



Prevalence and Incidence of tuberculosis infection and disease among household contacts of multidrug-resistant (MDR) TB cases

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MDR TB in Household Contacts (HHCs)

- MDR TB contact investigation is poorly implemented globally
- Studies of HHCs of MDR TB cases have largely been single site retrospective studies
- High quality data on prevalence and incidence of TB infection and disease needed to inform programs, epidemiologic models and trials of preventive therapies/vaccines



Shah et al. Clin Infect Dis 2014

Cain KP et al. Int J Tuberc Lung Dis 2010



PHOENix Feasibility Study Objectives

- **PHOENix Feasibility study (A5300/I2003)**
 - 2 US NIH-funded HIV clinical trials networks, ACTG and IMPAACT
 - 8 high TB burden countries at 16 sites
 - Prepare for a large multisite cluster randomized interventional trial of delamanid vs isoniazid for prevention of TB in high risk HHCs
- **Objectives**
 - Main
 - To describe feasibility of identifying, recruiting, and characterizing adults MDR TB index cases and their HHCs
 - Prevalence of TB infection, TB Disease, and HIV infection among HHCs
 - This analysis
 - To describe incidence of TB infection and disease 1 year later

*Gupta CID 2019
Suryavanshi CID 2019
Swindells IJTLD 2018
Kim CROI 2020*

Key Inclusion Criteria

Sites

- ACTG and IMPAACT sites with ability to enroll 10 MDR TB cases in a 16-week period

Population

• Index Cases:

- An adult (18+ years) with pulmonary RR/MDR TB by genotypic or phenotypic testing
- Started on TB treatment within past 6 months
- Willing to allow access to their households

• Household contacts:

- Residing in same dwelling unit or plot of land with shared housekeeping arrangements as the index case
- Reported exposure within 6 months prior to index case starting MDR TB treatment



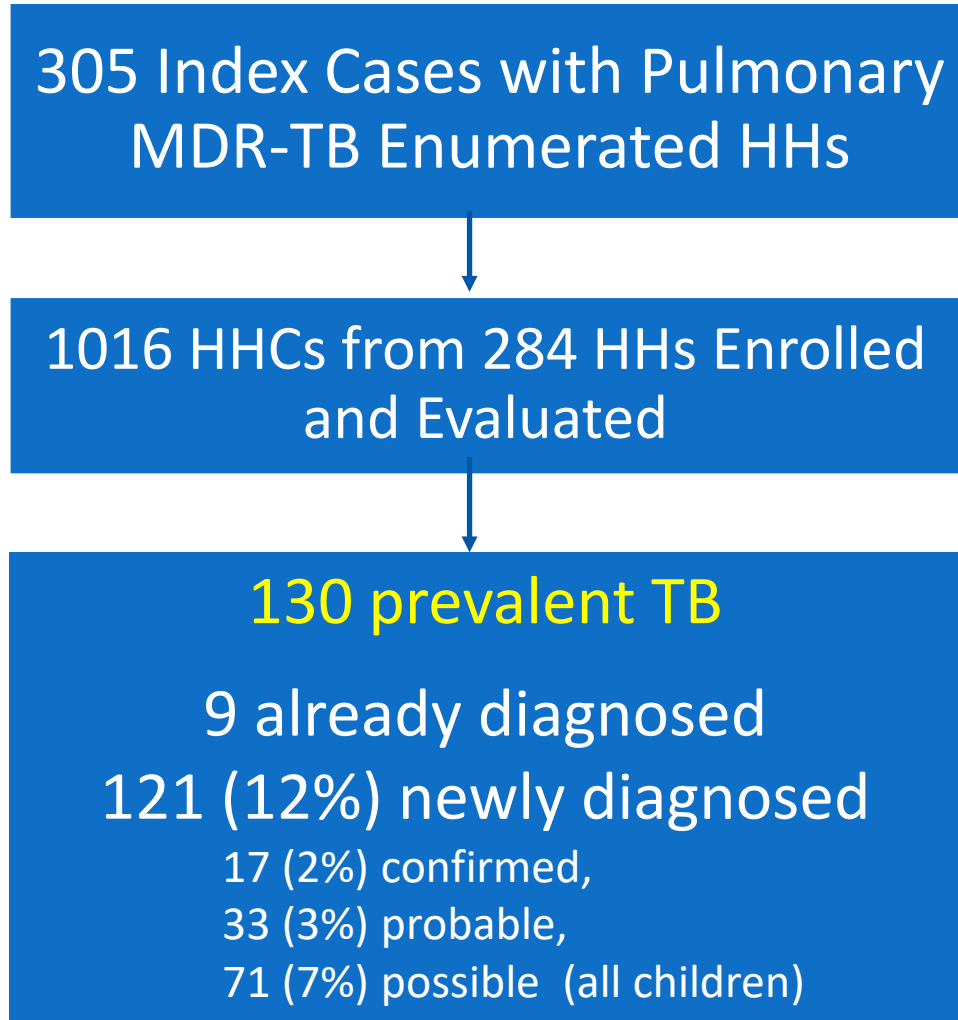
Methods

- **Outcomes**
 - **Incident TB Infection:** HHC \geq 5 years IGRA-negative or indeterminate at baseline and positive repeat IGRA at 1 year using QuantiFERON Gold-in-tube
 - **Incident TB Disease:** Negative symptom screen, chest radiography, mycobacteriology at baseline and positive at follow-up (routine program or via study)
 - Confirmed, probable, possible TB categories based on microbiology, clinical adjudication
- **High-risk groups** defined as:
 - Children <5 years
 - HIV-infected
 - TBI by either TST or IGRA
- **Statistical Analysis:** Cumulative incidence proportions and 95% CI estimated using Generalized Estimating Equations because of correlation within households



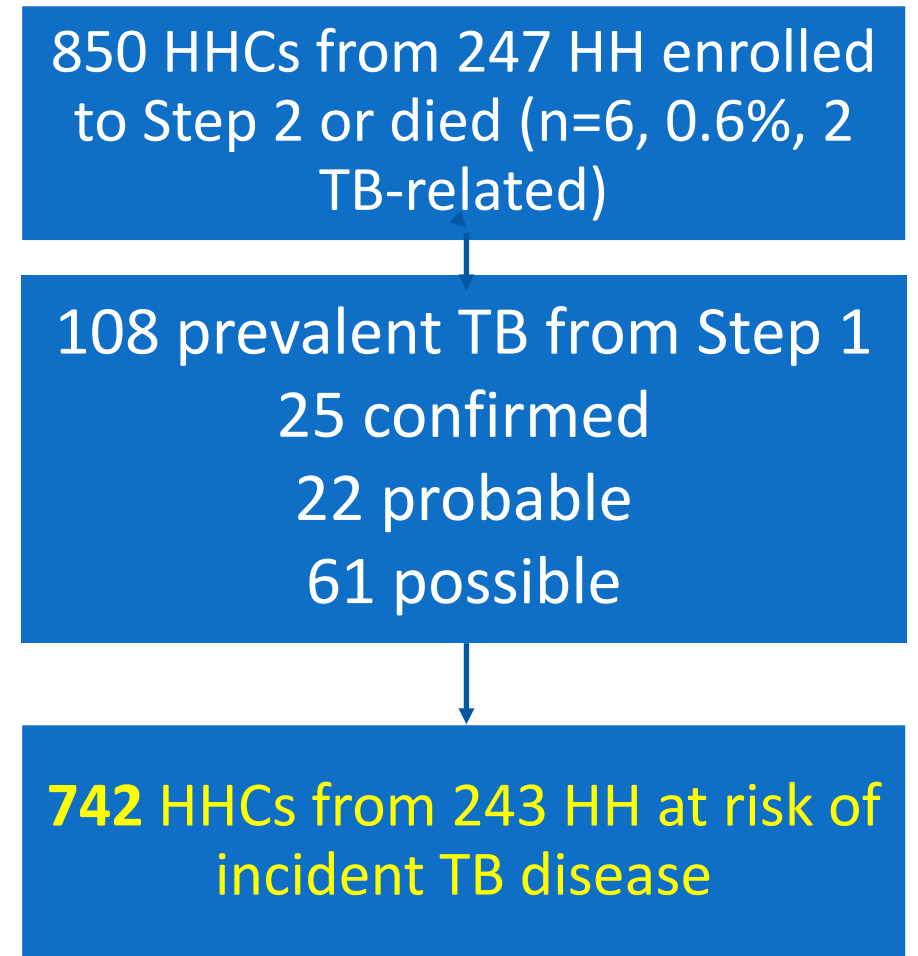
Flow Diagram for incident TB Disease

Step 1



Step 2

Median 51.4 weeks



Gupta CID 2019



Flow Diagram for incident TB Infection

Step 1

1016 HHCs from 284 HHs Enrolled and Evaluated

IGRA + prevalence

43/102 (**42%**) IGRA+ age <5
588/905 (**58%**) IGRA+ and age ≥5
1/102 (**1%**) indeterminate age <5
43 (4%) Step 1 IGRA not available

Step 2

720 not eligible for Step 2 IGRA testing

41 eligible but not enrolled in Step 2

242 HHCs from 131 HH at risk for incident TB infection and evaluated

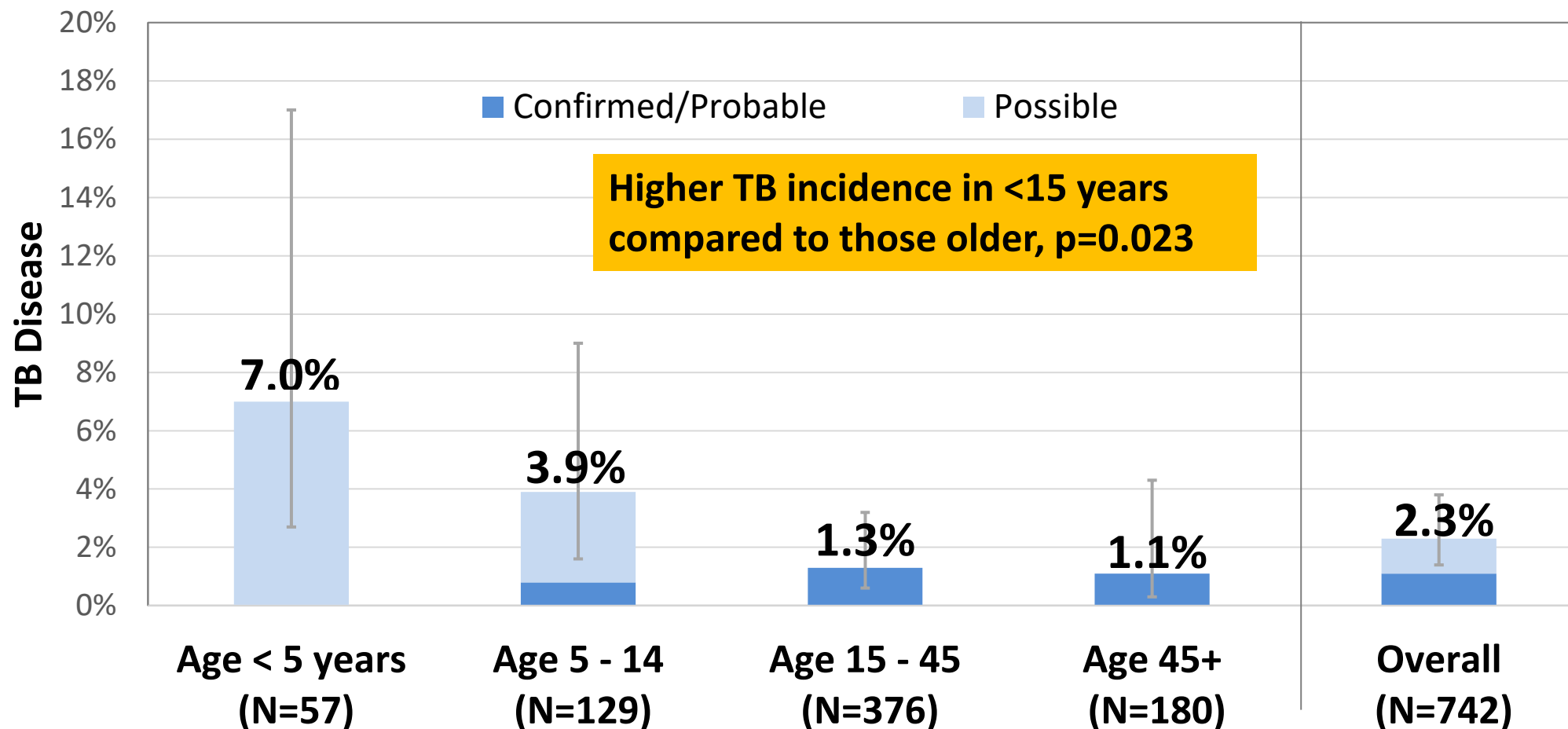


HHC Characteristics evaluated in Step 2 follow-up

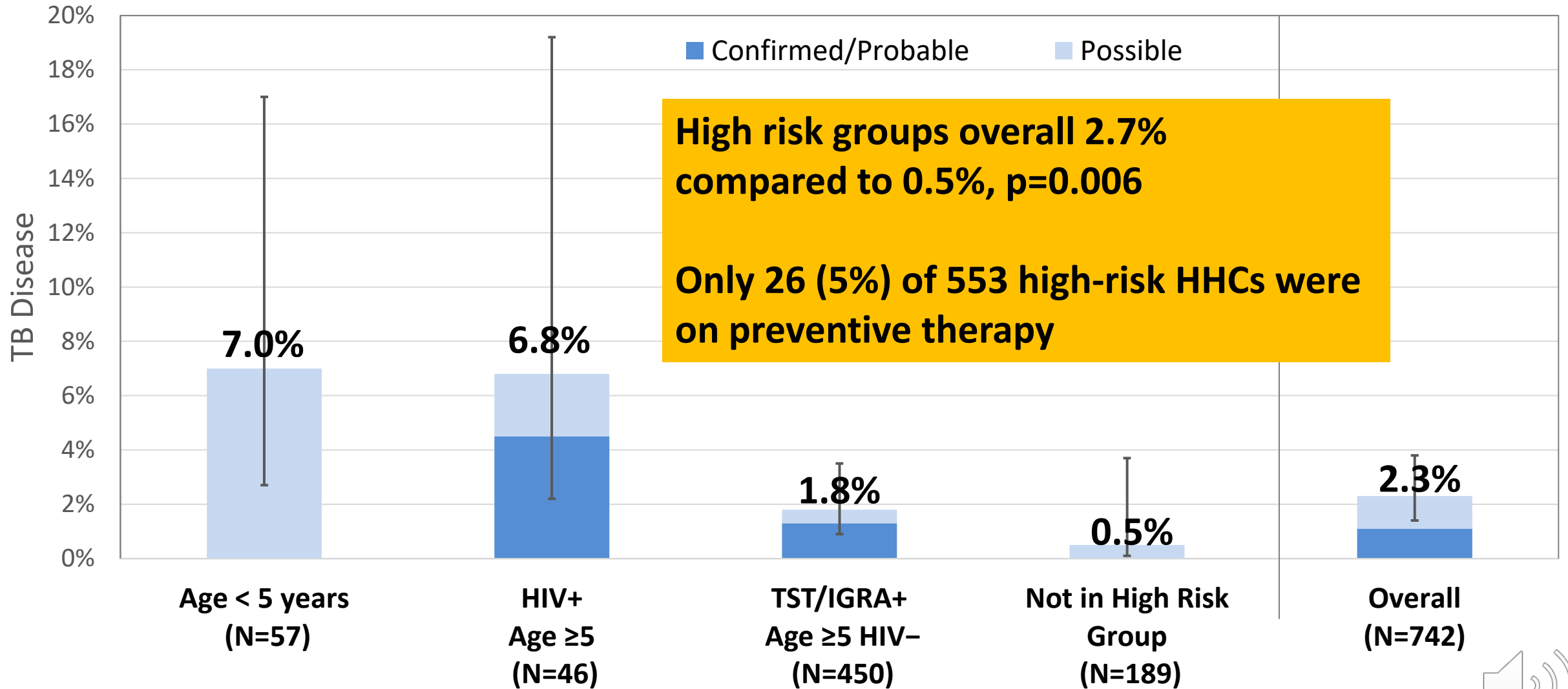
Characteristic	HHC (N=844)
Median age, years (interquartile range)	25 (11,43)
Female	497 (59%)
Countries (# sites)	
Botswana (1)	36 (4%)
Brazil (1)	17 (2%)
Haiti (1)	39 (5%)
India (2)	188 (22%)
Kenya (1)	10 (1%)
Peru (2)	181 (21%)
South Africa (7)	345 (41%)
Thailand (1)	28 (3%)
Risk group	
Group 1: < 5 years old	87 (10%)
Group 2: ≥5 years and HIV+	48 (6%)
Group 3: ≥5 years and HIV-/unknown and LTBI+	501 (59%)
Not in groups 1-3	200 (24%)
Active TB prior to Step 1	8 (1%)



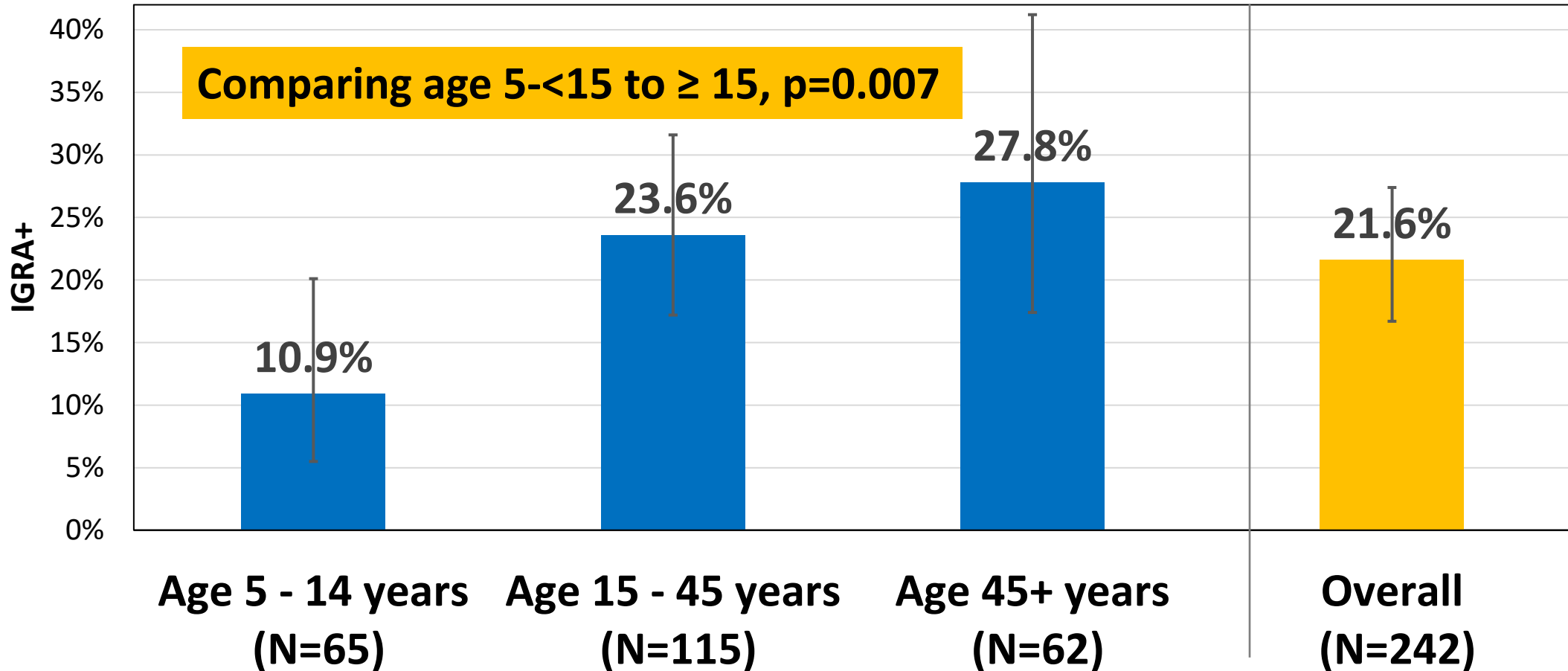
Significant differences in age-specific incidence of TB disease among household contacts



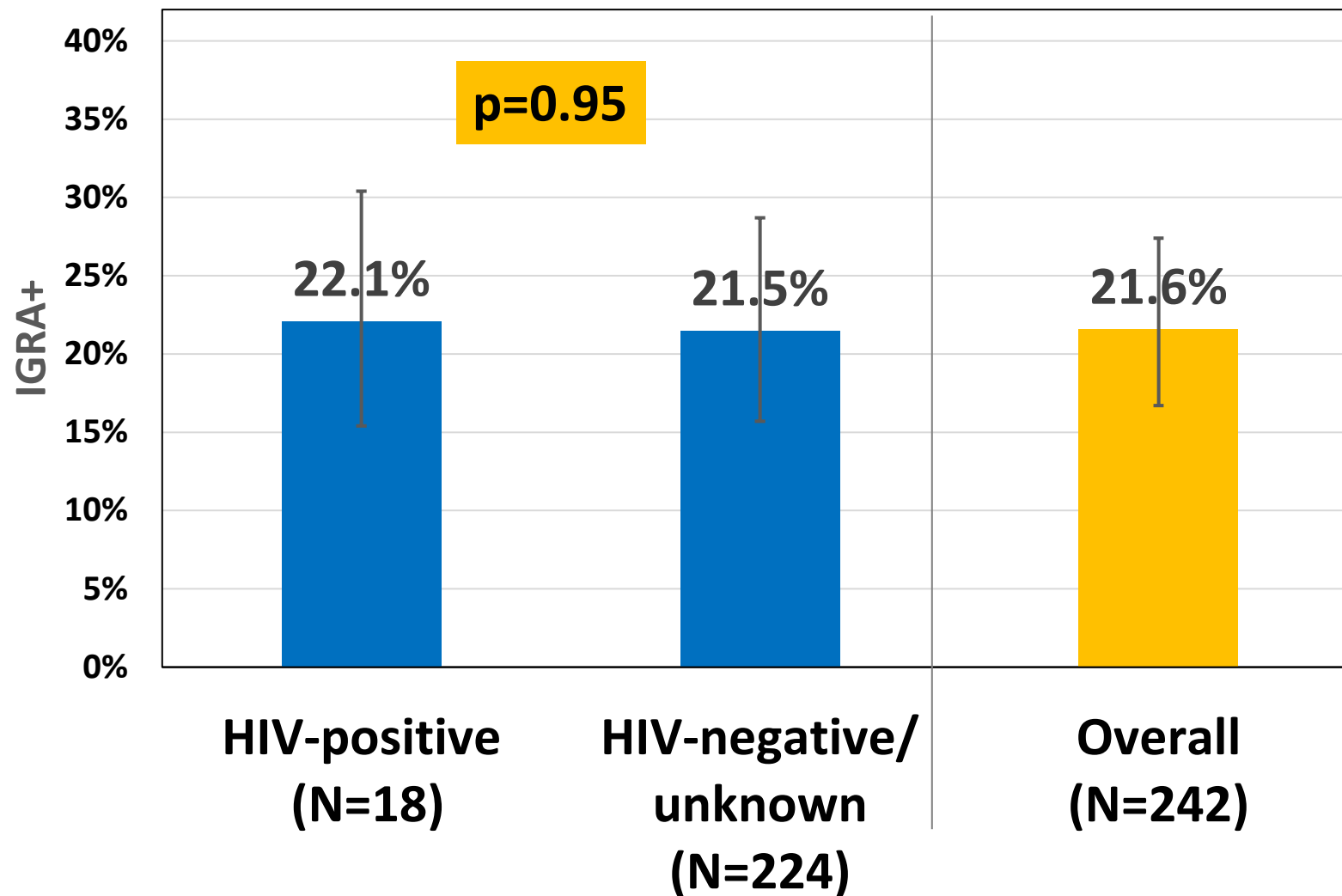
Cumulative incidence of TB Disease significantly differs by risk group



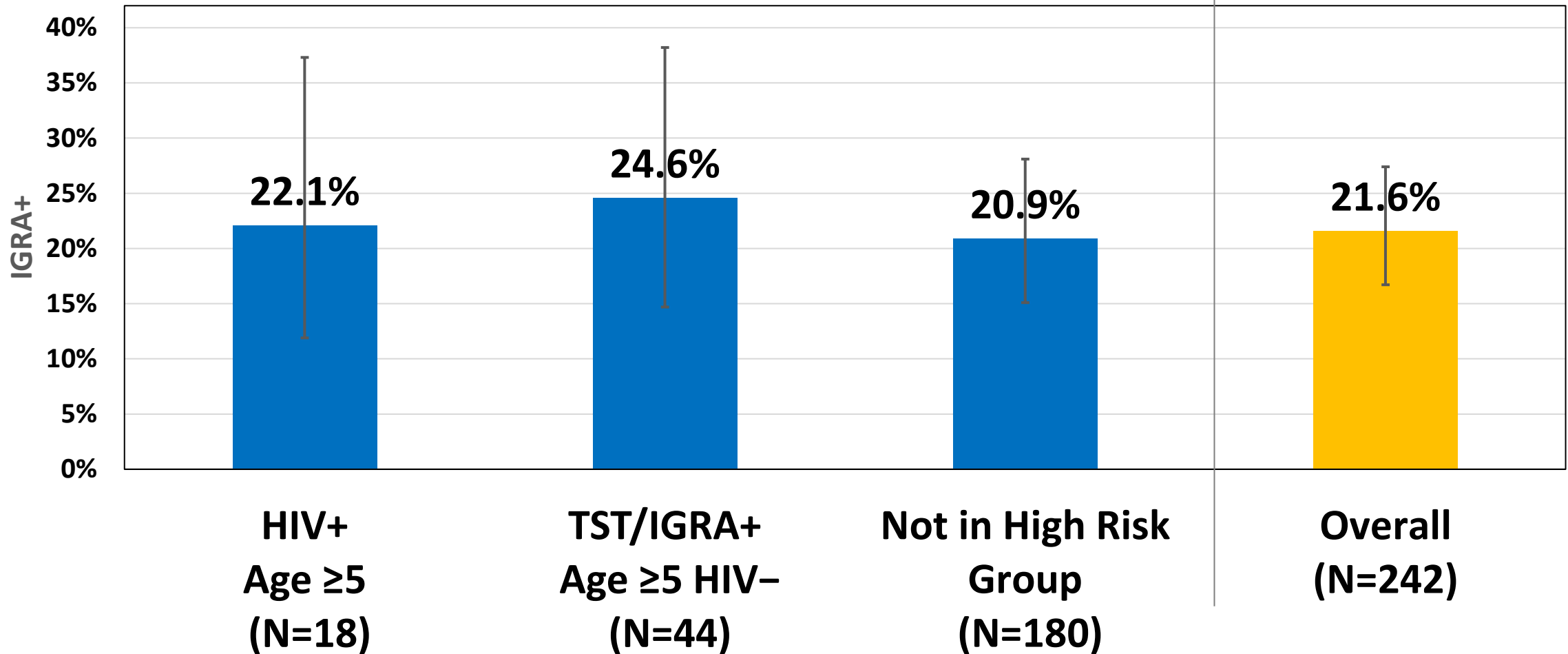
Increasing age-specific incidence of TB infection (IGRA conversion) at 1 year of follow-up among household contacts of RR/MDR TB cases



No observed difference in incident TB infection (IGRA conversion) by HIV status



Cumulative incidence of TB Infection by risk group



Summary

- Cumulative TB disease incidence was 2.7% in high risk HHCs compared to 0.5% not in high risk group
 - Highest in younger age but many were not confirmed microbiologically
 - Higher in HIV+ vs HIV- but small numbers so statistically non-significant
- Cumulative TB infection incidence high: 21% converted
 - Increased by age
 - No difference by HIV status
- Only 5% of high risk HHCs on preventive therapy
- Novel TB prevention strategies are urgently needed



Acknowledgments



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Thank you

