

## Evaluation of Interferon- $\gamma$ Release Assays in the Diagnosis of Latent TB Infection in U.S. Healthcare Workers:

Preliminary Results of Task Order #18

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On behalf of the  
CDC TB Epidemiological Studies  
Consortium



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## Background

- Diagnosis and treatment of LTBI are important components of U.S. TB control
- HCWs are an important group for targeted testing and treatment (~14 million in US)
- The IGRAs, QuantiFERON®-TB Gold In-Tube ("QFT") and T-SPOT®.TB ("T-SPOT"), are approved for use in the US
- There is limited information on use of these tests longitudinally in HCWs undergoing periodic testing
- The impact of a previous TST on IGRA results remains uncertain



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## Objectives

- To evaluate performance characteristics of QFT and T-SPOT compared with TST for detecting LTBI in HCWs undergoing routine screening
  - Test result stability over time (i.e. conversion, reversion)
  - Reproducibility
  - Test, re-test repeatability
  - Estimated sensitivity and specificity
  - Impact of TST on IGRA results
- To determine costs, cost-effectiveness
- To determine and compare acceptability of tests among participants



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## Design and Population



- Longitudinal study
- HCWs undergoing routine LTBI testing
- 4 sites: Denver, Houston, Baltimore, NYC
- Inclusion:
  - ≥18 yrs; informed consent; undergoing routine screening
- Exclusion:
  - Current or prior active TB; TST within 6 months prior to enrollment
- Target sample size 2500

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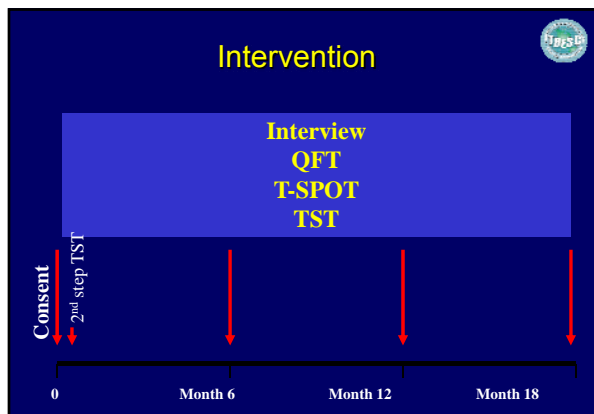
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## Intervention



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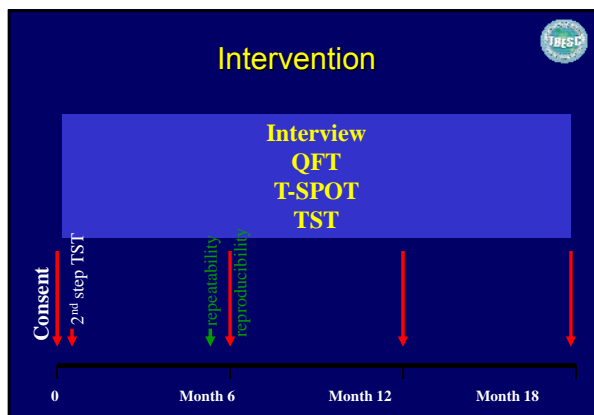
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## Intervention



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## Testing Methods



- TST
  - Administered, interpreted by study-trained personnel
  - Tubersol
- QuantiFERON®-TB Gold In-Tube (“QFT”)
  - Cellestis, Inc
  - Performed, interpreted by trained technologists according to manufacturer package insert
- T-SPOT®.TB (“T-SPOT”)
  - Oxford Immunotec, Ltd
  - Performed, interpreted by trained technologists according to manufacturer package insert

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## Characteristics of the Study Population (n=1208 to date)



	Number	%
Age (median)	34.5 (range 18-73)	
Female	885	73.5
Race/Ethnicity*		
Hispanic	213	17.6
African-American	163	13.5
Caucasian	701	58.0
Other	94	7.8
Born outside U.S.	186	15.4
h/o BCG vaccine	109	9.5

\*37 unknown

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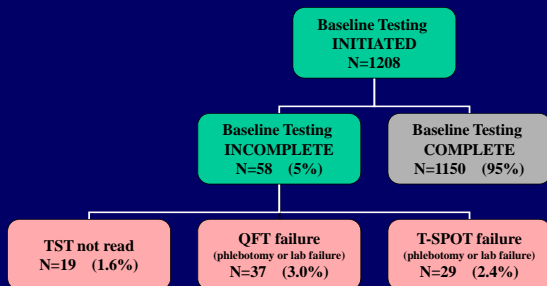
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## Testing Outcomes



\*Several incomplete on >1 test

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## Assay Results, by Method (completed tests with valid results)



	QFT N=1178	T-SPOT N=1171	TST* (10 mm) N=1189
Positive	73 (6.2%)	91 (7.8%)	110 (9.2%)
Negative	1085 (92.0%)	1021 (87.2%)	1079 (90.8%)
Borderline	n/a	49 (4.2%)	n/a
Indeterminate	20 (1.7%)	10 (0.9%)	n/a

\* Includes 2-step results

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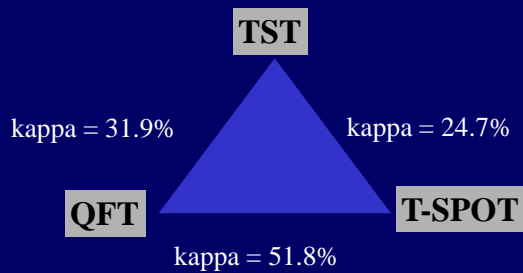
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## Test Agreement




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## Impact of a Recent TST Study Population and Methods



- Target enrollment:
  - 100 TST (-) and 100 TST (+)
- Participants must test negative on both QFT-GIT and T-SPOT at baseline
- Both IGRAs are repeated 1-3 weeks after the baseline TST was placed

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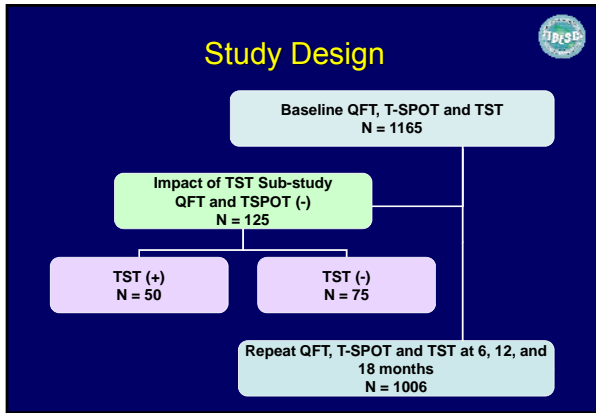
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### Results - Overall

Baseline QFT-GIT and T-SPOT Negative			
	TST (- n = 75	TST (+) n = 50	Total n (%)
Repeat QFT-GIT			
Negative	71 (95)	39 (78)	110 (88)
Positive	3 (4)	9 (18)	12 (10)
Indeterminate / Failed	1 (1)	2 (4)	3 (2)
Repeat T-SPOT			
Negative	67 (89)	38 (76)	105 (84)
Positive	5 (7)	7 (14)	12 (10)
Borderline	3 (4)	2 (4)	5 (4)
Indeterminate / Failed	0	3 (6)	3 (2)

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### Results – QFT-GIT

Impact QFT-GIT	Baseline QFT-GIT	
	<0.2	0.2-0.34
<0.2	104	0
0.2-0.34	5	0
0.35-0.49	3	1
0.5-0.69	0	0
≥ 0.7	6	2
Total	118	3

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## Results – T-SPOT



Impact T-SPOT	Baseline T-SPOT		
	≤ 3	4	5-7
≤ 3	97	2	2
4	2	3	0
5-7	5	0	0
8	3	1	0
≥ 9	7	0	0
Total	114	10	2

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## Definitions



- **Conversion:** change from a negative to a positive
- **Reversion:** change from a positive to a negative
- **Reproducibility:** lab variability when 2 samples are drawn simultaneously from an individual
- **Repeatability:** variability in an individual when the IGRAs are repeated within a short time frame (7-21 days)

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## Reproducibility



QFT-GIT			T-SPOT		
	n	%		n	%
Concordant Negative	91	73	Concordant Negative	77	65
Concordant Positive	29	23	Concordant Positive	26	22
Discordant (Pos/Neg)	5	4	Concordant Borderline	1	< 1
Total	125		Discordant Pos/Neg	5	4
			Border/Neg	5	4
			Border/Pos	4	3
			Total	118	

Excludes 7 with failed T-Spot

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## Summary and Conclusions



- LTBI prevalence is ~3% if defined as positive on all 3 tests; ~17% if defined as any test positive
- TST may "boost" a subsequent IGR and the change in IGRAs occurs early (within 2 weeks)
- Lab variability resulted in discordant results for 4% with QFT-GIT and 11% with T-SPOT
- Short-term variability (1-3 weeks) and long-term variability (6 months) for QFT-GIT and T-SPOT resulted in "conversions" in 3-4% and "reversions" in 15-33%.
- Alternative criteria establishing a minimum threshold for the amount of change necessary to define a conversion are needed

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## Thank you to TO #18 Team



- CDC: Paul Weinfurter, Denise Garrett, Grace Thiongo
- Denver: Charles Daley, Robert Belknap, Randall Reves, Kirsten Wall
- Houston: Ed Graviss, Larry Teeter
- Baltimore: Susan Dorman, Wendy Cronin, Elizabeth Munk, Jonathan Golub
- NYC: Neil Schluger, Daniel Brodie, Joyce Thomas, Yael Hirsch-Moverman

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