Introducing new TB diagnostics for those living with HIV: consequences for the South African health budget

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Starting point

- **In South Africa 2009, 58% of the people diagnosed with TB were also HIV positive**
- For persons living with HIV, TB can be quickly fatal (globally leading killer for those with HIV (19% of deaths))
- Yet, the diagnosis of TB in those with HIV is complex
- Conventional 'point of care' tests (smear microscopy) are not very sensitive for those with HIV . Other tests take time (culture)/ can be expensive , with many TB suspects not returning for results.
- New diagnostic Xpert MTB/RIF has much higher sensitivity, is quicker - potential for point of care use
- It also provides a signal for MDR-TB (Rif resistance)

First potential 'game changer' for TB control for many years (since SC regimens/MDR-TB treatment)

Boehme CC, Nabeta P, Hillemann D, et al. Rapid molecular detection of tuberculosis and rifampin resistance. N Engl J Med. 2010 Sep 9;363(11):1005-15

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Results and lessons learned using economic analysis

- Initial decision modelling
- Global recommendation
- Country roll-out – South Africa

- => Use of economic data during the process

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Background – Cost-effectiveness

- Decision analytic cohort model (Treeage Williamstown USA)
- Two scenarios: Xpert replaces smear microscopy, or in addition to smear microscopy
- 10,000 *TB suspects* including patients with S+ and S- pulmonary TB
  - Presenting with prolonged cough with or without systemic or other symptoms suggestive of pulmonary TB – as in field trial
- Separately for:
  - new and previously treated patients
  - HIV- and HIV+ patients
  - RIF-resistance/MDR
- *Three countries (SA, India, Uganda)*

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Model Parameterisation

- Test cost data (all TB test costs) empirical
- WHO choice estimates and literature sources treatment cost estimates
- Test performance from clinical trial sites

  Boehme CC, Nicol MP, Nabeta P et al. Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicentre implementation study. Lancet. 2011 Apr 30;377(9776):1495-505.
- Cohort pathway probabilities (ie initial default, default before diagnosis, adherence, return to system) literature based and assumptions
- Monte Carlo probabilistic sensitivity analysis
- A wide range of one and two sensitivity analysis for main assumptions

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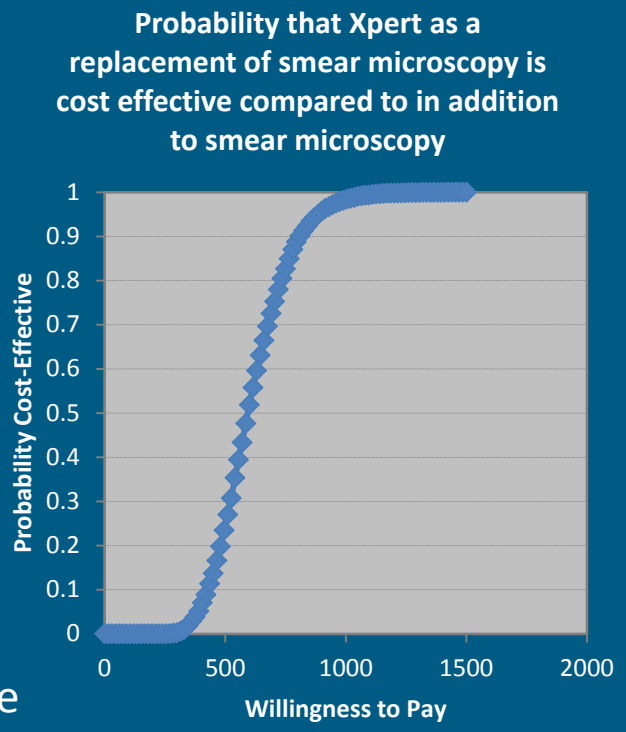
Incremental Cost Effectiveness Ratio (Cost per DALY) (US$2010)

Scenario	Cost per DALY	ICER compared to base case, mean	ICER compared to 'in addition to,' mean
Base Case	69		
In addition to smear	78	110	
Replacement of smear	85	138	582



Xpert MTB/RIF as a replacement of smear microscopy is predicted to be a highly cost-effective intervention at a willingness to pay threshold well below GDP per capita

Vassall A, van Kampen S, Sohn H, Michael JS, John KR, den Boon S, Davis JL, Whitelaw A, Nicol MP, Gler MT, Khaliqov A, Zamudio C, Perkins MD, Boehme CC, Cobelens F. Rapid diagnosis of tuberculosis with the Xpert MTB/RIF assay in high burden countries: a cost-effectiveness analysis. PLoS Med. 2011 Nov;8(11)

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Policy Impact

1. Policy decisions
   - WHO recommdendation to adopt Xpert
   - South Africa committed to roll-out Xpert
   - Global concern about budgetary implications (MDR-TB) and whether effectiveness could be achieved in practice (laboratory feasibility, health systems response)

Limitations of global exercise

- But influenced by the extent to which Xpert can to address loss to follow up (health systems/ quality/ patient costs) and the unit costs of diagnosis and treatment

- Technical and programmatic recommendation

  - *Evidence for Scale-up Group. Which new diagnostics for tuberculosis, and when? J Infect Dis. 2012 May 15;205 Suppl 2:S191-8.*
  - *Dowdy D, Vassall A, Cobelens F. Tuberculosis control in crisis: economic honesty and comparative effectiveness. Int J Tuberc Lung Dis. 2012 Aug;16(8):1131-2.*

- Does not providing sufficiently detailed data for financing at the country level

XTEND/XPHACTOR project

Step-wedged (random clusters of facilities) pragmatic trial

To measure the effectiveness of Xpert MTB/RIF in reducing early mortality in TB suspects – DURING ROLL-OUT.

To examine the effect of Xpert MTB/RIF availability on health care worker investigation practice (and changes in HR/ fixed resource capacity use)

To estimate the incremental cost per life saved and DALY averted from improved TB suspect outcomes from a provider and client perspective

To estimate the population-level impact of Xpert MTB/RIF roll-out using transmission modelling.

To examine screening/ triage in populations in HIV treatment and care

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Preparation for roll-out and trial

- Estimate the resource requirements of scaling up Xpert MTB/RIF in South Africa over a five year period
- Two groups asked – HE²RO/ UCT – existing planning model and cohort model
- In doing so, access to locally available data to better assess data gaps in the current knowledge in respect of Xpert MTB/RIF population level costs and affordability
- Strengthen links with policy makers
- Provide recommendations in terms of data collection and modeling during XTEND and beyond.

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Methods

- ASSA and TB incidence data used to establish population in need.
  - TB incidence based on static epidemic.
  - Suspect population from TB smear positives (limited)
- Model adjusted to newly available treatment, laboratory and other national data – plus confirmed algorithm
- Treatment/ MDR-TB cost impact
- Economies of scale (limited)
- 2 scale-up scenarios (case detection) - and extensive sensitivity analyses

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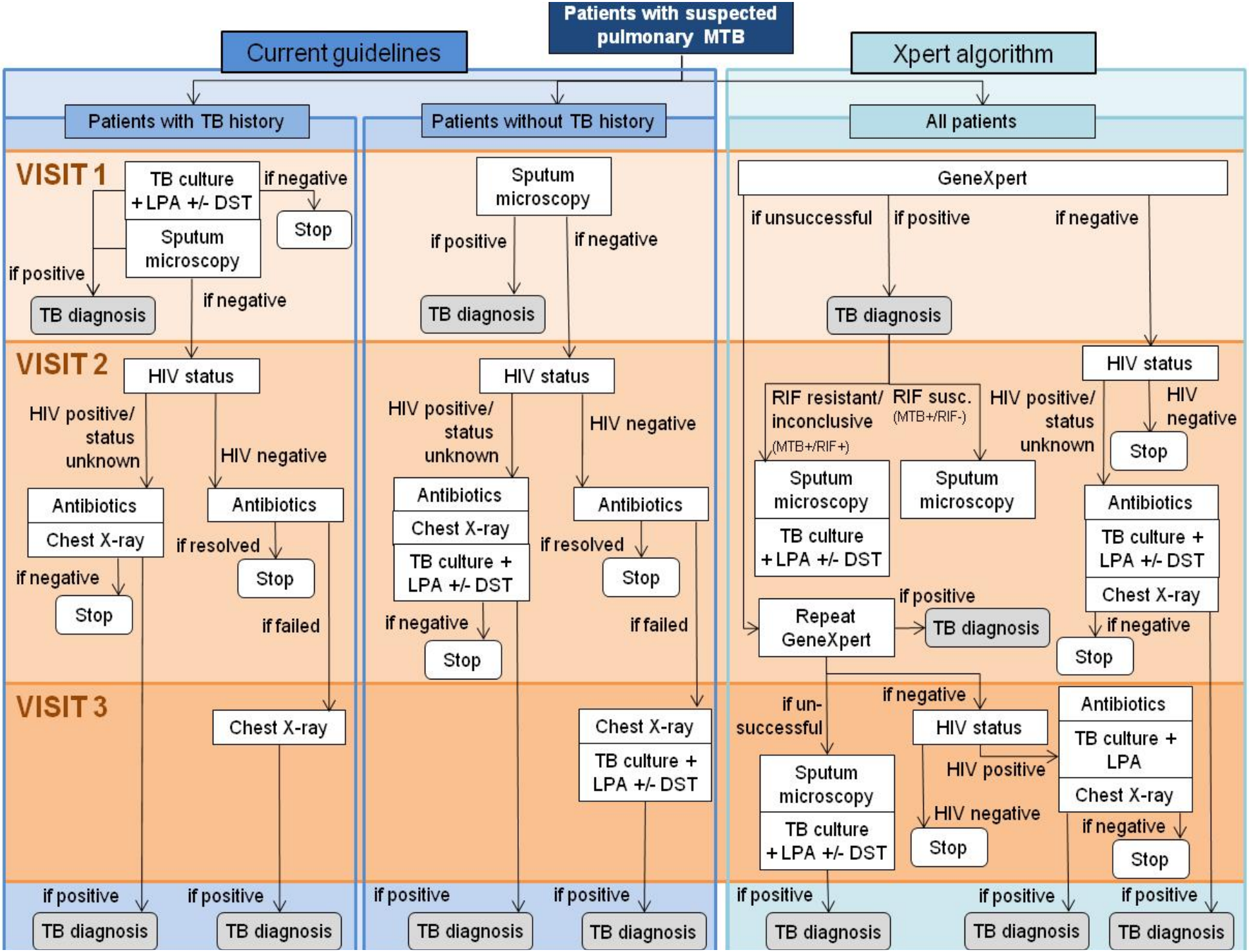
Patients with suspected pulmonary MTB
Current guidelines
Xpert algorithm
Patients with TB history
Patients without TB history
All patients
VISIT 1
TB culture + LPA +/- DST
Sputum microscopy
if negative
Stop
if positive
TB diagnosis
if negative
Sputum microscopy
if positive
if negative
TB diagnosis
GeneXpert
if unsuccessful
if positive
if negative
TB diagnosis
VISIT 2
HIV status
HIV positive/ status unknown
HIV negative
Antibiotics
Chest X-ray
if negative
Stop
Antibiotics
if resolved
Stop
if failed
HIV status
HIV positive/ status unknown
HIV negative
Antibiotics
Chest X-ray
TB culture + LPA +/- DST
if negative
Stop
Antibiotics
if resolved
Stop
if failed
RIF resistant/ inconclusive (MTB+/RIF+)
RIF susc. (MTB+/RIF-)
Sputum microscopy
TB culture + LPA +/- DST
Sputum microscopy
Repeat GeneXpert
if positive
TB diagnosis
HIV status
HIV positive/ status unknown
HIV negative
Stop
Antibiotics
TB culture + LPA +/- DST
Chest X-ray
if negative
Stop
VISIT 3
Chest X-ray
Chest X-ray
TB culture + LPA +/- DST
if un-successful
if negative
HIV status
Sputum microscopy
TB culture + LPA +/- DST
HIV positive
HIV negative
Stop
Antibiotics
TB culture + LPA
Chest X-ray
if negative
Stop
if positive
TB diagnosis
if positive
TB diagnosis
if positive
TB diagnosis
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TB diagnosis
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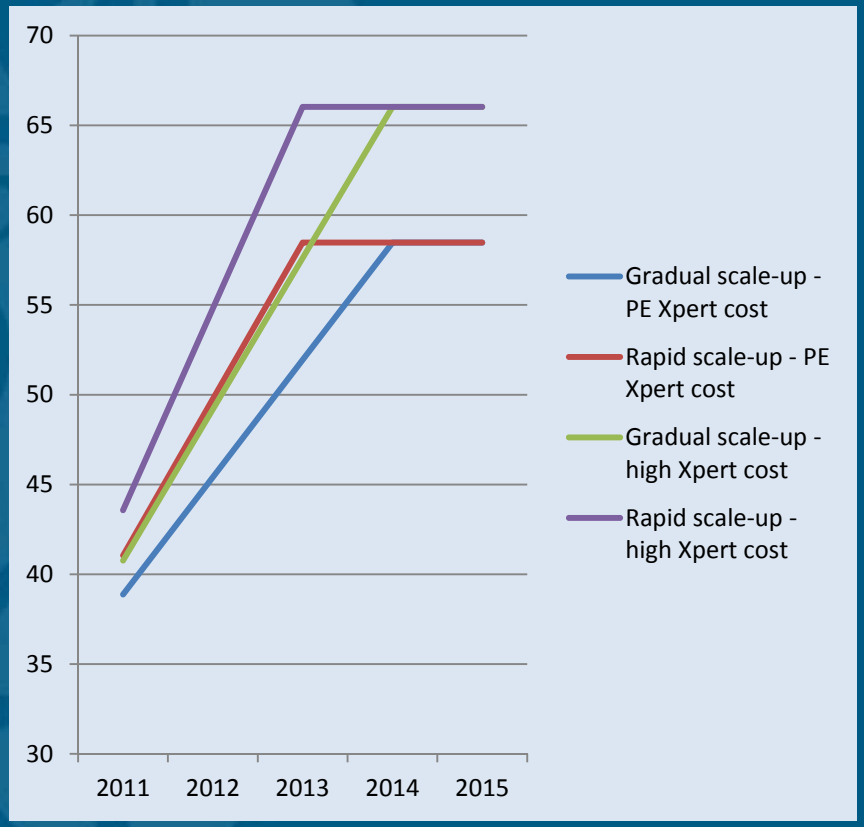
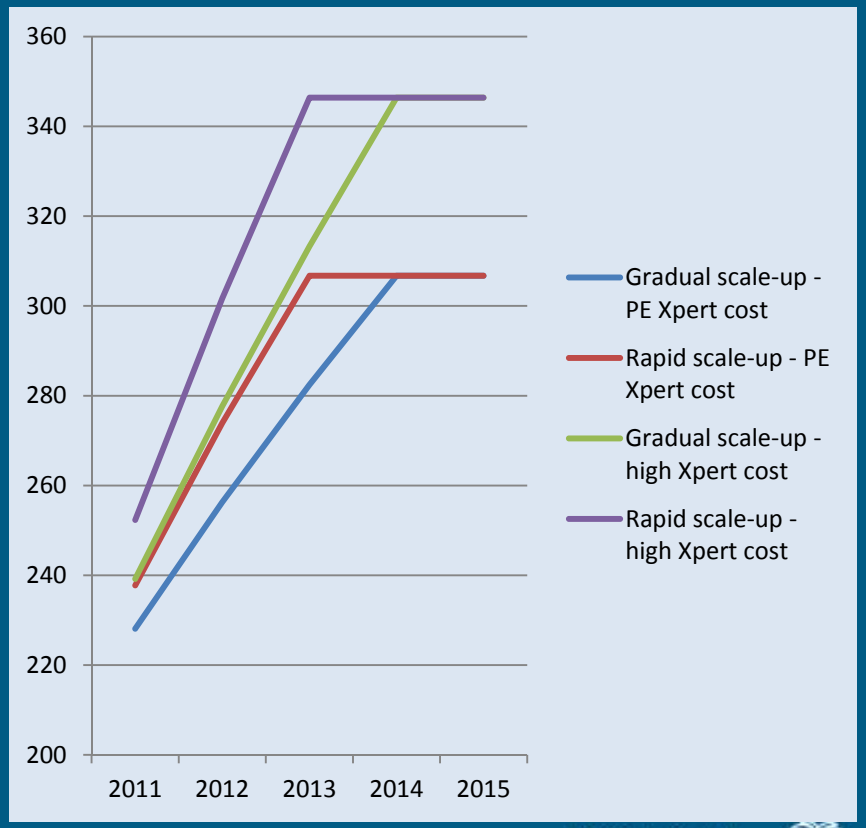
TB diagnosis
if positive
TB diagnosis

Mean cost per suspect and case diagnosed US$ 2011





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Predictions – Case detection increases at historical trends

Years	2011	2015	% increase
Numbers of suspects	1,878,274	1,992,897	6%
Diagnostic costs (US$)	73,014,526	116,525,404	60%
Treatment costs (US$)	533,679,235	636,933,809	19%
Total costs (US$)	606,693,762	753,459,213	24%
TB cases detected	311,751	364,129	17%
MDR TB cases detected	8,357	15,769	89%

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Predictions – case detection expands from 2010 SA policy

Years	2011	2015	% increase
Numbers of suspects	1,996,829	2,716,664	36%
Diagnostic costs (US$)	81,971,174	158,844,305	94%
Treatment costs (US$)	575,234,259	868,251,082	51%
Total costs (US$)	657,205,433	1,027,095,387	56%
TB cases detected	335,142	496,370	48%
MDR TB cases detected	9,653	21,495	123%

High-end estimate may be significantly reduced , if MDR- TB treatment costs can be reduced

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Policy implications

- In 2010/11 and 2011/12, health spending is projected to be US $14.4 billion and US $16 billion respectively, with around 5.2% of the total health budget was spent on TB in 2010/11
- Top-end 2.5% increase in SA health budget
- Joint presentation of both studies estimates
- Discussions with MoF - affordable in current fiscal climate
- Key issue remains is lives saved during roll-out (MoF aware of health systems limitations).
- MDR-TB costs less of a concern.

Questions remaining

- Direct effects in real world setting (pragmatic trial) – TB/HIV mortality
- Patient cost savings
- Effect of Xpert roll-out on transmission
- Costs (and models) of MDR-TB treatment
- Costs of TB treatment and diagnostics taking into account changing capacity (recent price reductions)
- Impact on ART costs
- Screening for those accessing HIV care and treatment

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