Cost-Effectiveness/Utility Analysis

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Outline

- Defining economic evaluation
- Cost-effectiveness/utility analysis
- Screening for M.tb infection in children (case study 1)
- XTEND trial (case study 2)

Introduction

- 'The only thing a minister of health is ever destined to discuss with the medical profession is money'
- Choosing between alternatives
- Which programmes to choose?
- Which interventions are 'worthwhile'?

What is economic evaluation?

- Economic evaluation is the comparative analysis of costs and consequences of alternative courses of action
  - linking the inputs going into procedures with the outputs resulting from the use of these inputs
  - improving decisions about the allocation of health care resources

Why economic evaluation?

- Helps identify neglected opportunities by highlighting interventions that are relatively inexpensive. Yet have the potential to reduce the disease burden substantially (oral rehydration therapy example)
- Economic evaluation helps identify ways to redirect resources to achieve more

Tasks of economic evaluation

- Four tasks of economic evaluation are to:
  - identify
  - measure
  - value, and
  - compare costs and consequences

Evaluations that precede economic evaluation

- Efficacy : can it work under ideal / controlled clinical trail conditions?
- Effectiveness: can it work under 'normal' conditions
    - Effectiveness = (efficacy x compliance)
- Availability: is the intervention accessible to people who could benefit from it?

Partial vs. full economic evaluation

- There are two characteristics that define economic evaluation:
    - Whether there is a comparison of at least two or more alternatives
    - Whether both costs (inputs) and consequences (outputs) of the alternatives are examined
- If the answer to both of these questions is YES, than you are dealing with a full economic evaluation

Key features of a good economic evaluation

- Well defined question (including viewpoint)
- Relevant alternatives
- Good medical practice
- Relevant range of costs and consequences identified
- Accurate measurement of costs and consequences
- Credible valuation of costs and consequences
- Adjustment for differential timing – discounting
- Incremental analysis
- Sensitivity analysis of the results
- Clear discussion of the relevance of the results

Types of full economic evaluation

- *Cost-effectiveness analysis (CEA)*
  - costs measured in monetary units and outcomes in natural units with the same outcome measure being used for all comparators
- *Cost-utility analysis (CUA)*
  - costs measured in monetary terms and outcomes in quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs)
- *Cost-benefit analysis (CBA)*
  - both costs and outcomes are measured in monetary units

CEA

- Often based on the net change in health care costs divided by the increase in health effects

"What is the best way of spending a given budget?"

- Always involves comparison of at least two options with the same goal
- Developed in the medical field (criticism about the use of the human-capital approach for valuing health changes)

CEA data sources

- Cost data sources
  - Retrospective data: financial records, activity data
  - Prospective data: obtain quantities (by types) of inputs required though interactive interviews with experts
- Effectiveness data sources: clinical trials and randomized controlled trials
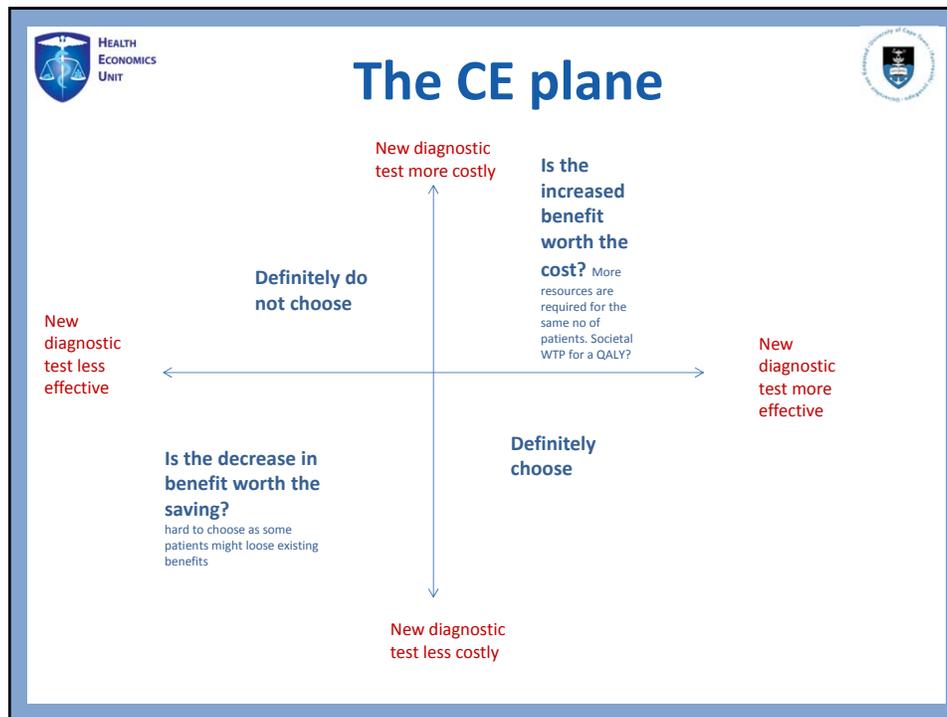
Choice of effectiveness data

- The effectiveness measure can relate to:
  - *final health output* (such as cases/ deaths averted, life years saved, number of heart attacks prevented)
  - *intermediate output* (such as cases detected, blood pressure reduction)

ICER

- In practice, CEA is based on the net change in costs divided by the increase in health effects
- ICER = incremental cost/the incremental effectiveness compared to the next most effective programme
- The ICER is a measure of the relative economic attractiveness of an intervention
- The cost-effectiveness plane (dominance issue)

The CE plane

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New diagnostic test more costly

Is the increased benefit worth the cost? More resources are required for the same no of patients. Societal WTP for a QALY?

Definitely do not choose

New diagnostic test less effective

New diagnostic test more effective

Definitely choose

Is the decrease in benefit worth the saving? hard to choose as some patients might loose existing benefits

New diagnostic test less costly

Decision-making rules

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- Which of the strategies is the most cost-effective in a specific setting?
  - If the ICER is below the WTP for a QALY threshold
  - Not available in the SA proposed economic evaluation guidelines
  - GDP as a threshold
- What are the key assumptions and parameters sensitive to?

CEA limitations

- CEA does not resolve problem of option selection whenever different options yield more than one kind of beneficial effect with the mix of benefits differing between options (e.g. quality of life can be as important an outcome as improving life expectancy)
- CEA does not allow comparison of interventions with differing impacts on both mortality and morbidity

When is CUA appropriate?

- When the quality of life is THE important outcome (e.g. pain treatments)
- When intervention(s) under evaluation affect both morbidity and mortality and you wish to have a common unit of outcome - a generic measure of outcome that combines both effects
- When interventions being compared have a wide range of different kinds of outcome

CUA issues

- Field of utility is relatively young and the methodology is still developing
- QALYs always represent individual preferences and therefore very strong assumptions have to be made
- Construction of culturally acceptable quality of life measurement instrument

QALYs

- A QALY is the product of quality and quantity (life expectancy) of life:

QALY = REMAINING LIFE EXPECTANCY x QUALITY OF LIFE

- With QALYs approach, both prolongation of life and quality of life can be given a single value
- QALYs are "good" that should be maximised

QALY: example

- Prof. Abel is 50 years old and HIV positive. His self-assessed quality of life is currently 0.20 utils. If he is not treated he would die in 5 years time. If he were to receive PEARL OMEGA treatment his remaining life expectancy might rise to say 13 years and his health related quality of life to 0.75 utils. The gain in treatment in this case would be measured as follows:

(A) Treatment option: 13 years x 0.75 utils = 9.75 QALYs

(B) No treatment option: 5 years x 0.2 utils = 1 QALY

(C) Gain from intervention (A − B) = 8.75 QALYs

DALYs

- The DALY, like the QALY, is a composite measure of health status, which combines the time lost to premature mortality and the time lived with a disability

- The concept of DALYs was developed to provide a single indicator of the burden of disease

DALYs calculation

- DALYs are calculated by adjusting a standard life expectancy for loss of healthy life resulting from disability and premature death
  - Two components are summed: Years Lost due to Disability (YLL) due to premature mortality AND Years Lost due to Disability (YLD) for incident cases of the health condition
  - One DALY = one lost year of "healthy" life

Calculating DALYs

- Time lost to premature death is measured in relation to a standard expectation of life, using a model life table
- Time lived with disability is translated into an equivalent time loss, using a set of weights which reflect reduction in functional capacity
- Discounting
- Non uniform age weights (less weight to years lives at young and older ages)

Applications of the DALY

- Defining the burden of disease
  - In 2001, the burden of disease per 1,000 population ranged from 128 DALYs in high-income countries to 282 DALYs in low- and middle-inclome countries
- Evaluating interventions and programmes
  - Less than $US100: vaccination, treatment of diarrhoea, malaria, respiratory infections, etc.
- Setting health service and research priorities
  - Allocation of funding by identifying the disease conditions responsible for the major health burden

Role of modelling in economic evaluations

- Extrapolating beyond the data observed in a trial
- Linking intermediate clinical endpoints to final outcomes
- Generalising results to other settings
  - From trials to regular practice e.g. compliance
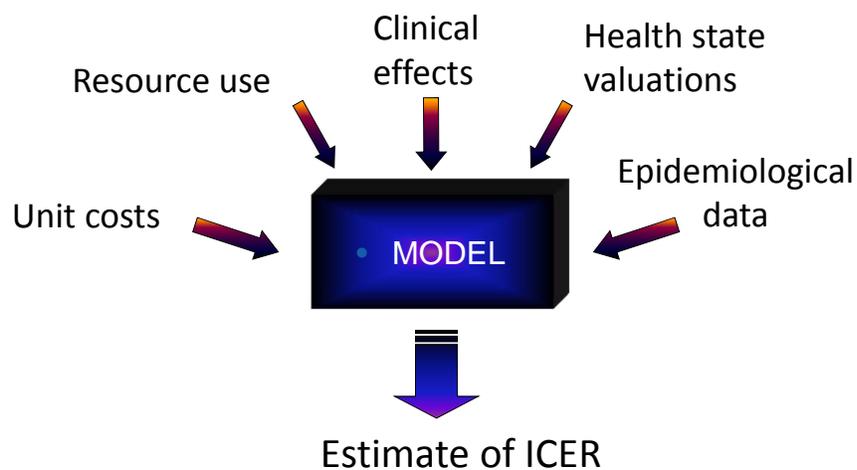 - From place to place (i.e. places with different contextual settings)

Role of modelling in economic evaluations

- Models can be used to simulate experiments and to explore alternative scenarios, where true experiments (e.g. RCTs) are infeasible or impractical
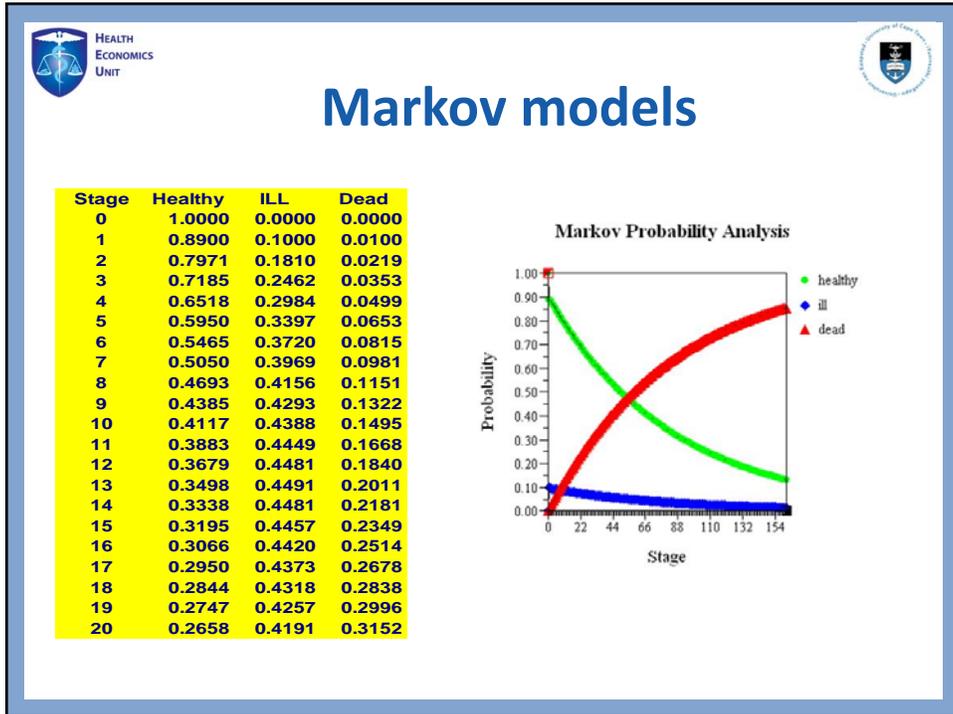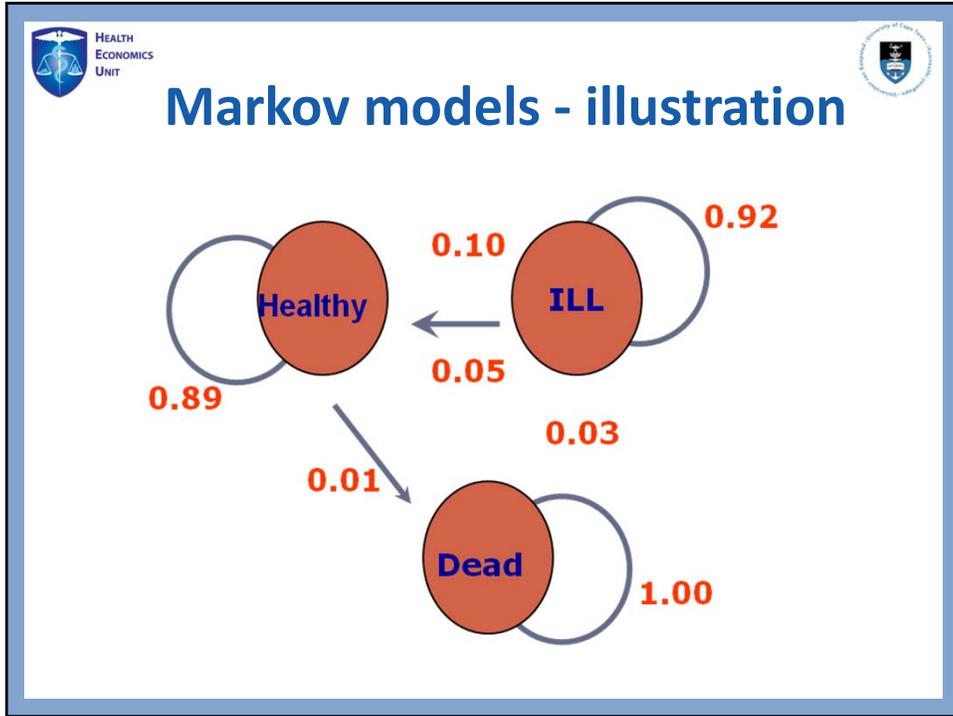- Informing decisions in the absence of hard data

Modelling in CEA

Markov models

- A Markov model is a decision-analytic model which describes the transitions a cohort of patients make between a number of health states during a series of time cycles

- Markov models are concerned with condition of a patient varying over time

- Particularly appropriate for recurring processes (such as chronic diseases)

Markov models

- Describes the condition at a given time as belonging to one of a (feasibly small) number of *mutually exclusive and collectively exhaustive* health states

- Transition probabilities out of each state, adding up to 1, can be constant or change over time

Markov models - illustration

Markov models

Stage	Healthy	ILL	Dead
0	1.0000	0.0000	0.0000
1	0.8900	0.1000	0.0100
2	0.7971	0.1810	0.0219
3	0.7185	0.2462	0.0353
4	0.6518	0.2984	0.0499
5	0.5950	0.3397	0.0653
6	0.5465	0.3720	0.0815
7	0.5050	0.3969	0.0981
8	0.4693	0.4156	0.1151
9	0.4385	0.4293	0.1322
10	0.4117	0.4388	0.1495
11	0.3883	0.4449	0.1668
12	0.3679	0.4481	0.1840
13	0.3498	0.4491	0.2011
14	0.3338	0.4481	0.2181
15	0.3195	0.4457	0.2349
16	0.3066	0.4420	0.2514
17	0.2950	0.4373	0.2678
18	0.2844	0.4318	0.2838
19	0.2747	0.4257	0.2996
20	0.2658	0.4191	0.3152

Markov Probability Analysis

2012/03/15

Limitations of Markov models

- No account taken of history (Markov assumption)
- Assumes uniform population and equal and constant risk
- May overcome these limitations by using a larger number of states, but also gets complicated with many health states

Summary

- Due to scarcity all choices involve opportunity costs
- Economic evaluation aims to maximise health gain subject to scarce resources
- Economic evaluation is not a substitute but a guide for decision making
- Decision criteria of economic evaluation techniques offer a basis for priority setting (especially in pursuit of efficiency goals)
  - not the only factor
  - relevance to local context
- Implementation of health care intervention policies should be preceded by economic evaluations

Cost-effectiveness of five different *M.tb* infection screening strategies in young household contacts (Case study 1)

Mandalakas AM, Hesseling AC, Gie RP, Schaaf HS, Marais BJ, Beyers N, Sinanovic E (2012) "Modelling the cost-effectiveness of strategies to prevent tuberculosis in child contacts in a high-burden setting" (accepted by *Thorax*)

Study question

- Which testing strategy is most cost-effective for diagnosis and treatment of *M.tb* infection in children in a setting with a high burden of TB (South Africa)?

Specific study objectives

- Develop a Markov state transition model to describe the screening and preventative therapy for *M.tb* infection in children within the SA context
- Estimate the cost-effectiveness of different testing strategies
- Compare the cost-effectiveness of five strategies defined as cost per life year gained (LYG) and cost per TB case prevented.

Model design

| Context	Alternative Strategies
- Children age 0-2, 3-5 - High risk of exposure (household contacts) - Poor IPT uptake and adherence - Resource-poor setting	1) TST 2) IGRA 3) -TST followed by IGRA 4) +TST followed by IGRA 5) No testing

Methodology

- The cost-effectiveness analysis, prospectively undertaken from a provider perspective and a societal perspective
- Markov modelling: cohort of 1,000 hypothetical children followed for 15 years (6 month cycles)
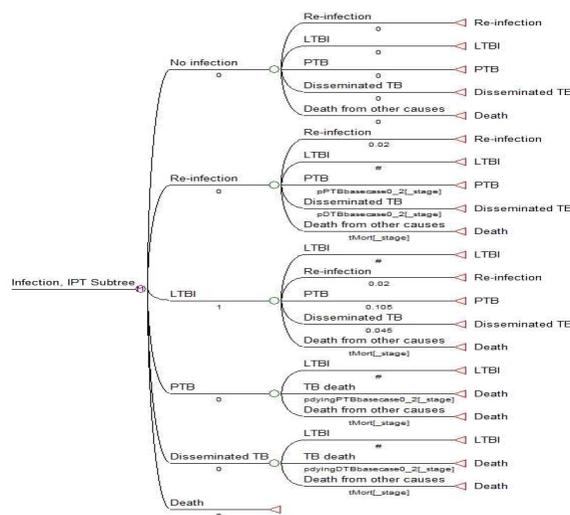
Decision Tree
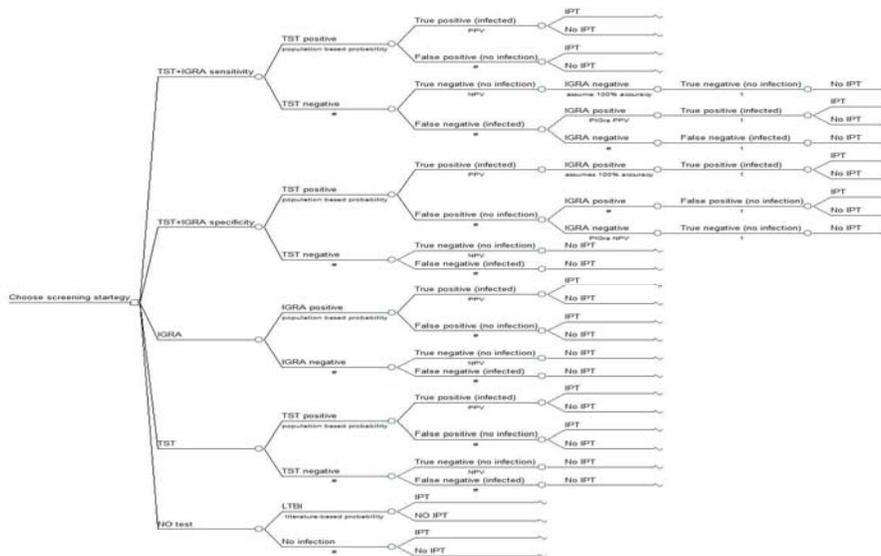
Markov model

- Seven health states
  - no infection
  - initial infection
  - subsequent infection due to future exposures
  - pulmonary TB
  - disseminated TB
  - TB death
  - death from other causes

Markov model: health states and possible transitions between states

Costs, Life Years Saved and Incremental Cost Effectiveness Ratios (0-2 year olds)

	15-year Cost (US$)*	Life years saved		Cost Effectiveness	ICER (life years)	
		Discounted[†]	Undiscounted		Societal Perspective	Provider perspective
Base-case scenario, 0-2 year old cohort, Quantiferon (QTF)						
No-testing	2,477	10.43	13.05	237		
TST	3,513	9.52	11.90	369	(Dominated)	(Dominated)
QFT after +TST	3,909	9.51	11.88	411	(Dominated)	(Dominated)
QFT after -TST	4,563	10.39	13.00	439	(Dominated)	(Dominated)
QFT	4,891	9.88	12.35	495	(Dominated)	(Dominated)
Base-case scenario, 0-2 year old cohort, T-Spot.*TB* (TSpot)						
No-testing	2,610	10.45	13.08	250		
TST	3,718	9.52	11.90	391	(Dominated)	(Dominated)
TSpot after +TST	4,180	9.51	11.89	440	(Dominated)	(Dominated)
TSpot after -TST	4,934	10.42	13.03	474	(Dominated)	(Dominated)
TSpot	5,317	9.89	12.37	538	(Dominated)	(Dominated)

Costs, Life Years Saved and Incremental Cost Effectiveness Ratios (3-5 year olds)

	15-year Cost (US$)*	Life years saved		Cost Effectiveness	ICER (life years)	
		Discounted[†]	Undiscounted		Societal Perspective	Provider perspective
Base-case scenario, 3-5 year old cohort, Quantiferon (QTF)						
No-testing	1,483	10.56	13.21	140		
TST	2,251	9.73	12.17	231	(Dominated)	(Dominated)
QFT after +TST	2,793	9.71	12.16	288	(Dominated)	(Dominated)
QFT after -TST	3,147	10.57	13.22	298	233,516	162,192
QFT	3,535	9.87	12.35	358	(Dominated)	(Dominated)
Base-case scenario, 3-5 year old cohort, T-Spot.*TB* (TSpot)						
No-testing	1,483	10.56	13.21	140		
TST	2,251	9.73	12.17	231	(Dominated)	
TSpot after +TST	2,893	9.71	12.16	298	(Dominated)	
TSpot after -TST	3,294	10.57	13.22	312	254,243	
TSpot	3,717	9.91	12.41	375	(Dominated)	Rank order changes

Conclusions

- Screening for *M.tb* infection and provision of IPT to young children is a highly cost-effective intervention

- Screening without testing for *M.tb* infection is the most cost-effective strategy in 0-2 year old children and the preferred strategy in 3-5 year old children
    - Lack of testing capacity should therefore not be a barrier to IPT delivery

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XTEND trial – GeneXpert MTB/RIF for tuberculosis: evaluating impact and cost-effectiveness in the routine roll-out in South Africa
(Case study 2)

Study collaborators: Aurum, NHLS, UCT, WHO, LSHTM, NDoH
2010 -2013

Background

- October 2010 promising results from demonstration sites in South Africa
- WHO Expert meeting to decide whether to approve Xpert MTB/RIF for programmatic use globally
- Concerns about costs and affordability
- Modelling to predict the cost-effectiveness of Xpert MTB/RIF roll-out

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Vassall, A et al Rapid diagnosis of tuberculosis with the Xpert MTB/RIF assay in high burden countries: a cost-effectiveness analysis. PLoS Med. 2011 Nov;8(11)

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

Findings from Vassall et al study, and recommendation

1. Diagnostic scenarios in which XPERT is used in addition to or instead of smear examination strongly and equally increase TB case finding in all three epidemiological settings.
2. Both these scenarios yield more DALYs than the baseline scenario
3. Both these scenarios are cost-effective cf. WHO criteria compared to the base case
4. Robust to sensitivity analysis, but influenced by the extent to which Xpert is about to address loss to follow up and the unit costs of diagnosis and treamtent
5. WHO recommdendation to adopt Xpert

XTEND trial study goal

- Overall, to better understand how Xpert MTB/RIF should be best used under conditions of national roll-out by determining its effectiveness and cost-effectiveness, and modelling these data to project the impact at population level in South Africa

Study aims: cost-effectiveness

- From a provider and patient perspective, to model:
  - the incremental cost per life year saved and DALY averted from improved TB suspect outcomes until the point of TB treatment cure or failure or death
  - the incremental cost per life saved/DALY averted, including reductions in transmission of drug susceptible and drug resistant TB

2012/03/15
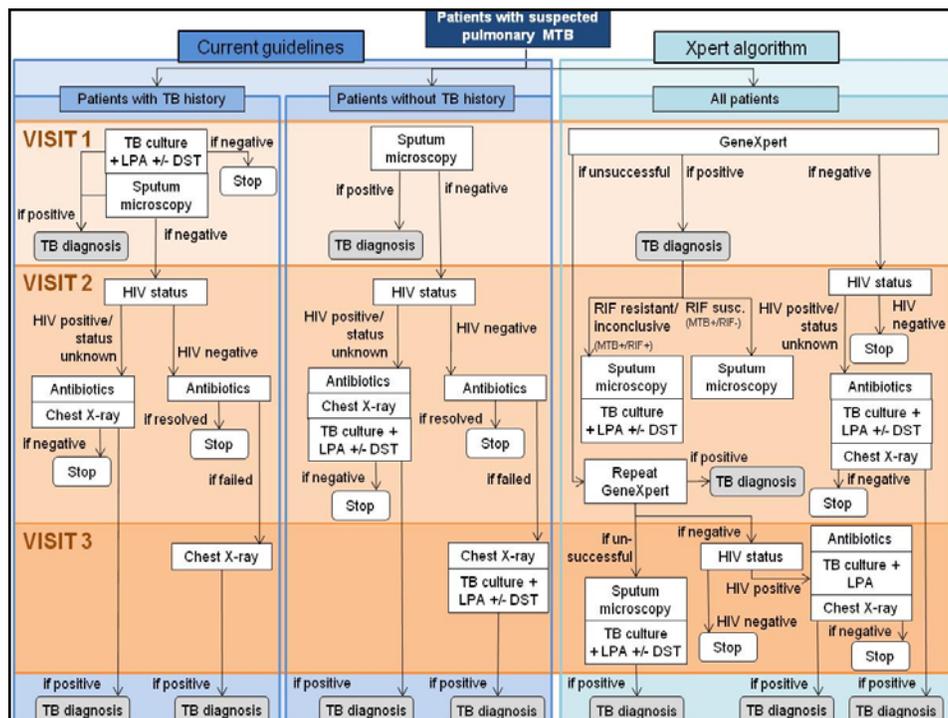
XTEND: Key areas being explored

- Accurate estimates of Xpert costs during roll-out to estimate economies of scale
- Extensive costing of all TB diagnostics
- Treatment costs of all categories of TB treatment
- Patient costs associated with an incorrect or lack of diagnosis of TB
- Linking TB cohort models with transmission modelling
- And..TB suspect cohort outcomes to validate initial CEA results

XPHACTOR

- A sub study focusing on HIV clinics where TB investigations should be prioritised
  - How best to prioritise?
- The study will identify an evidence-based algorithm for HIV-infected individuals
- It will complement the findings on the effectiveness and cost-effectiveness from the XTEND trial