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Effectiveness of contact investigations for tuberculosis control in Arkansas

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HIGHLIGHTS

- We evaluate the effectiveness of TB contact investigations in Arkansas in 2001–2014.
- We estimate that contact investigations have avoided about 20% of TB cases and deaths.
- Treatment of latent TB infections contributed marginally (2–3%) to this purpose.
- We show the importance of tracing contacts of sputum smear-negative index patients.
- Achieving national performance targets can significantly improve TB control.

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ABSTRACT

Comprehensive assessment of the effectiveness of contact investigations for tuberculosis (TB) control is still lacking. In this study, we use a computational model, calibrated against notification data from Arkansas during the period 2001–2011, that reproduces independent data on key features of TB transmission and epidemiology. The model estimates that the Arkansas contact investigations program has avoided 18.6% (12.1–25.9%) of TB cases and 23.7% (16.4–30.6%) of TB deaths that would have occurred during 2001–2014 if passive diagnosis alone were implemented. If contacts of sputum smear-negative cases had not been included in the program, the percentage reduction would have been remarkably lower. In addition, we predict that achieving national targets for performance indicators of contact investigation programs has strong potential to further reduce TB transmission and burden. However, contact investigations are expected to have limited effectiveness on avoiding reactivation cases of latent infections over the next 60 years.

1. Introduction

In high-income countries, the incidence of tuberculosis (TB) has seen a sustained decline since 1993, thanks to general improved health conditions and to control interventions applied by public health authorities (Verdier et al., 2011). In the United States, the backbone of TB control is based on three core elements: case detection and management, active investigation of contacts of infectious patients and treatment of latent TB infection (LTBI) (Coordinating Center for Health Information and Service, Centers for Disease Control and Prevention (CDC), 2005b). The cost-effectiveness of contact tracing in high-income countries has been evaluated in several epidemiological studies, yielding conflicting results, possibly due to limitations in study designs (Verdier et al., 2011). Randomized control trials would provide conclusive evidence of the effectiveness of contact investigation studies (Fox et al., 2011), but no such studies are available to date (Fox et al., 2013). Mathematical models can supplement epidemiological studies and aid the design and assessment of alternative strategies, but modeling studies for TB contact tracing are also lacking (Begun et al., 2013).

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In this work, we apply a computational model of TB transmission dynamics in Arkansas, USA, as an example of a low-burden, high-income setting, to assess the effectiveness of current contact investigation protocols and the potential impact of alternative intervention scenarios.

2. Methods

The epidemiological model used in this study is based on a previously published one, featuring a realistic, spatially explicit and time-evolving representation of the Arkansas socio-demographic structure by means of an individual based approach (Guzzetta et al., 2011). TB transmission within households, schools, workplaces, and casual, distance-dependent contacts is considered. Schools and workplaces are enclosed settings where individuals spend much of their day interacting with a significant number of contacts (Mossong et al., 2008; Fumanelli et al., 2012) thus representing transmission network hubs (Davidow et al., 2003). Indeed, TB outbreaks in schools are relatively common (e.g. Faccini et al., 2013), and both schools and workplaces are important settings for screening potential contacts of index cases (Davidow et al., 2003). The population in the model is spatially distributed according to estimates of the population density (Balk and Yetman, 2004) over 219 square cells covering the state territory. The demography and the network of contacts among individuals are updated at the end of each year: individuals are generated, grow older, create new households, procreate and die; the processes of school enrollment (following the educational career), new employment, job loss and retirement are also modeled. The evolution of the socio-demographic structure was validated in the original paper (Guzzetta et al., 2011). The model captures immigration via a yearly influx of a foreign-born population based on available age-specific data (Capps et al., 2013). Foreign-born individuals are characterized by a higher rate of LTBI prevalence (Bennett et al., 2008), and the model can accommodate a small fraction of new immigrants being infectious at the time of entry in the US. Since we do not explicitly model targeted TB screening during the immigration process, this fraction of infectious immigrants accounts for infectious individuals who may avoid the screening process (e.g. illegal immigrants), or with LTBI identified at screening who do not complete treatment and progress rapidly to TB disease.

Following the original model (Guzzetta et al., 2011), whose structure is proposed in Fig. 1, individuals are born uninfected and move to the recently infected class upon contact with an infectious (Active TB) individual. Recent infections are asymptomatic and progress to either of the following epidemiological outcomes: (i) complete healing, with pathogen clearance via immune response; (ii) active TB disease within a few years from infection episode (Vynnycky and Fine, 1997) ("primary TB"); (iii) LTBI. Individuals with LTBI are asymptomatic and non-infectious, and may develop endogenous TB reactivation (Vynnycky and Fine, 1997), even several decades after the infection episode. Individuals with LTBI can be re-infected by contacts with infectious hosts. Re-exposed individuals may develop active TB ("exogenous reinfection") within a few years, or revert to the latent class, just like recently infected individuals. However, the probability of exogenous reinfection is lower than that of primary TB, to account for the probability of protection from TB-specific immune memory arising after first exposure to TB (Guzzetta et al., 2011; Vynnycky and Fine, 1997; Guzzetta and Kirschner, 2013). The model considers extrapulmonary (non-infectious) and pulmonary (infectious) TB and assigns a higher infectiousness to smear-positive cases compared to smear-negative (Behr et al., 1999; Tostmann et al., 2008). Irrespectively of the site of TB and smear status, individuals with active TB may be diagnosed and cured and are at an increased risk of death.

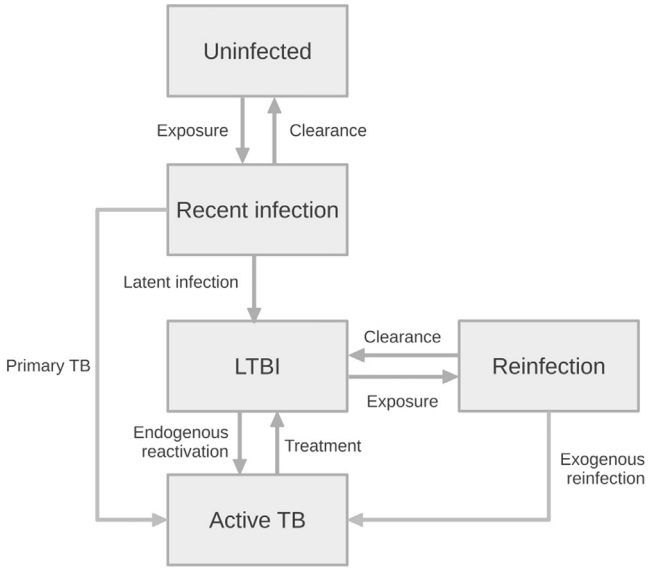

Fig. 1. Epidemiological workflow of the individual-based model. Individuals are born susceptible (uninfected), may be exposed to TB infection (recent infection) and either heal, develop primary TB or latent TB infection (LTBI). Latently infected individuals can develop endogenous reactivation or be re-exposed (reinfected). Re-exposed individual can revert to the latent compartment or develop TB from exogenous reactivation. Individuals with TB (active TB) can be diagnosed and treated, reverting to the latent compartment.

The original model (Guzzetta et al., 2011) was expanded to include contact investigation activities as per guidelines of the Centers for Disease Control (CDC) (Coordinating Center for Health Information and Service, Centers for Disease Control and Prevention (CDC), 2005). Full details on implementation are given in Technical Appendix. A summarizing graphical representation of the contact investigation procedures is provided in Fig. 2. More specifically, Fig. 2A represents a case management procedure, which includes a decision model for initiation of contact investigation and, where appropriate, elicitation of a list of contacts from the index case. We note here that the CDC does not prioritize investigation of contacts of smear-negative cases (although it is recommended when resources are available) (Coordinating Center for Health Information and Service, Centers for Disease Control and Prevention (CDC), 2005a). In Arkansas, the Department of Health applies the same protocol to smear-positive and smear-negative patients with equal priority (ARPE – Aggregate Reports for Program Evaluations). Fig. 2B depicts our procedure of tracing, testing and, where applicable, treating contacts on the list. Completed treatment of LTBI is assumed to have 100% and instantaneous efficacy in controlling the reactivation of LTBI. The contact investigation program applied in Arkansas (termed "Arkansas contact tracing" in the rest of the paper), was modeled by using yearly state-specific performance estimates from the Aggregate Reports on TB Program Evaluation (ARPE – Aggregate Reports for Program Evaluations) on the program coverage (proportion of index cases for which contacts are elicited), proportion of missed contacts, rates of treatment initiation and completion against LTBI.

The model is calibrated using surveillance data (Online Tuberculosis Information System (OTIS), 2014) and validated against data from four independent sources: a molecular epidemiology study in Arkansas (Berzkalns et al., 2014), surveillance data on TB in the foreign-born (Online Tuberculosis Information System (OTIS), 2014) and nation-wide epidemiological studies on contact tracing in households (Moran-Mendoza et al., 2007) and workplaces