

Informing decision-making for universal access to quality TB diagnosis? India: an economic-epidemic model

Incorporating health systems and costing models within the TB transmission model

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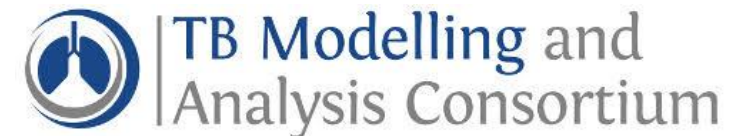
Acknowledgements of the work:

Study design: Hojoon Sohn & David Dowdy

ABS model: Parastu Kasie & Emily Kendall

Costing: Hojoon Sohn

External collaborators: Anna Vassall, Gaby Gomez, Madhukar Pai



Motivation

Xpert MTB/RIF is increasingly recommended as a first-line diagnostic test for TB, but the most cost-effective approach to implementation remains uncertain.

1. Centralized testing through sputum transport networks:
 - a. Higher volume of testing = economies of scale (less wasted capacity)
 - b. High-cost equipment can be maintained in central locations with infrastructure.
 - c. Quality can be more easily assured (fewer people performing the test).
2. Peripheral testing through point-of-care assays:
 - a. May reduce the need for expensive equipment altogether
 - b. Faster diagnosis may reduce pre-treatment losses to follow-up, reducing transmission.
3. Xpert Omni may strongly influence these decisions in the case of TB.
 - a. Flexible & mobile system with potentially lower cost than existing GeneXpert systems
 - b. Same high-quality diagnosis with minimal training & infrastructure
 - c. Capacity to penetrate into lower levels of the health system – increase physical diagnostic coverage

Overview of the research

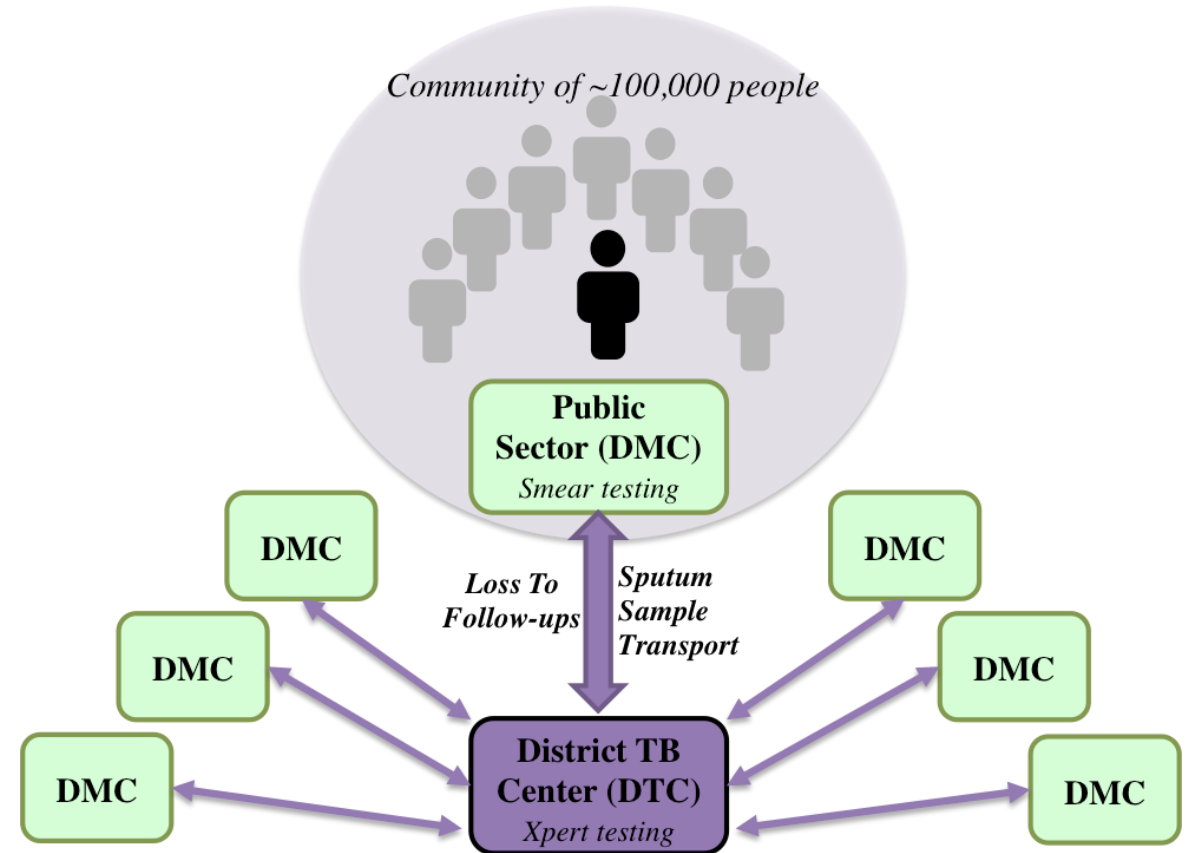
Intervention:

Decentralized Xpert testing using Xpert Omni at the Designated Microscopy Center level (population of 100,000)

Centralized Xpert using a specimen transport network to the District TB Center level (population of ≥ 1 million)

Outcomes:

Incremental cost-effectiveness (cost per DALY averted)



Methods

Transmission model

Agent-based agent-based simulation model

Demographics, household structure, TB natural history programmed at an individual level

Health system model

Incorporate patient movement within and between various health care sectors

Cost model

Health services cost:

Public sector: estimate an average unit cost of different types of patient's clinic encounters

Private sector: costs associated with clinic visits

Xpert & sample transport:

Dynamic unit cost estimates that factors supply and demand (i.e. workload, testing capacity, etc.)

Transmission Model

An individual agent-based simulation (ABS) model of TB transmission in a representative Indian setting

Population

- a. A self-contained population of 100,000 individuals corresponding to the catchment area of a single DMC
- b. Age- and gender- distribution calibrated to India
- c. Simplified household structure (using a uniform distribution of household sizes and maintaining the same distribution over time)

TB Infection

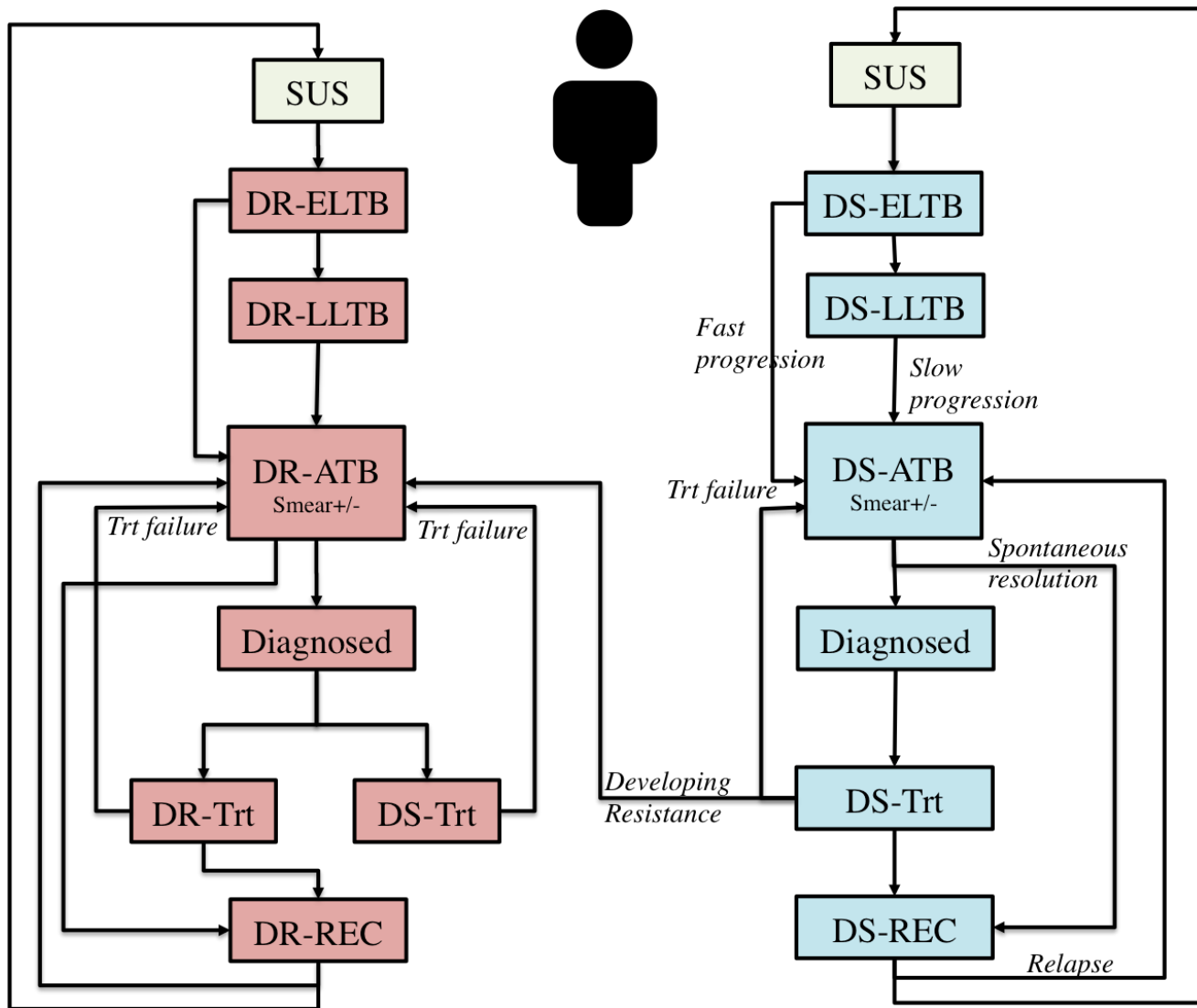
- a. Modeled as a combination of drug-susceptible (DS) and rifampin-resistant (DR) TB strains

Immunity:

- a. Latent disease: DS and DR imply immunity toward reinfection with both strains
- b. Individuals are immune toward reinfection during treatment period (TRDS/TRDR)

Treatment failure:

- a. Those failing treatment are subject to TB mortality during treatment and will return to active disease with full infectiousness



TB history model

Contact Network

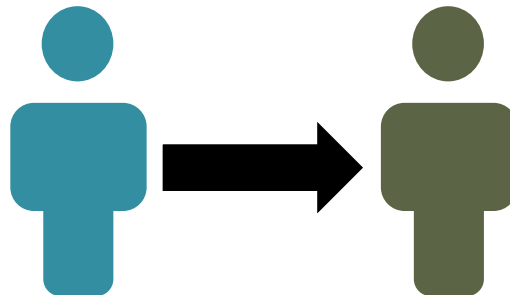
1. ***Close contacts*** between two individuals who belong to the same household
2. ***Casual contacts*** between random members of the community

Each network is characterized in terms of “frequency” and “effectiveness” of contacts for TB transmission

Model runs in a time step of 1 month

Transmission:

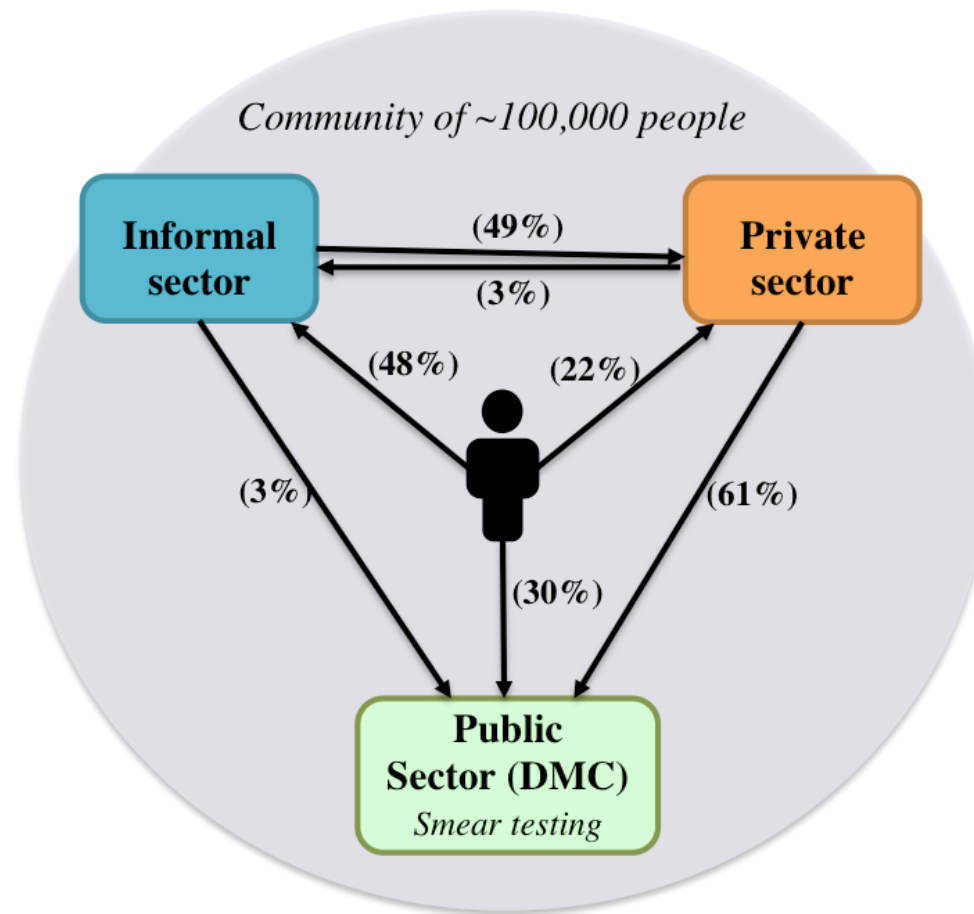
Computed as a function of the type of contact and the TB strain- and time-dependent infectiousness of the infectious person, and immunity of the susceptible/latent contact.



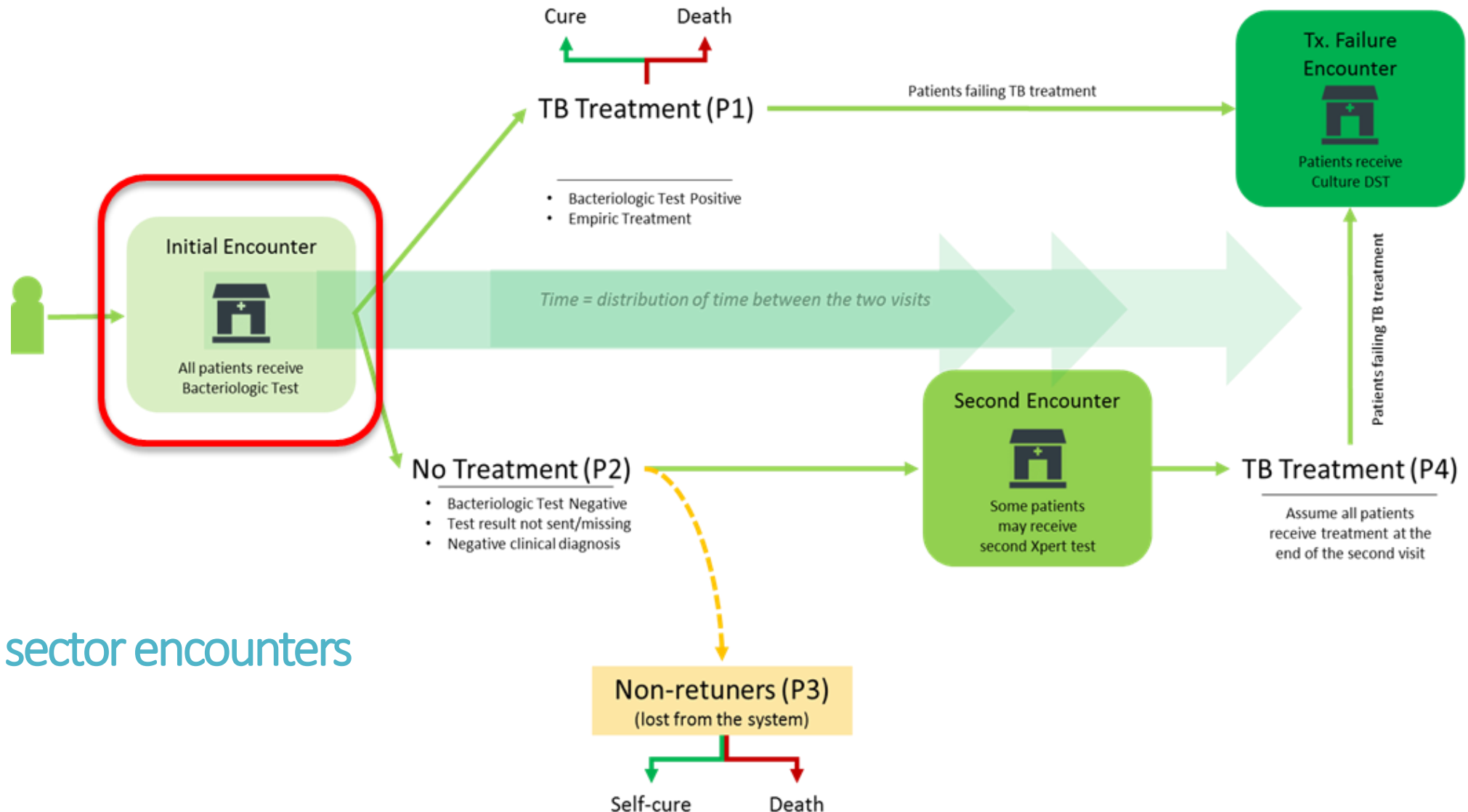
Healthcare System 1

Care seeking behavior

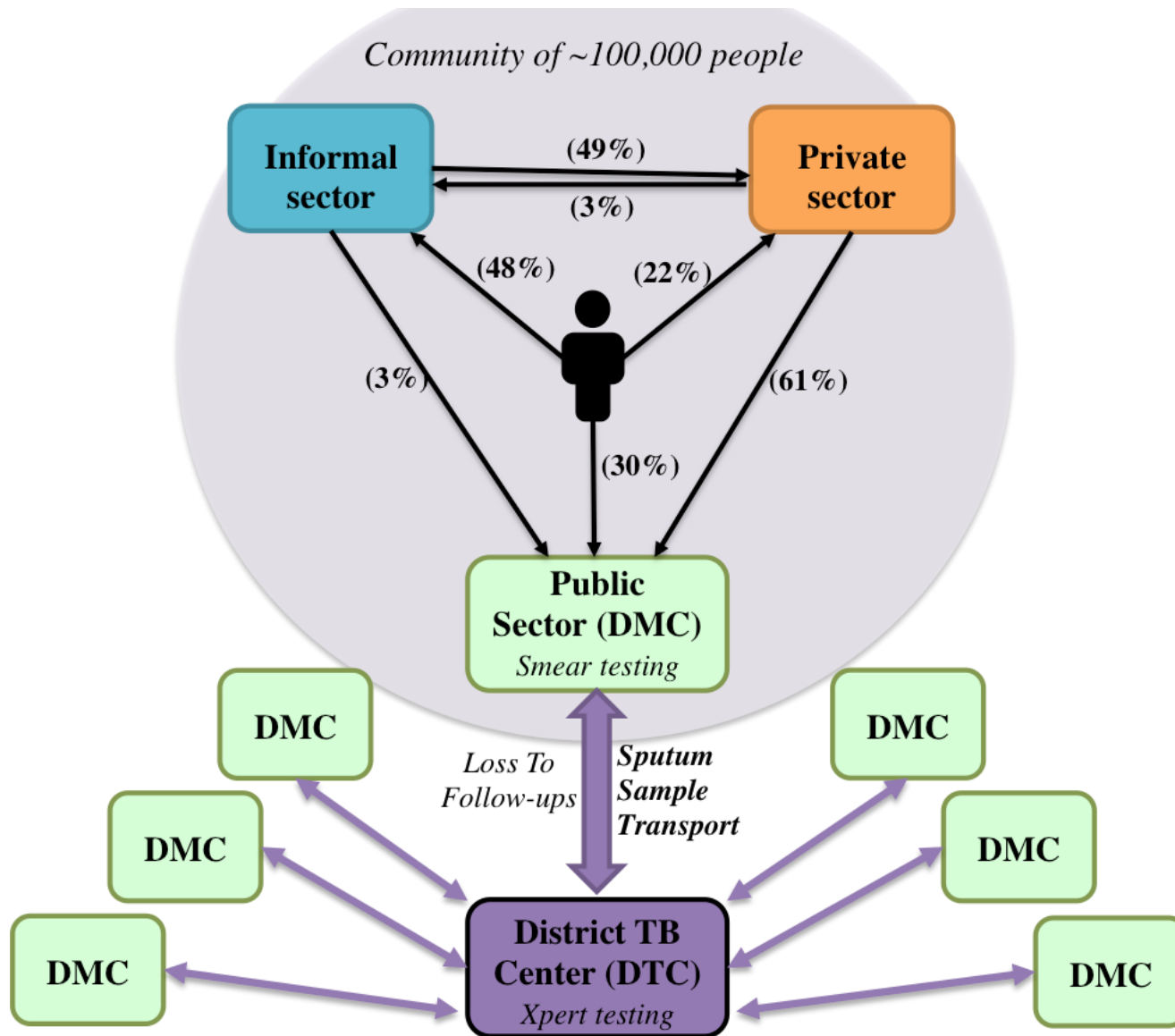
- a. *Probability of seeking care modeled as a function of time since infection*
- b. *Probability seeking care via each provide depends on the previous step*



Healthcare System 2



Public sector encounters



Xpert placement

Centralized Xpert scenario (CXP):

Not all patients intended to receive Xpert referral (67% in encounter 1)

Decentralized Xpert scenario (DXP):

All suspected TB patients (100%) will be tested with Xpert as an upfront test in addition to smear (smear as treatment monitoring tool) on the same day during the diagnostic visit

Clinical Encounter Costs

Informal & Private sector visits

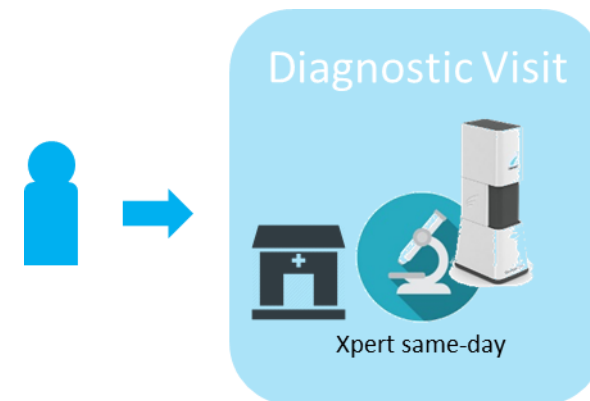
Type of clinical visits	Cost per visit		
	PE	Low	High
Informal & Formal allopathic private clinic visits	2.32	2.06	2.60

Public sector encounters

Categories of health service	Type of clinical encounter					
	Encounter 1		Encounter 2		Encounter 3	
	Utilization rate	Cost	Utilization rate	Cost	Utilization rate	Cost
Average # of clinic visits	3	6.42	2	4.28	1	2.14
X-ray (50%)	0.5	1.49	0.5	1.49	0.5	1.49
Anti-biotic trial (50%)	0.5	0.15	0	0	0	0
Biochemical Lab Test	1	0.30	0	0	0	0
Smear x 2	2	3.76	2	3.76	2	3.76
Total unit cost	PE	12.11	PE	9.53	PE	7.39
	Low	9.08	Low	7.15	Low	5.54
	High	15.14	High	11.91	High	9.24

Determining Xpert costs

Steps	Basis of calculation	Notes
1. Compute reference per-test cost	- Time and motion study of a range of laboratory workloads - Ingredients approach	Calculated based on a FIND study in India GX Omni unit price: \$2895 + 20% procurement cost
2. Simulate a range of laboratory workload scenarios	- Poisson distribution with lambda representing various per-day testing volumes 250 operational days / year	Simulated for 15 different laboratories with lambda ranging between 0.1 to 10
3. Evaluate # of GX Omni units required for 90% same-day testing	1 GX Omni unit has daily testing capacity of 4 tests - Calculate frequencies of days with workloads beyond capacity @ 4, 8, 12 tests/day	Per-day operating cost of GX Omni was calculated at \$4.6 *** (incurred daily cost for days with no test performed) ***
4. Average per-test cost for a DMC	- Each 'day' of laboratory operation has distinct per-test cost referenced from #1 - Average-per-test cost = Total annual cost / total # of tests performed	Assumed that laboratories with different workload have similar cost structure (overhead cost, laboratory technician salaries, procurement prices etc.)



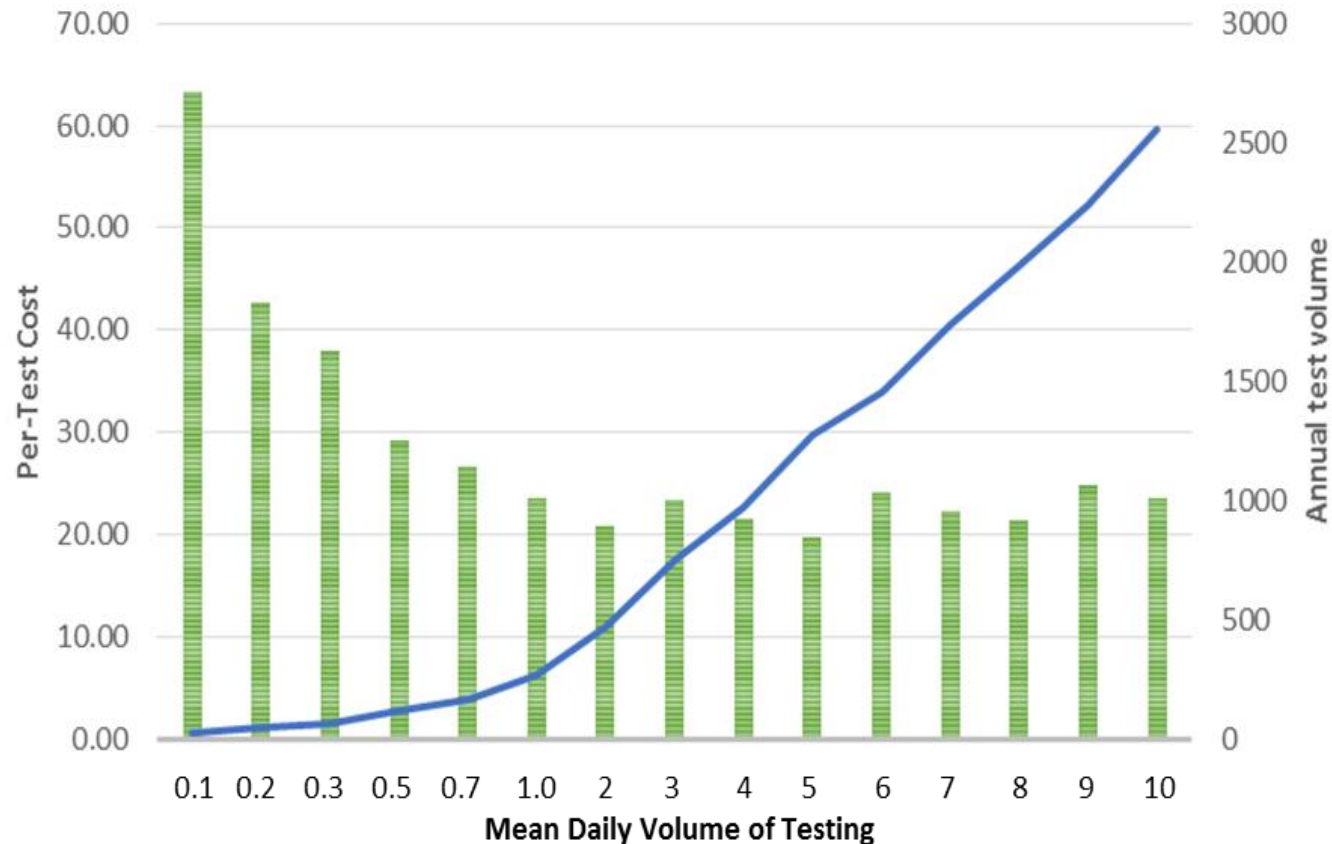
Factors influencing per-test cost of Xpert

Test workload	# of test performed per day
Unit prices of resources	HR, Overhead, Prices of equipment (e.g. Omni) & laboratory consumables (e.g. Xpert cartridges)
# of Omni Units required for 90% same-day testing	1 Omni unit = Maximum 4 tests per day (2 hr / run)

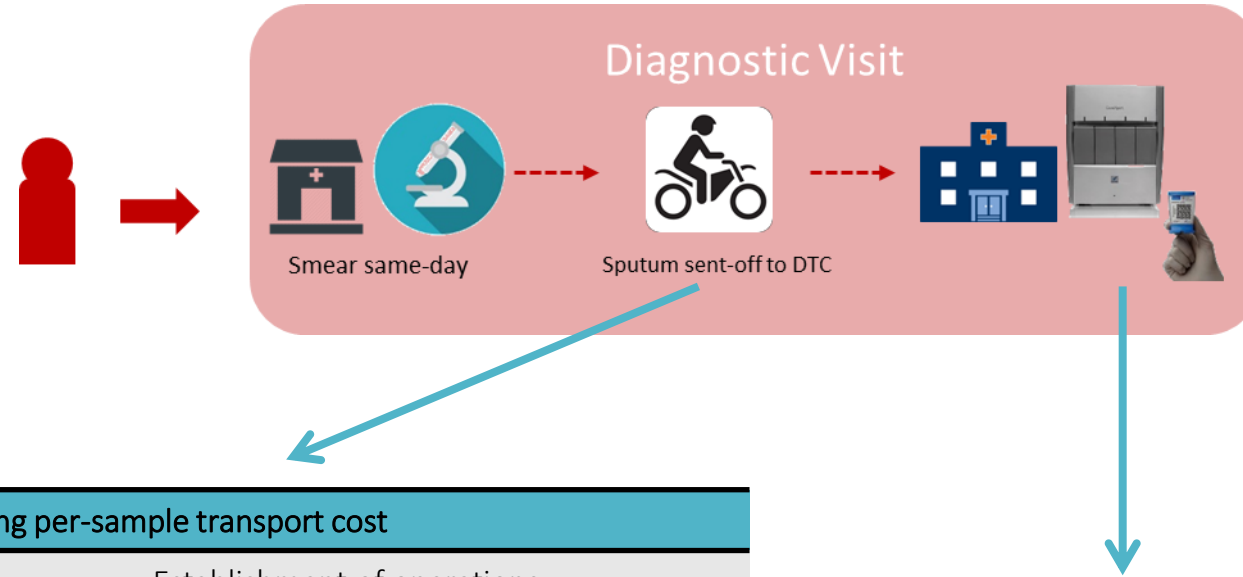
Reference per-test cost of Xpert (w/ Omni)

Per-test cost begins to rise sharply below average volumes of one test per working day (~1 TB diagnosis per week).

At higher volumes, unit cost stabilizes at \$20-\$25 per test.



Cost modeling of Centralized Xpert



Factors influencing per-sample transport cost

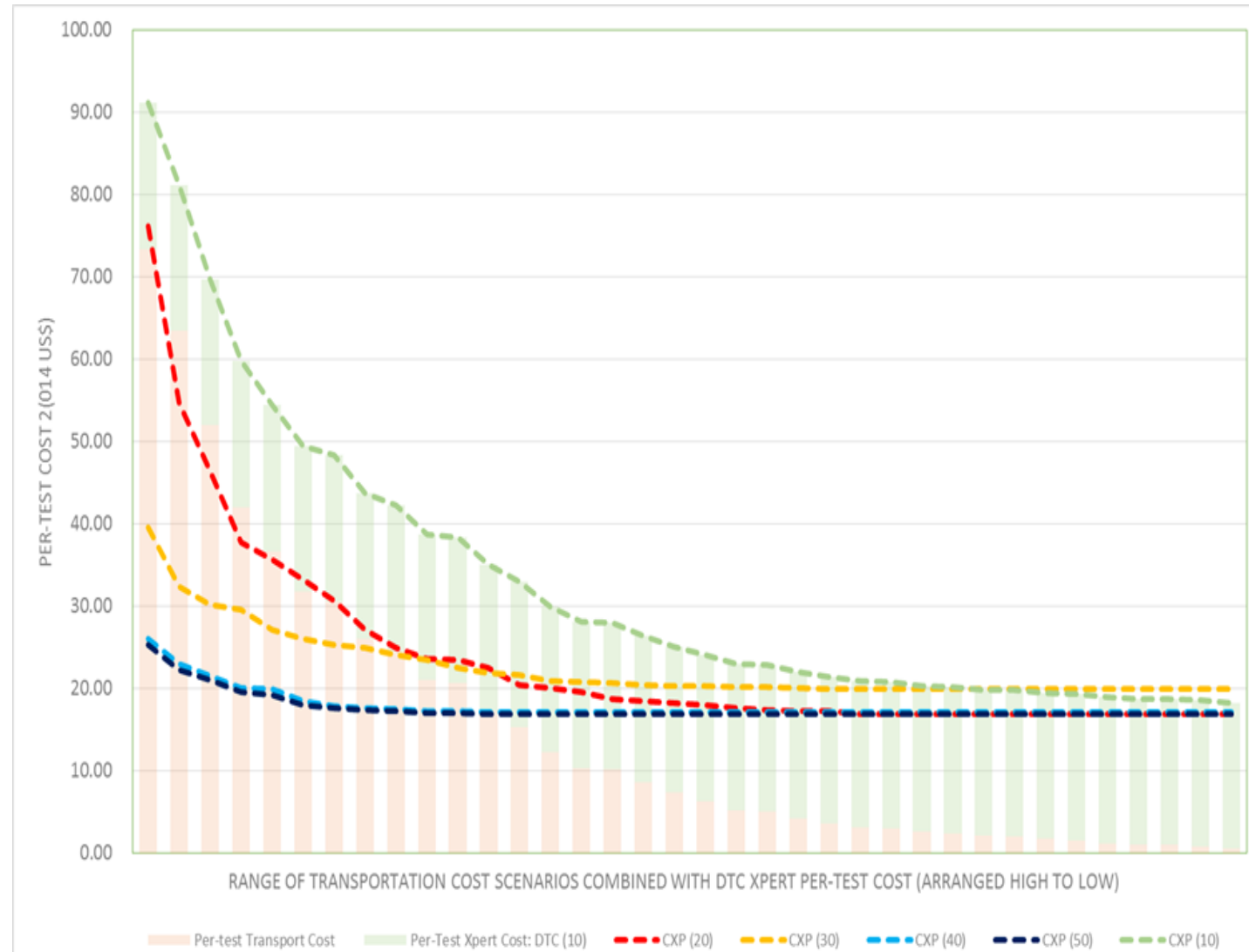
Overhead costs	Establishment of operations
Unit prices of resources	HR, prices of fuel & motorcycle
Operational factors	1. # of clinics visited 2. Total distance traveled 3. # of samples transported 4. Proportion of TB samples per sample transport

Factors influencing per-test cost of CXP

Test workload	# of test performed per day
Unit prices of resources	HR, Overhead, Prices of equipment (e.g. Omni) & laboratory consumables (e.g. Xpert cartridges)
# of GX4 units required for 90% 2-day turn-around	1 GX4 unit = Maximum 16 tests per day (2 hr / run)

Cost modeling of Centralized Xpert

- A. Per-test cost depends strongly on specimen transport cost.
- B. At high transport cost (left), unit cost can range from \$27 (highest volume, blue) to \$90 (lowest volume, green) per test.
- C. At lower transport costs (right), unit cost converges to ~\$20 per test.



Cost difference (CXP – DXP)

At higher transport cost (left), decentralized testing is cheaper (blue).

At lower transport cost (right), centralized testing is cheaper (red).

Volume of testing has relatively less impact.

Use volume of 10 per day at the central setting (CXP 10), under low and moderate transport cost assumptions, for further analysis.

		High transport cost					Low transport cost				
CXP Category	DXP Ave. Cost/Test	Per-test cost difference (CXP vs. DXP)									
CXP 10	27.03	64.09	39.25	18.90	9.29	0.47	-4.38	-6.46	-7.42	-8.24	-8.77
CXP 20	28.48	47.59	22.02	8.21	1.88	-4.83	-8.79	-10.22	-10.93	-11.18	-11.53
CXP 30	23.93	15.60	7.36	4.45	1.49	-0.96	-2.90	-3.58	-3.74	-3.90	-4.00
CXP 40	22.88	3.19	-0.60	-2.87	-2.92	-4.39	-4.96	-5.27	-5.42	-5.57	-5.72
CXP 50	22.17	3.14	-0.52	-2.64	-2.98	-4.17	-4.51	-4.81	-4.93	-5.10	-5.24

Epidemiological results

Small impact of incidence under both scenarios

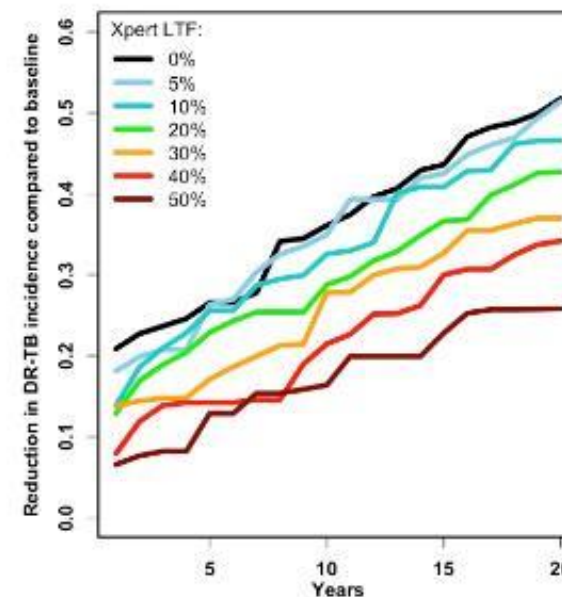
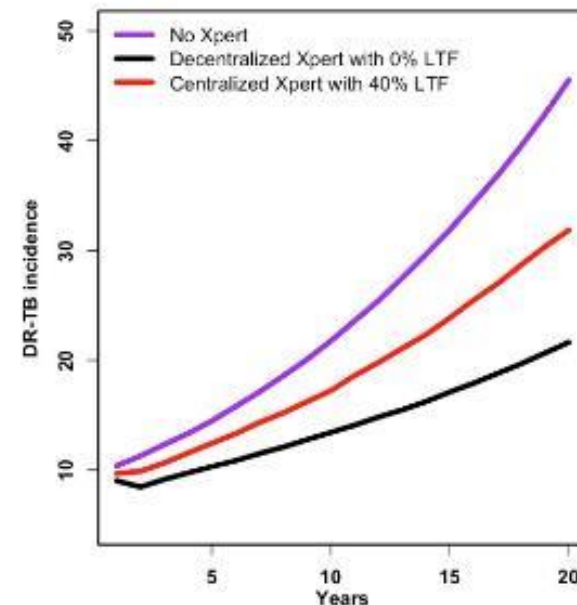
In the median of all simulations, centralized Xpert reduced the incidence of DR-TB by **1.9%** at 20 years after implementation, compared to a **3.1%** reduction under decentralized testing

Xpert testing caused a more immediate reduction in DR-TB incidence:

10.7% reduction after two years with centralized testing

21.4% reduction with decentralized testing

By the end of the 20-year analysis period, however, the incidence of DR-TB had begun to rise again in both Xpert scenarios, reflecting the underlying increasing trend in DR-TB incidence assumed at baseline



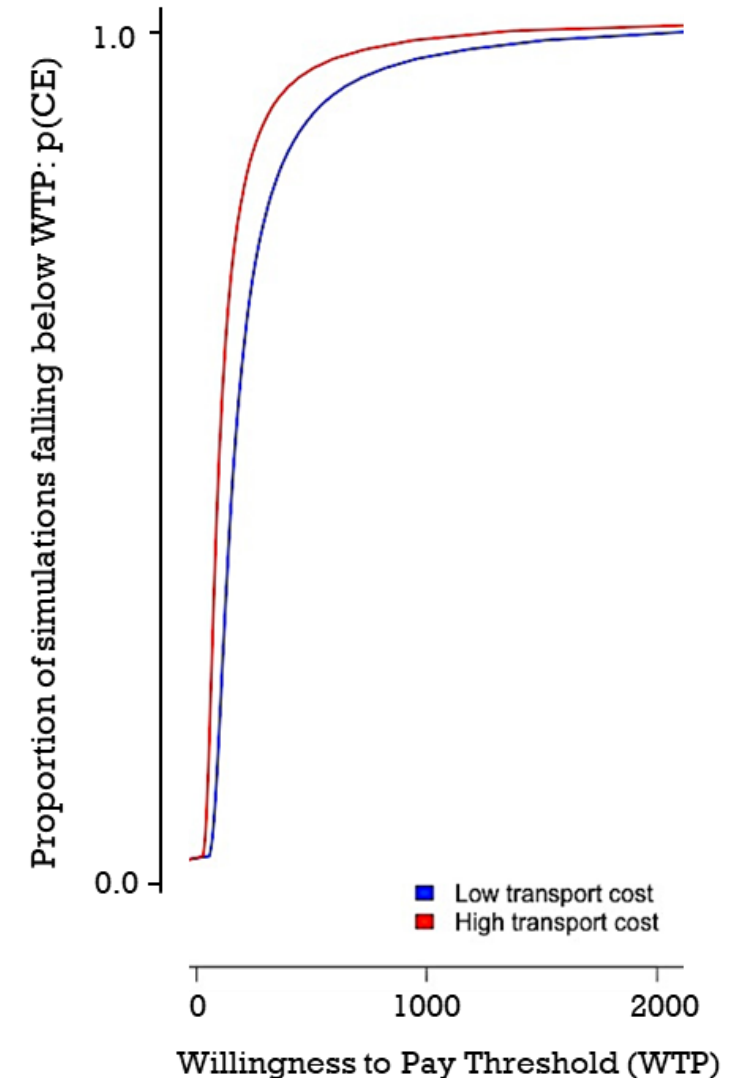
Cost-Effectiveness results

Relative to centralized Xpert, decentralized implementation averted an estimated 34 incident cases of TB (12 DS-TB cases and 22 DR-TB cases) and 3.5 TB deaths (1.9 DS-TB deaths and 1.6 DR-TB deaths), per 100,000 population over 10 years.

This translated into an estimated 8 DALYs averted by decentralized Xpert (relative to centralized Xpert) per 1,000 people, at an incremental cost-effectiveness of **\$141-\$241** per DALY averted.

The estimated number of DALYs averted by decentralized Xpert was a much stronger determinant of incremental cost-effectiveness than the cost of centralized Xpert:

- Varying the unit cost of centralized Xpert from the highest to the lowest reasonable cost caused the incremental cost-effectiveness ratio to vary by no more than 5%*
- Varying the estimated number of DALYs averted from the low to high bound of the 95% uncertainty range caused the incremental cost-effectiveness ratio to vary from \$125 to \$342 in the low transport cost scenario*



Discussion

In settings such as Uganda and South Africa, it has been argued that low-volume, point-of-care diagnosis is much more expensive relative to centralized testing.

Despite this, we find that – except in very low-volume settings – the cost of decentralized Xpert is unlikely to be substantially greater than that of centralized testing

Our projected epidemiological impact from Xpert is **smaller** than those of initial cost-effectiveness models, consistent with emerging evidence that **empiric treatment** practices may greatly attenuate the impact of Xpert at the population level.

Despite this relatively modest projected population-level impact, decentralized Xpert appears **highly likely to be cost-effective** relative to centralized testing.

Reflecting the small incremental cost of decentralized Xpert (approximately 50 cents per person over 10 years), such that even a modest reduction in TB morbidity and mortality is sufficient to justify this additional cost

Cost-effectiveness does not ensure affordability: Need for future research



Thank you!