

# **Xpert MTB/RIF for diagnosis of tuberculosis in South Africa: Evaluating impact and cost effectiveness in routine roll-out**

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# Overview

- Background
- Justification
- Objectives
- Study methods
- Significance



# Background

**SA has one of the worst TB epidemics in the world!**

- Ranked 3rd globally
- 4<sup>th</sup> greatest burden of MDR TB
- SA has the most number of HIV-infected TB patients in the world
- Case detection and cure rates below WHO targets
- In order to control TB in South Africa both the cure rate and the case detection rate need to be improved.



**WHO, Global TB control; 2010**

# More recently Xpert MTB/RIF has shown a lot of promise in diagnosis of TB

FIND evaluation studies

Single Xpert on unprocessed sputum

- Sensitivity

— Smear positives	98.2%
— Smear negatives	72.5%
— Rif resistant	97.6%



*Boehme et al, N Engl J Med; 2010*

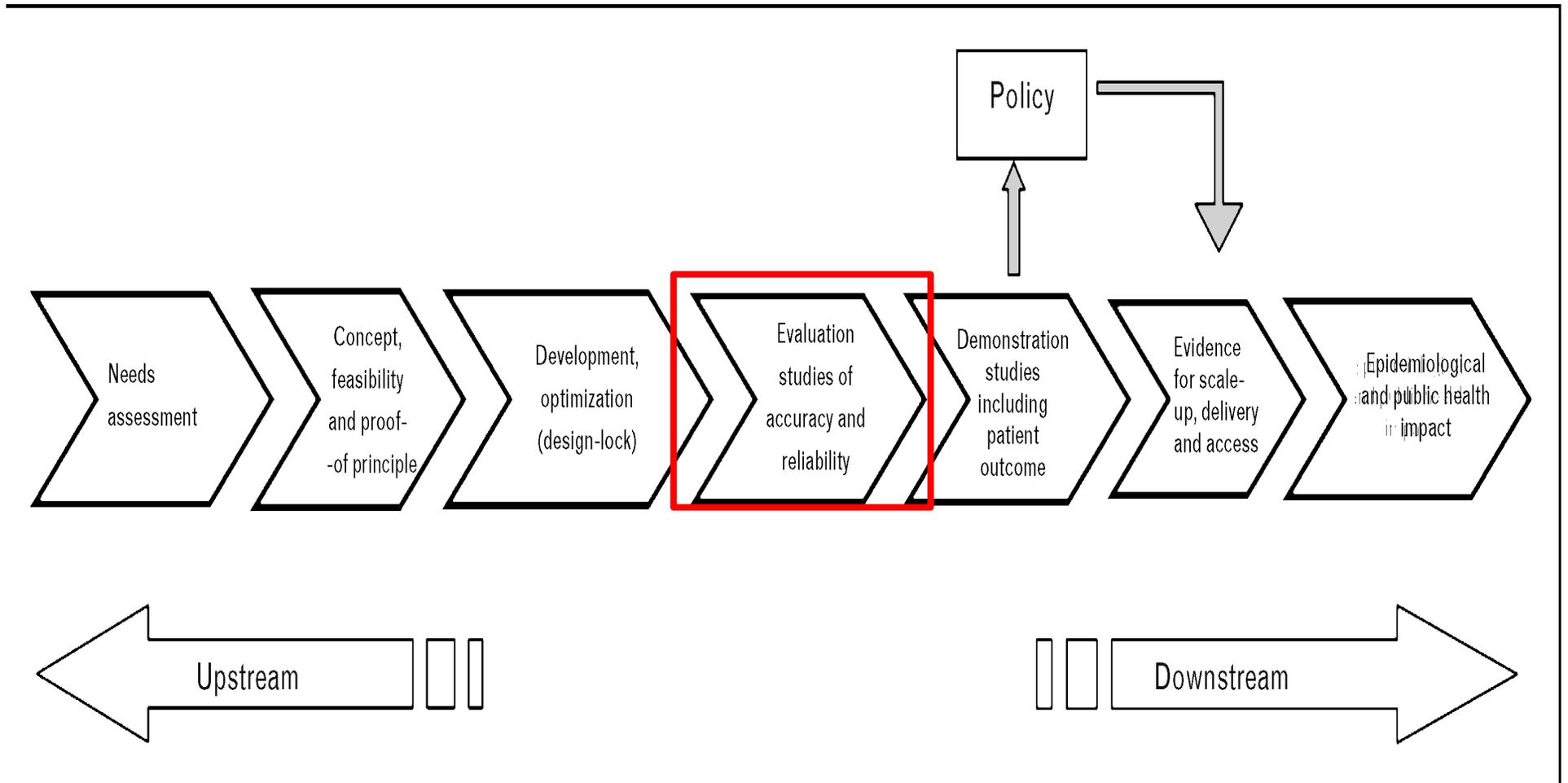
# Xpert MTB/RIF

- Specificity
  - Non-TB 99.2%
  - Rif sensitive 98.1%
- Markedly reduce turn around time
  - Smear negative and MDR TB

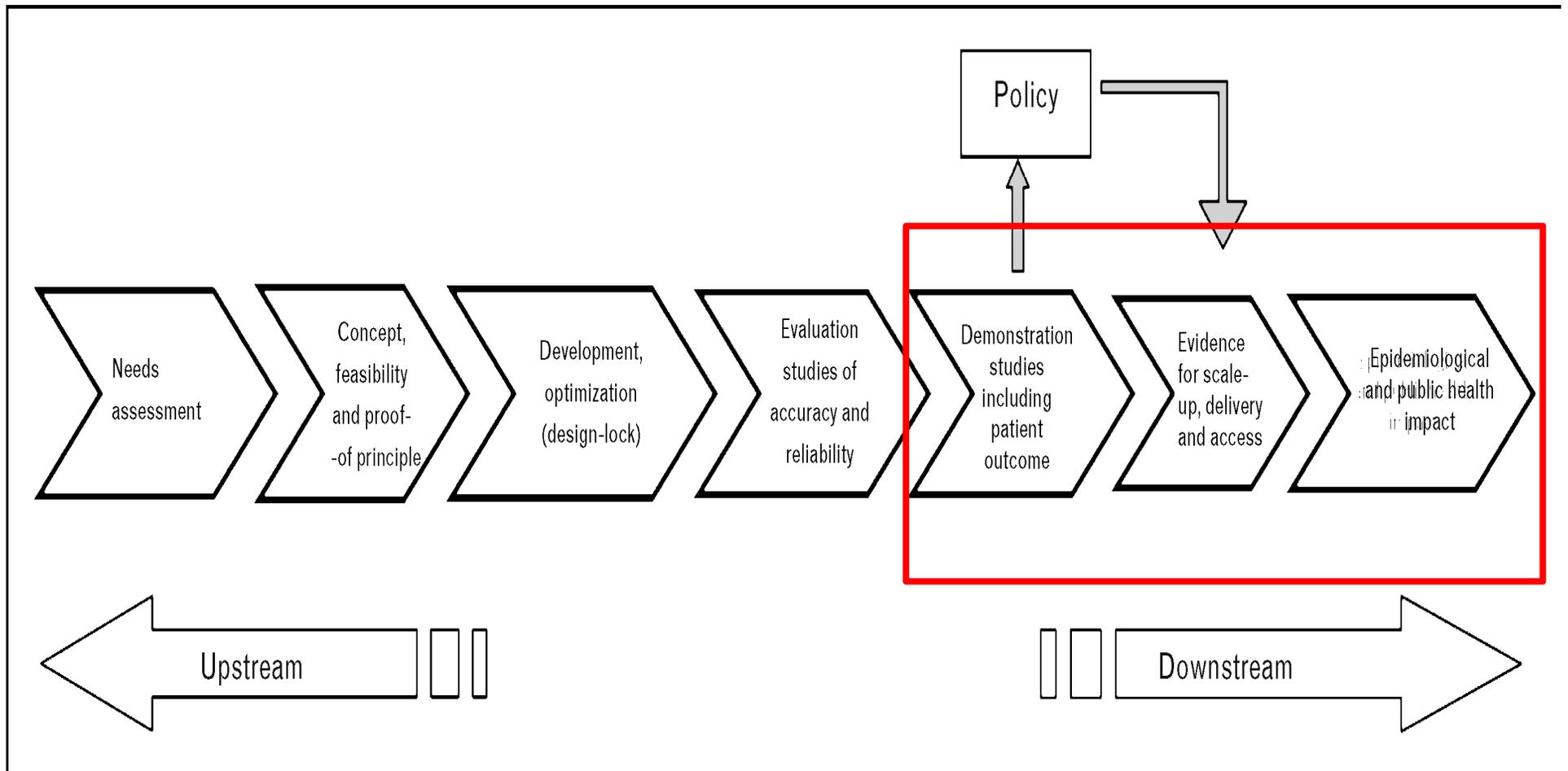


Boehme et al, *N Engl J Med*; 2010

# Levels of evidence required for policy



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# Aim

- The national rollout of Xpert MTB/RIF in South Africa affords us with a unique opportunity:
  - to evaluate effectiveness, cost and cost-effectiveness of implementing Xpert MTB/RIF in the investigation of TB and its impact on patient and programme outcomes and transmission at a population level

# Objectives

- To measure the effectiveness of Xpert MTB/RIF in improving patient and programme outcomes
- To determine the likely population level impact of using Xpert MTB/RIF in the investigation of TB on TB transmission, using mathematical modelling
- To estimate the cost-effectiveness of Xpert MTB/RIF from a patient and programme perspective

# Methods

## Study design

- A cluster randomised trial design
- A cluster is defined as a laboratory and two large clinics using that laboratory.
- Xpert MTB/RIF will be implemented in
  - Intervention labs at the start of the study (immediate arm)
  - Control labs after six months (deferred arm)
- 20 GX16 Labs chosen & randomized in partnership with NDOH & NHLS
  - Eastern Cape [8], Free State [2], Gauteng [8], Mpumalanga [2] or KZN [2])

# Methods

## TB investigations:

TB suspects will be investigated with

- Intervention arm
  - One sputum for Xpert MTB/RIF
    - Sputum Xpert MTB positive patients will have a second sputum specimen collected for smear microscopy
- Control arm (standard of care)
  - Two sputum for microscopy
  - Culture if smear negative and symptomatic, if HIV positive or if patient has a prior history of TB

# Methods

## Effectiveness of Xpert MTB/RIF Patient level outcomes

### Primary Outcome

- Mortality over six months following specimen collection

### Secondary outcomes

- Primary default
- Time to start of any TB treatment
- Time to start of appropriate treatment

### Exploratory outcomes

- TB treatment outcomes, amongst TB cases
- Proportion of TB suspects tested for HIV
- Time to start cotrimoxazole, IPT and ART among eligible patients
- CD4 count at time of specimen collection



# Methods

## Effectiveness of Xpert MTB/RIF Programme outcomes

- % of TB cases microbiologically confirmed
- Yield of microbiologically confirmed TB cases among TB suspects
  - All forms of TB
  - Rifampicin resistant TB



# Methods

## Economic outcomes

- Societal cost per DALY averted from improved suspect/patient outcomes
- Patient cost per TB suspect/ patient - from time of specimen collection until six months treatment
- Health service costs per TB diagnostic test, case detected and patient treated
- Societal cost per case, death and DALY averted due to reductions in transmission

# Sample size

- Assuming
  - A six month mortality among TB suspects of 5% in the “standard of care arm”
  - ***10 clusters per arm***
  - ***220 TB suspects per cluster***
  - A coefficient of variation of 0.25
- There would be 90% power to detect a 50% reduction of mortality in the Xpert MTB/RIF arm

# Timeline

<b>Total duration of study:</b>	<b>27 months</b>
– Cluster enrolment:	3 months
– Participant	
• Recruitment:	4 months
• Follow up:	8 months
– Data cleaning:	6 months
– Analysis and write up:	6 months

# Significance

- This study will yield essential data to guide evidence-based policy concerning implementation of Xpert MTB/RIF and other new TB diagnostics.

# Investigators

## Principal Investigator:

- Professor Gavin Churchyard.

## Investigators:

- *The Aurum Institute*: Dr. V Chihota, Dr S Charalambous
- *National Health Laboratory Service/University of Witwatersrand*: Prof. W Stevens, Dr G Coetzee, Dr L Erasmus
- *University of Cape Town*: Prof M Nicol, Dr E Sinanovic
- *The South African Centre for Epidemiological Modelling and Analysis*: Prof B Williams
- *World Health Organisation*: Dr C Dye
- *London School of Hygiene and Tropical Medicine*: Dr K Fielding, Dr A Vassall, Prof A Grant, Dr J Lewis

## Collaborators

- *National Department of Health*: Dr D Mametja, Dr L Mvusi, Dr N Ndjeka, K Vilakazi

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