

Integrating MDR TB Care in Burma, Uzbekistan and Uganda: Lessons learned for global scale up

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Objectives

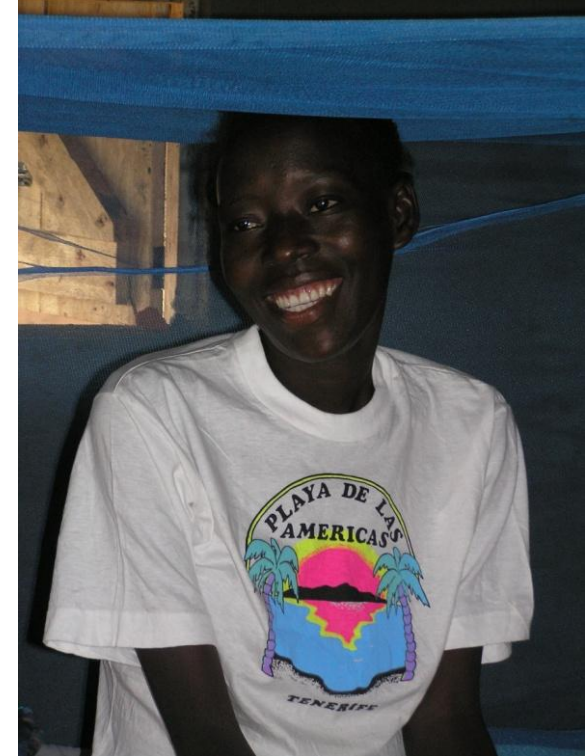
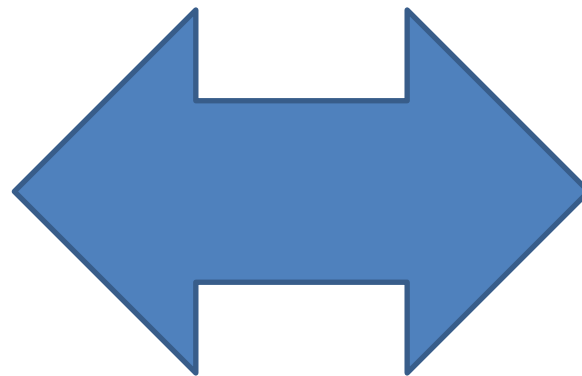
- Main principles in starting a DR TB programme
- Understand major global constraints to scale up of DR TB treatment
- Understand the main obstacles faced by medics in a programme
- Formulate potential solutions to these obstacles

Guidelines for the programmatic management of drug-resistant tuberculosis

2011 update

Guidelines for the programmatic management of drug-resistant tuberculosis

EMERGENCY UPDATE 2008



Overview



- Uzbekistan
 - Bringing MDR TB treatment to scale
 - Global Challenges
- Myanmar/Burma
 - Programmatic Challenges
- Manipur, India
 - Simplification and Task Shifting

Karakalpakstan, Uzbekistan



TB in Uzbekistan

- TB incidence Uzbekistan
128 / 100,000
- Estimated 62,000 cases
- 17540 cases notified
 - 7.8% DST
- 8700 MDRTB cases 2009
 - Approx 5% diagnosed



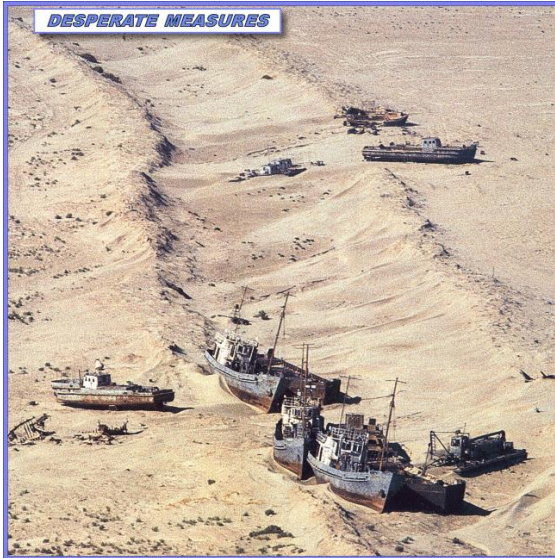
July - September, 1989



October 5, 2008

- Aral Sea Disaster

Aral Sea Environmental Disaster



- poisonous sandstorms, chronic health problems, dead fishing grounds and unemployment.



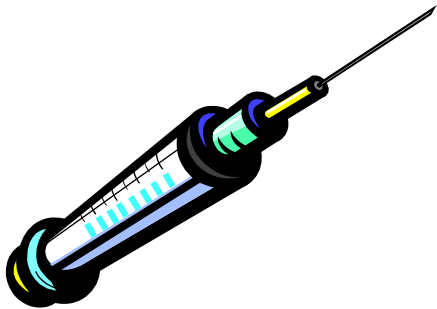
High prevalence of MDR TB in Central Asia

- Abrupt collapse of health system with break-up of soviet union
- Inefficient TB program which still uses outdated practices and concepts e.g. seasonal treatment
- Very centralized healthcare system
- Still existing non-DOTS (parallel NTP) and a clandestine private sector treatment providing inadequate TB regimens

Global Challenge 1: Health System Strengthening

Multi Drug Resistant Tuberculosis (MDR TB)

- Best drugs = isoniazid and rifampicin
- MDRTB resistant to both isoniazid and rifampicin
- Then for 2 years take
- With 8+ months



Problems With MDR TB Treatment

- Cost
- Duration
- Complexity
- Diagnostics
- Side Effects



PASer – after experiencing days of nausea and vomiting some patients get anticipatory nausea just on seeing this drug

History

- MSF: 1998 – 2004 DOTS tuberculosis program
- 2001: Drug resistance survey
 - 13% in new & 40% in retreated cases
- 2002: Green Light Committee application - (joint MSF-MoH)
- 2003: First patients admitted – treatment failures
- 2006: DST for all TB suspects



Global Challenge 2: Technical Capacity

- Lack of skilled staff to advise on commencing programmes
- Lack skilled staff to train and supervise

Rationale for the revision of current mechanism to support MDR-TB scale-up



- Slow scale up of MDR-TB management
- Limited political commitment and capacity of countries
- *The current mandate of the GLC acting as bottleneck*
- Member states have committed to achieve universal access to diagnosis and treatment of MDR-TB by 2015 (WHA Resolution 62.15)
- GLC not completely in conformity to WHO rules and practice

Stakeholder consensus to revise the Global Framework to support expansion of MDR-TB services which "should explicitly **shift from a controlling to a supporting mode**"

What the GLC Framework will do

- gGLC
 - Review global progress
 - Coordinate technical assistance strategy
 - Advise WHO and all partners in addressing priority issues in MDR-TB management scale up (see later)
 - Review secretariats' response to requests for advice from funding agencies
 - Coordinate with regional GLCs
- rGLCs
 - As above, with regional focus
 - Coordinate with gGLC
- Secretariat
 - Organize TA
 - Collate monitoring and evaluation, through global data collection, and national mission reports, and report to GLCs
 - Prepare bulk of advice for funding agencies, synthesize results for GLCs, discussing in detail difficult cases only
- GDF
 - (See later slide)

The Current Program

- According to WHO guidelines
 - Individualised regimens
 - Quality assured medications
 - Trained staff
 - Psychosocial support
 - Medical consultations to discuss difficult cases



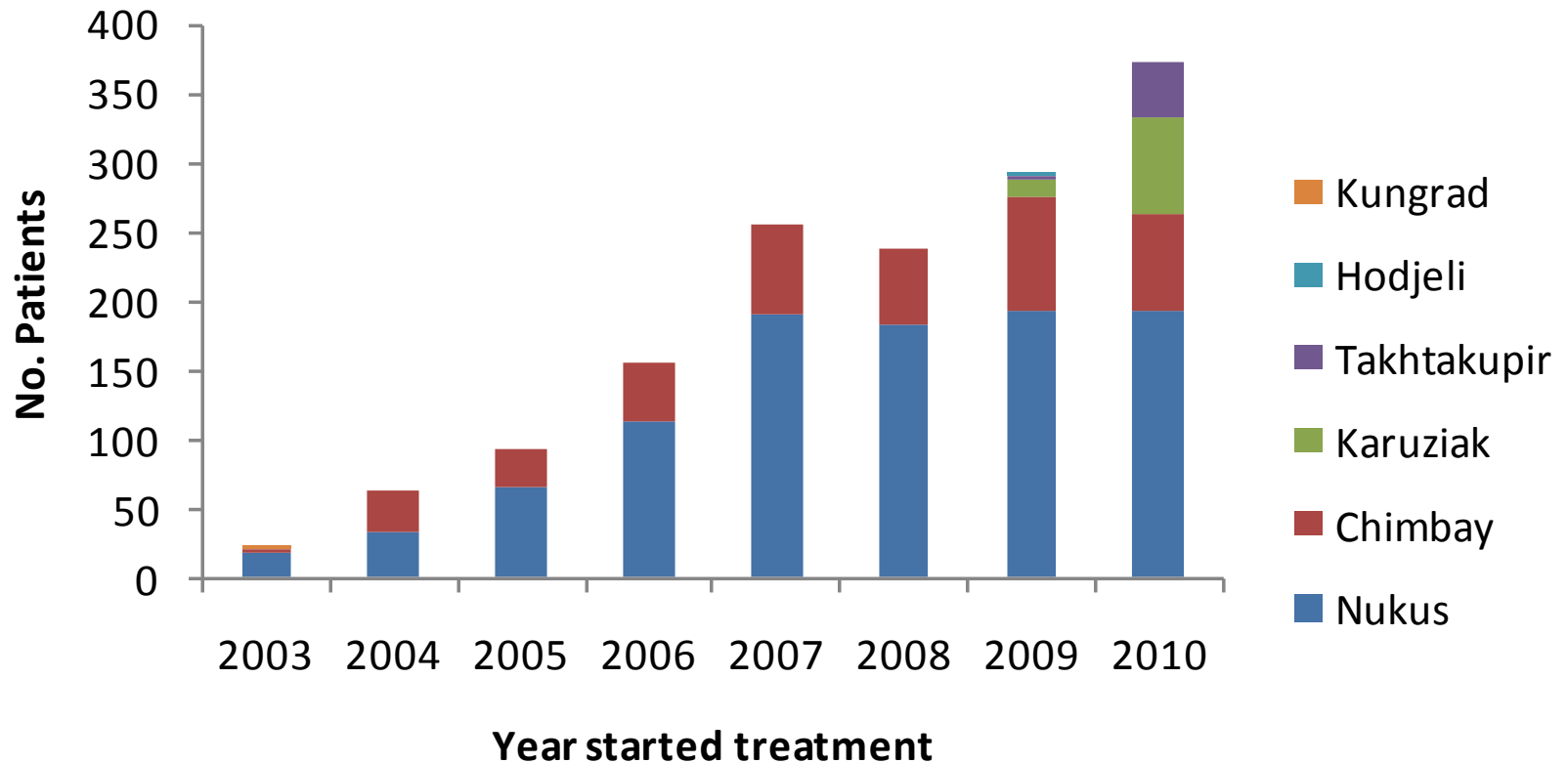
Global Challenge 3: Laboratory Capacity

- External proficiency testing of Laboratory
 - Liquid culture
 - Molecular test (GenoType MTBDR-plus assay)
 - 1st and 2nd line DST



Case Finding

DR TB Patients enrolled 2003-2010



Global Challenge 4: Funding

- Cost per patient \$4000+
- Cost 500 patients 2 million (drugs only)
- Uzbekistan 8700 = \$34.8 million
- Globally 2011-2015 estimated \$7 billion required for scale up MDR TB

Global Challenge 5: Drugs

- Drug availability
 - Most second line drugs 1 approved source
 - Companies produce what they are assured of selling
- Global shortages in 2011:
 - Streptomycin
 - Kanamycin
 - Capreomycin

Case Finding – Nukus and Chimbai

- Patients resistant to an average of 4.3 drugs.
- Most patients treated with
 - Pyrazinamide
 - Kanamycin (Capreomycin)
 - Levofloxacin (moxifloxacin)
 - Cycloserine
 - Prothionamide
 - Para-amino salicylic acid (PAS)
- 3rd line drugs available (clofazamine, amoxicillin/clavulante, clarithramycin)

Global Challenge 6: Restrict availability of Drugs

Research Article

Over the Counter Availability of Antituberculosis Drugs in Tbilisi, Georgia in the Setting of a High Prevalence of MDR-TB

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Recommended by Jonathan Mayer

Georgia, a country of 4.5 million people, has a high incidence of tuberculosis (TB) including drug resistant cases. Easy access and inappropriate use of anti-TB drugs are risk factors for further development of multidrug resistant (MDR)-TB. We carried out an investigation to assess the availability of over the counter anti-TB agents in pharmacies in Tbilisi. During February 2006, 15 pharmacies were randomly selected and the pharmacist at each store was interviewed. We found that all anti-TB medications stocked by these pharmacies were available and sold without a prescription. All 15 pharmacies sold isoniazid, rifampicin, and streptomycin; 13 (87%) of 15 pharmacies also sold pyrazinamide, ethambutol. Second line anti-TB drugs such as amikacin and kanamycin (injectable agents) and older fluoroquinolones (ofloxacin and ciprofloxacin) were available at 13 pharmacies while newer generation fluoroquinolones were less available (3 sold levofloxacin, none sold moxifloxacin). The ease access and availability of anti-TB agents is of a great concern given the high prevalence of TB including MDR-TB in Georgia. The potential for misuse of these anti-TB drugs can lead to the development of further drug resistance. These drugs should only be available by prescription in order to reduce the chance of amplifying drug resistance.

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Outcome Definitions

- **Cured**
- **completed treatment**
- at least five consecutive negative cultures
- From samples collected at least 30 days apart
- in the final 12 months of treatment.
- (or 1 positive with last 3 negative)

Outcome Definitions

Treatment completed

- **completed treatment** according to protocol
- but does not meet the definition for cure because of lack of bacteriological results

Outcome Definitions

Died

- **patient who dies for any reason during the course of MDR-TB treatment.**

Outcome Definitions

Failed

- **two or more of the** five cultures recorded in the final 12 months of therapy are positive,
- Or if any one of the final three cultures is positive
- if a clinical decision has been made to terminate treatment early because of poor clinical or radiological response or adverse events.

Outcome Definitions

Defaulted.

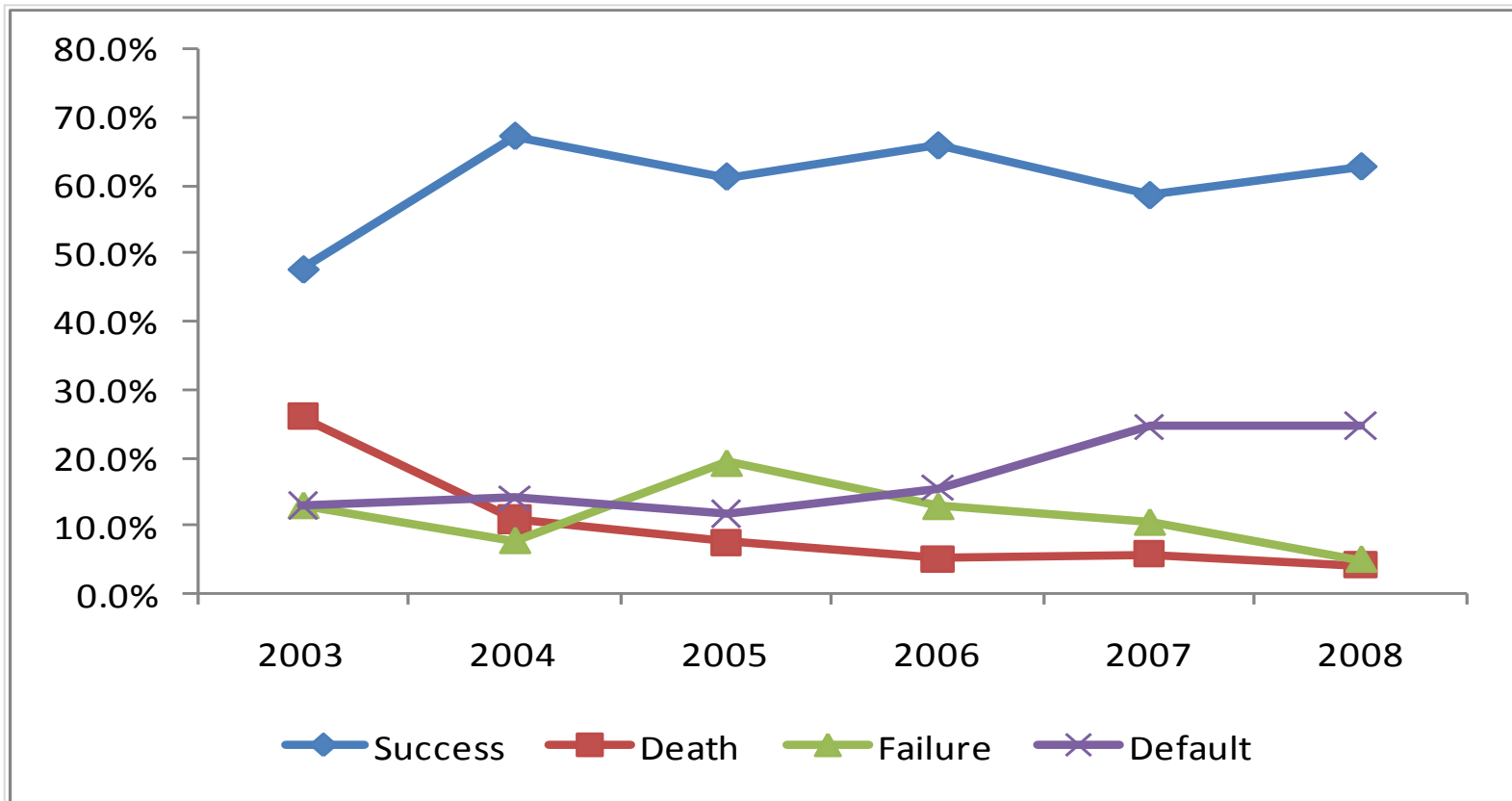
- **treatment interrupted for 2** or more consecutive months for any reason without medical approval.

Transferred out

- **transferred to another** reporting and recording unit and for whom the treatment outcome is unknown.

Outcomes

- 709 patients MDR TB enrolled b/w 2003 -2008
- The overall rate of success was 62%,
 - New patients (74%) compared to previously treated (60%).



Risk factors for default

- Preliminary univariate analysis

Risk Factor	Odds Ratio	95% Confidence Interval
male	1.45	1.00-2.10
age > 45 years	1.59	1.02-2.49
Health care worker	2.59	1.14-5.86
Previous travel outside the region	1.86	1.17-2.88

TB Anywhere is TB everywhere

- Infection Control
- Migration
- Prisons

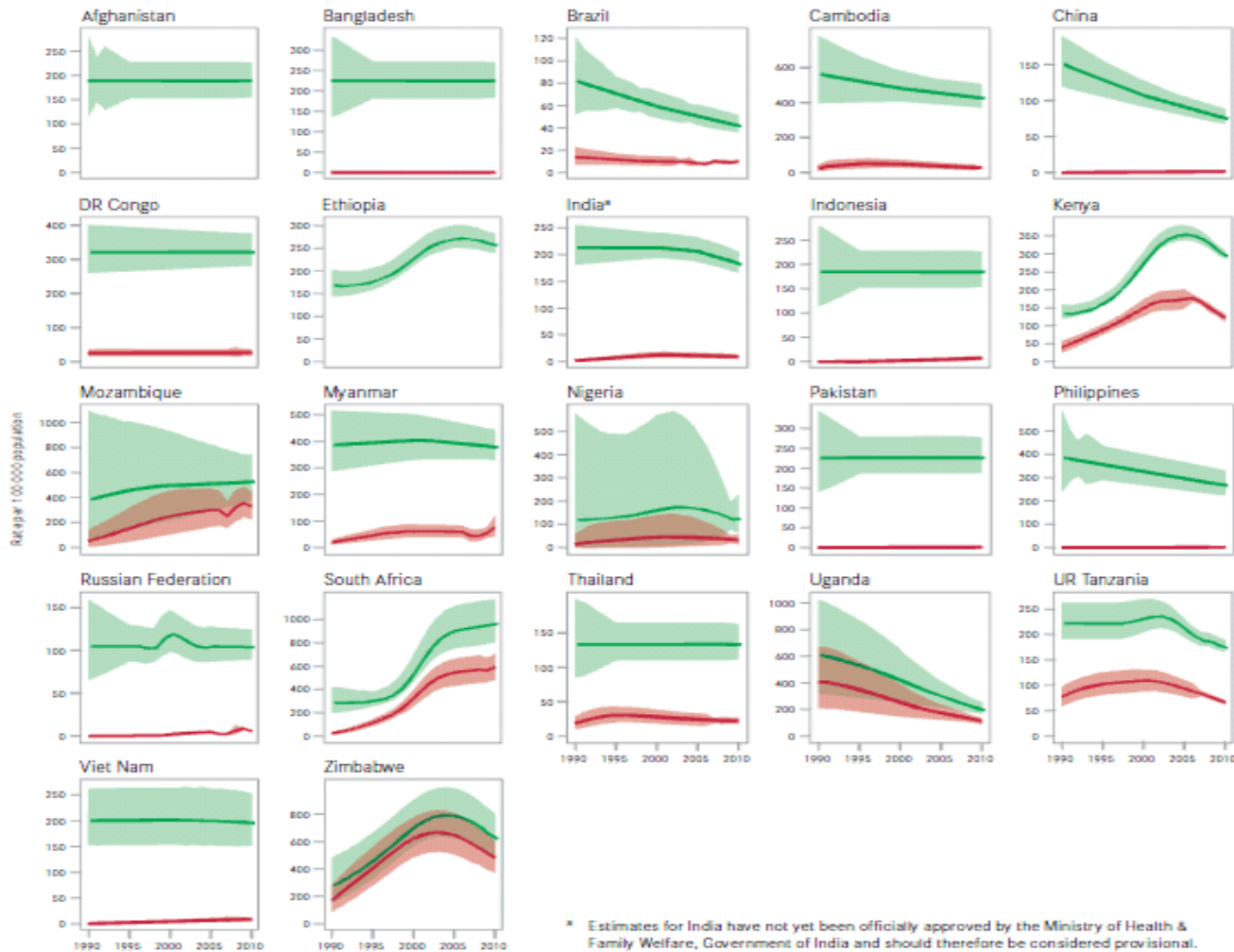


TB treatment, Kyrgyzstan Prison © William Daniels / Panos pictures and MSF

Global Challenge 7: Improve Surveillance Systems

FIGURE 2.7

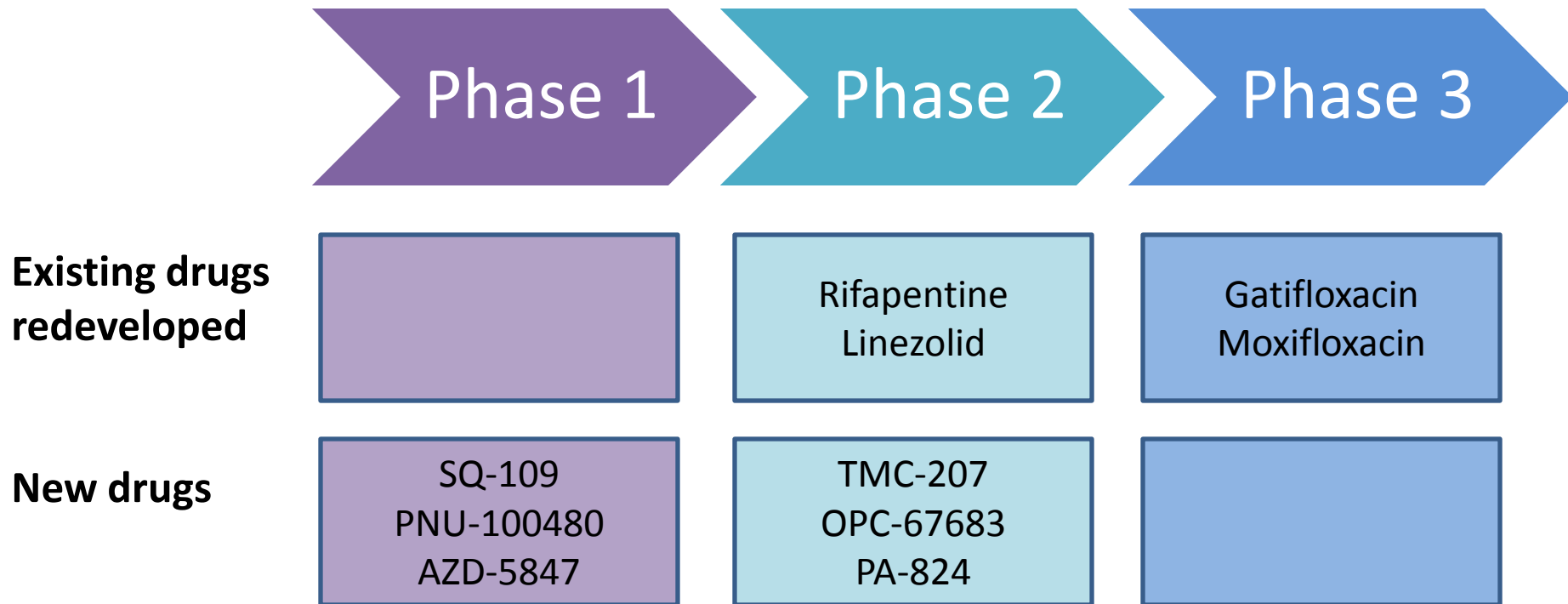
Estimated TB incidence rates, 22 high-burden countries, 1990–2010. Trends in estimated TB incidence rates (green) and estimated incidence rates of HIV-positive TB (red). Shaded areas represent uncertainty bands.



But what about failure cases?

- Patient with heavy alcohol use
- Failed MDR TB treatment
- Failed XDR TB treatment
- 3+ smear positive
- Resistance documented to all available TB drugs in country
- Should he be forced into isolation for community protection or allowed palliative care at home?

Global Challenge 8: Research New drugs, regimens, vaccine



Adapted from Zhenkun et al. Lancet. Published online May 19, 2010 DOI:10.1016/S0140-6736(10)60359-9

Comprehensive TB Care

- Rapid molecular diagnosis and treatment for drug sensitive and DR TB patients
- Expansion from 4 to 16 districts by 2013
- Ambulatory treatment from start of treatment
 - Less time in hospitals with inadequate infection control may also reduce cross-infection.
 - Decentralising care closer to where patients live aimed to increase case finding and reduce default
- Investing in improved psychosocial support
- Improving infection control.

Global Challenges

Funding

Drugs

Technical
Capacity

Laboratory
Capacity

Unrestricted
access TB
drugs

Surveillance
Systems

Research

Health System
Strengthening

Groups – 10 minutes

List all aspects you think are needed
to set up MDR TB care

Tuberculosis in Myanmar

- Estimated incidence
403 / 100,000
- Case Detection rate =
35% (smear +ve)
- 11% cases HIV positive
- MDR TB:
 - 4.2% new cases
 - 10% retreatment cases



Projects

- 15 years
- 5 States
- Focus: HIV and TB
- Also in Rakhine
 - Over 200,000 cases malaria treated per year



Working with Partners: National TB Programme, WHO and MSF



Programmatic Challenge 1: Drug Importation

- Delays
 - Drug order placed June 2008
 - Arrived 1 year later (world-wide shortage)
- Unable to import some drugs
 - E.g. for treatment of patients with failure or XDR TB (e.g. capreomycin, 3rd line TB drugs)
- Short expiry dates for some drugs (12-18 months)

Model of Care

- Patients admitted to hospital for 2 months to stabilise on DR TB treatment
- Standardised Regimen of 6 drugs
Z-Am-Lfx-Cs-Eto-PAS
Based on resistance survey results
- Injection for 8 months (or 4 months post conversion)
- 18 months continuation phase
- Ambulatory treatment home based or community clinic based

PC 2: Best Models of Care?

- The God Complex – “I am the expert and this is what should be done”
- What is the evidence for hospitalisation preventing transmission?

Advocate for Patients

Patient

- 32 year old
- Failed category 1 and 2 treatment
- Sputum smear +ve, culture → MDR TB
- HIV +ve; not on antiretrovirals; CD4 = 370
- Previous poor adherence
- Homeless, intermittently lives with sister and her 2 year old child.

PC3: Social/Financial Barriers

- Donors / Global fund often do not include necessary supports for patient treatment
 - Home infection control
 - Food
 - Side effect drugs
 - Incentives
 - Psychosocial support / counselling

PC 4: Stigma

- HIV/MDR TB
- Risk of death by 1 year without treating MDRTB is 70%+
- Stigma
 - from community?
 - From family/friends?
 - From health staff?

Listen to People with MDR TB

- DR TB patient Blogging platform
<http://msf.ca/blogs/tb/>
- Patients from 7 countries with MDR TB
- Issues
 - back biting (stigma)
 - Patient motivation
 - Side effects like becoming deaf
 - isolation

Myanmar DOTS Plus Pilot Project

- Planned enrolment of 275 patients in 2 years
- Estimated incident cases MDR TB 9300



PC 5: Infection Control

- Difficult to implement all recommendations from the WHO infection control guidelines
 - lack of budget,
 - limited time of staff members,
 - initial limited knowledge of staff members about TB infection control.

Infection Control

- Participatory approach → gradual improvements



Infection Control

- Participatory approach → gradual improvements

	Baseline	1 year after implementation
Facility-level managerial activities	1 of 6 items acceptable	4 of 6 items acceptable
Administrative controls	4 of 10 items acceptable	8 of 10 items acceptable
Environmental controls	1 of 3 items acceptable	2 of 3 items acceptable
Personal protective equipment	0 of 3 items acceptable	3 of 3 items acceptable
Staff members diagnosed with TB preceding year	3 /50	0 /50

PC 6: Timely diagnosis

- In 2009 – 64 HIV patients died in 4 HIV clinics
- Of these 12 patients confirmed MDR TB
- 1 of whom was started on treatment

- Need to diagnose and start treatment promptly

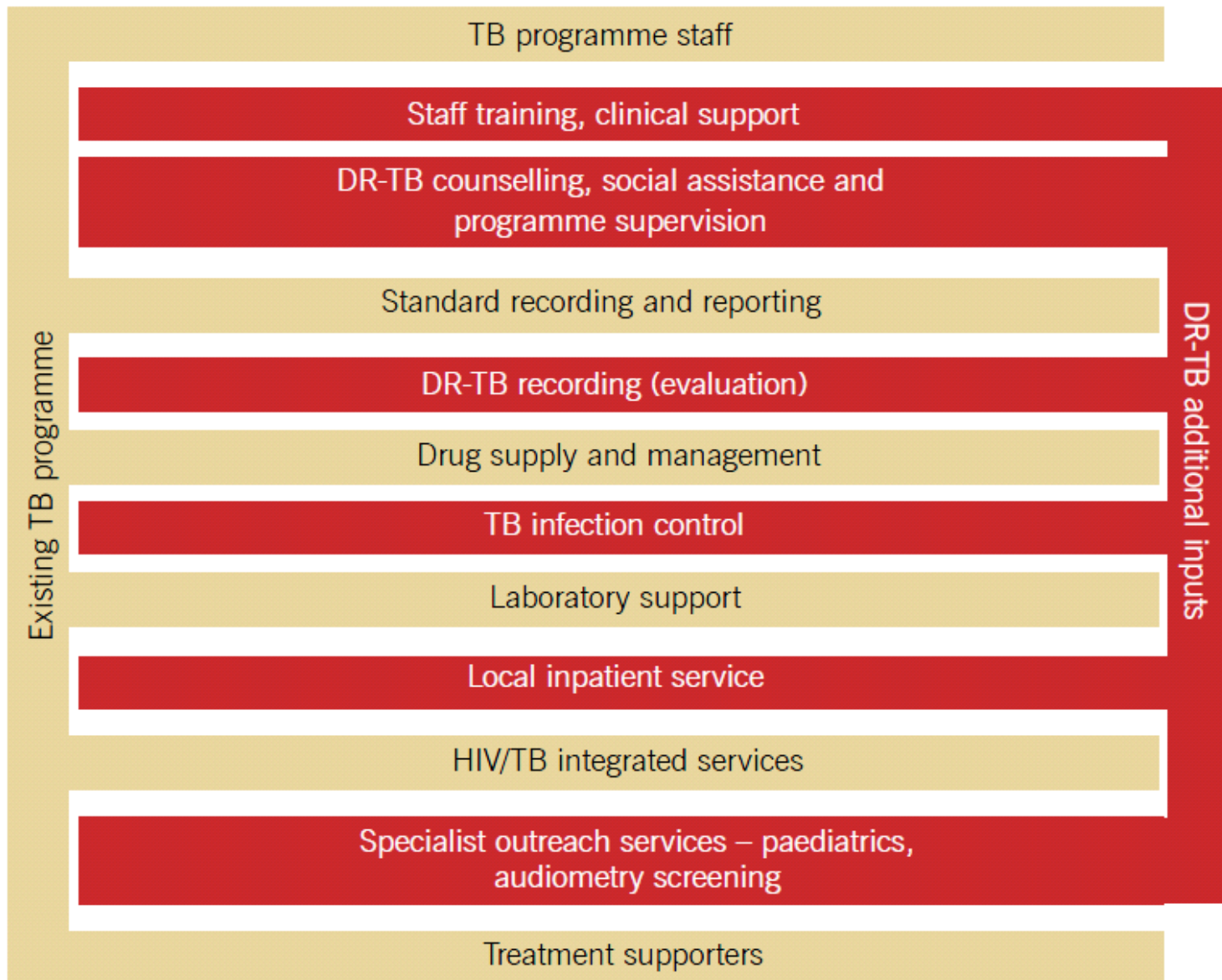
Timely laboratory diagnosis

- Solid culture – 2-3 months
- Liquid culture – 1-2 months
- Hain test – 1-2 days
- Xpert MTB rif – 2 hours

Empiric Treatment

- 1 year later
- On treatment
- Blogging on line from rural Uganda

PC 7: Integration



PC 8: Skilled Staff

- Training – need for on the job training
 - Telemedicine / teleradiology / discussion forums
- In Myanmar – in first 2 years – 3 programme managers trained → left to take jobs elsewhere
- Lack doctors: can we shift tasks to other health staff

Programmatic Challenges



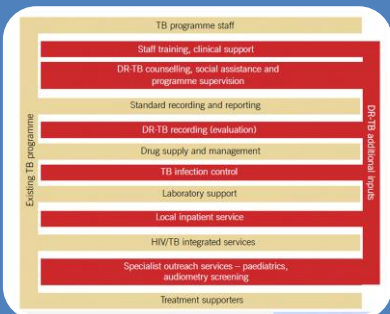
Stigma

Social & Financial
Adherence



Skilled human resources (task shifting)

Timely diagnosis and treatment
The God Complex



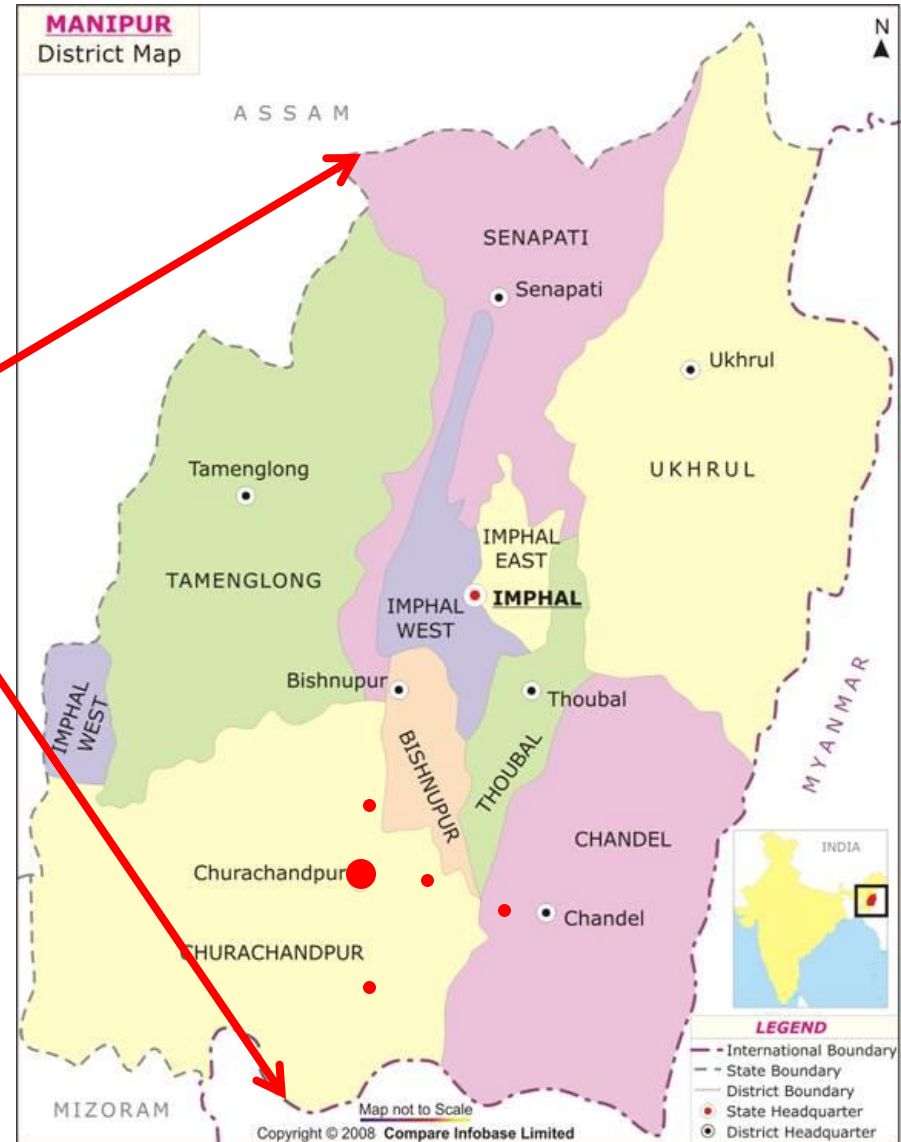
Integration (HIV/TB, primary health Care)

Infection Control
Local Regulations

Manipur India: How far can we go?



Manipur: Jewel of the North East

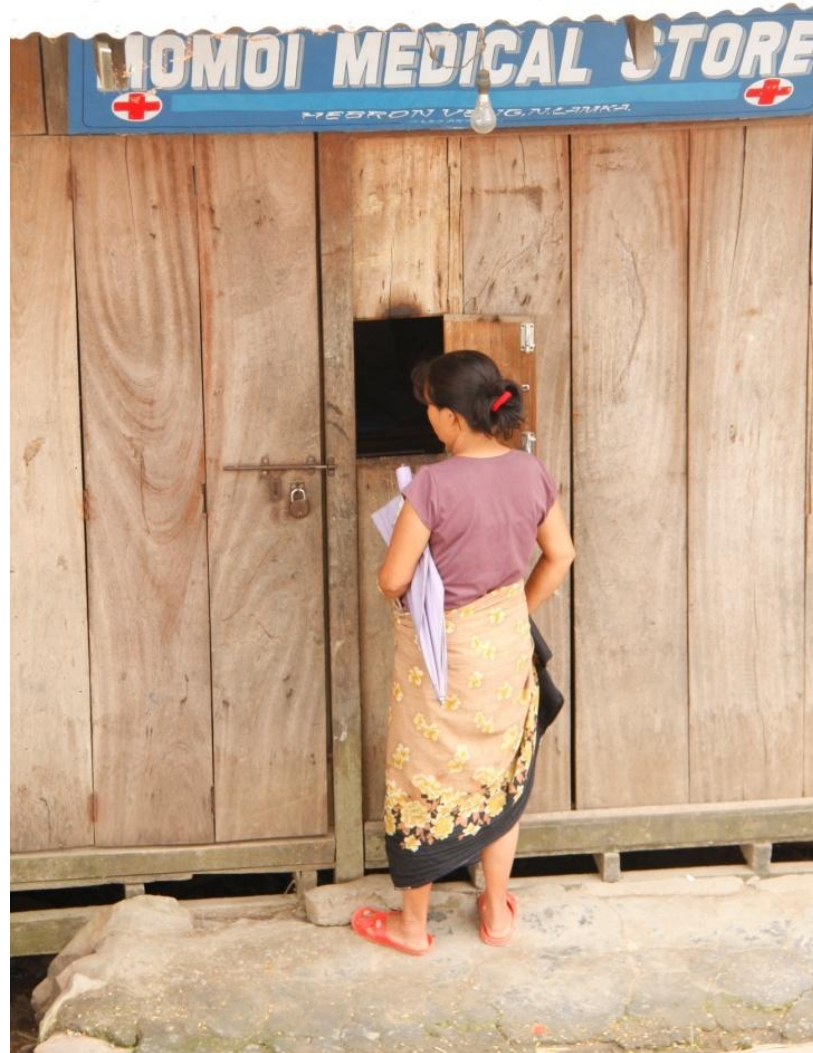


The Flaw in the Jewel

- Over 40 years of armed conflict
- 3 secessionist movements with overlapping claims
- Impacts on people:
 - Fear of travel (rival ethnic areas)
 - Targetted violence
 - Poor quality health services



Bandhs / Strikes



Health in Manipur

- Medical needs
 - Intravenous drug use
 - HIV-AIDS (>1% ; >15% high risk groups)
 - High rates of TB



Quality of TB Care in Manipur: State referral hospital



Simplified Approach

- Transport samples to Delhi
- 2 regimens for MDR TB (less choice)
- Simplified protocol
- Train nurses and counsellors to take on most tasks (side effect management by nurses)
- Home based care

Integrated Community Treatment

- Patient-centred care
- Community based models
- Task shifting – regular review and assessment for side effects initially by nurses
 - Patient supporters
- Contingency planning in unstable areas

Integration of MDR TB Care in Unstable Setting

- Small scale programme – after 1.5 years
 - 11 patients diagnosed MDR TB
 - 1 refused treatment
 - 1 default
 - 2 deaths
 - 7 patients on treatment



What is needed for scale up of MDR TB treatment

- Drugs
 - Reduce cost
 - Increase availability pre-qualified drugs
- Sense of urgency
 - Countries often have unambitious scale up plans

What is needed for scale up of MDR TB treatment

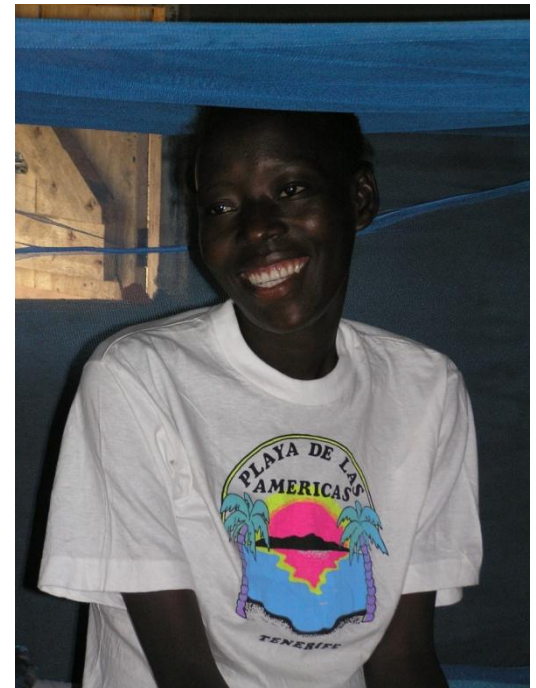
- Encourage best practice through operational research
 - e.g. community based models versus hospitalisation
- Quick but controlled access to new drugs
 - TMC 207 through compassionate use
 - RCTs into best regimens and duration of treatment
- Scale up of quality lab facilities
 - Rapid scale up of access to molecular tests

What is needed for scale up of MDR TB treatment

- Prioritise and appropriately fund infection control
- Address the human resources problems
 - Train more staff
 - Task shifting
- Greater involvement of patient groups / community
 - See website “TB and me” patients with MDR TB blogging about their experiences

Summary

- Scale up of Drug resistant TB treatment is
 - urgently needed
 - Feasible at programme and Global level
 - Must remain patient centred



Acknowledgements

- People with DR TB who shared their stories and pictures
- Ministry of Health Uzbekistan
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