Resistance to *Mycobacterium tuberculosis* infection among household contacts of MDR TB patients

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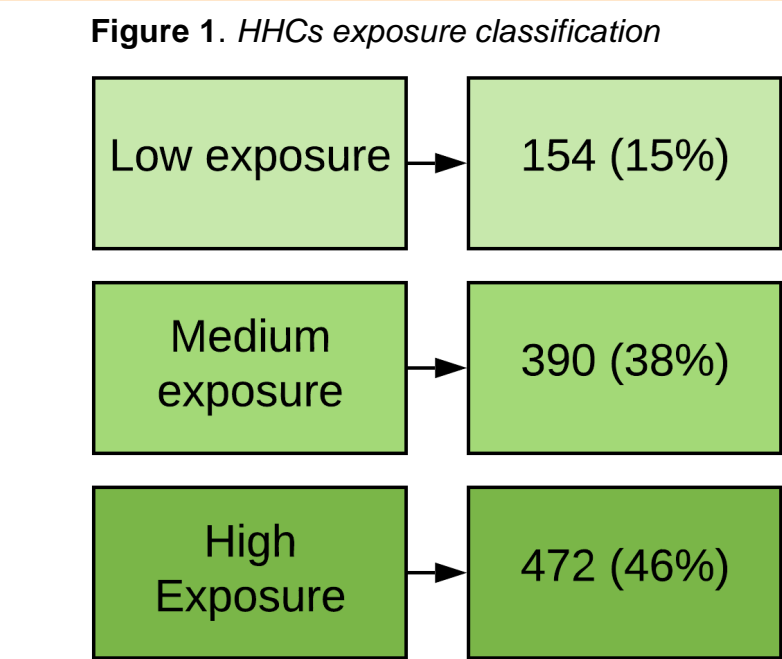Scientific Research

E-Poster No. EP-04-131-31

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Background

- Household contacts (HHC) of TB patients are at high risk for TB infection and disease
- Yet 10–50% of HHC remain negative on tuberculin skin test (TST) or interferon gamma release assays (IGRA)[1,2]
- These individuals may be "resistant" to *Mycobacterium tuberculosis (Mtb)* infection
- Accurate measures of exposure are critical to determine whether individuals are resistant to *Mtb* infection
- An additional challenge is defining *Mtb* infection because TST and IGRA measure adaptive immune response, not infection itself
- **We determined the proportion of HHC who may be "resistant" to *Mtb* infection despite high TB exposure**

Design/Methods

- Cross-sectional study from 10/2015–4/2016, with follow-up at 1 year after enrollment
  - **16 sites in 8 countries: Botswana, Brazil, Haiti, India, Kenya, Peru, South Africa, and Thailand**
- Adult pulmonary Rif-resistant or MDR-TB index cases and their HHC
- HHC tested for *Mtb* infection:
  - Baseline TST and/or IGRA
  - Follow-up IGRA after 1-year for HHC with negative baseline IGRA (age≥5)
- **Exposure variable**: 3-level variable (Figure 1) adapted from factors validated in published literature[3,4] including index case's infectiousness, interaction with HHC, and age of HHC
- **Definition of resistance to *Mtb* infection**:
  - Negative TST (0mm induration) <u>and</u> IGRA (<0.35 IU/ml) at baseline <u>and</u> negative IGRA after 1-year follow-up, if available; no active TB at baseline or after year.

Figure 1. *HHCs exposure classification*

Low exposure	→	154 (15%)
Medium exposure	→	390 (38%)
High Exposure	→	472 (46%)

Results

- **Enrollment:** 1016 HHCs of 284 index cases (Figure 2). 305 (30%) HHCs <15 years old
- **306 (30%) HHCs** without TST and IGRA results available and without active TB were excluded from resistance definition.
- **Resistance status defined for 710 HHC,** of whom **109 (15%)** were classified as resistant
  - Range: 0–50% across countries (Table 1)
  - Among HHCs with resistance defined, 328 were highly exposed, of whom **43 (13%)** were resistant
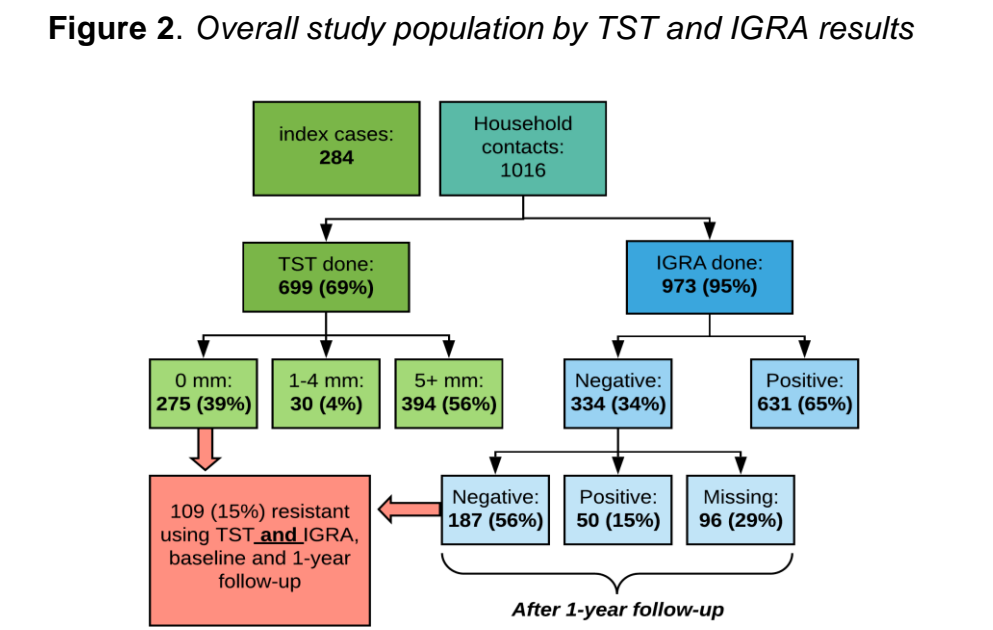
Figure 2. *Overall study population by TST and IGRA results*

Table 1. Distribution of resisters by country		Country*							
		Botswana	Brazil	Haiti	India	Kenya	South Africa	Thailand	Total
Resistance status defined		37	9	48	174	8	404	30	710
Resistant	N	15	0	8	19	0	52	15	109
	%	40	0	17	11	0	13	50	15

* Peru was excluded from the analysis because TST testing was not done

Conclusions

- Even with restrictive classification (i.e., TST and IGRA negative, baseline and 1-year follow-up), a substantial proportion of HHC remain negative on tests for *Mtb* infection (15%)
- Resister phenotype occurs across diverse geographical settings
- Future directions may involve identifying genetic or immunologic factors potentially responsible for resistance to *Mtb* infection TB HHC randomized prevention

Acknowledgements

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