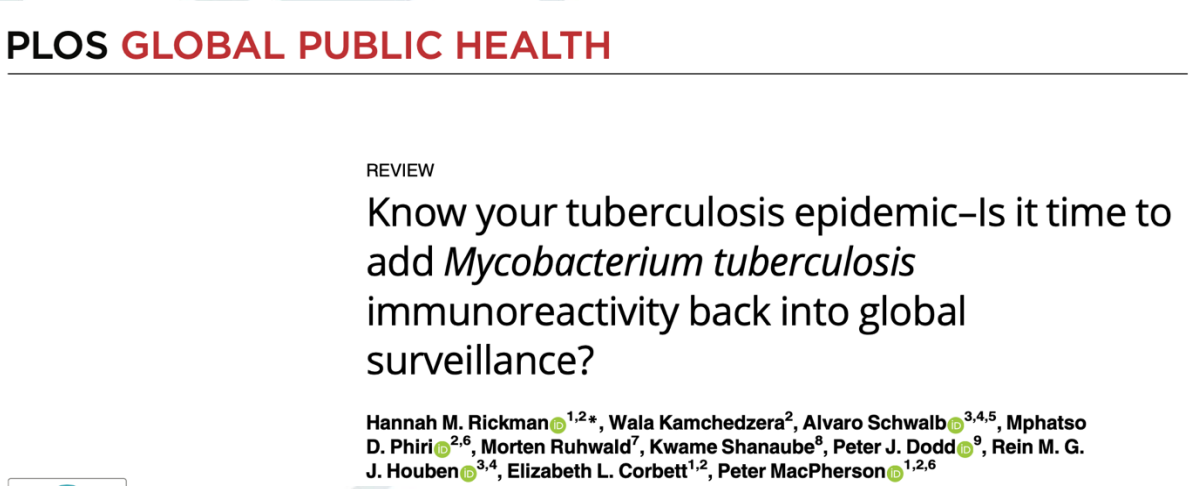
How to estimate trends
Remembering the past – repeat TBI surveys

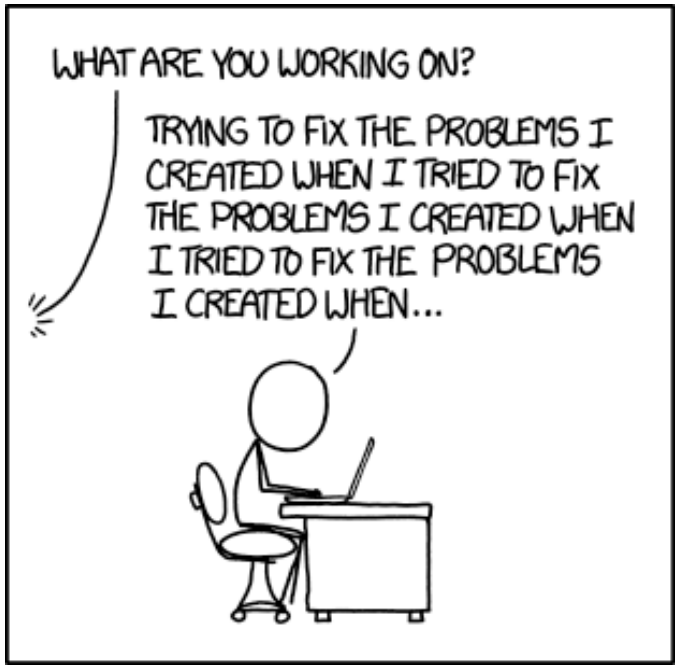
5-minute pitch

GTB Task Force meeting
27 Sep 2024



LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

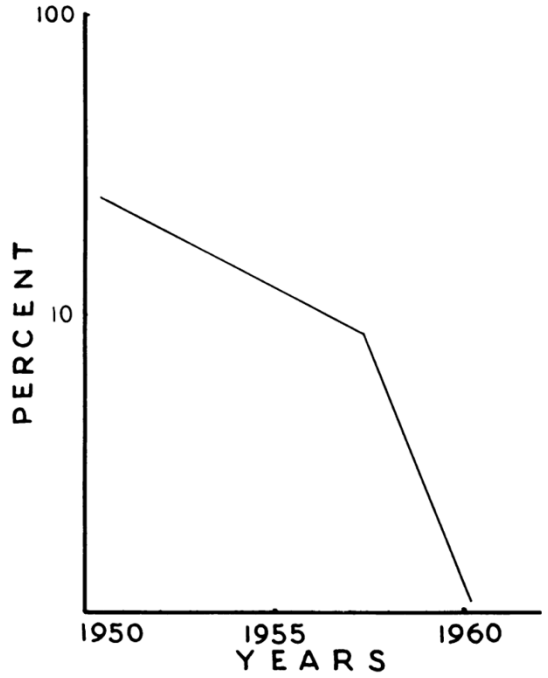
Problem



- *Need* to estimate trends
- Repeat prevalence surveys not possible
  - Human and financial resource constraints
- Other indicators (NNT, ACF, TPT, UCH SCI) have limitations
  - Measure programme performance
  - Unknown link to burden (or programmatic performance)
  - etc…

https://xkcd.com/1739/

Potential solution?



ARI reduction
Pre-trial = 24.5% (!!)
Trial start = 8.5%, Trial end = 1.1%

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REVIEW

Know your tuberculosis epidemic–Is it time to add *Mycobacterium tuberculosis* immunoreactivity back into global surveillance?

Hannah M. Rickman[1,2]*, Wala Kamchedzera[2], Alvaro Schwalb[3,4,5], Mphatso D. Phiri[2,6], Morten Ruhwald[7], Kwame Shanaube[8], Peter J. Dodd[9], Rein M. G. J. Houben[3,4], Elizabeth L. Corbett[1,2], Peter MacPherson[1,2,6]

$$ARTI = 1 - (1 - Prevalence)^{1/Age}$$

Rickman 2022 PLoS GPH, Comstock 1967 Am Rev Resp Dis

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- Repeat TBI surveys
- Measure immunoreactivity among population through IGRA/new TST
- Outcome of single TBI survey:
  - Estimate of prevalence of immunoreactivity
- Estimate of Annual Risk of Infection
  - Approximate measure of transmission in community

$$ARTI = 1 - (1 - Prevalence)^{1/Age}$$

Repeat TBI surveys --> Estimate of trend in transmission

Rickman 2022 PLoS GPH

Important notes

Prevalence of tuberculous infection and incidence of tuberculosis; a re-assessment of the Styblo rule

F van Leth,[a] MJ van der Werf[a] & MW Borgdorff[a]

- Immunoreactivity ≠ viable infection
- Several limitations
  - E.g. Threshold for positive test, lack of binomial distribution, age dynamics, test reversion rates
- However
  - BCG cross-reactivity solved, signals of responsiveness transmission
- *Not* suggesting to use TBI surveys for direct burden estimation
  - E.g. Incidence, prevalence or even single point ARI
- However, if methods constant, trends in estimated ARI provide strong signal for trend

van Leth 2008 Bull WHO

Upside(s)

- Surveys (much) smaller and simpler
  - N TBI survey: < 10,000
  - Procedures/tests: 1 or 2 (reading of TST)
- Can be linked to existing surveys
  - E.g. DHS, TB prevalence survey
- Repeat surveys can be done in sentinel populations
  - School children, military recruits, alongside vaccination
- Costs: 50-250k
  - For 1 TB prevalence survey, can do repeat TBI Survey in 6-15 countries
- Link between trend in ARI and e.g. TB incidence
  - More direct than other metrics considered

Survey	Ratio of prevalence (prevalence of infection / prevalence of disease) [3]	Ratio of survey size (infection survey size/ disease survey size)[4]
South Korea, 1995 [34]	15.49	0.084
Philippines, 1997 [35, 36]	16.36	0.034
Cambodia, 2002 [37]	11.16	0.20
Vietnam, 2007 [38]	55.19	0.15
Bangladesh, 2009 [39, 40]	44.53	0.088

Many challenges, but…

Costs/convenience
- 10-30x Cost differential with TB prevalence surveys
- Can be added onto e.g. DHS, prevalence survey

Relative value
- Improvement over other current/proposed solutions?

Developing field
- Many unknowns, but experience will build rapidly
  - TBI Surveys (will be) done in India, Malawi, Brazil, Indonesia, South Africa

Worth discussion in Task Force?

Thoughts/comments welcome

For more background, please see:

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