

OCB
June
2012

Cost-effectiveness study of
pre & post Xpert TB diagnosis
from patient & provider perspective
in a rural HIV/AIDS/TB programme,
in Buhera, Zimbabwe

Guillaume Jouquet - guillaume.jouquet@gmail.com

Helen Bygrave - helen.bygrave@joburg.msf.org

Index

I.	Introduction.....	5
A.	Background.....	5
B.	Objectives of the study.....	5
II.	Methods	6
A.	Cohort characteristics.....	6
B.	Costing methodology	6
C.	Effectiveness.....	8
D.	Cost effectiveness ratio	9
III.	Results	10
A.	Global cost / TB case detected	10
B.	Service provider perspective	11
C.	Patient perspective.....	13
IV.	Sensitivity analysis.....	15
A.	Price of Xpert cartridge	15
B.	Opportunity cost (1)	16
C.	Opportunity cost (2)	16
D.	X-ray cost in Patient perspective.....	17
V.	Discussion	18
A.	Conclusions.....	18
B.	Limits	18
C.	Way forward.....	18
VI.	Annexes	19
A.	Smear cost	19
B.	Xpert Cost	20
C.	X-ray cost.....	22
D.	Consultations Cost.....	23
E.	Cost by nature of Expenses	24
F.	Transport cost for patients.....	25
VII.	References	26

Figures

Figure 1: Pre-Xpert algorithm (July-December 2010)	8
Figure 2: Post-Xpert algorithm (July-December 2011).....	8
Figure 3: Cost / TB case diagnosed in Pre and Post Xpert interventions	10
Figure 4: Cost / TB case diagnosed in Pre and Post Xpert interventions (provider perspective)	11
Figure 5: Units of resources needed in each intervention (provider perspective)	11
Figure 6: Cost / unit of the ingredients (provider perspective).....	12
Figure 7: Comparison of the cost / diagnosis of smears and Xpert	12
Figure 8: Cost / TB case diagnosed in Pre and Post Xpert interventions (patient perspective).....	13
Figure 9: Units of resources needed in each intervention (patient perspective)	13
Figure 10: Cost / unit of the ingredients (patient perspective).....	14
Figure 11: Cost / TB cases diagnosed with Xpert current FIND negotiated price	15
Figure 12: Cost / TB cases diagnosed with Xpert FIND negotiated price for a volume of 1.5 million/y	15
Figure 13: Cost / TB cases diagnosed with Xpert UNITAID negotiated price	15
Figure 14: Cost / TB cases diagnosed with opportunity cost for consultation time at \$10/ day	16
Figure 15: Cost / TB cases diagnosed with opportunity cost for consultation time at \$23/ day	16
Figure 16: Cost / TB cases diagnosed with opportunity cost for consultation time & time to diagnosis at \$5/ day	17
Figure 17: Cost / TB cases diagnosed with opportunity cost for consultation time & time to diagnosis at \$10/ day	17
Figure 18: Cost / TB cases diagnosed with X-ray considered as a cost for the patient.....	17
Figure 19: Post-Xpert algorithm for Gutu project	18
Figure 20: # slides / year for ?PTB smear in MMH – Source: Lab stat	19
Figure 21: MMH lab workload for smear diagnosis in 2011 – Source: Lab follow-up	19
Figure 22: Calculation of FTE/ slide for ?PTB – Source: Lab technician interview + 2010 lab statistics	19
Figure 23: Calculation of smear annual cost in MMH lab in 2011	20
Figure 24: Breakdown of Cost/ smear in MMH in 2011.....	20
Figure 25: # Xpert done in the 4 first months of 2012– Source: Lab stat	20
Figure 26: Calculation of FTE / Xpert.....	21
Figure 27: Cost of investment for Xpert machine in MMH in 2011	21
Figure 28: Calculation of Xpert annual cost in MMH lab	21
Figure 29: Breakdown of Cost/ Xpert in MMH.....	21
Figure 30: MMH X-Ray activity 2011 – Source: MMH X-Ray register	22
Figure 31: X-Ray Film Consumption in MMH – Source: MMH Pharmacy stock cards + Isystock.....	22
Figure 32: Calculation of X-Ray annual cost in MMH in 2011	22
Figure 33: Breakdown of Cost/ X-ray in MMH in 2011	22
Figure 34: Breakdown of nurses in the 27 clinics of Buhera district in 2011 (exclusion of MMH, BBH and Buhera hospital) – Source: MOH District administrator	23
Figure 35: Breakdown of activity in the 27 clinics of Buhera district in 2011 (exclusion of MMH, BBH and Buhera hospital) – Source: MOH District Statistician.....	23
Figure 36: Calculation of the average annual cost of nursing staff in the 27 clinics of Buhera district in 2011 (exclusion of MMH, BBH and Buhera hospital).....	23
Figure 37: Calculation of the cost/ consultation for a nurse or a doctor in Buhera district in 2011	23
Figure 38: Cost of staff in Buhera district – Source: MMH accountant.....	24

Figure 39: % overhead/ nursing staff for OPD consultation in Hospital and clinic in 2009 in Morija District, Lesotho.....	24
Figure 40: % overhead/ lab staff for smear in 2009 in Morija District, Lesotho	24
Figure 41: Costs including freight of consumables and equipment provided by MSF Supply to Murambinda project – Sources: MSF supply documents + SAGA.....	24
Figure 43: Average transport cost / patient (way and back)– Source: SAGA.....	25

I. Introduction

A. Background

Zimbabwe is one of 22 high TB burden countries that collectively account for approximately 80% of all new TB cases reported each year. According to current World Health Organization (WHO) estimates for Zimbabwe, 80% of TB patients have known HIV status, and 75% of TB patients with known HIV status are HIV-positive. TB case detection is low (approximately 56%). All HIV-positive patients with TB are eligible for ART, but currently only about 30% are initiated. The low TB case detection rate and low proportion of HIV-positive TB patients that start ART, results in considerable, but unquantifiable, morbidity and mortality.

Xpert® MTB/RIF (Xpert) is a promising new technology for TB diagnosis. Despite its high sensitivity and specificity, and potential to reduce delays in TB diagnosis and treatment initiation, concerns about affordability serve as a barrier to implementation in resource-limited settings. Cost issues withstanding, Singh and Bhan have argued that there are public health, ethical, and human rights imperatives to implement the use of novel diagnostic technologies, including Xpert, in high TB burden, low-income countries wherever this is feasible. Recent cost effectiveness studies using analytical modelling have also suggested that Xpert is cost effective.

Singh and Bhan have pointed out that use of Xpert is likely to result in increased TB detection rates, and more specifically, increased detection of drug-resistant TB (DR-TB). This will put pressure on governments to provide and increase access to first- and second-line TB regimens, and this will in turn place pressure on drug and diagnostics manufacturers to lower the prices of their products.

Medecins Sans Frontieres (MSF) has been at the forefront of implementing Xpert to diagnose TB in resource-limited settings with high TB burden settings. MSF's South African Medical Unit (SAMU) has been providing support to HIV/TB projects in seven sites in Southern Africa that started implementing Xpert, including a site in Buhera District, Zimbabwe.

MSF has been supporting health services in Buhera District in Manicaland Province in eastern Zimbabwe since 2002 and has been providing ART to eligible patients in Buhera District since 2004. In 2011, MSF provided two Xpert instruments in order to improve TB diagnosis. One instrument is located at Murambinda Mission Hospital (MMH) and the other is located at Birchenough Bridge Hospital (BBH). Each hospital serves several satellite clinics. Clinical staff visit the satellite clinics once a week to collect sputum samples from TB suspects and take them to the nearest hospital for testing. Prior to the introduction of Xpert, sputum samples were tested using sputum fluorescence microscopy. Since the introduction of Xpert, sputum samples have had parallel testing with sputum microscopy and Xpert but from November 2011 Xpert has been used as the first diagnostic test.

Prior to the introduction of Xpert, smear-negative TB suspects who remained symptomatic had TB diagnosed on the basis of chest X-ray (CXR) and clinical assessment. CXR is currently available only at MMH, thus patients from peripheral clinics need to travel to MMH for a CXR. Although MSF pays for CXRs and patient transport, the need to travel to MMH for a CXR results in delays in making a TB diagnosis, and also results in some TB suspects not following through on referrals for CXR, and thus not having a diagnosis of TB confirmed or ruled-out.

B. Objectives of the study

The objective of the study is to compare the cost / TB case detected from the patient and provider perspective before and after introduction of Xpert in Buhera district (respectively Pre-Xpert and Post-Xpert interventions).

II. Methods

A. Cohort characteristics

	Pre-Xpert	Post-Xpert
Location	Buhera District, Zimbabwe	
HIV prevalence		13.5%
HIV/ TB co-infection rate		65%
Period of time	Jul-Dec 2010	Jul-Dec 2011
TB suspects	3,211	2,220
TB cases detected	717	600
% TB case detected	22%	27%

There was NO dramatic increase in case detection pre and post Xpert. This may be explained due to the high level of implementation of the standard smear negative algorithm prior to implementation of Xpert. MSF doctors attended all clinics weekly and MSF paid for CXR and transport costs allowing most patients to proceed to a final diagnosis efficiently. Hence comparing the comparative costs in a setting where prior smear negative diagnosis was so effectively implemented made this an ideal setting to assess the costs of diagnosis pre and post Xpert.

B. Costing methodology

1. Methods

The costs were estimated:

- from a service provider and patient perspective
- using ingredient costing approach

Ingredient costing approach has two key elements:

- 1) identifying the quantities of resources utilized;
- 2) establishing the unit cost or price for each.

The cost per patient is therefore estimated in each intervention as follows:

$$C = Q_1P_1 + \dots + Q_nP_n$$

Where:

C = Cost per patient

$Q_1 \dots Q_n$ = quantities of ingredients (consultations, Xray, smear, Xpert etc)

$P_1 \dots P_n$ = prices (or unit costs) for each of the quantified ingredient

The quantities of ingredients are determined by the data collected in the project for the 2 interventions (see II.C.1)

The unit costs are estimated using both empirical (“top-down”) and normative (“bottom-up”) analysis so that discrepancies could be reconciled.

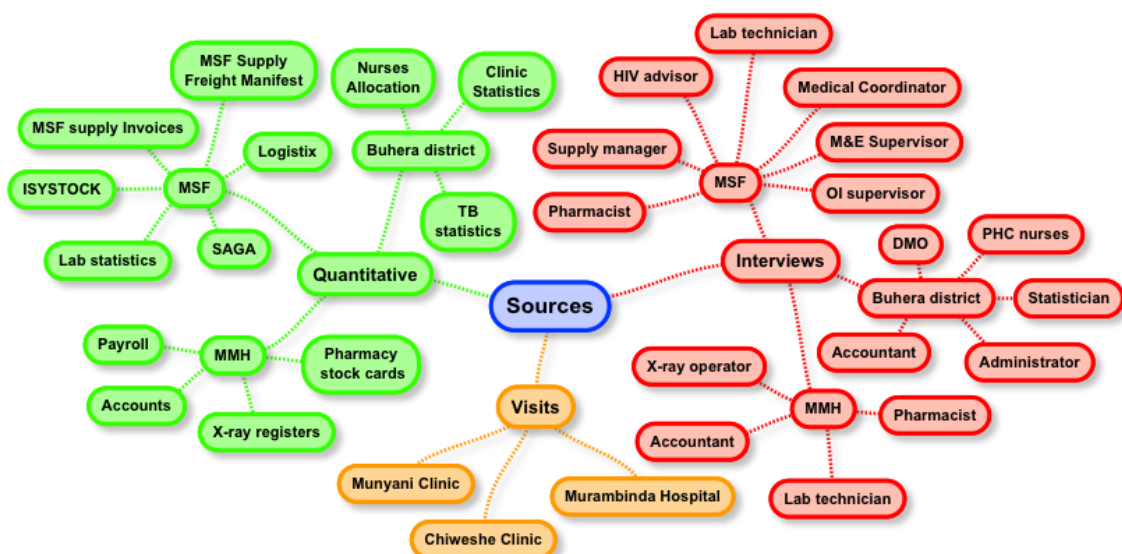
These costs include:

- Staff: estimated at MOH salary and allowances (see Annex VI.E.1 Cost of staff)
- Overhead: estimated with % of staff cost (see Annex VI.E.2 Overhead cost)
- Consumables: estimated at MSF supply price including freight by air (see Annex VI.E.3 Cost of supply (Drugs, reagents, consumables & equipment))
- Equipment: estimated at MSF supply price including freight by air (see Annex VI.E.3 Cost of supply (Drugs, reagents, consumables & equipment))

All costs are reported in 2011 US\$

2. Sources of information

Data were collected in the sites of the interventions between the 29/05/2012 and the 12/06/2012



3. Identified ingredients of the cost



C. Effectiveness

1. Methodology

In the 2 interventions, effectiveness is measured in terms of % TB case detected / TB suspects

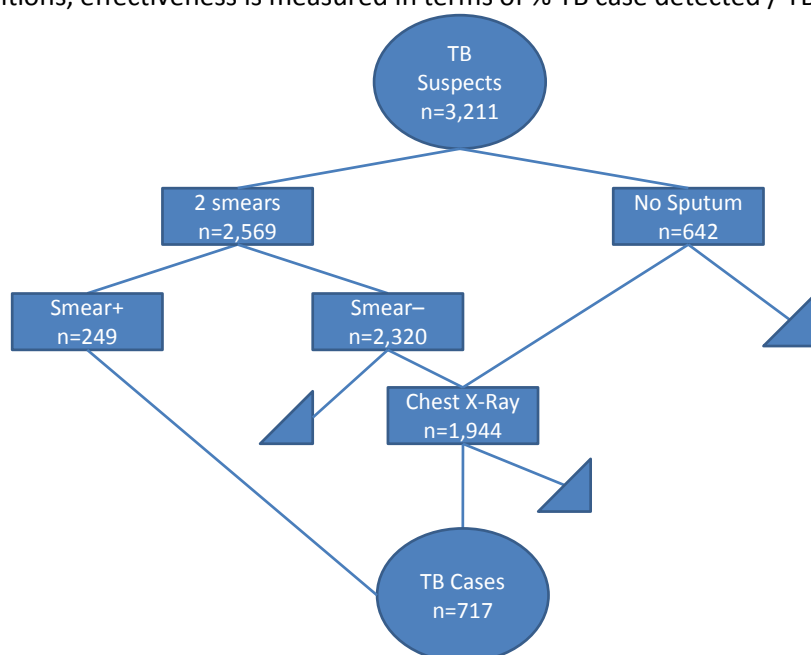


Figure 1: Pre-Xpert algorithm (July-December 2010)

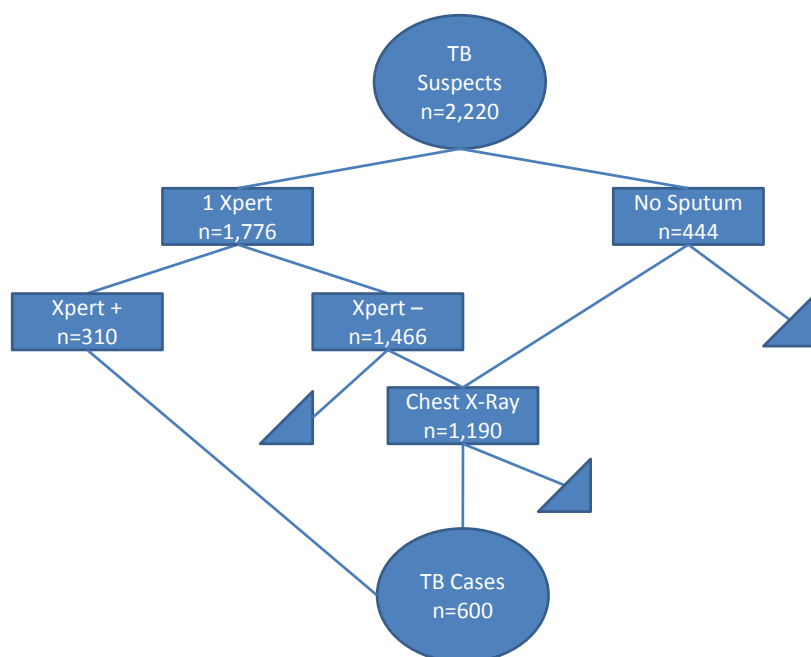


Figure 2: Post-Xpert algorithm (July-December 2011)¹

2. Sources:

- Assumption: 80% of TB suspect have smears or Xpert done (MMH CXR statistics)
- MMH & BBH lab statistics: # patients with smears or Xpert done (including EPTB samples)
- MMH & BBH X-Ray register: # PTB Chest X-Ray done
- Buhera TB case finding data (TB Alert Database)

¹ For all Xpert positive results one smear was performed for classification of the TB case

D. Cost effectiveness ratio

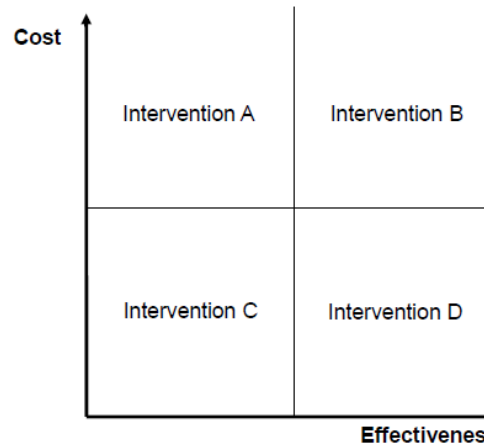
1. Calculation of cost effectiveness ratio

$$\text{ICER} = (\text{Cost A} - \text{Cost B}) / (\text{Effectiveness A} - \text{Effectiveness B})$$

where A and B are the 2 interventions we want to compare

2. Interpretation of cost effectiveness ratio

- If $\text{ICER} \leq 0$, it means one intervention is dominating the other (D is dominating A, B or C; A is dominated by B, C or D).
- If $\text{ICER} > 0$ (ICER B vs. C), the choice between 2 interventions will depend whether your strongest constraint is effectiveness over cost (more quality & less equity) or cost over effectiveness (less quality and more equity)



III. Results

A. Global cost / TB case detected



Cost / TB case diagnosed	Pre-Xpert	Post-Xpert	Incremental cost
Service provider	\$ 72	\$ 125	\$ 53
Patient	\$ 87	\$ 65	\$ -23
Total	\$ 159	\$ 190	\$ 31

Figure 3: Cost / TB case diagnosed in Pre and Post Xpert interventions

Our estimations of cost show:

- From a service provider perspective, the cost Post-Xpert intervention / TB case diagnosed is \$53 more than Pre-Xpert
- From a patient perspective, the cost Post-Xpert intervention / TB case diagnosed is \$23 less than Pre-Xpert
- From a global perspective, the cost Post-Xpert intervention / TB case diagnosed is \$31 more than Pre-Xpert (ICER > 0, the post-Xpert intervention is both more costly and more effective in terms of TB detection)

The cost driver in the Post-Xpert intervention is the price of the Xpert cartridges. Otherwise, the post-Xpert intervention is using fewer resources per TB case diagnosed in terms of doctors and nurses. Despite the fact that the cost of an Xpert diagnosis per se is 10 times the cost of a smear diagnosis, the cost of the Post Xpert intervention in our estimation is only 16% more per TB case detected.

The limits of our study are:

- we are considering MSF supply cost instead of local suppliers for consumables and equipment
- we are not considering the opportunity cost for the patient being sick waiting the diagnosis
- We are not considering the added value of DRTB detection in post-Xpert intervention

Details of the cost for both perspectives are explained in the following chapters

B. Service provider perspective

1. Cost/ TB case detected

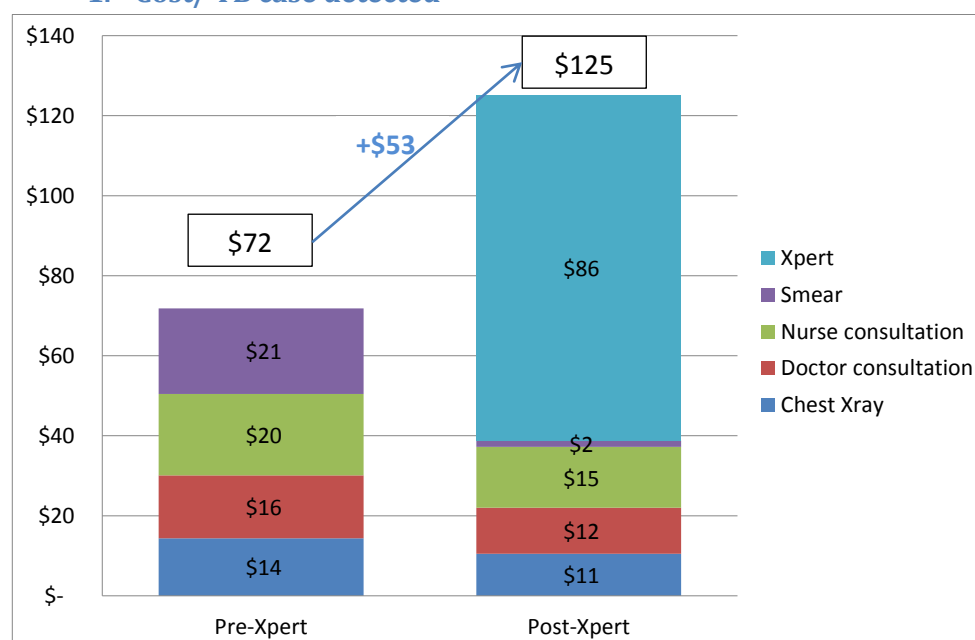


Figure 4: Cost / TB case diagnosed in Pre and Post Xpert interventions (provider perspective)

From service provider perspective:

- The use of resources such as Doctors, Nurses and X-ray is about 25% less in the Post-Xpert intervention. This is mainly explained by the better sensitivity of Xpert diagnosis compared to smear diagnosis which means:
 - less chest X-Ray and less doctor consultations are required in proportion to the population of TB suspects (impact on the numerator of the cost)
 - more TB cases are detected in proportion to the population of TB suspects (impact on the denominator of the cost)
- The cost of the diagnosis itself is 4 times more in the Post-Xpert intervention and represents 70% of its cost.

2. # units

.	Units / ingredient	# Patients concerned	Total units
Pre-Xpert			
Xpert	0.0	0	0
Smear	2.0	2 569	5 138
Chest Xray	1.0	1 944	1 944
Doctor consultation	1.0	1 944	1 944
Nurse consultation	2.1	3 211	6 743
Post-Xpert			
Xpert	1.0	1 776	1 776
Smear	1.0	310	310
Chest Xray	1.0	1 190	1 190
Doctor consultation	1.0	1 190	1 190
Nurse consultation	1.9	2 220	4 218

Figure 5: Units of resources needed in each intervention (provider perspective)

Explanations for the calculation of total number of units for each intervention:

- For Xpert, Smear and chest X-ray in each intervention, see II.C Effectiveness
- For Nurse consultation in each intervention- A folder review of TB cases diagnosed during the pre and post Xpert periods was performed. The average number of nurse consultations performed between identifying a TB suspect and determining a TB case was then calculated.
- For Doctor consultation, all patients referred for a CXR would require a doctor consultation for CXR interpretation.

3. Cost / unit

Cost of ingredients	Cost / unit
Smear	\$ 2.99
Xpert	\$ 29.22
Chest Xray	\$ 5.30
Nurse consultation	\$ 2.16
Doctor consultation	\$ 5.80

For more details on the different costs, see Annexes:

- VI.A Smear cost
- VI.B Xpert Cost
- VI.C X-ray cost
- VI.D Consultations Cost

Figure 6: Cost / unit of the ingredients (provider perspective)

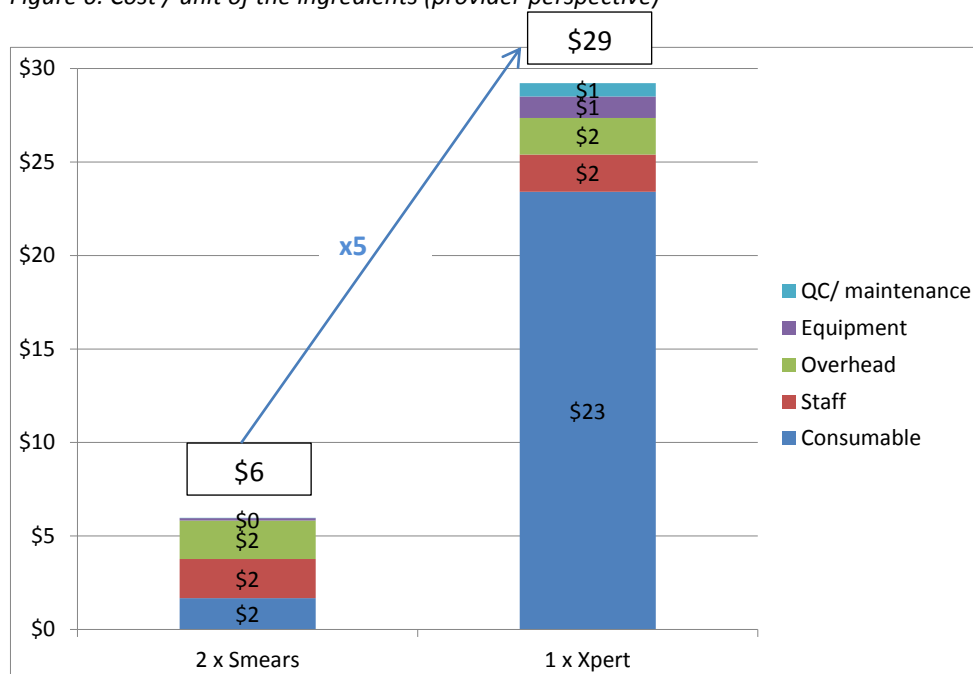


Figure 7: Comparison of the cost / diagnosis of smears and Xpert

- Cost of 1 Xpert is about 5 times the cost of 2 smears
- 80% of the cost of Xpert is the cartridge
- Cost of staff and overheads for 1 Xpert is the same as for 2 smears
- Cost of equipment (GeneXpert machine + training & installation cost, UPS and air conditioner) represents only 4% of the cost of 1 Xpert

Conclusions:

- From a service provider perspective, the Xpert diagnosis is the main cost driver of the Post-Xpert intervention (70% of the cost)
- The cartridge is the main cost driver of the Xpert diagnosis (66% of the cost). It is where the priority should be in terms of cost reduction

C. Patient perspective

1. Cost/ TB cases detected

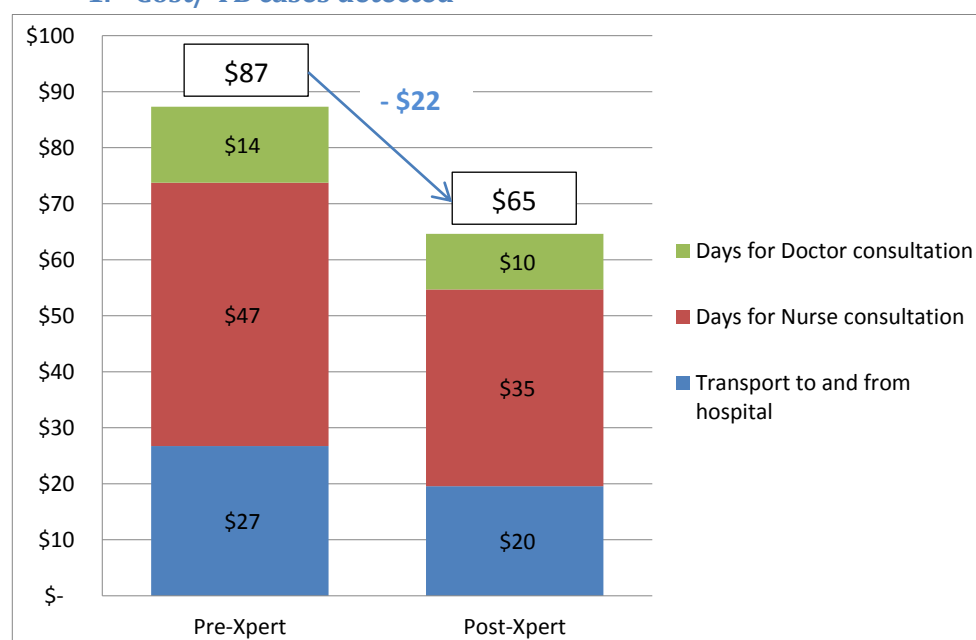


Figure 8: Cost / TB case diagnosed in Pre and Post Xpert interventions (patient perspective)

From the patient perspective, both the opportunity cost (wasted time to go to a consultation) and the transport cost are about 25% less in the Post-Xpert consultation. The reason is because of the improved sensitivity of Xpert compared to smear. Hence the Post-Xpert intervention requires less nurse consultations (at clinic level) and less doctor consultations (at hospital level) and therefore less transport cost / TB case diagnosed.

One limit of our analyses is that we did not consider the opportunity cost due to delay for the patient to receive their result. In the Post-Xpert intervention “Time-to-initiation of TB treatment at the decentralized clinics was reduced, which has the potential to reduce morbidity in individuals and reduce the risk of TB transmission to others”². Taking this into consideration, this opportunity cost will increase the difference of cost between the 2 interventions in favour of the Post-Xpert algorithm. This component will be analysed in the sensitivity analysis.

2. # units

.	Units / nature of cost	# Patients concerned	Total units
Pre-Xpert			
Transport to and from hospital	1.0	1 944	1 944
Days for Nurse consultation	2.1	3 211	6 743
Days for Doctor consultation	1.0	1 944	1 944
Post-Xpert			
Transport to and from hospital	1.0	1 190	1 190
Days for Nurse consultation	1.9	2 220	4 218
Days for Doctor consultation	1.0	1 190	1 190

Figure 9: Units of resources needed in each intervention (patient perspective)

² Bygrave et al., 2011 IAC 2012

Explanations for the calculation of total number of units for each intervention:

- Days for consultation: everybody needing a doctor and/or nurse consultation has an opportunity cost of one day.
- Transport to and from hospital: anybody having a chest-Xray and a doctor consultation has to pay public transport (we didn't consider the cost of transport to and from the clinic for the nurse consultation as this is done most of the time by foot).

3. Cost / unit

Cost of ingredients	Cost / unit
Days for consultation	\$ 5.00
Transport to and from hospital	\$ 9.86

Figure 10: Cost / unit of the ingredients (patient perspective)

The transport cost / patient to and from the hospital is based on the amount MSF reimbursed in the year 2011 to patients coming from different areas of Buhera district to Murambinda hospital with or without a caretaker. The reimbursement is based on public transport fees for the different areas of Buhera district. (For more details, see Annex VI.F Transport cost for patients)

The opportunity cost for 1 day of a patient from Buhera rural district is considered at the price that the community would pay for 1 day of work for farming activities: \$5/ day

In the sensitivity analysis, we will consider other estimates of the daily opportunity cost such as:

- National policy minimum wage: \$23/ day
- Commercial farming wage: \$10/ day

IV. Sensitivity analysis

A. Price of Xpert cartridge

The actual cost Buhera project is paying for a cartridge provided by MSF supply is \$21.71 (including transport which is \$1.87). The 1st sensitivity analysis will be by modifying ceteris paribus the price of a cartridge according to FIND and UNITAID negotiated prices:

- FIND negotiated price³
 - Current: \$19.4 including transport
 - for 1.5 million cartridges/y: \$15.5 including transport
 - for 3.0 million cartridges /y: \$11.7 including transport
- UNITAID negotiated price: \$9.90⁴ excluding transport or \$11.7 including transport at MSF supply cost

1. Current FIND negotiated price

Cost / TB case diagnosed	..				Incremental
.		Pre-Xpert	Post-Xpert		cost
Service provider	\$	72	\$ 114	\$	42
Patient	\$	87	\$ 65	\$	-23
Total	\$	159	\$ 179	\$	19

Figure 11: Cost / TB cases diagnosed with Xpert current FIND negotiated price

2. FIND negotiated price for 1.5 million cartridges /year

Cost / TB case diagnosed	..				Incremental
.		Pre-Xpert	Post-Xpert		cost
Service provider	\$	72	\$ 102	\$	31
Patient	\$	87	\$ 65	\$	-23
Total	\$	159	\$ 167	\$	8

Figure 12: Cost / TB cases diagnosed with Xpert FIND negotiated price for a volume of 1.5 million/y

3. UNITAID negotiated price⁵

Cost / TB case diagnosed	..				Incremental
.		Pre-Xpert	Post-Xpert		cost
Service provider	\$	72	\$ 91	\$	19
Patient	\$	87	\$ 65	\$	-23
Total	\$	159	\$ 156	\$	-3

Figure 13: Cost / TB cases diagnosed with Xpert UNITAID negotiated price

4. Conclusion

At \$11.70 (the price per cartridge Cepheid have agreed to drop to + freight at MSF supply cost), the post-Xpert intervention is more cost-effective than the pre-Xpert intervention ceteris paribus. The higher cost / TB case detected in the post-Xpert intervention from the service provider perspective is compensated by its lower cost/ TB case detected from a patient perspective (ICER <0, Pre-Xpert intervention is dominated by post-Xpert intervention).

³ Vassall A et al. 2011

⁴ Feedback from Durban TB Conference, 26th June 2012

⁵ Equal to FIND negotiated price for 3.0 million cartridges /year

B. Opportunity cost (1)

In our study, we have estimated the opportunity cost of patients coming to clinics or hospital at the daily rate of \$5 corresponding to the community salary for one day of farming activities in Buhera district.

This second sensitivity analysis considers modifying ceteris paribus this daily rate at:

- Commercial farming wage: \$10/ day
- National policy minimum wage: \$23/ day

1. Consultation time at private farming wage

Cost / TB case diagnosed	..			Incremental
.		Pre-Xpert	Post-Xpert	cost
Service provider	\$	72	\$ 125	\$ 53
Patient	\$	148	\$ 110	\$ -38
Total	\$	220	\$ 235	\$ 15

Figure 14: Cost / TB cases diagnosed with opportunity cost for consultation time at \$10/ day

2. Consultation time at national minimum wage

Cost / TB case diagnosed	..			Incremental
.		Pre-Xpert	Post-Xpert	cost
Service provider	\$	72	\$ 125	\$ 53
Patient	\$	305	\$ 227	\$ -79
Total	\$	377	\$ 352	\$ -25

Figure 15: Cost / TB cases diagnosed with opportunity cost for consultation time at \$23/ day

3. Conclusion

If we value the opportunity cost for the patient time spent for a consultation at the national policy minimum wage, ceteris paribus, the cost/ TB case detected is \$25 less in post Xpert intervention compared to pre-Xpert intervention (ICER <0, Pre-Xpert intervention is dominated by post-Xpert intervention).

C. Opportunity cost (2)

The opportunity cost due to delay for the patient to get their result was not taken into consideration. The median time to TB treatment initiation among HIV/TB co-infected patients with sputum-smear-negative TB decreased at decentralised sites (from 18.5 days to 7 days)⁶. For all patients at decentralised sites the time to initiation of treatment decreased from 13 to 7 days.

In this 3rd sensitivity analysis, we are considering, ceteris paribus, time to diagnosis for patients' opportunity cost:

- Time to diagnosis = 6 days less for smear negative TB case detected in Post-Xpert
- 50% of patient with TB waiting for diagnosis can't work
- Opportunity cost at:
 - either \$5 / day (Buhera district daily wage)
 - \$10 / day (private farming daily wage)

⁶ Bygrave et al., 2011 IAC 2012

1. Time to diagnosis at Buhera district wage

Cost / TB case diagnosed	..				Incremental
.		Pre-Xpert	Post-Xpert		cost
Service provider	\$	72	\$ 125	\$	53
Patient	\$	120	\$ 82	\$	-38
Total	\$	192	\$ 207	\$	16

Figure 16: Cost / TB cases diagnosed with opportunity cost for consultation time & time to diagnosis at \$5/ day

2. Time to diagnosis at private farming wage

Cost / TB case diagnosed	..				Incremental
.		Pre-Xpert	Post-Xpert		cost
Service provider	\$	72	\$ 125	\$	53
Patient	\$	213	\$ 145	\$	-68
Total	\$	285	\$ 270	\$	-15

Figure 17: Cost / TB cases diagnosed with opportunity cost for consultation time & time to diagnosis at \$10/ day

3. Conclusion

If we consider the opportunity cost of the patient consultation time + time to diagnosis at private farming daily wage ceteris paribus, the cost/ TB case detected is \$15 less in the post Xpert intervention compared to pre-Xpert intervention (ICER < 0, Pre-Xpert intervention is dominated by post-Xpert intervention).

D. X-ray cost in Patient perspective

If MSF was not present in Buhera district the patients would have to pay the X-ray fee which in MMH is \$10. In our estimates we have considered X-ray at a cost of \$5.3 from a service provider perspective and no cost from the patient perspective.

In our last sensitivity analysis, we have considered the X-ray at a \$10 cost from the patient perspective and no cost from the provider perspective.

Cost / TB case diagnosed	..				Incremental
.		Pre-Xpert	Post-Xpert		cost
Service provider	\$	57	\$ 115	\$	57
Patient	\$	114	\$ 84	\$	-30
Total	\$	172	\$ 199	\$	27

Figure 18: Cost / TB cases diagnosed with X-ray considered as a cost for the patient

V. Discussion

A. Conclusions

Whereas **Xpert diagnosis** costs **5 times more** than smear diagnosis, our estimates on primary data from the HIV/AIDS/TB programme in Buhera district in Zimbabwe show that the **Post-Xpert intervention** for TB diagnosis cost only **19% more** per TB case diagnosed than Pre-Xpert intervention (**provider + patient perspectives**). The reasons are:

- Pre-Xpert intervention is slightly less effective than Post-Xpert intervention in terms of TB cases detected amongst TB suspects
- Pre-Xpert intervention required more X-ray and more doctor consultations / TB suspects as smear is less sensitive than Xpert

Our estimates on primary data demonstrate that the Post-Xpert intervention is more cost effective than the Pre-Xpert intervention (ICER<0) from a **patient** perspective. The Pre-Xpert intervention requires higher transport and opportunity cost for patients than the Post-Xpert intervention (because of more X-Ray and doctor consultations / TB case detected).

The sensitivity analyses show that **Post-Xpert** intervention is **more cost effective** than Pre Xpert intervention (ICER <0) in 3 scenarios ceteris paribus:

- **Price of Xpert** cartridge at **\$11.7** including transport (UNITAID negotiated price +freight)
- Opportunity cost for the **patient consultation** time estimated at **\$23/ day** (daily national policy minimum wage)
- **Time to diagnosis** considered as an opportunity cost for **half of the TB cases** detected and estimated at **\$10/ day** (private farming daily wage)

B. Limits

Some important elements in favour of the Post-Xpert intervention in terms of cost-effectiveness are not taken in consideration in our study:

- Cases averted by earlier initiation of treatment
- DRTB detection not taken into consideration (including spreading the disease)
- Prices from MSF supply instead of local suppliers

C. Way forward

It could be considered to use the findings of our study in terms of unit costs to calculate the cost-effectiveness of the protocol 2nd Xpert for Xpert -. Data from Gutu project before and after Xpert could be used to determine the number of units needed for each ingredient of the diagnosis cost following this protocol.

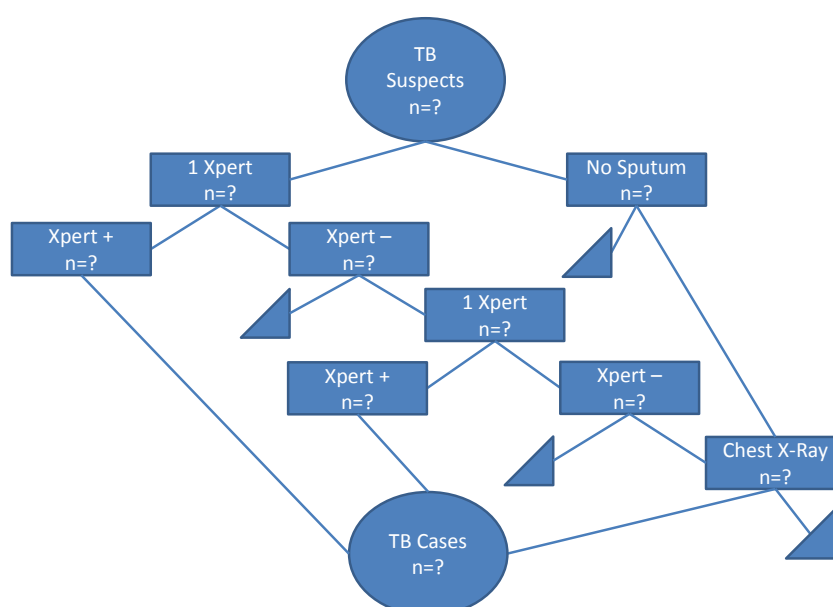


Figure 19: Post-Xpert algorithm for Gutu project

VI. Annexes

A. Smear cost

1. Smear activity

# Slides	2010	2011	2012 (4 months)
Diagnosis	6 629	4 891	648
Follow-up	737	386	158
Quality control	478	333	48
Total	7 844	5 610	854

Figure 20: # slides / year for ?PTB smear in MMH – Source: Lab stat

2. Estimation of lab FTE / slide for ?PTB (bottom-up methodology)

Description	No. Tests	Average time/ test	Total time
Tb Smears prep	5 277	2	10 554
Staining:10slides/batch	528	10	5 277
Reading slides			-
Negative	4 579	3	13 737
Scanty	125	3	375
1+	166	2	332
2+	140	1	140
3+	188	1	94
Control/IQC/EQC	333	5	1 665
Total Time (minutes)			32 174
# smears prepared			5 277
Average time/ smear (minutes)			6.10

Figure 21: MMH lab workload for smear diagnosis in 2011 – Source: Lab follow-up

3. Estimation of lab FTE / slide for ?PTB (top-down methodology)

	2010
# FTE dedicated to ?PTB Smear (year)	1
# FTE dedicated to ?PTB Smear (minutes)	100 800
# slides for ?PTB smear	7 366
Average time/ slide (min)	14
Average FTE/ slide (year)	0.000136

Figure 22: Calculation of FTE/ slide for ?PTB – Source: Lab technician interview + 2010 lab statistics

- We have considered 2010 data as the introduction of Xpert diagnosis in 2011 brings confusion to estimate the FTE dedicated to Smear (the microscopists are doing both)
- We have considered a FTE working 7 hours a day (exclusion of pauses), 5 days a week, 48 weeks a year (4 weeks leaves)

4. Discrepancy between bottom-up and top-down methodology

The top-down methodology shows a time/ slide twice longer compared to bottom-up strategy. We consider the top-down methodology being less biased than bottom-up methodology:

- in bottom-up methodology:
 - Misestimating by 1 or 2 minutes each step of the process leads to major variation in average time/ smear.
 - Hidden times are not taken in consideration

- The time calculated with top-down methodology seems more realistic for the 2 lab technician interviewed.

5. Smear annual cost (2011)

Description	# units / year	Cost/ unit (\$)	Cost / Year (\$)
Microscopist	0.8	7 730.50	5 888
Overhead	0.8	7 575.89	5 770
Sputum container	2 626.0	0.17	454
Slides	5 722.2	0.11	631
Auramine	6.0	47.78	287
Ethanol	48.0	69.06	3 315
Quality control	4.0	15.00	60
Fluorescent microscope	0.1	3 468.62	347
Total			16 751

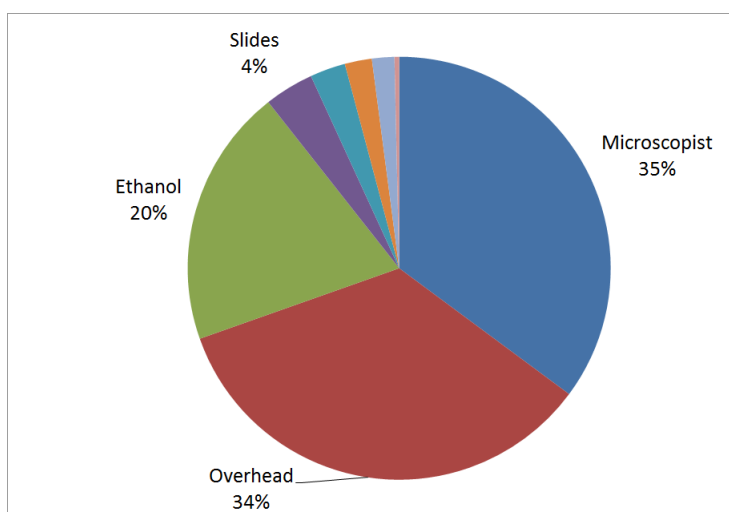
Figure 23: Calculation of smear annual cost in MMH lab in 2011

- Costs/ unit for staff, overhead and supply: see Annex E: Cost by nature of Expenses
- # units/ year for slides includes 2% waste
- Life expectancy for Fluorescent microscope (10 years), # units / year for consumables, unit & cost for QC: lab technician interview

6. Cost / Smear

Description	Cost / smear (\$)
Microscopist	\$ 1.05
Overhead	\$ 1.03
Ethanol	\$ 0.59
Slides	\$ 0.11
Sputum container	\$ 0.08
Fluorescent microscope	\$ 0.06
Auramine	\$ 0.05
Quality control	\$ 0.01
Total	\$ 2.99

Figure 24: Breakdown of Cost/ smear in MMH in 2011



B. Xpert Cost

1. Xpert activity

# Xpert	2012 (4 months)	Extrapolation (12 months)
Diagnosis	842	2 526
Error (7%)	59	177
Total	901	2 703
Full capacity	1 387	4 160
%	65%	65%

Figure 25: # Xpert done in the 4 first months of 2012– Source: Lab stat

2. Estimation of lab FTE / Xpert (top-down methodology)

Description	2012 (4 months)	Explanation
# FTE dedicated to ?PTB Smear & Xpert (year)	0.33	A= 4months/12months
# FTE dedicated to ?PTB Smear & Xpert (minutes)	33 600	B=A x (48 weeks x 5 days x 7 hours x 60 min)
# slides for ?PTB smear	854	C= see Annex A1
Average time/ slide (min)	14	D= see Annex A3
# FTE dedicated to ?PTB Smear (minutes)	11 691	E = C x D
# FTE dedicated to Xpert (minutes)	21 909	F= B-E
# Xpert done	901	G= see Annex B1
Average time/ Xpert (min)	24	H= F/G
Average FTE/ Xpert (year)	0.00024	I= H/(48 weeks x 5 days x 7 hours x 60 min)
# Xpert done / FTE/ Year	4 145	J=1/I

Figure 26: Calculation of FTE / Xpert

3. Investments related to Xpert

Description	Cost	Source
Xpert machine	\$ 20 712.97	See Annex G3
UPS	\$ 881.00	
Air conditioner (lab)	\$ 1 053.00	Logistix (bought locally)
Installation & training	\$ 506.00	SAGA 2011
Total	\$ 23 152.96	

Figure 27: Cost of investment for Xpert machine in MMH in 2011

4. Smear annual cost (2011)

Description	# units / year	Cost/ unit (\$)	Cost / Year (\$)
Microscopist	0.65	7 730.50	5 041
Overhead	0.65	7 575.89	4 940
Sputum container	2 526.00	0.17	437
Cartridge	2 702.82	21.71	58 689
Maintenance	1.00	1 800.00	1 800
Equipment	0.13	23 152.96	2 894
Total			73 800

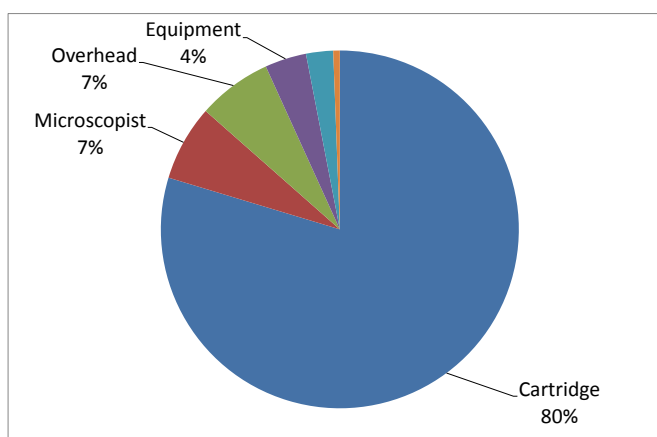
Figure 28: Calculation of Xpert annual cost in MMH lab

- Costs/ unit for staff, overhead and supply: see Annex E: Cost by nature of Expenses
- # cartridge / year for includes 7% error
- Maintenance cost from Pascale Chaillet, Laboratory Advisor, MSF
- Life expectancy for equipment (8 years): from F. Leme, Programs Manager, Cepheid

5. Cost / Xpert

Description	Cost / Xpert (\$)
Cartridge	\$ 23.23
Microscopist	\$ 2.00
Overhead	\$ 1.96
Equipment	\$ 1.15
Maintenance	\$ 0.71
Sputum container	\$ 0.17
Total	\$ 29.22

Figure 29: Breakdown of Cost/ Xpert in MMH



NB: The cost of cartridge includes 7% waste due to inconclusive results

C. X-ray cost

1. X-Ray activity

Month	1	2	3	4	5	6	7	8	9	10	11	12	Total
X-Ray patients	374	386	299	347	402	375	363	345	354	417	405	349	4 416

Figure 30: MMH X-Ray activity 2011 – Source: MMH X-Ray register

2. Films consumption

	stock 1/1/11	IN		OUT		Stock 31/12/11
		From MSF	From BBH	Expired	Consumptions	
FILM 24/30	700	3 400	200	400	3 700	200
FILM 35/43	-	3 800	-	-	3 800	-
FILM 30/40	800	1 000	200	500	1 500	-
Total	1 500	8 200	400	900	9 000	200

Figure 31: X-Ray Film Consumption in MMH – Source: MMH Pharmacy stock cards + Isystock

3. Discrepancy between X-ray activity and film consumption

2 raisons for the discrepancy have been identified:

- % waste of films: 5% estimated
- Number of films / patient: estimated average of 2 (1 for chest X-ray but can be many for fractures when the doctor asked for different angles)

Consistency control:

- 4.416 patients x 2 films x 1,05 waste= 9274 films
- Time spent by X-ray
 - Estimated by X-Ray technician (bottom-up method): 10 minutes
 - Estimated by Top-down method: 100.800 minutes / 9.000 films = 11 minutes / film

Estimated activity: 95% consumptions (5% error) = 8.550 X-ray films produced

4. X-Ray annual cost

Description	# units / year	Cost/ unit (\$)	Cost / Year (\$)
Film	9 000	2.58	23 216
Radiographer	1	11 443.00	11 443
Overhead	1	7 552.38	7 552
Developer	12	88.17	1 058
X-ray machine	0.05	17 000.00	850
Maintenance	1	638.50	639
Fixer	12	48.34	580
Total			45 338

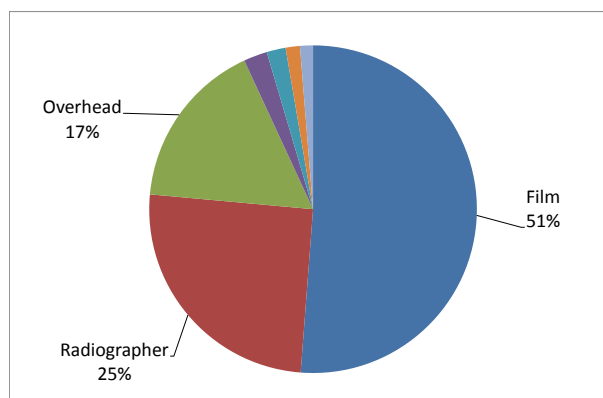
Figure 32: Calculation of X-Ray annual cost in MMH in 2011

- Unit costs for staff and supply: see Annex E: Cost by nature of Expenses
- Unit cost for X-ray machine is from quotation by Phillips to replace X-Ray machine in BBH
- Life expectancy for X-Ray machine (20 years) is from X-Ray technician
- Maintenance cost is from SAGA 2011

5. Cost / X-Ray

Description	Cost / X-Ray (\$)
Film	\$ 2.72
Radiographer	\$ 1.34
Overhead	\$ 0.88
Developer	\$ 0.12
X-ray machine	\$ 0.10
Maintenance	\$ 0.07
Fixer	\$ 0.07
Total	\$ 5.30

Figure 33: Breakdown of Cost/ X-ray in MMH in 2011



D. Consultations Cost

1. # Nurses in clinics

	Government	MSF	Council	Mission	Private	Total
Nurse RGN	1	2	1	3	2	9
Nurse PCN	12	4	38	1	0	55
Nurse Aid	5		18	2	0	25
Total	18	6	57	6	2	89

Figure 34: Breakdown of nurses in the 27 clinics of Buhera district in 2011 (exclusion of MMH, BBH and Buhera hospital) – Source: MOH District administrator

2. Nurse activity in clinics

	# visits	Weight	# consultations
ANC VISITS	12 080	1.0	12 080
OI/ART	61 960	1.0	61 960
VCT	9 427	1.0	9 427
OPD	224 700	1.0	224 700
STI	7 630	1.0	7 630
Chronic desase	14 788	1.0	14 788
EPI	64 002	0.3	21 334
Growth monitoring	57 108	0.2	11 421.60
Family planning	34 379	1.0	34 379
Total			397 720
# consultations / day			1 530
# nursing staff			89
# consultation /day/ nursing staff			17

Figure 35: Breakdown of activity in the 27 clinics of Buhera district in 2011 (exclusion of MMH, BBH and Buhera hospital) – Source: MOH District Statistician

3. Nursing staff average cost in clinics

	#	Annual cost	Total Cost
Nurse RGN	9	\$ 7 741	\$ 69 669
Nurse PCN	55	\$ 6 907	\$ 379 885
Nurse Aid	25	\$ 6 257	\$ 156 425
Total	89	\$ 6 809	\$ 605 979

Figure 36: Calculation of the average annual cost of nursing staff in the 27 clinics of Buhera district in 2011 (exclusion of MMH, BBH and Buhera hospital)

4. Nursing staff average cost in clinics

	Nurse	Doctor
Annual cost for 1 staff	\$6 809	\$17 075
Daily cost for 1 staff	\$28	\$71
# consultations/ day	17	17
Staff cost / consultation	\$1.65	\$4.14
Overhead	\$0.51	\$1.66
Total cost/ consultation	\$2.16	\$5.80

Figure 37: Calculation of the cost/ consultation for a nurse or a doctor in Buhera district in 2011

- Annual cost for nurse, doctor and overhead: see Annex E: Cost by nature of Expenses
- A nurse or a doctor is working 48 weeks a year x 5 days a week
- We consider # consultation/ staff/ day being the same for nurse and doctor

E. Cost by nature of Expenses

1. Cost of staff

Job description	Monthly Gross salary	Monthly Incentive	Annual cost
Doctor	\$575	\$800	\$17 075
Nurse in charge	\$457	\$150	\$7 741
Nurse RGN	\$439	\$100	\$6 907
Nurse PCN	\$389	\$100	\$6 257
Nurse Aid	\$327	\$23	\$4 527
General hand	\$308	\$23	\$4 280
Lab Scientist	\$511	\$400	\$11 443
Lab Technician	\$429	\$180	\$7 731
Radiographer	\$511	\$400	\$11 443

Figure 38: Cost of staff in Buhera district – Source: MMH accountant

- Monthly gross salary: from Zimbabwe Salary Services Bureau (SSB) including:
 - basic salary
 - transport & housing allowances
 - taxes
- Monthly incentive: from hospital donors
- Annual cost = Gross salary x 13 + Incentive x 12

2. Overhead cost⁷

Cost/ Consultation	Hospital OPD	Clinic OPD
Nursing Staff	\$ 2.39	\$ 1.57
Overhead	\$ 1.58	\$ 0.49
Total	\$ 3.97	\$ 2.06
% overhead / nursing staff	66%	31%

Figure 39: % overhead/ nursing staff for OPD consultation in Hospital and clinic in 2009 in Morija District, Lesotho

Overhead in OPD mainly includes:

- Management and administrative staff
- Water and electricity
- Transport
- Cleaning supplies
- Repairs and maintenance of buildings

Cost/ smear	Lab
Lab Staff	\$ 0.85
Overhead	\$ 0.83
Reagents & consumables	\$ 0.45
Total	\$ 2.13
% Overhead / staff	98%

Figure 40: % overhead/ lab staff for smear in 2009 in Morija District, Lesotho

Overhead in lab includes:

- Same nature of expenses as hospital OPD
- + Transport of samples between clinics and hospital by motorbike (driver + motorbike cost)

3. Cost of supply (Drugs, reagents, consumables & equipment)

Invoice	Code	Description	€/unit	\$/unit	Freight cost (air) \$	Total cost \$/unit
10408665	DORAAMOX5T	AMOXICILLIN, 500 mg, tab.	0.03	0.04	0.00	0.04
10406341	ELAECONT1S	CONTAINER, SAMPLE, sputum, plastic, non sterile	0.09	0.13	0.04	0.17
29403641	ELAEFLUO2--	FLUORESCENCE ILLUMINATOR (FluoLED Royal blue) for microscope	1 099.40	1 540.15	24.34	1 564.49
11401285	ELAEGENX1--	REAL TIME PCR SYSTEM (GeneXpert GX-IV), 4 modules +computer	14 661.77	20 539.67	173.29	20 712.97
91403500	ELAEGENX101	(GeneXpert) Test MTB/RIF, cartridge	14.17	19.84	1.87	21.71
29404625	ELAEIMCR5--	MICROSCOPE (Olympus CX21), COMPLETE (bin.,mirror/mains, box)	1 303.97	1 826.73	77.40	1 904.13
10406196	ELAESLID1F-	SLIDE, frosted, 76 x 26 mm, 1-1.2 mm thickness	0.02	0.03	0.08	0.11
11401610	PELEZBE0532	UPS, ON-LINE DOUBLE CONVERSION, 2000VA 230VAC 50Hz	458.46	642.26	238.74	881.00
11405099	SDIMDEVE2P-	DEVELOPER, X-RAY, powder for 22.5 l	50.34	70.52	17.65	88.17
91402668	SDIMFILMG35	FILM X-RAY, green sensitivity, 35 x 43 cm	1.71	2.40	0.18	2.58
91402669	SDIMFIXA2P-	FIXER, X-RAY, powder for 22.5 l	21.91	30.69	17.65	48.34
91402434	SLASETHA9B1	ETHANOL, denaturated, 95%, 1 l, bot.	44.60	62.48	6.57	69.06
10404294	SLASZTF0336	AURAMINE O (C.I. 41000) 50 g, powder, bottle.	32.37	45.34	2.43	47.78

Figure 41: Costs including freight of consumables and equipment provided by MSF Supply to Murambinda project – Sources: MSF supply documents + SAGA

⁷ We are taking % overhead / staff in Morija district Lesotho in 2009 as a proxy – cf. Jouquet G. & al.; 2011

F. Transport cost for patients

Year	2011	
IDPROJET	30	
IDCOMPTA	6440	
IDDEWISE	USD	
.		
Total amount paid by MSF for patient busfare	\$7 631	
Total # patients transported	774	
Average transport cost / Patient	\$9.86	

Figure 42: Average transport cost / patient (way and back)– Source: SAGA

VII. References

Singh JA, Bhan A. The ethics of national tuberculosis programmes in low-income countries not rolling out Xpert® MTB/RIF. *Int J Tuberc Lung Dis* 2011; 15(12): 1563

Vassall A, van Kampen S, Sohn H, Michael JS, John KR, et al. (2011) Rapid Diagnosis of Tuberculosis with the Xpert MTB/RIF Assay in High Burden Countries: A Cost-Effectiveness Analysis. *PLoS Med* 8(11): e1001120. doi:10.1371/journal.pmed.1001120

H. Bygrave, S. Simons, D. Munyaradzi, B. Nyagadza, C. Metcalf1, K. Ncube, S. Van Den Broucke (2011); Implementing Xpert® MTB/RIF in rural Zimbabwe: impact on diagnosis of smear-negative TB and time-to-initiation of TB treatment in smear-negative patients co-infected with HIV. *THAB0105 AIDS* 2012 Washington

Jouquet, Guillaume; Bygrave, Helen; Kranzer, Katharina; Ford, Nathan; Gadot, Laurent ; Lee, Janice; Hilderbrand, Katherine; Goemaere, Eric; Vlahakis, Natalie; Trivino, Laura; Makakole, Lipontso; Cleary, Susan (2011) Cost and Cost-Effectiveness of Switching From d4T or AZT to a TDF-Based First-Line Regimen in a Resource-Limited Setting in Rural Lesotho. *JAIDS Journal of Acquired Immune Deficiency Syndromes*: November 2011 - Volume 58 - Issue 3 - p e68–e74 doi: 10.1097/QAI.0b013e31822a9f8d