Treat TB Modelling Project

TB,HIV and Lung Health Department Consultants Meeting – October 2011

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The Opportunities

❑ The introduction and scale-up of new tools for the diagnosis of Tuberculosis (TB) in developing countries has the potential to make a huge difference to the lives of millions of people living in poverty e.g.

LED Fluorescence Microscopy

Line Probe Assay HAIN

GeneXpert MTB/RIF

Liquid Culture MGIT

Small PM, Pai M. (2010), Tuberculosis diagnosis - time for a game change. N Engl J Med. 2010; 363(11): 1070-1.
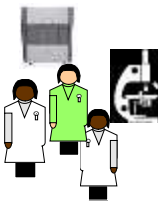
Providing evidence

❑ **Critical evidence is provided by :-**

- ▪ Laboratory Tests
- ▪ Demonstration Studies
- ▪ Explanatory Trials (Does it work?)
- ▪ Pragmatic Trials (Does it work in normal practice in a particular context?)

❑ **Modelling complements trials by applying the evidence to other similar or different contexts to**
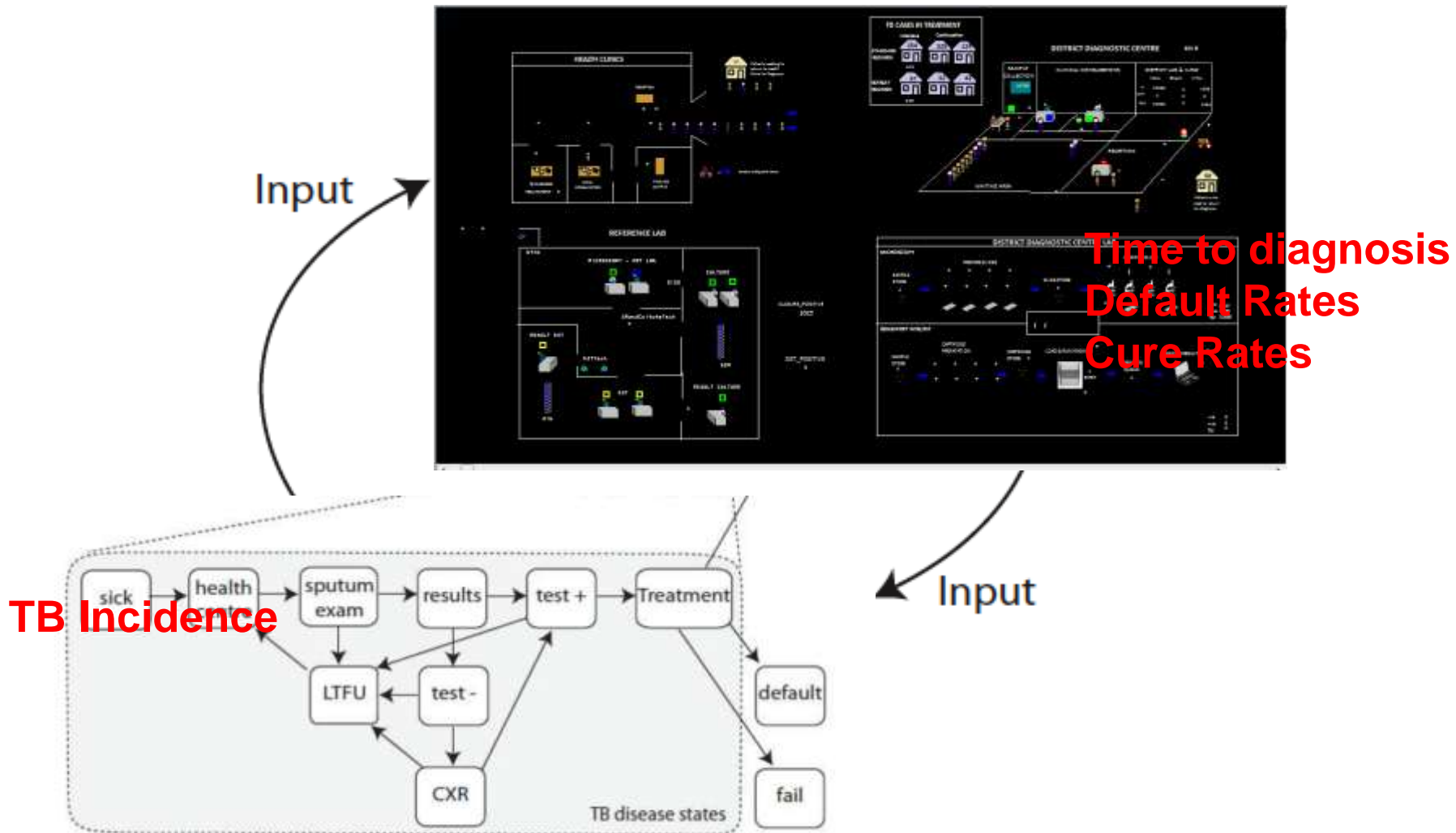
- ▪ Project *patient* effects across a wide spectrum of measures
- ▪ Project *health system* impacts and *costs*
- ▪ Project impacts of *scale-up*
- ▪ Assess incremental *cost effectiveness* models
- ▪ Project *TB incidence impacts* when linked to transmission models

Providing evidence

Impact Assessment Framework*	Patients	Health System	Community
EFFICACY - How well does it work?	How many more patients with TB will be diagnosed? How many more patients will be cured?		
EQUITY - Who benefits and why?	Which patients will benefit? - The poor, HIV+?		
HEALTH SYSTEM - Operational effects?		What will be the effect on staffing, Infrastructure, procurement, bottlenecks and capacity?	
SCALE-UP - Impacts of national rollout?	How will it effect access to care and patient costs?	How much will it cost to Implement , maintain, & run? Is it sustainable?	How will it effect transmission? TB & MDR-TB incidence? TB prevalence?
HORIZON SCANNING - How does it compare to other new/future technologies?		How cost effective is it compared to other approaches? Now and in the future?	

* Mann G, Squire SB, Bissell K, Eliseev P, Du Toit E, Hesseling A, et al. (2010), Beyond accuracy: creating a comprehensive evidence base for TB diagnostic tools. Int J Tuberc Lung Dis. 2010; 14(12): 1518-24.

The Treat TB modelling approach

Input

Time to diagnosis
Default Rates
Cure Rates

TB Incidence

sick → health → sputum exam → results → test + → Treatment
LTFU ← test -
CXR
default
fail
TB disease states

Input

Operational model

The operational model can be seen as a 'Virtual Implementation' and its utility is greatly enhanced when it is:-

A. **Sufficiently detailed -** to take account of the complex interactions that affect outcomes, cause bottlenecks, and limit capacity

B. **Visual-** to give a representation of the operation that enables non modellers (e.g. policy makers) to engage with the modelling and assist in its validation – not a 'black box'.

C. **Flexible-** so the effects of many new and existing diagnostics options and contexts can be modelled. Also enabling 'what if?' questions to be addressed.

D. **Output rich** - so outcomes can be analysed using readily available database and statistical tools e.g. matching the WHO output requirements for monitoring implementations of Xpert MTB/RIF

E. **Powerful** – to enable many iterations of the process to be rapidly completed e.g. simulating 5-10 years of TB diagnosis in under an hour of real time

Such approaches are widely used to model changes to health systems in the developed world, but have not been used previously in the developing world

Operational model design – Inputs

DIAGONSTIC CENTRE CURRENT PERFORMANCE	
Annual Smear Positive TB Cases	**255**
Annual Smear Negative TB Cases	**64**
Annual Retreatment Cases	**91**
HIV+ rate in TB cases	**42.0%**
Proportion of new suspects Smear Poitive	**11.6%**
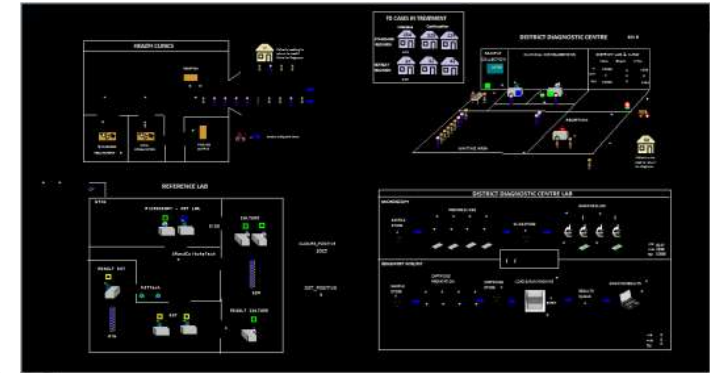
EXCEL WORKBOOK

DIAGNOSTIC DEMAND MATRIX						DISTRICT1	Parameters marked in yellow must be input	
SMEAR		+ve	-ve	-ve	-ve	-ve	Default	N0.
X-RAY			No	Yes	Yes	No	Diagnosis	Seeking
TREATMENT		Yes	Yes	Yes	No	No	No	TOTAL
PATIENT CATEGORY								
NEW/ RETREAT	HIV							
NEW	+ve	95	0	39	789	0	163	1,086
	-ve	160	0	25	1,090	0	225	1,500
	TOTAL	255	0	64	1,879	0	388	2,586
RETREAT	+ve	38					2	40
	-ve	53					3	56
	TOTAL	91					5	96

The Diagnostic Options

❑Assumptions validated with experts, published literature, and subject to sensitivity analysis e.g.

- Accuracy (Sensitivity and Specificity of each test)
- TB suspect and treatment default rates
- Diagnostic processes and treatment times
- Costing information

Operational model design – Diagnostic Centre
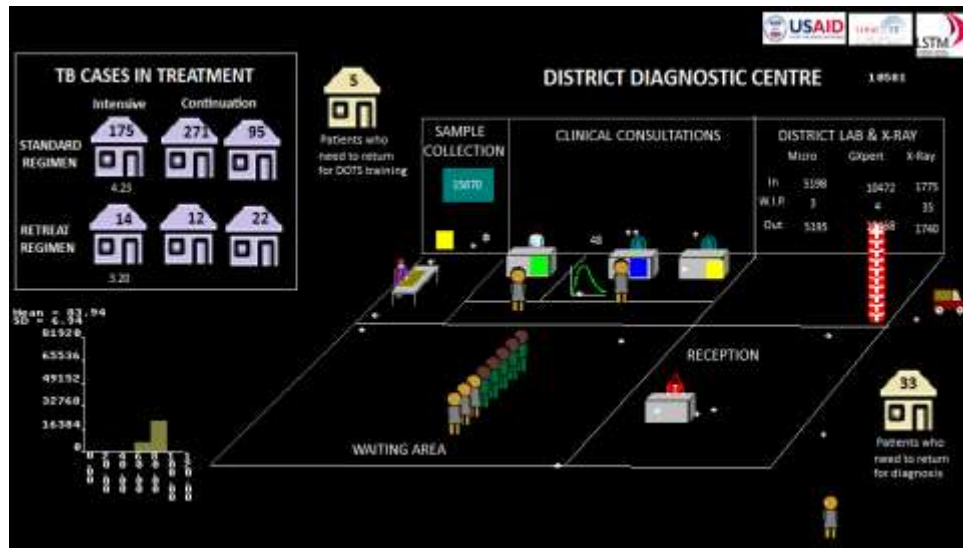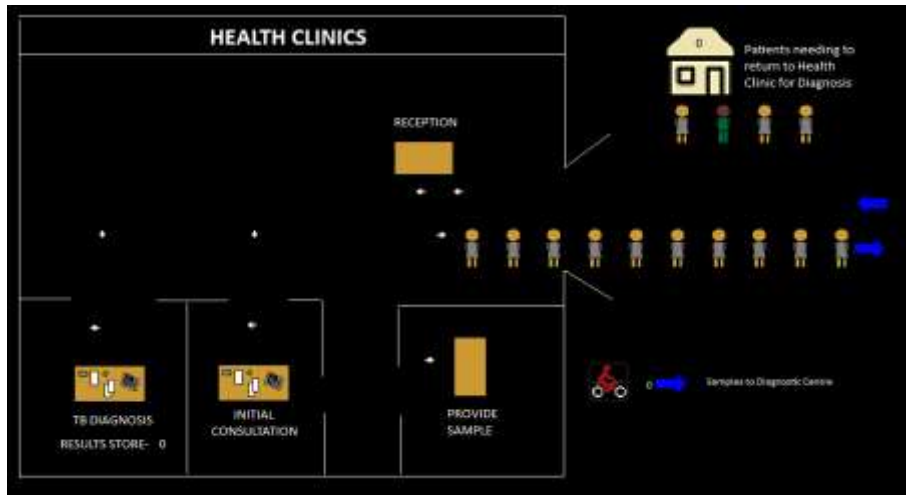
A detailed model was developed using the WITNESS Simulation Software. Patients are modelled through each process from Health Clinics into a TB Diagnostic Centre and through to Treatment where appropriate.

Operational model design – Diagnostic Lab

Sputum samples are modelled through the lab process. The lab model shows a schematic of the process and includes microscopy and Xpert MTB/RIF with flows defined for each sample by rules defined in an input data files
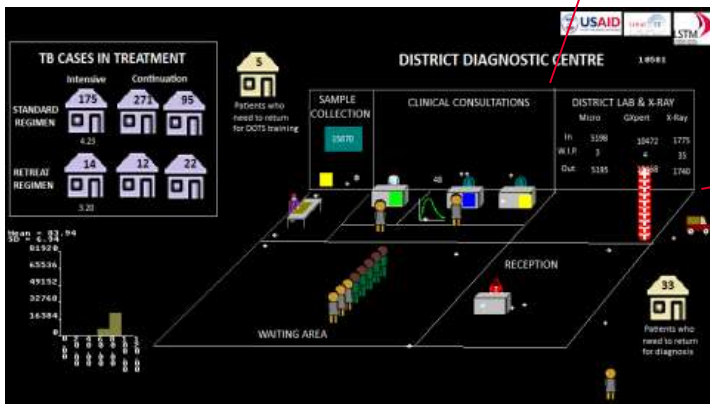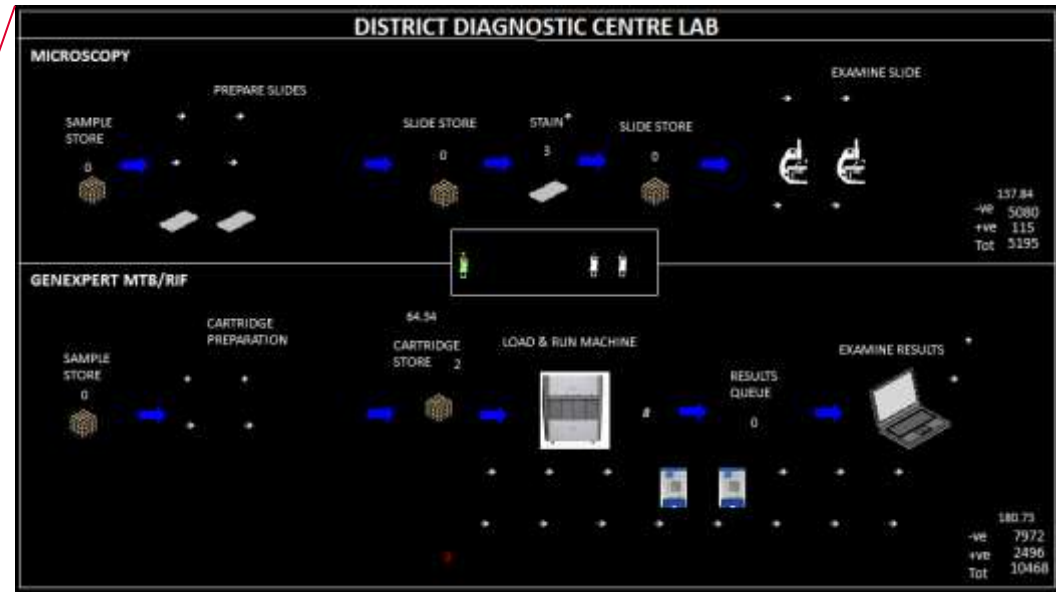
Lab technicians and assistants as well as clinical staff are modelled as resources

Operational model design – Drug Sensitivity
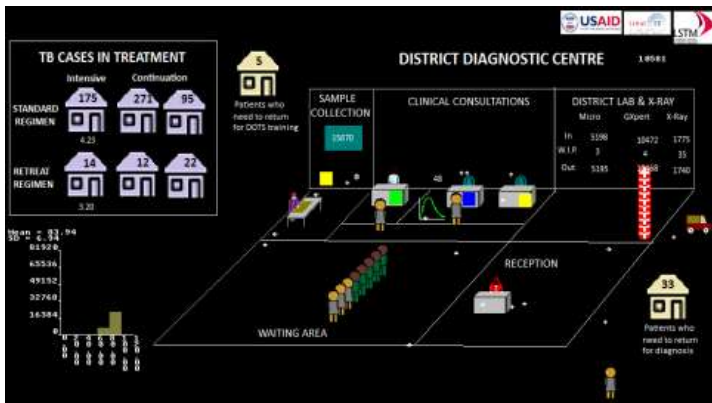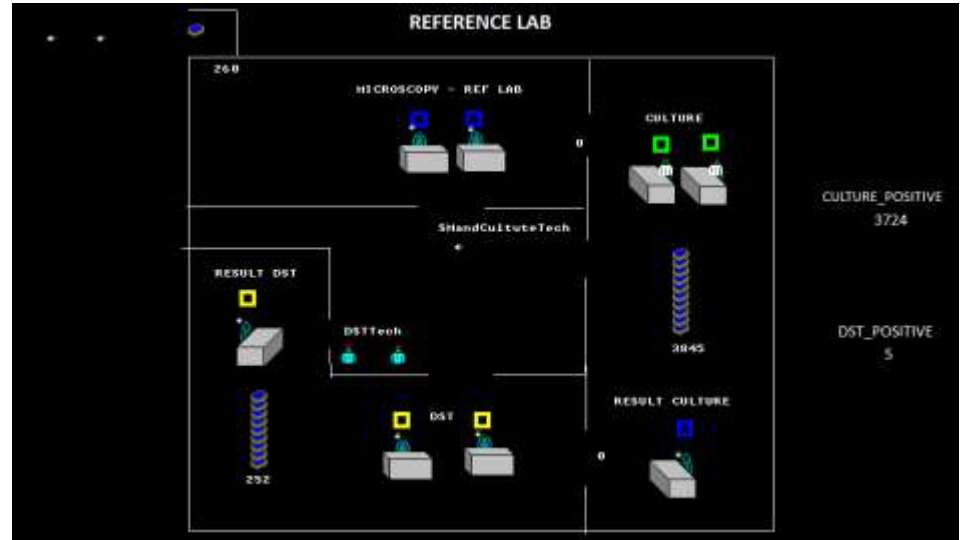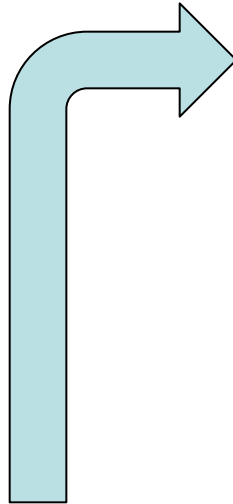
Samples from patients where there is a risk of drug resistance are transported to the Central TB Reference Lab for Drug Sensitivity Testing.

Operational model design – Outputs
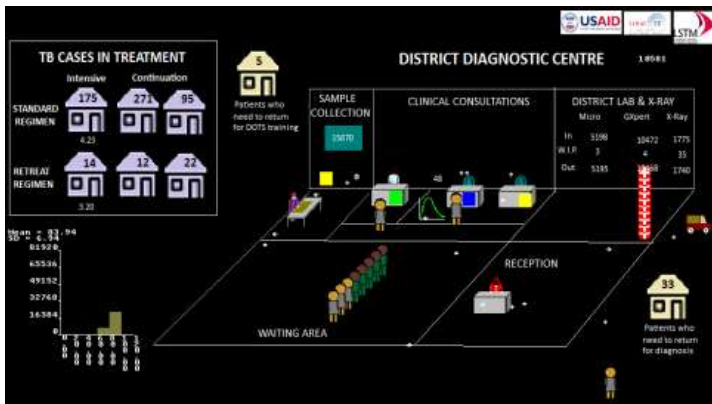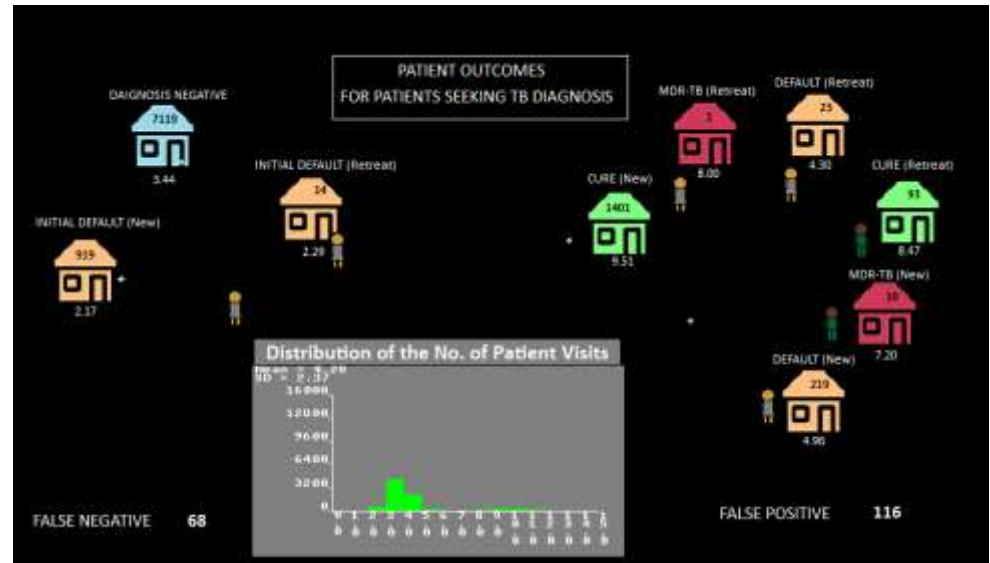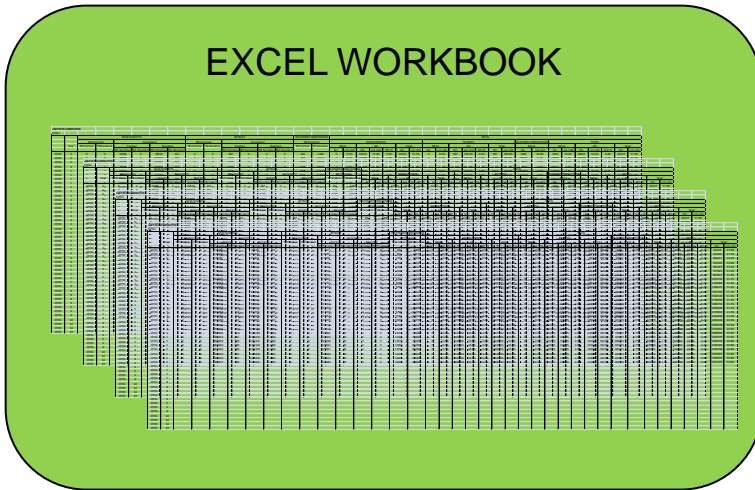
EXCEL WORKBOOK

Data is output to an Excel Workbook every Quarter in line with the World Health Organisation requirements for trials of TB diagnostics

Modelling Approach? – Data Collation & Model Calibration


```
1 - Dar es Salaam
2 - Pemba North
3 - Pemba South
4 - Zanzibar Central/South
5 - Zanzibar North
6 - Zanzibar Urban/West
```

Testing approach in Tanzania.

Measure	Count
Population	44million
New TB cases per year	80k p.a.
TB cases Treated	64k p.a.
HIV+% in TB Incidence	47%
Treatment Cure Rate	87%

Health Facility	Count
Central TB Reference Lab	1
Zonal Laboratories	2
Regions	27
Districts	168
TB Laboratories	>900

Sources
Basra Doulla , Ministry of Health, Dar es Salaam, Tanzania

Options to be considered for a diagnostic centre

DIAGNOSTIC OPTIONS				CURRENT	OPTION	OPTION	OPTION
Patient	Test	HIV Status	Smear Status	0	1	2	3
New Suspects							
	Primary	HIV+		MICRO	XPERT	XPERT	MICRO
		HIV-		MICRO	XPERT	XPERT	MICRO
	Secondary	HIV+	Smear+	-	-	-	-
			Smear-	XRAY	XRAY	XRAY	XPERT
		HIV-	Smear+	-	-	-	-
			Smear-	XRAY	XRAY	XRAY	XRAY
	Tertiary	HIV+	Smear-	-	-	-	XRAY
		HIV+	Smear-	-	-	-	-
Retreat				MICRO	XPERT	XPERT	XPERT
Treatment Monitoring				MICRO	MICRO	MICRO	MICRO
DIAGNOSTIC CENTRE LAB RESOURCES							
Lab Technicians				2	1	2	2
Lab Assistants				0	1	0	1
Microscopes LED				2	1	1	2
Microscopes ZN				0	0	0	0
XPERT Cartridge Positions				0	8	4	4

DIAGONSTIC CENTRE CURRENT PERFORMANCE

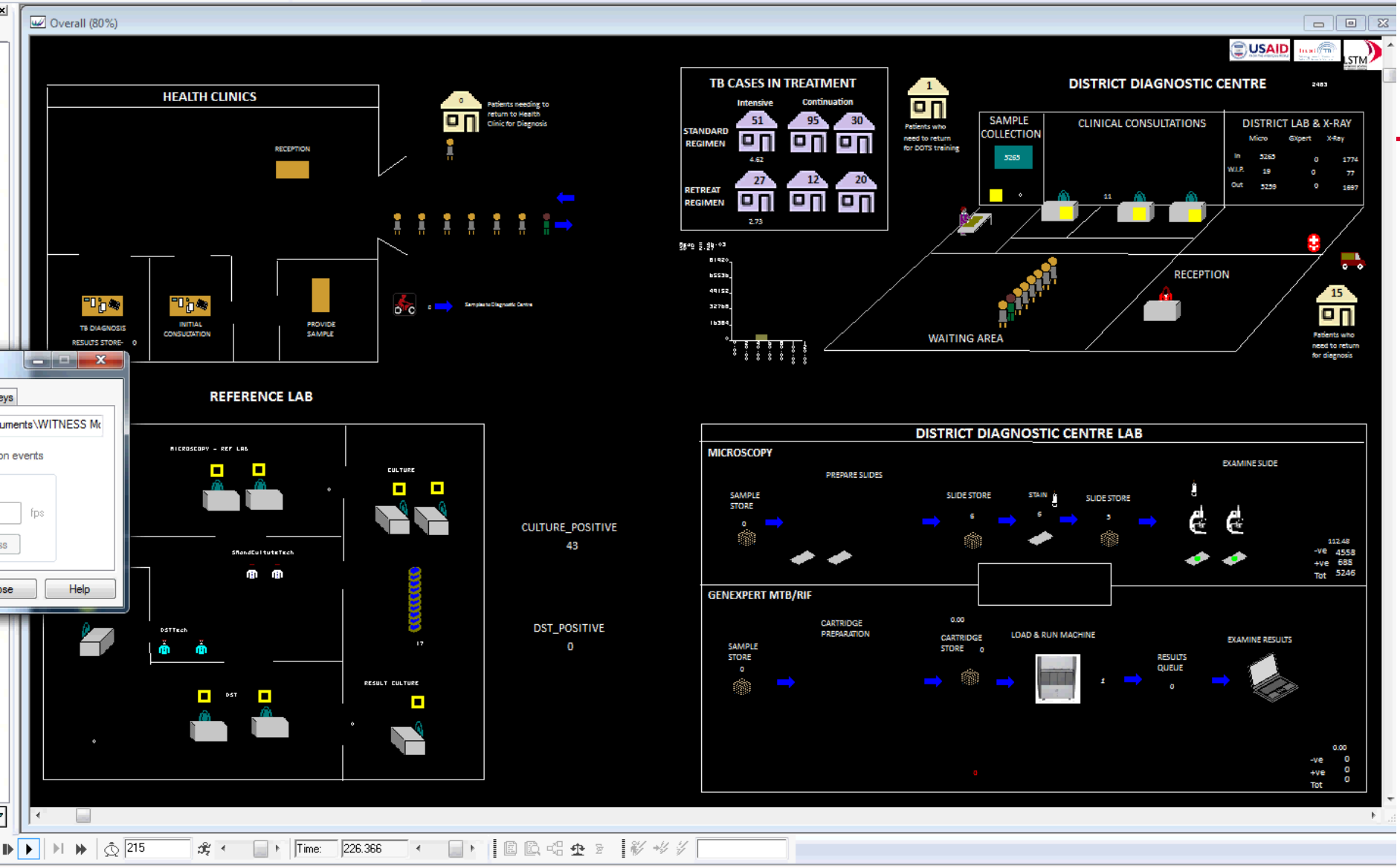|	
Annual Smear Positive TB Cases	255
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Annual Retreatment Cases	91
HIV+ rate in TB cases	42.0%
Proportion of new suspects Smear Poitive	11.6%

MODEL OPTION	0

Run Base Case

DIAGNOSTIC OPTIONS				CURRENT	OPTION	OPTION	OPTION
Patient	Test	HIV Status	Smear Status	0	1	2	3
New Suspects							
	Primary	HIV+		MICRO	XPERT	XPERT	MICRO
		HIV-		MICRO	XPERT	MICRO	MICRO
	Secondary	HIV+	Smear+	-	-	-	-
			Smear-	XRAY	XRAY	XRAY	XPERT
		HIV-	Smear+	-	-	-	-
			Smear-	XRAY	XRAY	XRAY	XRAY
	Tertiary	HIV+	Smear-	-	-	-	XRAY
		HIV+	Smear-	-	-	-	-
Retreat				MICRO	XPERT	XPERT	XPERT
Treatment Monitoring				MICRO	MICRO	MICRO	MICRO
DIAGNOSTIC CENTRE LAB RESOURCES							
Lab Technicians				2	1	2	2
Lab Assistants				0	1	0	1
Microscopes LED				2	1	1	2
Microscopes ZN				0	0	0	0
XPERT Cartridge Positions				0	8	4	4

DIAGONSTIC CENTRE CURRENT PERFORMANCE

Annual Smear Positive TB Cases	**255**
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MODEL OPTION	1

Run Xpert All

DIAGNOSTIC OPTIONS				CURRENT	OPTION	OPTION	OPTION
Patient	Test	HIV Status	Smear Status	0	1	2	3
New Suspects							
	Primary	HIV+		MICRO	XPERT	XPERT	MICRO
		HIV-		MICRO	XPERT	MICRO	MICRO
	Secondary	HIV+	Smear+	-	-	-	-
			Smear-	XRAY	XRAY	XRAY	XPERT
		HIV-	Smear+	-	-	-	-
			Smear-	XRAY	XRAY	XRAY	XRAY
	Tertiary	HIV+	Smear-	-	-	-	XRAY
		HIV+	Smear-	-	-	-	-
Retreat				MICRO	XPERT	XPERT	XPERT
Treatment Monitoring				MICRO	MICRO	MICRO	MICRO
DIAGNOSTIC CENTRE LAB RESOURCES							
Lab Technicians				2	1	2	2
Lab Assistants				0	1	0	1
Microscopes LED				2	1	1	2
Microscopes ZN				0	0	0	0
XPERT Cartridge Positions				0	8	4	4

Example results for a single diagnostic centre
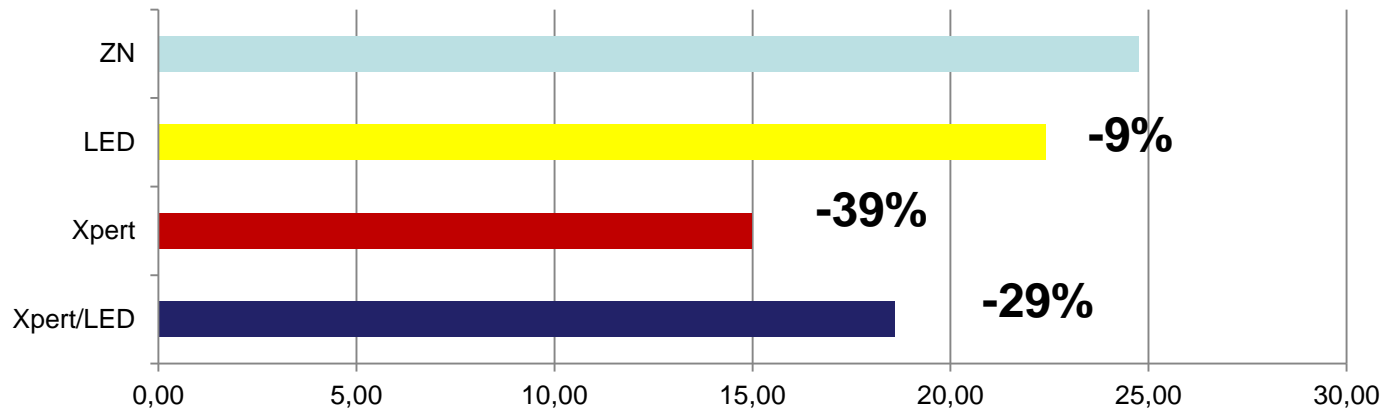
❑ **Options considered**
  - Base Case - ZN Microscopy
  - Optimised LED Fluorescence Microscopy
  - Xpert MTB/RIF as frontline tool for all suspects
  - Xpert MTB/RIF for HIV+ suspects, LED Microscopy for HIV- suspects
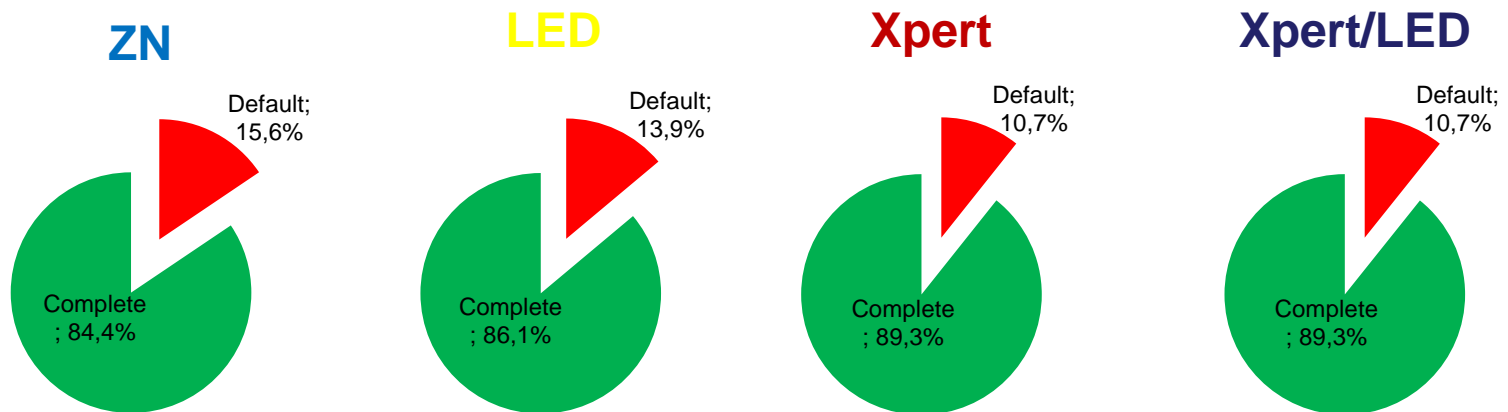
❑ **LED Microscopy for Treatment follow-up**

❑

Parameter	Example Data from Tanzania
Current Diagnostic Tools	ZN Microscopy & X-ray
Laboratory Staff	2 lab technicians
TB cases per year New TB Smear +ve	560
New TB Smear -ve	450
Retreatment	93
HIV+ rate in TB Cases	42.0%
Smear +ve Rate - New Suspects	11.4%

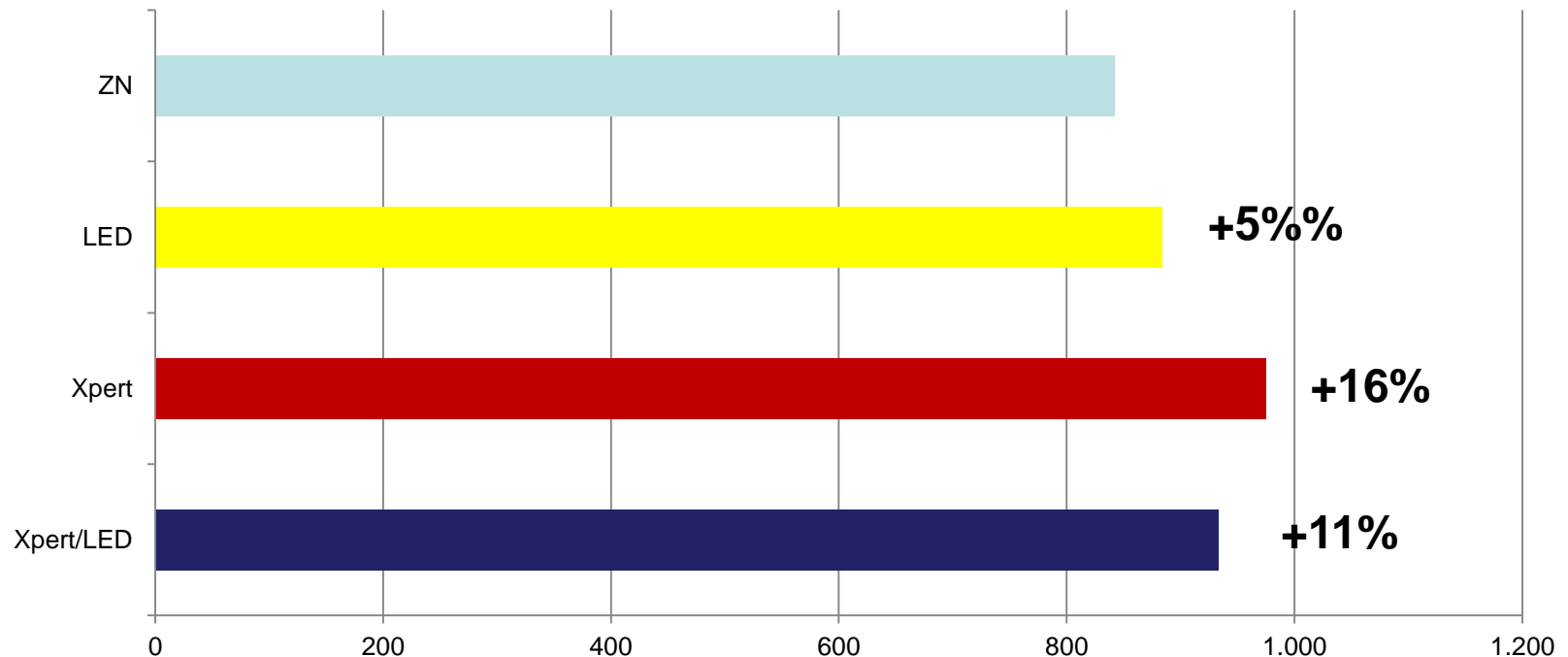# Example Results - Patient Outcomes

Time to Diagnosis (DAYS)

- ZN
- LED — **-9%**
- Xpert — **-39%**
- Xpert/LED — **-29%**

(axis: 0,00 — 5,00 — 10,00 — 15,00 — 20,00 — 25,00 — 30,00)

Diagnostic Default rates

ZN
Default; 15,6%
Complete; 84,4%

LED
Default; 13,9%
Complete; 86,1%

Xpert
Default; 10,7%
Complete; 89,3%

Xpert/LED
Default; 10,7%
Complete; 89,3%

No. of TB Patients Cured each Year

Example Results – Health System Outcomes

No. of Sputum Samples Analysed p.a.

Running Costs ($k p.a.)

+0.2%

+49%

+27%

PATIENT OUTCOMES – XPERT/MICROSCOPY
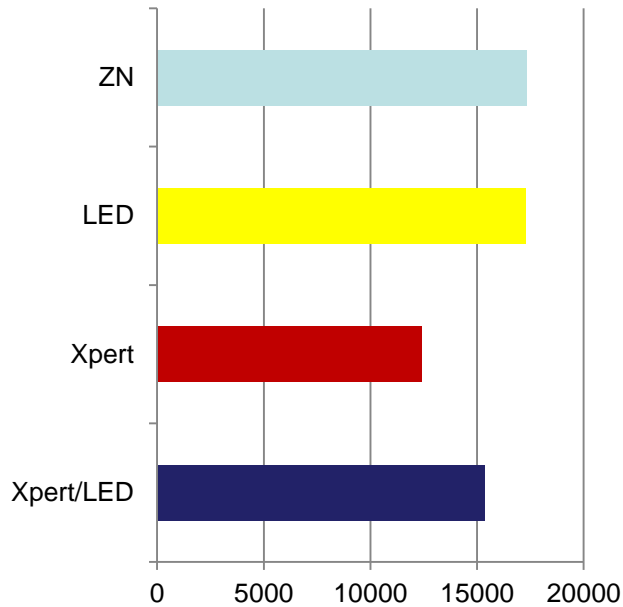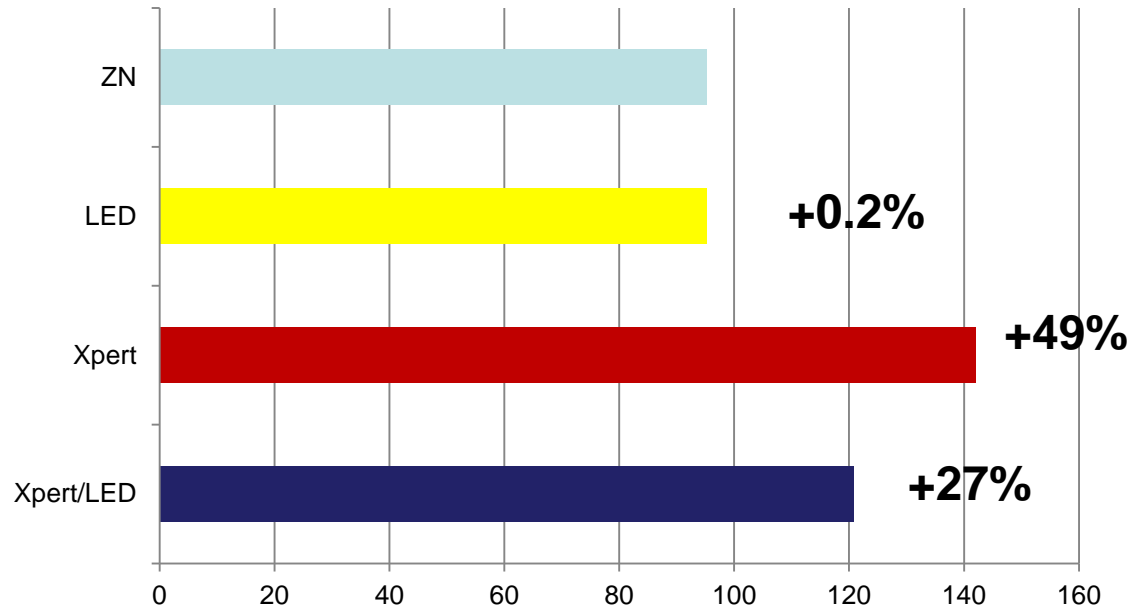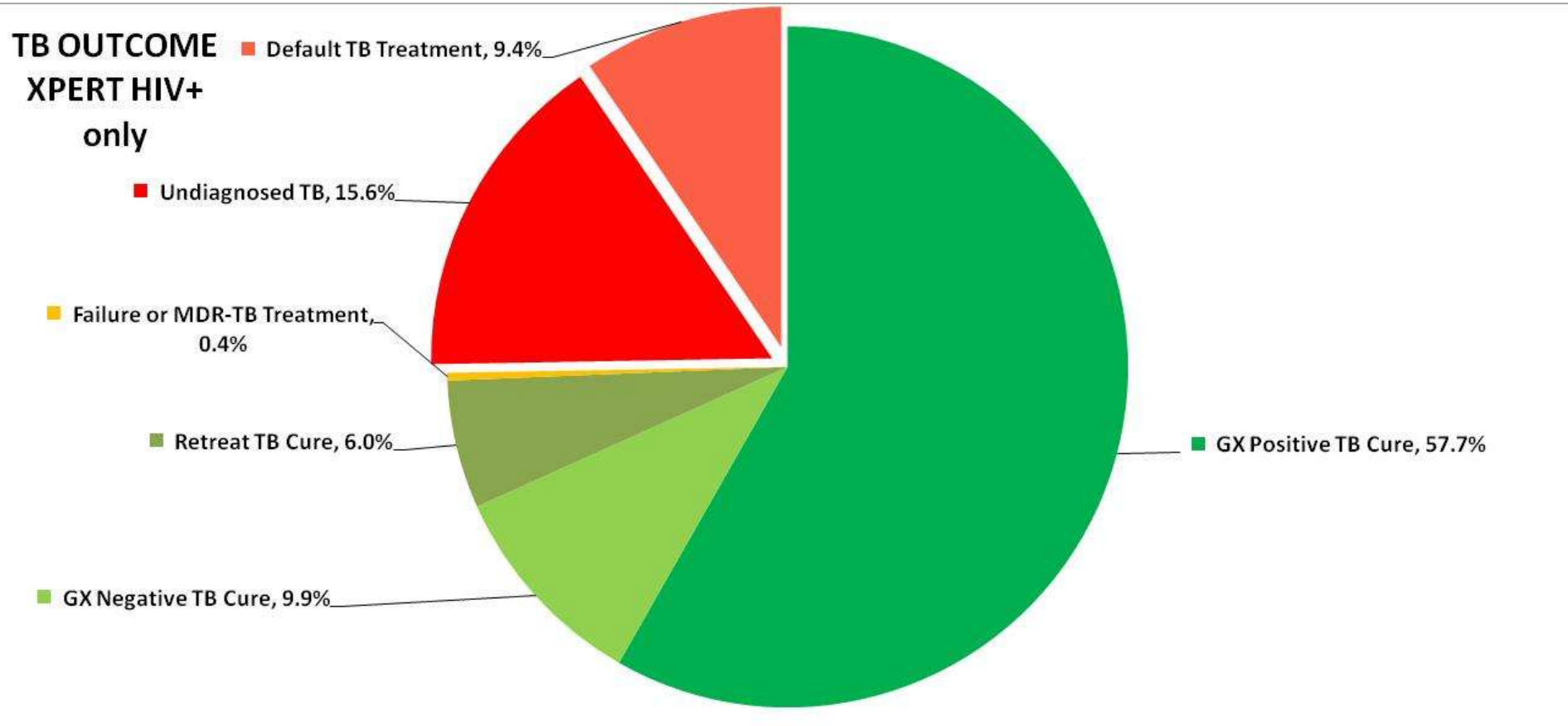
AROUND 73.5% OF PATIENTS/SUSPECTS SEEKING DIAGNOSIS ARE CORRECTLY DIAGNOSED AND TREATED FOR TB

Conclusions

❑ **The modelling approach of options for TB diagnostics in the developing world:-**

- is practical

- provides comprehensive outcome projections

- can be linked effectively to transmission models

- engages policy makers in validation and questioning

- enables complex interactions to be taken into account

- can take longer to develop than some other approaches, but once developed can be quickly adapted to similar contexts

What Next?

❑ **IMPACT ASSESSMENT IN TANZANIA**

- Of *scale-up* of the options
- Of the proposed Xpert MTB/RIF implementations in the 5 diagnostic centres (supporting Tanzanian staff to conduct their own evaluations)
- Present results to a meeting of policy makers in Tanzania

❑ **PUBLISH**

- Publish in a pier reviewed journal

❑ **RESEARCH**

- Apply the models to other settings e.g. Malawi and Brazil
- Develop transmission models for MDR-TB
- Apply the models to High MDR Setting

- ❑ **USAID**
  - ▪ YaDiul Mukadi
- ❑ **Tanzania NTLP**
  - ▪ Dr Saidi Egwaga
  - ▪ Basra Doulla
  - ▪ Raymond Shirima
  - ▪ Dr Riziki Kisonga
- ❑ **Malawi MOH**
  - ▪ Reuben Mwenda
- ❑ **The Union (Treat-TB)**
  - ▪ I.D. Rusen
  - ▪ Anne Detjen

- ❑ **Liverpool School of Tropical Medicine**
  - ▪ Bertie Squire
  - ▪ Gillian Mann
  - ▪ Kerry Millington
- ❑ **National Taiwan University**
  - ▪ Hsien-Ho Lin
- ❑ **Harvard School of Public Health**
  - ▪ Ted Cohen
  - ▪ Megan Murray
- ❑ **Lanner Group**
  - Geoff Hook