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TB prevention among previously treated people

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Overview

- Recurrence of TB after treatment: knowns
 & unknowns
- Targeting prevention to previously treated people in high-incidence settings
- Conclusions

Natural history of TB after treatment



G. Walzl et al., *Nat Rev Imm*, 2011

Rates of recurrent TB in Southern Africa, 1993 - 2013



HIV-uninfected, recurrences per 100,000 person-years

TB recurrence due to reinfection vs. reactivation



Uys et al., Roy Soc Interface, 2009

Recurrent and other previously treated TB in 52 South African health districts



Percentage of bacteriologically-confirmed TB cases

Marx et al., *IJTLD* (under review)

Evidence from the ZAMSTAR prevalence surveys (2010)



Marx et al., *ERJ*, 2016

Effect of secondary preventive therapy on recurrence of tuberculosis

| study | year | type | | | | | RR (95% CI) |
|-------------------|------|--------|-----|----|------|---------|-------------------|
| Perriens et al. | 1995 | RCT | - | • | | | 0.22 (0.06, 0.66) |
| Haller et al. | 1999 | RCT | | • | | | 0.30 (0.03, 0.94) |
| Fitzgerald et al. | 2000 | RCT | | | | | 0.18 (0.04, 0.83) |
| Churchyard et al. | 2003 | cohort | | _ | • | | 0.45 (0.26, 0.78) |
| | | | | | | | |
| | | | .01 | .1 | .5 1 | 2 | 5 |

Bruins & van Leth, Inf Dis, 2017

Knowns

- High rates of TB after successful TB treatment, exacerbated by reinfection
- In high-incidence settings, previously treated people contribute substantially to incident and prevalent TB
- Preventive therapy is effective to reduce recurrent TB

Unknowns

- Determinants of high rates of recurrence?
 - Heterogeneity in exposure/infection/progression risk?
 - Quality of treatment?
 - Role of inflammation and lung destruction?
- Extent and duration of infectiousness among previously treated TB cases?
- Drug resistance acquisition?

Tuberculosis control interventions targeted to previously treated people in a high-incidence setting: a modelling study



Florian M Marx*, Reza Yaesoubi*, Nicolas A Menzies, Joshua A Salomon, Alyssa Bilinski, Nulda Beyers, Ted Cohen





Marx et al., *The Lancet GH*, 2018

Calibration data (2 suburban communities, Cape Town)



Marx et al., The Lancet GH, 2018

Projections



Targeted active case finding: 14% (0.4-28.0) of incident TB cases and 21% (2.5-39.0) of TB deaths averted over 10 years

Targeted active case finding & Secondary isoniazid preventive therapy: 40% (21–56) of incident TB cases and 41% (16–55) of TB deaths averted over 10 years.

Marx et al., The Lancet GH, 2018

Cost-effectiveness of post-treatment follow-up (PTFU) and secondary IPT (work in progress)



Conclusions

- In high-incidence settings, preventing TB among previously treated people may be an attractive strategy to reduce TB
- <u>Example of targeted prevention</u>: models of TB prevention should consider population heterogeneity in the risk of exposure/infection, disease progression, and transmission

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