Implementation Science Case Study:

Tuberculosis Guideline Observation and Adherence in Low-income countries (TB GOAL study)

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Advanced TB Diagnostics Research Course

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Outline

- Background
- Overview of study setting
- Progress to date: Aims 1-3
- Lessons Learned

Implementation defined

–noun

1. any article used in some activity, esp. an instrument, tool, or utensil: agricultural implements.

2. an article of equipment, as household furniture, clothing, ecclesiastical vestments, or the like.

3. a means; agent: human beings as an implement of divine plan.

–verb (used with object)

4.to fulfill; perform; carry out: Once in office, he failed to implement his campaign promises.

5.to put into effect according to or by ***means of a definite plan or procedure.***

6.to fill out or supplement.

7.to provide with implements.

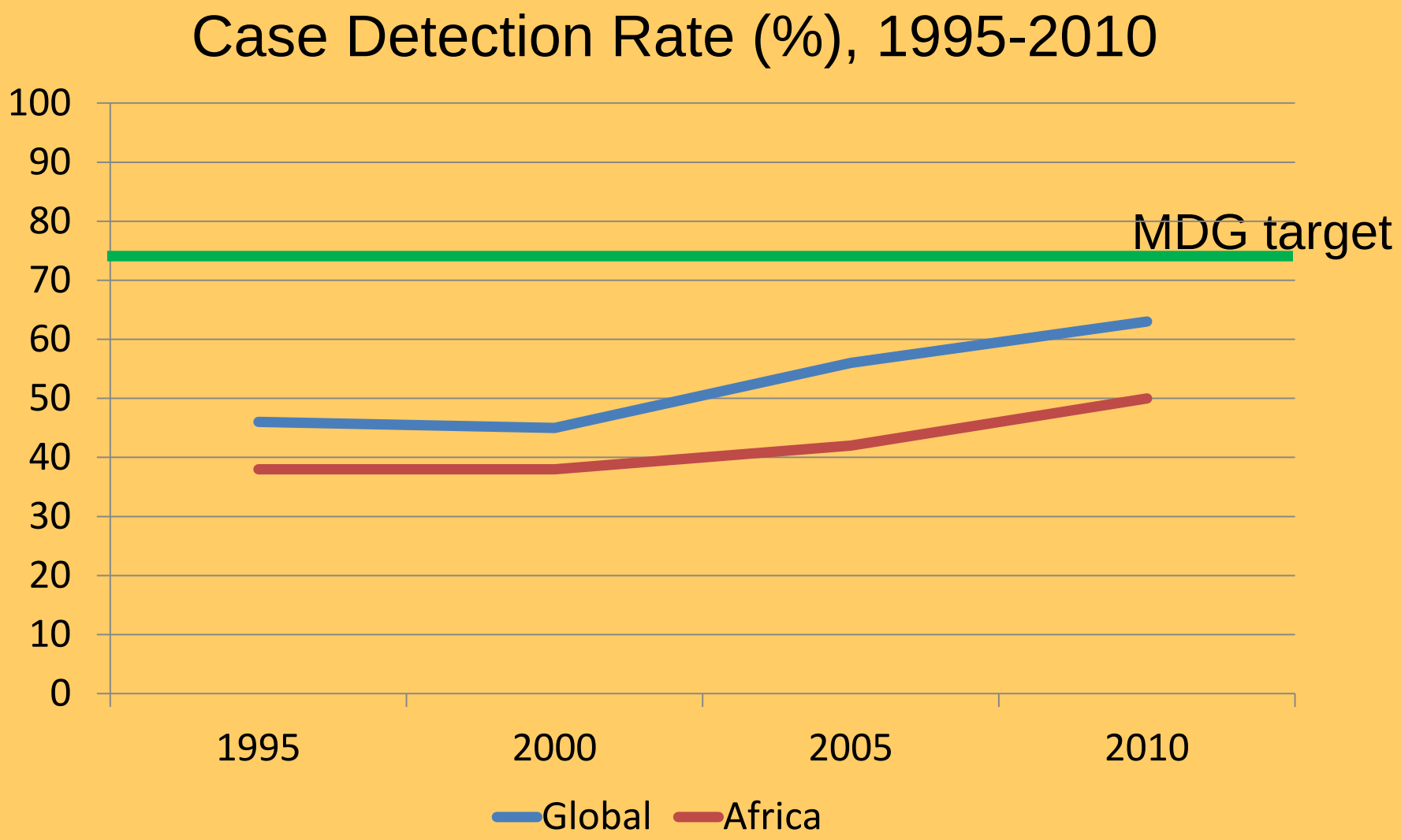
Implementation Science

- The **study of methods or strategies** to promote uptake of research findings into routine clinical practice

- NOT simply the validation of evidence-based practices or interventions in “real world” settings

- Contributes to an understanding of factors that help ensure similar outcomes in studies and in the “real world”

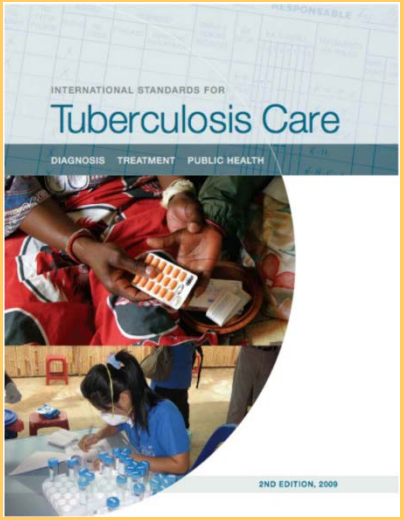
Estimated vs. Notified Cases



Reasons for low case detection rates

- Cases are diagnosed but not reported
- Cases do not seek care
- Cases seek care but are not diagnosed
  - Insensitive diagnostic tests
  - Poor TB evaluation practices

TB evaluation guidelines



International Standards for Tuberculosis Care
Standard 1. All persons with otherwise unexplained productive cough lasting 2-3 weeks or more should be evaluated for tuberculosis.
Standard 2. All patients who are capable of producing sputum suspected of having pulmonary tuberculosis should have at least two sputum specimens submitted for microscopic examination in a quality-assured laboratory.
Standard 8. All patients diagnosed with TB should receive an internationally accepted first-line treatment regimen.

Hopewell P. Lancet. 2006

- Initial aim: To describe adherence to ISTC at government health centers in Uganda

- Additional aims
  - To determine barriers to ISTC adherence
  - To develop and test a theory-driven intervention to increase ISTC adherence and TB case detection

- Overall hypothesis
  - Improving ISTC adherence will increase TB case detection at peripheral health centers in Uganda

Outline

- Background and specific aims
- Overview of study setting
- Methods/Results to date: Aims 1-3
- Conclusions and future directions

Study Setting:
Uganda TB Surveillance Project

- Network of 6 government health centers
- Partners
  - Uganda Ministry of Health
  - Makerere University
- Electronic data collection (>100,000 patients/year)
- Web-interface to monitor indicators tied to ISTC

Patient Record Form

Clinic_____

Date	OPD Number	Patient's Last Name	First Name	New attendance
[ ][ ]/[ ][ ]/[ ][ ]	[ ][ ][ ][ ]			☐Yes ☐ No
Parish	**Village**	**Age:**	**Sex**	**Weight**
		[ ][ ] Yrs [ ][ ] Mos	☐Male ☐Female	[ ][ ].[ ] kg

History & Exam findings

Fever or history of fever? ☐ Yes ☐ No | History of cough ≥ 2 weeks? ☐ Yes ☐ No **(BOTH these questions must be completed)**

☐BS for Malaria ☐Pos ☐ Neg

Parasite density: _____(If positive)

☐RDT for Malaria ☐Pos ☐ Neg

Malaria Lab number [ ][ ][ ][ ]

☐HIV test ☐CTBR ☐ CTR

HIV Lab number [ ][ ][ ][ ]

☐TB exam

1st smear ☐Pos ☐Neg (today's date)
2nd smear ☐Pos ☐Neg Date: __/__/__
3rd smear ☐Pos ☐Neg Date: __/__/__

TB Lab number [ ][ ][ ]

☐ Stool ordered - Results:

☐ Urinalysis ordered – Results:

☐Hb [ ][.][ ] g/dl

☐VDRL test ☐Pos

☐Other (test/result)

Diagnosis (Check all that apply)

Reportable diseases			
☐ Acute flaccid paralysis	☐ Malaria (not during pregnancy)	☐ Animal and Snake bites	☐ Haemorrhage during pregnancy
☐ Cholera	☐ Malaria (during pregnancy)	☐ Asthma	☐ High BP during pregnancy
☐ Dysentery	☐ Meningitis (Non meningococcal)	☐ Cardiovascular- High BP	☐ Obstructed labour
☐ Guinea worm	☐ Onchocerciasis	☐ Cardiovascular- Other	☐ Pneumonia
☐ Hemorrhagic fever	☐ Pelvic Inflammatory Disease	☐ Childhood mental disorder	☐ Severe anaemia
☐ Measles	☐ Pneumonia	☐ Diabetes Mellitus	☐ Dog bite
☐ Meningitis (Meningococcal)	☐ Schistosomiasis	☐ Epilepsy	☐ Eye injury
☐ Plague	☐ Sleeping Sickness	☐ GI disorders (non infective)	☐ Burns
☐ Rabies	☐ STI	☐ Injuries- Road traffic accidents	☐ Snake bite
☐ Tetanus (0-28 days age)	☐ Tetanus (over 28 days age)	☐ Injuries- Trauma of other origin	☐ Other
☐ Yellow Fever	☐ Typhoid Fever	☐ Malnutrition- low weight for age	☐ Burns
Infectious Disease	☐ Urinary Tract Infections (UTI)	☐ Malnutrition- severe	
☐ AIDS/HIV	**Tuberculosis**	☐ Mental Illness- Anxiety	
☐ Cough or Cold (no pneumonia)	☐ New case – No prior TB treatment	☐ Mental Illness- Depression	
☐ Diarrhea- Acute	☐ New case – Previous TB treatment	☐ Mental Illness- Mania	
☐ Diarrhea- Persistent	☐ Known TB Case – Med Refill	☐ Mental Illness- Schizophrenia	
☐ Intestinal worms	**Non Infectious Diseases**	☐ Mental Illness- Other	
☐ Leprosy	☐ Alcohol and drug abuse	**Maternal and Perinatal Diseases**	
	☐ Anaemia	☐ Abortions	

Treatment (Check all that apply)

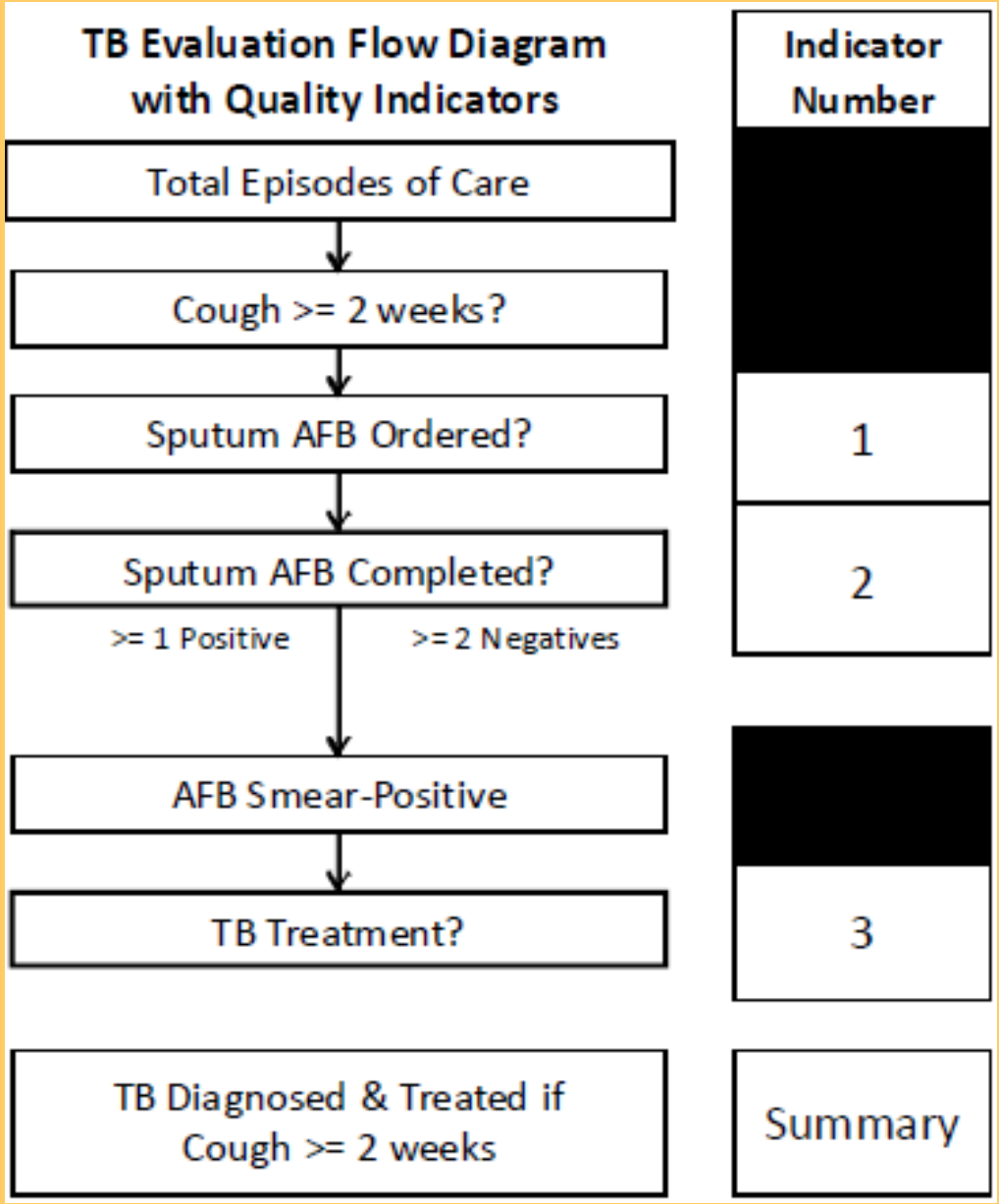
Drug	Dose	Drug	Dose
Antimalarial		Other Drugs	
☐ Coartem		☐ Aspirin	
☐ Quinine		☐ Cough linctus	
☐ Chloroquine		☐ Diazepam	
☐ Amodiaquine		☐ Dexamethasone	
☐ SP		☐ Diclofenac	
☐ Artesunate		☐ Folic Acid	
☐ Daxocetacrin		☐ Gentian violet	
Antimicrobials		☐ Hydrocortisone	
☐ Albendazole		☐ Ibuprofen	
☐ Amoxicillin		☐ Magnesium	
☐ Chloramphenicol		☐ Multivitamin	
☐ Ciprofloxacin		☐ Nystatin	
☐ Cloxacillin		☐ Paracetamol	
☐ Cotrimoxazole		☐ Phenytoin	
☐ Doxycycline		☐ Pirition	
☐ Erythromycin		☐ Salbutamol	
☐ Gentamicin		☐ Vit. B group	
☐ Mebendazole		Other	
☐ Metronidazole		Other	
☐ PPF		Other	
☐ Tetracycline		Other	
☐ X-pen		Other	

Referrals and additional notes

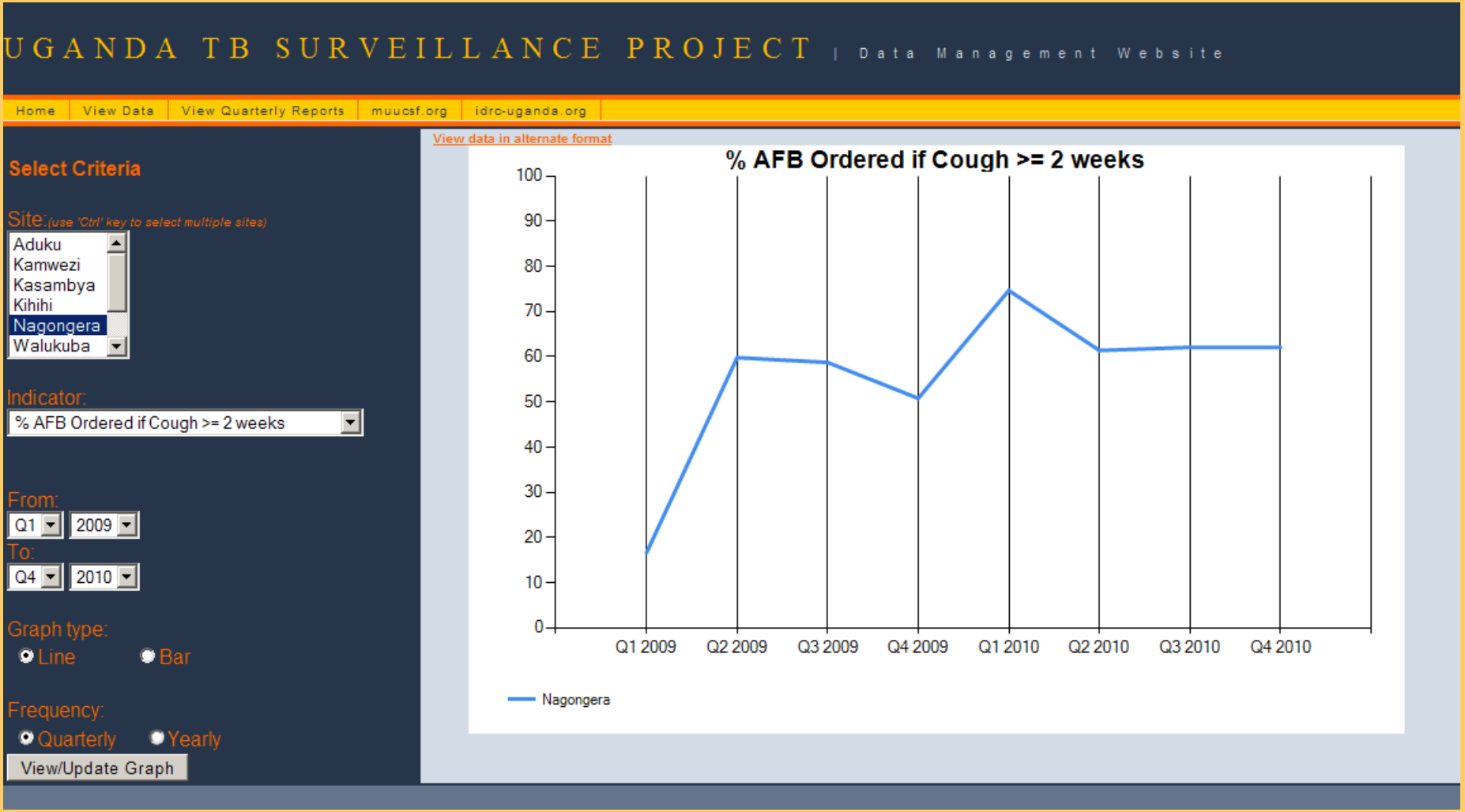
☐Admitted to ward	Notes	TB Drug Regimen (Check if prescribed)
☐Referred to HIV care		☐ **Initial Phase**
☐Referred for TB care		☐2HRZE ☐2HRZES ☐2RHZ
☐Referred for other services		☐ **Continuation Phase**
		☐4HR ☐6HE ☐4RH

Full Name _____ Signature _____

ISTC Quality Indicators



Data website: http://www.mu-ucsf.org/tb



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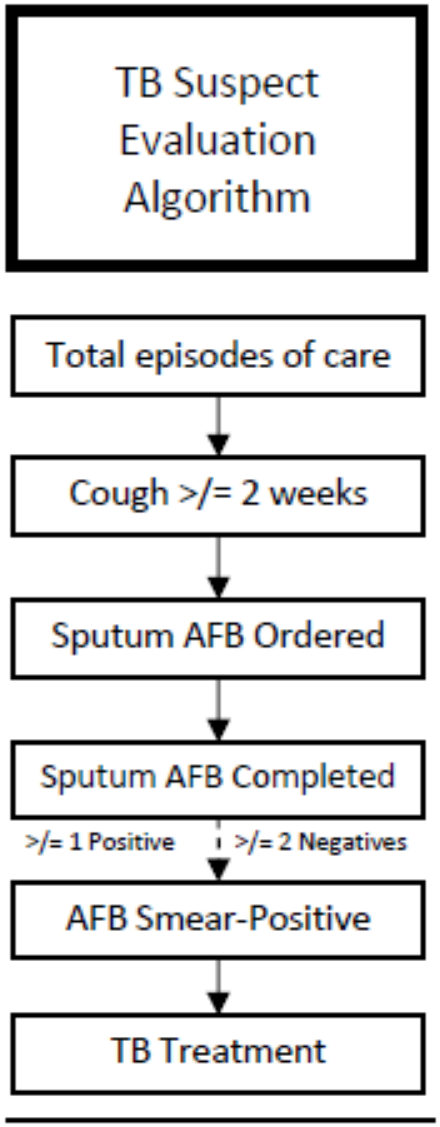
Aim 1: “Define quality gap”

- Prospective study Jan-Dec 2009
- Descriptive analysis of ISTC quality indicators
  - Point estimates (95% CI), by quarter
  - Change over time
- Study population

N (range)	62,909
Female, % (95% CI)	70 (69-71)
Age, median (IQR)	29 (21-40)

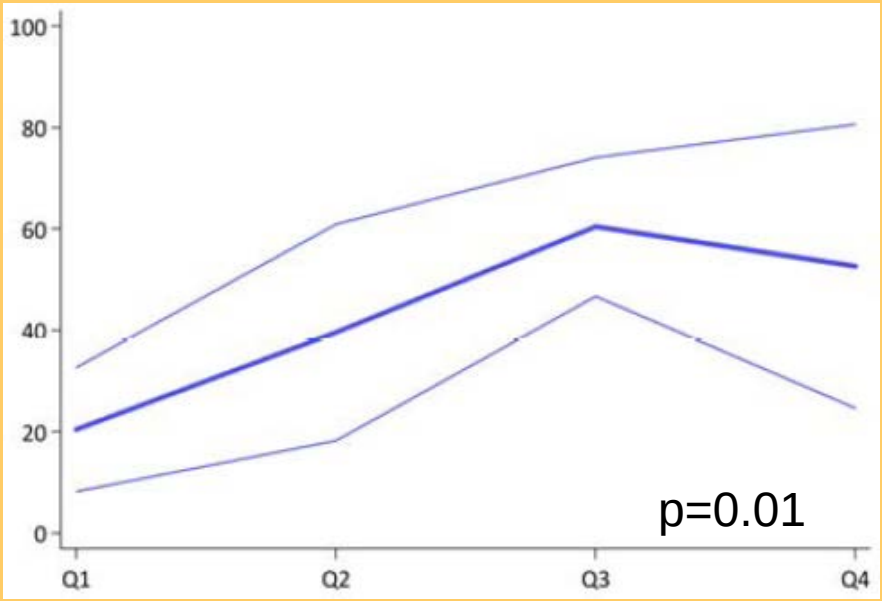
Davis et al. AJRCCM 2011



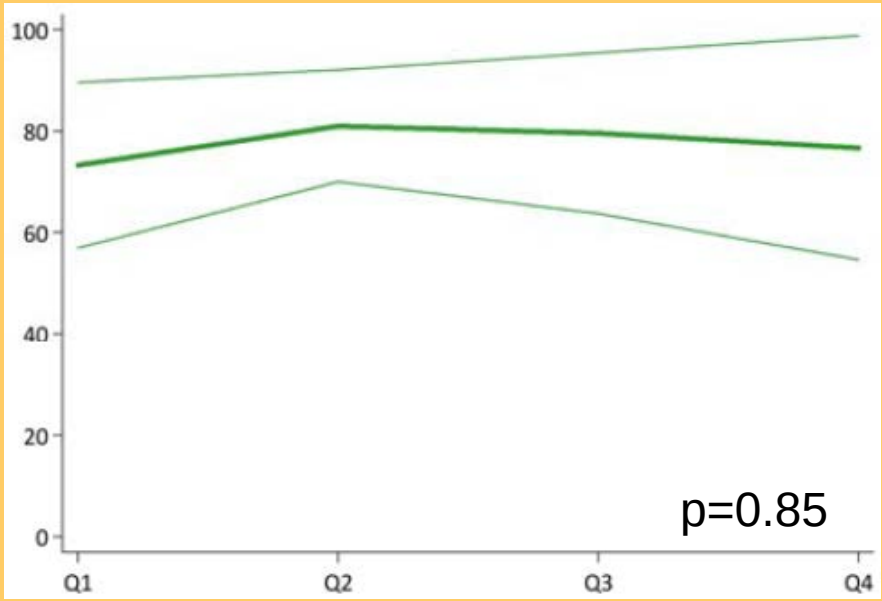
Indicator	Proportions*, by quarter
	Q1
	14,852
	365 2.5%
1	75 21%
2	55 73%
	7 13%
3	5 71%
Cumulative Probability of Diagnosing and Treating Smear-Positive TB	11%

*Proportions account for clustering by site, and therefore differ from the proportions that would be calculated directly from the numbers displayed in the table.

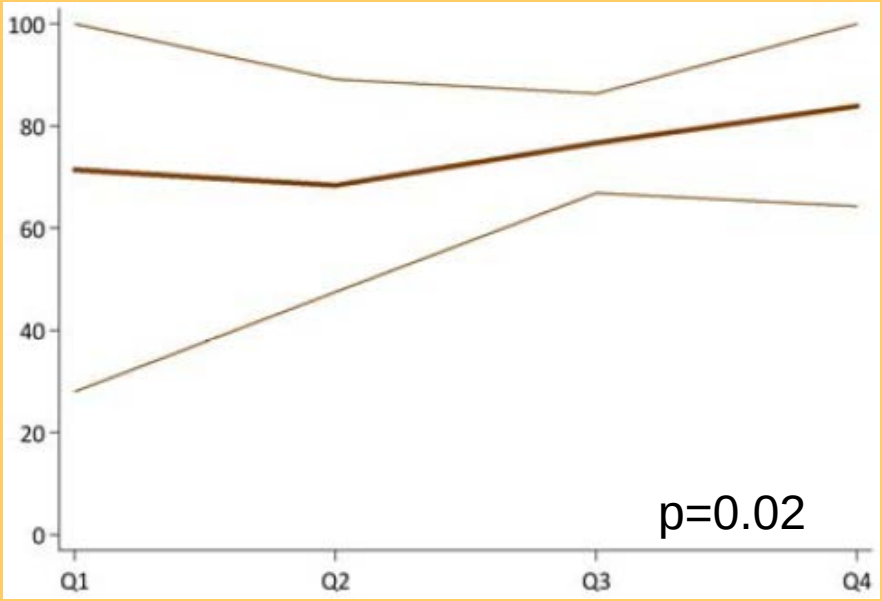
Indicator 1: Referred for TB exams



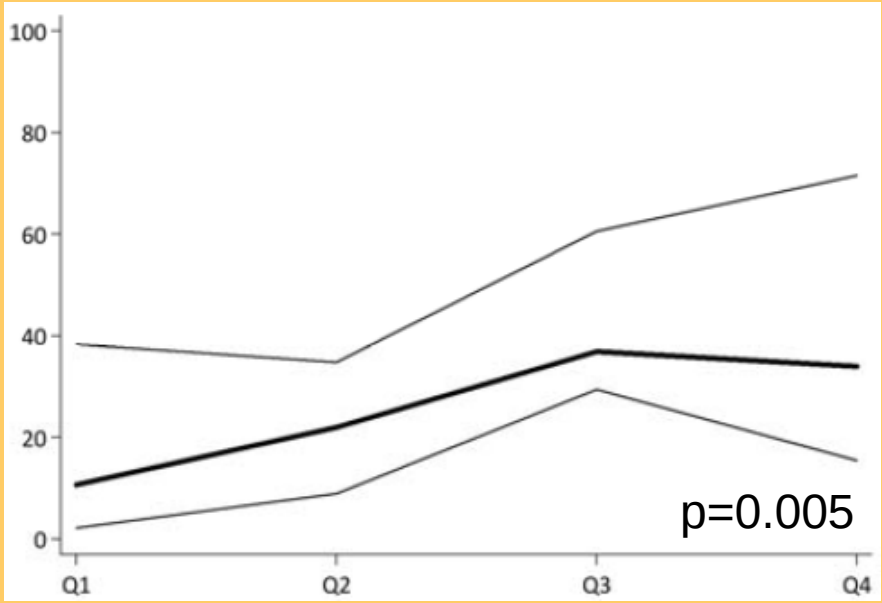
Indicator 2: Completed TB exams



Indicator 3: Treated if AFB-positive

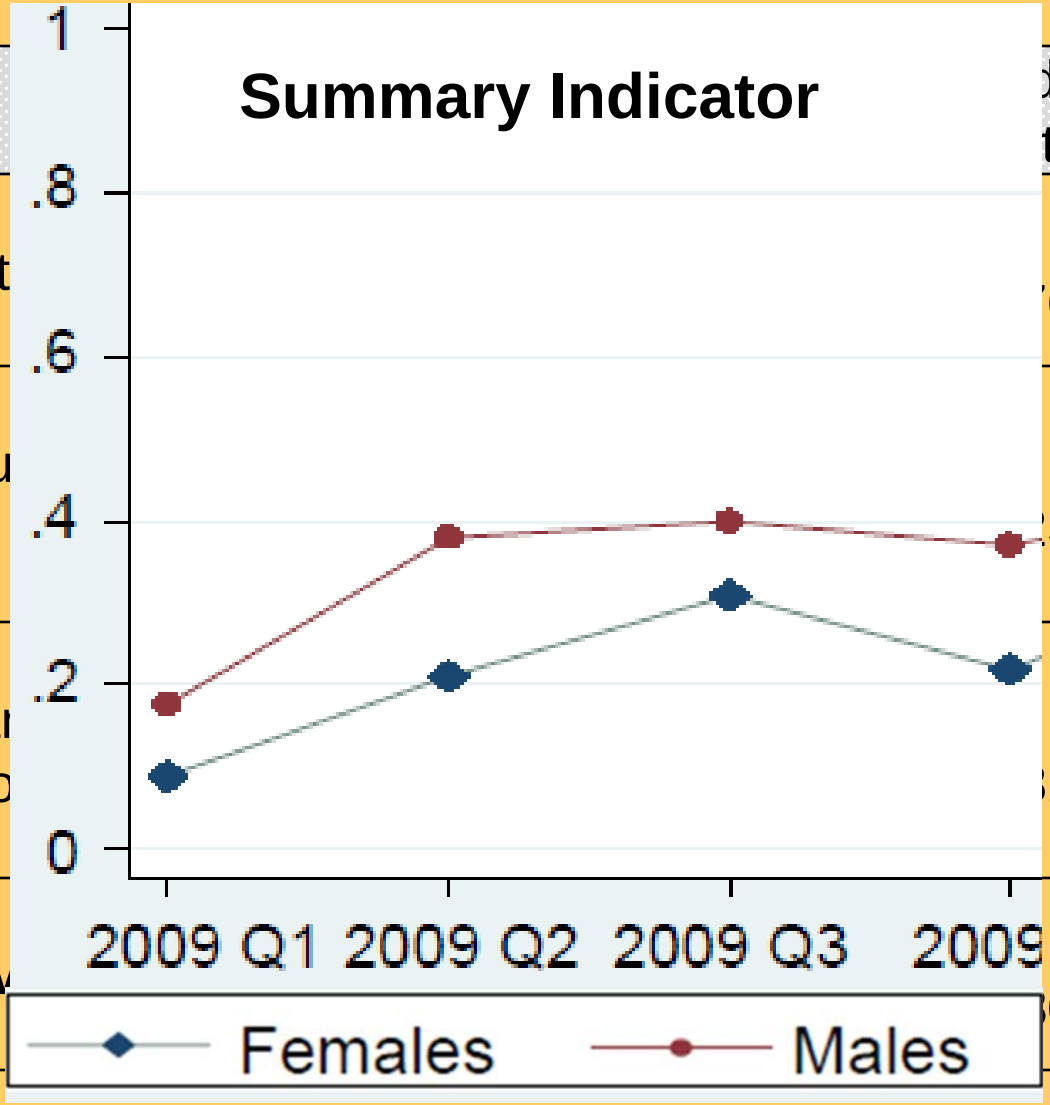


Summary Indicator



Gender disparities

ISTC	d* tio	p-value
Referred for sput	0)	<0.001
Completed sputu if referred	3)	0.66
Initiated TB treatr if sputum AFB po	2)	0.54
Summary TB Ev	**6)**	**0.001**



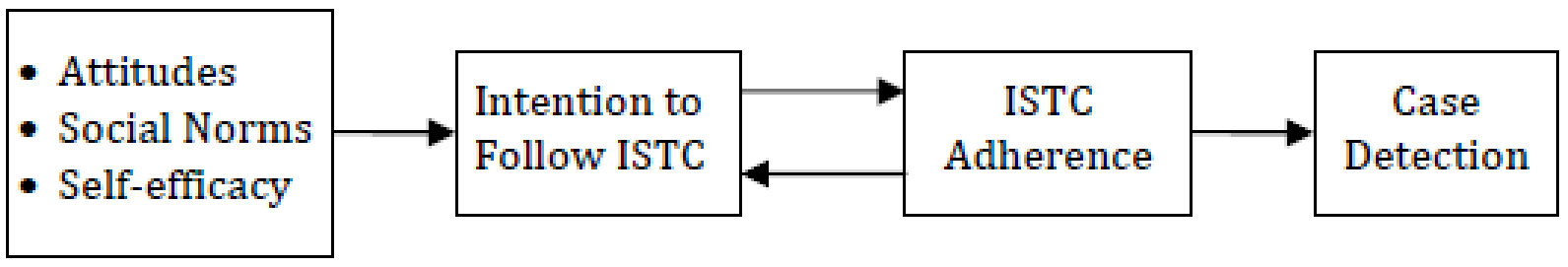
* Adjusted for site and date of clinical encounter. Reference group is male gender.

Aim 1: Summary

- Poor adherence to ISTC at baseline
- Modest improvements → 4-fold increase in TB case detection (7 to 25 cases/quarter)
- High yield of smear examination (13-21%)
- Strong need for strategies to enhance ISTC implementation

Aim 2: “Understand quality gap”

- Conceptual Framework: Theory of Planned Behavior

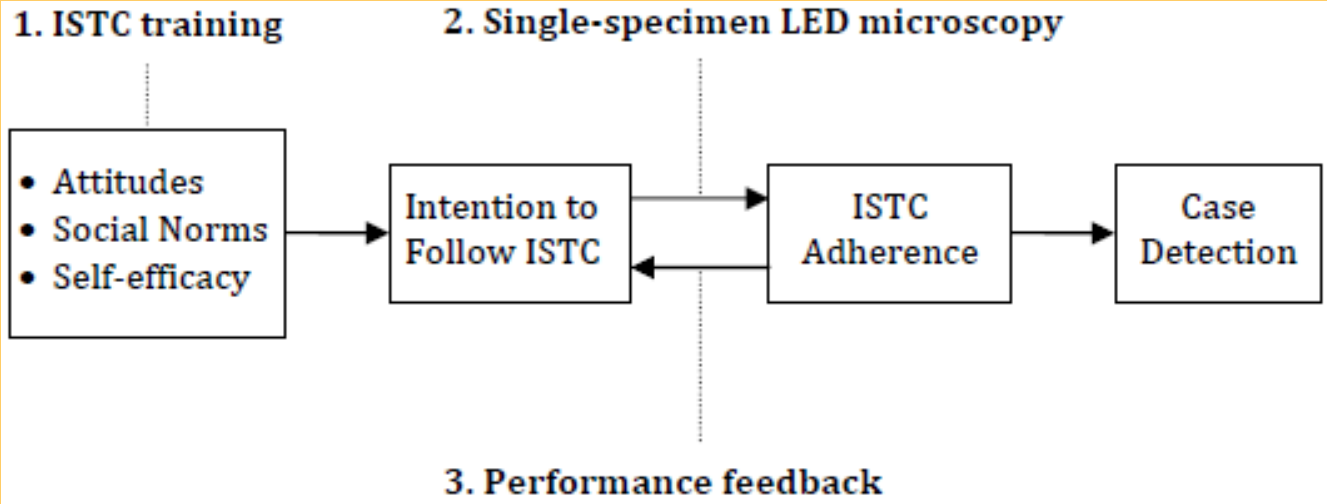


- Data collection
  - Key informant interviews
  - Semi-structured surveys
  - Field Observation
- Analysis
  - Transcribe interviews, surveys, field notes
  - Apply standard coding scheme to transcripts

Aim 2: Preliminary findings

Variable	Recurring themes
Knowledge/ Attitudes	• Lack of familiarity with ISTC • Minimal opportunities for CME/training updates
Subjective Norms	• Inconsistent support/guidance from clinic supervisors and the NTP • Tendency to focus on high suspicion patients • Competing important health concerns (*e.g.*, malaria, HIV/AIDS)
Behavioral Control/ Self-efficacy	• Belief that patients will not complete diagnostic evaluation • Inability to track patients who are lost-to-follow-up • Belief that successful TB screening reduces risks for rest of community
Ecologic/ Structural Factors	• Stock-outs of reagents, supplies, medications • Low motivation – low salaries, delays in payments • Substandard workflow and recordkeeping • Lack of feedback to guide improvement

Aim 3: “Improve quality gap”

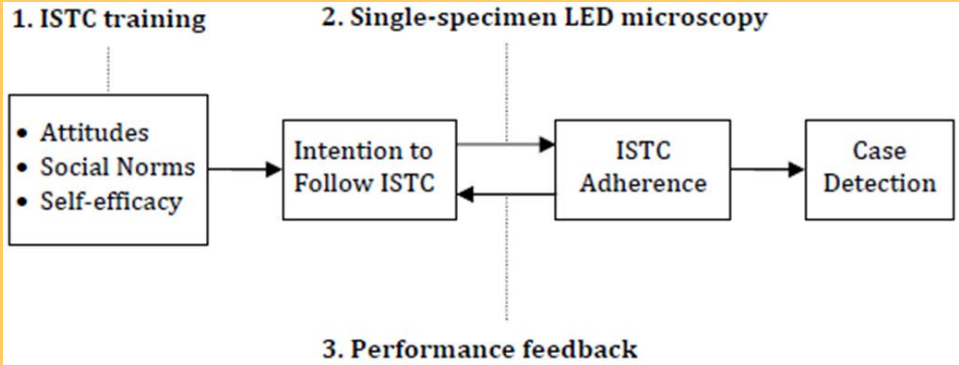


- ISTC training
  - Interactive, case-based training modules
- Single-specimen LED microscopy*
  - Facilitate same-day TB evaluation and treatment
- Performance feedback
  - Facilitate continuous quality improvement

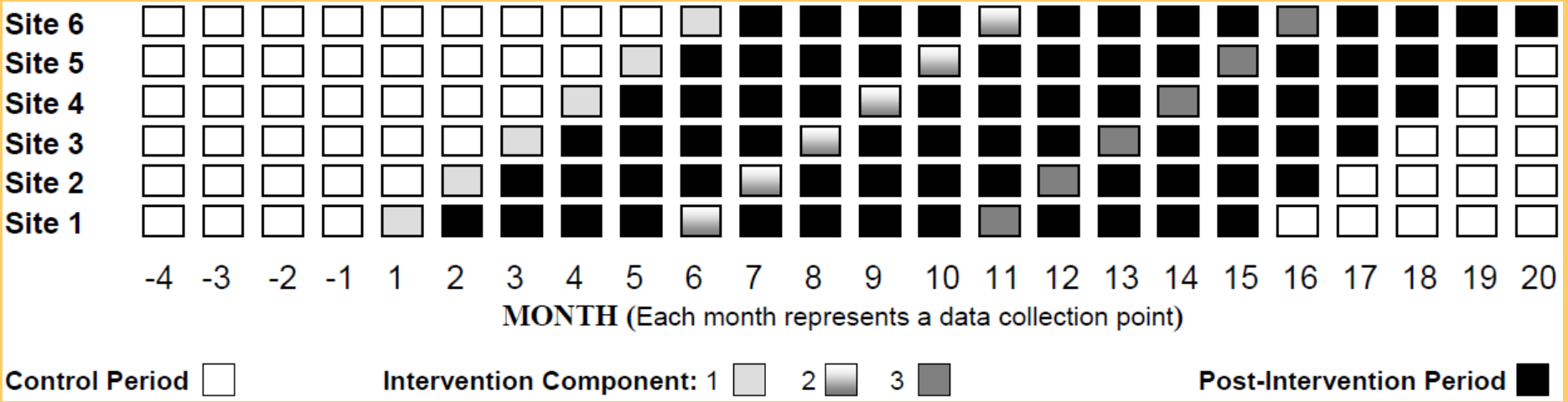
Cattamanchi et al. AJRCCM. 2011.

Study Design

- Pilot study – quantify impact of each component
  - Interrupted time series design
  - Primary Outcome: TB case detection
  - Secondary Outcomes
    - ISTC quality indicators
    - Behavioral model inputs
  - Predictors
    - Intervention component
    - Time trend
    - Patient- and site-level factors



Interrupted Time Series Design



KEY DESIGN FEATURES FOR PILOT STUDY

- Intervention components evaluated individually
- Sequential introduction of intervention at study sites (order selected randomly)
- Outcomes measured at multiple time points
- Utilize statistical methods (GEE, mixed models) to account for clustered data
- All sites receive intervention by end of the study

KEY LIMITATIONS

- Hawthorne effect
- Generalisability

Lessons Learned

- Poor quality of TB suspect evaluation is likely a major contributor to low case detection rates

- Methods to improve the quality of TB suspect evaluation are likely to enhance the impact of better diagnostics

- Implementation science
  - External assessment often different from reality on the ground
  - Theoretical frameworks can help identify secondary outcomes that help explain intervention efficacy or lack of efficacy
  - Quasi-experimental designs can improve upon the standard before-and-after comparison

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Questions/Comments