Session 4: Health Systems Thinking

September 22nd, 2017

It's time to think about health systems factors more closely

What and how do the health systems factors influence the costs and effectiveness of TB intervention(s)?

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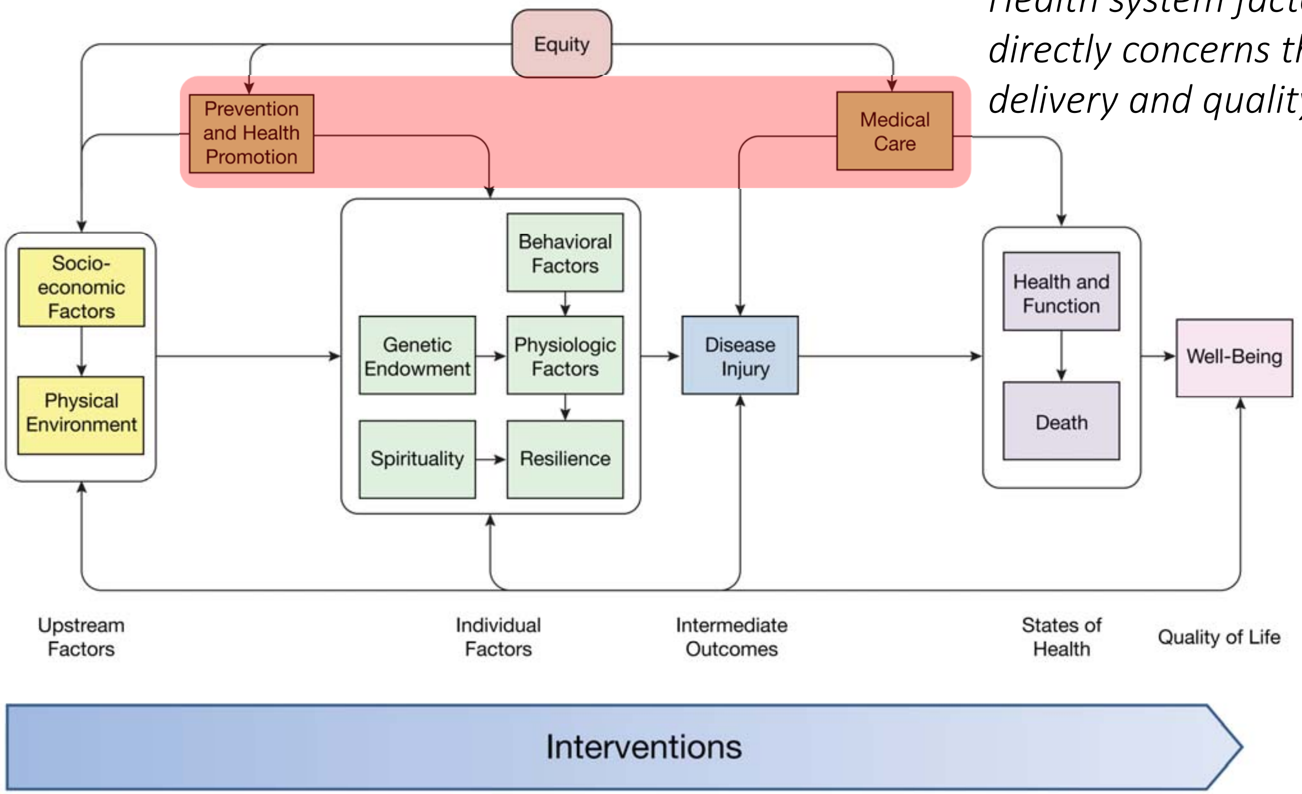
TB Modelling and Analysis Consortium

The pathway to promoting patient's well-being

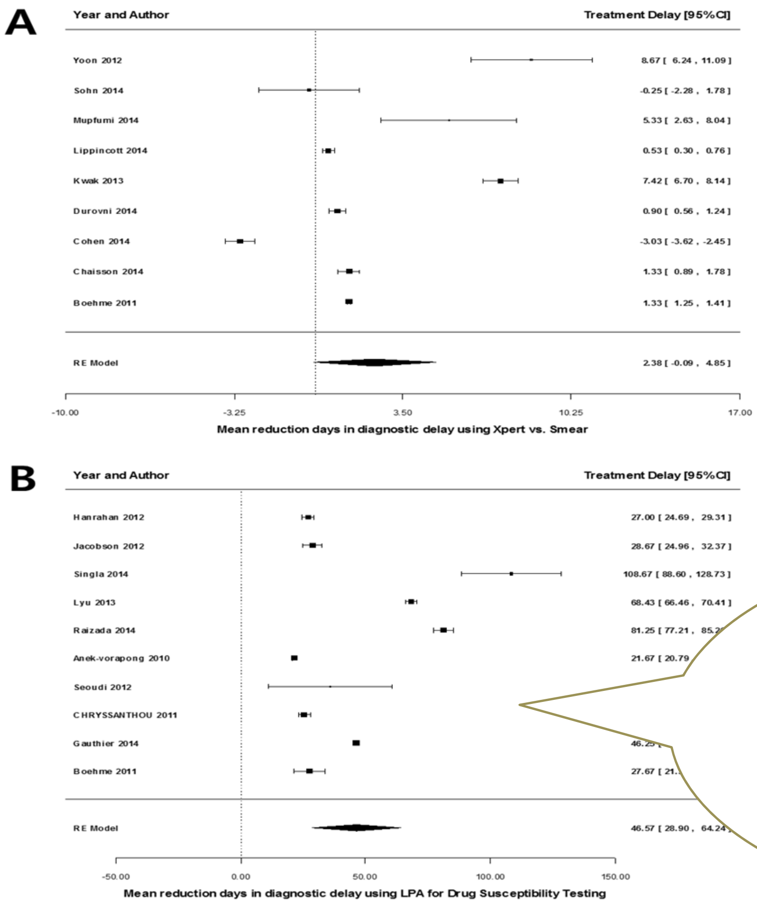


Health system factors directly concerns the delivery and quality of care

Institute for Healthcare Improvement (IHI) Composite Model of Population Health – Stoto, 2014

Let’s think in terms of delays

Would introducing new diagnostics alone improve delays?



- Screening 7,995 titles led to 39 eligible studies (21 for DS-TB w/ Xpert & 18 for DR-TB w/ LPA, where 2 were also for Xpert)
- Use of Xpert (vs. smear microscopy) reduced 2.83 days (95% CI: 0.09, 4.85) for diagnosis and 16.54 days* (95% CI 6.79, 26.35) for treatment for DS-TB

  *Exclusion of hypothetical studies reduced the effect to 4.75 days (95% CI 0.94, 8.57)**

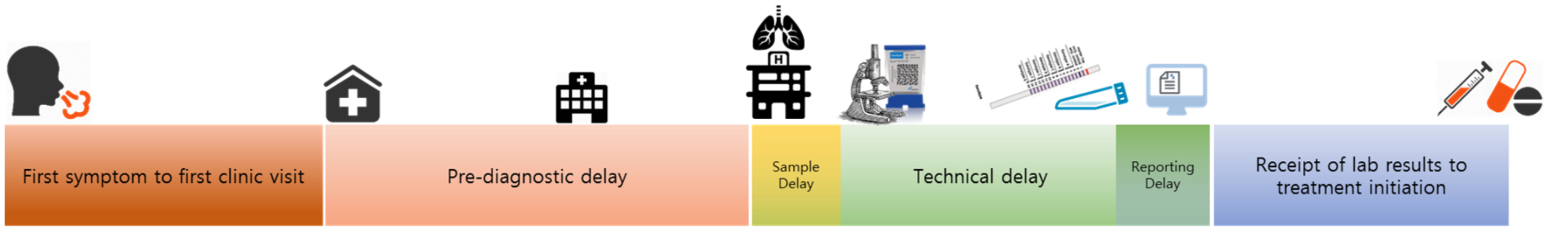
- … (vs. culture DST) reduced 45.57 days (95% CI … 8 days (95% CI 27.72, 97.24) for … f DR-TB
- … observed (types of study … on of time delay components, … MA)

How can a 2 hr. test end up delaying diagnosis and treatment for more than 40 days**?!

** e.g. Hanrahan & Jacobson reported overall 55 and 60 days for treatment initiation of MDR-TB using LPA results

Each components of delay is associated with health systems

Dissecting causes of delays in diagnosis and treatment of TB



Patient Delay

Definition:
Time between onset of the first symptom(s) and the time when the patient first contacted any type of health care service

Time components
- Time to seeking health care

Pre-diagnostic delay

Definition
Time between patient's first contact with the health care service and specimen collection got TB diagnosis (or first visit for TB specific consultation)

Time components
- Time to TB clinic visit

Sample delay is defined as time of specimen collect to specimen arrival at the laboratory.
Reporting delay is defined as time of result at the laboratory to availability of results at the clinic. Technical delay is defined as time between sample arrival at the laboratory to test result

Diagnostic Delay

Definition
Time between specimen collection (or first TB specific visit or study recruitment) and reporting or receipt of results at the clinic.

Time components
- Sample delay
- Technical delay
- Reporting delay

Treatment Delay

Definition
Time between test result reporting and treatment decision for TB disease (or to confirm no TB)

Time components
- Time to seeking health care

Therapeutic Delay

Definition
Time between first specimen collection (for diagnosis of TB) and treatment decision for TB disease (or to confirm no TB)

Time components
- Diagnostic delay
- Treatment delay

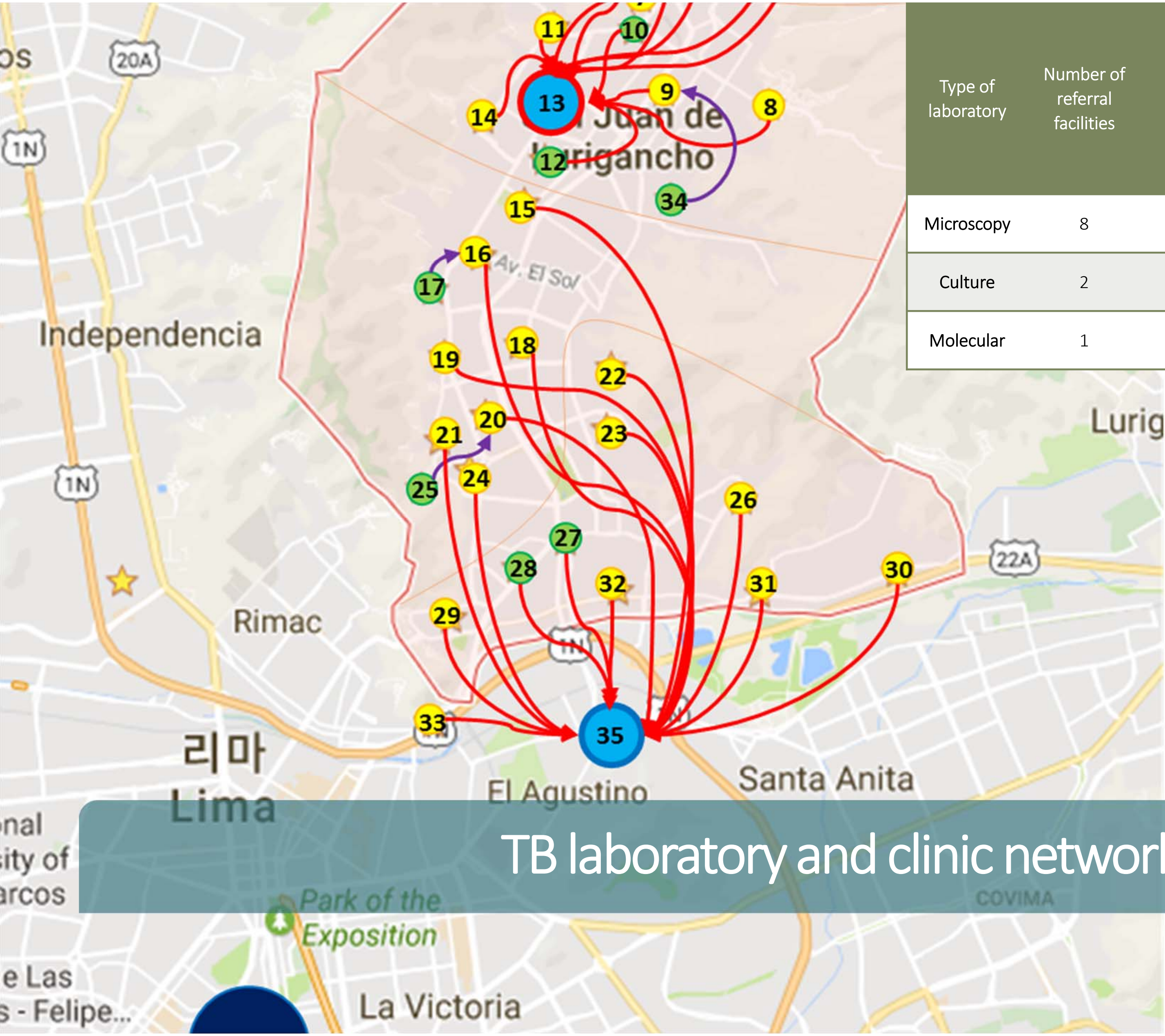
Health Systems Delay

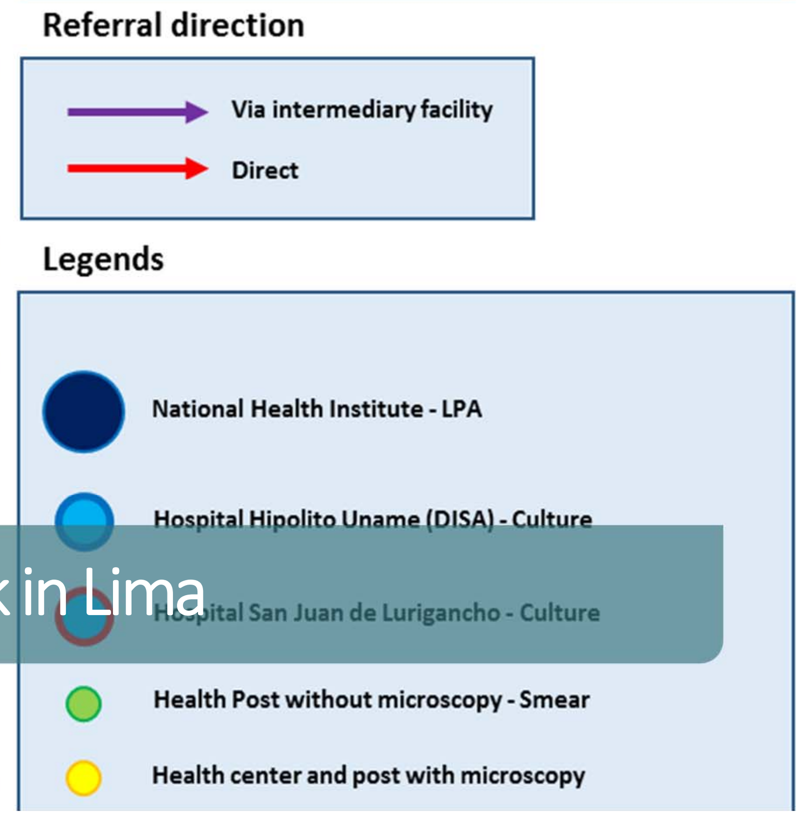
Definition
Time between patient's first contact with the health system to treatment decisions for TB disease

Time components
- Pre-diagnostic delay
- Diagnostic delay
- Treatment delay

TB laboratory and clinic network in Lima

Type of laboratory	Number of referral facilities	Ave. distance (km)	Ave. Freqeuncy / wk	Ave. Samples/ Transport	Number of TB samples referred to laboratories		
					via intermediary facility/lab	direct	Total
Microscopy	8	1.30	5.14	8.10	N/A	12589	12589
Culture	2	3.34	2.98	6.43	1377	24092	25469
Molecular	1	7.57	1.94	3.08	3953	156	4109





Incorporating health systems and costing models within the TB transmission model

Evaluating the cost-effectiveness of Xpert decentralization in India

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

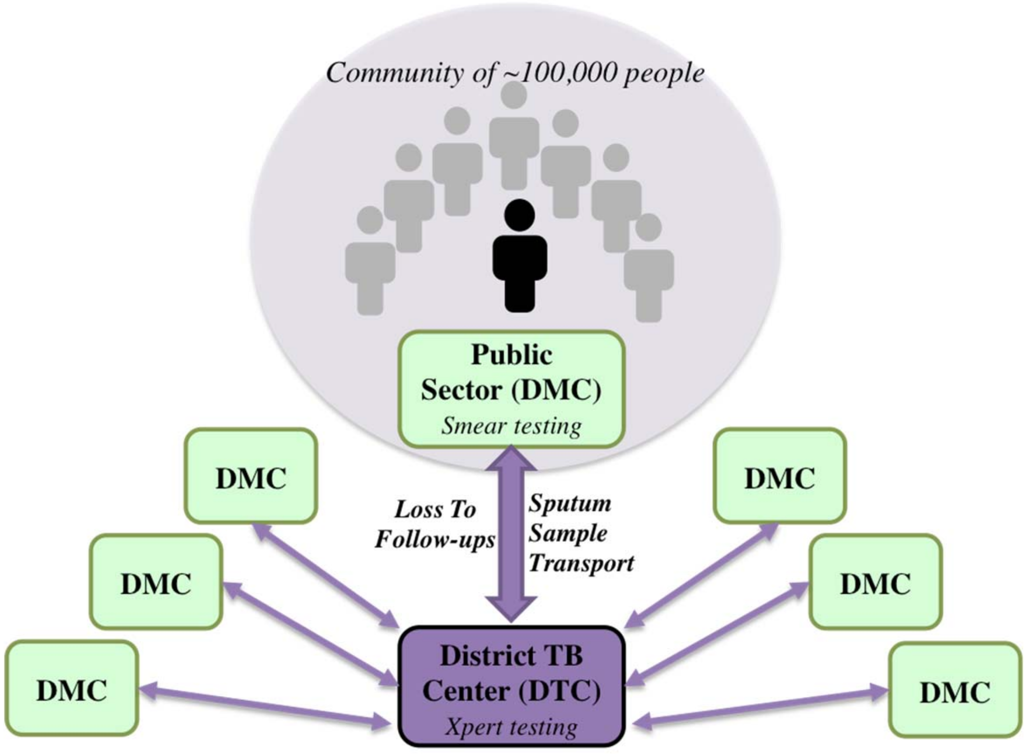
Overview of the research

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

<u>Health services cost:</u>

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

Private sector: costs associated with clinic visits

<u>Xpert & sample transport:</u>

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

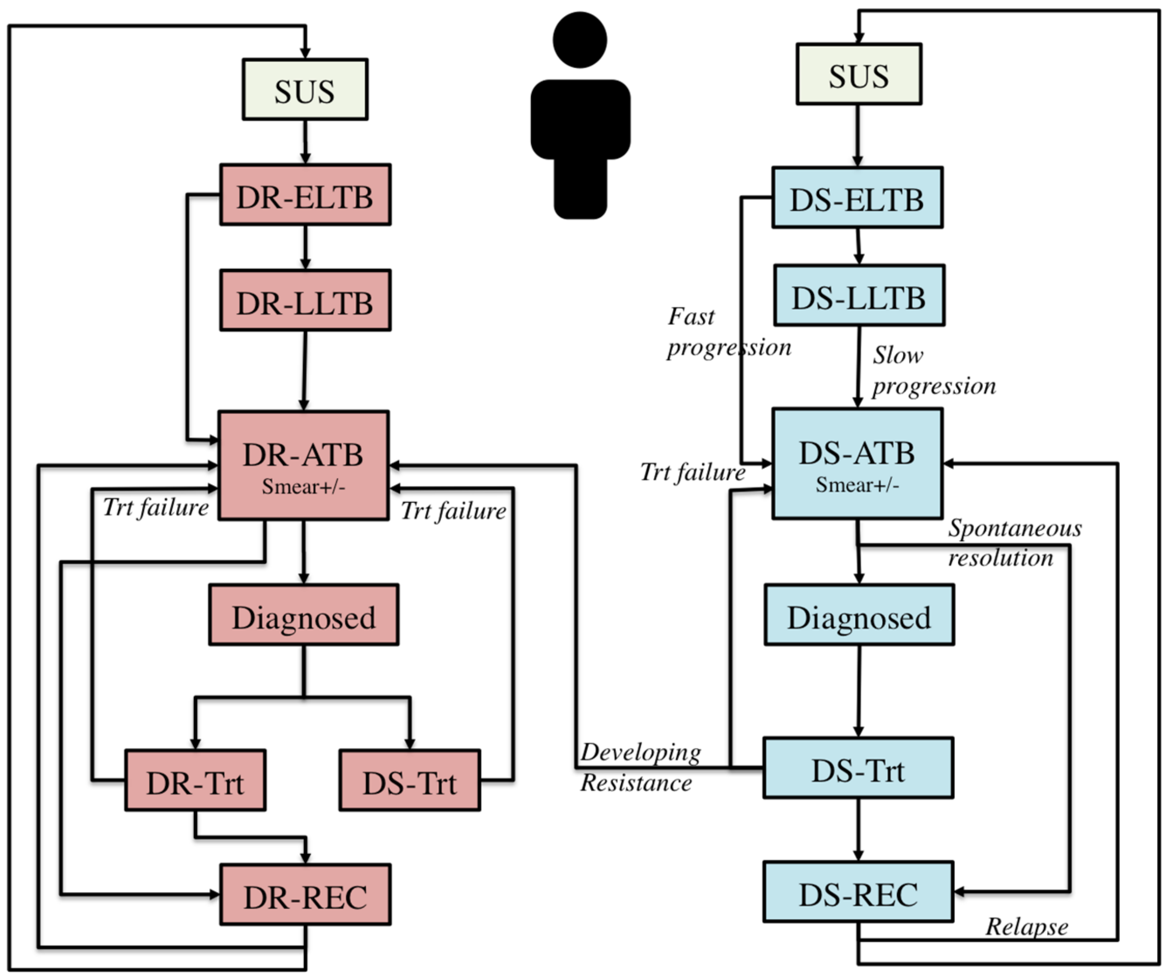
Immunity:

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

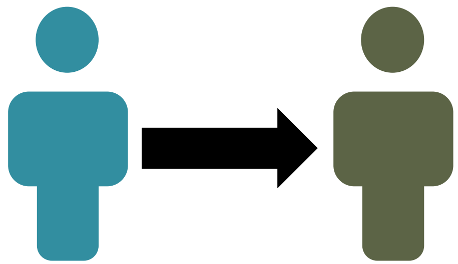
1. ***Close contacts*** between two individuals who belong to the same household
2. ***Casual contacts*** between random members of the community

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.

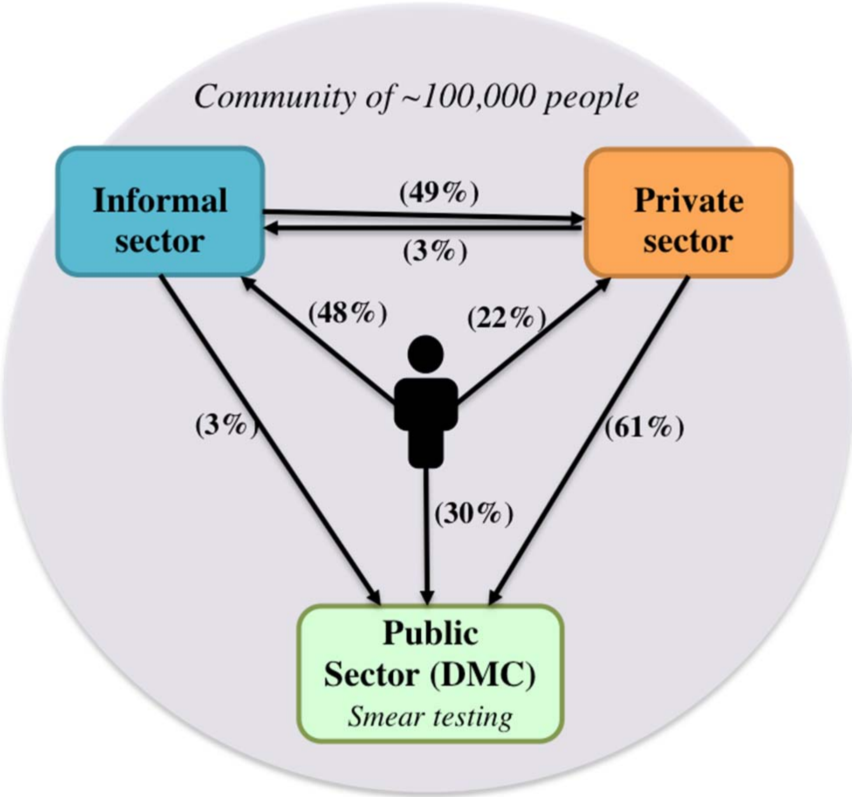


Healthcare System 1

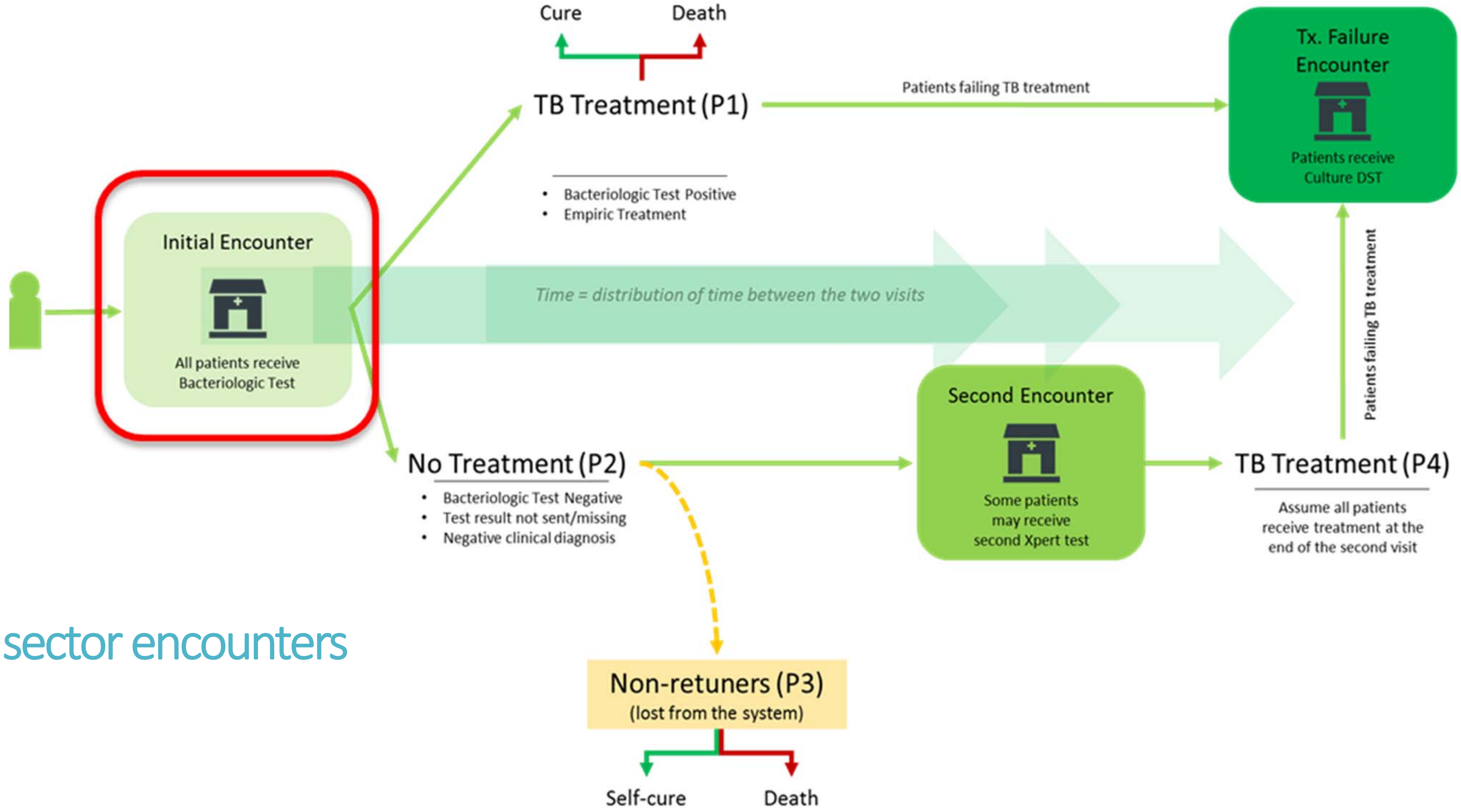
Care seeking behavior

a. *Probability of seeking care modeled as a function of time since infection*

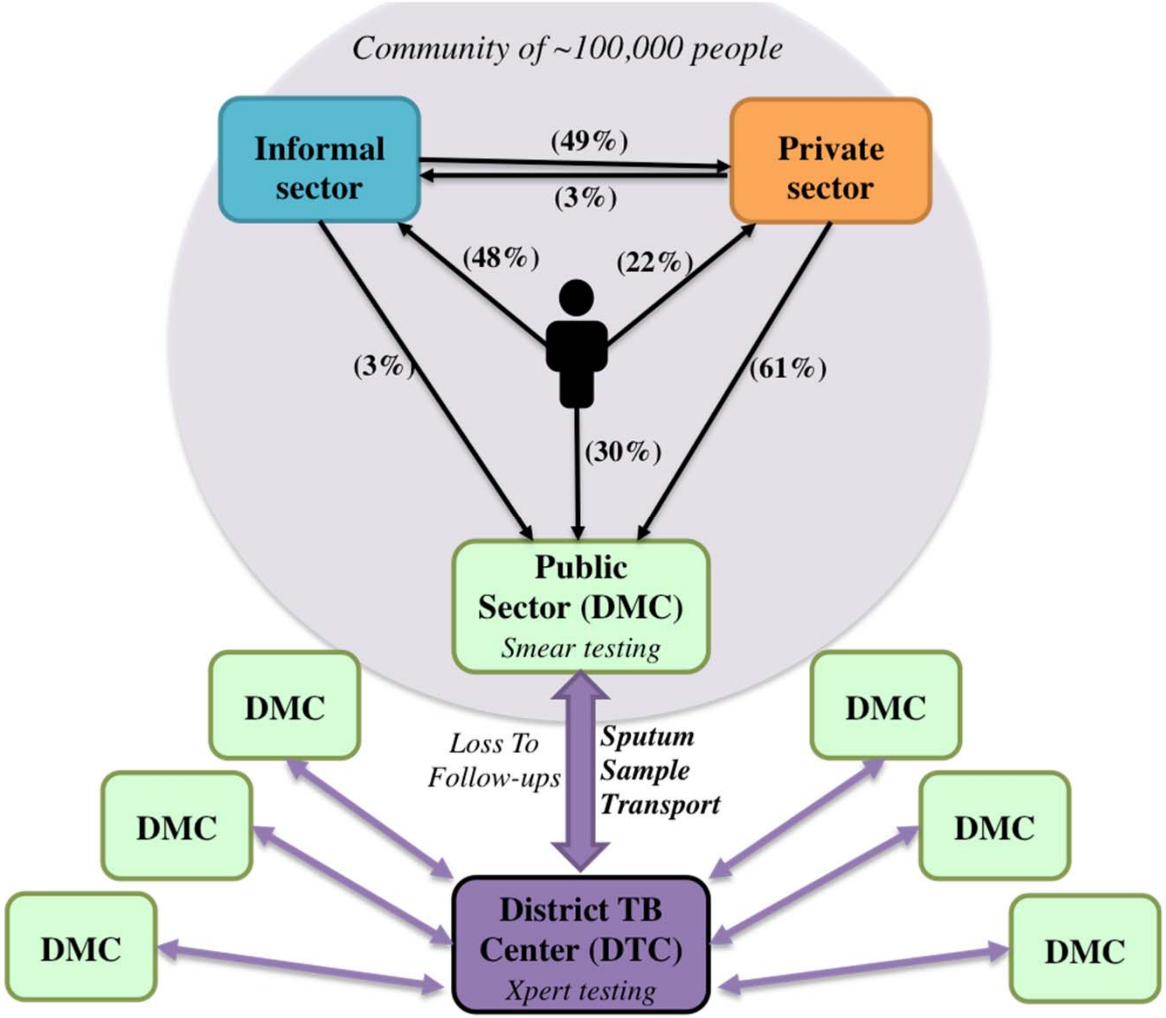
b. *Probability seeking care via each provide depends on the previous step*



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

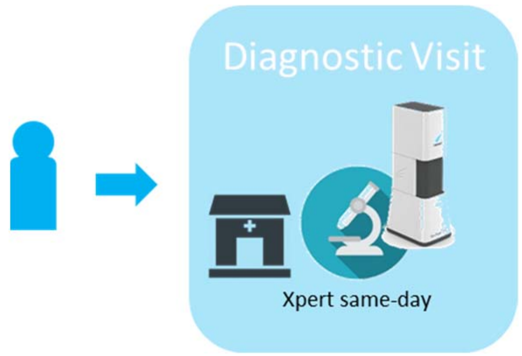
Type of clinical visits	Cost per visit		
	PE	Low	High
Informal & Formal allopathic private clinic visits	2.32	2.06	2.60

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.)

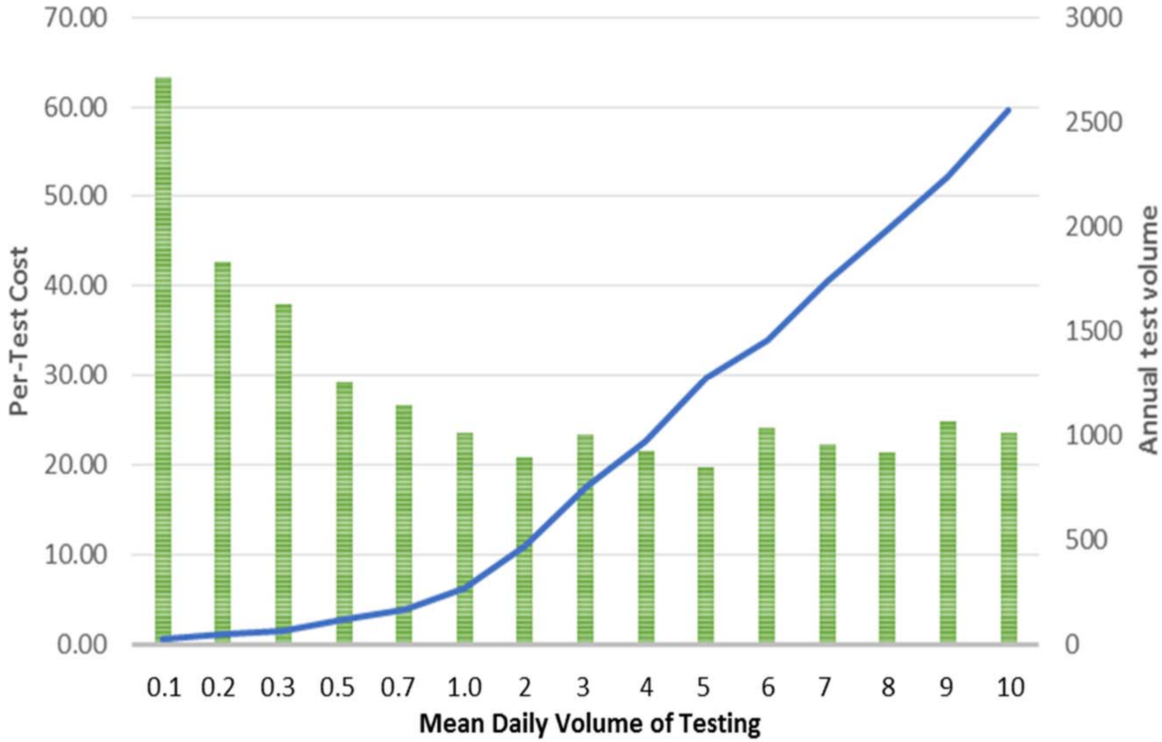


Factors influencing per-test cost of Xpert	
Test workload	# of test performed per day
Unit prices of resources	HR, Overhead, Prices of equipment (e.g. Omni) & laboratory consumables (e.g. Xpert cartridges)
# of Omni Units required for 90% same-day testing	1 Omni unit = Maximum 4 tests per day (2 hr /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

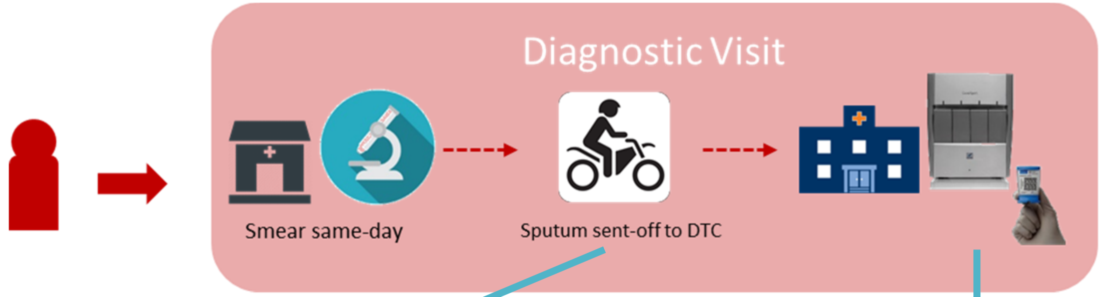
Reference per-test cost of Xpert (w/ Omni)

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

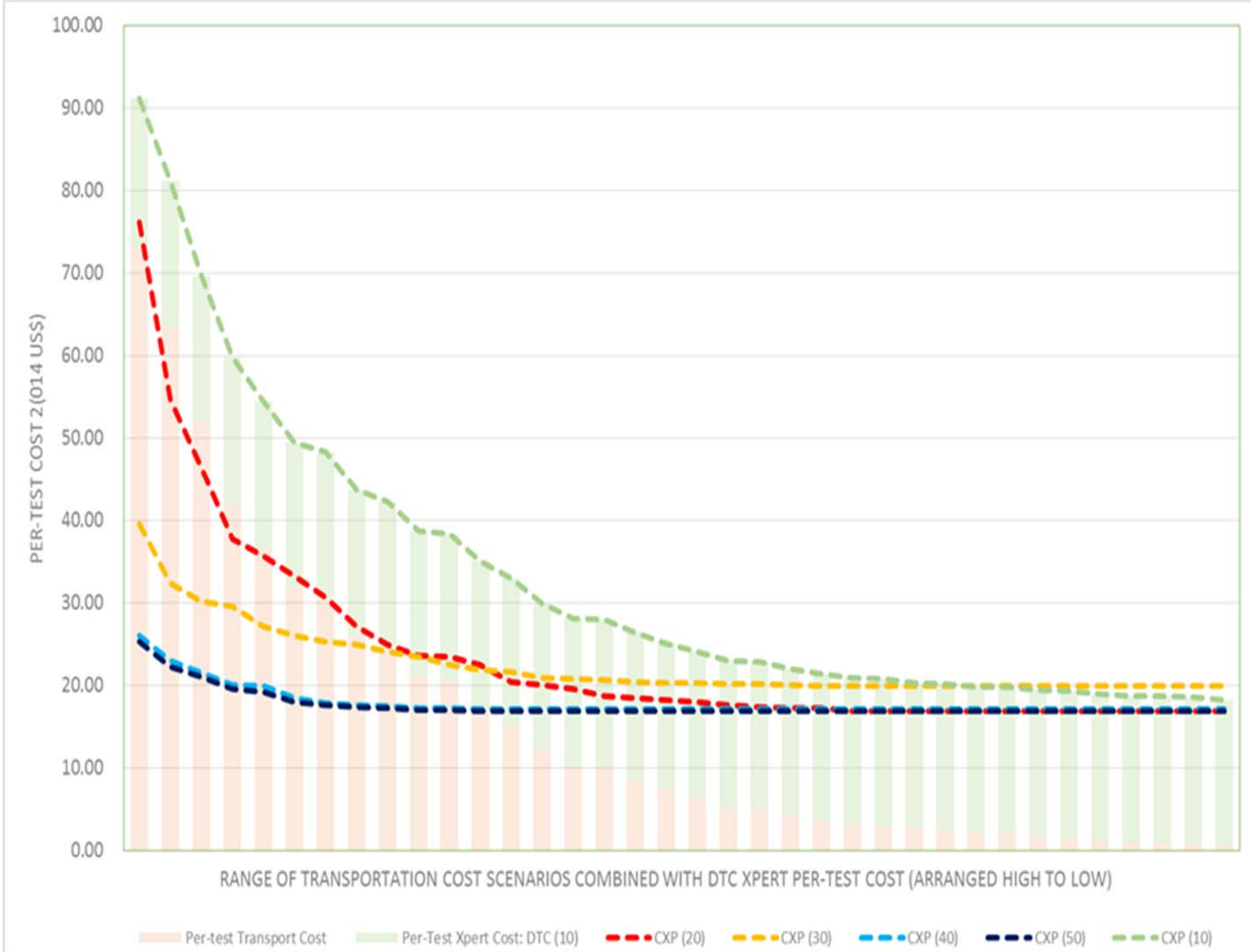
Factors influencing per-test cost of CXP	
Test workload	# of test performed per day
Unit prices of resources	HR, Overhead, Prices of equipment (e.g. Omni) & laboratory consumables (e.g. Xpert cartridges)
# of GX4 units required for 90% 2-day turn-around	1 GX4 unit = Maximum 16 tests per day (2 hr / run)

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 DS-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:

a. *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%*
b. *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