Challenges in Modeling TB Diagnostics: A Case Study

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Background

- India is scaling up Xpert, though primarily for purposes of DST.
- The impact of that scale-up is likely influenced by India's complex healthcare system.
- Models of Xpert scale-up need to account not only for the diagnostic test, but also for the system into which that test is deployed.
- *Construct a model of Xpert scale-up in India that accounts for patient behavior and the healthcare system*

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The Importance of Implementation Strategy in Scaling Up Xpert MTB/RIF for Diagnosis of Tuberculosis in the Indian Health-Care System: A Transmission Model

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Question

treatment—early in the diagnostic pathway. To better understand the potential epidemiological impact and resource requirements for strategies in which Xpert is scaled up across different health-care sectors, we constructed a transmission model of TB that incorporates provider and patient behavioral patterns within the Indian health-care system.

Population

Table 3. Model calibration.

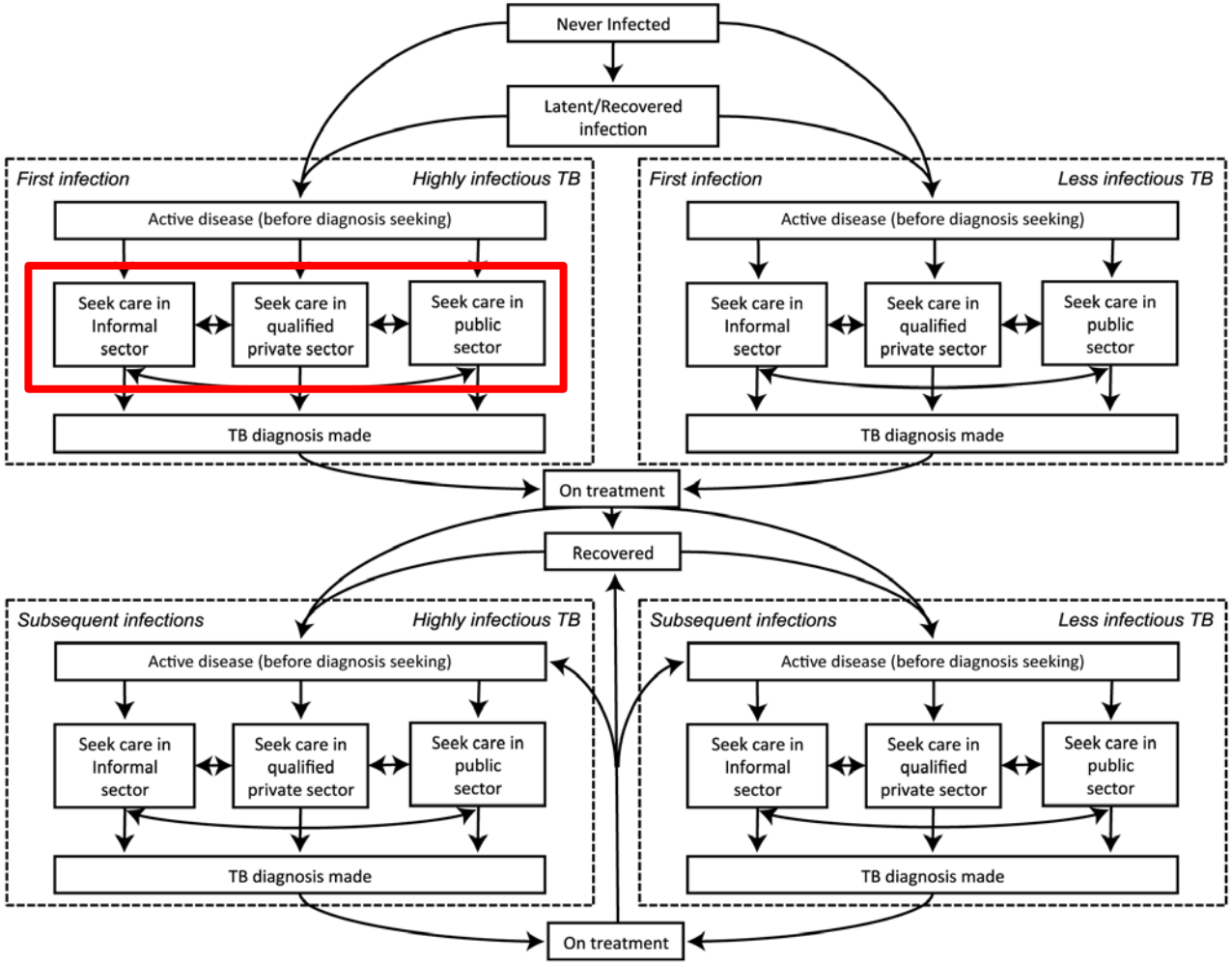
Data point	Reported Value	Adjusted Value	Fitted Value
Prevalence (per 100,000)	249	293	293
Annual incidence (per 100,000)	181	213	213
TB mortality (per 100,000)	24	29	29
Proportion of TB infections in HIV+ individuals	0.042	0.042	0.042
Proportion MDR-TB in all infections	0.021	0.021	0.021
Proportion of diagnoses made in qualified private sector	0.4	0.4	0.4

Interventions

Table 4. Scenario overview.

Scenario	Public Sector (High Risk for MDR-TB)	Public Sector (Low Risk for MDR-TB)	Qualified Private Sector	Informal Sector
Baseline	Sputum smear microscopy, no Xpert	Sputum smear microscopy, no Xpert	Existing mix of tests in private sector, no Xpert	Existing mix of tests in private sector, no Xpert
1. Public sector, HIV/high MDR-TB risk only	Baseline + Xpert for 40%	Baseline	Baseline	Baseline
2. Broad public sector	Baseline + Xpert for 40%	Baseline + Xpert for 20%	Baseline	Baseline
3. Qualified private sector	Baseline + Xpert for 40%	Baseline	Baseline + Xpert for 20%	Baseline
4. Public plus qualified private sectors	Baseline + Xpert for 40%	Baseline + Xpert for 20%	Baseline + Xpert for 20%	Baseline
5. Broad cross-sector access	Baseline + Xpert for 40%	Baseline + Xpert for 20%	Baseline + Xpert for 20%	Baseline + Xpert for 20%
6. Increased referral	Baseline	Baseline	Baseline	Baseline

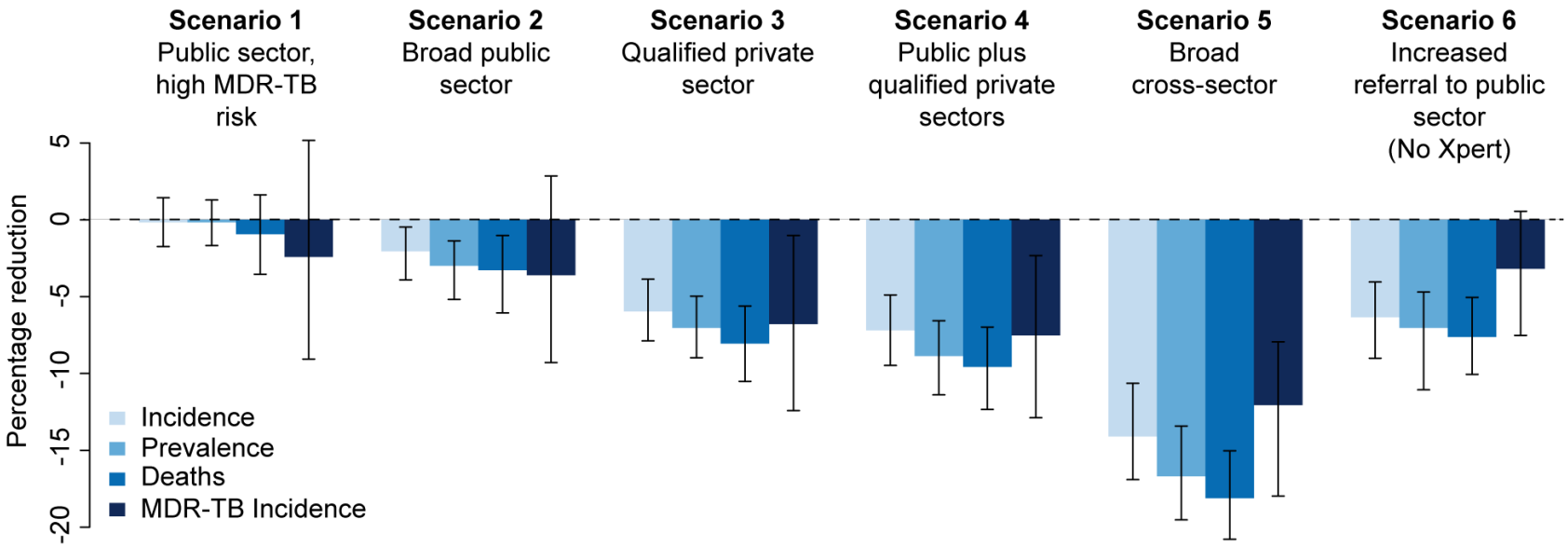
Model Structure



Parameters: TNTC

Time infectious before symptoms	4.1 mo	0–6 mo	Fitted value
Time from symptoms to seek diagnosis	4.8 mo	1–6 mo	[12]
Initial sector visited by TB suspect			[12]
Informal sector	0.69	0.61–0.77	
Qualified private sector	0.31	0.23–0.39	
Public sector	0.00	0–0.2	
Time to seek second opinion	1.9 mo	1.5–2.4 mo	[12]
Site of next diagnostic attempt (informal/qualified private/public)		—[e]	[12]
Current diagnostic attempt: informal sector	0.48/0.49/0.03	—	
Current diagnostic attempt: qualified private sector	0.03/0.36/0.61	—	
Current diagnostic attempt: public sector	0/0/1	—	
Probability of being diagnosed correctly, primary infection, highly infectious TB[f]			
Informal sector (without Xpert)	0	Unchanged	Model assumption
Qualified private sector (without Xpert)	0.38	0.27–0.45	Fitted value
Public sector (without Xpert)	0.98	0.85–1	Model assumption
Xpert	0.98	0.85–1	[22]
Probability of being diagnosed correctly, primary infection, less infectious TB[f]			
Informal sector (without Xpert)	0	Unchanged	Model assumption
Qualified private sector (without Xpert)	0.2	0.1–0.5	Model assumption
Public sector (without Xpert)	0.2	0.1–0.5	Model assumption
Xpert	0.73	0.6–0.8	[22]

Xpert Impact



Xpert Impact

Table 5. Effect of Xpert rollout on annual TB incidence and mortality after 5 y compared to baseline scenario with no Xpert.

Scenario	Cases Averted[a]	Deaths Averted[a]	MDR-TB Cases Averted[a,b]	Additional MDR-TB Diagnoses ($\times 10^3$/y, All India[a,c])	Total Number of Xpert Tests Conducted ($\times 10^3$/y, All India[a,c,d])	Minimum Number of Xpert systems Required (All India[a,c,e])
1. Public sector, HIV/high MDR-TB risk only	0.2% [−1.4, 1.7] (0.3 per 100,000)	0.9% [−1.6, 3.5] (0.2 per 100,000)	2.4% [−5.2, 9.1] (0.1 per 100,000)	2.5 [1.4, 4.4]	300 [250, 420]	60 [50, 90]
2. Broad public sector	2.1% [0.5, 3.9] (4.0 per 100,000)	3.3% [1.0, 6.1] (0.9 per 100,000)	3.6% [−2.9, 9.3] (0.2 per 100,000)	4.7 [3.0, 6.6]	3,200 [2,400, 4,000]	700 [490, 840]
3. Qualified private sector	6.0% [3.9, 7.9] (11.5 per 100,000)	8.1% [5.6, 10.5] (2.1 per 100,000)	6.8% [1.0, 12.4] (0.3 per 100,000)	5.9 [3.9, 7.7]	3,500 [2,600, 3,900]	700 [530, 810]
4. Public plus qualified private sectors	7.2% [4.9, 9.5] (13.9 per 100,000)	9.6% [7.0, 12.3] (2.5 per 100,000)	7.5% [5.7, 10.6] (0.3 per 100,000)	7.2 [5.0, 9.1]	5,100 [3,700, 5,800]	1,100 [770, 1,220]
5. Broad cross-sector access	14.1% [10.6, 16.9] (27.2 per 100,000)	18.1% [15.0, 20.8] (4.7 per 100,000)	12.1% [7.9, 18.0] (0.5 per 100,000)	7.7 [5.2, 9.2]	10,800 [8,000, 12,100]	2,200 [1,670, 2,510]
6. Increased referral	6.3% [4.0, 9.0] (12.2 per 100,000)	7.6% [5.0, 10.1] (2.0 per 100,000)	3.2% [−0.6, 7.5] (0.1 per 100,000)	—	—	—

Effect of 100 Xpert Systems

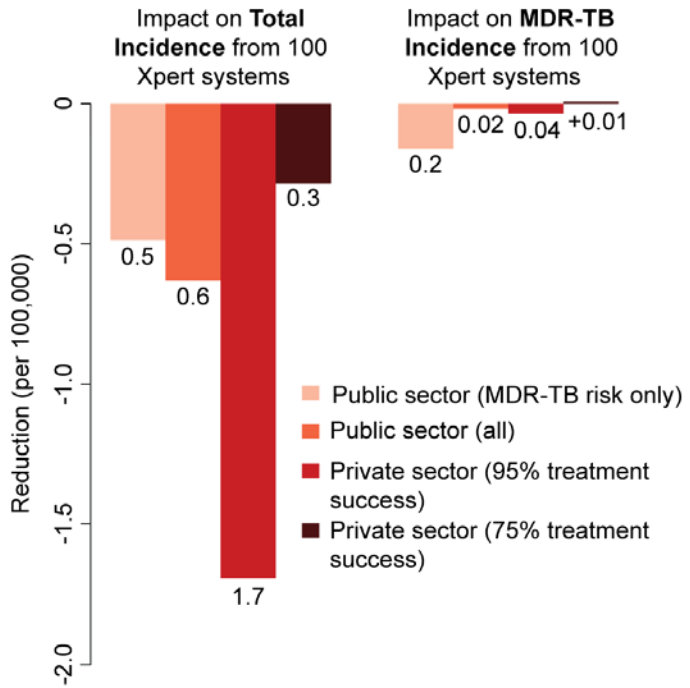
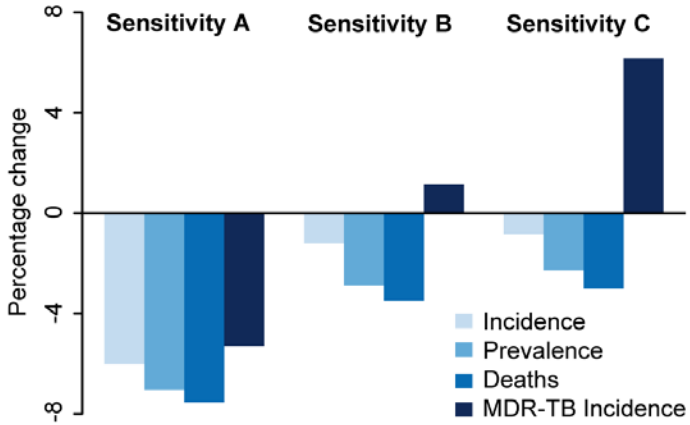


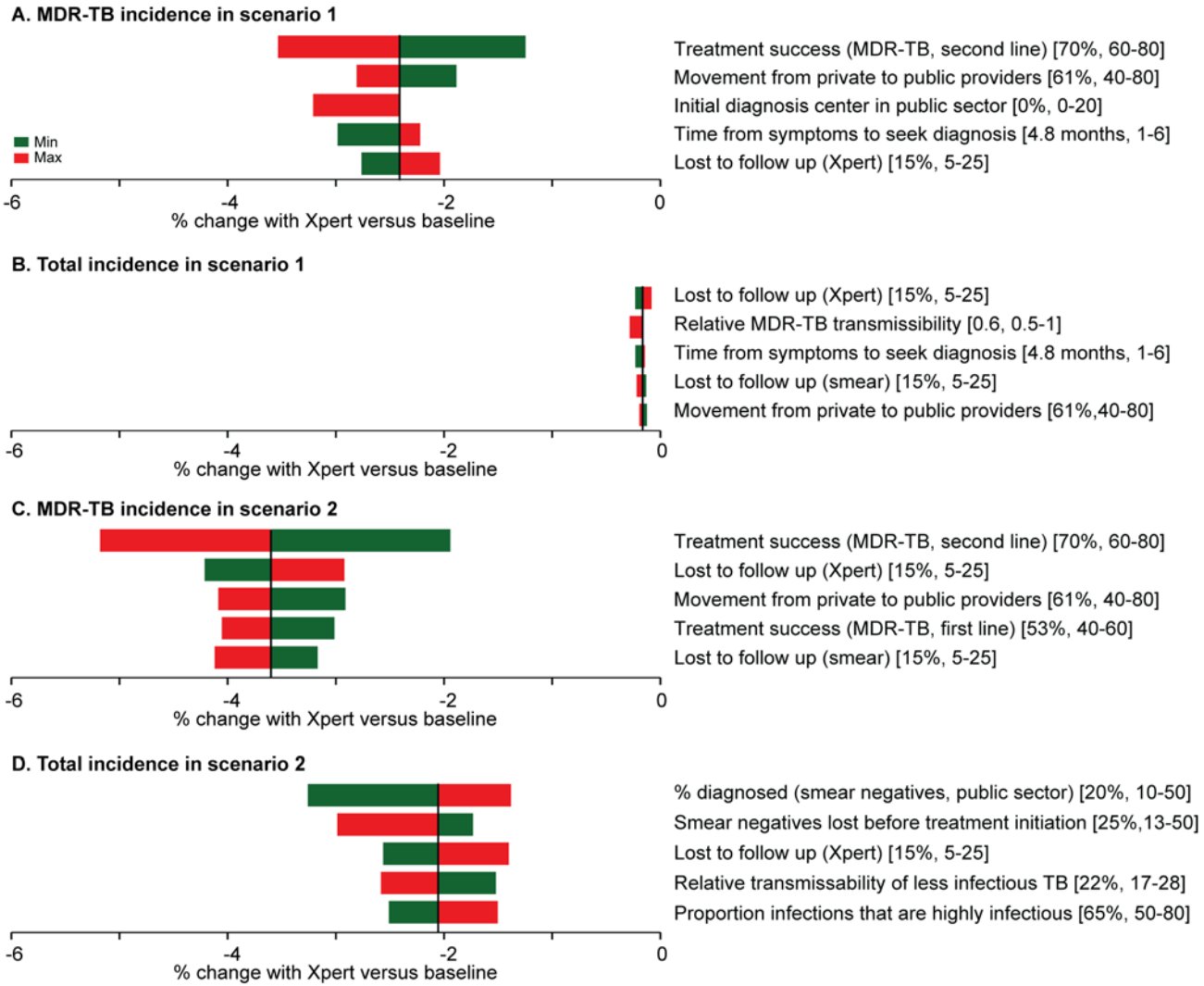
Figure 3. Impact of 100 Xpert systems rolled out in different sectors after 5 y. Reduction in total annual incidence and MDR-TB incidence per 100,000 individuals from a rollout of 100 Xpert machines. The scenarios are as described in the Methods. Rollout of 100 Xpert machines in the private sector has substantially greater impact than a similar rollout in the public sector, but only if high treatment success can be assured. If treatment is poor, use of Xpert machines in the private sector has no epidemiological benefit.

Effect of Treatment Success

Treatment parameter	A	B	C
% developing MDR-TB while on treatment (private sector)	0.8%	1.6%	4.0%
% developing MDR-TB while on treatment (public sector)	0.8%	0.8%	0.8%
% treatment of non-MDR-TB resulting in cure (private sector)	95%	75%	75%
% treatment of non-MDR-TB resulting in cure (public sector)	95%	95%	95%
% treatment of MDR-TB with non-first line regimen resulting in cure (private sector)	70%	60%	53%
% treatment of MDR-TB with non-first line regimen resulting in cure (public sector)	70%	70%	70%



Sensitivity Analysis



Just Increasing Referrals by 50%

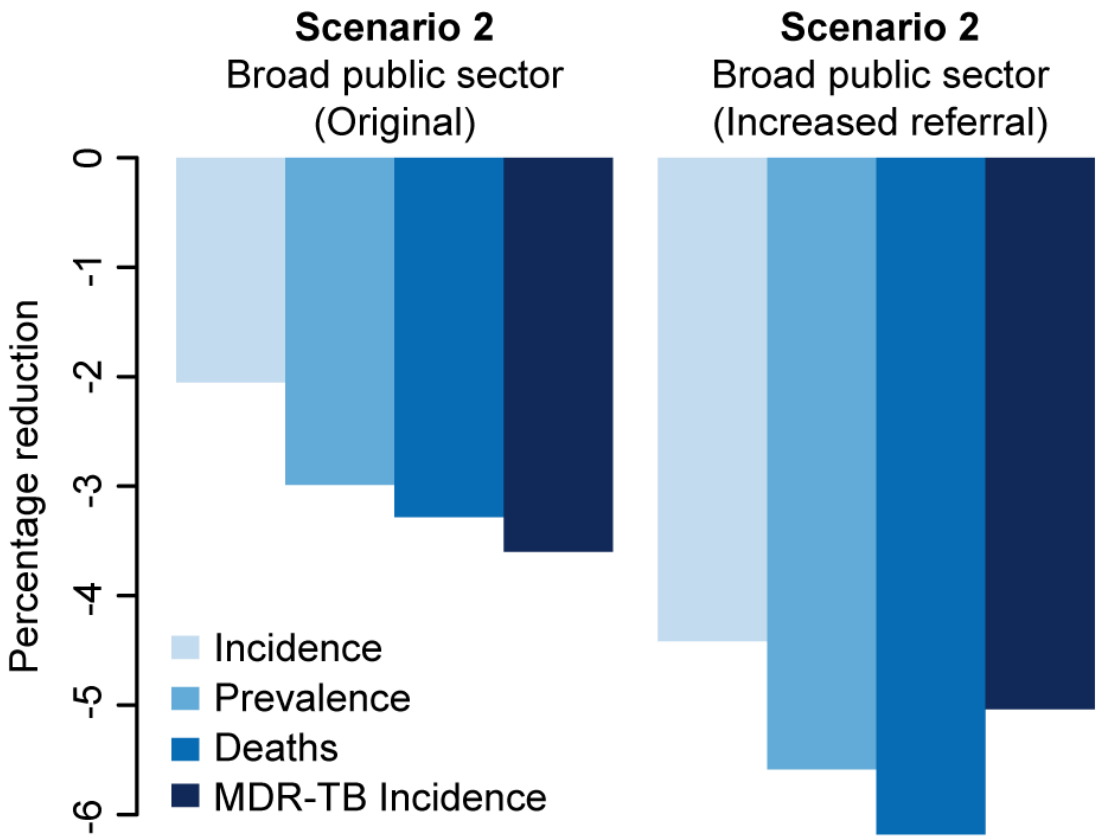


Figure 6. Impact of behavioral changes. We explored the impact

Conclusions

- **The impact of TB diagnostics depends on patient behavior and health systems.**
  - We need better data on interactions in different systems to make informed decisions about “which diagnostic test, when, and where”.
- **Xpert and other diagnostics can make a difference, but…**
  - They must be situated at the right place in the system.
  - They must be linked to appropriate treatment.
  - They must be scaled up for more than just DST and HIV.
- **Models can help us to understand complex interactions.**
  - Assumptions and structure can be challenged in transparent fashion.
  - Decisions can benefit from modeling input, but models can’t make the decision.
  - *How to incorporate models into the decision-making process?*