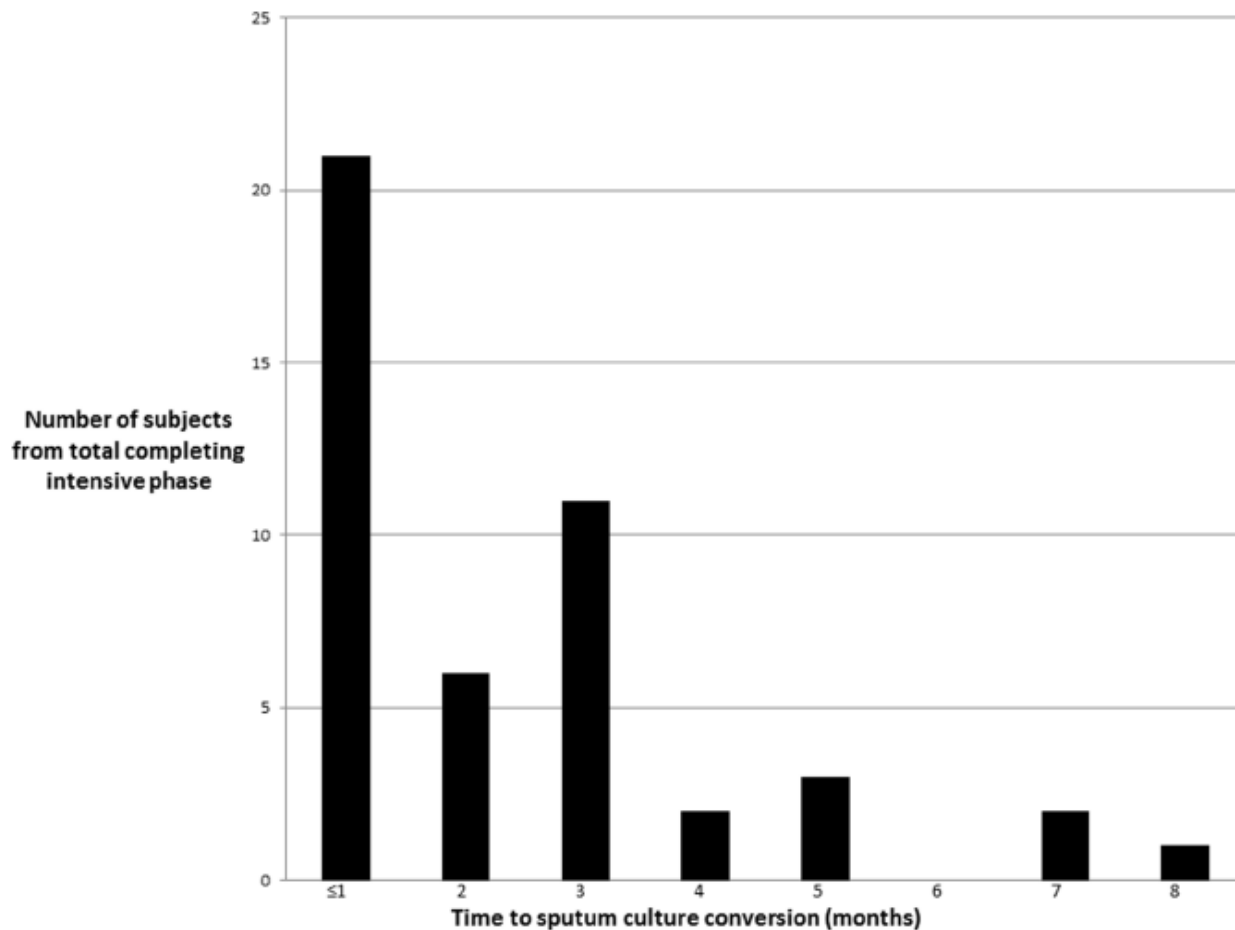
Continuation phase = 12-18

Microbiological monitoring
Monthly culture/smear

Adverse events monitoring
Daily

Background

Distribution of culture conversion in MDR-TB Patients



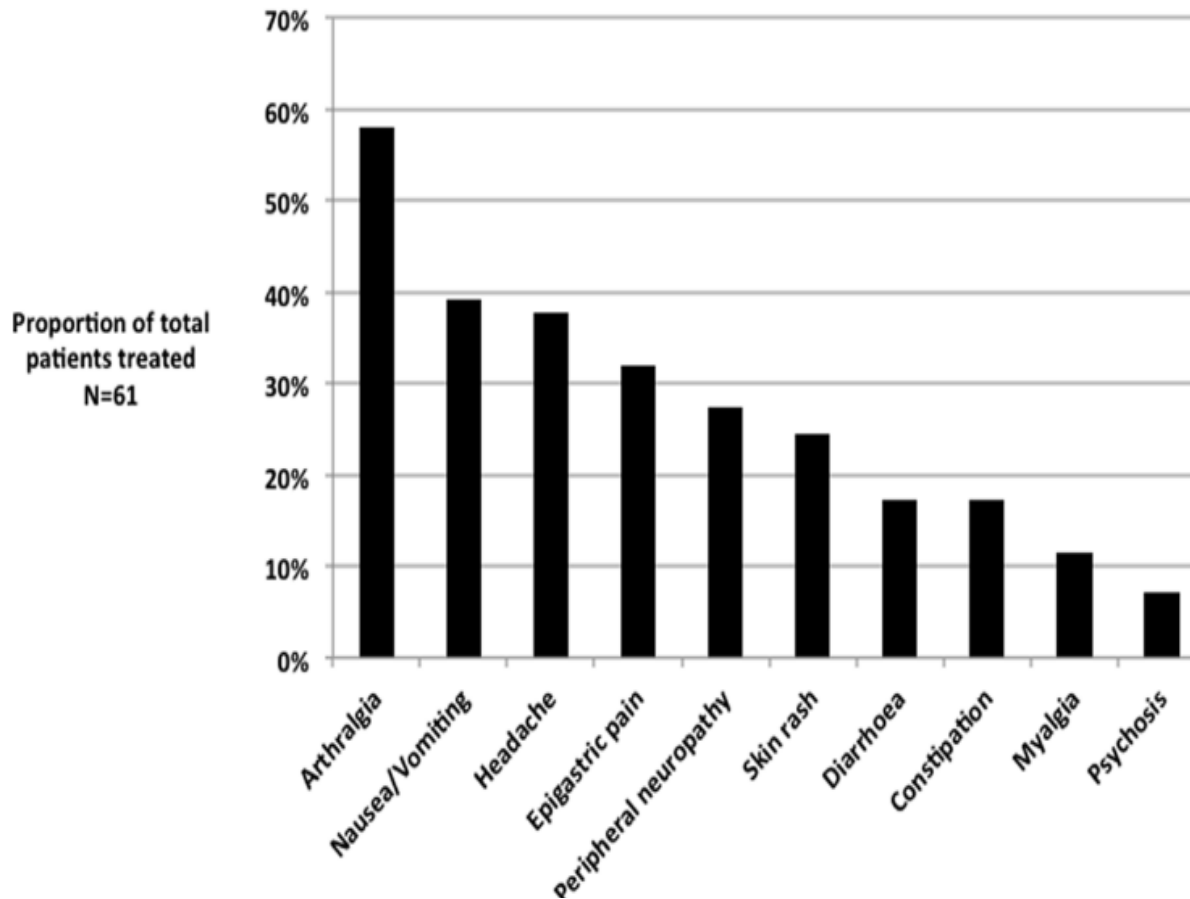
Mpagama et al, PLoS ONE. 2013

Drug Susceptibility Testing of MTB from MDR-TB Patients

Characteristics	Sub-category	Number
Secondline(DST) resistant MTB	XDR-TB	2 (13%)
	Ethionamide	6 (40%)
	PAS	5 (23%)
	Moxifloxacin	1 (5%)
	Amikacin/Kana mycin	2(10%)

Treatment monitoring

Distribution of adverse events (reported top 10 events)



Ototoxicity = 3 (1%)

Nephrotoxicity = (2%)

Both nephrotoxicity
Ototoxicity = (1)

Challenges in diagnosis

Estimate of MDR-TB Burden in 2012 (WHO Report 2013)

TB case notification 2012	Prevalence of MDR-TB	# Tested	MDR-TB diagnosed
New (61,126)	1.1%	639 (3%)	12
Retreatment (2, 766)	5.9%	108 (4%)	12

Challenges in MDR-TB treatment

Treatment Regimen

❖ Lengthy

❖ Complex

❖ Poor tolerated

Principles for designing future regimens for multidrug-resistant tuberculosis

Bridgden et al , 2013

- ❖ Regimen contain at least 1 new class of drug
- ❖ Treat both MDR or XDR TB
- ❖ Contain 3 -4 effective drugs from a different drug class
- ❖ Exclusive oral delivery

Principles for designing future regimens for multidrug-resistant tuberculosis

- ❖ Simple dosing schedule
- ❖ Good side effect profile that allow limited monitoring
- ❖ Minimal interaction with ART drugs
- ❖ Maximal duration of 6 months

Am J Respir Crit Care Med. 2010 Sep 1;182(5):684-92. doi: 10.1164/rccm.201001-0077OC. Epub 2010 May 4.

Short, highly effective, and inexpensive standardized treatment of multidrug-resistant tuberculosis.

[Van Deun A](#)¹, [Maug AK](#), [Salim MA](#), [Das PK](#), [Sarker MR](#), [Daru P](#), [Rieder HL](#).

+ Author information

Abstract

RATIONALE: Based on expert opinion, the global guidelines for management of multidrug-resistant tuberculosis impose lengthy and often poorly tolerated treatments.

OBJECTIVES: This observational study evaluates the effectiveness of standardized regimens for patients with proven multidrug-resistant tuberculosis previously untreated with second-line drugs in low-income countries.

METHODS: Consenting patients were sequentially assigned to one of six standardized treatment regimens. Subsequent cohorts were treated with regimens adapted according to results in prior cohorts. The study was designed to minimize failure and default while reducing total treatment duration without increasing relapse frequency.

MEASUREMENTS AND MAIN RESULTS: We report the treatment outcome of all patients with laboratory-confirmed, multidrug-resistant tuberculosis enrolled from May 1997 to December 2007. The most effective treatment regimen required a minimum of 9 months of treatment with gatifloxacin, clofazimine, ethambutol, and pyrazinamide throughout the treatment period supplemented by prothionamide, kanamycin, and high dose isoniazid

1997 - 2007

Treated 207

Short regimen 9 month

Containing Gatifloxacin, Clofazimine, Ethambutol, Pyrazinamide throughout

Supplemented by Kanamycin, High dose Isoniazid and Prothionamide for a minimum of 4/12

Relapse free 87.9%

http://www.controlled-trials.com/ISRCTN78372190 — ISRCTN78372190 - The evaluation of a standardised treatment regimen of anti-tuberculosis drugs for patients with multi-drug-resistant tuberculosis (MDR-TB) — Yahoo!

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ISRCTN78372190 - The evaluation of a standardised treatment regimen of anti-tuberculosis drugs for patients with multi-drug-resistant tuberculosis (MDR-TB)

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ISRCTN REGISTER

- Trial registration
- Unique identification scheme
- International databases

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ISRCTN FAQs

data set

letter of agreement

request information

guidance notes

statistics

The evaluation of a standardised treatment regimen of anti-tuberculosis drugs for patients with multi-drug-resistant tuberculosis (MDR-TB)

ISRCTN	ISRCTN78372190
DOI	10.1186/ISRCTN78372190
ClinicalTrials.gov identifier	
EudraCT number	
Public title	The evaluation of a standardised treatment regimen of anti-tuberculosis drugs for patients with multi-drug-resistant tuberculosis (MDR-TB)
Scientific title	The evaluation of a standardised treatment regimen of anti-tuberculosis drugs for patients with multi-drug-resistant tuberculosis (MDR-TB): a multi-centre international parallel group randomised controlled trial
Acronym	STREAM
Serial number at source	N/A
Study hypothesis	<p>To determine whether a standardised regimen utilising existing drugs that has been used in one country setting with excellent treatment outcomes can be used in other settings with comparable success.</p> <p>Patients with Multidrug-Resistant Tuberculosis (MDR-TB) are currently treated for 18-24 months, based on recommendations by the World Health Organisation (WHO). Treatment success rates are poor.</p> <p>In a study carried out by Dr. Van Deun (2010) in Bangladesh, patients with MDR-TB were treated for only nine months with excellent results.</p> <p>The STREAM trial assesses whether a treatment closely similar to that used in Bangladesh is as good as the treatment for MDR-TB recommended by WHO. If the results are positive, it will be possible to treat patients with MDR-TB in different countries for only nine months.</p> <p>On 28/09/2011 the following changes were made to the trial record:</p> <ol style="list-style-type: none"> 1. Ethiopia and South Africa were added to the countries of recruitment. 2. The anticipated start date was changed from 03/01/2011 to 15/11/2011. 3. The source of funding was changed from 'International Union Against Tuberculosis and Lung Disease (The Union) (France)' to 'The United States Agency for International Development (USAID) (USA)' <p>On 13/11/2012 the following changes were made to the trial record:</p> <ol style="list-style-type: none"> 1. The anticipated end date was changed from 15/05/2015 to 30/10/2016. 2. India was added to the countries of recruitment <p>Please note that as of 15/11/2012, this trial is now recruiting</p>

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-Ethiopia
-South Africa

**Not yet
recruiting**

A Phase 2 Open Label Partially Randomized Trial to Evaluate the Efficacy, Safety and Tolerability of Combinations of Bedaquiline, Moxifloxacin, PA-824 and Pyrazinamide in Adult Subjects With Drug-Sensitive or Multi Drug-Resistant Pulmonary Tuberculosis.

Condition: Tuberculosis

Interventions: Drug: Pa-824; Drug: bedaquiline; Drug: moxifloxacin; Drug: pyrazinamide; Drug: isoniazid, rifampicin, pyrazinamide and ethambutol combination tablet

A large white cross is centered on a dark purple background. A dark purple diagonal banner with a thin white border crosses the center of the cross. The banner contains the text "Thank you for your attention" in white, bold, sans-serif font, oriented diagonally from the bottom-left to the top-right.

Thank you for your attention