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Title: Modelling the social and structural determinants of TB: opportunities and challenges

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Running head: Mathematical modelling of TB socioeconomic drivers

Summary

Introduction

Despite the close link between tuberculosis (TB) and poverty, most mathematical models of TB have not addressed underlying social and structural determinants (SD). In this paper, we review studies employing mathematical modelling to evaluate the epidemiological impact of SD of TB.

Methods

We systematically searched PubMed and personal libraries to identify eligible papers. We extracted data on modelling techniques employed, research question, type of SDs modelled, and setting.

Results

From 232 records identified, we included eight papers published between 2008 and 2015; six employed population-based dynamic TB transmission models and two non-dynamic analytic models. Seven studies focused on proximal TB determinants (four on nutritional status, one on wealth, one on indoor air pollution, and one examined overcrowding, socioeconomic and nutritional status), and one focused on macroeconomic influences.

Conclusions

Few modelling studies have attempted to evaluate SD of TB, resulting in key knowledge gaps. Despite challenges of modelling such a complex system, models must broaden their scope to remain useful for policy making. Given the inter-sectoral nature of the interrelations between SD and TB outcomes, this work will require multi-disciplinary collaborations. A useful starting point would be to focus on developing relatively simple models that can strengthen our knowledge regarding the potential effect of SD on TB outcomes.

Introduction

Tuberculosis (TB) is widely recognised as a disease of poverty (1-3) with disproportionate disease burden falling on the poorest in society and the most vulnerable communities. The need to design and implement comprehensive strategies to achieve TB elimination through Universal Health Coverage and interventions to address the underlying social determinants (SD) of TB is a key element of the World Health Organization's (WHO) End TB strategy for the 2015-2035 era (4, 5).

The targets and indicators of this new TB action framework are anchored in the seventeen Sustainable Development Goals (SDGs) that were adopted by the United Nations and that mark the global development agenda that began on 1 January 2016. By placing their emphasis on the interdependence and synergies between socioeconomic development and health (6), these offer unique entry points for addressing TB social and structural determinants.

In this article, we follow the definition of social and structural determinants of health of the WHO Commission on Social Determinants of Health (7): structural determinants of TB are those conditions that generate or reinforce social stratification (e.g. socioeconomic inequalities, population growth, urbanisation), and therefore give rise to unequal distribution of key social determinants of TB epidemiology, such as poor housing, poverty and malnutrition, that in turn influence exposure to risk, vulnerability and ability to recover after developing the disease (8). Table 1 summarises these definitions.

[Table 1 about here]

Quantitative analytical tools such as mathematical modelling can play an important role in informing the End TB Strategy, evaluating the impact of novel poverty-reduction interventions nested in its vision (including in combination with existing biomedical tools), and exploring the contribution of socioeconomic drivers to the epidemic. However, to do so, inevitably TB models will need to expand their focus beyond diagnosis and treatment to

incorporate SDs, but the potential of modelling as well as its main limitations in supporting this research agenda remain unclear.

In this paper, we report findings from a systematic review of the literature which we carried out with the aim to provide an overview of the current state of knowledge in the field of mathematical modelling of social and structural determinants of TB. We then go on to discuss key methodological challenges and gaps in empirical evidence that existing mathematical models need to overcome to be able to incorporate SDs and remain relevant to policy-making.

Methods

Search strategy and selection criteria

For the purposes of this review "mathematical model" was defined based on Garnett et al (9) as mechanistic representations for how disease burden is established, and this included both dynamic transmission and decision (non-dynamic) analytic models.

We searched PubMed for any relevant paper on modelling and socioeconomic determinants of TB (e.g. nutrition, crowding, poverty). The full search string is included in Box 1. Titles and abstracts were screened for eligibility. Papers were eligible for full-text review if they were written in English (due to limited resources), the target population was human individuals and mathematical modelling assessed the epidemiological impact of social and structural determinants of TB.

[Box 1 about here]

We excluded systematic reviews, epidemiological studies that did not use mathematical modelling techniques and ecological analyses looking at social and structural determinants of TB. The search focused on socioeconomic factors (i.e. the intervention or exposure involves a socioeconomic factor), and excluded studies focusing only on diabetes, HIV and behavioural risk factors such as alcohol consumption and smoking unless their association with socioeconomic factors were also considered. We applied no restrictions as to the year or status of publication.

Additional relevant articles were identified in the authors' personal libraries and included in the review. DP selected the papers with support from RMGJH, DB and KL; data extraction was performed by DP and RMGJH.

Data abstraction and synthesis

Figure 1 presents details of the selection process. The aim of the study, first author and publication dates, type and feature of the model, the socioeconomic factor, the setting and the main findings were extracted into a pre-designed form. We focused on a qualitative synthesis of the methods employed in the articles we identified.

[Figure 1 about here]

Results

A total of 229 unique records were found in the literature search; 3 additional papers were added from the authors' personal libraries. Of these, 53 underwent full-text evaluation. After full-text screening, we included eight papers, published between 2008 and 2015, with four articles published in 2015 only. Table 2 summarises the main features of the selected studies.

[Table 2 about here]

Socioeconomic factors investigated. The study by Reeves et al. (10) was the only one that looked at the impact of distal determinants (i.e. government expenditure per capita on public health services, GDP and cumulative decline in GDP as a measure of the severity of the economic recession) on TB control. The remainder modelled proximal TB determinants: four focused on nutritional status (BMI and undernutrition) (11-14), one on wealth (15), one on smoking and indoor air pollution (16), and one on nutritional status, overcrowding and socioeconomic status (17). All studies looked at one factor at a time, with the exception of the study by Dye et al. which also explored the combined effect of nutritional status and demographic changes (including age structure and urbanisation) on TB incidence.

Modelling methods, structure and parameters. Compartmental population-based dynamic TB transmission models were the most common simulation approach employed in the selected papers (75%, 6/8); two studies used non-dynamic analytical models and both

investigated the effect of both diabetes and nutritional status on TB epidemics. Most studies included a conceptual framework to illustrate the mechanics of the models and the hypotheses behind their research questions.

Transmission models employed standard SLIR ("Susceptible-Latent-Infectious-Recovered") models that were adapted to explore the research question set in each study: the model by Oxlade et al, for instance, was stratified by levels of undernutrition by wealth quartile. Andrews et al implemented a parallel structure for two wealth groups to a standard TB model to explore the benefit of assortative mixing to interventions targeting the poor, highlighting the potential importance of including mixing parameters in TB models even if data are currently not available to inform these.

As to the model parameters, Ackley et al explored changes in differences in susceptibility to infection and progression to disease in hypothetical scenarios. Different levels of BMI drive changes in reactivation and progression parameters in the model by Oxlade et al. The study by Reeves et al used an econometric analysis to estimate changes in relevant model parameters controlling case detection. Bhunu et al divided the population in rich and poor communities, and compared the reproduction numbers for these two strata (Appendix 1).

Data on the different exposures were mainly drawn from the literature (12, 14), national population based surveys (11, 13, 15, 16) or publicly available databases (10). Very few data employed in these studies were local or regional. The majority of studies were calibrated to TB data (e.g. incidence trends or point estimates) from WHO estimates.

Key findings of the modelling studies. The studies in our review support the notion that TB control is linked to and would benefit from action on TB social determinants. Reeves et al. found that a decrease in funding to control TB due to an economic recession (distal factor) can lead to a decline in TB case detection, and consequently in higher TB rates. Lin et al. showed that interventions on smoking and indoor air pollution (proximal factors) can accelerate TB decline. The studies that focused on nutritional status (proximal factor) found that reducing undernutrition would substantially reduce TB incidence. Andrews and colleagues showed that preferential targeting toward the poor can benefit TB control

(wealth as proximal factor). From the analysis of reproduction numbers for the poor and rich communities, Bhunu et al found that overcrowding, poor nutrition, lower socioeconomic status (proximal factors) and reduced TB treatment uptake worsen TB transmission. Finally, the study by Dye et al concluded that the combination of nutritional and demographic changes (proximal factors) operating over the decade from 1998 tended to increase TB incidence per capita in high-burden India and reduce it in lower-burden Korea.

Discussion

This review has highlighted the paucity of mathematical modelling studies looking at the effects of socioeconomic factors on TB pathogenesis and epidemiology, but has also shown that, although fairly recent, work in this field seems to be growing as the number of papers published has increased in the later years (i.e. from 2011 onwards). This is plausibly a reflection of changing policy priorities that are now embedded in the End TB Strategy.

Our findings point to the need, at this stage, to develop relatively simple models that improve and expand the current body of work to incorporate available evidence and strengthen our knowledge of the potential effect of SDs on TB outcomes. For instance, most models focused on one or two factors only, and those that considered two factors did not account for possible interactions between these. Notably, most mathematical modelling studies focussed on assessing the effect of nutritional status and changes in BMI on TB epidemiology. This is not surprising as undernutrition has long been acknowledged as a key, socially determined, TB risk factor. We found no modelling work looking at the impact of improved socioeconomic macro-indicators on TB outcomes, or of social protection interventions targeting TB patients and their households. As to the proximal risk factors, only one model assessed the effect of crowding on TB epidemiology, possibly a reflection of the fact that data on crowding and TB are not rich enough to unpick causality for a model.

Challenges in translating from determinant to model

The narrow focus of past global health and development policies and TB control strategies only partly explains why TB modelling has so far shown some reluctance in including social and structural determinants. This has also been due to the real and perceived weaknesses in

183 the empirical evidence which is needed to populate models and quantify the pathways from
184 socioeconomic factors to changes in the natural history of TB in a population. Figure 2
185 provides a conceptual framework that outlines how distal/structural determinants (such as
186 macroeconomic policies), work through a potential array of more proximal determinants
187 (e.g. crowding and nutrition), which in turn affects the dynamics of a standard mechanistic
188 TB model at multiple points (18, 19), such as the intensity of transmission (through
189 crowding) or the rate of progression after recent and/or latent infection (e.g. through
190 nutrition).

191 [Figure 2 about here]

192

193 While there are some data to inform parts of, for instance, the pathway from
194 macroeconomic policies (e.g. GDP) to TB incidence (10), our ability to quantify the exact
195 relationship of each step is still limited. However, it should be noted that the same
196 limitations apply to current TB models, ranging from capturing the impact of HIV, or when
197 models look to evaluate the potential impact of interventions, including current approaches
198 to improving case detection and reducing patient delay, or future hypothetical tools (20,
199 21).

200 When translating the effect of changing a socioeconomic determinant into a mechanistic
201 model, it does not suffice to have an estimate of the magnitude of the effect (see examples
202 in Table 3). One needs to know, or make assumptions about, the model parameters that
203 should be changed to achieve the estimated impact. As illustrated in Figure 2, changes in
204 disease risk may be due to influences at one or several of the stages on the pathway
205 between exposure and disease that are captured by transmission models. As direct
206 evidence is often still lacking, this means that choices need to be made based on biological
207 plausibility.

208 [Table 3 about here]

209 The range of these potential model parameters includes those directly capturing the
210 intensity of transmission, e.g. social mixing or crowding in households, but also parameters
211 guiding progression to disease after infection, which can be affected, for instance, by
212 nutritional status. It is also plausible that different paths to progression (primary,

213 reactivation, reinfection) are affected at different pathway stages. In addition, any
214 interventions that reduce barriers to care and treatment completion will change model
215 parameters capturing the time to diagnosis as well as retention in care (e.g. alcohol and
216 drug abuse).

217 In addition to effects on incidence, SDs may alter the natural history of disease (e.g. reduced
218 infectiousness and disease duration in people living with HIV) or disease outcomes (e.g. HIV,
219 undernutrition, diabetes, and smoking). Clustering of these risk factors for behavioural or
220 biological reasons, requires an understanding of their interactions, and further increases the
221 level of knowledge required. Finally, separating out composite phenomenological quantities
222 into their mechanistic components may also improve transferability between settings if the
223 data are available to quantify how these components differ.

224 **Conclusions and recommendations**

225 Mathematical modelling is a powerful and flexible tool to inform policy discussions and
226 estimate the potential impact of various interventions relative to one-another (9). However,
227 to be useful, models need to be able to reflect the relevant aspects of the epidemic and
228 address the questions faced by policymakers. In the SDGs and End TB Strategy era, this
229 means that mathematical models of TB must translate the impact of socioeconomic
230 determinants in their mechanistic components. As a starting point, the TB modelling
231 community should use the existing scientific evidence to construct relatively simple
232 mechanistic models that add to our understanding of the effect of SDs on TB, and help
233 improve specific policy decisions.
234
235 As we showed in this paper, there exists a scarcity of TB models that include SD, but also a
236 small but increasing body of work that has explored initial ideas. Some modelling of
237 proximal risk factors and related public health interventions has been done, but, for
238 example, this has never moved upstream. TB models can leverage the existing data, and
239 highlight the value of collecting those that are missing, such as the exact link between
240 changes in nutritional status and changes in progression to disease, or the relationship
241 between transmission intensity and living environments (e.g. urban slums compared to rural
242 settings).

To further our knowledge, projects are urgently needed that advance the field whilst avoiding the pitfall of developing overly complex models that include population or pathway structures not adequately supported by empirical evidence or fully understood. In addition, the complexity of the pathways involved and the multi-sectoral nature of new approaches to end TB evidently require collaborations from different disciplines, including social scientists, epidemiologists, economists, policymakers as well as mathematical modellers (11). While recognising the importance of such projects but at the same time the struggle to identify suitable funding opportunities for such cross-disciplinary collaborative work, the TB Modelling and Analysis Consortium organised a meeting at the end of 2015 to discuss existing experiences and potential path forward. A range of projects was developed that would both advance the field and be feasible given current data (22). Two of these projects have been funded and preliminary results are expected by the end of 2016: an interdisciplinary project looking at how social protection interventions can accelerate TB elimination (the Social Protection to Enhance the Control of TB (S-PROTECT) Consortium), and a project assessing the relative contribution of TB programme (DOTS) expansion and improvements in socio-economic indicators on TB epidemiology in China.

In this paper we highlighted that the literature on mathematical modelling of social determinants of TB remains limited. We argue that to maintain its key role in policy discussions in the era of the SDGs and End TB Strategy, the TB modelling community needs to embrace the technical challenges to adequately represent the interplay between TB and its socioeconomic drivers. While some work is underway, more funding, data and capacity are urgently needed to ensure TB modelling remains a useful tool for the ultimate goal of TB elimination.

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Table 1: Structural and social determinants, and social protection: definitions and examples

Term	Definition	Examples
Structural determinants	Those factors that generate or reinforce socioeconomic stratification in the society and that defines the differential distribution of risk factors in a given population(7). Structural determinants are also referred to as upstream or distal factors.	Global socioeconomic inequalities, high level of population mobility, rapid urbanisation, population growth, macroeconomic policies, social protection policies (including welfare, social protection, labour legislation, education), socioeconomic position
Social determinants	All those material, psychological and behavioural circumstances linked to health and generically indicated as 'risk factors' in the conventional epidemiological language (7). Social determinants are also referred to as downstream, proximal factors or intermediary determinants.	Poor housing and environmental conditions, food insecurity and malnutrition, alcohol consumption, smoking, drug consumption, co-morbidities (e.g. HIV/AIDS, diabetes, mental health), imprisonment
Social protection	All public and private initiatives that provide income or consumption transfers to the poor, protect the vulnerable against livelihood risks, and enhance the social status and rights of the marginalised; with the overall objectives of reducing the economic and social vulnerability of poor, vulnerable and marginalised groups (23). At least four types of interventions fall under this definition: social transfers (such as food, cash and inputs); public works programmes (food for work and cash for work); education and vocational training; and financial resources (micro-credit, savings and insurance).	Bolsa Familia, Ghana National Health Insurance, Intervention with Microfinance for AIDS and Gender Equity (IMAGE) in South Africa (24)

Box 1: Full search string for literature review in PubMed

Search Term Group		
Modelling	**Tuberculosis**	**Social/structural determinants of TB**
((mathem AND (model OR models)) OR (mathem* modell*) OR (mathem* modelling) OR (modeling OR modelling)) OR "Populations dynamics" OR "System dynamics" OR "Computer simulation" OR microsimulation)) AND*	TB OR tuberculosis OR "Tuberculosis"[Mesh]	*OR "Populations dynamics" OR "System dynamics" OR "Computer simulation" OR microsimulation)) AND ((socioeconomic OR socio-economic OR social OR structural) AND (determinant* OR driver* OR factor* OR protection OR status)) OR poverty OR poor OR deprivation OR ("gross domestic product" OR GDP) OR migration OR wealth OR "financial crisis" OR "economic recession" OR poor OR inequalit* OR under-nutrition OR undernutrition OR nutrition OR malnutrition OR incarceration OR prison OR crowding OR "air pollution"))* [Mesh]

Figure 1: Systematic review flow chart for selection of papers.

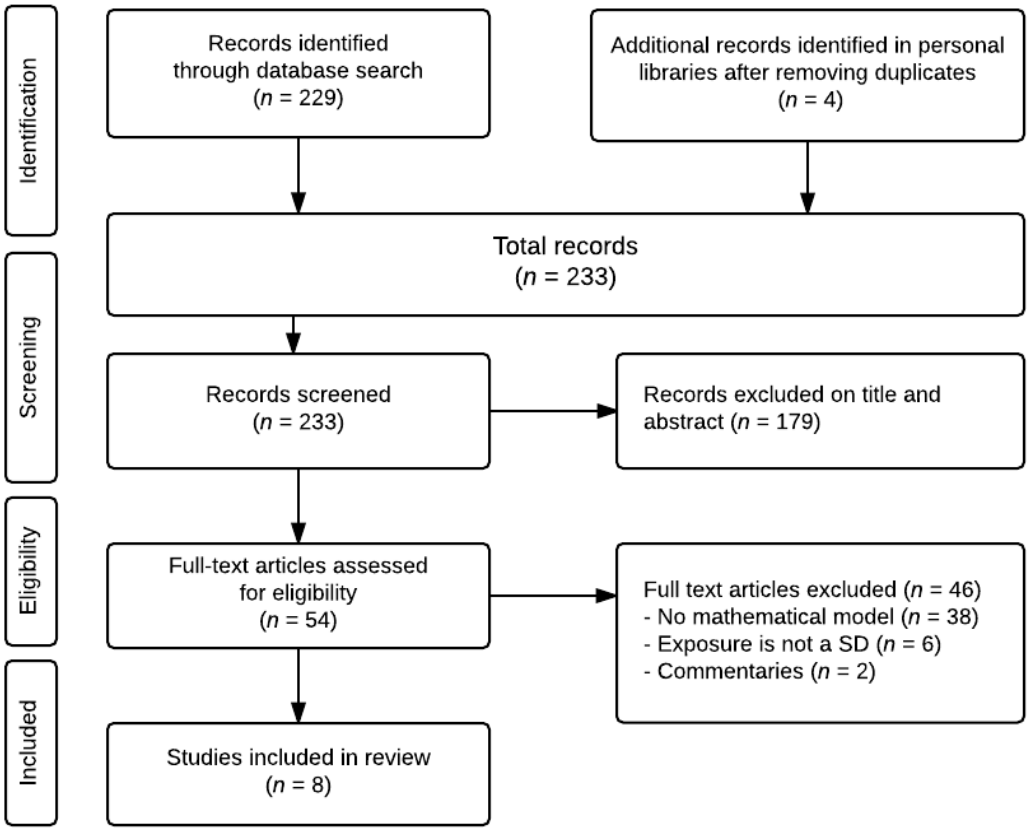


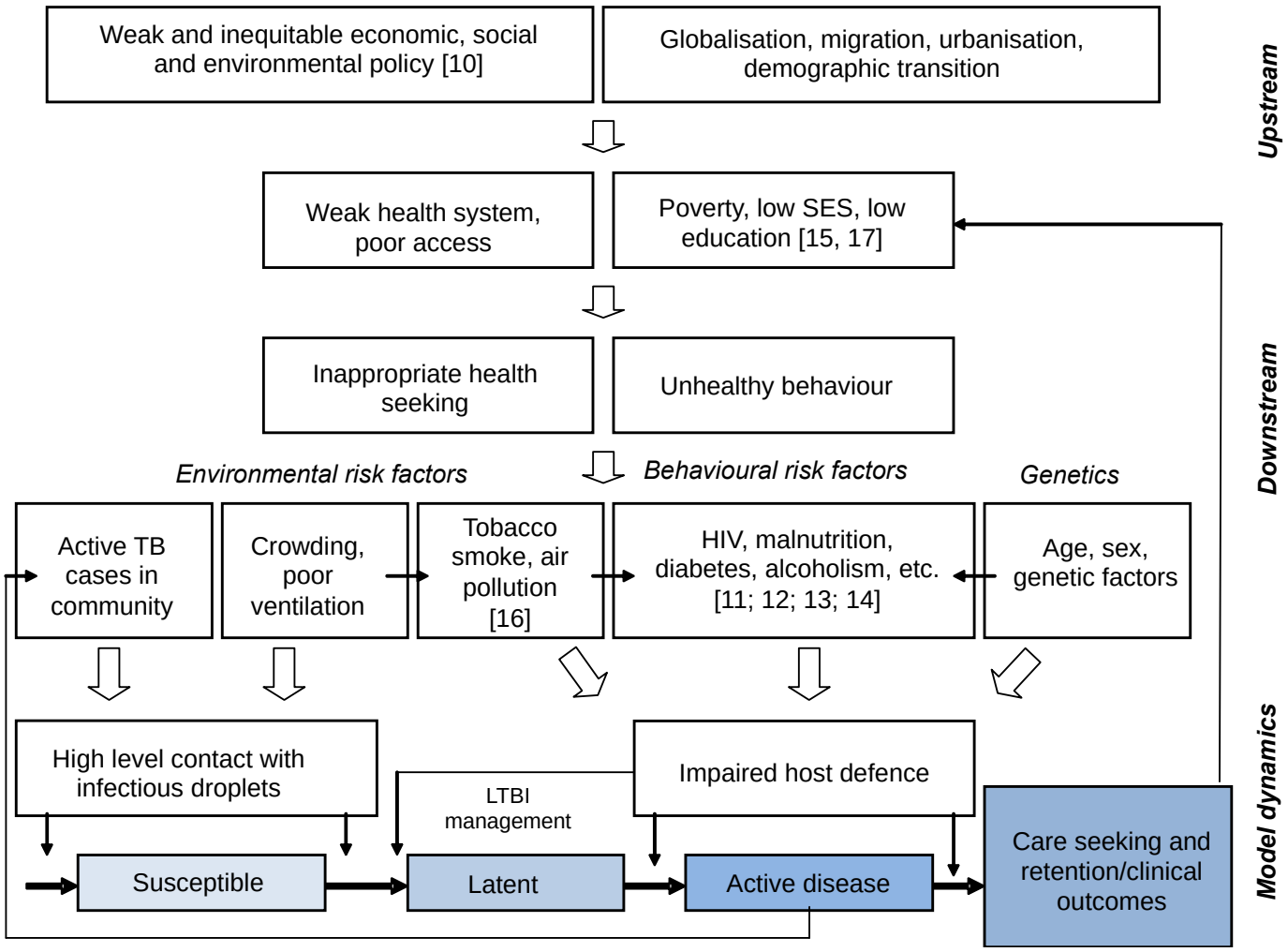
Table 2: Summary of studies identified in the systematic review

Ref	Aim of the study	Key socioeconomic factors investigated	Mathematical modelling methods/Type and features of the simulation model	Setting	Conclusion(s)
(10) (Reeves, 2015)	To project the potential influence of the economic recession on TB epidemiology in Europe until 2030.	Government expenditure per capita on public health services. GDP and cumulative decline in GDP during the recession period as a measure of the severity of the recession	Dynamic model SLIR (susceptible-latent-infectious-recovered) model. Authors applied the findings from the preceding econometric models to dynamic mathematical models of TB transmission and mortality. The mathematical models simulated longitudinal TB rates in each country – given the data on case detection observed before, during and after the financial crisis – as well as a counterfactual scenario in which case detection was unaffected by either the recession or the related austerity.	Europe	Recession can lead to short-term reductions in the financial support of programmes for TB control. The associated decrease in the detection of TB is projected to result in sustained, long-term rises in TB incidence, prevalence and mortality.
(15) (Andrews, 2015)	To illustrate the role of social mixing in shaping disparities in the distribution of TB, and demonstrate how the concentration of disease risk and transmission among the poor presents challenges and opportunities for TB control	Wealth	Dynamic Deterministic, compartmental model with parallel structure for two wealth groups with varying parameters, contact rates and social mixing.	India	TB control efforts may benefit from preferential targeting toward the poor.
(16) (Lin, 2008)	To predict the effects of risk-factors trends on COPD, lung cancer and TB	Smoking, solid fuel use	Dynamic Dynamic TB transmission model: deterministic compartmental (SLIR)	China	Reducing smoking and solid-fuel use can substantially reduce predictions of COPD and lung cancer burden and would contribute to effective TB control in China (even when DOTS implementation is less effective)

(11) (Oxlade, 2015)	To project future trends in TB related outcomes under different scenarios for reducing under-nutrition in the adult population in the Central Eastern states of India	Under-nutrition	Dynamic Compartmental TB transmission model stratified by body mass index (BMI) parameterised using national and regional data from India (model population is stratified into four exposure levels defined by the mean BMI for each quartile).	India	Intervening on under-nutrition could have a substantial impact on TB incidence and mortality in areas with high prevalence of under nutrition
(14) (Ackley, 2015)	To explore the population-level effects of malnutrition and genetic heterogeneity in TB susceptibility on TB epidemics	Malnutrition, genetic heterogeneity	Dynamic Dynamic TB transmission model: deterministic compartmental susceptible-latent-infectious-recovered model.	First Nations community in Canada	I) Changes in a population's nutritional status can have significant effects on TB dynamics II) Inclusion of heterogeneity in susceptibility to *M.tb* infection or risk of TB disease yields improved fit to data
(17) (Bhunu, 2012	To assess the impact of socioeconomic conditions on TB transmission, taking into account heterogeneous mixing patterns.	Socioeconomic conditions (overcrowding, increased endogenous reactivation, reduced socioeconomic status, reduced treatment uptake and poor nutrition on TB dynamics).	Dynamic Dynamic TB transmission model: deterministic compartmental Susceptible-Exposed-Infectious-Recovered model	Zimbabwe	Poverty enhances TB transmission as overcrowding, poor nutrition, reduced treatment uptake and lower socioeconomic status worsen TB; therefore, TB transmission rates are higher in poor communities than in the rich ones.
(12) (Odone, 2014)	I) To review epidemiological and biological evidence to describe the relationship between TB, diabetes, and nutritional status. II) To review past trends, present burden, and available future global projections for diabetes, overweight and obesity, as well as undernutrition and food insecurity.	Diabetes, overweight and obesity, undernutrition and food insecurity	Non-dynamic Analytical model to estimate the effect of diabetes and undernutrition on TB incidence per person per year in different age groups, WHO regions, and over time in various scenarios.	World	Reduction of undernutrition and better prevention and care for diabetes combined with improved access to prevention of infection, quality diagnosis, and treatment for all people with TB, could produce a large preventive effect on TB and is crucial to reach the post-2015 TB targets.

	III) To estimate how different scenarios of future trends for diabetes and undernutrition could affect TB epidemiology until 2035				
(13) (Dye, 2011)	To explore the consequences for TB epidemiology and control of changes in BMI, diabetes, population age structure and urbanization in India and Korea	BMI, diabetes, population age structure and urbanization	Non-dynamic Analytical model	India, Republic of Korea	The combination of nutritional and demographic changes operating over the decade from 1998 tended to increase TB incidence per capita in high-burden India and reduce it in lower-burden Korea.

Figure 2: Framework for proximate risk factors, upstream determinants and TB mechanics.



Source: Adapted from Lönnroth et al, 2009

This framework provides an example of the complexity when considering SD in TB models, and it illustrates the complicate cascade of parameters from distal to downstream determinants affecting development of disease, and care and prevention. Studies identified during the literature review are in square brackets.

Table 3: Known relationships between proximal determinants and risk of developing TB disease

Proximal determinant	Relative risk of TB disease	References
HIV infection	2-20, 1.4 per 100 cells/mm^3 decrement in CD4	Corbett, 2013 (25) Sonnenberg, 2005 (26) Williams, 2005 (27)
Low BMI	1.14 per decrement in BMI	Lönnroth, 2010 (28)
Diabetes	2-4	Jeon, 2008 (29) Stevenson, 2007 (30)
Alcohol use (>40g/day)	2-5	Lönnroth, 2008 (31) Rehm, 2009 (32)
Smoking	1-5	Bates, 2007 (33) Lin, 2007 (34)
Indoor air pollution	1-6	Lin, 2007 (34) Sumpter, 2013 (35)

Appendix 1: Summary of model structure and parameters employed in the studies included in the review.

Study	**Model structure**			**Parameters employed to capture the effect of socioeconomic factors**
	Dynamic	Non-dynamic	Description	
Reeves et al, 2015 (10)	•		SLIR (Susceptible-Latent-Infectious-Recovered) deterministic compartmental model. Authors applied the findings from the preceding econometric models to dynamic mathematical models of TB transmission and mortality. The mathematical models projected TB incidence rates in each country (given the data on case detection observed before, during and after the financial crisis) as well as a counterfactual scenario in which case detection was unaffected by either the recession or the related austerity.	Parameter: diagnostic rate *(the rate (%/year) that TB cases get diagnosed per year).* Quantitative relationship: authors used the cumulative fall in GDP during the recession associated with falling case detection rates (from regression analysis, -0.22%) and applied it to dynamic models as a reduction in diagnosis rate.
Oxlade et al, 2015 (11)	•		SLIR (Susceptible-Latent-Infectious-Recovered) deterministic model. Compartmental TB transmission model stratified by body mass index (BMI) parameterised using national and regional data from India (model population is stratified into four exposure levels defined by the mean BMI for each quartile).	Parameter: rapid progression and reactivation rates by BMI stratum. Quantitative relationship: Relative risks of TB disease by BMI status directly applied to rapid progression and reactivation parameter values in each BMI stratum, i.e. relative risk of two for disease implemented as double the value for rapid progression and reactivation parameter values.
Lin et al, 2008 (16)	•		SLIR deterministic compartmental model. Smoking and indoor air pollution are introduced into the model by stratifying the model population into the four possible combinations of exposure to these risk factors, proportional to their actual (time-varying) prevalence in each of the nine Chinese province considered.	Parameter: Transmission and progression to disease. Quantitative relationship: Relative risks from systematic reviews, applied to specific strata. Effect on prevalence of latent infection applied as change in transmission.

Ackley et al, 2015 (14)	•		SLIR deterministic compartmental model for historical TB epidemics amongst First Nation populations in Canada.	Parameters: rapid progression to disease, reactivation, TB specific mortality, immunity. Quantitative relationship: model sampled from a range of relative risks of 1-3 to find fit to data.
Andrews et al, 2015 (15)	•		SLIR deterministic compartmental model. Parallel model structure for two wealth classes (poorer and wealthier), based on TB epidemic in India.	Parameter: mixing between wealth classes Quantitative relationship: hypothetical scenarios of differential mixing between wealth classes.
Bhunu et al, 2011 (17)	•		SEIR (Susceptible-Exposed-Infectious-Recovered) deterministic compartmental model. The model subdivides the population into 'rich' and 'poor' strata, which is defined according to health status and living conditions. Poverty-stricken individuals are defined as those who live in overcrowded living situations, suffer from poor health, are less likely to receive treatment and who have an increased risk of death from TB.	Parameters: contact rate, transmission upon contact, progression to disease, treatment access, death due to TB. Quantitative relationship: Theoretical scenarios where being poor leads to a higher probability of TB or death, and lower probability of accessing treatment.
Odone et al, 2014 (12)		•	Analytic model where change in TB incidence is directly estimated based on prevalence of diabetes and undernutrition, and relative risk of disease given that risk factor. Authors estimate the effect of diabetes and undernutrition on TB incidence per person per year in different age groups, WHO regions, and over time in various scenarios.	Parameter: prevalence of diabetes and/or undernutrition. Quantitative relationship: Relative risk of TB disease for diabetes and undernutrition.
Dye et al, 2011 (13)		•	Analytic model where change in TB incidence is estimated based on changes in prevalence of diabetes, BMI and urbanization in India and Korea from 1998 to 2008.	Parameter: prevalence of diabetes, undernutrition, and urbanization. Quantitative relationship: Relative risk of TB disease for diabetes and undernutrition.