TB infection treatment eligibility among household contacts of microbiologically confirmed pulmonary TB patients in high TB settings

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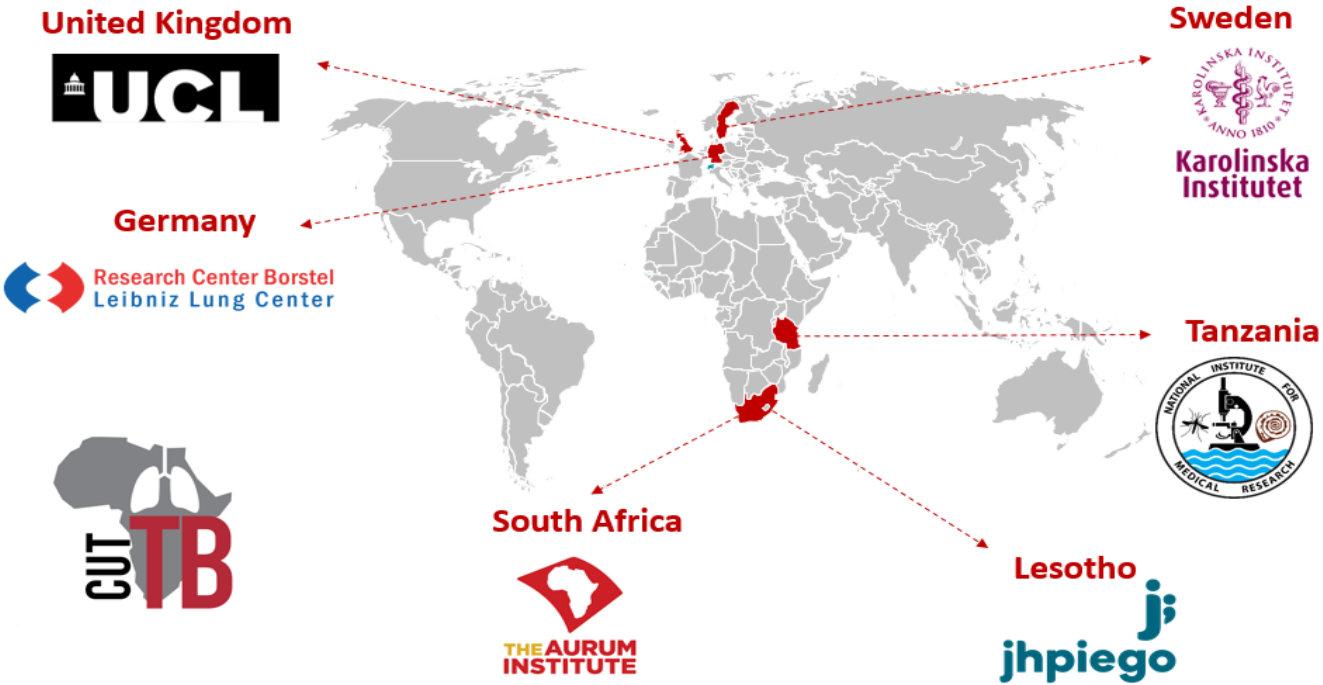
Background – CUT-TB Trial



Background – TB Infection

Tuberculosis infection (TBI) is the seedbed from which TB cases arise

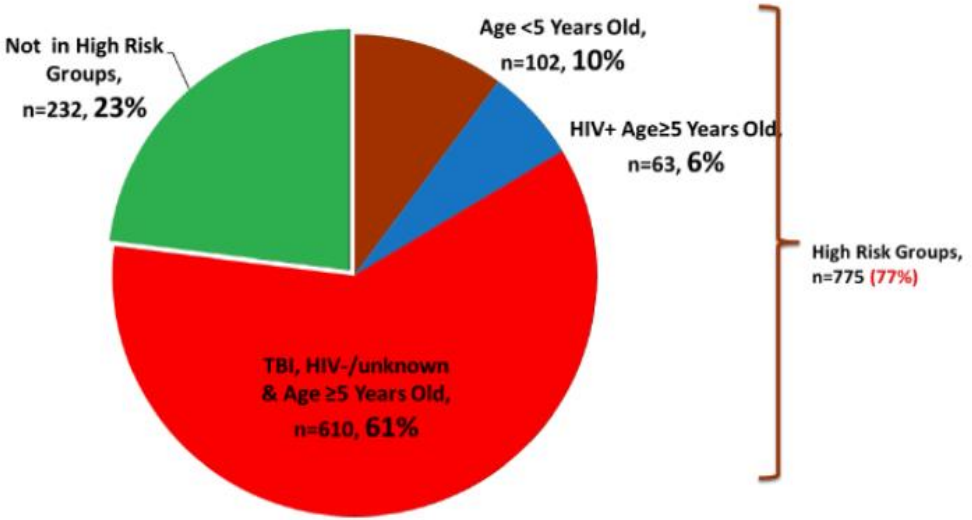
United Nations high-level meeting targeted to provide TB Preventive Therapy (TPT) to 30 million including 24 million household contacts (HHCs)

TPT trials have shown most benefit in those with TBI but testing for TBI is cumbersome and may result in reduced uptake of TPT

Current WHO guidelines (2020) do not mandate TBI testing for PLHIV or HHCs

Background – PHOENIx Trial

- Evidence from a multi-country feasibility study among HHCs of multi-drug resistance TB (MDR-TB) persons (PHOENIx trial)
- This could be different for drug sensitive TB (DS-TB) as people are infectious for shorter period of time



(Gupta et al, 2019, CID)

Aim

- To characterise HHCs of DS-TB patients to estimate the proportion who would be eligible for TPT (<5 years, PLHIV or having TBI) among HHCs of microbiologically confirmed pulmonary TB patients in high TB settings

Methods – Study Design and Setting

Study Design

- Cross-sectional study

Study Setting

- Lesotho – Maseru, Thaba -Tseka, Berea, and Quthing Districts
- South Africa – Ekurhuleni District, Gauteng Province
- Tanzania – Songwe and Mbeya City Districts

Study Population

- TB index patients: Microbiologically confirmed TB within ≤6 weeks, age ≥18 years
- HHCs: Anyone identified by TB index patient and found in the household

Sample Size

- We planned to recruit 100 Index patients and all listed HHCs (300) in each country

Methods – Study Procedures

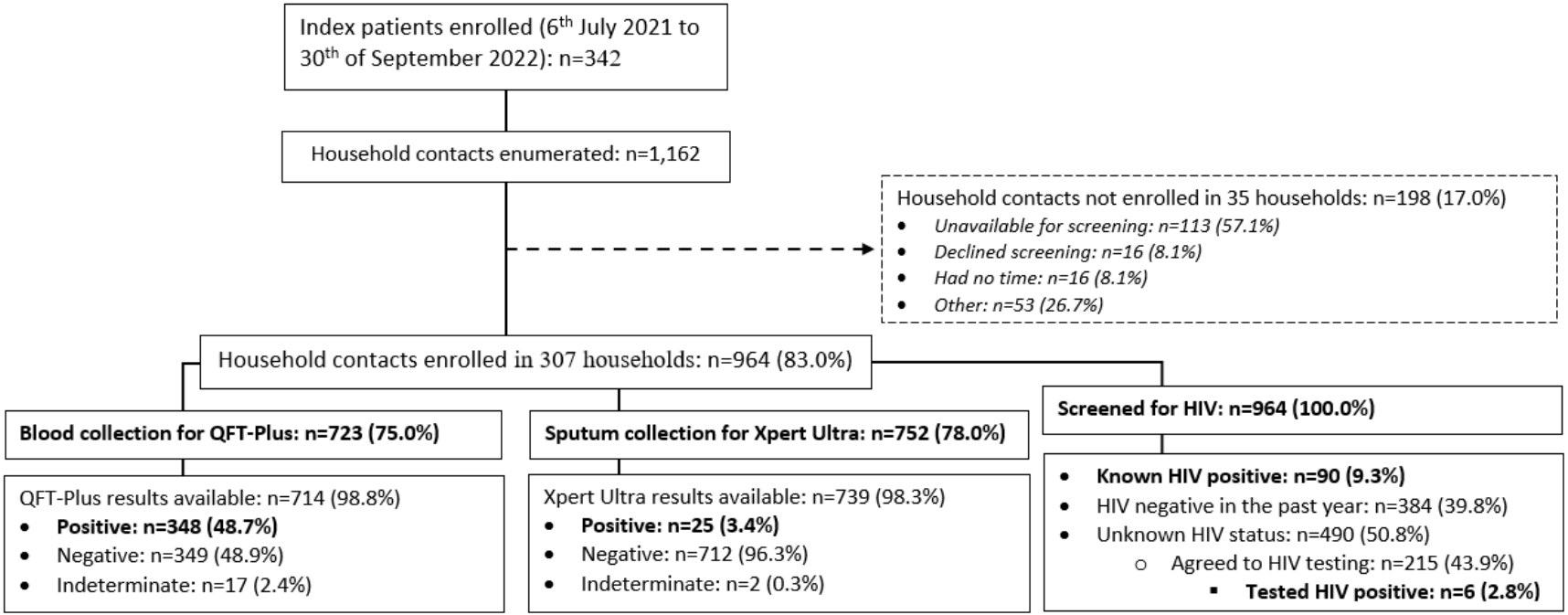
Index patients

- Informed consent
- Enumeration of HHCs

Household contacts

- Informed consent
- Demographic and medical history questionnaire
- Symptom screening
- Offered HIV testing
- Single sputum collection for Xpert Ultra testing
- Blood collection for TBI testing (6 ml single lithium heparin tube) for ≥5 years by a trained phlebotomy nurse
- Samples were transported and tested at Aurum Clinical Research Laboratory (quality assured) for TBI testing using QuantiFERON-TB-Gold-Plus (QFT-Plus) according to manufactures' instructions

Results – Consort Diagram



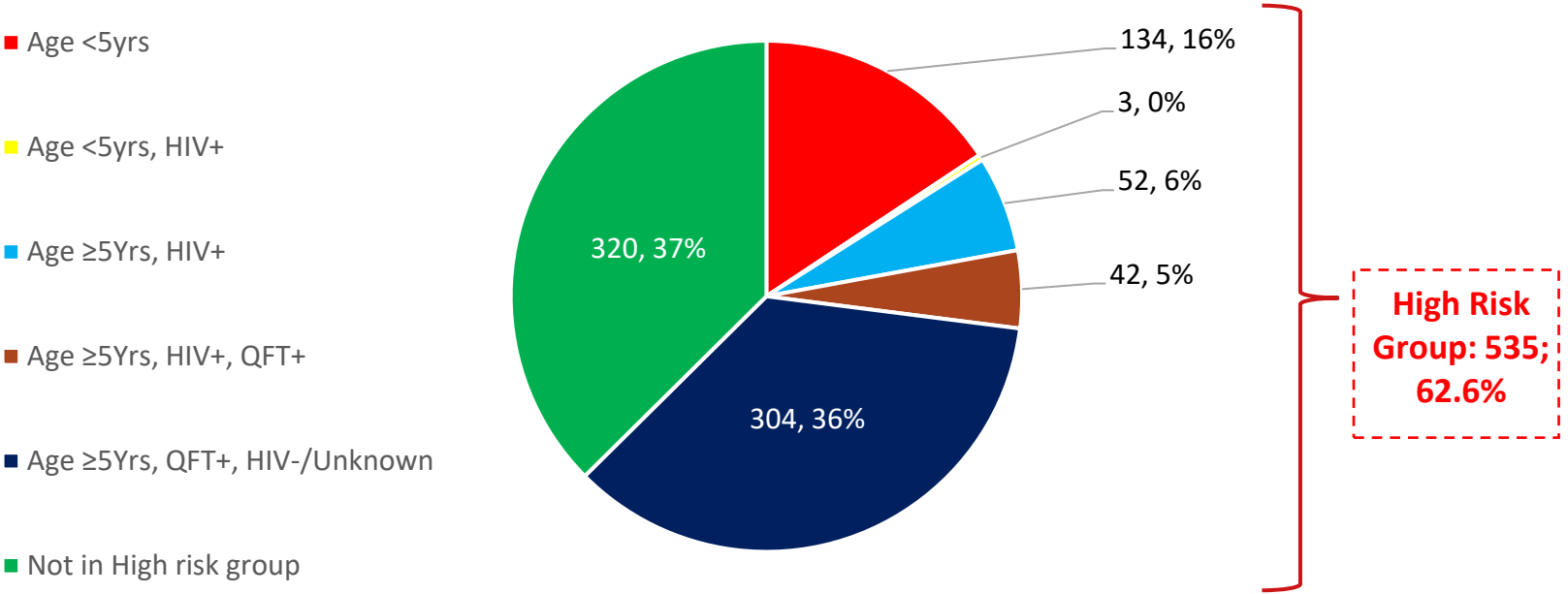
Demographic Characteristics

Variable (N=964)	Frequency (n)	Percent (%)
	964	100.0%
Median (IQR)	18 (8 - 39)	
Gender		
Female	597	61.9%
Age Category		
0-9 yrs	281	29.2%
10-19 yrs	221	22.9%
20-29 yrs	111	11.5%
30-39 yrs	113	11.7%
40-49 yrs	82	8.5%
50-59 yrs	62	6.4%
≥60 yrs	94	9.6%
Site Country		
South Africa	300	31.1%
Lesotho	343	35.6%
Tanzania	321	33.3%
Sleep in the same room with Index		
Yes	310	32.2%
Previous TB		
Yes	51	5.3%
Previous TPT Treatment		
Yes	123	12.8%
HIV status		
Positive	96	10.0%
Negative	593	61.5%
Unknown	275	28.5%

QFT-Plus Results by Demographic Characteristics

Variable (N=693)	N (%)	LTBI +ve – n (%)	p-Value
	693 (100.0%)	346 (49.9%)	<0.001
Median (IQR)	26 (13, 45)	32 (18, 50)	
Gender			0.791
Male	255 (36.8%)	129 (50.6%)	
Female	438 (63.2%)	217 (49.5%)	
Age Category			<0.001
0-9 yrs	102 (14.7%)	37 (36.3%)	
10-19 yrs	187 (27.0%)	62 (33.2%)	
20-29 yrs	93 (13.4%)	53 (57.0%)	
30-39 yrs	103 (14.9%)	60 (58.3%)	
40-49 yrs	75 (10.8%)	47 (62.7%)	
50-59 yrs	54 (7.8%)	34 (63.0%)	
≥60 yrs	79 (11.4%)	53 (67.1%)	
Site Country			<0.001
South Africa	238 (34.3%)	135 (56.7%)	
Lesotho	215 (31.0%)	121 (56.3%)	
Tanzania	240 (34.6%)	90 (37.5%)	
Sleep in the same room with Index *			0.470
Yes	198 (28.8%)	103 (52.0%)	
Previous TB **			0.001
Yes	42 (6.1%)	31 (73.8%)	
Previous TPT Treatment ***			0.509
Yes	63 (9.1%)	29 (46.0%)	
HIV status			<0.001
Positive	82 (11.8%)	39 (47.6%)	
Negative	379 (54.7%)	271 (71.5%)	
Unknown	232 (33.5%)	90 (38.8%)	

TPT eligibility characteristics (N=855)



TPT eligibility by country (N=855)

Eligibility status	Lesotho (N=277)			South Africa (N=259)			Tanzania (N=319)			Total (N=855)			
	n	%	95% CI	N	%	95% CI	n	%	95% CI	n	%	95% CI	
Eligible	190	68.6%	62.8 - 74.0	166	64.1%	57.9 - 69.9	179	56.1%	50.5 - 61.6	535	62.6%	59.2 - 65.8	p-Value=0.006
Not eligible	87	31.4%	26.0 - 37.2	93	35.9%	30.1 - 42.1	140	43.9%	38.4 - 49.5	320	37.4%	34.2 - 40.8	

Conclusion

- Approximately two thirds of TB exposed HHCs were classified as high-risk group for progressing from TBI to TB disease and would therefore benefit from TPT

- Our results suggest that the recommendation not to test for TBI is warranted, and there would only be a place for TBI testing if more cost-effective and field-friendly tests had to become available

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