Modeling to inform implementation strategies of TB vaccines.

Sourya Shrestha
TB MAC
Washington DC, Sep 14, 2018

Motivation

TB is heterogenous — factors that drive (and/or show the manifestation) could be geographic, demographic, socio-economic, immunological/biological, etc.

Motivation

PLOS | ONE

Tuberculosis and Poverty: Why Are the Poor at Greater Risk in India?

Olivia Oxlade[1], Megan Murray[1,2,3]

TB prevalence (per 100,000) by Wealth Quintile

Socio-economic condition

Heterogeneity in tuberculosis transmission and the role of geographic hotspots in propagating epidemics

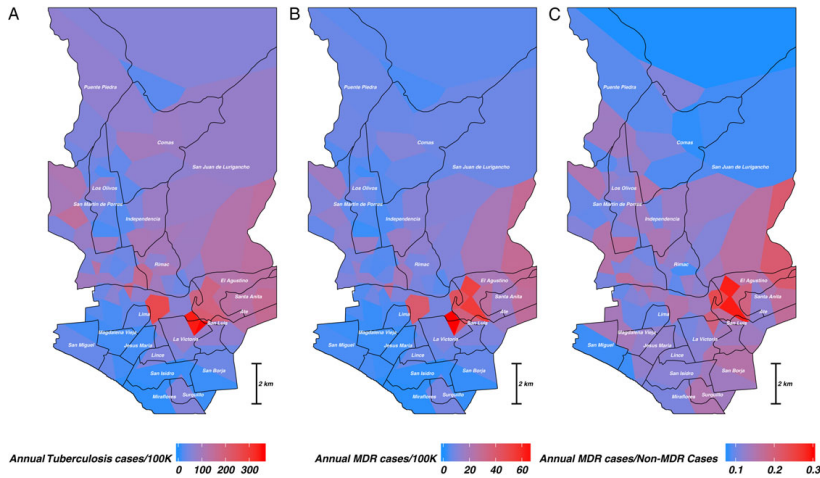David W. Dowdy[a,b,1], Jonathan E. Golub[a,b], Richard E. Chaisson[a,b], and Valeria Saraceni[c]

Geography

The Journal of Infectious Diseases

MAJOR ARTICLE

IDSA — Infectious Diseases Society of America

hivma — hiv medicine association

OXFORD

Identifying Hotspots of Multidrug-Resistant Tuberculosis Transmission Using Spatial and Molecular Genetic Data

Jonathan L. Zelner,[1] Megan B. Murray,[2] Mercedes C. Becerra,[3] Jerome Galea,[4] Leonid Lecca,[4] Roger Calderon,[4] Rosa Yataco,[4] Carmen Contreras,[4] Zibiao Zhang,[5] Justin Manjourides,[6] Bryan T. Grenfell,[7,8] and Ted Cohen[9]
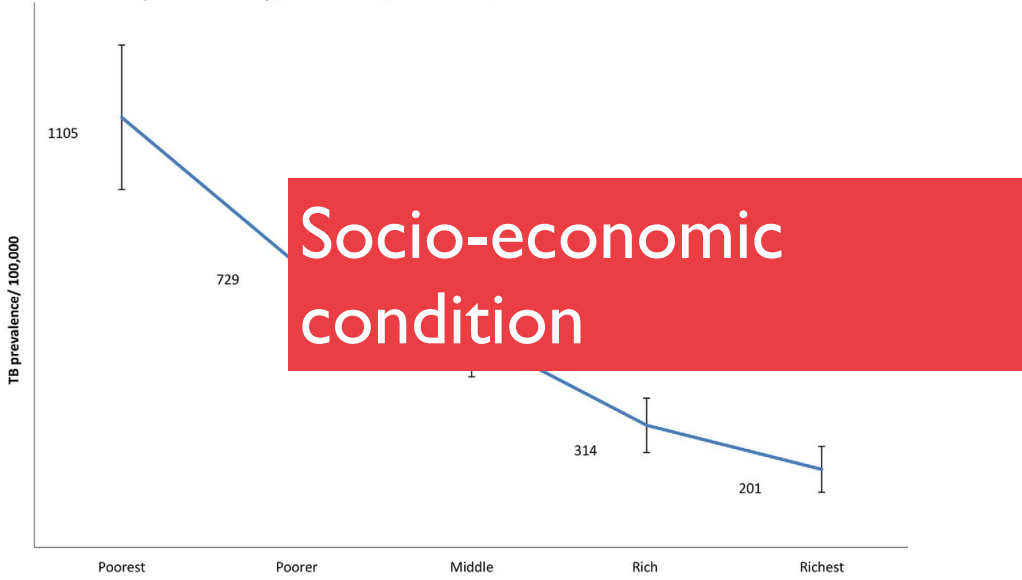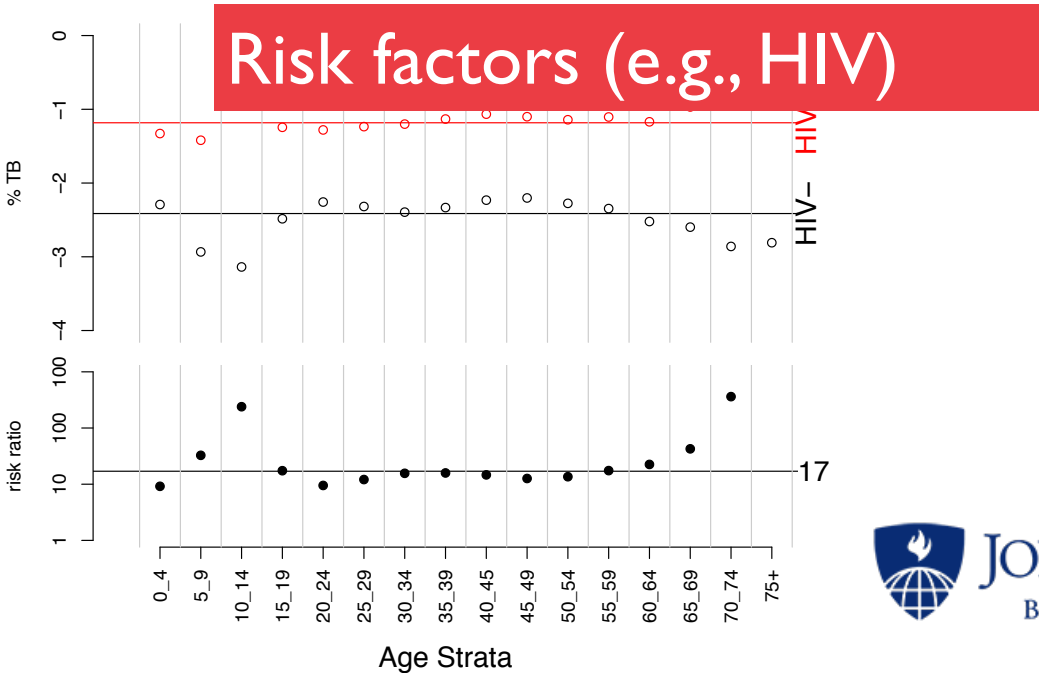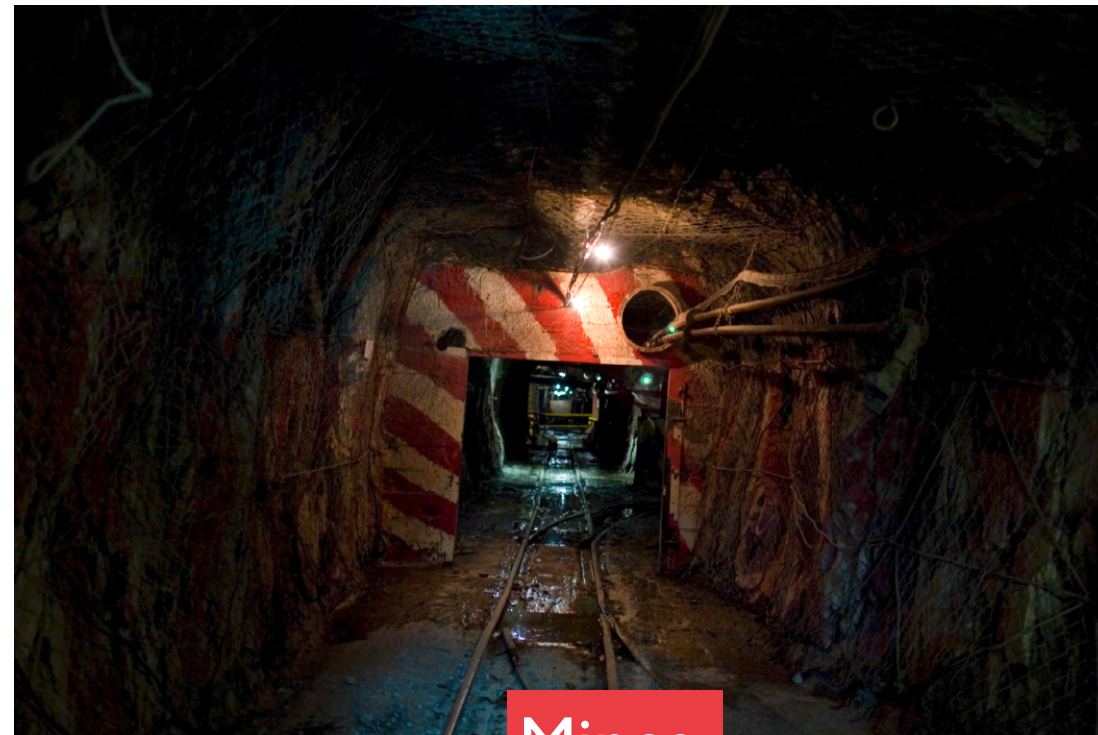
PLoS one

Burden of New and Recurrent Tuberculosis in a Major South African City Stratified by Age and HIV-Status

Robin Wood[1,2,3], Stephen D. Lawn[1,2,4], Judy Caldwell[5], Richard Kaplan[1,2], Keren Middelkoop[1,2], Linda-Gail Bekker[1,2]*

Risk factors (e.g., HIV)

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Motivation

Prisons

Mines

Slums

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Motivation

TB is heterogenous — factors that drive (and/or show the manifestation) could be geographic, demographic, socio-economic, immunological/biological, etc.

Targeted interventions that leverage these heterogeneities could be more effective.

Outline

**Part I: Geographically targeted adult TB vaccination in Gujarat, India.**
- Model conceptualization to capture heterogeneity & mixing in this settings.
- Data limitations.

Part II: Targeted TB vaccination in South African mining communities.
- Modeling South African mining communities.
- Comparing adult TB vaccination strategies.

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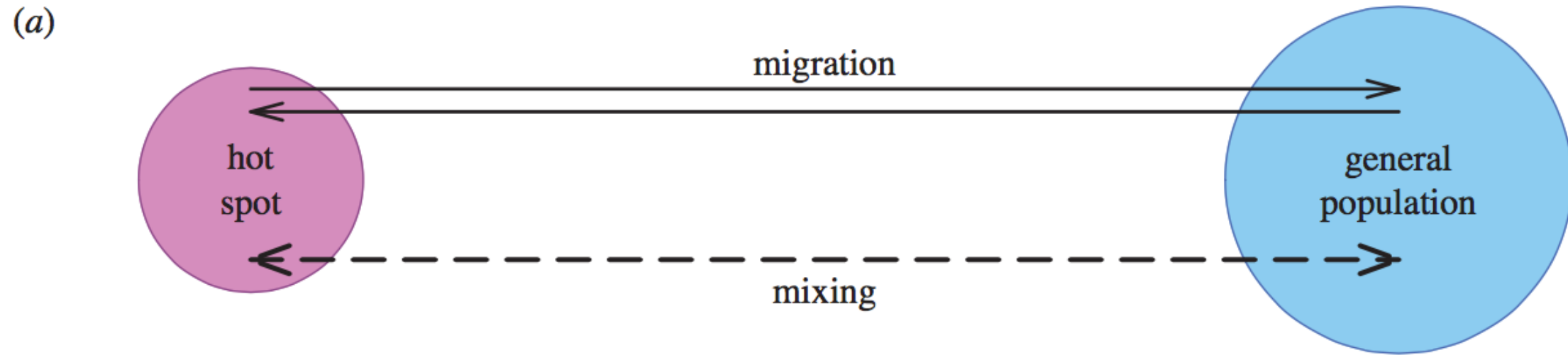*of* PUBLIC HEALTH

Part I

Geographically targeted adult TB vaccination in Gujarat, India (Shrestha et al, Interface, 2016)

Data
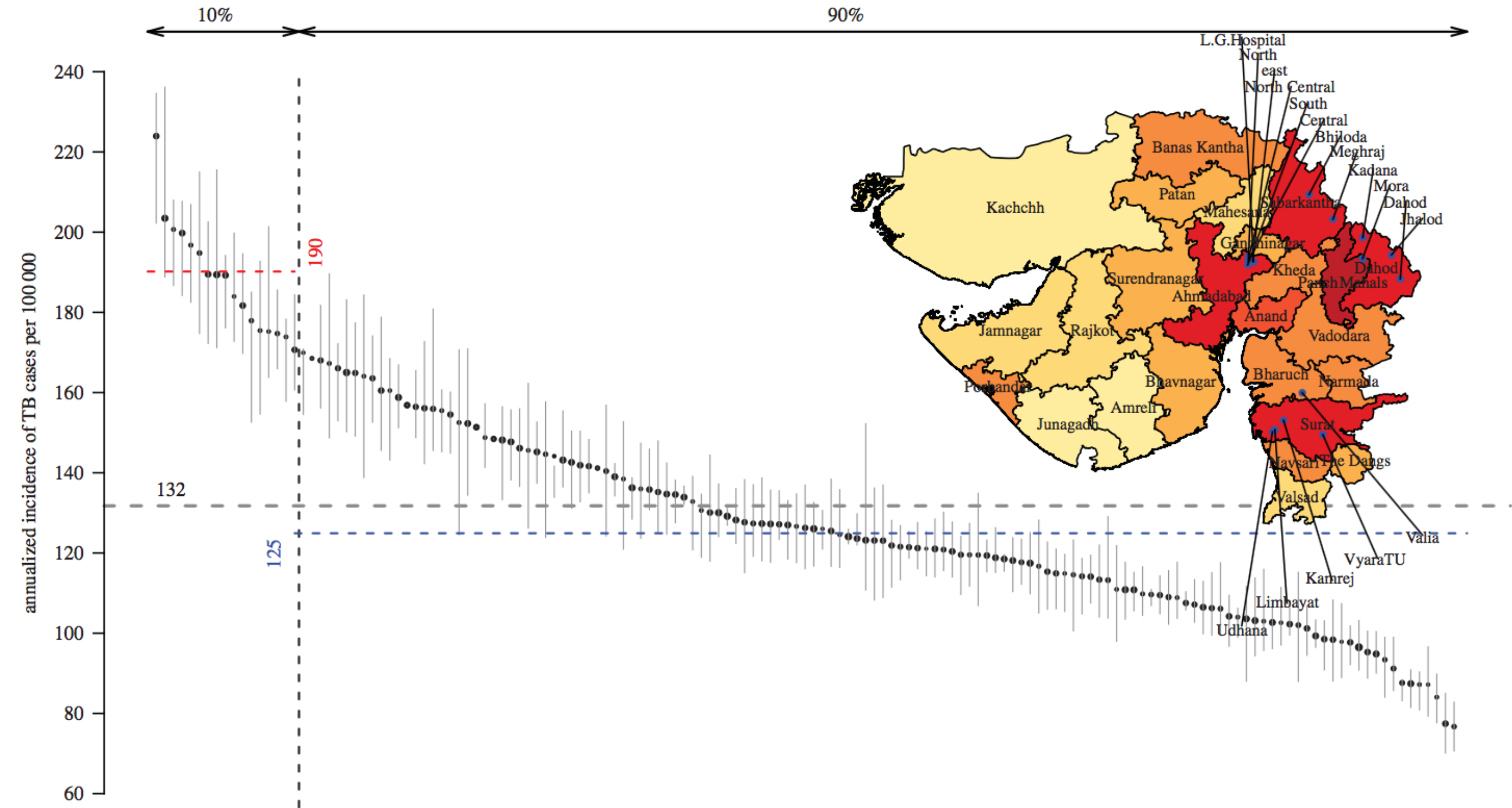
- Ordered TB units (subdistrict level with ~.5 mil pop) based on TB notification rates
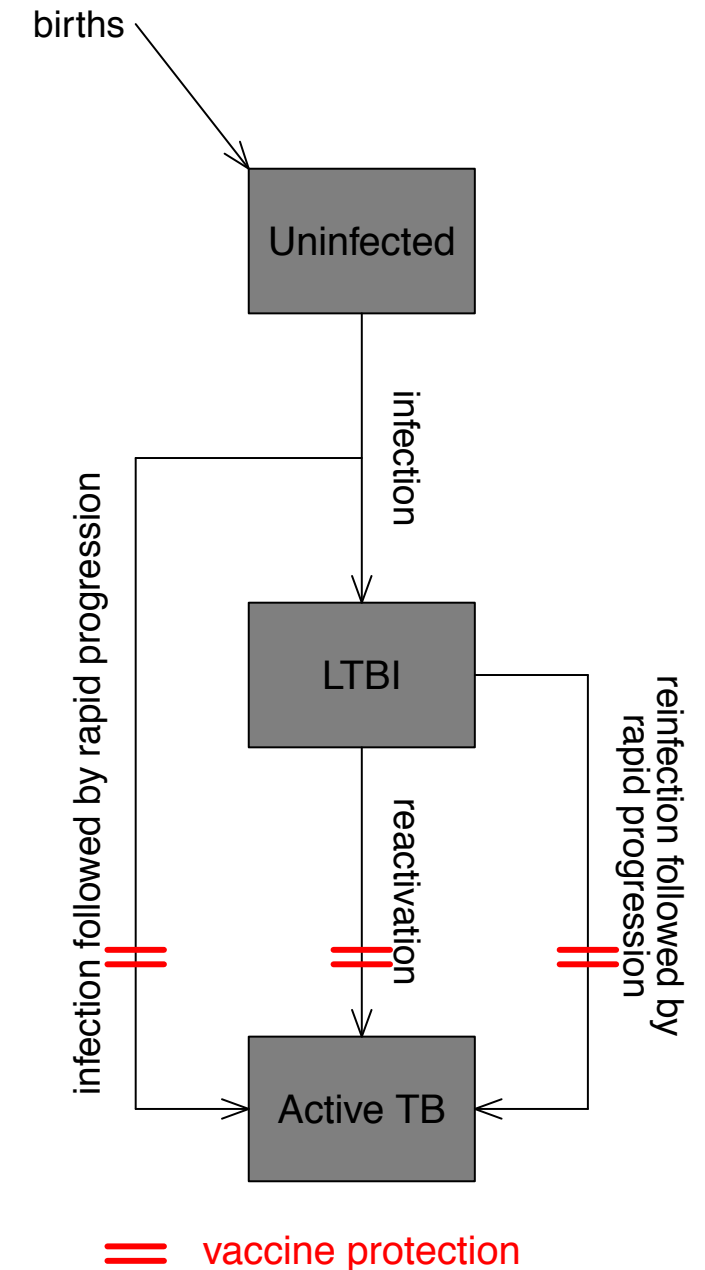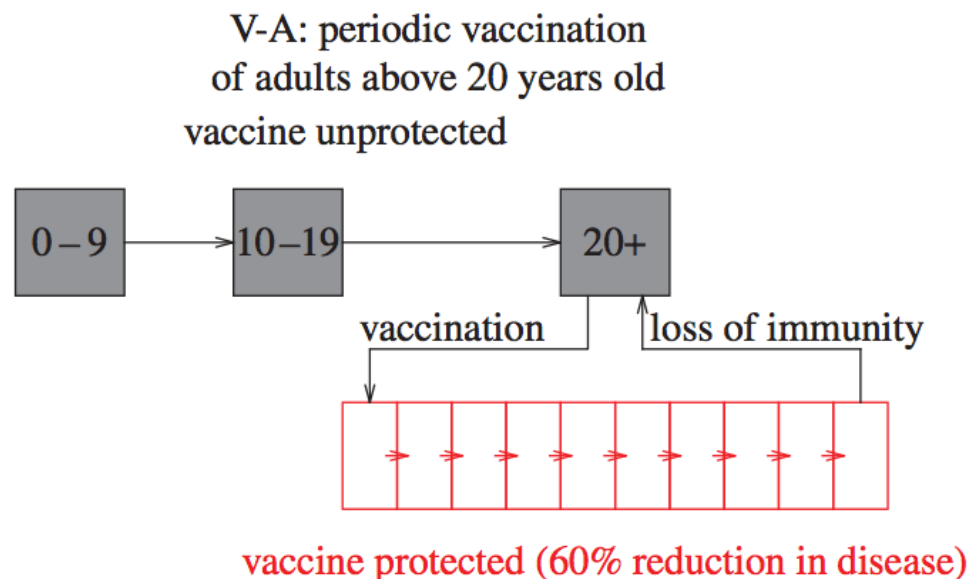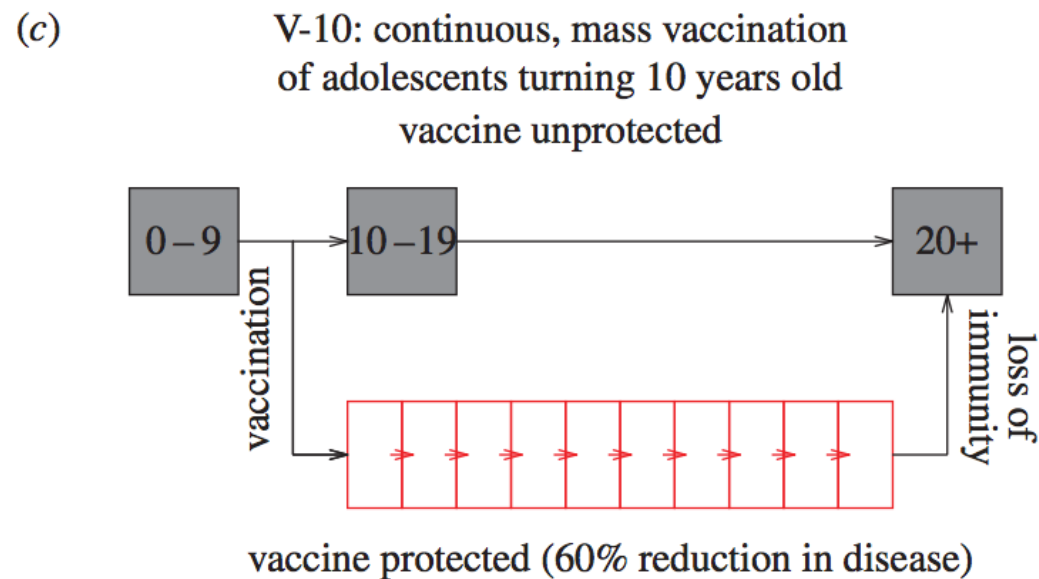- "hotspot": units with the highest TB reporting rates, comprising of 10% of the population

Model

(a)

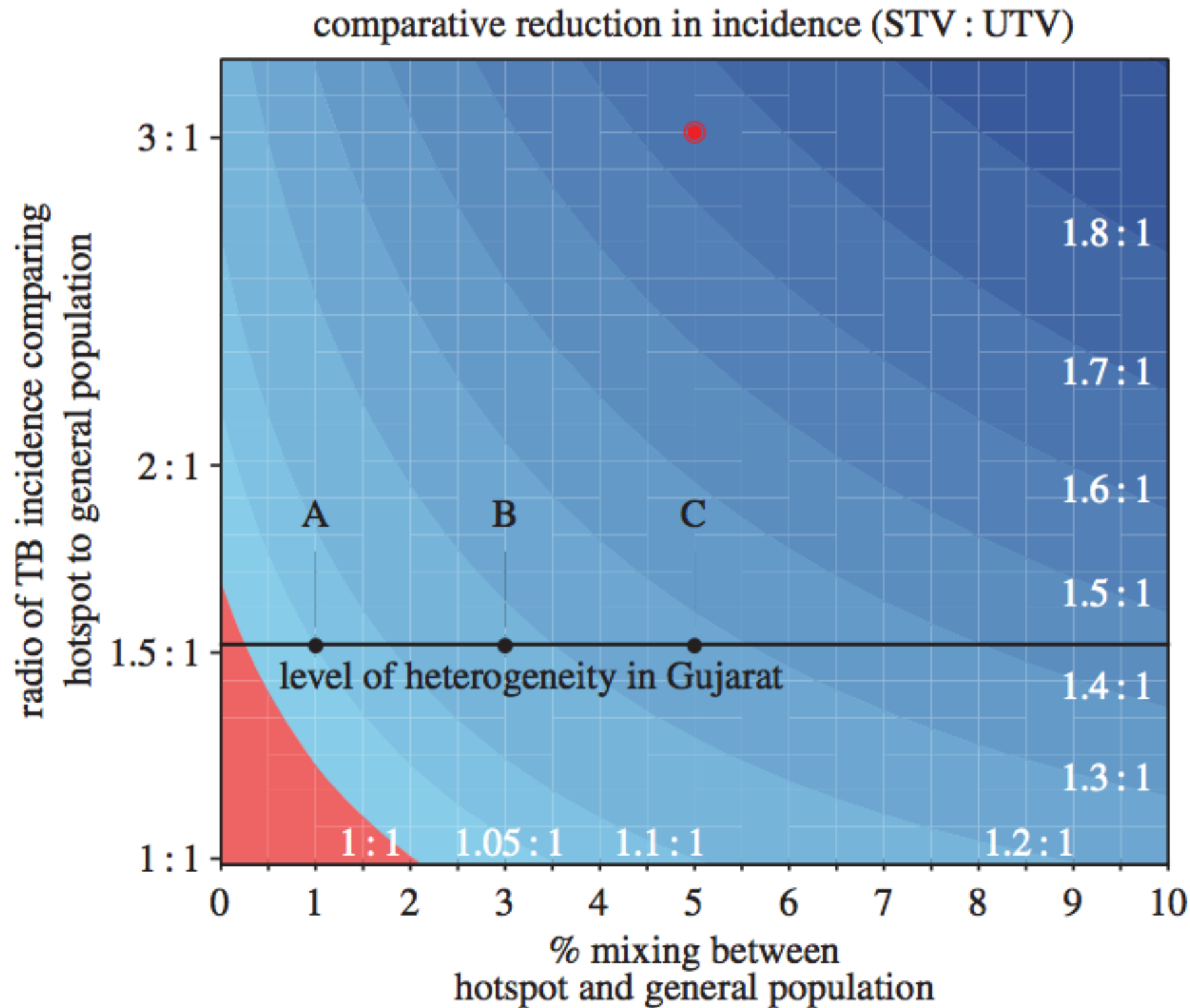hot spot   —migration→   general population

mixing

TB vaccination

Vaccine characteristics:

- Post-infection vaccine that protects against disease (not infection).
- 10 years of protection with 60% efficacy.

(c) V-10: continuous, mass vaccination of adolescents turning 10 years old
vaccine unprotected

vaccine protected (60% reduction in disease)

V-A: periodic vaccination of adults above 20 years old
vaccine unprotected

vaccine protected (60% reduction in disease)

births

Uninfected

infection

infection followed by rapid progression

LTBI

reinfection followed by rapid progression

reactivation

Active TB

== vaccine protection

Results

comparative reduction in incidence (STV : UTV)

radio of TB incidence comparing hotspot to general population

% mixing between hotspot and general population

level of heterogeneity in Gujarat

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Limitations/Challenges

- Data from Gujarat rely on official notification data.
  - Ignores the role of private sector—may distort the true geographical TB distribution.
  - TB Unit designations may be optimal for TB care provision—may underestimate heterogeneity.
- Data on key parameters are necessarily limited.
  - Social mixing for airborne infections: understudied.
  - Unknowable vaccine parameters (e.g., distribution of duration of effect) also play an important role in spatial targeting.
- Spatial targeting may be difficult in practice.
  - This model assumes idealized scale-up.
  - Hotspots may have the least infrastructure.

Summary

Spatial targeting of TB vaccines: modest but important added value.
- Mixing between hotspot and general population is the most important determinant of the magnitude of this benefit.
- Low spatial heterogeneity in Gujarat may limit the impact of spatial targeting in this setting.
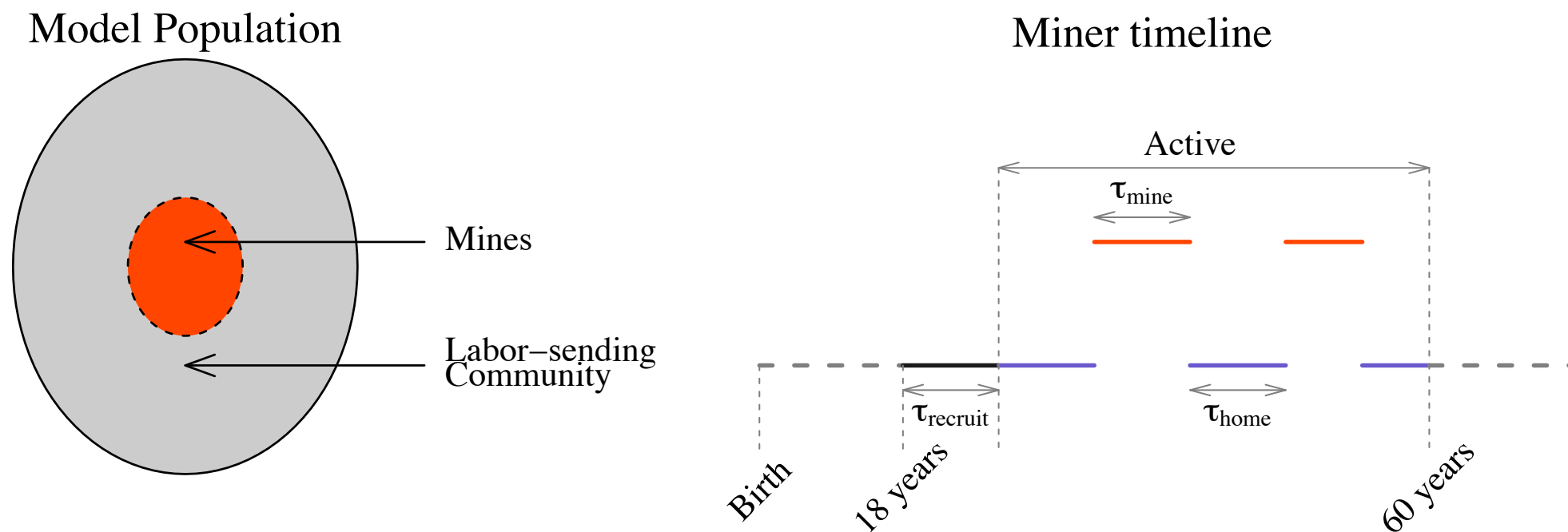
Model suggests important areas for future data collection efforts.
- Daily social mixing patterns from an airborne pathogen's perspective, at the scale of a TU (more important than migration)
- Better data (e.g., from animal studies) as to the likely mechanism of vaccine protection and the distribution of its durability
- Operational feasibility of identifying and targeting more intense hotspots (e.g., finer spatial scale)

Part II

Targeted TB vaccination in South African mining communities. (Shrestha et al, AJE, 2017)

Model

- Conceptualized the model population to comprise of mines and the associated labor sending community.

- Explicitly modeled life trajectory of miners, with recruitment and travels back and forth between the mines and their home community.

Model Population

Mines

Labor–sending Community

Miner timeline

Active

τ_{mine}

$\tau_{recruit}$

τ_{home}

Birth

18 years

60 years

- Natural history of TB and HIV (as described previously).

Setting

Mines (Thibela TB study)

Labor sending communities
Ugu (KwaZulu–Natal)
Sisonke (KwaZulu–Natal)
OR Tambo (Eastern Cape)
Alfred Nzo (Eastern Cape)
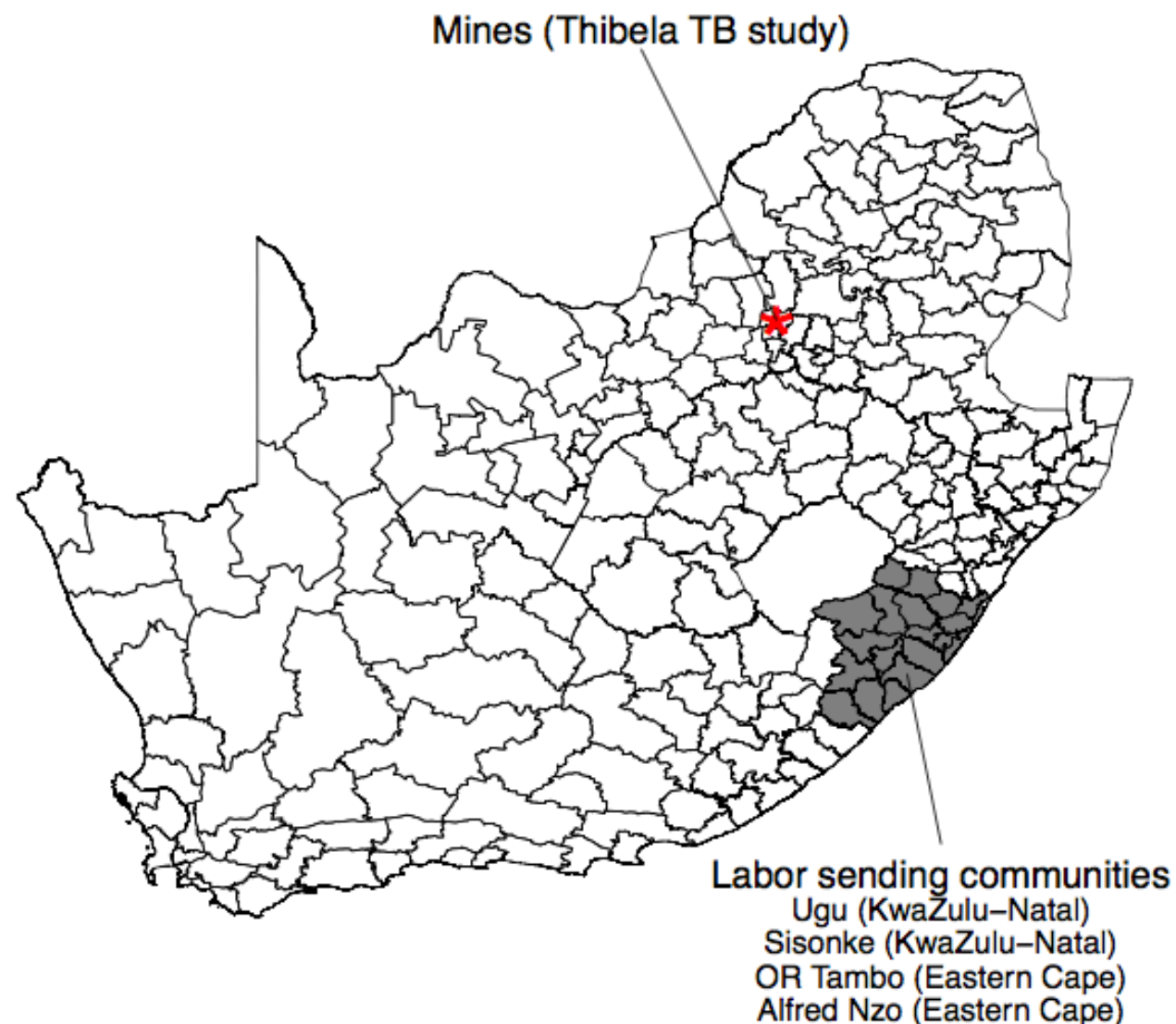
- Anchored our model to data on miners are collected from the Thibela TB study (Churchyard et al, 2014).

- We identified 4 districts from KZN and Eastern Cape as communities representative of labor sending communities.

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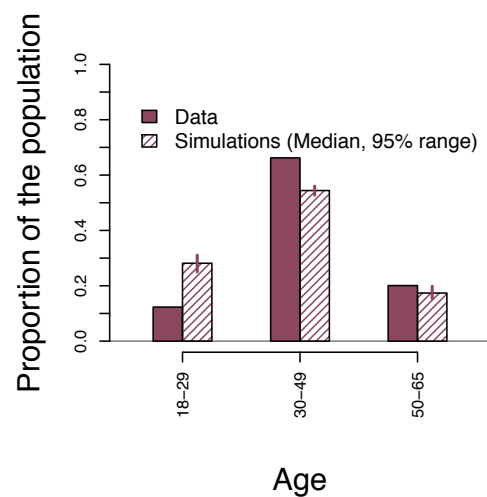BLOOMBERG SCHOOL
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Results

Deomographics
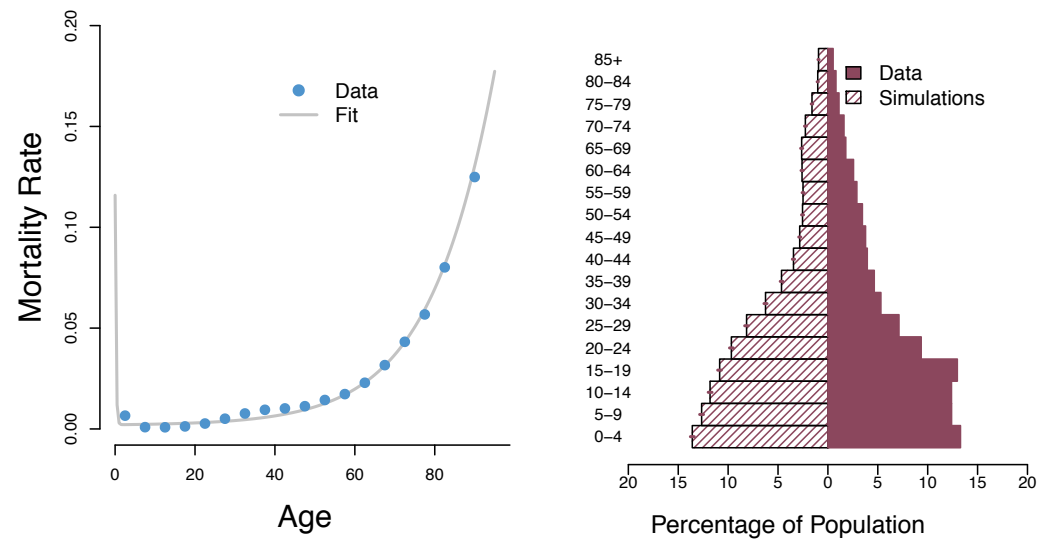
HIV prevalence
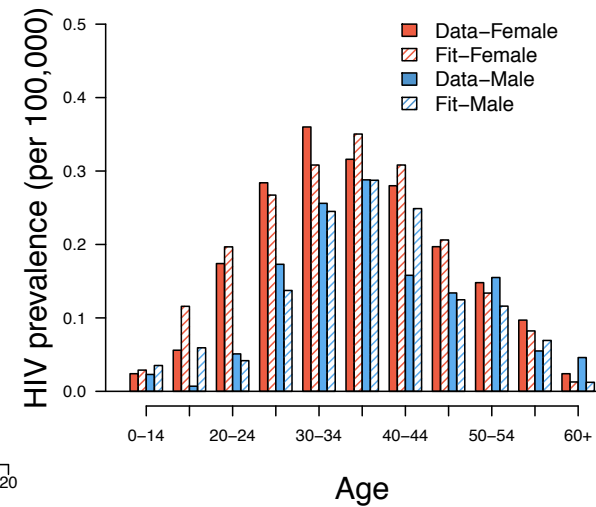
TB incidence
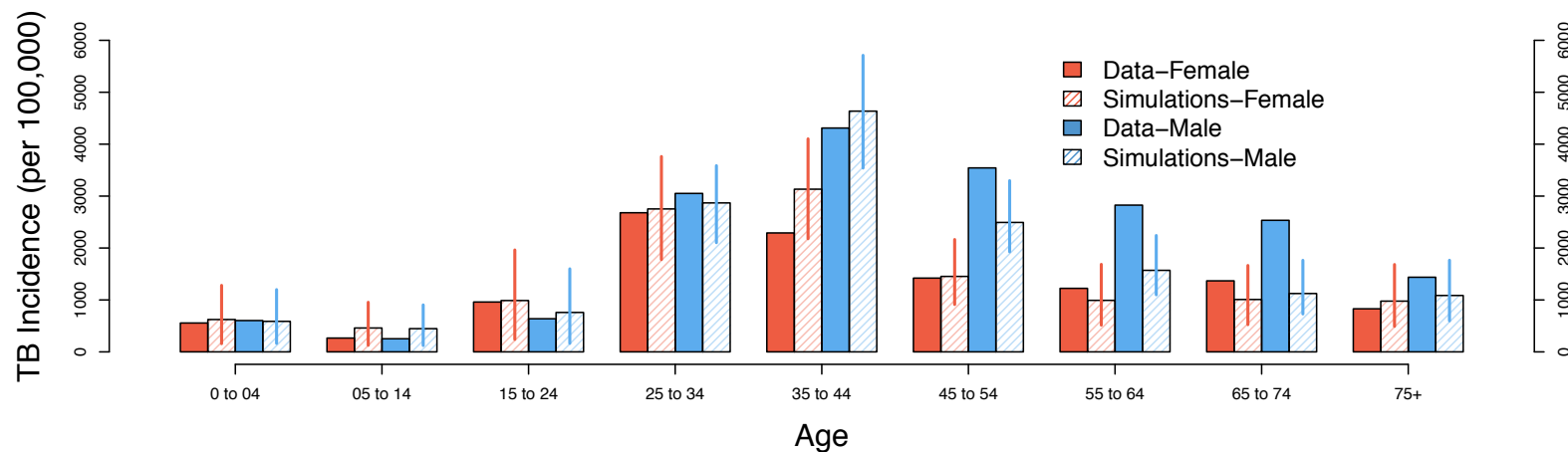
Mines
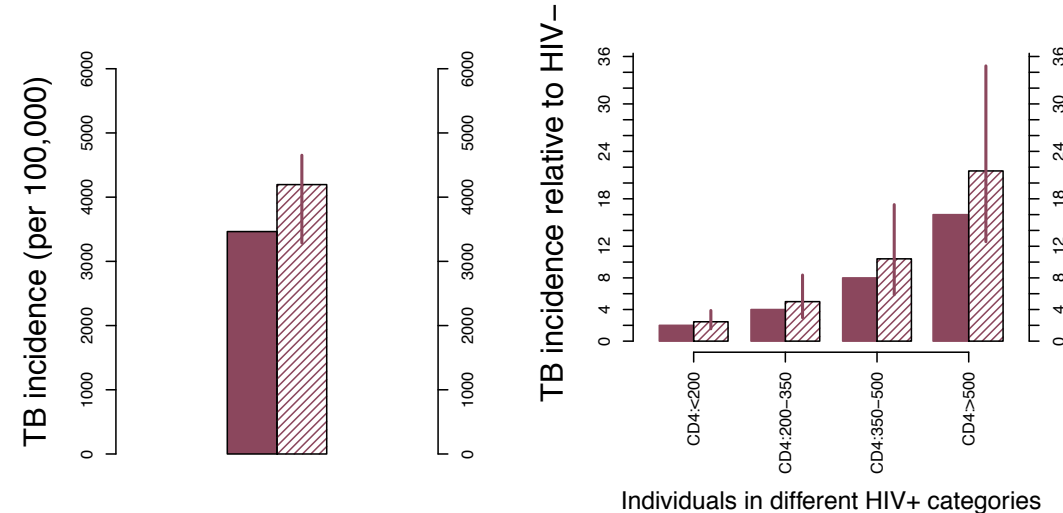
HIV-TB

Model calibrated to data on demography, TB and HIV.

TB vaccination
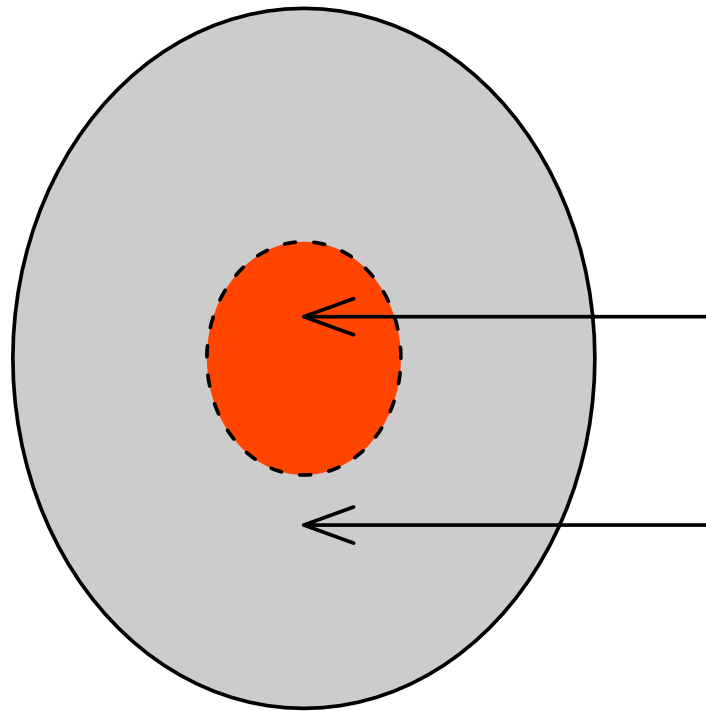
20 year adult TB vaccination campaigns:

Mine-targeted vaccination:
All miners are vaccinated (as they enter the mining workforce).
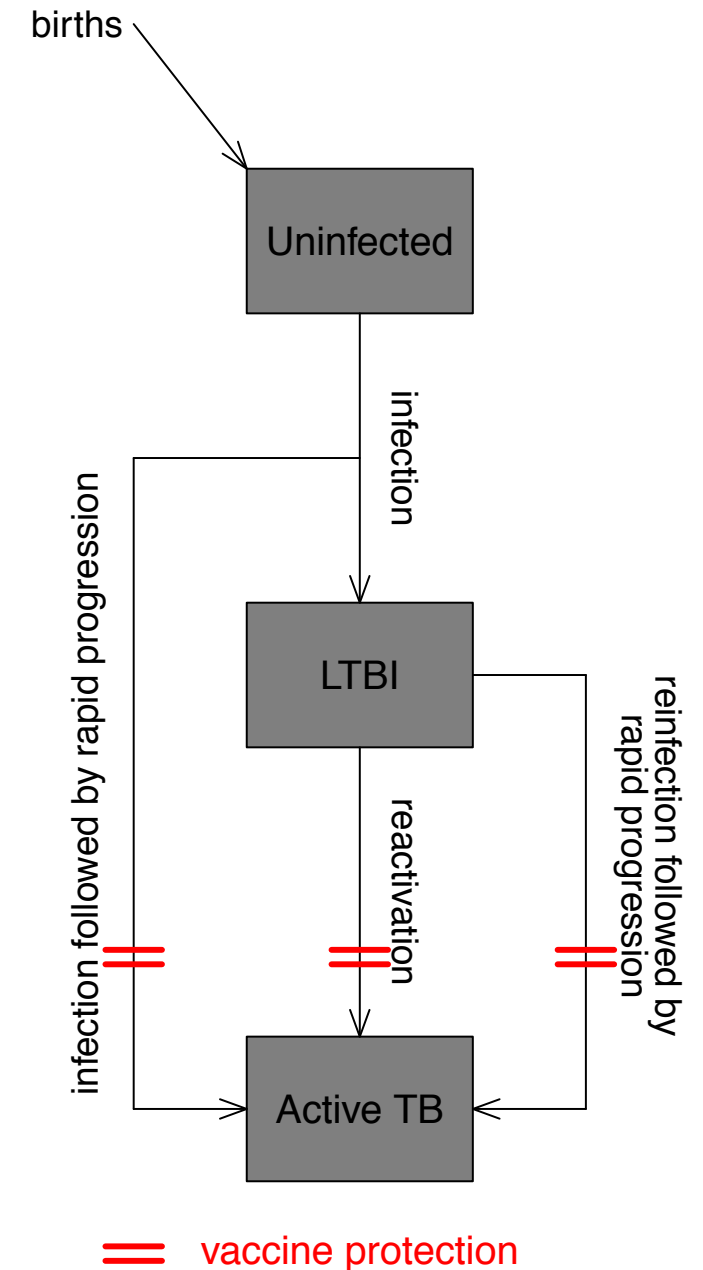
Community-targeted vaccination:
Random adults in the community are vaccinated.

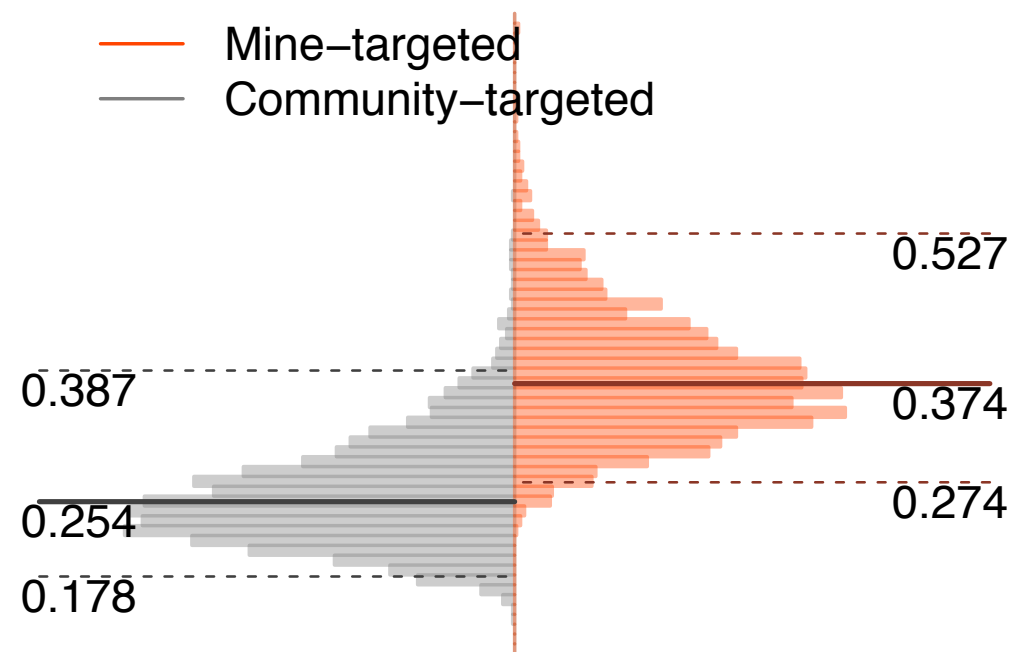- Vaccination rates are matched (for comparison).

TB vaccination

Vaccine characteristics:

- Post-infection vaccine that protects against disease (not infection).
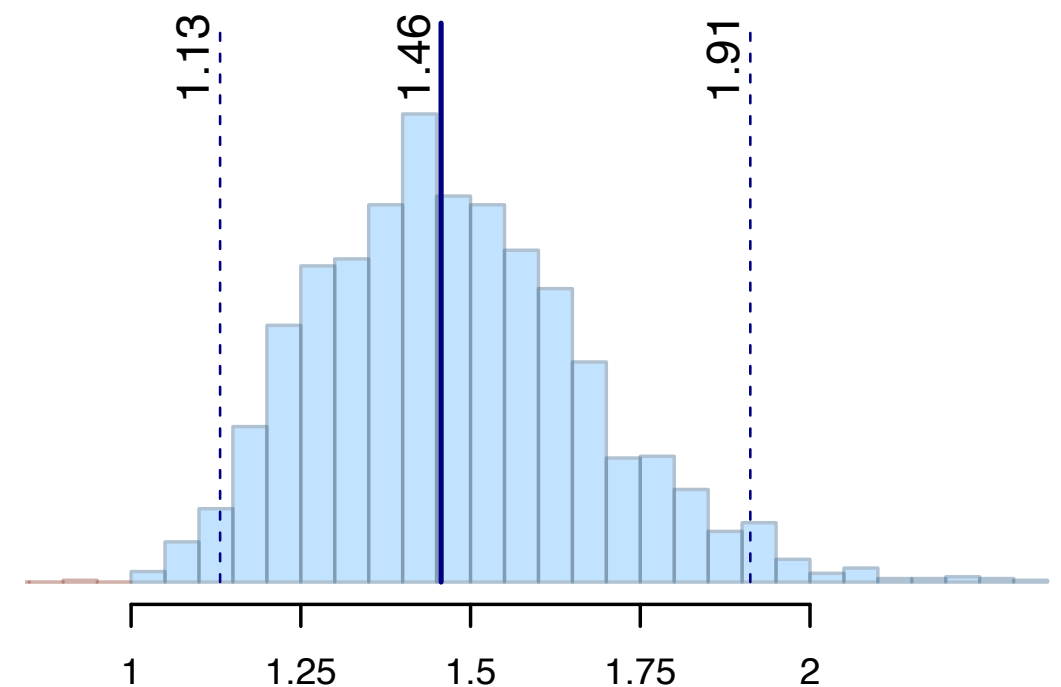- 10 years of protection with 60% efficacy.

Results

9660

Over 20 year period of vaccination:

Mine-targeted
Community-targeted

0.527

0.387

0.374

0.254

0.274

0.178

TB cases averted per vaccine

1.13

1.46

1.91

1   1.25   1.5   1.75   2

Relative impact of mine-targeted vaccine
(Mine-targted:Community-targeted)

Results
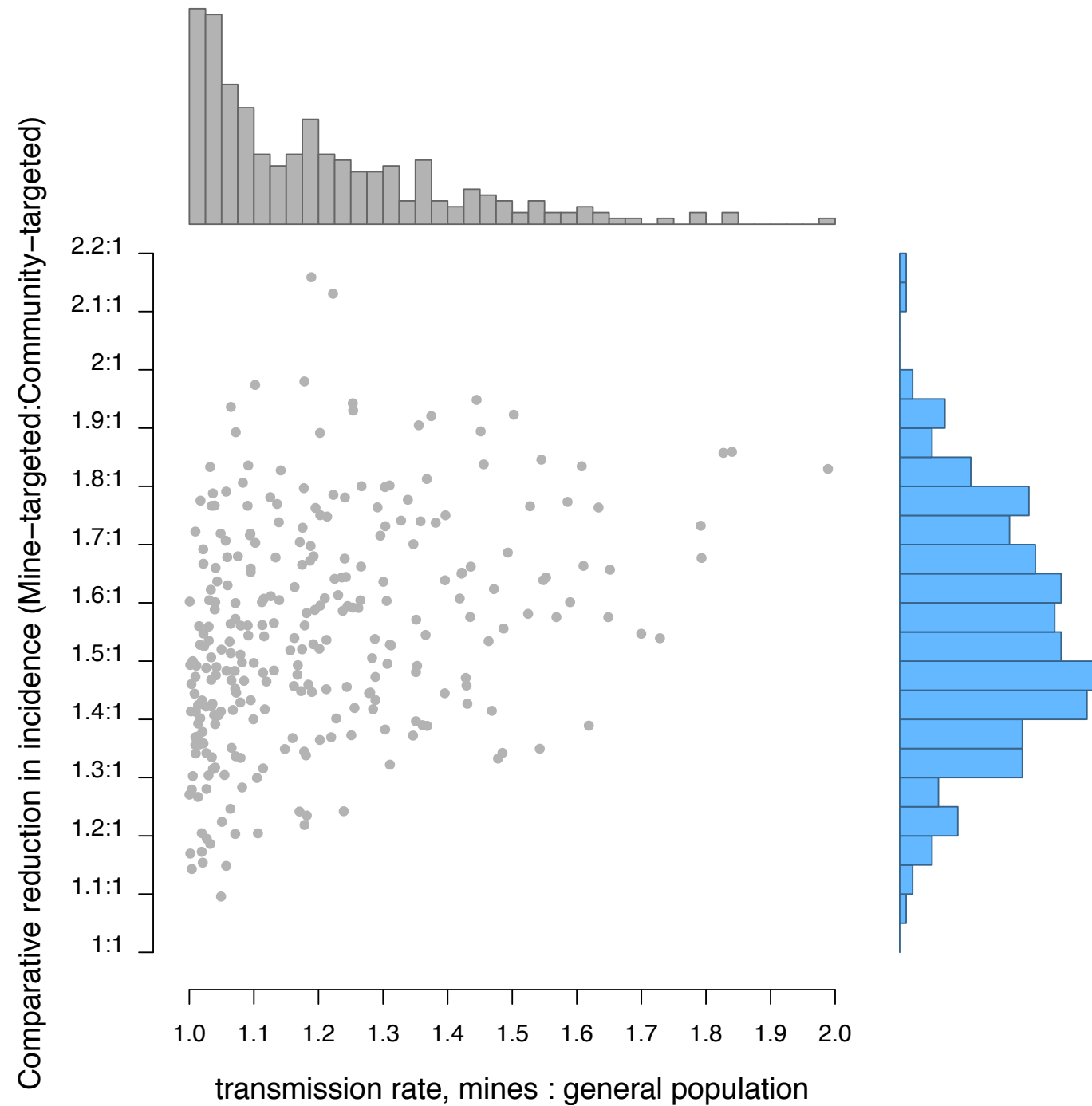

% TB occurring in adult males correlated strongly with relative impact of targeting mines.
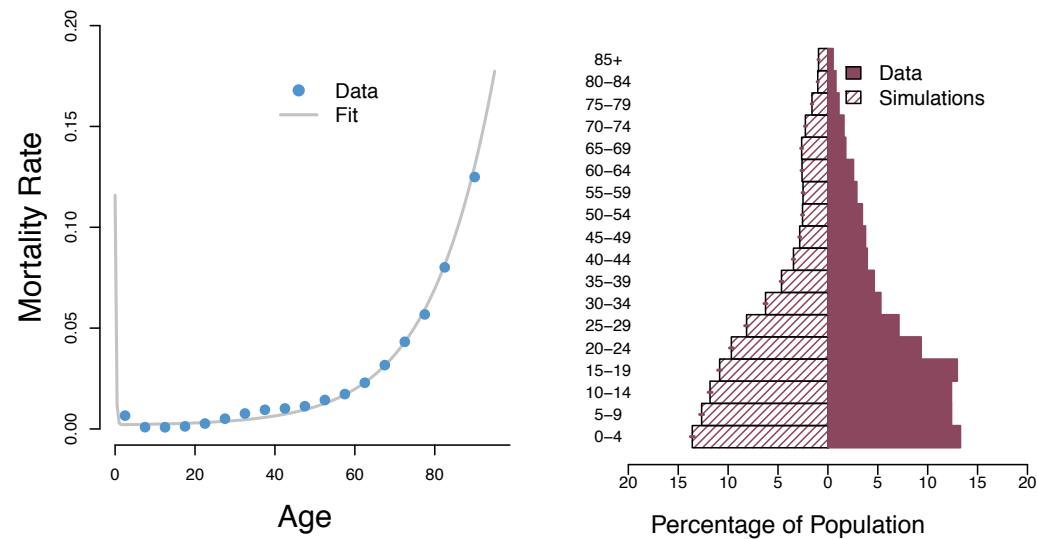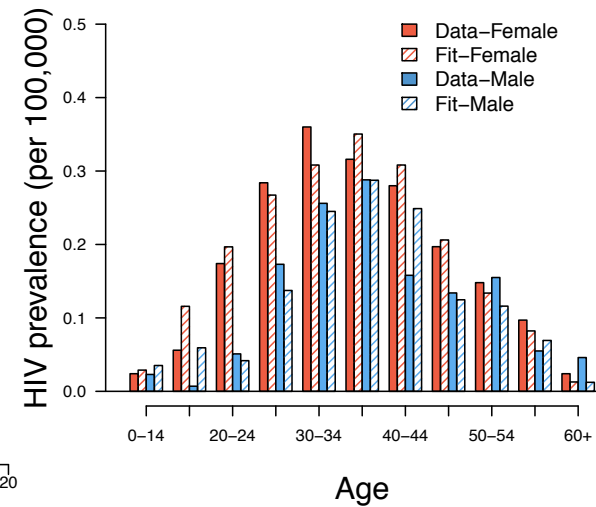
Results

Differential transmission rate in the mines (compared to the community) was not supported by data.
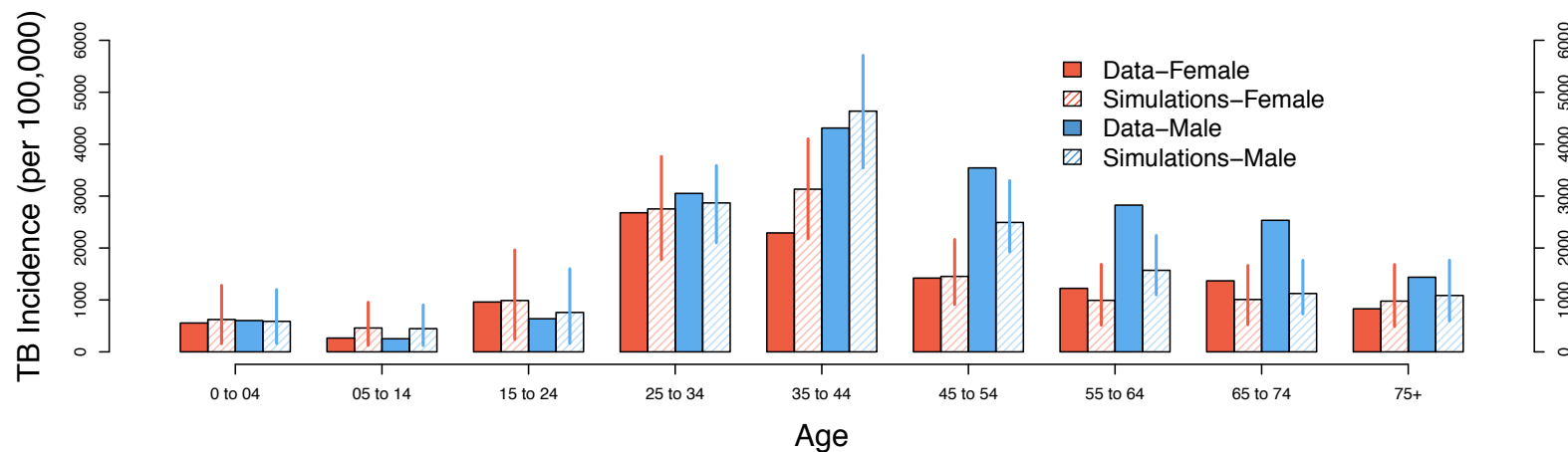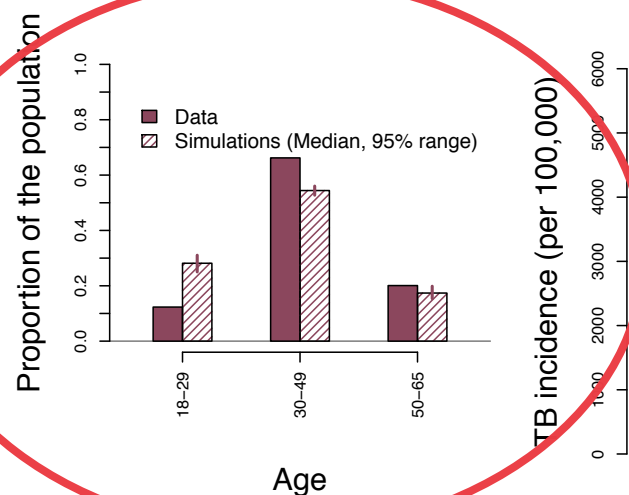
Results

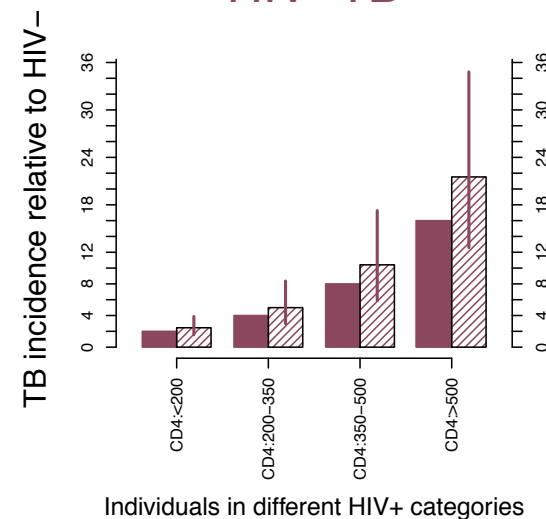Deomographics

HIV prevalence

TB incidence

Mines

HIV–TB

Miners were exclusively all adult males

Summary

- **The absolute impact of adult TB vaccination was substantial, reflecting the tremendous incidence of TB in the population as a whole.**

- **Mine-targeted vaccination strategy provided modest but sizeable relative improvement over community-targeted strategy.**

- **The relative benefit achieved by targeting the mines largely reflected the fact that mine-focused strategies target a demographic group with higher TB incidence: adult males. (Knight et al, Chang et al)**

- **Mines, in this context, even when they are not "transmission hotspots", may nonetheless serve as a mechanism via which demographic groups with higher risk of TB can be identified, and they may also be logistically more accessible than general adult populations.**

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Acknowledgements

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THANK YOU!