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Cost-Effectiveness Analysis of TB Diagnostics

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Challenges and Future Directions

Protecting Health, Saving Lives—*Millions at a Time*

Objectives

- Provide an overview of cost-effectiveness analysis (CEA) as applied to TB diagnostics
  - Focus on one sample CEA model rather than overview all models
- Discuss limitations and challenges of CEA, with emphasis on relevance to TB diagnostics
- Mention current areas of interest for CEA of TB diagnostics

"First we're going to run some tests to help pay off the machine."

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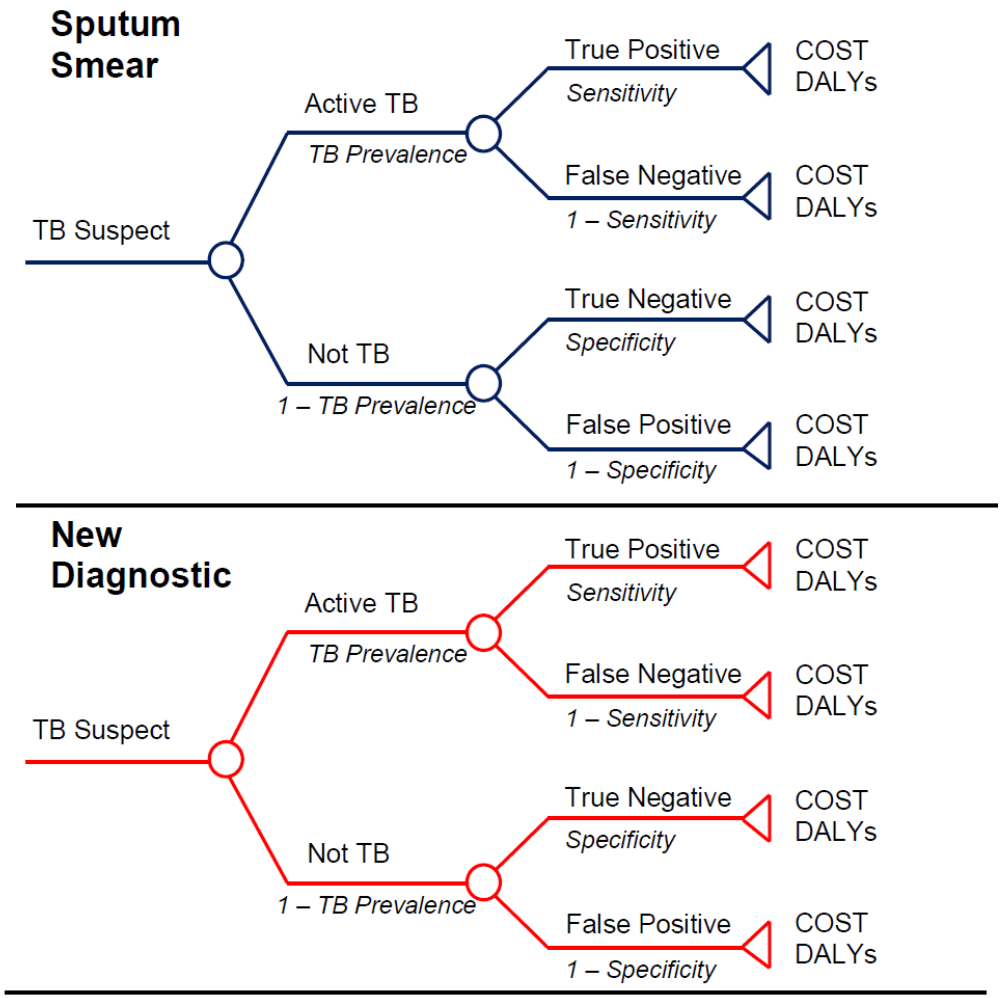
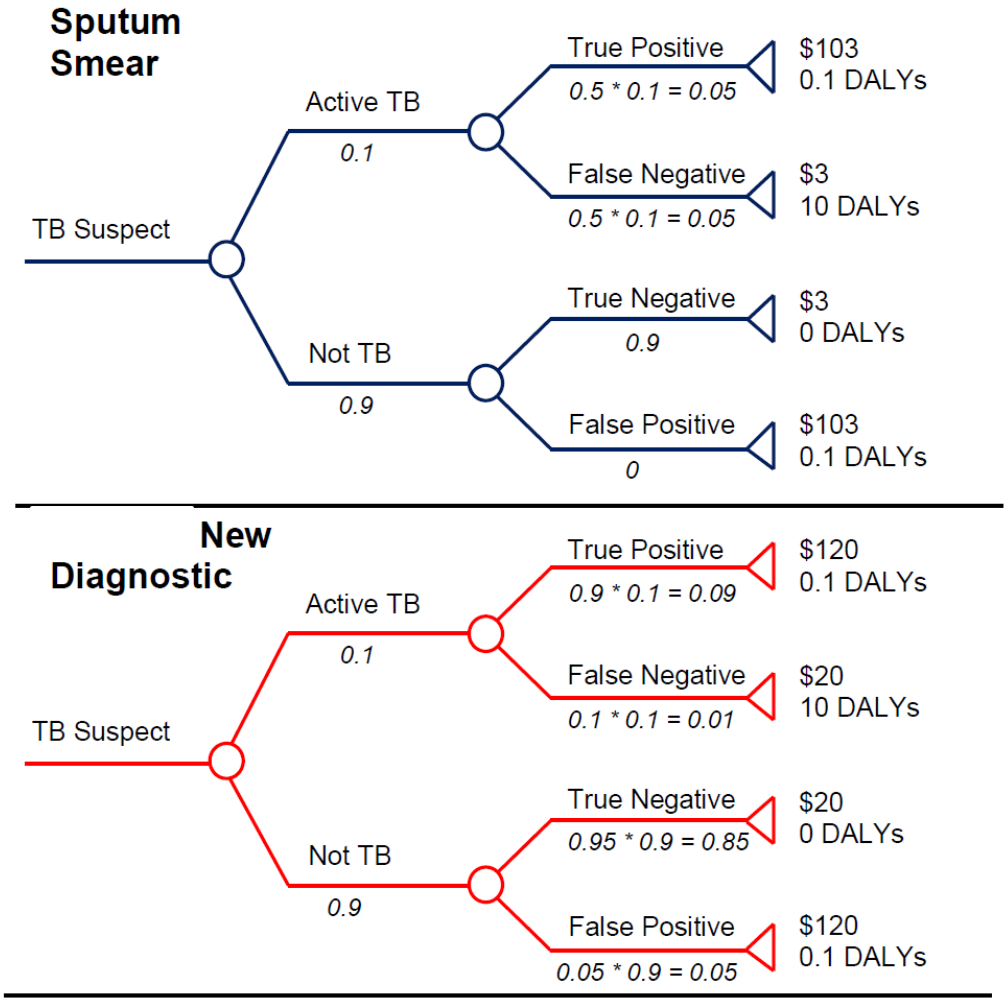
CEA of TB Diagnostics: Prototype Model



Mean Cost = Σ(Cost * Probability)
Mean Effectiveness = Σ(DALYs * Probability)

$$\text{Incremental Cost-Effectiveness Ratio (ICER)} = \frac{(\text{Cost of New Test} - \text{Cost of Smear})}{(\text{Effectiveness of New Test} - \text{Effectiveness of Smear})}$$

Add in Some Realistic Numbers



TB Prevalence: 0.1

Smear Sensitivity: 0.5
Smear Specificity: 1.0

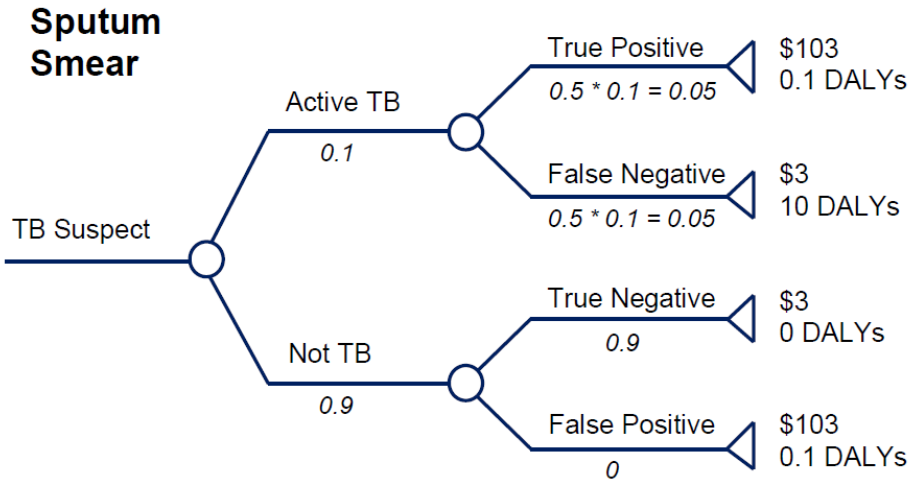
New Test Sensitivity: 0.9
New Test Specificity: 0.95

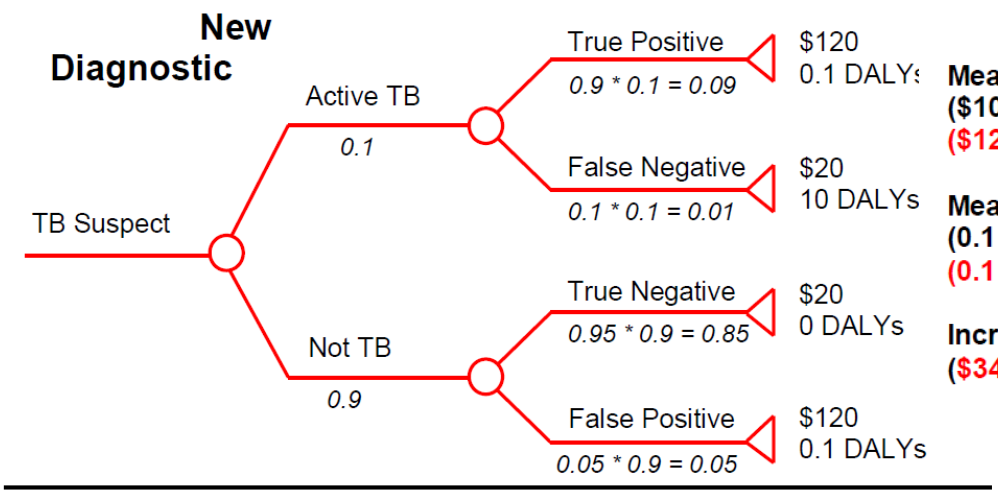
Cost of Smear: $3
Cost of New Test: $20
Cost of TB Treatment: $100

DALYs for Untreated TB: 10
(20 years * 50% risk of death)

DALYs for TB Treatment: 0.1
(6 months * 20% QOL loss)

Add in Some Realistic Numbers





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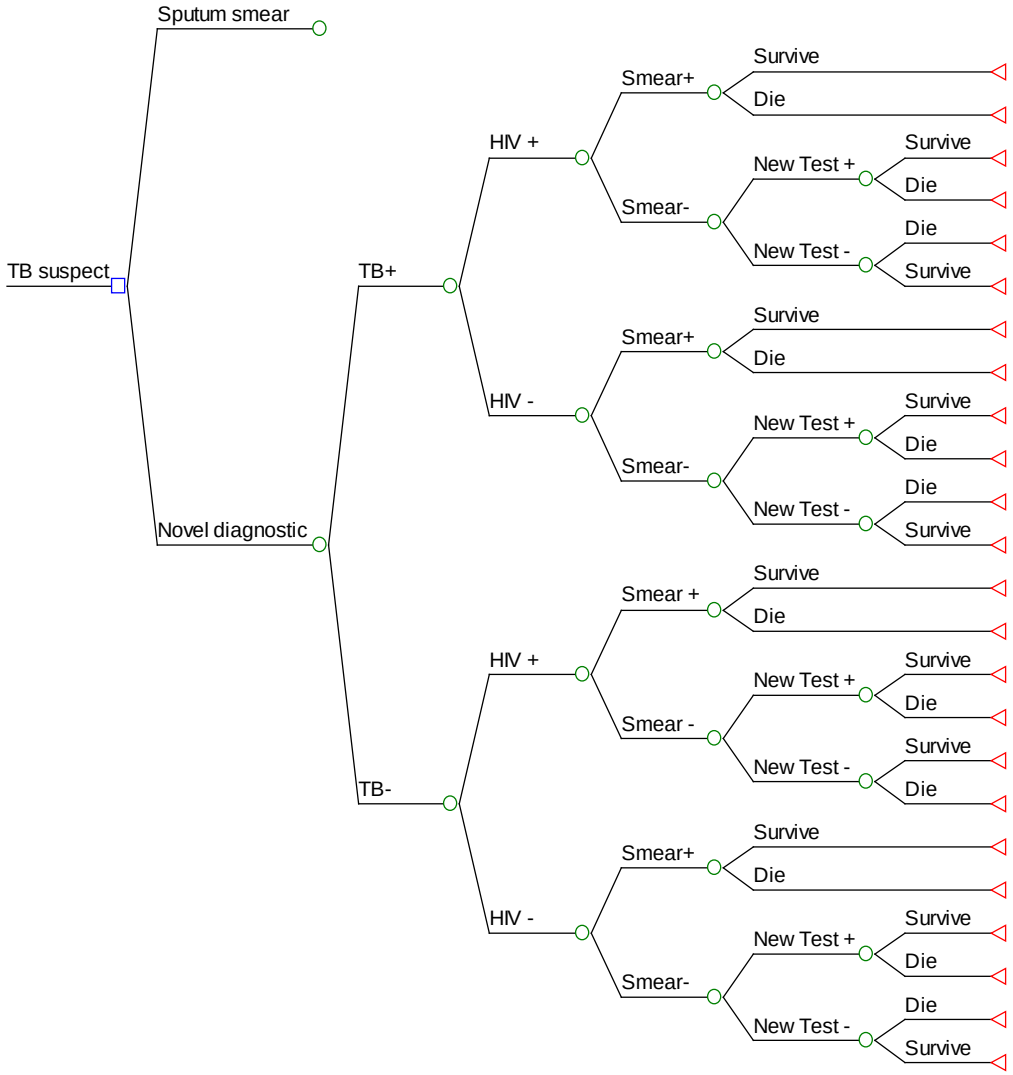
Mean Cost:
($103 * 0.05) + ($3 * 0.05) + ($3 * 0.9) + ($103 * 0) = $8 (smear)
($120 * 0.09) + ($20 * 0.01) + ($20 * 0.85) + ($120 * 0.05) = $34 (new test)

Mean Effectiveness = Σ(DALYs * Probability)
(0.1 * 0.05) + (10 * 0.05) + (0 * 0.9) + (0.1 * 0) = 0.505 (smear)
(0.1 * 0.09) + (10 * 0.01) + (0 * 0.85) + (0.1 * 0.05) = 0.114 (new test)

Incremental Cost-Effectiveness Ratio (ICER) =
($34 – $8)/(0.114 – 0.505) = $66 per DALY averted

Adding Complexity to the Prototype Model



Cost-Effectiveness of TB Diagnostics in a Low-Income Country (Kenya)

- Sputum smear microscopy: $38 per DALY averted
- New test (90% sens, 95% spec, $20/test): $115/DALY
  - More expensive than in our analysis because undiagnosed TB doesn't suffer 10 DALYs
    - *Dowdy et al, IJTLD 2008; 12:1021*

Reference values:

- MDR-TB treatment in Peru: $211/DALY
  - *Suarez et al, Lancet 2002; 359:1980*
- WHO standard for "highly cost-effective": <GDP per capita
  - >$300 in all countries except for Zimbabwe
  - $50,000/DALY as one benchmark in developed countries
    - *Commission on Macroeconomics and Health, WHO, 2001*
    - *CIA World Factbook*

Summary: Prototype CEA of TB Diagnostics

- A simplified decision-analysis model provides a “ballpark” figure for the cost-effectiveness of TB diagnostics.
- Complexity can be built into models as necessary.
- TB diagnostics will generally appear highly cost-effective.
  - Depending on the assumptions used

So, what's the problem? Limitations of CEA for TB diagnostics

- False-positive diagnostic results
- Misrepresentation of the diagnostic process
- Failure to account for transmission
- Output that is not useful to end-users

- *Dowdy DW, Cattamanchi A, Steingart KR, Pai M. PLoS Med 2011*

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PLoS MEDICINE

Essay

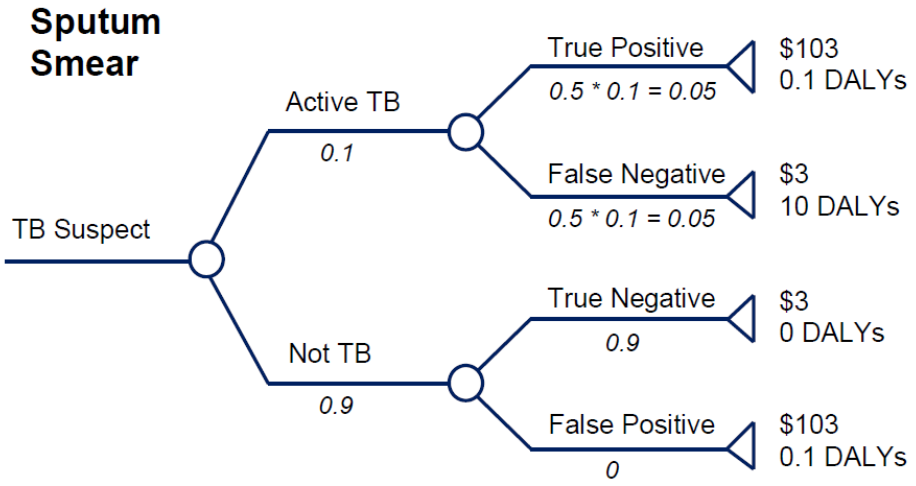
Is Scale-Up Worth It? Challenges in Economic Analysis of Diagnostic Tests for Tuberculosis

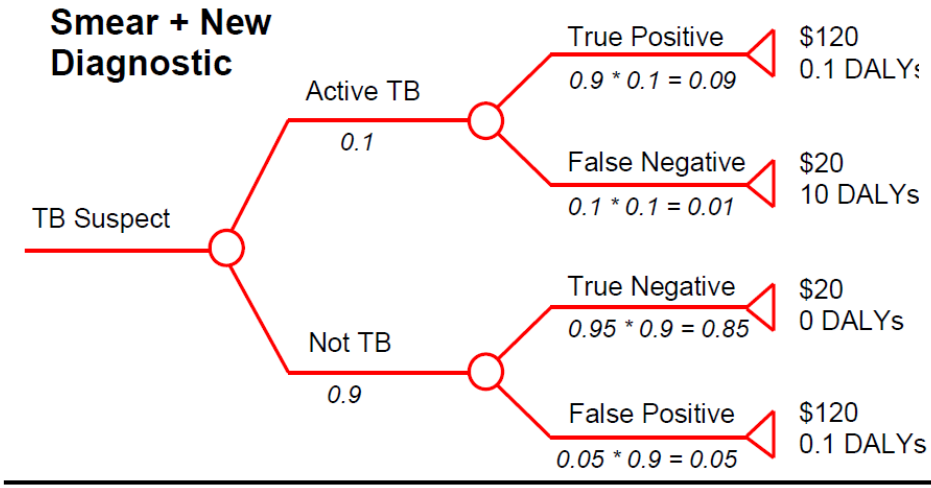
David W. Dowdy[1¤*], Adithya Cattamanchi[2], Karen R. Steingart[3], Madhukar Pai[4]

Limitation 1: False-Positive Results

- Treatment for TB is highly cost-effective.
  - Young people who might otherwise die
- The cost of TB treatment is relatively low.
  - $100 is a small price to pay, and complications are relatively rare.
- As a result, any intervention that increases TB diagnosis appears cost-effective.
  - Even if the test is so poor that nobody would consider using it
  - This is one argument for empiric TB treatment, but in most places of the world, patients and doctors will not commit to 6 months of treatment without an attempt at diagnosis.
- An illustrative example:

Take This Good Test…





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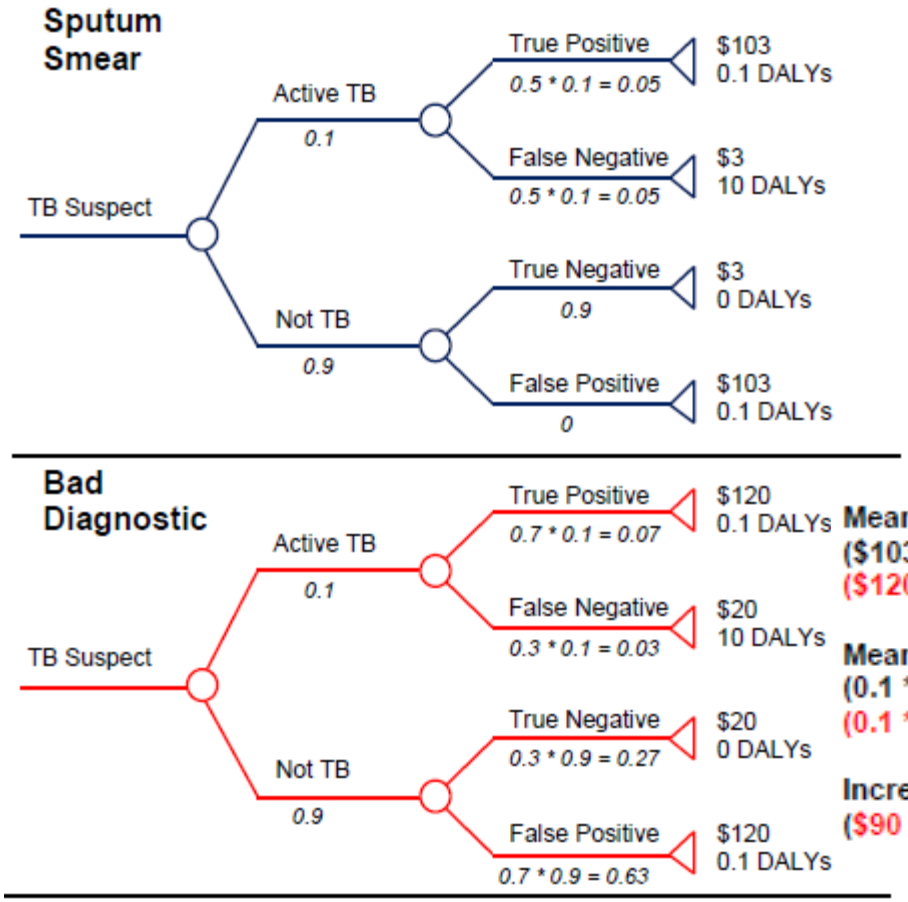
Incremental Cost-Effectiveness Ratio (ICER) =
($34 – $8)/(0.114 – 0.505) = $66 per DALY averted

...and Replace it with a Bad One



Sensitivity = 70%
Specificity = 30%
(i.e., randomly treat 70% of all pts)
Cost = $20

Mean Cost:
($103 * 0.05) + ($3 * 0.05) + ($3 * 0.9) + ($103 * 0) = $8 (smear)
($120 * 0.07) + ($20 * 0.03) + ($20 * 0.27) + ($120 * 0.63) = $90 (new test)

Mean Effectiveness = Σ(DALYs * Probability)
(0.1 * 0.05) + (10 * 0.05) + (0 * 0.9) + (0.1 * 0) = 0.505 (smear)
(0.1 * 0.07) + (10 * 0.03) + (0 * 0.27) + (0.1 * 0.63) = 0.370 (new test)

Incremental Cost-Effectiveness Ratio (ICER) =
($90 – $8)/(0.370 – 0.505) = $607 per DALY averted

$670/DALY = Highly Cost-Effective in Most Settings

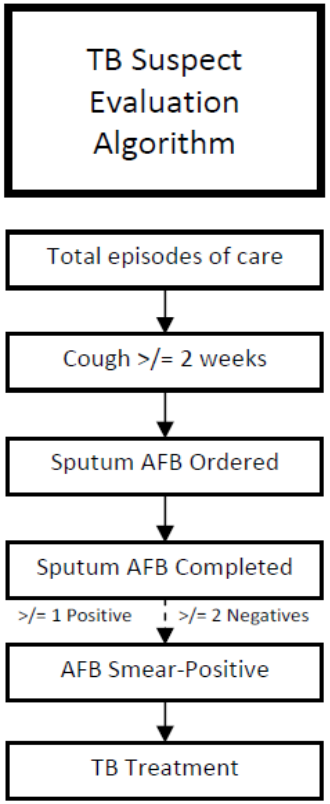
False Positives

- Standard cost-effectiveness methods suggest that treating 30 false-positives for every 1 true-positive is cost-effective.
  - *Basinga P et al, Med Decis Making 2007;27:53.*
- Most patients or physicians would not accept such a high false-positive rate.
  - Erosion in trust of the healthcare system
  - Misuse of TB resources
  - Questions the purpose of a diagnostic test
- Most tests, if added to sputum smear in the field, will diagnose more new false-positives than true-positives.
  - 70% sensitivity for smear-negative TB & 95% specificity (e.g., Xpert)
  - TB prevalence of 10%, 50% of TB smear-positive
  - 50% of smear-negative TB treated on basis of clinical suspicion
  - New test identifies 2.6 false-positives for every new true smear-negative

Limitation 2: Misrepresenting the Diagnostic Process

- Simple decision analysis assumes that a patient receives a diagnosis and is treated/suffers outcomes accordingly.
- In reality, many steps happen in between.
  - Diagnostic delay: time of diagnosis as important as correct diagnosis
  - Loss to follow-up: diagnostic results not acted upon
  - Repeat diagnosis: false-negatives may return to clinic
  - Other conditions: inappropriate TB diagnoses may increase morbidity from other diseases
- Failure to incorporate these steps likely results in overestimation of diagnostics' cost-effectiveness.

Link from Diagnosis to Treatment in Uganda



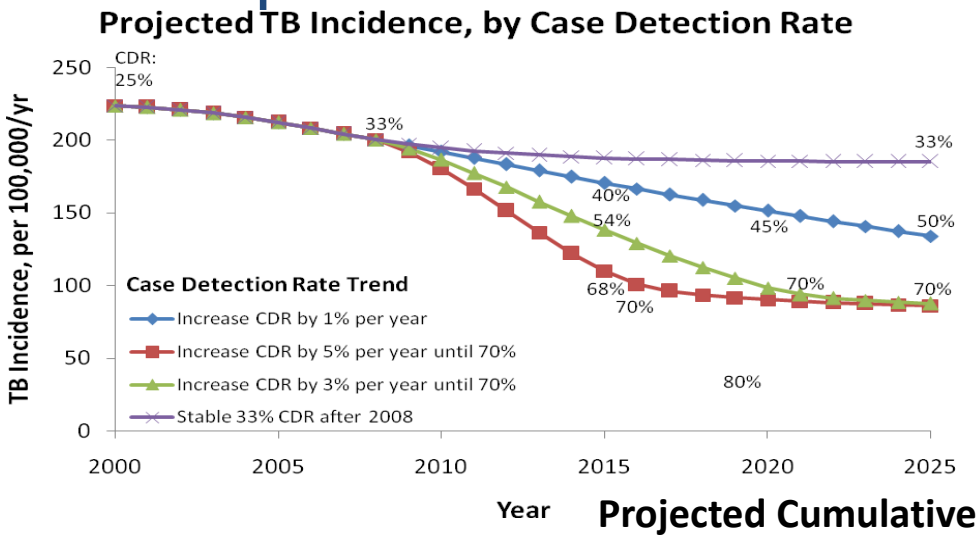
Indicator	Numbers, by quarter				Proportions*, by quarter				p-Value
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	
	14,852	14,652	17,369	16,036	--	--	--	--	--
	365	280	349	294	2.5%	2.0%	2.1%	1.8%	0.27
1	75	111	211	155	21%	40%	60%	53%	0.014
2	55	90	168	119	73%	81%	80%	77%	0.85
	7	19	30	25	13%	21%	18%	21%	0.25
3	5	13	23	21	71%	68%	77%	84%	0.016
Cumulative Probability of Being Diagnosed with and Treated for TB[†]					11%	22%	37%	34%	0.005

- *Davis JL et al, AJRCCM 2011 (epub ahead of print)*

Limitation 3: Failure to Account for Transmission

- "Public health imperative" of TB diagnostics is to reduce total burden of transmission
  - Results in control of the epidemic over time
- CEA methods have evolved separately from transmission models.
  - Economists vs. mathematicians
- Most cost-effectiveness models of TB diagnostics do not account for transmission over time.
  - If diagnostics lead to increased/faster TB treatment, their impact will likely be underestimated.

Example: TB Control in Rural China



Dowdy D, Wong A, Peeling R. unpublished data

Projected Cumulative Outcomes 2010-2025 (per 1 million population)

	Incident TB Cases[a]		TB Deaths		Treatment Costs (US$)[b]	
	15-year total	Cases Averted	15-Year Total	Deaths Averted	15-Year Total	Added Cost
Increase CDR to 33%, then stabilize	29,100	0	7900	0	$1.82 million	$0
Increase CDR by 1% per year	24,700	4400	6200	1700	$2.01 million	$190,000
Increase CDR by 3% per year to 70%	18,600	10,500	3900	4000	$2.06 million	$240,000
Increase CDR by 5% per year to 70%	16,500	12,600	3000	4900	$2.02 million	$200,000

Limitation 4: Output Not Useful to End-Users

- Statement that “TB diagnostic is cost-effective” is not useful to decision-makers.
  - Most TB-related interventions meet standard thresholds for cost-effectiveness.
  - However, money for TB diagnostics often comes from TB-designated funds, not health funds in general.
  - CE models often don’t compare actual alternatives being considered.
  - Example: Serological testing of 15% of India’s TB suspects would consume the entire Revised National TB Control Programme budget.
    - Dowdy D, Steingart K, Pai M. PLoS Med, in press.
- Cost-effectiveness models of TB diagnostics need to think beyond “is this test cost effective?”

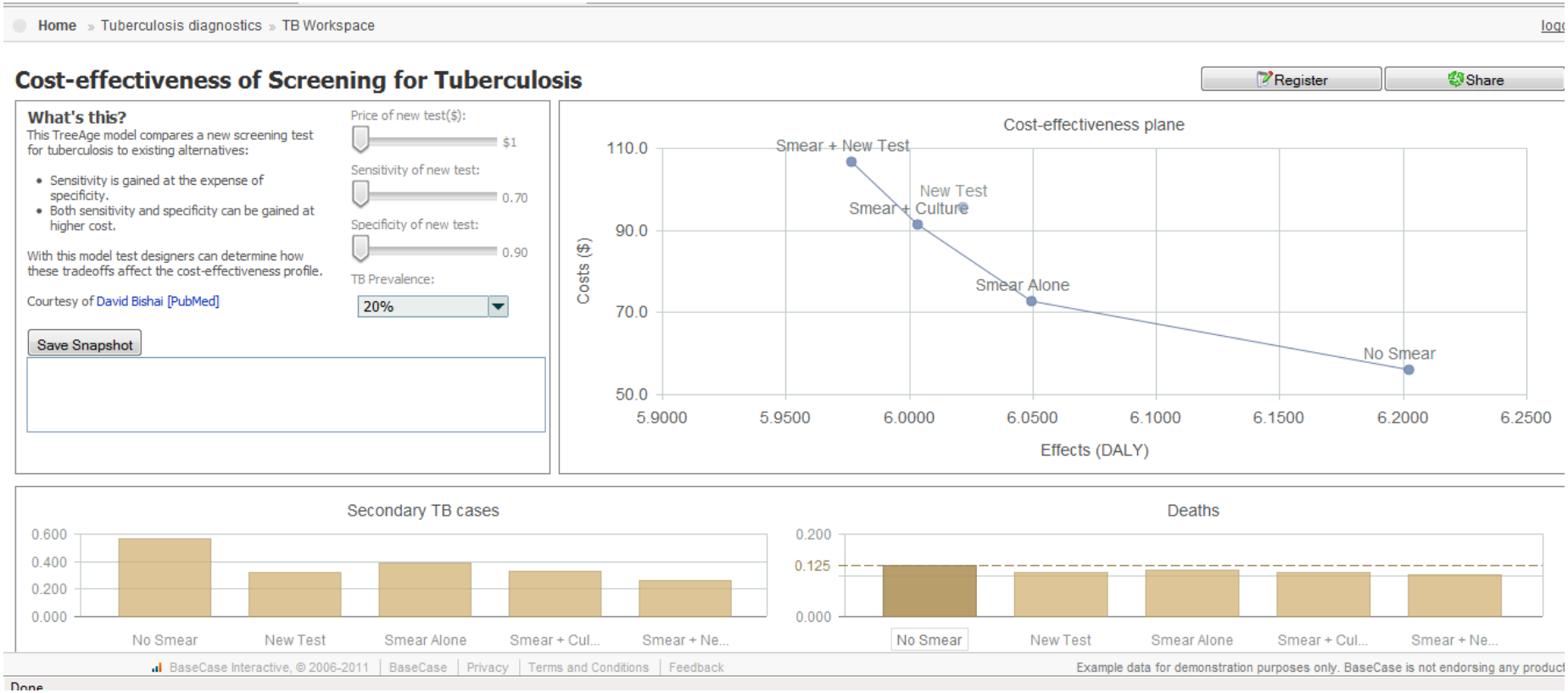
Summary: Limitations of CEA for TB diagnostics

- False-positive diagnostic results
  - Standard models favor any test that increases TB case detection
  - Consequences of excessive false-positive rates rarely considered
- Misrepresentation of the diagnostic process
  - Most TB suspects presenting to care do not get started on treatment
  - Models generally do not consider these losses
- Failure to account for transmission
  - Standard models focus only on the cohort at hand
  - Fail to capture the “public health imperative” of TB diagnostics
- Output that is not useful to end-users
  - Not just “is a test cost-effective,” but rather “is implementation of this test the best use of actual resources available”

Potential Solutions: A Brief Listing

- Estimate the true cost of false-positives.
  - Ask patients and physicians what false-positive rate they would be willing to tolerate.
  - Consider empiric therapy in selected circumstances.
- Model the diagnostic process more accurately.
  - Collect data on diagnostic losses and operational accuracy in the field.
- Combine transmission and economic models.
  - Example of TB control in China
  - Potentially incorporate costs of non-TB treatments that are hindered/facilitated by inaccurate/accurate TB diagnosis.
- Set appropriate cost-effectiveness thresholds.
  - Ask end-users what alternatives they are considering.
  - Benchmark diagnostics against those alternatives.

User-Friendly Cost-Effectiveness Analysis: A Field in its Infancy



www.tbtools.org

Conclusions

- Cost-effectiveness analysis is an essential tool for guiding the development and implementation of TB diagnostics.
- Current approaches suffer from important limitations.
  - Impact of false-positives
  - Misrepresentation of the diagnostic process
  - Failure to account for transmission
  - Generation of output not useful to end-users
- Future cost-effectiveness models of TB diagnostics may:
  - Aim to better represent the process of TB diagnosis
  - Combine economic and epidemic modeling techniques
  - Produce user-friendly output that can be instantly utilized by decision-makers

Thank you for your attention!