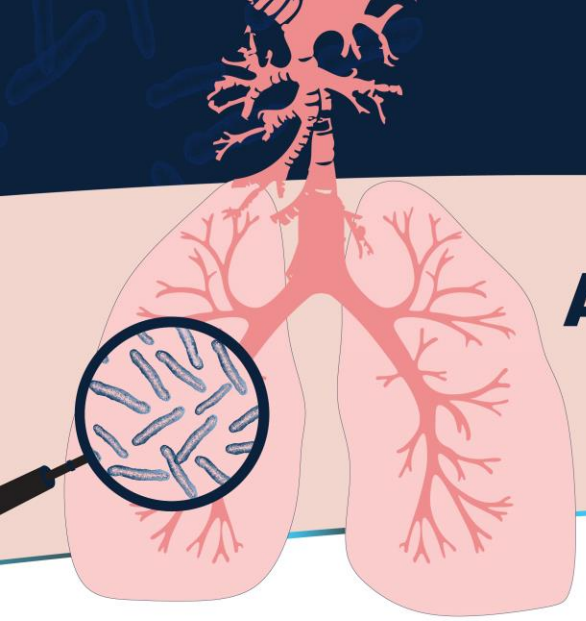

Accelerating progress to end TB

8th SA TB Conference
04 - 07June 2024
Durban ICC

Implementing in-home molecular point-of-care TB testing of household contacts using sputum and tongue swab specimens: Interim Results of the TB Home Study

Professor Andrew Medina-Marino, PhD
Desmond Tutu HIV Centre, University of Cape Town
For the TB Home Study Team

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FIND Diagnosis for all

Province of the EASTERN CAPE HEALTH

Global TB and The Cases We Miss – 2022

- In 2022, an estimated:
  - 10.6 million people fell ill with TB
  - 3.1 million people with TB were missed by the health system

- Missing people with TB:
  - Do not get diagnosed
  - Do not receive treatment
  - Are not notified by national TB programs

- Individuals with TB not detected by health systems significantly contribute to on-going transmission

Active Case Finding (ACF)

- Targeted screening/testing of those at ↑ risk for active TB disease:
  - People living with HIV
  - People treated for TB in past 2 years
  - Household contacts of TB patients

- Benefits of ACF:
  - Improves early case detection
  - Decreases # of people with TB missed by passive detection

- ACF Approaches:
  - Household contact investigations
  - Community-based screening/testing platforms

Household Contact Investigations

- ✓ Targeted screening of individuals at increased risk for TB disease
- ✓ Decreases barriers to clinic-based screening services
- X Low uptake of community-to-clinic referrals for clinic-based testing
-  Integrate diagnostic services into household contact investigations (i.e., Home-based TB testing)

In-Home TB Testing is Acceptable

Tropical Medicine and International Health doi:10.1111/tmi.13533

VOLUME 26 NO 3 PP 343–354 MARCH 2021

"I got tested at home, the help came to me": acceptability and feasibility of home-based TB testing of household contacts using portable molecular diagnostics in South Africa

Andrew Medina-Marino[1,2,3], Lindsey de Vos[1], Dana Bezuidenhout[1], Claudia M. Denkinger[4,5], Samuel G. Schumacher[4], Sanghyuk S. Shin[6], Wendy Stevens[7], Grant Theron[8], Martie van der Walt[9] and Joseph Daniels[10]

Qualitative Paper

- Convenient
- Overcame apathy to testing
- Mitigated barriers to clinic-based testing
- Alleviated health insecurities

JOURNAL ARTICLE ACCEPTED MANUSCRIPT

In-home TB Testing Using GeneXpert Edge is Acceptable, Feasible and Improves the Proportion of Symptomatic Household Contacts Tested for TB: A Proof-of-Concept Study

Andrew Medina-Marino ✉, Dana Bezuidenhout, Charl Bezuidenhout, Shelley N Facente, Bernard Fourie, Sanghyuk S Shin, Adam Penn-Nicholson, Grant Theron

Open Forum Infectious Diseases, ofae279, https://doi.org/10.1093/ofid/ofae279

Published: 13 May 2024 **Article history** ▾

Quantitative Paper

- Significant increase in proportion of contacts receiving test results

Study Aims

1. Describe the outcomes of TB patient's household contacts who receive a positive sputum test result following in-home TB testing

2. Evaluate the predictive value of pooled individual tongue swab specimens as a household-level triage test for TB during household contact investigations using the GeneXpert Omni and Edge platforms

Study Design

Design: Longitudinal cohort

Population: Households of TB index patients

Location: Duncan Village and Scenery Park Communities, BCM

Specimen: Tongue Swabs and Sputum

Test Devices: GeneXpert 1 and Omni

Test Cartridge: MTB/Rif Ultra

Adapted GXI Device

Omni Device

Approach, Eligibility and Specimen Collection

- **Initiation of Investigation:**
  - Household visits are scheduled after receiving consent from TB Index Patients in health facilities

- **Eligibility Criteria:**
  - Household contact of index patient
  - Age ≥18 years
  - Not currently on TB treatment;
  - Provision of individual written informed consent

- **Testing Procedures:**
  - Implemented Targeted Universal TB Testing
  - All eligible individuals asked to provide:
    - Two tongue swabs (collected 1st)
    - One sputum specimen (collected 2nd)

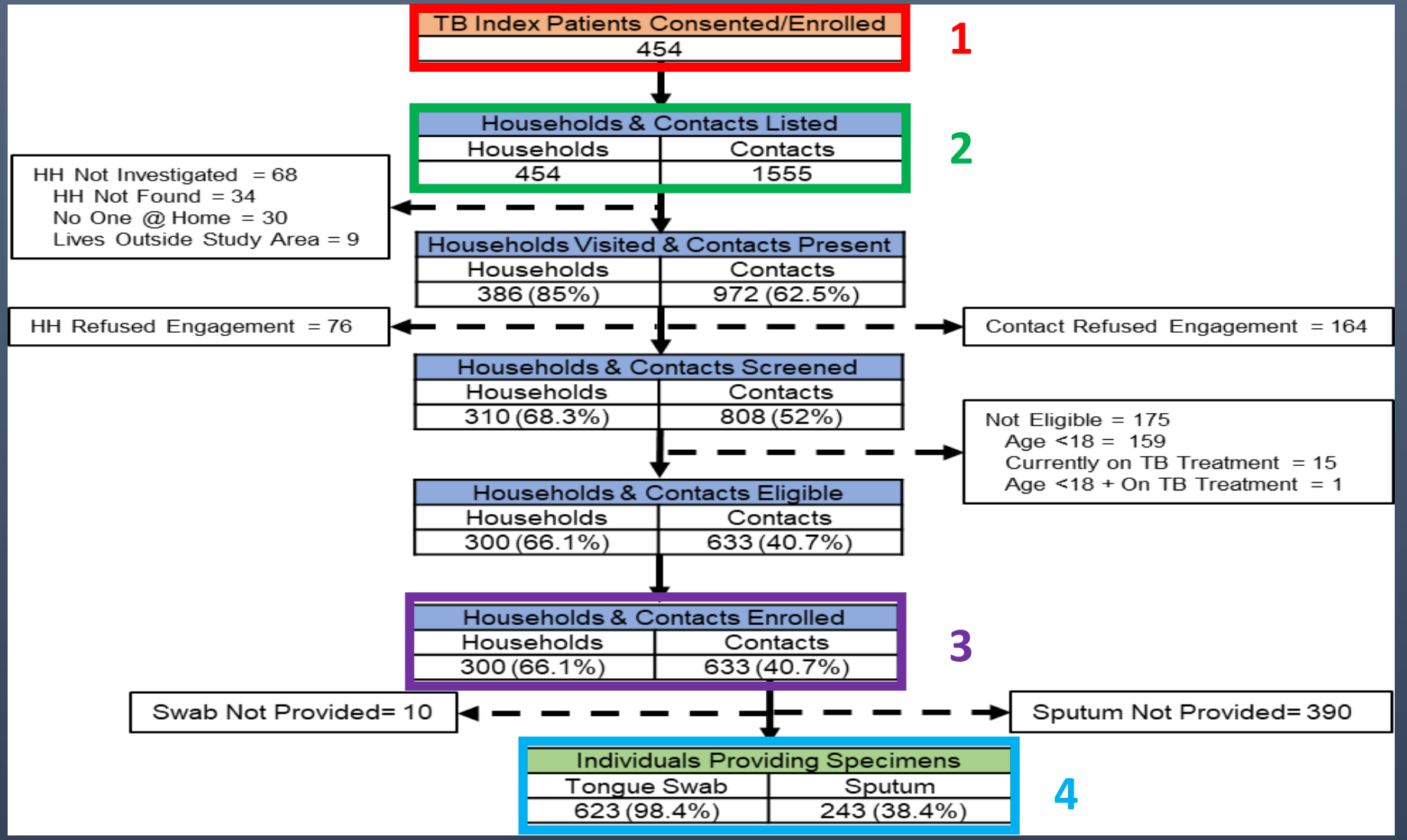
Specimen Testing

TONGUE SWABS:
Pooled into a single tube
(up to 3 swabs per tube)

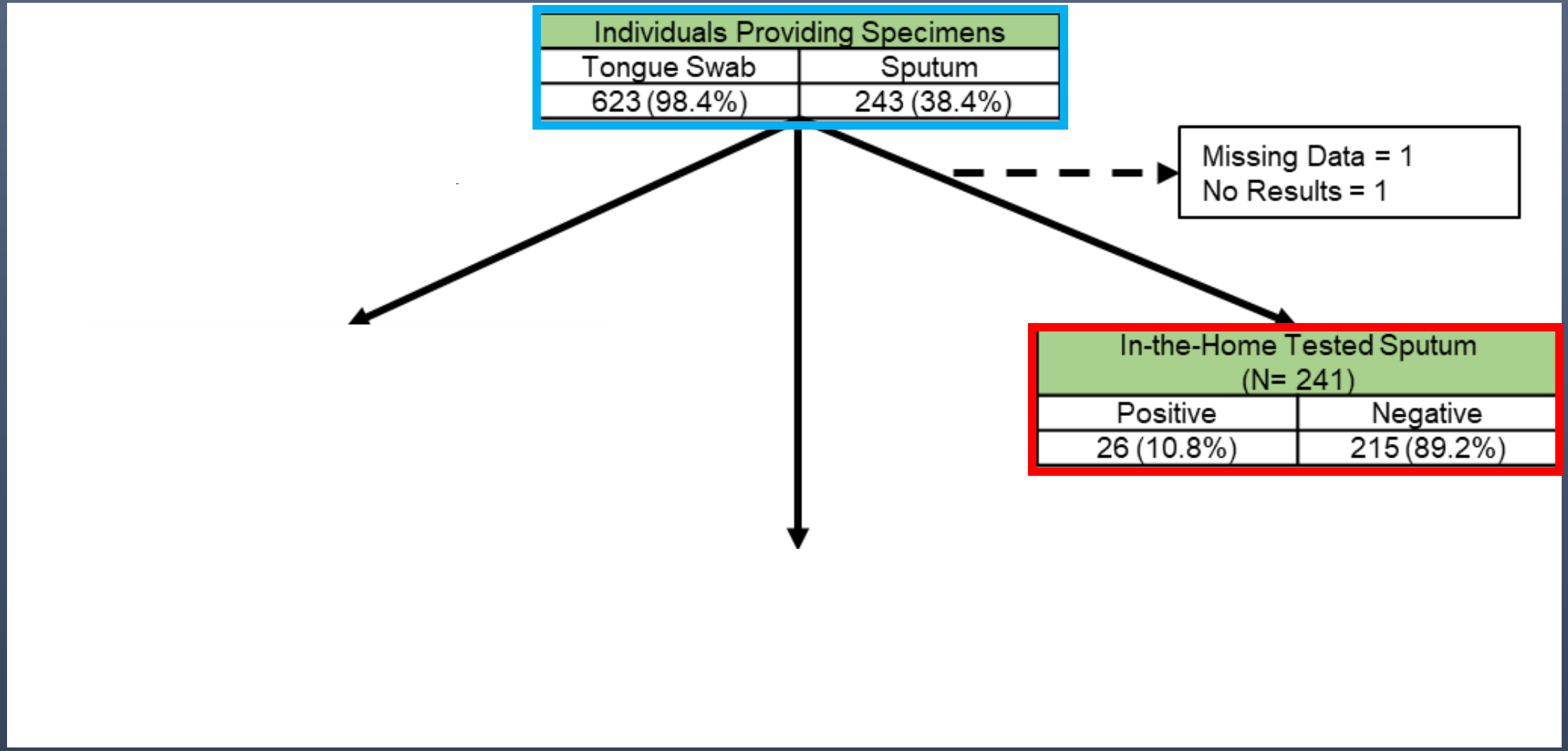
TESTING INSTRUMENTS:
GeneXpert Omni
GeneXpert Edge

SPUTUM SPECIMEN:
Individually tested and compared to pooled test

Participant Recruitment Flow Diagram



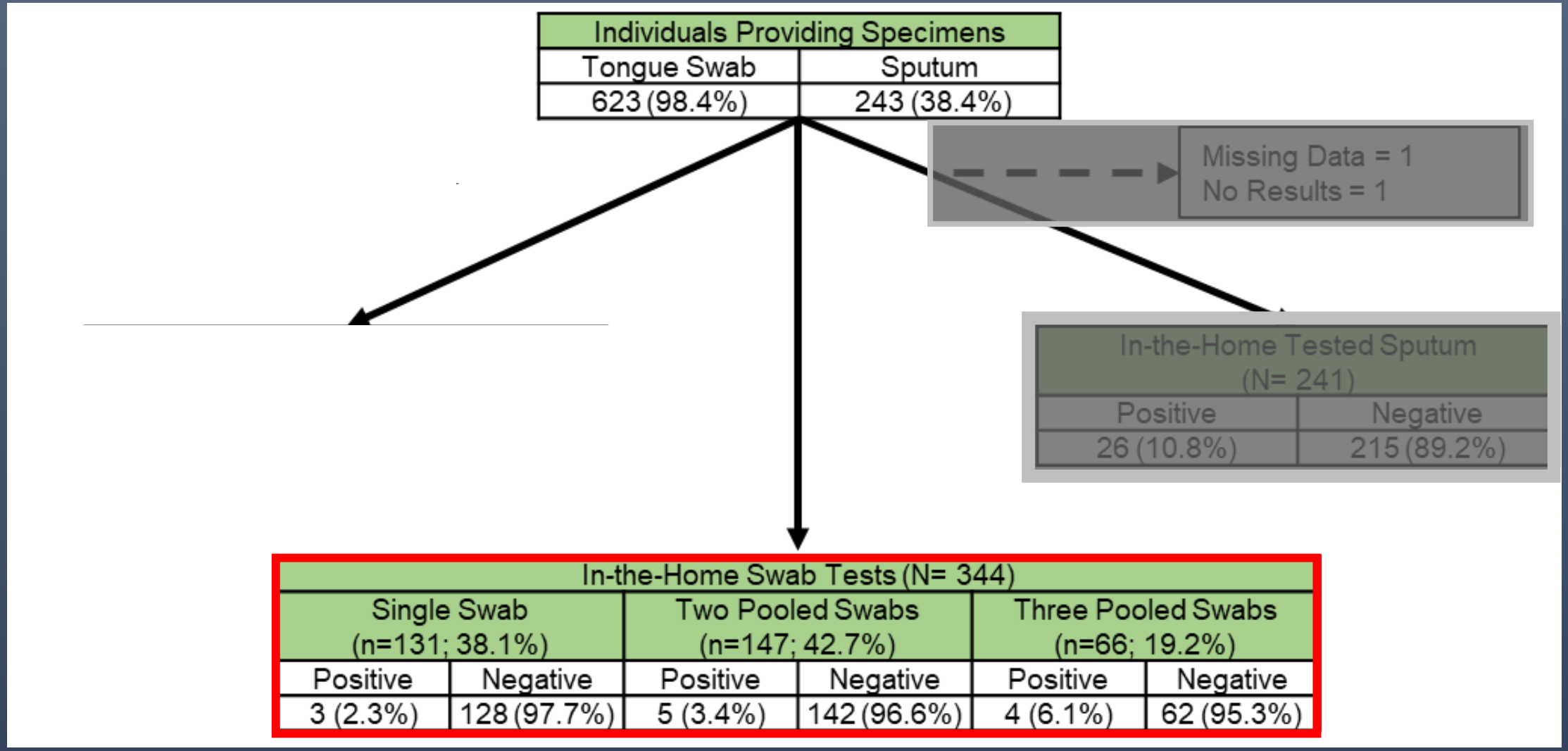
Results: Sputum Test Positivity



Outcomes: Contacts w/ Positive Sputum Result

- **Referral Uptake:**
  - **22 of 26 (84.6%) were confirmed to have presented to a clinic**
- **Time-to-Clinic Presentation (days):**
  - **Median (IQR): 1 day (1)**
  - **Mean (SD): 1.62 (2.2)**
  - **Range: 0-9 days**
- **Clinic-based Testing Conducted:**
  - **All 22 individuals provided sputum for testing**
  - **21 of 22 (95.5%) received a positive test result**
- **Initiated on Treatment:**
  - **All 21 (100%) with a positive sputum via clinic-testing initiated treatment**

Results: In-home Swab Test Positivity



Individuals Providing Specimens	
Tongue Swab	Sputum
623 (98.4%)	243 (38.4%)

Missing Data = 1
No Results = 1

In-the-Home Tested Sputum (N= 241)	
Positive	Negative
26 (10.8%)	215 (89.2%)

In-the-Home Swab Tests (N= 344)					
Single Swab (n=131; 38.1%)		Two Pooled Swabs (n=147; 42.7%)		Three Pooled Swabs (n=66; 19.2%)	
Positive	Negative	Positive	Negative	Positive	Negative
3 (2.3%)	128 (97.7%)	5 (3.4%)	142 (96.6%)	4 (6.1%)	62 (95.3%)

2x2 Tables of Paired Sputum vs. In-home Tested Swabs

Sputum vs. Single Swab

	Sputum +	Sputum -	
Swab +	3	0	3
Swab -	0	39	39
	3	39	42

Sputum vs. Two Pooled Swabs

	Sputum +	Sputum -	
Swab +	5	0	5
Swab -	7	71	78
	12	71	83

Sputum vs. Three Pooled Swabs

	Sputum +	Sputum -	
Swab +	2	0	2
Swab -	4	29	33
	6	29	35

To be included in Sputum vs. Single Swab 2x2 Table: Individual must have provided BOTH a swab and sputum

To be included in Sputum vs. Pooled Swabs 2x2 Tables: At least one individual in the pool must have provided a sputum

Diagnostic Accuracy of In-home Tested Swabs

	Sputum vs. Single Swab (n= 42 paired results)	Sputum vs. 2-Pooled Swabs (n= 83 paired results)	Sputum vs. 3-Pooled Swabs (n= 35 paired results)
Sensitivity	100% (95% CI: 29.2-100%)	41.7% (95% CI: 15.2-72.3%)	33.3% (95% CI: 4.3-77.7%)
Specificity	100% (95% CI: 91.0-100%)	100% (95% CI: 94.9-100%)	100% (95% CI: 88.1-100%)
Positive Predictive Value	100% (95% CI: 29.2-100%)	100% 95% (CI: 47.8-100%)	100% (95% CI: 15.8-100%)
Negative Predictive Value	100% (95% CI: 91.6-100%)	93.9% (95% CI: 86.1-98.1%)	93.1% (95% CI: 78.6-99.0%)

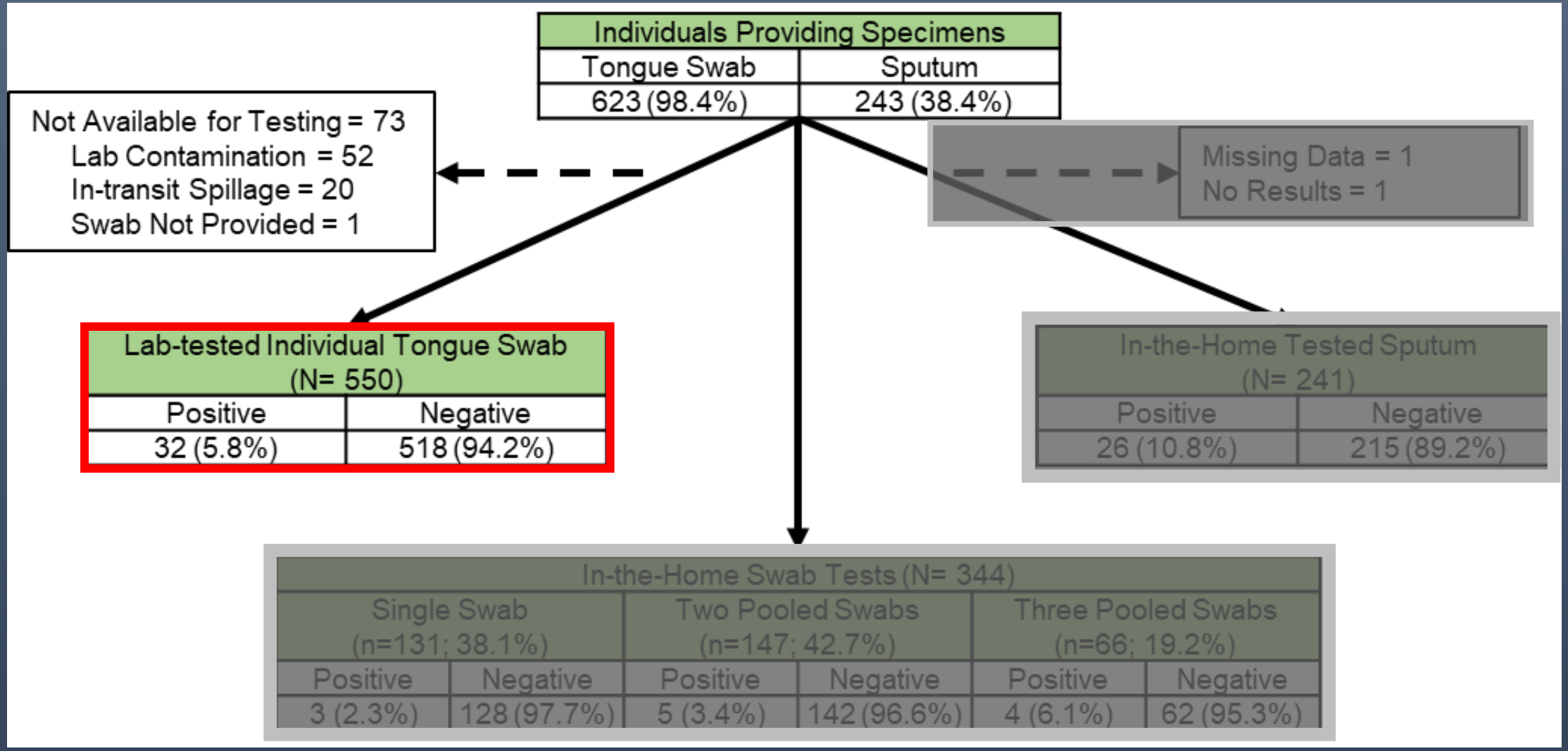
Relationship between Positive Sputum and Negative Pooled Swabs Results (False Negatives)

HOUSEHOLD #	HOUSEHOLD ID	SAMPLE ID	POOLED RESULT	SPUTUM RESULT
3	**313**	H2942117-1-OSS H2942117-2-OSS	Negative Pooled	Negative **Positive (MTB Detected Low)**
4	**315**	H4942181-1-OSS H4942181-2-OSS	Negative Pooled	**Positive (MTB Detected Low)** Could not produce Sputum
15	**529**	H2941713-1-OSS H2941713-2-OSS	Negative Pooled	**Positive (MTB Detected Low)** Negative
16	**534**	H2041809-1-OSS H2041809-3-OSS	Negative Pooled	Negative **Positive (MTB Trace Detected)**
17	**577**	H3041769-1-OSS H3041769-2-OSS	Negative Pooled	**Positive (MTB Trace Detected)** Negative
18	**617**	H3941616-2-0SS H3941616-7-OSS	Negative Pooled	**Positive (MTB Trace Detected)** Negative
21	**698**	H4941599-1-0SS H4941599-4-0SS	Negative Pooled	Negative **Positive (MTB Detected Low)**
7	**322**	H6942120-1-OSS H6942120-2-OSS H6942120-3-OSS	Negative Pooled	**Positive (MTB Detected Very Low)** Could not produce Sputum Could not produce Sputum
13	**477**	H7041692-1-OSS H7041692-2-OSS H7041692-6-OSS	Negative Pooled	**Positive (MTB Detected Low)** **Positive (MTB Trace Detected)** **Positive (MTB Trace Detected)**
14	**511**	H1941834-1-OSS H1941834-2-OSS H1941834-3-OSS	Negative Pooled	**Positive (MTB Detected Very Low)** Negative Negative
20	**688**	H5041652-1-OSS H5041652-3-OSS H5041652-4-OSS	Negative Pooled	**Positive (MTB Detected Very Low)** Could not produce Sputum Could not produce Sputum

Relationship between Positive Sputum and Positive Pooled Swabs Results (True Positives)

HOUSEHOLD #	HOUSEHOLD ID	SAMPLE ID	POOLED RESULT	SPUTUM RESULT
1	256	H1942112-1-OSS H1942112-3-OSS H1942112-4-OSS	Positive (MTB Detected Low)	Positive (MTB Detected High) Positive (MTB Detected High) Positive (MTB Detected Medium)
2	285	H4042100-3-OSS	Positive (MTB Detected Low)	Positive (MTB Detected High)
6	330	H2942132-2-OSS H2942132-3-OSS	Positive (MTB Detected Very Low)	Could not produce Sputum Positive (MTB Detected High)
8	375	H1942092-5-OSS H1942092-1-OSS	Positive (MTB Trace Detected)	Positive (MTB Detected Low) Could not produce Sputum
9	413	H2941750-1-OSS	Positive (MTB Detected Low)	Positive (MTB Detected Medium)
10	408	H7941780-1-OSS	Positive (MTB Detected Low)	Positive (MTB Detected High)
11	466	H7041808-2-0SS H7041808-4-0SS	Positive (MTB Detected Very Low)	Positive (MTB Detected High) Could not produce Sputum
12	476	H6941842-2-OSS H6941842-7-OSS H6941842-8-OSS	Positive (MTB Detected Low)	Negative Positive (MTB Trace Detected) Positive (MTB Detected High)
19	686	H2941725-1-OSS H2941725-3-OSS	Positive (MTB Detected Very Low)	Could not produce Sputum Positive (MTB Detected Low)
22	726	H4941656-1-OSS H4941656-3-OSS	Positive (MTB Trace Detected)	Positive (Positive (MTB Detected Medium) Could not produce Sputum

Results: Lab-tested Single Swab Test Positivity



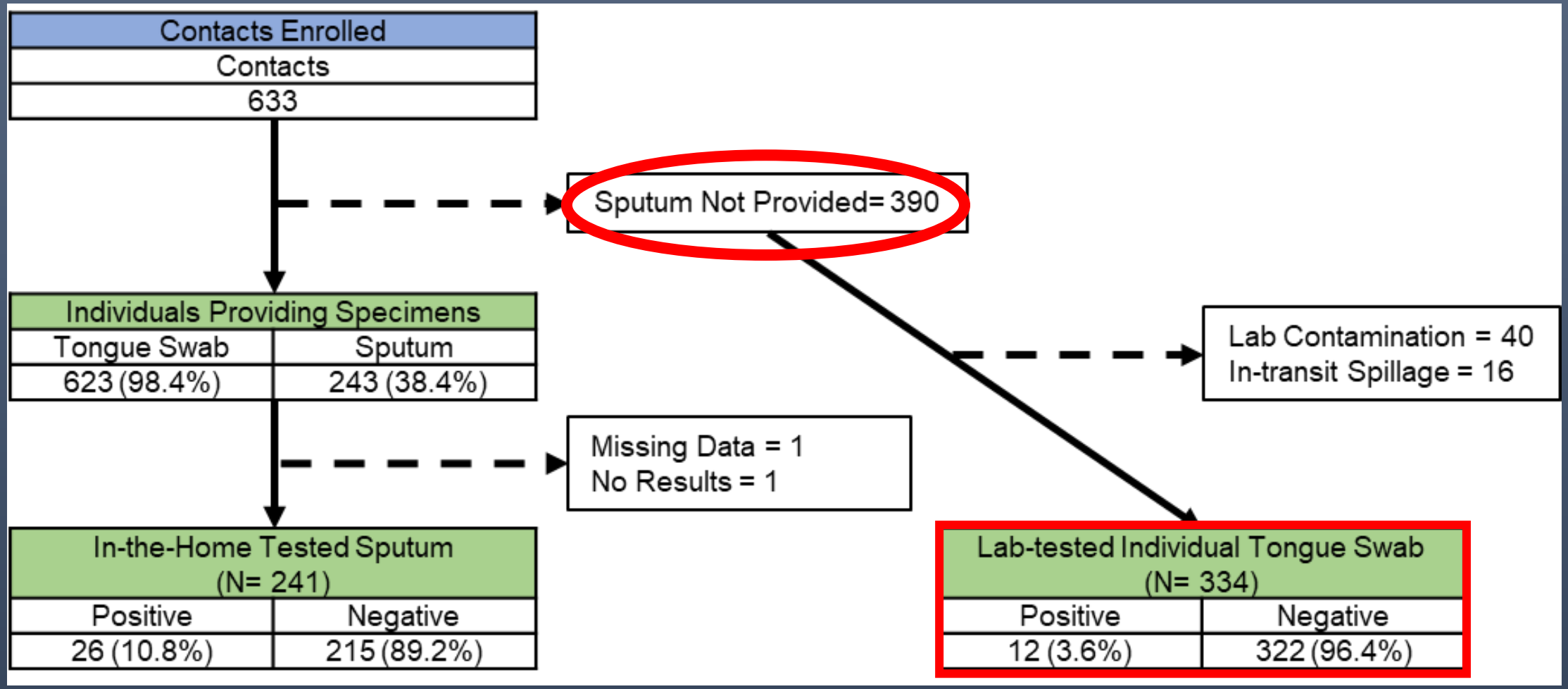
2x2 Table of Paired Sputum vs. Lab Tested Swabs and Diagnostic Accuracy of Lab Tested Swabs

	Sputum +	Sputum -	
Swab +	14	5	19
Swab -	12	186	198
	26	191	217

	Sputum vs. Lab-tested Single Swab (n= 217 paired results)
Sensitivity	53.9 (95% CI: 33.4-73.4%)
Specificity	97.4% (95% CI: 94.0-99.1%)
PPV	73.7% (95% CI: 52.4-87.7%)
NPV	93.9% (95% CI: 91.1-95.9%)

Individual must have provided BOTH a swab and sputum to be included in this 2x2 Table

Tongue Swab Specimens Increase Yield of TB Case Finding Among Those Unable to Produce Sputum



Failure Rate of Tests Performed In-the-Home

	Sputum (N= 250)	Tongue Swabs Tests (N= 379)		
		Single (n= 152)	Two Pooled (n= 153)	Three Pooled (n= 74)
Valid Test Result	241 (96.4%)	131 (86.2%)	147 (96.1%)	66 (89.2%)
Test Failures	9 (3.6%)	21 (13.8%)	6 (3.9%)	8 (10.8%)
Error	6 (66.6%)	13 (61.9%)	1 (16.7%)	6 (75%)
No Results	3 (33.3%)	8 (38.1%)	0 (90%)	2 (25%)
Invalid	0 (0%)	0 (0%)	5 (83.3%)	0 (0%)

Conclusions

- **In-home TB testing may significantly improve upon current household contact investigation approaches by:**
  - Increasing referral uptake (linkage-to-care) for clinic-based TB services
  - Decreasing time-to-presentation for clinic-based TB services
  - Decreasing time-to-treatment initiation
- **Low sensitivity of pooled tongue swabs may be related to specimen dilution and impacted by an individual's sputum bacterial load**
- **Positive test result of pooled tongue swabs indicative of a contact with high bacterial load requiring individual level testing and urgent linkage-to-care**
- **Tongue swabs increase yield of case finding among those unable to produce sputum**

Ongoing Work and Next Steps

Ongoing Work:

- Implementing optimized protocol for pooled swab testing
- Implementing consensus protocol for processing of single swabs
- Expanded inclusion criteria to test contacts ≥12 years old
- Complete cost-effectiveness modeling for home-based TB testing using sputum and swabs

Next Steps:

- Conduct rigorous evaluation of home-based TB testing on case detection and time-to-treatment initiation of those with TB disease
- Explore other diagnostic platforms for use in home-based TB testing

Acknowledgments

Collaborators

- Bernard Fourie, University of Pretoria (co-PI)
- Adam Penn-Nicholson, FIND (co-I)
- Ndumie Ngcelwane, Eastern Cape DoH (Partner)
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- Mbasa Njomane, DTHF (Data Coordinator)
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