Projection of tuberculosis incidence with increasing immigration trends ☆

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ABSTRACT

Tuberculosis (TB) incidence rates vary substantially from regions to regions and from countries to countries. In countries such as Canada where TB incidence rate is low, increasing immigration trends may have significant impact on the TB transmission patterns in these countries. In this study we formulate a deterministic epidemiological model of TB transmission in two demographically distinct populations: Canadian born and foreign born populations, in order to investigate the effects of this demographic distinction on the short-term incidence and long-term transmission dynamics, and with special emphasis on the impact of immigration latent TB cases on the overall TB incidence rate in the whole population.

1. Introduction

The primary objective of this study is to forecast future trends in the incidence of infectious tuberculosis (TB) in Canada using a deterministic mathematical model. While the study will predict future TB trends in the Canadian born and foreign born populations individually, it will also take into consideration the spread of TB between these two populations and their effect on national TB incidence rates as a whole.

TB is a bacterial infection that spreads from one person to another by the airborne route. Initial infection with TB occurs when bacteria within aerosolized droplets are inhaled into the lung (Smith and Moss, 1994). Characteristics of the host immune response dictate whether an exposed individual will develop latent infection, in which the bacteria are contained, or active disease, where the host develops clinical symptoms and can transmit manifestations of disease. It is in general felt that about

5% will develop active TB within 2 years of exposure, and another 5% will develop active TB more than 2 years from the time of exposure (i.e., adding up to a 10% lifetime risk) (Adler and Rose, 1996; Comstock, 1982; Karus, 1983; Styblo, 1986; WHO Fact Sheet).

TB infects roughly one-third of the world's population, killing more than three million people every year today and potentially could cause the death of another 40 million people over the next 20 years (Bleed et al., 2001; WHO, 2004). TB is also the number one killer of HIV-positive individuals, accounting for more than 30% of AIDS deaths (WHO, 1996). The figure of worldwide new infection is staggering: someone in the world is newly infected with TB every second and nearly 1% of the world's population is newly infected with TB each year.

While most cases and deaths occur in developing countries, TB still maintains a presence in industrialized parts of the world. With the deterioration of health services in many developing nations and the emergence of multi extensively drug resistant TB, the prospect of a global TB epidemic is a very real threat to nations throughout the world and many industrialized nations recognize that the growing global TB epidemic poses a national threat to their health and economic security. In 1993, driven by these related concerns, the World Health Organization declared TB to be a global emergency—the first disease to carry this status in the organization's history.

In the industrialized world, TB disproportionately affects immigrant and refugee populations. In Canada, for example, two-thirds of the country's TB cases occur in the nation's foreign born population, which comprises less than one-fifth of the

Canadian population. In the Great Toronto Area, approximately 95% of TB cases are reported among foreign born persons, who account for just one-half of the city's inhabitants. The proportion of TB cases among foreign born individuals has been on the rise in Canada since the 1970s (Health Canada, Tuberculosis in Canada, 2001b).

Although TB has become less common in Canada as a result of improvements in housing, nutrition and the introduction of antibiotics, there have been significant concerns about the increasing proportion of TB cases among immigrants as a result of immigration from TB-endemic countries. Since the Second World War, approximately 7.8 million immigrants (almost 150,000 per year) have arrived in Canada (Health Canada, Immigration and Health,). Since 1990, Canada has accepted approximately 230,000 immigrants per year, representing about 0.7% of the Canadian population. In 1996, almost five million people, or 17.4% of the Canadian population, were foreign born.

Understanding the impact of immigration on the transmission dynamics of TB within the immigration population and across the whole community is therefore of considerable importance. The purpose of this project is to construct a mathematical model of disease transmission that takes into account both epidemiological and demographic factors associated with the stratification of the population into the subpopulation of the Canadian born and the subpopulation of immigrants and refugees. More specifically, we shall consider the case where the total population is divided into two subgroups: Canadian born individuals and immigrants, with both the Canadian born and foreign born populations being further divided into four epidemiological groups: susceptible, latent infection, infectious and recovery/treated classes. The model will then become a system of coupled difference equations, and some qualitative and quantitative analysis of the long-term behaviors of the transmission dynamics either within the subpopulation of foreign born or within the whole population will be carried out.

The parameters involved in the model are related to social, economical and cultural factors, and can be altered by various immigration policies and public health prevention and control measures. The data used for parameter identification here is compiled from various sources including TB data from Public Health Agency of Canada, annual demographic data from Statistics Canada, and citizenship and immigration data from Citizenship and Immigration Canada. Identified parameters then allow us to carry out some model-based simulations to provide a projection of socio-demographic profile of affected populations under various immigration policies and immigration medical screening conditions. This analysis should produce useful health policy tools to understand and to predict the epidemiological consequences of medical and behavioral interventions.

The focus of this study is to incorporate immigration subpopulation into a compartmental model and to use real data for parameter identification. We note that Waale et al. formulated a mathematical model of TB in 1962 and intensive work has been done. The work of Waaler et al. (1962) used data from a rural area in South India for the period 1950–1955 to identify the model parameters, and these parameters then set useful ranges for the estimation of parameters in developing nations. There are now many results on the modeling and analysis of TB transmission. In parallel to the historical evolution of dynamical models of TB that follows a common pattern in mathematical biology from linear to nonlinear, from one strain to multiple strains, from homogeneous to heterogeneous, from deterministic to stochastic, and from empirical to theoretical, remarkable progress in the development of a theoretical framework for the study of the dynamics of TB and other epidemiological processes, based on the use of systems of difference equations, differential equations, integro-differential equations and Markov chains, has been made. See, for example, Arino et al., 2003; Blower et al., 1996; Castillo-Chavez and Feng, 1997; Feng et al., 2002; Murphy et al., 2002, 2003; Travis and Blower, 1998 and a recent survey article Castillo-Chavez and Song, 2004.

The paper is organized as follows. The TB transmission model among foreign born and Canadian born populations is formulated and simplified in Section 2, and the long-term dynamics is described in Section 3. Statistical data and parameter identification are presented in Section 4, together with some simulation results and projection profiles of TB cases under different immigration rates of latent TB cases. The final section contains a short discussion of the main results and some remarks where the model and analysis can be further improved.

2. Model formulation and simplification

We consider the case where the total population is divided into two subgroups: Canadian born population and foreign born population, with both subgroups being further divided into four epidemiological compartments: susceptible (S), latent infection (E), infectious (I) and recovery/treated (R). The susceptible individuals can become infected and enter the latent infection class, while the latent infection individuals will develop active TB and enter infectious or treated class. Persons with active TB can recover spontaneously or with treatment, or die.

Here by foreign born population we mean first generation immigrants: any one born in Canada is grouped into the Canadian born population, in other words, foreign born individuals are only those not born in Canada regardless of their ancestry. This assumption that all Canadian born individuals are epidemiologically equivalent is certainly an approximation of the reality. Further refinement should be made, once relevant data become available, to account for the epidemiological distinction of individuals with different immigration backgrounds and histories.

Note that not all persons who are exposed will develop latent (i.e., dormant) TB infection that generally requires fairly close contact for a reasonable period of time (generally several hours). Note also that only about 10% individuals with latent infection will develop active disease. Here, we use latent TB infection for those who will go on to develop active TB with the mean latent period. Therefore, the transmission rate β in our model is the rate at which a susceptible is so effectively exposed that he/she will eventually enter the infectious or treated class. As such, the rate from the latent infection to the infectious or treated class will be larger than the rate from the exposed class to the infectious class.

Assumed in the model below is the "effective" transmission rate: all infected individuals will develop active-TB (if they survive latency period). Therefore, we implicitly assume that latently infected individuals who are not going to progress to active-TB are fully susceptible to reinfection. See Nardell et al., 1986; Small et al., 1993; de Viedma et al., 2002 for supporting references of reinfection using molecular fingerprinting for TB.

We also note that individuals with different disease ages (time since the exposure) have different degrees of risk of developing the clinical diseases. In our formulation, all individuals in the latent infection class will become infectious with the mean latent period. To better describe the contribution to the disease dynamics of those who will develop the clinical diseases after the mean latent period, one may consider the approach introduced in Aparicio et al. (2002) and Ziv et al. (2001), by adding an extra low-risk class.

Note also that if persons with active TB develop disease involving their respiratory tract, they become infectious and can

potentially spread TB to others. It is important to note, however, that many individuals who develop active TB will not be infectious since the disease will involve a site other than their lungs. We also remark that persons with active TB can spontaneously recover from TB without treatment, recover with treatment, or die with or without treatment. Again it is important to note that "active" does not necessarily mean the same thing as "infectious".

The flow of individuals among the eight compartments is shown in Fig. 1, where the subscripts 0 and 1 stand for the Canadian born and foreign born populations, respectively. The parameters involved are as follows:

b: the per capita natural intrinsic birth rate,
μ: the per capita natural death rate,
α: the per capita rate at which an individual leaves the latent infection compartment,
q: the proportion of infectious TB cases,
$p = 1 - q$: the proportion of non-infectious TB cases,
δ: the per capita TB induced death rate,
γ: the per capita recovery (completely treated) rate,
A_s: the immigration rate of susceptible individuals,
A_e: the immigration rate of latent infection individuals.

The model describing the transmission dynamics is the following system of difference equations:

$$
\begin{cases}
S_0(t+1) - S_0(t) = B(t) - \mu_0 S_0(t) - g_0(t)S_0(t), \\
E_0(t+1) - E_0(t) = g_0(t)S_0(t) - (\mu_0 + \alpha_0)E_0(t), \\
I_0(t+1) - I_0(t) = q\alpha_0 E_0(t) - (\mu_0 + \delta_0 + \gamma_0)I_0(t), \\
T_0(t+1) - T_0(t) = p\alpha_0 E_0(t) + \gamma_0 I_0(t) - \mu_0 T_0(t), \\
S_1(t+1) - S_1(t) = A_s - \mu_1 S_1(t) - g_1(t)S_1(t), \\
E_1(t+1) - E_1(t) = A_e + g_1(t)S_1(t) - (\mu_1 + \alpha_1)E_1(t), \\
I_1(t+1) - I_1(t) = q\alpha_1 E_1(t) - (\mu_1 + \delta_1 + \gamma_1)I_1(t), \\
T_1(t+1) - T_1(t) = p\alpha_1 E_1(t) + \gamma_1 I_1(t) - \mu_1 T_1(t), \\
B(t) = bN(t)K(N(t)), \\
N_i(t) = S_i(t) + E_i(t) + I_i(t) + T_i(t), \quad i = 0, 1, \\
N(t) = N_0(t) + N_1(t).
\end{cases}
\tag{1}
$$

Note that for the sake of simplicity, we use b as the common intrinsic birth rate for individuals in different compartments and subpopulations. In the formula for $B(t)$, one can replace

$bN(t)$ by

$$
b_S[S_0(t) + S_1(t)] + b_E[E_0(t) + E_1(t)] + b_I[I_0(t) + I_1(t)] \\
+ b_T[T_0(t) + T_1(t)]
$$

with different b_S, b_E, b_I and b_T without changing much of the analysis and conclusions in the remaining part of this paper.

In the above formulation, the factor $K(N)$ involved in the natural birth rate describes the crowding effect. In particular, this together with the per capita natural death term $\mu_0 N$ should lead to logistic growth for the overall population. The function $K(N)$ thus satisfies the following property

$$
K(0) > 0, \quad K(+\infty) = -\infty, \quad K'(N) \leqslant 0 \text{ and} \\
K''(N) \leqslant 0 \quad \text{for } N > 0,
\tag{2}
$$

which will be used in the analysis of the long-term behaviors of our model (1).

Also, the forces of infection are given, using the standard incidence, by

$$
\begin{cases}
g_0(t) = \beta_0 I_0(t)/N_0(t) + \beta_{01} I_1(t)/N_1(t), \\
g_1(t) = \beta_{10} I_0(t)/N_0(t) + \beta_1 I_1(t)/N_1(t),
\end{cases}
\tag{3}
$$

where β_0 is the TB transmission rate from Canadian born TB infectious individuals to Canadian born susceptible individuals; β_{01} is the TB transmission rate from foreign born TB infectious individuals to Canadian born susceptible individuals; β_{10} is the TB transmission rate from Canadian born TB infectious individuals to foreign born susceptible individuals; β_1 is the TB transmission rate from foreign born TB infectious individuals to foreign born susceptible individuals.

The mathematical analysis of model (1) is complicated for the long-term incidence prediction, and a full account of all possible scenarios in terms of long-time transmission patterns is still remote at this stage. Nevertheless, as will be shown, some useful observations can be obtained.

Available statistical data shows that TB transmission between foreign born and Canadian born persons is considered a fairly uncommon event. See Kulaga et al. (2002) and Hernandez-Garduno et al. (2002) for supporting data from Montreal and Vancouver, similar results from a Toronto fingerprinting study support this as well, though these results have not been published yet. Hence, it is a good approximation to take $\beta_{01} = \beta_{10} = 0$ in our preliminary analysis and simulations. Mathematically, the qualitative results presented below will remain unchanged when these

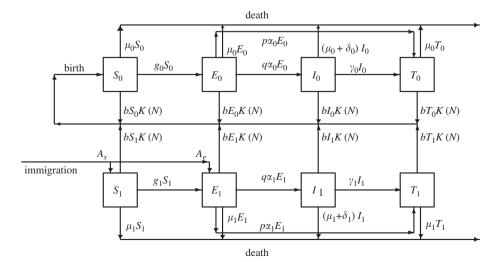Fig. 1. Transmission diagram of TB in Canada whose population consists of two subgroups: Canadian born (denoted by the subindex 0) and foreign born (denoted by the subindex 1), with each subgroup being further divided into four compartments (susceptible, latent infection, infectious and treated). In the figure, $g_0(t)$ and $g_1(t)$ are the forces of infection from the Canadian born and foreign born populations.

two transmission rates are both small, by using a standard perturbation theory. Nevertheless, we should emphasize that increasing the mixing between foreign born and Canadian born populations may alter this assumption and lead to a higher level of infection in the Canadian born population. We shall carry out some numerical simulations to illustrate this point by increasing β_{01} and β_{10} (see Figs. 3 and 9, and Appendix A).

Note that in the case where $\beta_{01} = \beta_{10} = 0$, the last four equations for the foreign born population are decoupled from the first four equations and we have the following isolated subsystem:

$$\begin{cases} S_1(t+1) - S_1(t) = A_s - \mu_1 S_1(t) - \beta_1 S_1(t) I_1(t)/N_1(t), \\ E_1(t+1) - E_1(t) = A_e + \beta_1 S_1(t) I_1(t)/N_1(t) - (\mu_1 + \alpha_1) E_1(t), \\ I_1(t+1) - I_1(t) = q\alpha_1 E_1(t) - (\mu_1 + \delta_1 + \gamma_1) I_1(t), \\ T_1(t+1) - T_1(t) = p\alpha_1 E_1(t) + \gamma_1 I_1(t) - \mu_1 T_1(t). \end{cases} \quad (4)$$

Hence, we can study this isolated system for the foreign born population first and then substitute the limit values into the first four equations in order to understand the long-term dynamics of the Canadian born population.

3. Long-term behaviors

In this section, to qualitatively understand the impact of immigration on the transmission of both foreign born and Canadian born populations, we shall assume the rates A_s and A_e are constants, although they vary in time and we shall use time-dependent rates later for numerical simulations.

The introduction of a new infectious individual produces $\beta_1/(\mu_1 + \delta_1 + \gamma_1)$ new infections but only the fraction $q\alpha_1/(\mu_1 + \alpha_1)$ survives the latency period and becomes infectious, resulting in new cases. Therefore, the basic reproduction number for the foreign born population is

$$R_0^1 = \frac{q\beta_1\alpha_1}{(\mu_1 + \alpha_1)(\mu_1 + \delta_1 + \gamma_1)}. \quad (5)$$

As shall be shown, this basic reproduction number, along with the rate of immigration A_s and the rate A_e of admitting latent TB cases, plays a crucial role in the transmission dynamics in both the foreign born and Canadian born populations.

The transmission dynamics is related to the structure and stability of equilibria, obtained by solving a system of algebraic equations. In particular, we have

$$\begin{cases} T_1 = \frac{\alpha_1(\gamma_1 + p(\mu_1 + \delta_1))}{\mu_1(\mu_1 + \delta_1 + \gamma_1)} E_1, \\ I_1 = \frac{q\alpha_1}{\mu_1 + \delta_1 + \gamma_1} E_1, \\ S_1 = \frac{A_s + A_e}{\mu_1} - \frac{\mu_1 + \alpha_1}{\mu_1} E_1, \\ N_1 = \frac{A_s + A_e}{\mu_1} - \frac{q\alpha_1\delta_1}{\mu_1(\mu_1 + \delta_1 + \gamma_1)} E_1, \end{cases} \quad (6)$$

where E_1 is determined by

$$(\mu_1 + \alpha_1)E_1 = A_e + \frac{q\alpha_1\beta_1/(\mu_1 + \delta_1 + \gamma_1)[A_s + A_e - (\mu_1 + \alpha_1)E_1]}{A_s + A_e - q\alpha_1\delta_1/(\mu_1 + \delta_1 + \gamma_1)E_1} E_1. \quad (7)$$

3.1. Role of R_0^1 and A_s

In the simplest case where $A_s = A_e = 0$, the foreign born population will go extinct naturally. This is true mathematically, since $N_1(t+1) = (1 - \mu_1)N_1(t) - \delta_1 I_1(t) \leqslant (1 - \mu_1)^{t+1} N_1(0) \to 0$ as $n \to \infty$.

The more realistic and the most ideal case is when $A_s > 0$ and $A_e = 0$. In this case, a straightforward calculation shows that

(i) when $R_0^1 < 1$, model (4) has only the disease free equilibrium $W_0^f = (A_s/\mu_1, 0, 0, 0)$ that is globally asymptotically stable;
(ii) where $R_0^1 > 1$, model (4) has two equilibria: the disease free equilibrium W_0^f that is unstable, and the asymptotically stable endemic equilibrium $W_0^e = (S_1^*, E_1^*, I_1^*, T_1^*)$ with E_1^* being the unique positive solution of Eq. (7), and other components being determined from the relationship (6). This positive solution is given by

$$E_1^* = \frac{\mu_1 + \delta_1 + \gamma_1}{q\alpha_1(\beta_1 - \delta_1)}(R_0^1 - 1)A_s. \quad (8)$$

Note that $\delta_1 < \beta_1$ if $R_0^1 > 1$.

Therefore, whether there will be a TB epidemic in the foreign born population is determined by the value of R_0^1: when $R_0^1 < 1$ the foreign born population will eventually be TB free, while if $R_0^1 > 1$ the foreign population will remain at a sustained level of TB infection. This level of infection is determined by the immigration rate A_s and the parameter α_1, among others. The first (A_s) is related to the immigration policy and the second (α_1) is associated with the disease progression within the foreign born population: the quicker the latent foreign born TB cases develop the disease, the larger the α_1, and thus the higher level of TB infection among the foreign borns.

3.2. Role of A_e

In the case where $A_e > 0$, model (4) has only the endemic equilibrium $W_1^e = (S_1^e, E_1^e, I_1^e, T_1^e)$ which is stable, with E_1^e being the unique positive solution of Eq. (7).

Eq. (7) has a unique positive solution, because the right-hand side equals A_e at the endpoints of the interval $(0, (A_s + A_e)/(\mu_1 + \alpha_1))$ and gives a concave down curve C_R on this interval, while the left-hand side gives a straight line C_L rising from below to above C_R. See Fig. 2 (top-right) for an illustration.

A careful examination of the intersection of the above curves shows that the location of the E_1 coordinate of this unique intersection increases with R_0^1: the ratio of the slope of C_R over the slope of C_L at $E_1 = 0$ is exactly R_0^1.

It is possible to calculate the additional number of latent individuals due to the imported latent cases at the equilibrium, and this is given by the difference of the equilibrium E_1^e and the value given in (8), namely,

$$\Delta = E_1^e - E_1^* = E_1^e - \frac{\mu_1 + \delta_1 + \gamma_1}{q\alpha_1(\beta_1 - \delta_1)}(R_0^1 - 1)A_s. \quad (9)$$

This quantity provides an important measure for determining the role of medical screening of immigrants, as effective medical screening of immigrants should reduce the number A_s.

We now use model (4) with a fixed set of parameter values to numerically illustrate our discussions so far, and we defer to later sections for the justification of these model parameters. We let

$$q = 0.57, \quad \alpha_1 = 1/60, \quad \mu_1 = 0.0071/12, \quad \delta_1 = 0.060/12,$$
$$\gamma_1 = 1/2, \quad A_s = 18414,$$

where the time unit is month. Substituting these parameter values to (5) we have

$$R_0 = 1.0887\beta_1.$$

Therefore, in the case $A_e = 0$, model (4) has no endemic equilibrium if $\beta_1 < 0.9185$, and admits one endemic equilibrium W_0^e with equilibrium coordinate

$$E_1^e = 1066963 \times \frac{\beta_1 - 0.9185}{\beta_1 - 0.005} \quad \text{for } \beta_1 > 0.9185.$$
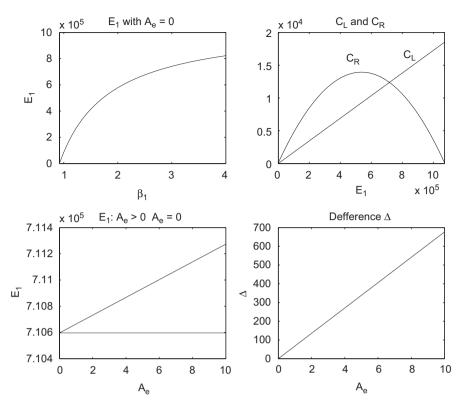
Fig. 2. Influence of importing the latent. Top-left: the equilibrium E_1-component as a function of β_1 when $A_e = 0$. Top-right: The curve C_R and the straight line C_L as functions of E_1, their intersection gives the equilibrium value E_1^e. Bottom-left: the E_1 component E_1^e at the equilibrium is almost a linear function of $A_e > 0$, while the horizontal line corresponds to E_1^* or E_1^e with $A_e = 0$. Bottom-right: the difference Δ as a function of A_e has the slope 67.6.

Fig. 2 (top-left) shows the impact of β_1 on the endemic: the E_1-component of the endemic equilibrium increases sharply after $\beta_1 = 0.9185$ and reaches the level of 8.6×10^4 when β_1 is close to 1. Fig. 2 (top-right), with $\beta_1 = 2.74$ and $A_e = 97$, illustrates the argument that when $A_e > 0$, Eq. (8) always has a unique positive solution given by the intersection of the curve C_R and the line C_L. The bottom figures show that the E_1 component E_1^e at the equilibrium is almost a linear function of $A_e > 0$ (the bottom-left straight line with positive slope, while the horizontal line corresponds to E_1^* or E_1^e with $A_e = 0$) and the difference Δ is almost a linear function of $A_e \in (0, 10)$ with slope 67.6. It is clear that E_1^e increases very fast with respect to the infection rate β_1, and the new infection generated by an importing latent infection is large.

3.3. Long-term impact on Canadian born population

As the size of each compartment within the foreign born population eventually reaches its equilibrium state, the subsystem for the Canadian born can then be regarded as an asymptotically autonomous system and the limiting system can be obtained by simply replacing $S_1(t)$, $E_1(t)$, $I_1(t)$ and $T_1(t)$ with their corresponding limits. The limiting equation for the Canadian born population is

$$
\begin{cases}
S_0(t+1) - S_0(t) = B_0(t) + B_1^e(t) - \mu_0 S_0(t) - g_0(t)S_0(t), \\
E_0(t+1) - E_0(t) = g_0(t)S_0(t) - (\mu_0 + \alpha_0)E_0(t), \\
I_0(t+1) - I_0(t) = q\alpha_0 E_0(t) - (\mu_0 + \delta_0 + \gamma_0)I_0(t), \\
T_0(t+1) - T_0(t) = p\alpha_0 E_0(t) + \gamma_0 I_0(t) - \mu_0 T_0(t), \\
B_0(t) = b(S_0(t) + E_0(t) + I_0(t) + T_0(t))K(N_0(t) + N_1^e), \\
B_1^e(t) = bN_1^e K(N_0(t) + N_1^e), \quad N_1^e = S_1^e + E_1^e + I_1^e + T_1^e.
\end{cases}
\tag{10}
$$

Again, the structure of equilibria determines the long-term dynamics of this subsystem. To be more precise, we note that

the equilibria are given by solving a system of algebraic equations:

$$
\begin{cases}
T_0 = \dfrac{(\gamma_0 + p(\mu_0 + \delta_0))\alpha_0}{\mu_0(\mu_0 + \delta_0 + \gamma_0)}E_0 := a_T E_0, \\
I_0 = \dfrac{q\alpha_0}{\mu_0 + \delta_0 + \gamma_0}E_0 := a_I E_0
\end{cases}
\tag{11}
$$

with E_0 being determined by

$$
(\mu_0 + \alpha_0)E_0 = \beta_0 a_I E_0 S_0 / N_0.
\tag{12}
$$

Therefore, either $E_0 = 0$, or

$$
N_0/S_0 = \frac{\beta_0 a_I}{\mu_0 + \alpha_0} = \frac{q\beta_0 \alpha_0}{(\mu_0 + \alpha_0)(\mu_0 + \delta_0 + \gamma_0)} := R_0^0.
\tag{13}
$$

Immediately, we obtain that if $R_0^0 < 1$ then the subsystem (10) has only disease free equilibrium.

The S_0 component of the disease free equilibrium, when $R_0^0 > 1$, is given by solving

$$
0 = K(S_0 + N_1^e)[bS_0 + bN_1^e] - \mu_0 S_0.
\tag{14}
$$

The right-hand side gives a concave down curve, its value is positive at $S_0 = 0$ and negative at $S_0 = +\infty$. Therefore, there is always a unique positive solution S_0^f of Eq. (14). That gives a non-trivial unstable disease free equilibrium $(S_0^f, 0, 0, 0)$ for system (10).

If $R_0^0 > 1$, and if there is an endemic equilibrium, then we must have $S_0 = (S_0 + E_0 + a_I E_0 + a_T E_0)/R_0^0$ from which it follows that

$$
S_0 = a_S E_0 := \frac{1}{R_0^0 - 1}(1 + a_I + a_T)E_0.
\tag{15}
$$

Substituting this into the first equation of system (10), we obtain

$$
K((1 + a_S + a_I + a_T)E_0 + N_1^e)b[(1 + a_S + a_I + b_T)E_0 + N_1^e]
$$
$$
= \mu_0 a_S E_0 + (\mu_0 + \alpha_0)a_I E_0.
\tag{16}
$$

Again, the left-hand side of the above equation gives a concave down curve while the right hand is a straight line rising from below to above this concave curve, and thus the equation has a unique positive solution E_0^e. This gives the E_0 component of an endemic equilibrium, whose other components are determined by E_0^e and the relationships in (11) and (15).

To summarize, whether there is a sustained level of infection in the Canadian born population is fully determined by whether or not $R_0^0 > 1$, and this observation has nothing to do with whether there is an endemic in the foreign born population, that is determined by R_0^1. Of course, this observation holds only when the transmission from the foreign born to the Canadian born is zero. Our simulation shows that this observation is no longer true if the transmission from the foreign born to Canadian born is not small. Substituting parameters specified in Fig. 3 into models (4) and (10), we obtain $R_0^1 = 0.0523$, $R_0^0 = 0.6561$, $S_1^e = 31113266$, $E_1^e = 5929$, $I_1^e = 111$, $T_1^e = 165949$, $N_1^e = 31285255$. In the case where $\beta_{01} = 0$, model (4) has no endemic equilibrium since $R_0^0 < 1$. The endemic equilibrium W_0^e, however, exists if the transmission rate from the foreign born population to the Canadian born population is non-zero. Fig. 3 depicts the temporal evolution of the annual TB case number of Canadian born population with different values of β_{01}: $\beta_{01} = 0$, 0.2, 0.4, 0.6, respectively. The simulation shows that an endemic equilibrium of (10) exists if $\beta_{01} > 0$ though $R_0^0 < 1$. This endemic equilibrium of (10) seems to be globally asymptotically stable, with $(E_0(t), I_0(t)) \to (3733, 70)$ for $\beta_{01} = 0.2$; $(7432, 140)$ for $\beta_{01} = 0.4$; and $(11100, 209)$ for $\beta_{01} = 0.6$. This simulation clearly shows the significant impact of mixing between the Canadian born and the foreign born on the long-term dynamics of TB transmission in the total population.

4. Projection of the Canadian TB incidence and demographic profile

4.1. Statistical data

The worldwide estimated TB incidence rates vary from regions to regions. The largest number of cases occurs in the South-East Asia Region, which accounts for 33% of incident cases globally. The estimated incidence per capita in sub-saharan Africa is nearly twice that of the South-East Asia, around 350 cases per 100 000 population. Europe and Americas have the lowest TB incidence rates (http://www.who.int/mediacentre/factsheets/fs104/en/).

TB has become less common in Canada, as a result of improvements in housing, nutrition and the introduction of antibiotics. However, a dramatic increase in the proportion of foreign born cases of TB has been observed over the past 20 years in Canada, and an increasing immigration trend has been noticed recently. Consideration of the impact of immigrants on the TB incidence rates becomes necessary as the following immigration data show: since the Second World War, approximately 7.8 million immigrants (almost 150,000 per year) have arrived in Canada; since 1990, Canada has accepted approximately 230,000 immigrants per year, or about 0.7% of the Canadian population. In 1996, almost five million people, or 17.4% of the Canadian population, were foreign born (http://www.hc-sc.gc.ca/iacb-dgiac/arad-draa/english/rmdd/wpapers/Immigration.pdf,). Details of the immigration data are listed in Table 2 (Citizenship and Immigration Canada, 2005, 2006; http://www.hc-sc.gc.ca/iacb-dgiac/arad-draa/english/rmdd/wpapers/Immigration.pdf), based on which we calculate the value of $A_s(t)$ shown in Fig. 4. The average between 1985 and 2005 is $205,351$ per year, or $17,113$ per month. The

Fig. 3. Simulation based on model (10) with different β_{01} to illustrate the impact of the mixing between Canadian and foreign born populations on the TB transmission in the total population. The horizontal axis is time, and the unit is year. The vertical axes is TB case numbers of Canadian born population. In the simulation, we used the following parameters (the birth rate and death rate are from Statistics Canada,): $b = 0.0105/12$, $\alpha_0 = \alpha_1 = 1/60$, $\mu_0 = \mu_1 = 0.0071/12$, $\delta_0 = \delta_1 = 0.060/12$, $\gamma_0 = \gamma_1 = 1/2$, $q = 0.57$, $p = 0.43$, $A_s = 18414$, $A_e = 97$, $\beta_0 = 0.6026$, $\beta_1 = 0.048$. Also $K(x) = 1 - x/150\,000\,000$.

Fig. 4. The numbers (stars) of immigrants and reported TB cases during 1985–2005, and their fitted curves.

number of immigrants is well fitted by a cubic curve

$$A_s(t) = 137.5(t - 1984)^3 - 5133.4(t - 1984)^2 + 59057.8(t - 1984) + 15233.$$

We do not know how many immigrants newly accepted into Canada are infected in a specific year, but we have the yearly reported TB case numbers among foreign born and Canadian born populations, shown in Table 3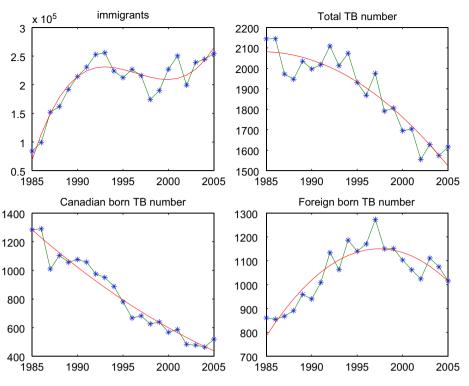 (Health Canada, Tuberculosis in Canada, 2001a) and Fig. 4. Note that the sum of the Canadian born and the foreign born is less than the total number in the table, and the difference is the number of those whose origins are unclear.

It is reported that the latency period is significantly shorter for Asian immigrants (mean of 9.1 years) compared to immigrants from other countries (http://www.hc-sc.gc.ca/iacb-dgiac/arad-draa/english/rmdd/wpapers/Immigration.pdf,). The mean latency period for TB among immigrants and refugees to Ontario during 1989–1995 between immigration and diagnosis was 9 years, and 53% of patients presented within five years of resettlement (Kerbel, 1997). An analysis of TB data from Toronto revealed that the highest rates of TB occurred among immigrants within five years of arrival in Canada (PHRED, 2000). The reported new active and relapsed foreign born TB cases by year of arrival in Canada is shown in Table 4 (Health Canada, Tuberculosis in Canada, 1996, 1997, 1998, 1999, 2000, 2001b; Public Health Agency of Canada, Tuberculosis in Canada, 2002, 2003, 2004, 2005a).

The TB death number from 1996 to 2001 is shown in Table 5, and the average yearly death rate during this period is 6.7%.

In 2005, 43% of all active disease cases were non-infectious (Public Health Agency of Canada, Tuberculosis in Canada, 2005b). The proportions over the past few years have ranged in 41–43%.

An important issue in simulation is the sensitivity on the transmission rates β_0 and β_1, since the total number of susceptibles is extremely large compared with the infected. This sensitivity is related to the assumption that the infected is uniformly distributed among the whole population and hence each individual has the same probability to be infected.

To avoid this sensitivity, we use the following procedure: we first use $\beta_0^*(t) = \beta_0 S_0(t)/N_0(t)$ and $\beta_1^*(t) = \beta_1 S_1(t)/N_1(t)$ and focus on the following systems for the latent and infectious compartments:

$$\begin{cases} E_0(t+1) = E_0(t) - (\mu_0 + \alpha_0)E_0(t) + \beta_0^*(t)I_0(t), \\ I_0(t+1) = I_0(t) + q\alpha_0 E_0(t) - (\mu_0 + \delta_0 + \gamma_0)I_0(t), \\ E_1(t+1) = A_e + E_1(t) - (\mu_1 + \alpha_1)E_1(t) + \beta_1^*(t)I_1(t), \\ I_1(t+1) = I_1(t) + q\alpha_1 E_1(t) - (\mu_1 + \delta_1 + \gamma_1)I_1(t). \end{cases} \quad (17)$$

We then use available data to backcalculate $\beta_0^*(t)$ and $\beta_1^*(t)$ and use this for short-range prediction. For long-term prediction, we use the average values of $\beta_0^*(t)$ and $\beta_1^*(t)$ during the period where data are available.

4.2. The simulation and projection of Canadian born TB

A key issue before a reliable simulation is the parameter identification from aforementioned data and the choice of initial values. We set, using month as the time unit, $\mu = 0.0071/12$, $\delta = 0.067/12$, $\alpha = 1/60$, $\gamma = 1/2$. In other words, we assume that the population death rate is 0.71% yearly, the TB induced death rate is 6.7%, the average TB latent period is 5 years, and the TB infectious period is 2 month.

We use 10 year data (1991–2000) to estimate the infection rate $\beta_0^*(t)$ in our simplified model (17), and then use the next 5 year data (2001–2005) to validate the model and the parameters. The procedure is as follows: we first fit the Canadian born TB case numbers to a quadratic curve. This, using Matlab, is given by

$$3.424(t - 1990)^2 - 92.842(t - 1990) + 1162.$$

The real data and the fitted curve are shown in Fig. 5 (top-left). The monthly reported numbers of Canadian born infectious TB
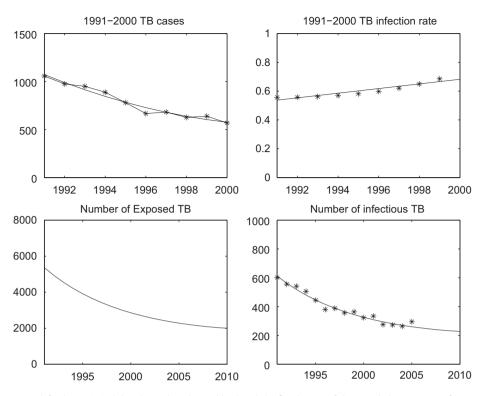
Fig. 5. The Canadian born TB. Top-left: the statistical data (stars, based on Table 3) and the fitted curve of the Canada born TB cases from 1991 to 2000; Top-right: the estimated Canadian born TB infection rate and its fitted curve. Bottom-left: the number of Canadian born latent infection TB. Bottom-right: the projection of Canadian born TB cases until 2010.

cases can then be computed on the basis of this fitting curve, and these numbers correspond to the item $\alpha_0 E_0(t)$ in the first equation of model (17). From the second equation of (17) we obtain the monthly number of infectious TB cases, since the transferring number $\alpha_0 E_0(t)$ and parameters μ_0, δ_0 and γ_0 have been determined, i.e.,

$$I_0(t+1) = I_0(t) + q\alpha_0 E_0(t) - (\mu_0 + \delta_0 + \gamma_0)I_0(t).$$

Then, $\beta_0^*(t)$ can be derived by the first equation of (17):

$$\beta_0^*(t) = \frac{E_0(t+1) - (1 - \mu_0 - \alpha_0)E_0(t)}{I_0(t)}.$$

A linear function fits the infection rate curve $\beta_0^*(t)$ well, and this gives

$$\beta_0^*(t) = 0.521258 + 0.0013447t,$$

where $t = 1$ corresponds to the first month of 1991. The infection rate and its fitted curve are shown in Fig. 5 (top-right).

The average value of the Canadian born TB infection rate between 1991 and 2000 is 0.6026. This means that every infectious TB case generated 0.6026 new infection per month, and each infectious person thus produced 1.2052 infected individual (0.687 infectious TB case and 0.5182 non-infectious TB case) during the infection period.

The estimated Canadian born latent infection is given in Fig. 5 (bottom-left). It shows that there was a large pool of Canadian exposed TB. These become active some years later. The small average infection rate explains why reported TB cases among the Canadian born population have been decreasing in the last two decades, and the large pool of exposed TB gives the reason that reported TB cases in the Canadian born population drops very slowly. We also note that the TB infection rate in Canadian born population is growing slowly, and if nothing to be changed, this

infection rate will reach 0.8818 in 2012. That is, after 2012 every infectious TB case will produce more than one new infectious TB case during the two month infectious period. The TB cases will substantially increase again among Canadian born population, and we will have to deal with the re-emergence of TB in Canadian born population.

Substituting the above fitted curves in the first two equations of (17), we obtain a linear discrete model for the Canadian born TB case

$$E_0(t+1) = 0.98275E_0(t) + (0.521258 + 0.0013447t)I_0(t),$$
$$I_0(t+1) = 0.0095E_0(t) + 0.4944I_0(t). \tag{18}$$

This gives the predictive formula for future Canadian born TB.

All we need now is to determine the initial values for the model. The latent TB number $E_0(t)$ is a good reference for the initial value. Our estimate of $\alpha_0 E_0(t)$ at the first month of 1991 is 93, hence we set the initial value of $E_0(t)$ to be 5586. To determine the initial value for $I_0(t)$, we assume that the number of infectious TB cases at the first two months are the same. Using the second equation of (18), we can calculate the initial value for $I_0(t)$, which is 106. We use the linear model (18) to carry out simulations month by month. The monthly numbers are then added to obtain the yearly data. The simulated result is shown in Fig. 5 (bottom-right) for the number of infectious TB cases, where stars are the statistical data and the curve is obtained through the simulation. The curve gives the prediction of Canadian born TB from 2006 to 2010.

4.3. The simulation and projection of foreign born TB

It is estimated that the vast majority (95–98%) of all TB infections in immigrants occur in their country of origin

(Hernandez-Garduno et al., 2002; Kulaga et al., 2002). To run the simulation, we first focus on the estimation of the infection rate β_1 and the number of immigrant latent TB cases. The foreign born TB case numbers are best fitted by a quadratic curve, given by

$$-6.01520(t - 1990)^2 + 76.4152(t - 1990) + 949.2000,$$

as shown in Fig. 6 (top).

The monthly numbers of foreign born infectious TB cases are then computed on the basis of the curve. These numbers correspond to the item $\alpha_1 E_1(t)$ in the last equation of model (17). We divide the infected TB number of the new entering $E_1(t)$ into two part, 95% infection occurred in their origin countries, which gives the latent infection TB number among immigrants $A_e(t)$, 5% for the infection after arrival in Canada, which gives the last part of the third equation in (17). In order to estimate $\beta_1^*(t)$, we first calculate $I_1(t)$ from the last equation of model (17),

$$I_1(t + 1) = I_1(t) + q\alpha_1 E_1(t) - (\mu_1 + \delta_1 + \gamma_1)I_1(t),$$

with the initial value 94. After obtaining $I_1(t)$, we use the third equation of model (17) to estimate $A_e(t)$ and $\beta_1^*(t)$ by

$$A_e(t) = 0.95[E_1(t + 1) - (1 - \mu_1 - \alpha_1)E_1(t)],$$
$$\beta_1^*(t) = 0.05 \times \frac{E_1(t + 1) - (1 - \mu_1 - \alpha_1)E_1(t)}{I_1(t)}.$$

We then calculate the average values of $A_e(t)$ and $\beta_1^*(t)$ as $A_e = 97$ and $\beta_1 = 0.048$.

The infection within Canada of the foreign borne populations contributed to only 5% of the TB infections reported and the majority comes from their original countries. This explains the relatively small average value of $\beta_1^*(t)$. We also note that the average value of $\beta_1(t) = 0.048$ is much smaller than the average 0.6026 for the Canada born TB infection rate. This seems to be puzzling as it is widely believed that the risk of TB transmission within the entire Canadian born population should be lower than the risk of TB transmission within the entire foreign born population. We think this arises from our model baseline assumption that the Canadian born population is a homogeneous group. A close look at the Canadian born population shows that high-risk Canadian born populations, namely homeless persons and aboriginal populations, have a very high number of TB cases although their relative sizes are small. If we follow our basic modeling setting and split the total Canadian born population into two distinct subgroups—a core and small subgroup (such as the aboriginal and the homeless group) and the rest—and if these two distinct subgroups do not interact much, then we obtain

$$\beta_0(t) = \beta_c(t)q + \beta_r(t)(1 - q).$$

This can be obtained by comparing the equation for $S_0(t + 1) - S_0(t)$ with the corresponding equation for $S_c(t) = S_c(t + 1) - S_c(t)$ and the equation for $S_r(t + 1) - S_r(t)$, where subindex c denotes the core subgroup and r for the rest of the Canadian born population. q is the ratio $I_c(t)/[I_c(t) + I_r(t)]$ which is, for the sake of simplicity here, assumed to be relatively unchanged (this is not too far from the real data, see, Public Health Agency of Canada, Tuberculosis in Canada, 2006a). Therefore, the average value 0.6026 for the entire Canadian born population considered as a homogeneous group is the linear combination of the average numbers β_c^a of β_c and β_r^a of $\beta_r : 0.6026 = \beta_c^a q + \beta_r^a(1 - q)$. Consequently, 0.6026 is the weighted average rate of infection (per month) for the entire Canadian born population. The average rate of infection among the high-risk group can be large, and the average rate of infection among the rest of the Canadian born can be much less than 0.048, specially when q is large. Of course, a more careful analysis is needed since q in general is not a constant and there are cross-infection between the core and the rest of the Canadian born population. This shows the importance of further stratification of the Canadian born population.
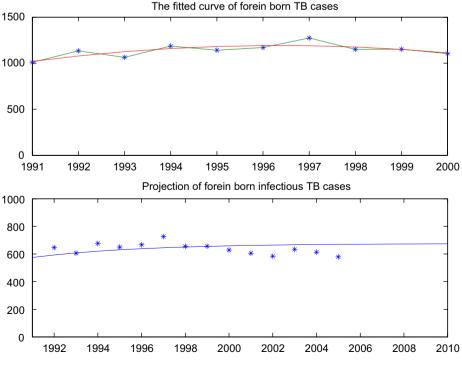

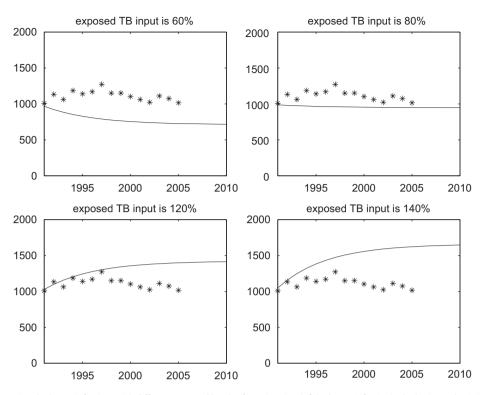Fig. 6. The foreign born TB infection rate and the projection until 2010.

Fig. 7. The influence of importing the latent infection, with different assumed levels of immigration (of the latent infection). The horizontal axis is year (starting from 1990), and the vertical axis is the number of foreign born TB cases.

Table 1
Simulation, validation and prediction of TB cases in Canada, 2001–2010

Year	reported	Prediction	ITB	DR TB	MDR TB
2001	1704	1704	971	206	25
2002	1555	1683	959	203	25
2003	1628	1664	948	201	24
2004	1574	1647	939	199	24
2005	1616	1632	930	197	24
2006	1621	1618	922	196	24
2007		1606	916	194	24
2008		1596	910	193	23
2009		1588	905	192	23
2010		1581	901	191	23

Remark: The TB case number of 2006 is obtained from the pre-released version of "Tuberculosis in Canada 2006" after the first version of this manuscript was submitted. The predicted result is very close to the statistical data (Public Health Agency of Canada, Tuberculosis in Canada, 2006c).

Fig. 8. Simulation, validation and prediction of all cases in Canada during 1991–2010.

After choosing the initial value, in the same way as we did for Canadian born, we obtain the simulation results shown in Fig. 6 (bottom).

The influence of the latent foreign born TB cases is shown in Fig. 7 with different levels of exposed immigrants per month. The stars are based on the statistical data (Table 3), and the smooth curves are the model-based simulated foreign born TB cases. The latent foreign born TB cases are chosen to be 0.6, 0.8, 1.2 and 1.4 times of the reported averaged level, respectively. It clearly shows that the foreign born TB cases grow up with the increase of the latent immigration level. The number of foreign born TB cases will be 717, 949, 1414, 1646, respectively, in 2010 under the above assumed levels of importing latent cases.

Validation of the model and prediction based on the validated model are presented in Table 1 and Fig. 8. Numbers in the prediction column during 2001–2005 are used to compare with the statistical data in the reported column. These numbers include the numbers of active and relapsed TB cases. ITB is the number of the infectious TB cases (57% of the active and relapsed TB), DR TB (drug resistant TB) is calculated by the formula $0.121 \times Prediction$, and MDR TB(multiple drug resistant TB) is calculated by the

formula $0.015 \times Prediction$ (Public Health Agency of Canada, Turberculosis in Canada, 2006b).

5. Discussions

We studied the TB transmission in Canada, assuming the total population is divided into two subgroups: Canadian born and foreign born populations. A deterministic compartmental model was formulated and qualitatively analyzed. The qualitative analysis shows that

(a) In the current situation where the transmission from one subgroup to another is small, two basic reproduction numbers R_0^0 and R_0^1 for the Canadian born and foreign born populations, respectively, together with the averaged immigration rate and the level of importing the latent infection, decide whether there will be a TB epidemic in these subgroups, and determine the levels of such an endemic if it occurs.

(b) Increasing the mixing between the two subgroups, and in particular, increasing the transmission from the foreign born to the Canadian born has very significant impact on the endemic level and the long-term prediction.

We estimated model parameters, using a set of Canadian immigration and TB incidence case data during the period 1991–2000. We also validated the model and the parameter values using similar data during 2001–2005. We then carried out some model-based simulations and projected the profiles of TB cases among the Canadian born and the foreign born. In particular, we noted that

(c) The average value of the Canadian born TB infection rate between 1991 and 2000 is 0.6026 per month, therefore every infectious TB case generated about 0.687 infectious individuals and 0.5812 non-infectious individuals during the infection period.

(d) There was a large pool of Canadian latent TB, between the period 1991 and 2005. The small average infection rate explains why the reported TB cases among Canadian born population have been decreasing in the last two decades, and the large pool of latent TB gives the reason why the reported TB in Canadian born population drops very slowly.

(e) The TB infection rate in Canadian born population is growing slowly and this infection rate will reach 0.8818 (per month) in 2012 (if nothing changes), and every infectious case will produce more than one new infectious TB case and 0.7583 non-infectious TB case. That is, after 2012 every active TB case will produce more than one new individual, on average. As a result, TB cases will increase again among Canadian born population, and we will have to deal with the re-emergence of TB in Canadian born population.

The main reason for TB to re-emerge in Canada by 2012 is a consequence of the (linear) polynomial fit to the data (Fig. 5 top-right). As the total Canadian population is at present time almost increasing linearly, if nothing changes the transmission rate $\beta_0^*(t)$ should be approximately an increasing linear function. The coefficients of this function were estimated to best fit the available data. Errors in estimating these coefficients could alter the prediction of the year when TB will re-emerge, but not the conclusion that TB will re-emerge in the near future.

We used the technique of polynomial fitting to the data. These fitted polynomials were then used to help us to estimate some model parameters so that we can make some short-term predictions. Our use of polynomials for interpolating does generate results fitting well with the 10 year statistical data (Fig. 4) from 1991 to 2000, and the 5-year data from 2000 to 2005

validated well the model prediction based on the parameters estimated with the help of the fitted polynomials. We must, however, note the potential large errors when extrapolating based on polynomial fitting, specially for long-term predictions. We believe repeating/iterating our process of polynomial interpolation, parameter estimations and validation based on updated information is the best way to ensure accurate prediction.

TB is indeed strongly linked to socioeconomic factors. Here we considered all Canadian born individuals epidemiologically equivalent. As such, our analysis does not fully capture the depth of heterogeneity within the Canadian born population. Nonetheless for this initial analysis, we considered the Canadian-born population to be homogeneous given that the incidence rate of TB in the Canadian-born population is quite low relative to the nation's foreign-born population. Future analyses we conduct will evaluate Canada's domestic in greater depth. It is not so clear how much additional insights we could gain from re-categorizing children of foreign born parents with the foreign born population. This re-categorization would entail the mixing of two very heterogeneous groups. While not extensively studied, there are no compelling data to indicate the children of foreign born parents are at significantly elevated risk of developing active TB. A majority of persons born overseas acquire their infection abroad (as substantiated by the many published molecular fingerprinting studies in industrialized countries like Canada) while children of foreign born parents spend most of their lives living domestically and such have a much lower risk of developing active TB than their parents (they might acquire infection if their parents or family members developed active TB or if they spent a significant amount of time traveling in their parents country of origin). For these reasons, it would make sense to keep these two populations separate, at least for this study.

Admittedly, like other models our proposed mathematical formulation is an approximation of the real situation in the overall picture of Canadian TB transmission dynamics. TB transmission, unlike other diseases modeled by the traditional SIR model, involves an important issue of fast–slow dynamics, addressing this issue requires a complete set of models which should be developed in a future study. Our model, following the main idea of the classical SEIR epidemiological model, attempted to address the transmission heterogeneity essential to an immigration country like Canada by dividing the whole population into two groups: the Canadian born population and the foreign born population. We do notice from available statistics data that the TB incidence rate of aboriginal Canadian is much higher than the non-aboriginal Canadian born population, and there is also great diversity of incidence rates among immigrants from different regions. A more realistic model would require further stratification of the whole population, and reliable data related to immigration and incidence rates associated with different regions in the world.

Acknowledgments

Appendix A. Statistical data and some sensitivity analysis

In this appendix, we provide some statistical data compiled from various sources. We also provide some additional numerical

simulations to further illustrate the impact of the transmission between two subgroups on the short-term projection (Tables 2–5).

Table 2
The annual number of immigrants to Canada during 1985–2005

Year	1985	1986	1987	1988	1989	1990	1991
Number	84,302	99,219	152,098	161,929	192,001	214,230	230,781

Year	1992	1993	1994	1995	1996	1997	1998
Number	252,842	255,819	223,875	212,504	226,773	216,014	174,100

Year	1999	2000	2001	2002	2003	2004	2005
Number	189,816	227,209	250,346	229,091	221,352	235,824	262,236

Table 3
The TB number, stratified in terms of Canadian born and foreign born, in Canada during 1985–2001

Year	1985	1986	1987	1988	1989	1990	1991
Canadian total	2144	2145	1972	1947	2035	1997	2018
Canadian born	1283	1290	1009	1104	1056	1076	1009
Foreign born	861	855	868	891	959	940	1009

Year	1992	1993	1994	1995	1996	1997	1998
Canadian total	2109	2013	2074	1931	1868	1976	1791
Canadian born	975	950	888	780	667	682	626
Foreign born	1134	1063	1186	1140	1170	1273	1150

Year	1999	2000	2001	2002	2003	2004	2005
Canadian total	1806	1695	1704	1555	1628	1574	1616
Canadian born	639	568	587	484	476	464	519
Foreign born	1151	1103	1062	1024	1111	1075	1016

Table 4
The number of TB cases by year of arrival in Canada during 1996–2001

Year 1996	−85	−90	91	92	93	94	95	96						XX
	110	225	77	71	66	89	113	125						47

Year 1997	−62	−72	−82	−92	93	94	95	96	97					XX
	66	73	155	396	67	94	89	118	117					93

Year 1998	−62	−72	−82	−92	93	94	95	96	97	98				XX
	65	50	145	329	61	74	65	84	117	93				68

Year 1999	−62	−72	−82	−92	93	94	95	96	97	98	99			XX
	59	55	121	314	48	63	59	56	80	74	136			86

Year 2000	−62	−72	−82	−92	93	94	95	96	97	98	99	00		XX
	39	33	116	239	52	39	54	50	54	64	124	121		117

Year 2001	−62	−72	−82	−92	93	94	95	96	97	98	99	00	01	XX
	44	37	113	240	36	34	32	44	39	45	63	107	120	108

Year 2002	−62	−72	−82	−92	93	94	95	96	97	98	99	00	01	02	XX
	38	45	110	200	28	45	32	45	41	33	48	71	152	126	76

In the first row of the table, −85 means the arrival time is 1985 and early. −90 means the arrival time is between 1986 and 1990. In the second row of the table; −62 means the arrival time is 1962 and early; −72 means the arrival time is between 1963 and 1972; −82 means the arrival time is between 1973 and 1982; −92 means the arrival time is between 1983 and 1992. The other numbers with the minus sign have the similar meaning. XX stands for the number of TB cases whose arrival time is not clear.

Table 5
The TB death number in Canada during 1996–2001

The cause	1996	1997	1998	1999	2000	2001
TB underlying cause	35	27	19	26	23	28
TB contributed but not underlying	42	42	54	52	67	56
TB did not contribute	36	47	41	43	16	32
Cause not stated	4	4	8	8	5	10
Total	117	120	122	129	111	126

To further illustrate the impact of the transmission between two subgroups on the short-term projection, we provide here an additional simulation based on the linear birth rate

$$B(t) = bN(t) = b[S_0(t) + E_0(t) + I_0(t) + T_0(t) \\ + S_1(t) + E_1(t) + I_1(t) + T_1(t)]$$

with $b = 0.000875$, and the initial value (with the initial time as the beginning of the year 1991): $S_0(1991) = 23,000,000$, $E_0(1991) = 5584$, $I_0(1991) = 106$, $T_0(1991) = 4000$ for the Canadian born and $S_1(1991) = 5,000,000$, $E_1(1991) = 4959$, $I_1(1991) = 94$, $T_1(1991) = 3500$ for the foreign born. The parameters to be used are the average values estimated in the main body of the paper: $A_s = 18,414$, $A_e = 97$ for the immigration rates, $\beta_0 = 0.6026$, $\beta_1 = 0.048$ for the transmission rates within the subgroups; $\mu = 0.0005917$, $\delta = 0.005$, $\gamma = 0.5$ for the disease progression, as well as the assumed transmission rates between the two subgroups:

$$\beta_{01} = 0, 0.2\beta_0, 0.4\beta_0, 0.6\beta_0, \\ \beta_{10} = 0, 0.1\beta_0, 0.2\beta_0, 0.3\beta_0, \quad \text{respectively.}$$

We use the model incorporating the coupling of the two subgroups via the transmission

$$\begin{cases} S_0(t+1) = S_0(t) + bN(t) - \mu_0 S_0(t) - \dfrac{\beta_0 S_0(t)I_0(t)}{N_0(t)} - \dfrac{\beta_{01}S_0(t)I_1(t)}{N_0(t)}, \\ E_0(t+1) = E_0(t) + \dfrac{\beta_0 S_0(t)I_0(y)}{N_0(t)} + \dfrac{\beta_{01}S_0(t)I_1(t)}{N_0(t)} - (\mu_0 + \alpha_0)E_0(t), \\ I_0(t+1) = I_0(t) + q\alpha_0 E_0(t) - (\mu_0 + \delta_0 + \gamma_0)I_0(t), \\ T_0(t+1) = T_0(t) + p\alpha_0 E_0(t) + \gamma_0 I_0(t) - \mu_0 T_0(t), \\ S_1(t+1) = S_1(t) + A_s - \mu_1 S_1(t) - \dfrac{\beta_{10}S_1(t)I_0(t)}{N_1(t)} - \dfrac{\beta_1 S_1(t)I_1(t)}{N_1(t)}, \\ E_1(t+1) = E_1(t) + A_e + \dfrac{\beta_{10}S_1(t)I_0(y)}{N_1(t)} + \dfrac{\beta_1 S_1(t)I_1(t)}{N_1(t)} - (\mu_1 + \alpha_1)E_1(t), \\ I_1(t+1) = I_1(t) + q\alpha_1 E_1(t) - (\mu_1 + \delta_1 + \gamma_1)I_1(t), \\ T_1(t+1) = T_1(t) + p\alpha_1 E_1(t) + \gamma_1 I_1(t) - \mu_1 T_1(t). \end{cases}$$

(19)

The simulation result is reported in Fig. 9 with the parameters mentioned above. The top-left is the projection of total TB case number in Canada without transmission between the two subgroups, i.e., $\beta_{01} = 0$, $\beta_{10} = 0$. The stars are the statistical data from 1991 to 2005, the curve is the projection. The other three show the results for different level of the transmission rates between the two subgroups. The simulation clearly shows that the increasing transmission between the Canadian born and the foreign born both have significant influence on the TB infection in the whole population of Canada.
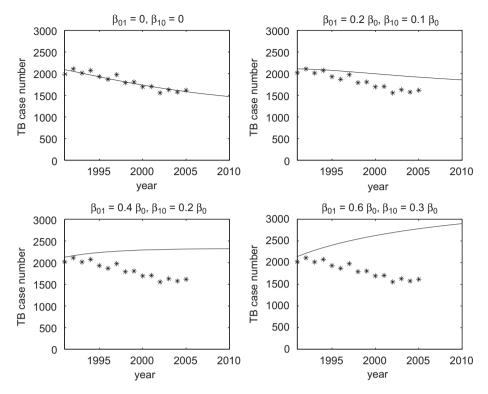
Fig. 9. The simulation and prediction of TB cases in the whole population of Canada during 2001–2010, when we vary the transmission rates between the two subgroups.

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