

Measuring TB transmission and its impact at community level: what is missing?

Peter Godfrey-Faussett

Hospital for Tropical Diseases, London

London School of Hygiene and
Tropical Medicine





La Belle Dame sans Merci

I see a lily on thy brow,
With anguish moist and fever-dew,
And on thy cheeks a fading rose
Fast withereth too.

I saw pale kings and princes too,
Pale warriors, death-pale were they all;
They cried -'La Belle Dame sans Merci
Hath thee in thrall!'

I saw their starved lips in the gloam,
With horrid warning gaped wide,
And I awoke and found me here,
On the cold hill's side.



John Keats 1819



Nobel laureate address 1905

"One of the most powerful weapons, if not the most powerful, which we can bring into use against TB are ***social welfare centres***:

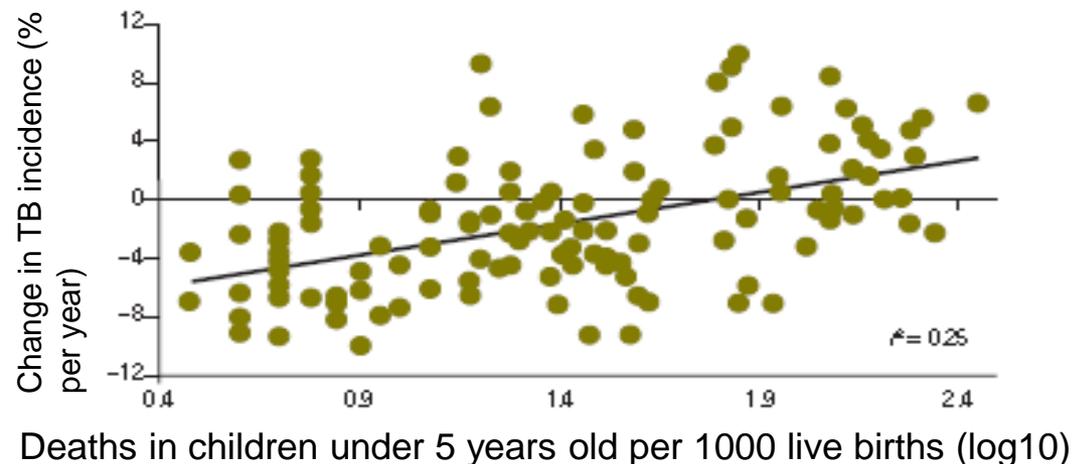
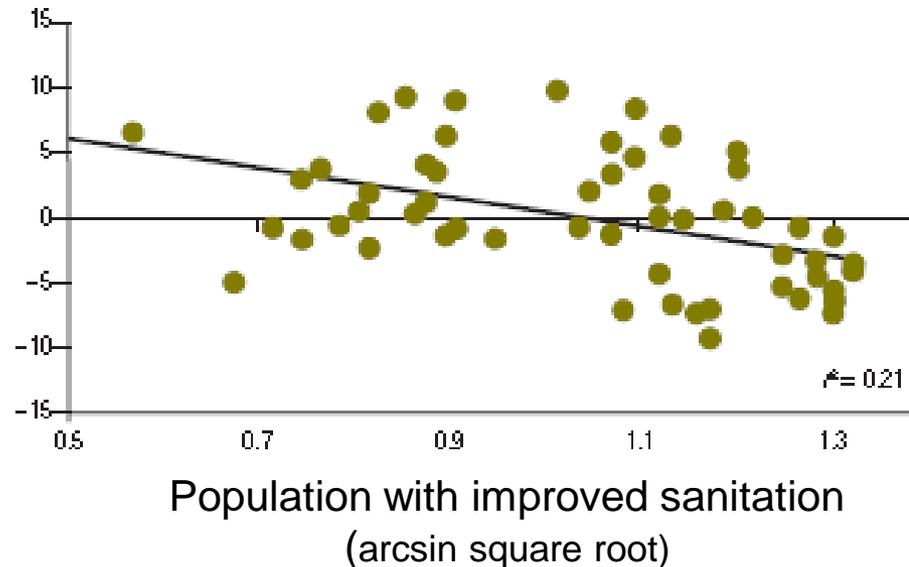
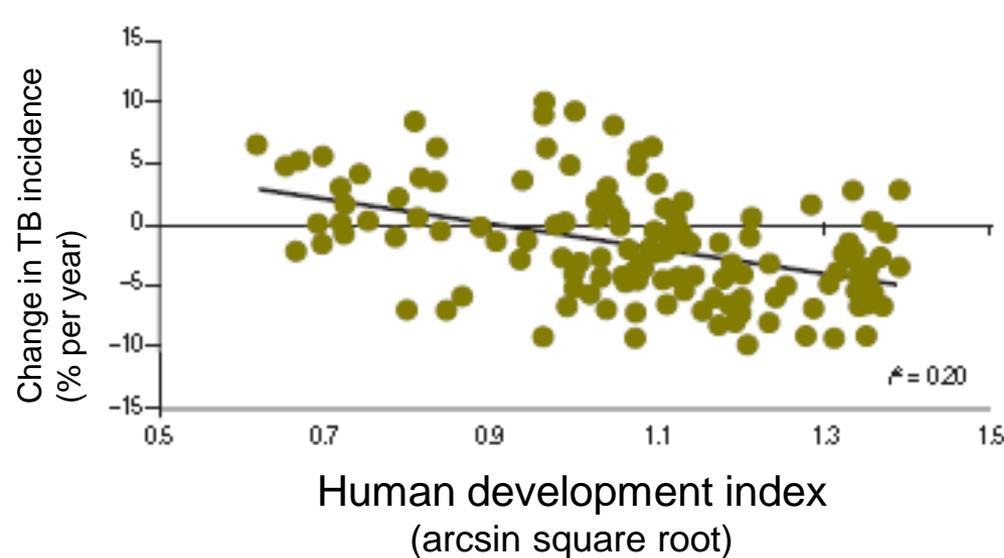
- ...the sick person is visited in his home, and is given instruction and advice concerning cleanliness.
- ...If living conditions are bad, then money is granted...
- ...poor families are supported by granting them appropriate food, fuel, etc".
- ...private action is virtually powerless against this nuisance, while the State can easily remedy the situation with suitable laws"



Trends in tuberculosis incidence and their determinants in 134 countries

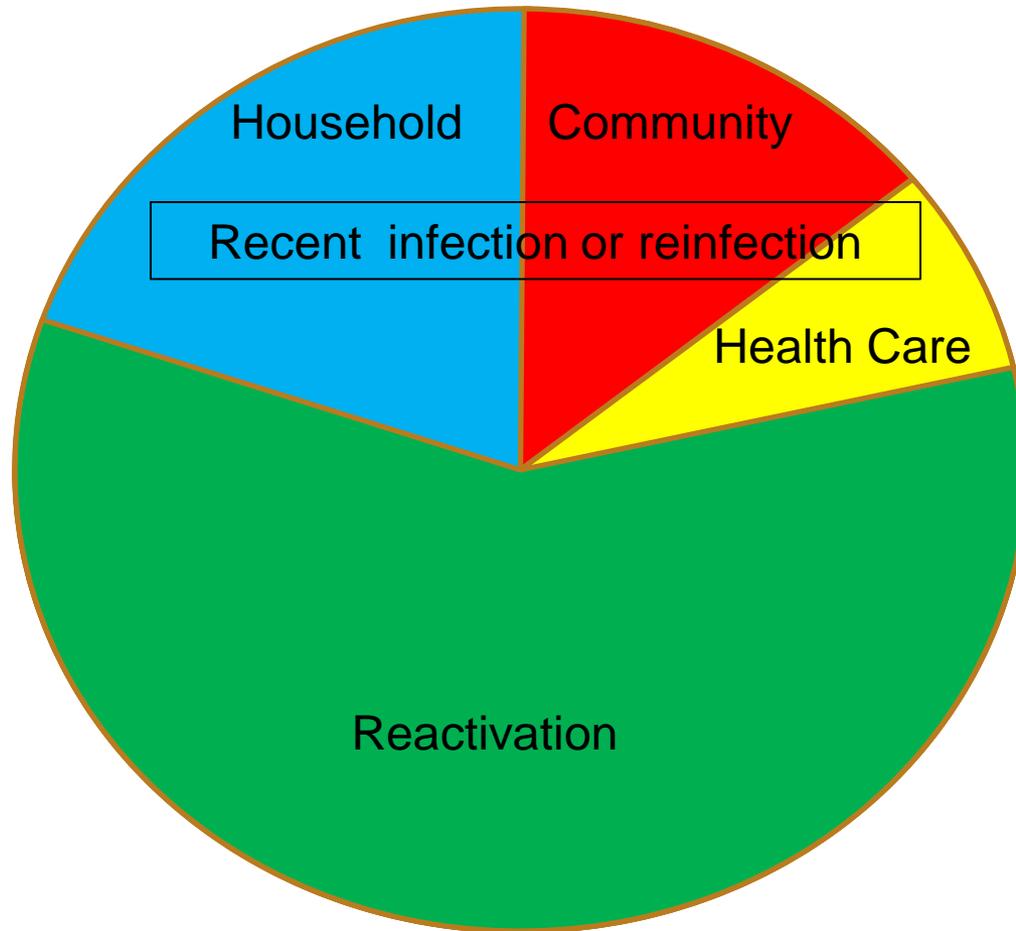
C Dye, K Lonroth, B Williams and M Raviglione

Bull World Health Organ 2009;**87**;683-691



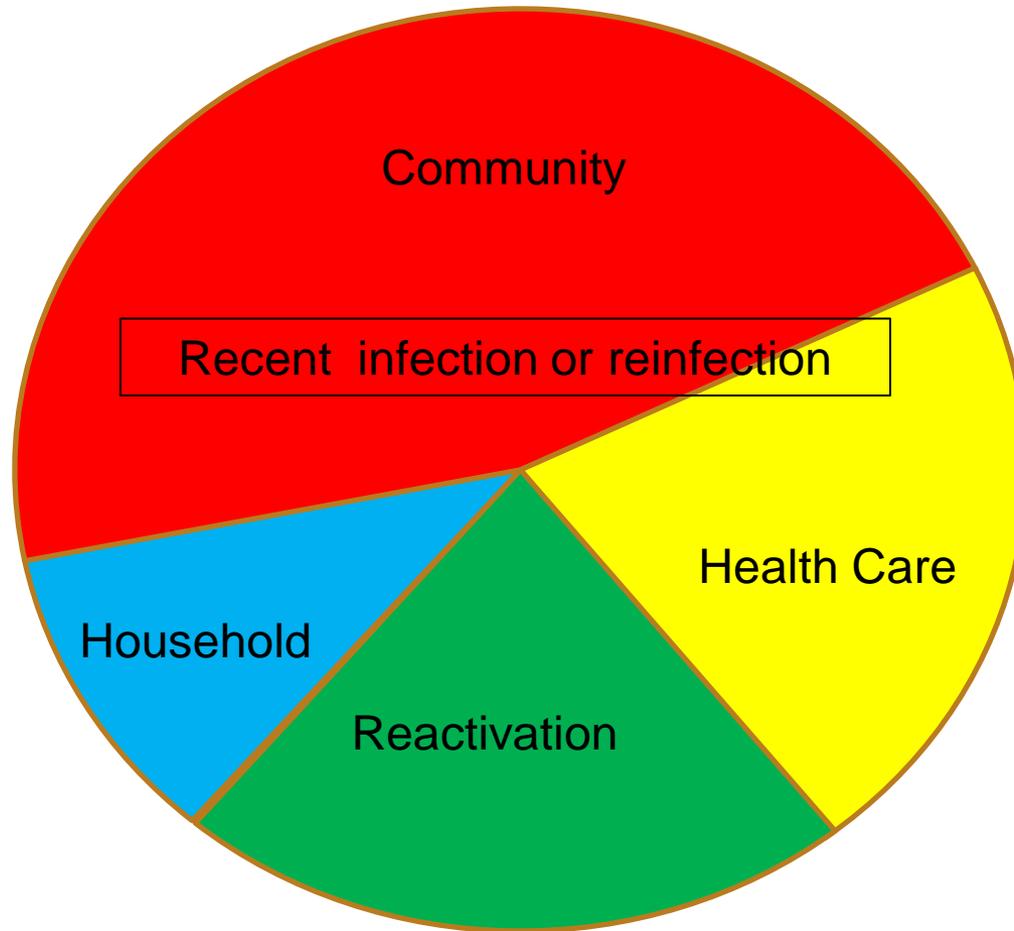
Poverty causes TB

Why did your last 100 patients develop tuberculosis?



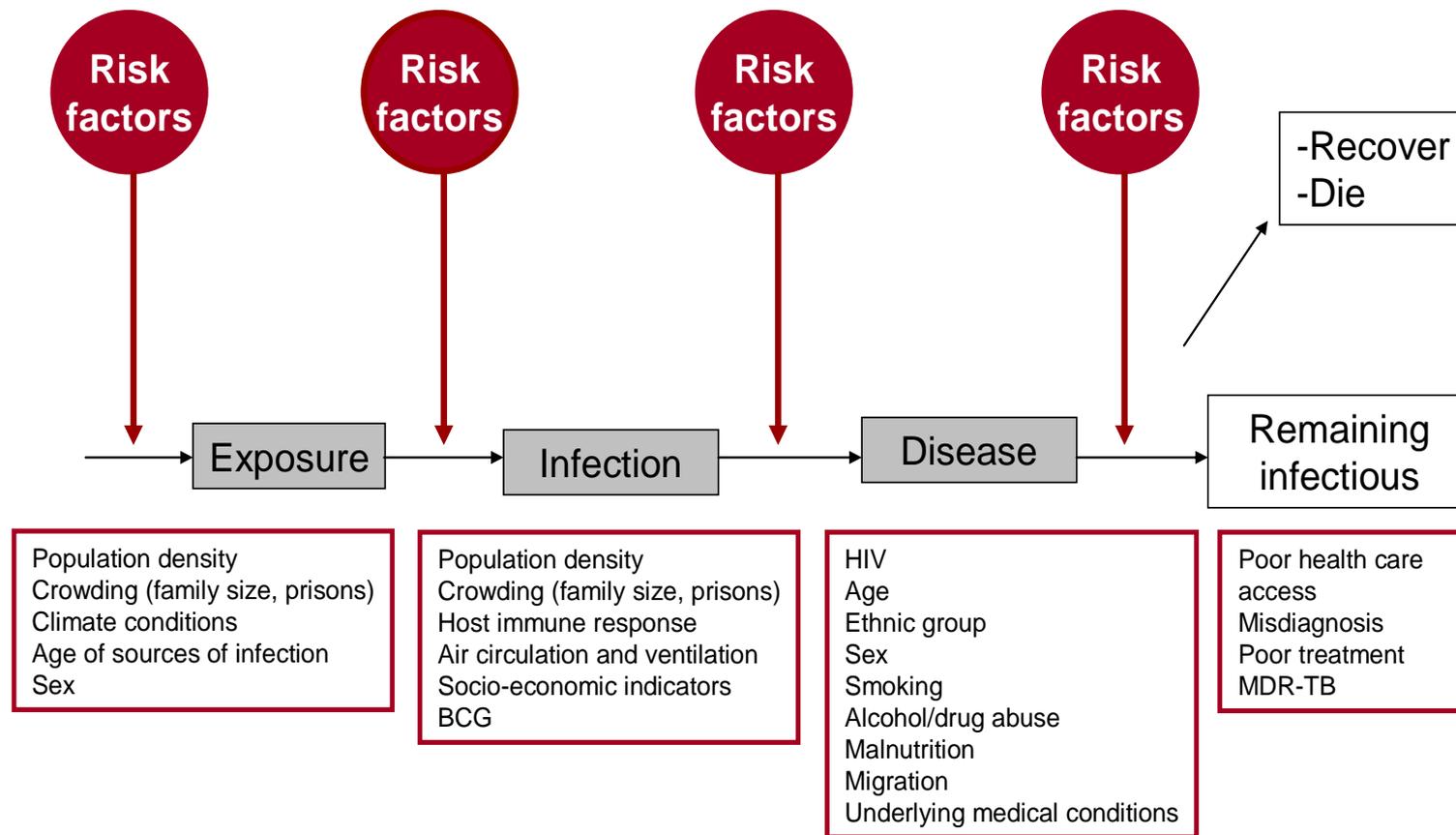
IPT, ART > Contact tracing > Enhanced case finding > Infection control

Why did your last 100 patients develop tuberculosis?



Enhanced Case Finding > Infection control > IPT, ART > Contact tracing

HIV or AIDS – Infection or Disease

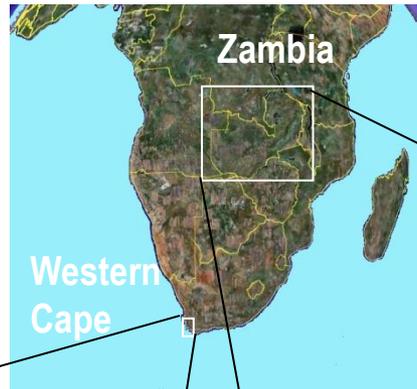


- Various poverty measures associated with prevalent culture positive tuberculosis in ZAMSTAR baseline studies
- Negatively associated with IGRA positivity



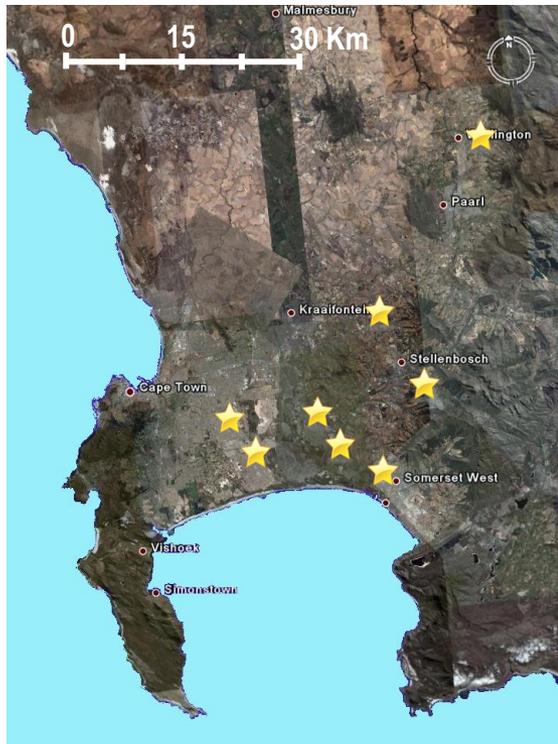
Location of the 24 communities selected

Southern Africa

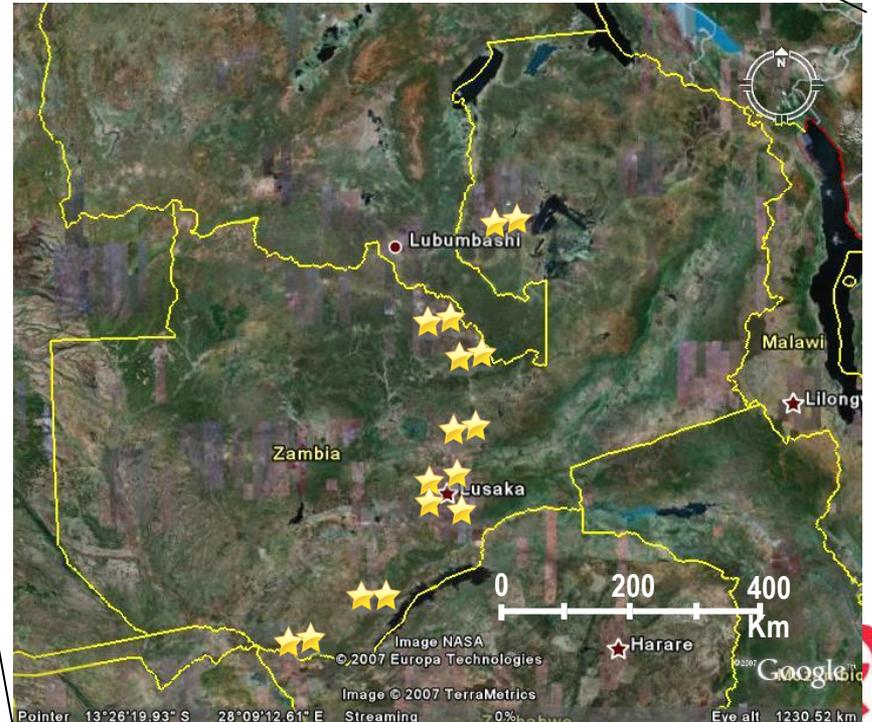


A community randomized trial of two interventions delivered to ~1,200,000 people while strengthening the existing health systems

Western Cape



Zambia



ZAMSTAR Interventions

Enhanced Case Finding

- Community Mobilisation and sputum collection
- School intervention
- Open Access at the clinic
- Guiding Principles
 - Every person able to give sputum within 30 min walk
 - Sputum smear results within 48 hours

Household Counselling

- Using a TB patient as the Gateway to a household at risk of TB and HIV
- 3 visits (0,2, completion TB treatment)
- Group education TB/HIV
- TB screening
- HIV testing (group, couple, individual)
- Counselling and referral for care



ZAMSTAR Trial Design

- Total Population 962,655
- 6 communities per arm
- Primary endpoint:
 - Prevalence of TB
 - Enhanced case finding (ECF) Vs no ECF
 - Household Intervention (HH) Vs no HH
- Secondary Endpoint:
 - Community level: TB transmission
 - Household level: TB outcomes, TB incidence, HIV incidence



TB/HIV at the clinic: 257,698



Enhanced Case Finding: 148,090



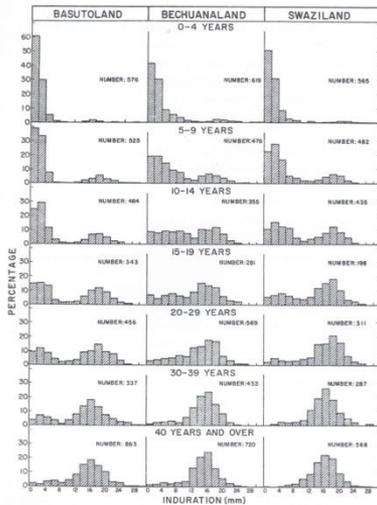
Household: 257,729



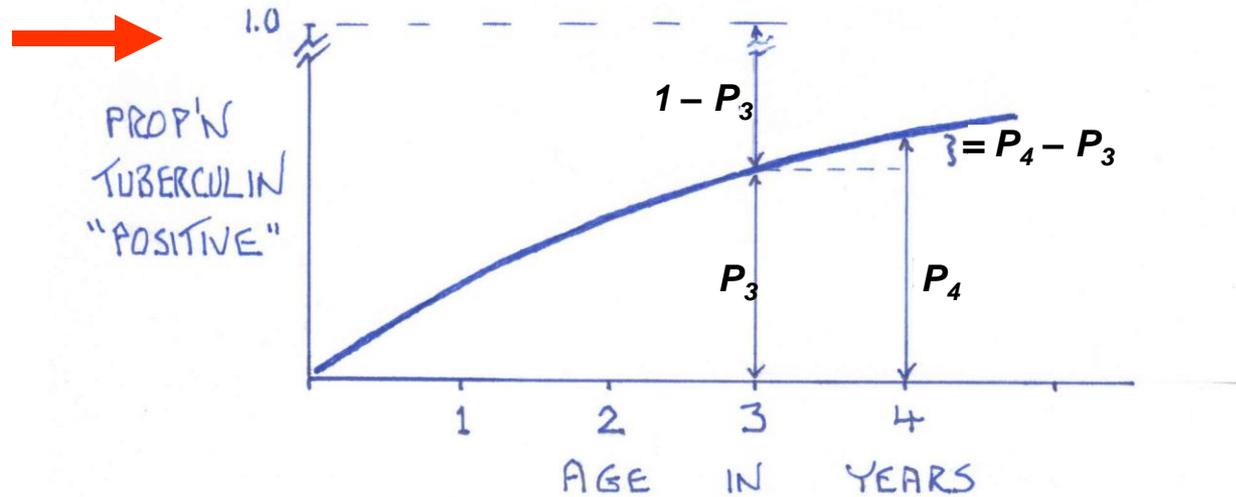
ECF & Household: 299,138



Fig. 4 Distributions by size of reactions to Mantoux 5 TU in specified age-groups



CALCULATION OF ANNUAL RISK OF INFECTION



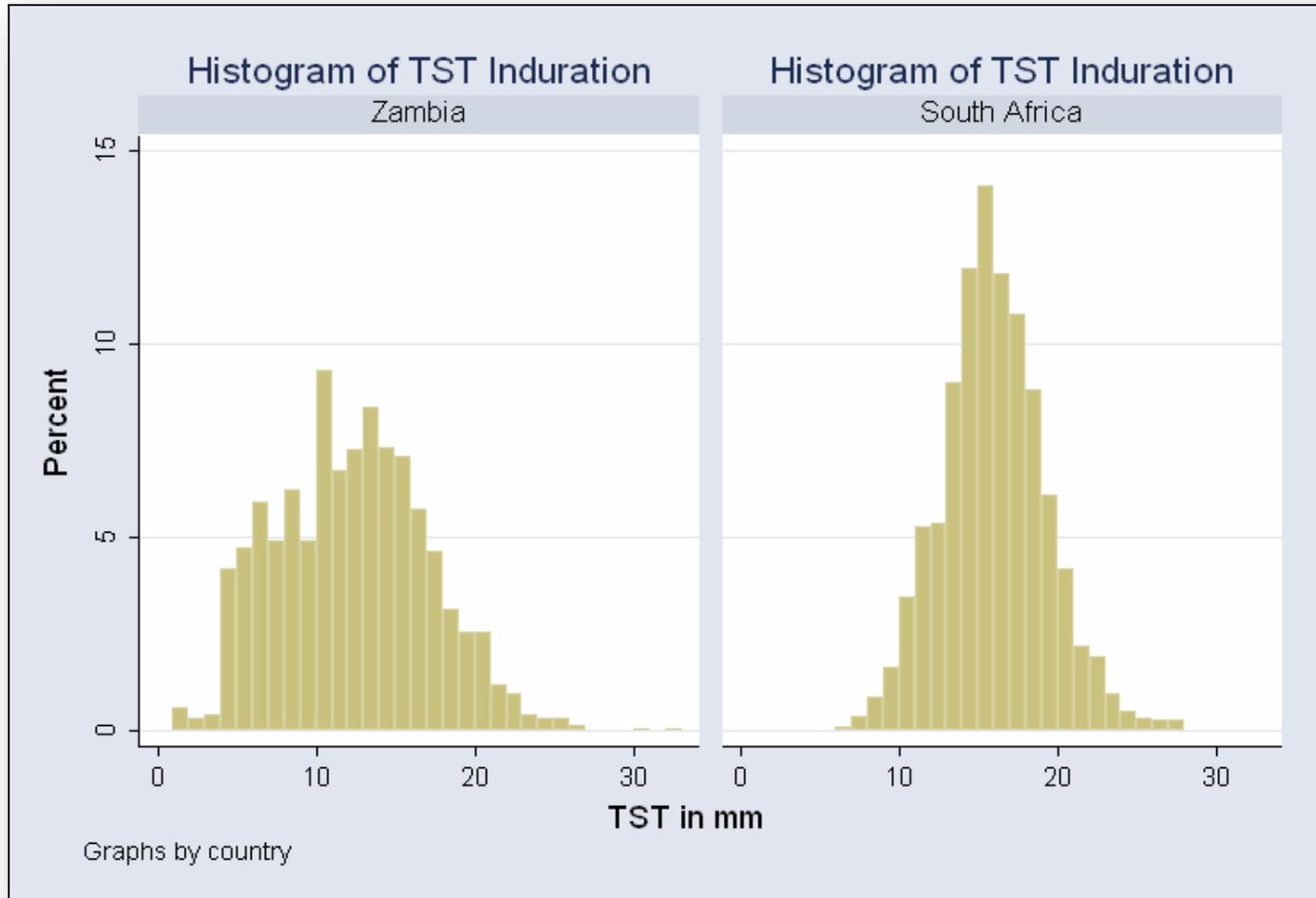
- Cumulative risk of infection
- Constant risk of infection over time
- Constant risk of infection over age
- School children
- BCG

$$\text{Annual risk of infection } (r) = 1 - (1 - P_3)^{1/3}$$

Baseline survey results

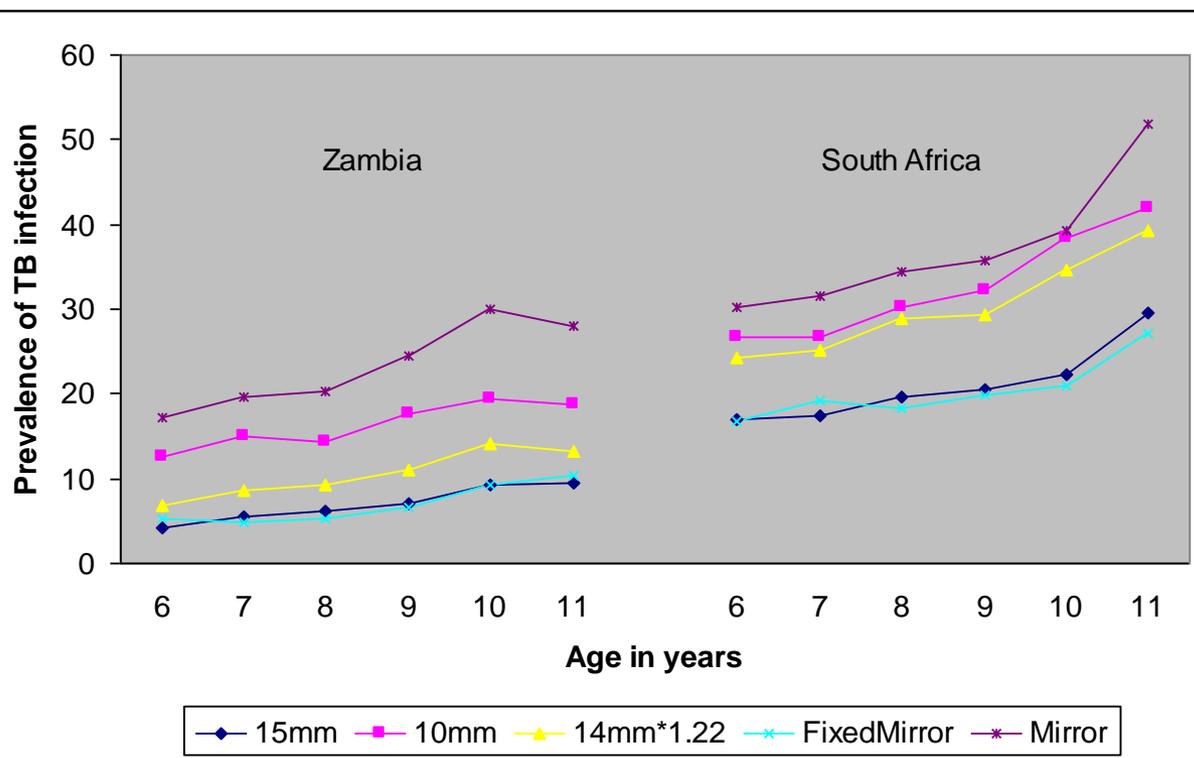
- TST surveys conducted in 98 schools in the 24 communities
- 21,393 children had tests administered and read
- Sex-51% female
- Mean age at baseline-8.5 years
- % children TST positive (10 mm)
 - Zambia: 16.5% (95% CI:12-21.1)
 - SA: 30.5% (95% CI:22.9-38.2)
- Little difference among children with a BCG scar and those without.

TST frequency distributions by country



Distribution restricted to non-zero TST indurations

Prevalence of infection depends on method used

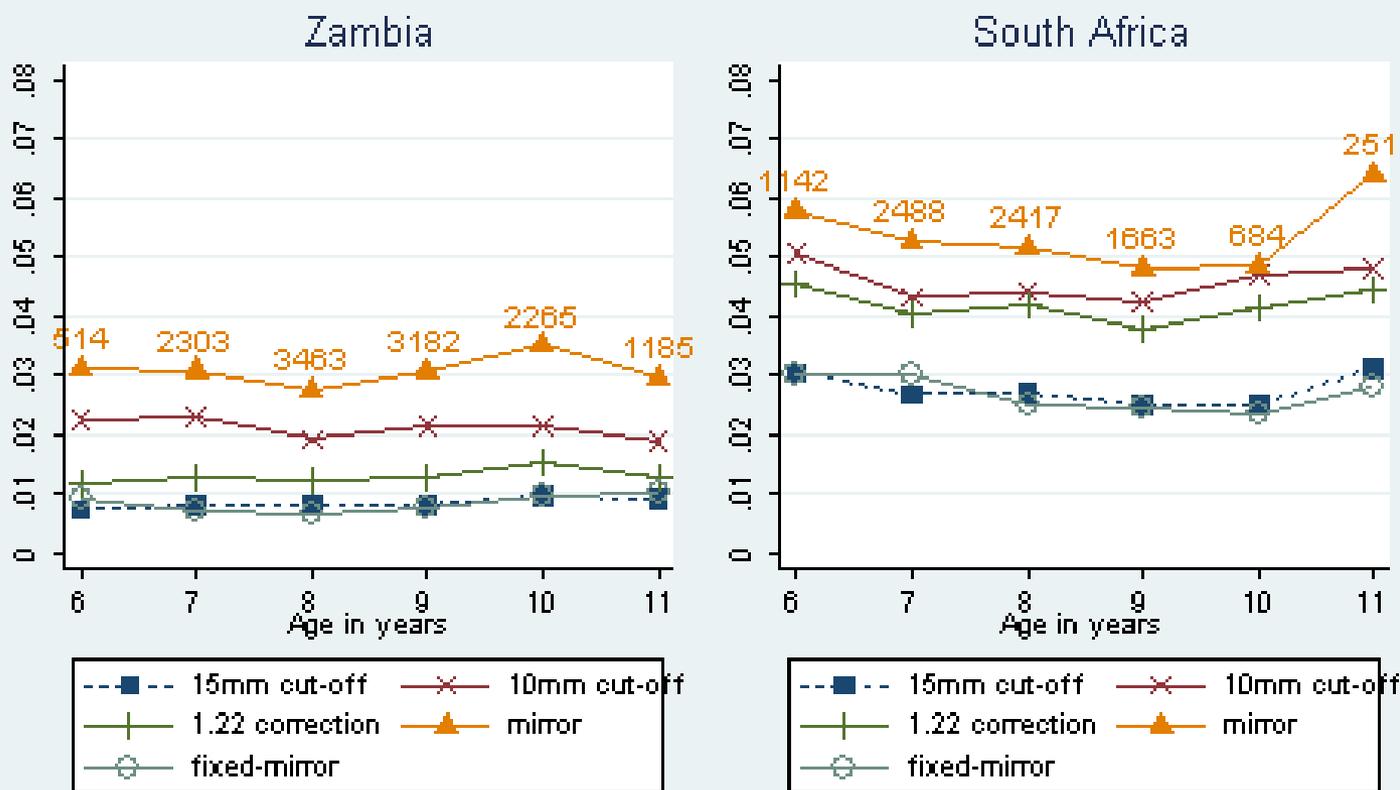


- Individual
- Community
- Cut-offs
- Mirrors
- Mixtures

Shanaube et al. **PLoS One** 2009;4:e7749

ARI by age group

Figure 2: Annual risk of tuberculous infection, as calculated using five methods, by country and age



How to detect changes in risk of infection?

TB

- Modelling from prevalence
- IGRA vs. TST
- ARI
- Cohorts

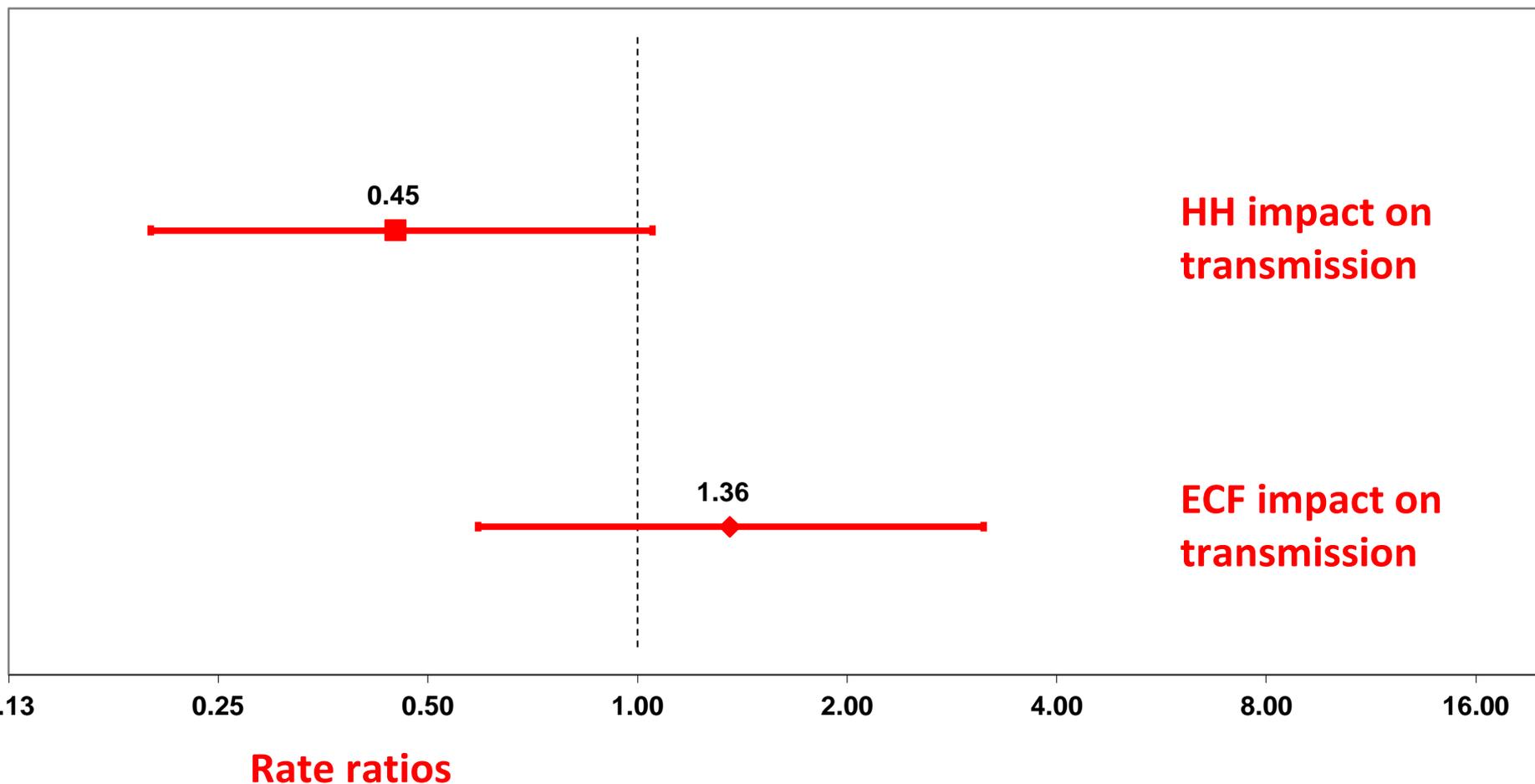
HIV

- BED assays
- Pyrosequencing in an individual
- High resolution melting point methods
- Modelling from young adults
- Cohorts

Study Design

- Longitudinal design
 - Direct measure of incidence of tuberculous infection
 - Follow children TST negative at baseline and measure rate of TST conversion
 - Advantage over repeated cross sectional design in that cumulative incidence would be acquired throughout child's life and not just for the duration of the interventions
 - Trial outcome, so favour specificity over sensitivity

Rate ratios for intervention effect at the community level, comparing communities with intervention to those without



Conclusions

- TB transmission three times higher in Western Cape communities than in Zambian communities (4.5 vs. 1.2%/pyrs).
- For both countries wide variability among communities in TB infection prevalence
- Longitudinal design practical & met the objectives of our study.
- Results suggest HH intervention reduced TB transmission in these 24 communities.
- Consistent with evidence that suggests that HH intervention also reduced TB prevalence in the same communities.
- Focus on transmission of infection (rather than disease) would be a useful step forward
- New tools/algorithms to determine recent infection needed



**Chipolopolo win Africa Cup of Nations
12th February 2012**