Are household-based interventions robust to neighborhood-level variation in TB exposure?

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Original article

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Protective effects of household-based TB interventions are robust to neighbourhood-level variation in exposure risk in Lima, Peru: a model-based analysis

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Roadmap

1. Passive, active, and targeted TB screening.

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2. Estimating variation in household and community TB exposure and incident TB risk among household contacts of TB cases in Lima, Peru.

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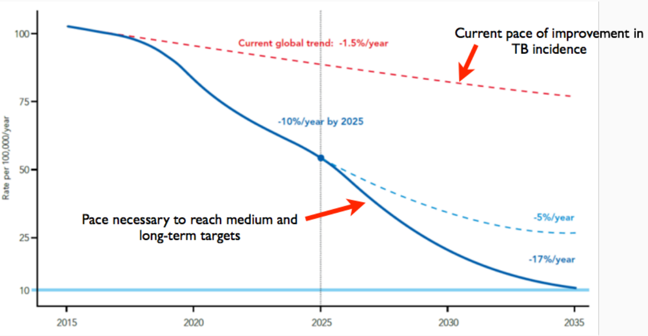
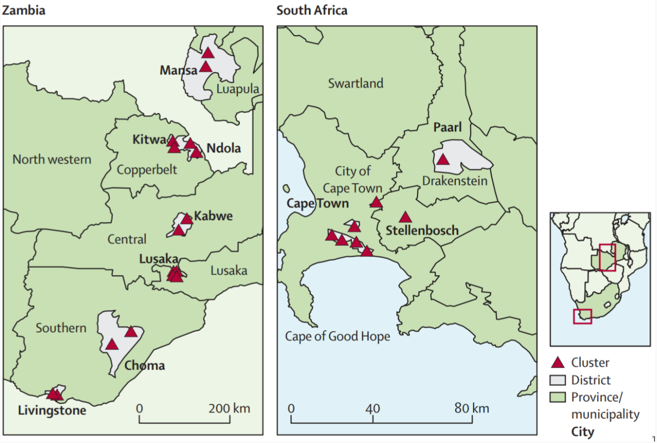
2. Estimating variation in household and community TB exposure and incident TB risk among household contacts of TB cases in Lima, Peru.
3. Simulating outcomes from hypothetical untargeted and targeted screening and treatment programs in Lima.

Passive approaches have not achieved pace of improvement necessary to meet long term goals



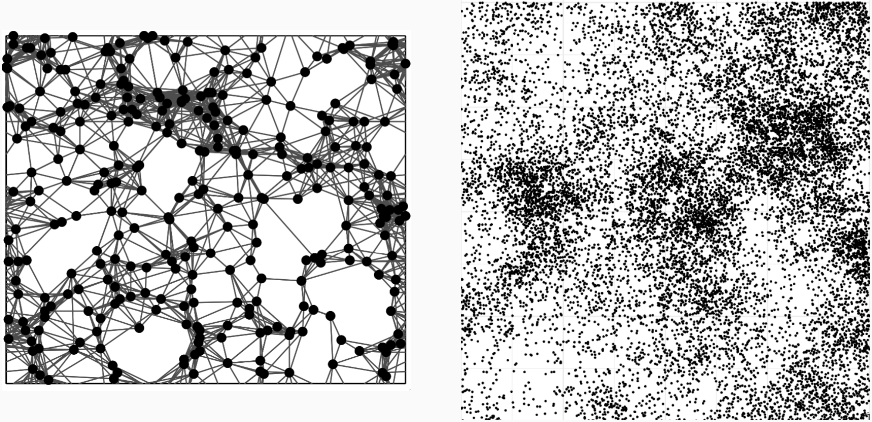
Long-term goals for TB incidence reduction vs. current trends. From 2016 WHO Global TB Report(1).

Community-wide active case-finding (ACF) not sufficiently effective to justify cost



Location of intervention communities from ZAMSTAR cluster-randomized trial. (Image from Ayles et al. 2013 (2))

Targeted interventions leverage heterogeneity in contact and susceptibility to maximize impact



Network and spatial contact heterogeneity.

Patterns of household and community transmission reflect unequal living and working conditions

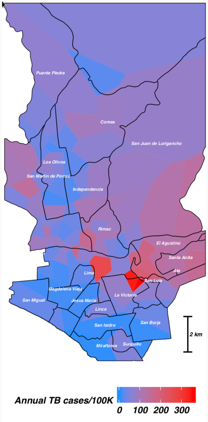
Densely populated, crowded conditions that facilitate TB transmission

Household transmission is canonical example of contact heterogeneity

- Evidence of increased TB risk among household contacts of TB cases in two large cohorts in Lima (3,4).
- Targeting household and neighborhood contacts of TB cases reduced TB mortality rates from 14% to 2% among screened individuals in Cambodia (5).

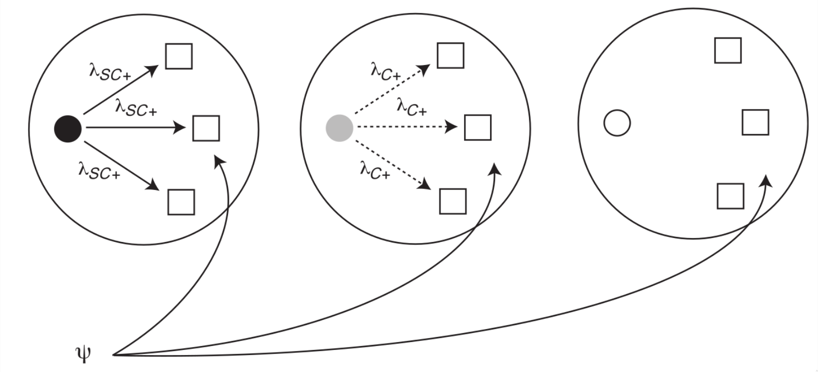
However: Variation in community risk may impact efficacy of intervention targeting

Where disease risk from community exposure > risk from HH exposure, efficacy of household-based interventions may be limited.



Neighborhood-level variation in annual TB incidence in Lima (Figure from Zelner et al., *JID* 2016)

Model varying household and community exposure



Infection risk from community exposure (ψ), smear-positive (λ_{SC+}) and culture-positive (λ_{C+}) household exposure. (Figure from Zelner et al., *AJE* 2014.)

Hierarchical model of variation in community ARTI

$$log(\alpha_i) \sim Normal(log(\mu_\alpha), \sigma_\alpha)$$

$$\lambda_{ij}^{COM} = \alpha_i a_j$$

- α_i: HC-level annual risk of TB infection
- μ_α: HC-wide mean ARTI.
- σ_α: SD of ARTI across HC areas.
- λ_{ij}^{COM} : Total community force of infection (FOI) from birth to age a_j.

Is household-based preventive therapy robust to variation in community exposure in Lima, Peru?

Data

Data come from large, household-based TB cohort

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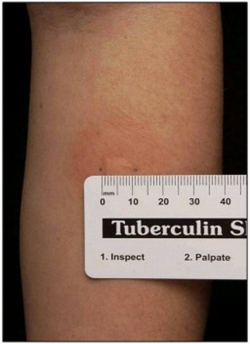
- Low HIV context.

Ideal setting to assess impact of household-based preventive therapy

- Current analysis focused on individuals aged ≤ 30 years.
- 8144 household contacts exposed to 2829 household index cases.
- All household contacts offered isoniazid preventive therapy (IPT).
- About half of household contacts initiated on IPT.

Modeled outcomes

- Baseline Tuberculin skin test result from household contacts to measure latent TB infection (LTBI).
- Incident TB in household contacts over the 1-year follow-up period.



Measurement of Tuberculin skin test.
Source: CDC

Analysis Goals

- Estimate health center level annual risk of TB infection (ARTI).

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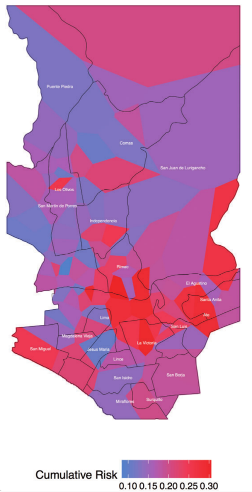
- Estimate protective effects of IPT and risks of incident TB associated with household and community-acquired infection.
- Using posterior simulation from fitted models, estimate number of TB cases prevented under three screening and treatment scenarios reflecting increasing intensity of targeting}.

Results

Wide variation in HC-level annual risk of TB infection (ARTI)



Cumulative TB exposure from birth to age 10 by HC catchment area.

Risk of household infection driven by infectiousness of index case

- Smear/Culture Positive Exposure: 14% risk of infection (95% CI = 12%, 17%)
- Smear-negative/Culture-positive Exposure: 7% risk of infection (95% CI = 4%, 10%)
- Co-prevalent case: 18% risk of infection (95% CI = 10%, 27%)

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- Household crowding: Hazard of infection increased by 1.1x (95% CI = 1.0, 1.3)

Individuals receiving IPT have $\leq$ 50% risk of incident TB

- IPT: OR = 0.37 (95% CI = 0.25, 0.56)
- BCG: OR = 0.36 (95% CI = 0.19, 0.71)

However: To understand pop'n impact of screening and treatment strategies we need to weight estimates by likelihood of disease among IPT recipients under that regime.