Diagnosing Xpert MTB/RIF negative TB suspects: Impact and cost of an alternative algorithm

Kathryn Schnippel[1], Gesine Meyer-Rath[1,2], Lawrence Long[1], Wendy Stevens[3,4], Ian Sanne[1,2], and Sydney Rosen[1,2]

[1]Health Economics and Epidemiology Research Office (HE[2]RO), Department of Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

[2]Center for Global Health and Development, Boston University, Boston, USA

[3]Department of Molecular Medicine and Haematology, University of the Witwatersrand, Johannesburg, South Africa

[4]National Health Laboratory Service, Johannesburg, South Africa

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The Impact and Cost of Scaling up GeneXpert MTB/RIF in South Africa

Gesine Meyer-Rath[1,2]*, Kathryn Schnippel[1], Lawrence Long[1], William MacLeod[1,2], Ian Sanne[1,2], Wendy Stevens[3,4,5], Sagie Pillay[3,4], Yogan Pillay[6], Sydney Rosen[1,2]

- National TB Cost Model (NTCM)
  - Population-level decision model
  - Compared Xpert diagnostic algorithm to old guidelines
  - Estimated incremental impact and cost of Xpert roll-out 2011-2016

HIV+, Xpert negative TB suspects

- 56% to 70% of TB suspects HIV-infected
- 50% to 75% of TB disease in HIV-infected is smear negative
  - High morbidity and mortality
- Sensitivity of single Xpert if Sm- 63% to 79%
- In 2014, 1.4 million TB suspects (53% of all TB suspects) need further diagnosis

Scott et al, 2011; Lawn et al, 2011; Boehme et al, 2010; Boehme et al, 2011; Meyer-Rath et al, 2012

High cost, low yield

- Current algorithm calls for Xpert-, HIV+ TB suspects to have
  - Culture (2-6 weeks for results)
  - Chest x-ray
  - Examination
  - Antibiotics
- 10% of all TB cases
- 60% of the cost of the entire PTB diagnostic program in South Africa

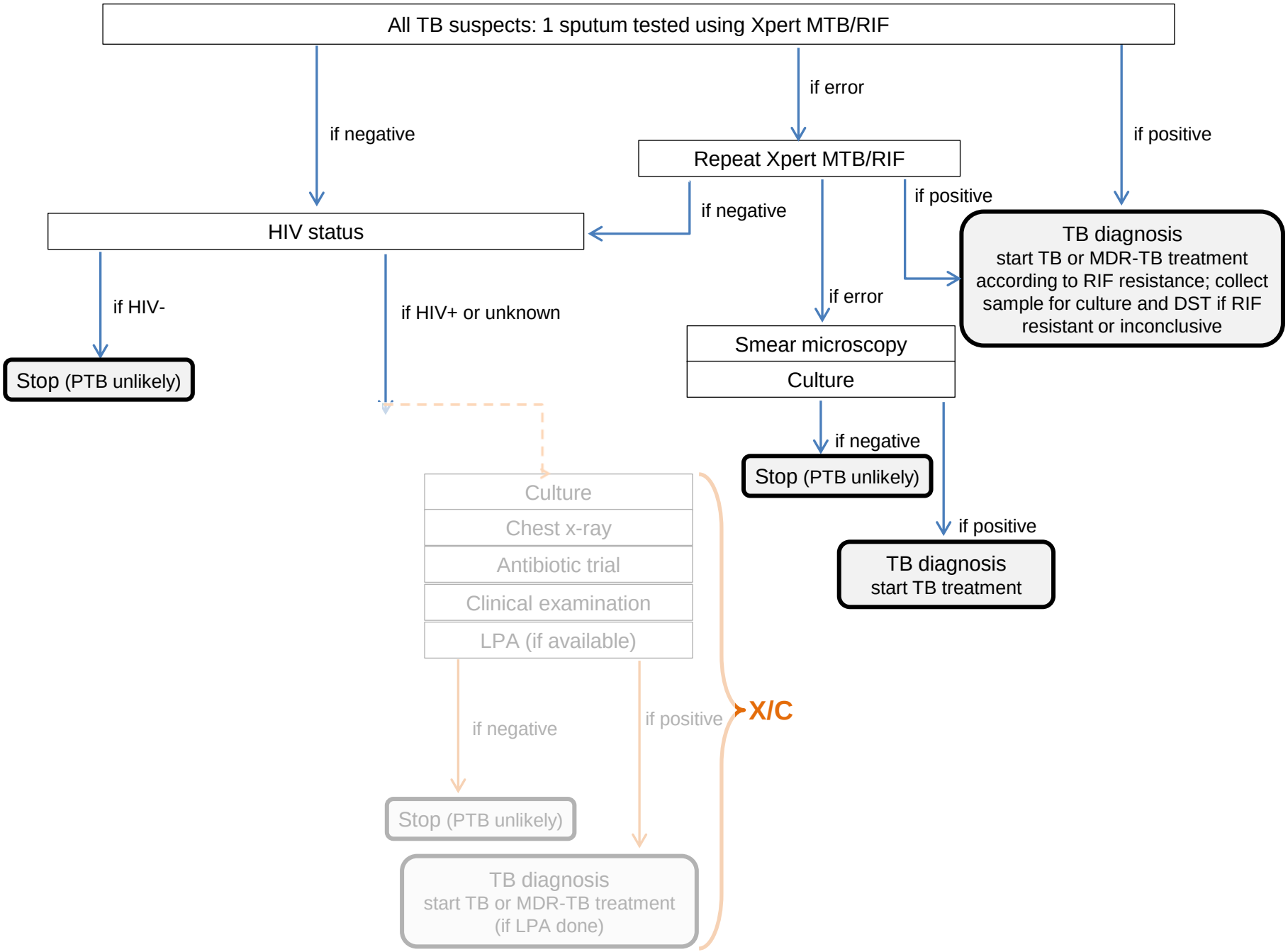
Meyer-Rath et al, 2012

Costs of Xpert vs culture

- Xpert test = R166
  Xpert MTB/RIF cartridge in 2014=$10.72
- Culture = R103 to R270
  average for HIV+/Xpert- = R107

NTCM: incremental cost and impact of an Xpert/Xpert algorithm

- Is a diagnostic algorithm using a second Xpert test for HIV+/Xpert- TB suspects (**X/X**) cost-effective compared to the current Xpert algorithm using culture/chest x-ray/antibiotic trial (**X/C**)?


All TB suspects: 1 sputum tested using Xpert MTB/RIF
if negative
if error
if positive
Repeat Xpert MTB/RIF
if negative
if positive
HIV status
TB diagnosis
start TB or MDR-TB treatment according to RIF resistance; collect sample for culture and DST if RIF resistant or inconclusive
if HIV-
if HIV+ or unknown
if error
Smear microscopy
Culture
Stop (PTB unlikely)
if negative
if positive
TB diagnosis
start TB treatment
Culture
Chest x-ray
Antibiotic trial
Clinical examination
LPA (if available)
if negative
if positive
X/C
Stop (PTB unlikely)
TB diagnosis
start TB or MDR-TB treatment
(if LPA done)

NTCM updates and adjustments

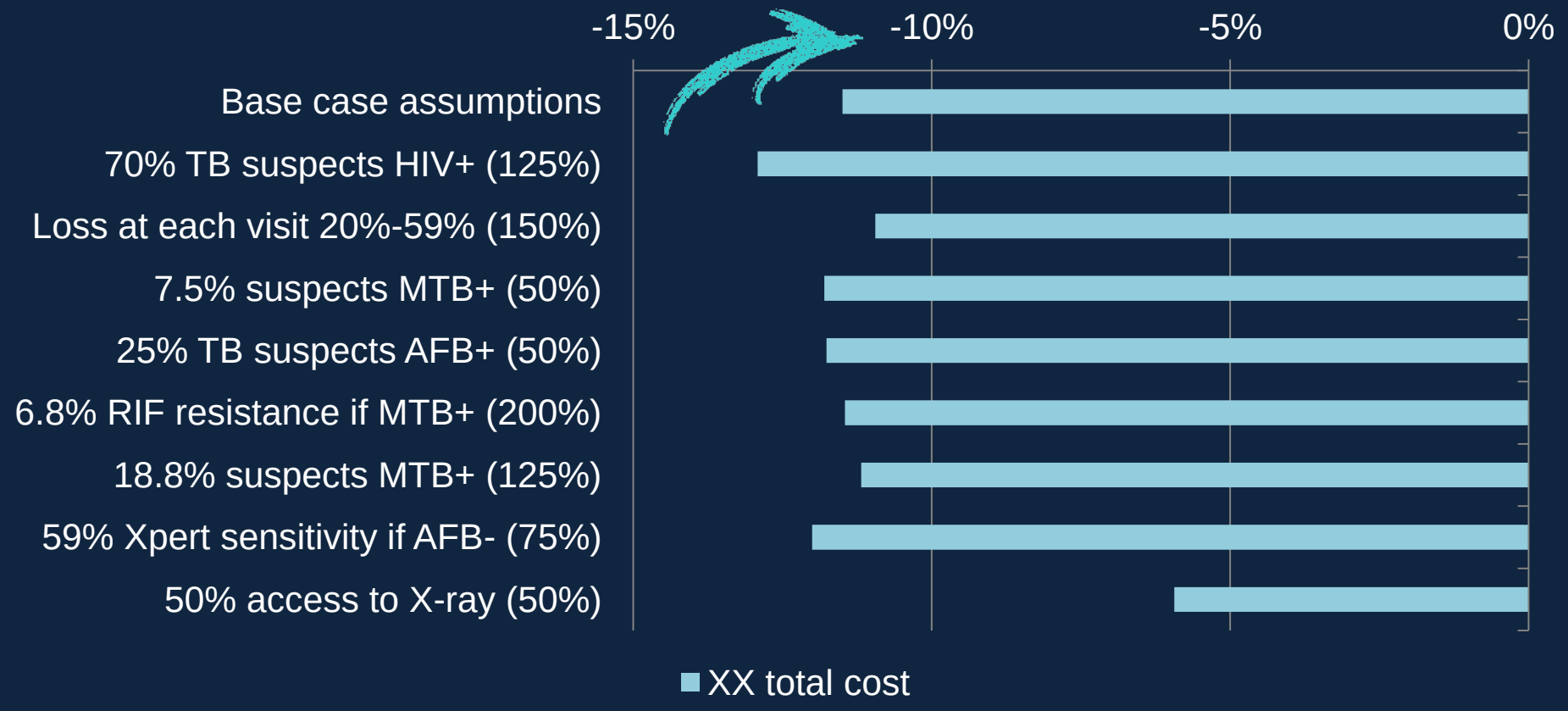
- 2011 smear microscopy, line probe assay, and Xpert laboratory volumes
- 2011 drug and laboratory costs
- MDR-TB treatment guidelines
  - MDR-TB smear negative cases treated as outpatient
- loss to follow-up and death during treatment
- XDR-TB (10% of MDR-TB patients)
- WHO CHOICE unit costs for non-drug treatment costs

Incremental cost of X/X vs X/C

Base case scenario	X/C	X/X	Incremental change of X/X over X/C	
Total annual cost of PTB diagnosis	R1,094 million	R969 million	-R126 million	-11%
Cost per suspect	R426	R376	-R51	-12%
Cost per case diagnosed	R2,567	R2,314	-R246	-10%
Cost per case initiated on treatment	R3,044	R2,682	-R362	-12%
Total annual cost of PTB diagnosis and treatment	R2,312 million	R2,194 million	-R118 million	-5%

Parameters varied systematically in sensitivity analysis; total cost sensitive only to cost of Xpert test; cost savings across all tested scenarios.

Uncertainty analysis: Total diagnostic cost savings under X/X



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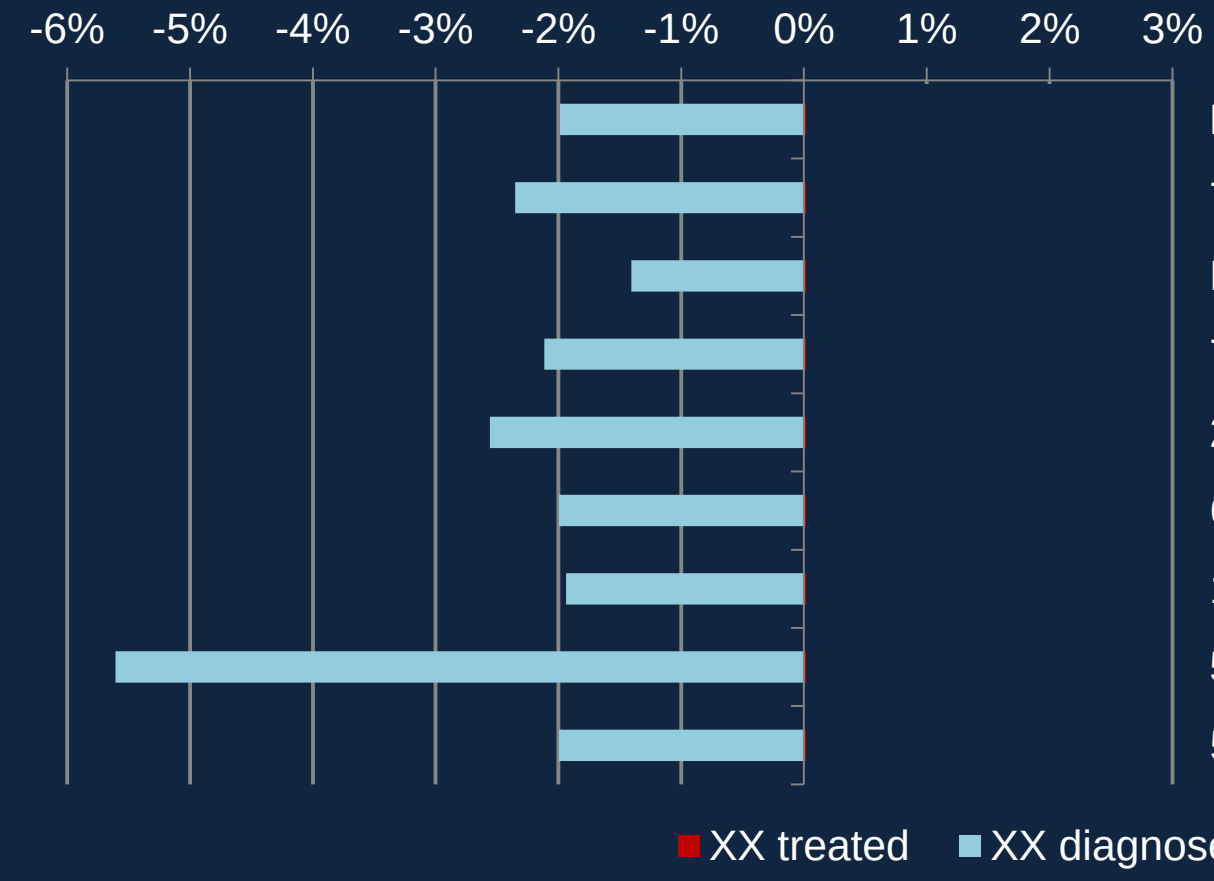
Results: Incremental impact of X/X

Base case scenario	X/C	X/X	Incremental change of X/X over X/C	
Number of TB cases diagnosed	426,558	418,079	- 8,479	-2%
Number of MDR-TB cases diagnosed	11,033	10,861	- 172	-2%
Number of TB cases initiated on treatment	359,274	361,136	+1,862	+1%
Number of MDR-TB cases initiated on treatment	9,341	9,397	+56	+1%

Uncertainty analysis: Patients diagnosed and treated



Base case assumptions

70% TB suspects HIV+ (125%)

Loss at each visit 20%-59% (150%)

7.5% suspects MTB+ (50%)

25% TB suspects AFB+ (50%)

6.8% RIF resistance if MTB+ (200%)

18.8% suspects MTB+ (125%)

59% Xpert sensitivity if AFB- (75%)

50% access to X-ray (50%)

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Conclusions

- Across a wide range of assumptions, modifying the pulmonary TB diagnostic algorithm from **X/C** to **X/X** could:
  - provide rapid results
  - simplify diagnostic processes
  - improve HIV/TB treatment outcomes
  - generate cost savings

Thank you

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Model inputs and assumptions

Parameter	Value in 2014	Variation (Sensitivity)	Source
TB suspects	2,573,504		Meyer-Rath et al 2012
Proportion TB suspects HIV+	56%	42-70%	ETR 2010
Proportion TB suspects sputum smear+ (2 sputa)	7%	3.5-10.5%	Meyer-Rath et al 2012
Proportion TB suspects culture+ if smear-	9%	4.5-13.5%	Meyer-Rath et al 2012
RIF+INH resistance (MDR-TB)	3%	1.5 – 4.5%	Weyer et al 2007
Xpert sensitivity, smear-	79%	63%-95%	Boehme et al 2011
% loss-to-follow-up at visit 1, 2, 3	13%, 26%, 39%	7-20%	Boehme et al 2011
% lost to follow-up or dead, 1st line treatment	14%		WHO 2011
% lost to follow-up or dead, MDR-TB treatment	30%		NDOH 2011
% of patients who die during XDR-TB treatment	36%		Dheda et al 2010

Model inputs: costs

Parameter	ZAR	Source
Xpert MTB/RIF test (including cartridge)	R166	Meyer-Rath et al 2012
Chest x-ray	R119	Public sector charges 2011
Empirical antibiotics	R11	Public sector drug prices 2011
Nurse visit	R72	OSD 2011
Doctor visit	R130	OSD 2011
Drug-sensitive TB	R2,769	NDOH TB treatment guidelines 2009; NDOH DR-TB treatment 2011; Public sector drug prices 2011; WHO CHOICE 2008 SA unit prices (inflated to 2011)
RIF mono-resistant TB	R17,330	
INH mono-resistant TB	R4,931	
MDR-TB (in-patient)	R55,440	
XDR-TB	R205,910	