

Vuka! Let's unite towards a TB-free world!

9th SA
TB
Conference
8 - 11 June 2026



**Improved detection of undiagnosed
tuberculosis and intra-household
transmission using differentially culturable
tubercle bacteria**

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Closing the Gap: Missed Tuberculosis Cases in South Africa



The Diagnostic Gap in South Africa

- Estimated **249,000** TB cases vs. **184,000** diagnosed (WHO 2025).
- **26% of TB cases** remain undiagnosed or unreported.
- **Reasons:**
 - Low bacterial load.
 - Extrapulmonary or paucibacillary disease.
 - Sample type limitations.

Estimated TB Case Detection in South Africa

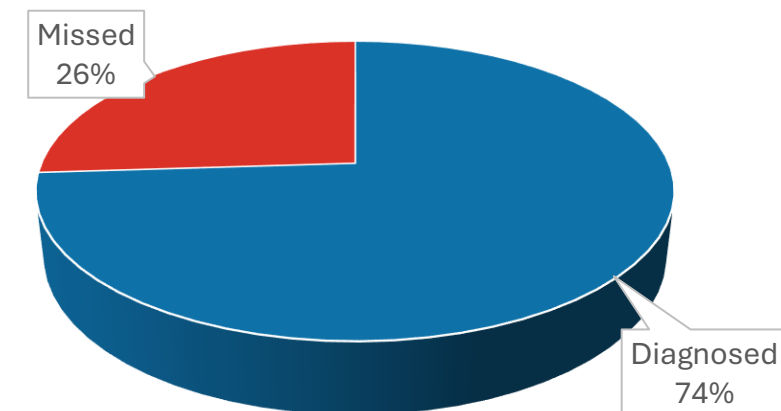
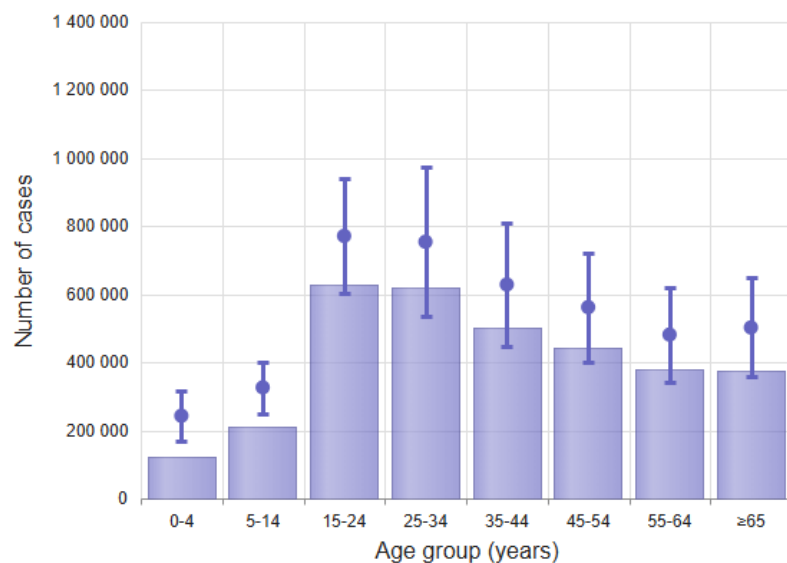


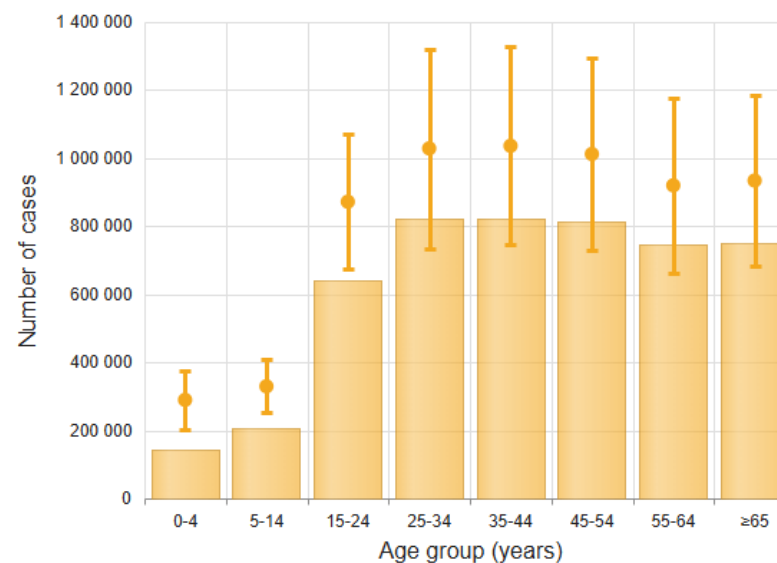
Fig. 1.1.6 Global estimates of TB incidence (absolute numbers) disaggregated by age group and sex, compared with case notifications (female in purple; male in orange), 2024

Bars show TB notifications. Dots and error bars show best estimates of incidence and 95% uncertainty intervals, respectively.

(a) Female



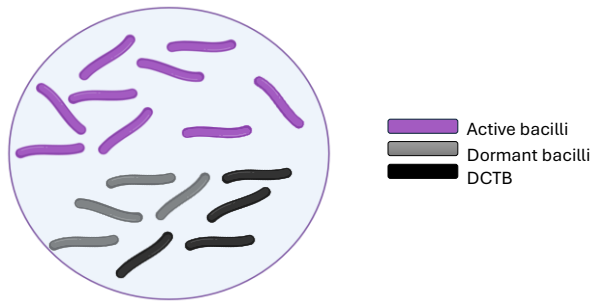
(b) Male



Understanding DCTB Populations

What Are DCTB Populations?

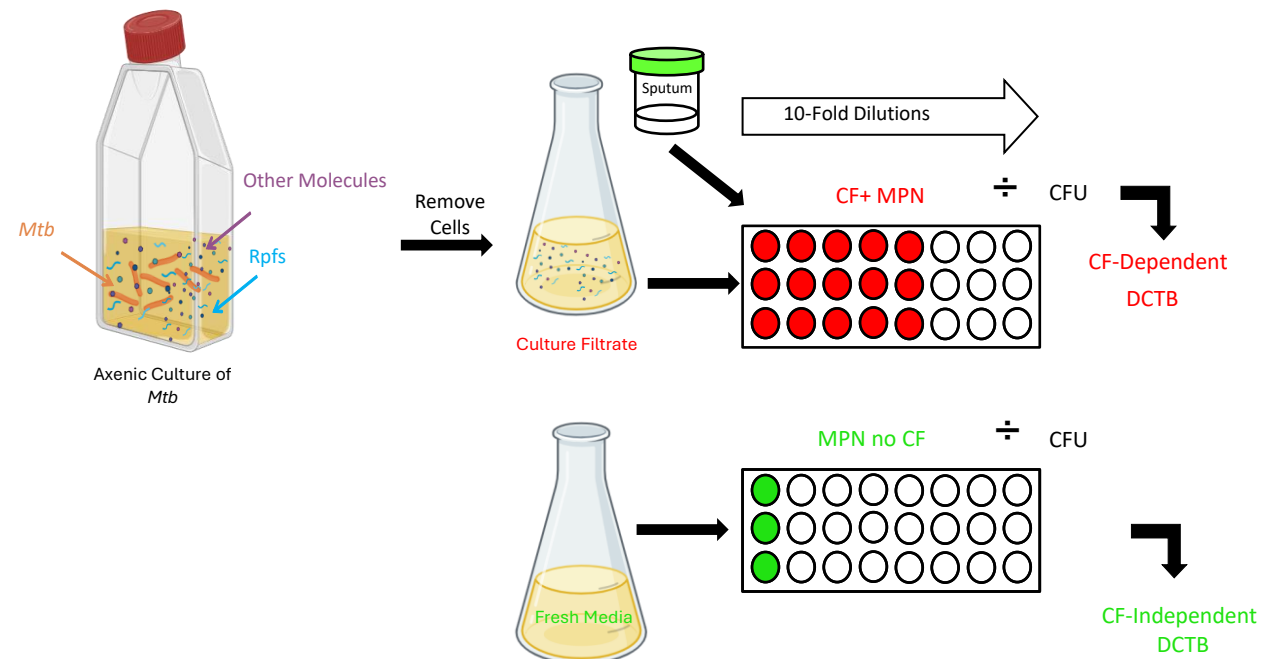
DCTB = **D**ifferentially **C**ulturable **T**ubercle **B**acilli – bacteria that can't grow on standard solid media but can be recovered in liquid media supplemented with resuscitation-promoting factors (Rpfs) or other growth stimulatory factors



- Represent metabolically active but non-replicating or dormant subpopulations of *M. tuberculosis*.
- Often undetected by standard culture
- Detected using culture filtrate (CF) supplementation or resuscitation-promoting factors (Rpfs).

Importance of Culture Filtrate in DCTB Detection

- CF = a filtrate derived from *M. tuberculosis* culture supernatant, containing secreted proteins and Rpfs.
- Acts as a growth stimulant, resuscitating non-culturable bacilli.



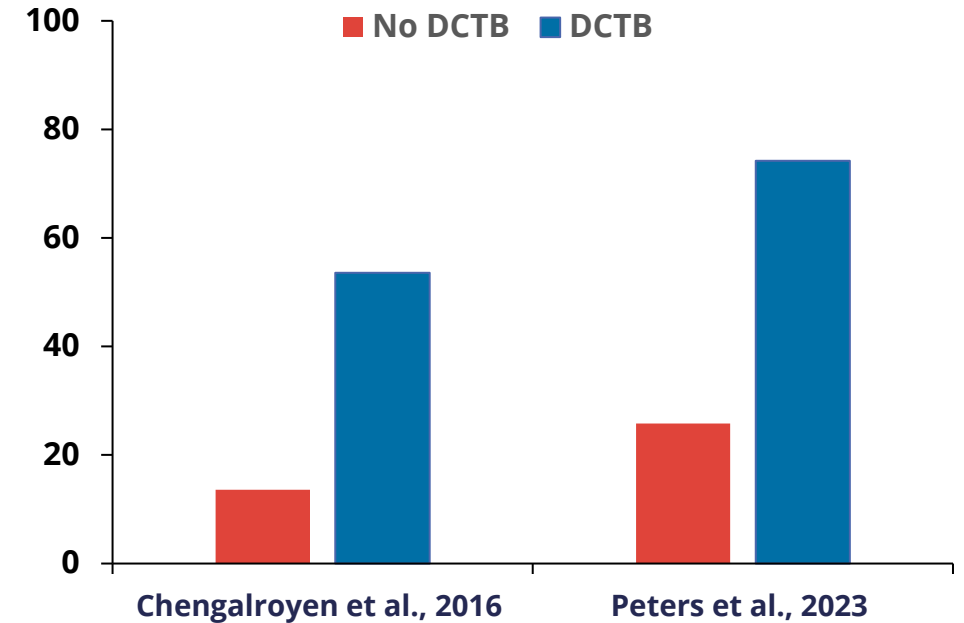
How DCTB Can Help Bridge the Diagnostic Gap

Detects *Mtb* populations missed by conventional diagnostics.

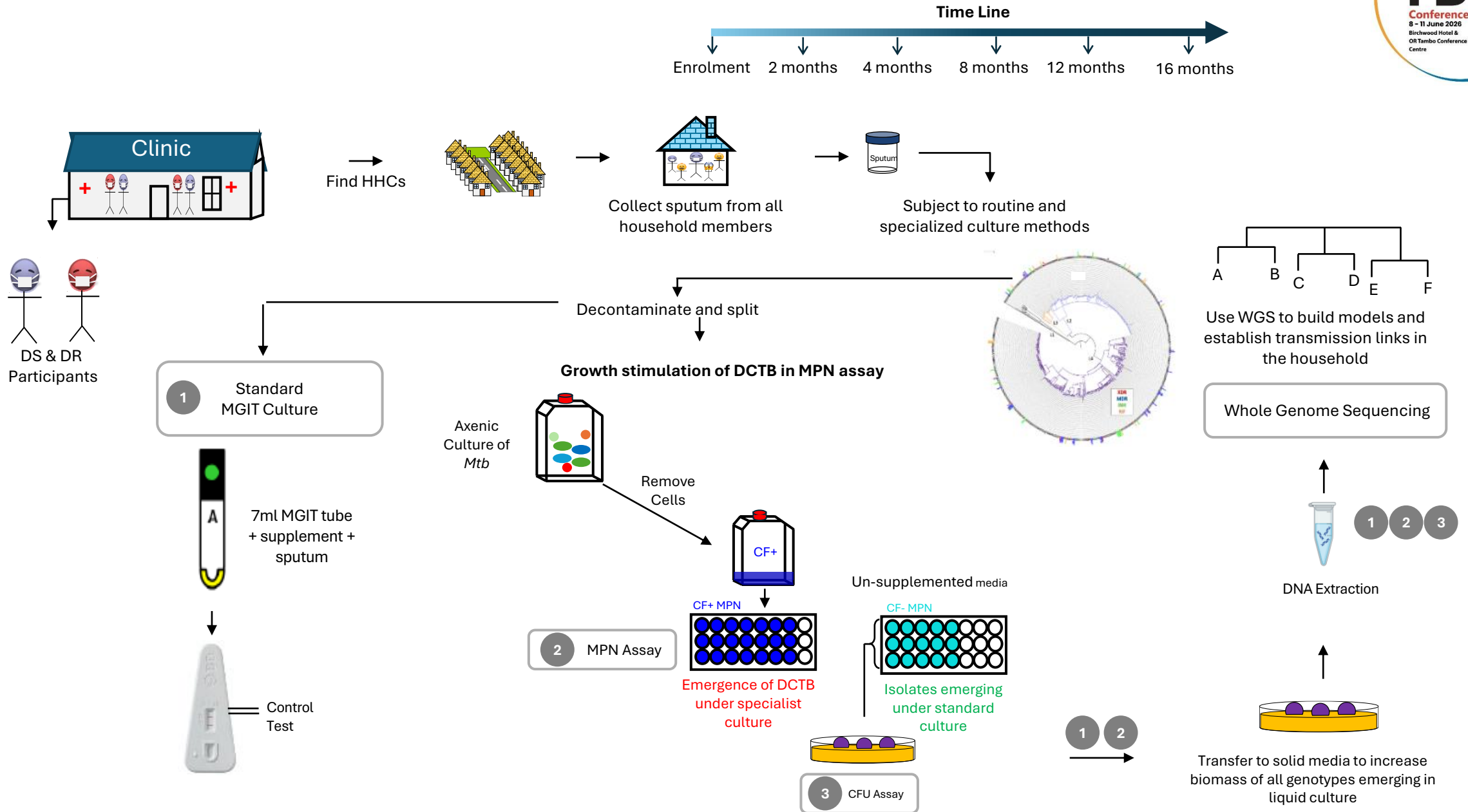
Improves sensitivity in paucibacillary, latent, and non-sputum samples.

Supports better understanding of *Mtb* persistence and transmission.

Can enhance early detection, treatment monitoring, and infection control strategies.



HoTT DCTB Study Overview

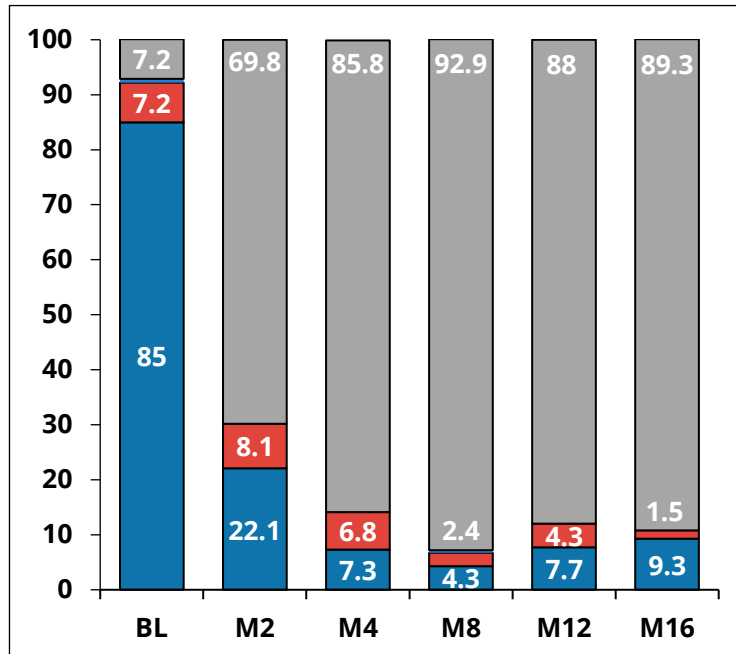


Demographics and lab data

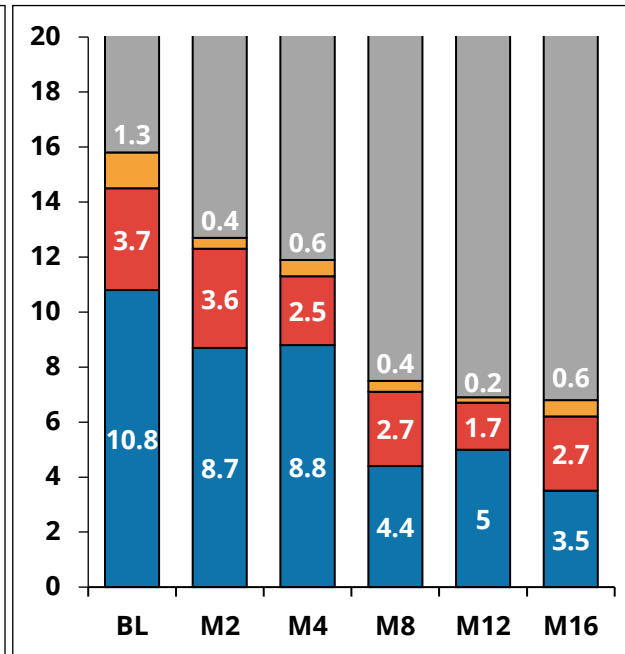
	Index Households (n=293)		Control Households (n=43)
	Index participants (n=293)	HHCs (n=701)	Control Participants (n=122)
Participant demographics			
Sex, n (%):			
Women	110 (37.5)	453 (64.6)	67 (54.9)
Men	183 (62.5)	248 (35.4)	55 (45.1)
Age, yr, median (IQR)	37 (27 – 48)	33 (20 – 51)	33 (22-45)
BMI, median (IQR)	18.7 (16.5 – 21.3)	23.1 (19.1 – 29.7)	23.7 (20.4-30.1)
HIV status at baseline, n (%)			
Positive	168 (57.3)	201 (28.7)	32 (26.2)
On ART	94 (56.0)	156 (77.6)	29 (90.6)
Negative	125 (42.7)	500 (71.3)	90 (73.8)
CD4 count*, median (IQR)	213.5 (42.5 – 3112)	565 (361 – 823)	686 (312.5-1057)
Viral load*, copies/ml, median (IQR)	294 (96.5 – 5007)	-	-
Laboratory data at baseline, median (IQR)			
MGIT time to positivity, h	173 (117 – 279)	984 (984 – 984)	984 (984 – 984)
Log bacterial load by MPN assay			
CF-dependent MPN	5.7 (4.0 – 6.9)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)
CF-independent MPN	4.3 (2.7 – 5.9)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)
Log bacterial load by CFU	5.0 (3.2 – 6.0)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)

Overall *M. tuberculosis* detection

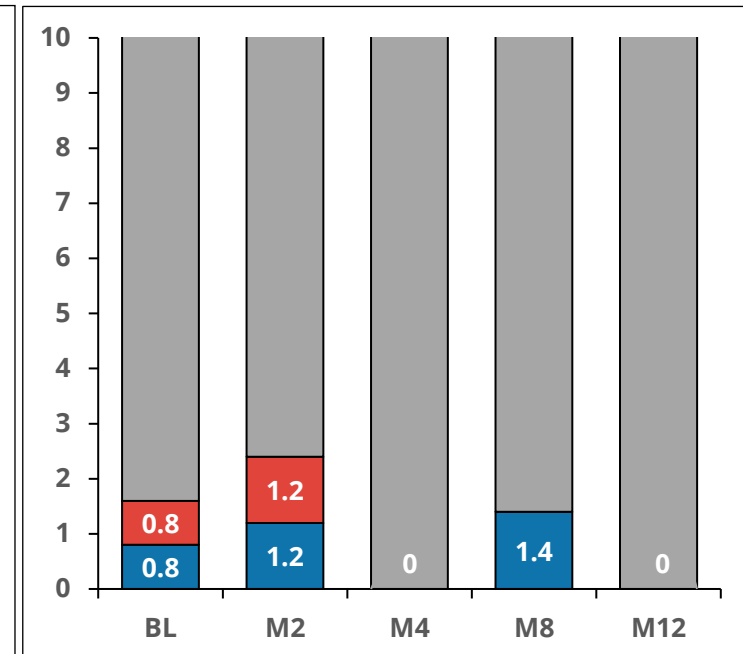
Index Participants



HHCs



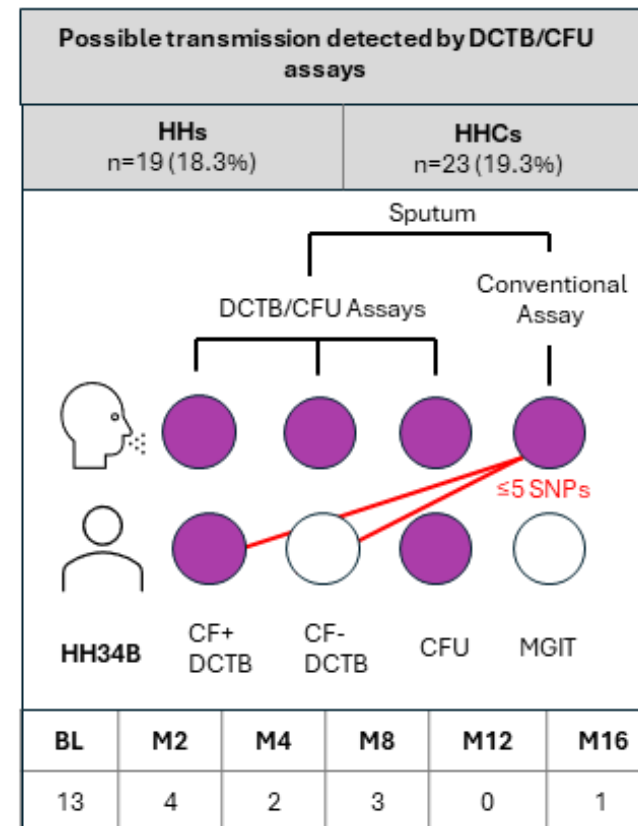
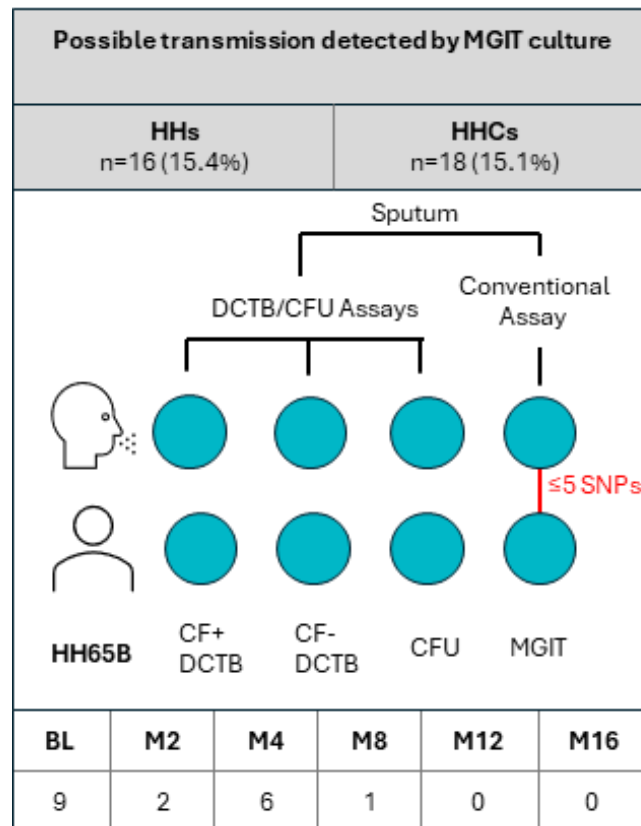
Control Participants



MGIT + Negative MGIT - / DCTB + MGIT - / CFU+

DCTB assays can identify additional *Mtb*-positivity in index participants and household contacts

Transmission linkages based on conventional and DCTB assays for *M. tuberculosis* strain identification

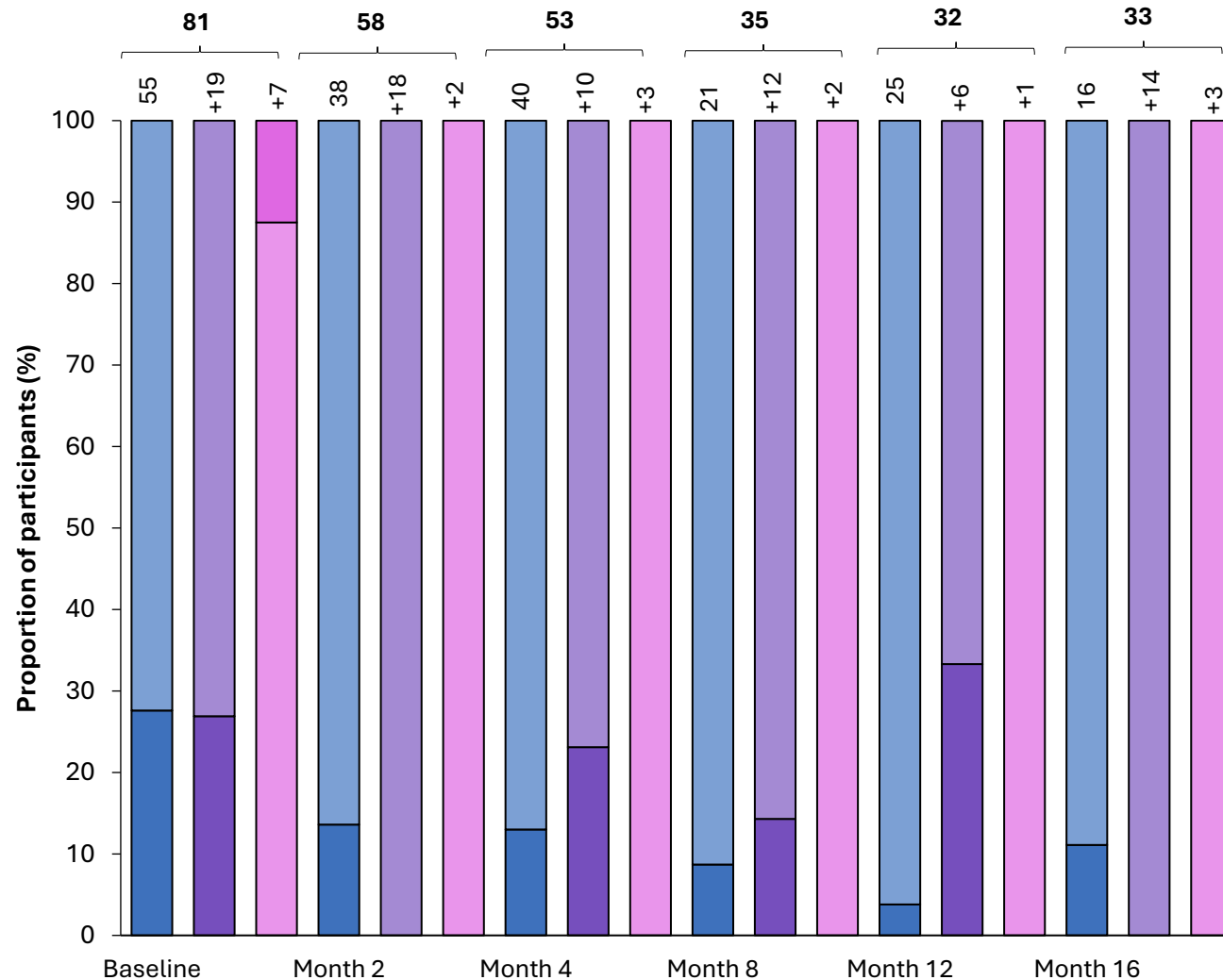


DCTB assays detected additional transmission links within 23% of households, missed/undetected by standard culture.

Key

- Lineage 1.1
- Lineage 2.2
- Lineage 3
- Lineage 4.1
- Lineage 4.3
- Lineage 4.4
- Lineage 4.9
- >5 SNPs
- Transmission Links (≤5 SNPs)

Detection of asymptomatic HHCs using MGIT culture and DCTB assays over a 16-month period



Asymptomatic household contacts, n=292

MGIT+: n=195

MGIT-/DCTB+: n=79

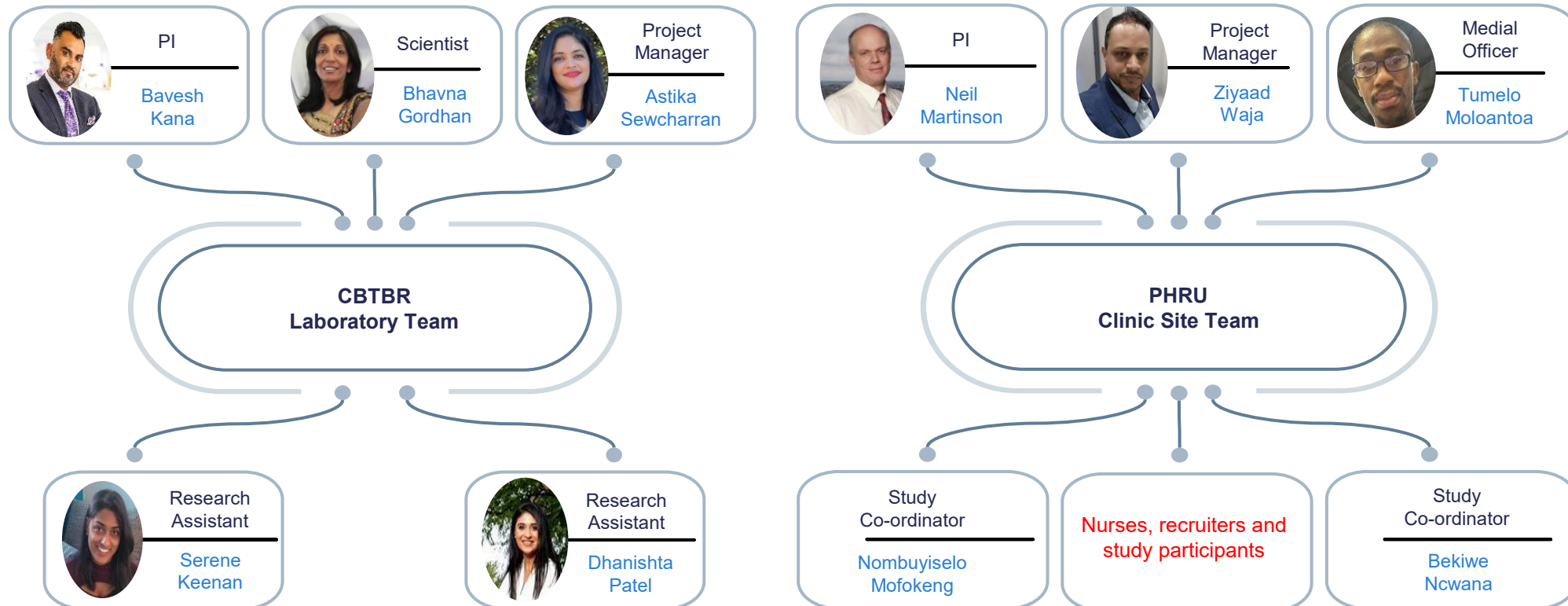
84% (79/94) of additional HHCs detected by DCTB assays were MGIT negative and asymptomatic by WHO criteria.

Conclusion



- **1. The way we culture matters**
 - Integrating DCTB assays into TB contact tracing and diagnostic workflows enables detection of *Mtb* in HHCs missed by standard culture alone.
 - HHCs of TB index cases in high-burden settings should undergo standard screening and testing irrespective of symptom status.
 - Combining DCTB with standard culture improves detection of diverse *Mtb* populations, enhances early diagnosis and detection of asymptomatic cases.
- **2. DCTB Assays uncover hidden transmission links**
 - DCTB assays identify greater genetic heterogeneity within samples, thereby allowing for a better understanding of the transmission dynamics at play within households.

Acknowledgements



Funder