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WORLD CONGRESS OF EPIDEMIOLOGY 2024

Sex differences in *Mycobacterium tuberculosis* immunoreactivity risk in Blantyre, Malawi: a community-based prevalence survey

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26th September 2024

Objectives of this talk

1. Sex differences in global TB epidemiology

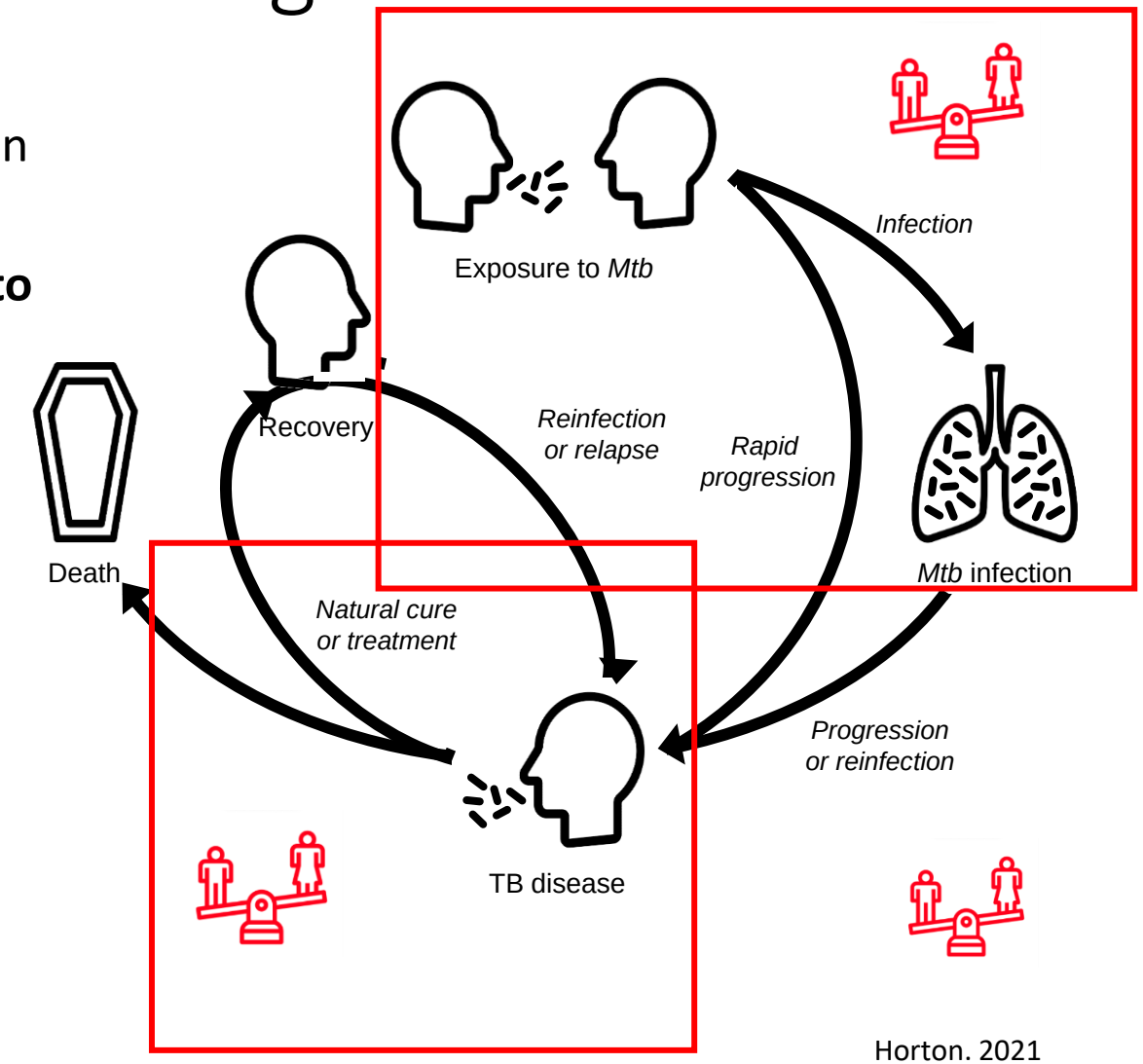
2. Rapidly changing TB epidemiology in Malawi

3. *Mtb* infection prevalence survey: objectives, study design & preliminary findings

4. Discussion: summary of findings & relevance for future pre- & post-infection interventions

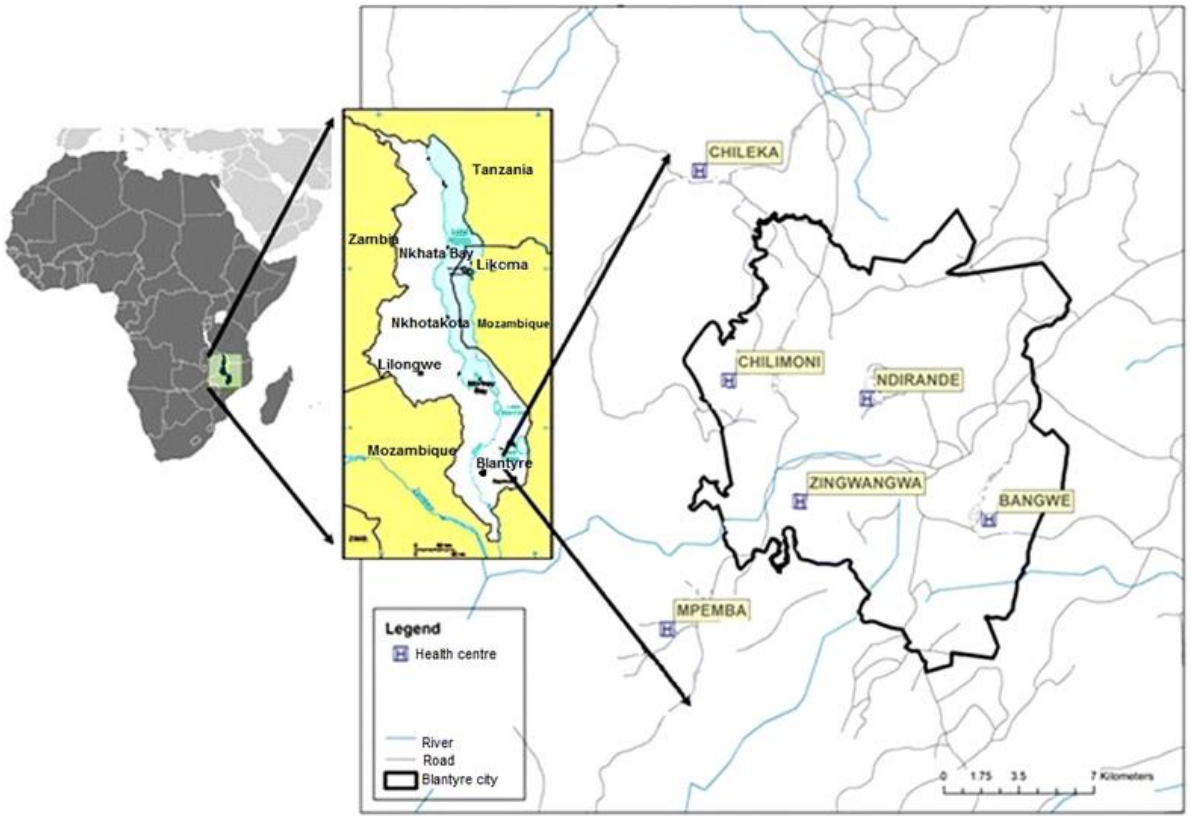
Sex differences in TB disease: from *Mycobacterium tuberculosis* (*Mtb*) exposure through to TB disease

- Men account for 2x TB case incidence globally, and a majority of transmission towards women and children
- Sex differences in **exposure to** and/or **susceptibility to infection with** *Mtb*
- **Progression** from *Mtb* infection to TB disease
- **Access to case detection & treatment** and/or mortality
- **Understanding origins of sex differences in TB disease could inform targeted interventions to address sex differences in TB disease.**



Horton. 2021

TB epidemiology in Blantyre, Malawi



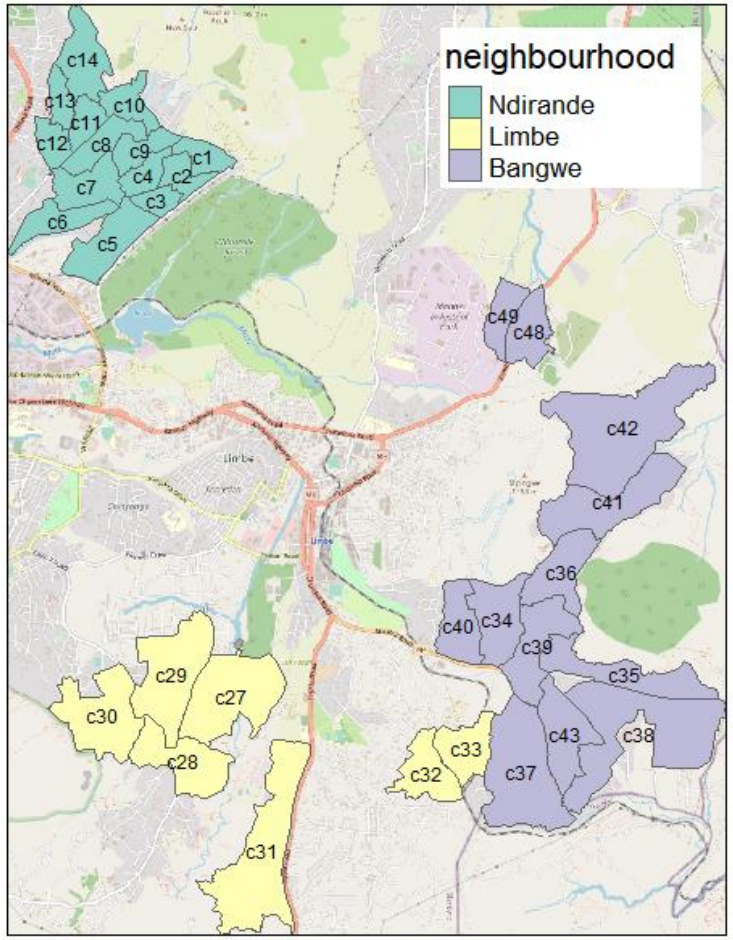
- Malawi: country population: 20 million (Blantyre City: ~1.2millon (NSO))
- TB incidence: 125 (61-212) per 100,000 (WHO, 2023); neonatal BCG vaccine coverage ≥95%
- Outdated population-representative age/sex-specific *Mtb* infection prevalence data for adolescents & adults

Source: Mathanga et al. Mal J. DOI: 10.1186/s12936-016-1623-9

Study objectives & design

- What is the sex-specific prevalence of *Mtb* infection ("immunoreactivity") among adolescents (10-17 y/o) and adults (18-40 y/o) in urban Blantyre, Malawi?
- To detect Male-to-Female (M:F) prevalence ratios: 1.2 to 2

- Cross-sectional study, randomly sampled households in 3 peri-urban townships of Blantyre (high incidence, previous studies)
- Sample size: ≥640 adolescents & ≥1920 adults to detect M:F prevalence ratios ≥ 1.34 (assuming prevalence ≥20% in females, 80% power, alpha=95%)
- Children 1-5 y/o in same households & from primary health clinics (Dr H Rickman, Wellcome Clinical PhD Fellow, LSHTM)



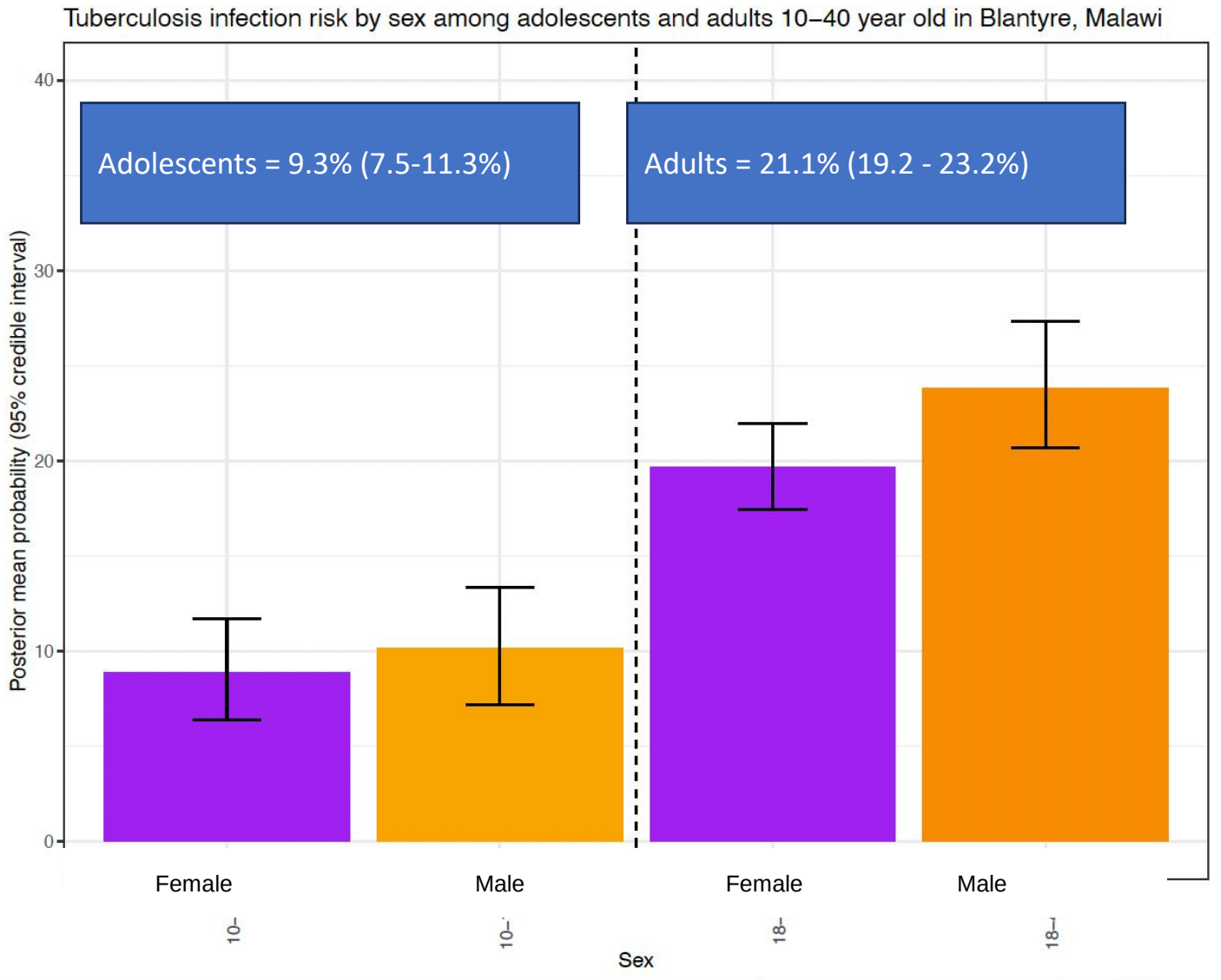
- Household- & individual-level sociodemographic & clinical characteristics
- **QuantiFERON® Plus** (QFT-Plus): interferon gamma release assay (IGRA), KUHeS TB lab

Participant characteristics (N = 2,656, excluding 59 participants with indeterminate QFT-Plus result)

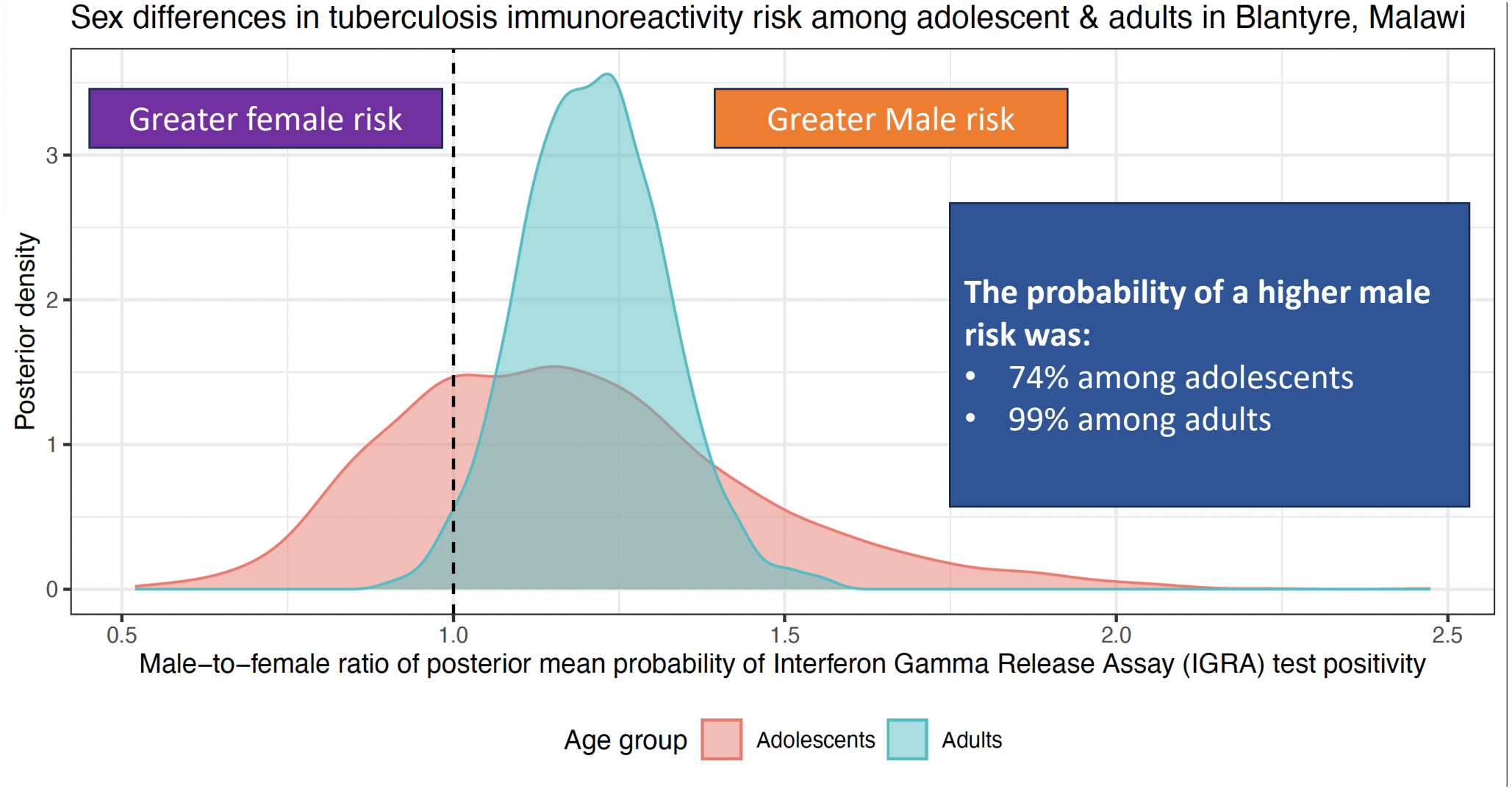
Characteristic	**Adolescent 10-17**, N = 850	**Adult 18-40,** N = 1,806
Age, median (IQR)	14 (12, 16)	25 (21, 31)
Sex, n (%)		
Female	444 (52%)	1151 (64%)
Male	406 (48%)	655 (36%)
HIV status (self-reported)		
Positive	16 (1.9%)	152 (8.4%)
Negative	301 (35%)	1442 (80%)
Unsure	533 (63%)	212 (12%)
QFT-Plus result		
Positive	78 (9.2%)	380 (21%)
Negative	772 (91.0%)	1426 (79%)

Phiri et al. Unpublished. 2024

IGRA positivity risk by age & sex: unadjusted analysis (N=2656, excluding 59 participants with indeterminate results)



Male-to-female IGRA positivity probability ratios: unadjusted analysis



Summary of preliminary findings

- *Mtb* immunoreactivity **overall prevalence was lower than expected**, and compared with Zambia & South Africa (? impact of IGRA resistance, reversion/loss of immunological response unclear)
- *Mtb* immunoreactivity **unadjusted prevalence appears to increase with age, as expected, and higher in males compared to females among both adolescents & adults**, but data are preliminary, 95% compatibility intervals overlap
- Possible explanation for sex differences: ↑ exposure +/- susceptibility among males compared to females, due to biological and/or sociobehavioural factors (alcohol, smoking, employment & social contact)
- Age- & sex-specific *Mtb* infection prevalence data will inform planning of imminent TB infection interventions for adolescents & adults, e.g. new vaccines, preventive therapy

Acknowledgements






THE LIGHT CONSORTIUM

UKaid from the British people

wellcome

& the TB lab team at Kamuzu University of Health Sciences