

Evaluating the Effectiveness of Contact Tracing on Tuberculosis Outcomes in Saskatchewan Using Individual-Based Modeling

Health Education & Behavior
40(1S) 98S–110S
© 2013 Society for Public
Health Education
Reprints and permissions:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/1090198113493910
heb.sagepub.com



Yuan Tian, MSc¹, Nathaniel D. Osgood, PhD¹,
Assaad Al-Azem, PhD², and Vernon H. Hoepfner, MD^{1,2}

Abstract

Tuberculosis (TB) is a potentially fatal disease spread by an airborne pathogen infecting approximately one third of the globe. For decades, contact tracing (CT) has served a key role in the control of TB and many other notifiable communicable diseases. Unfortunately, CT is a labor-intensive and time-consuming process and is often conducted by a small and overworked nursing staff. To help improve the effectiveness of CT, we introduce a detailed, individual-based model of CT for the Canadian province of Saskatchewan. The model captures the detailed operation of TB CT, including loss to follow-up, and prophylactic and case treatment. This representation is used to assess the impact on active TB cases and TB infection prevalence of differential scoping, speed, prioritization of the CT process, and reduced loss to follow-up. Scenario results are broadly consistent with—but provide many additional insights beyond—our previously reported findings using an aggregate model. In the context of a stylized northern community, findings suggest that age- and ethnicity-prioritized schemes could improve CT effectiveness compared to unprioritized schemes by dramatically reducing TB infection and preventing on average roughly 11% ($p < .0001$) of active TB cases over a period of 20 years. Reducing loss to follow-up to 10% could yield 5.4% ($p = .02$) TB cases prevented on average with lower prevalence of TB infection, but improving the CT speed does not yield significant improvement in TB outcomes. Finally, although the work emphasized the value of social network analysis, we found that caution should be exercised in directly translating social network analysis—observed associations into prioritization recommendations.

Keywords

agent-based modeling, contact tracing, individual-based modeling, infection control, scale-free network, tuberculosis

A variety of mathematical models have been built to understand the dynamics of the mycobacterial infectious disease tuberculosis (TB). Such models have been used to explore “what-if” questions to better understand control and prevention options (Aparicio & Hernandez, 2006; Lich, 2007; Osgood et al., 2011; Vynnycky & Fine, 2000; Ziv, Daley, & Blower, 2001), study dynamics interaction of TB with smoking (Lich, 2007), investigate the distinct impacts of age and calendar year of infection on individual- and population-level infection lifelong risk (Vynnycky & Fine, 2000), and understand the impact of temporary lapses in TB control (Osgood et al., 2011).

Contact tracing (CT)—the process of identifying, notifying, and testing individuals who have contacted an infected individual—is recognized as an integral part of many notifiable disease control programs by virtue of its capacity to locate high-risk contacts, identify and treat active cases among them before they spread the infection widely, and

provide prophylaxis for other traced contacts. Many epidemiological models have been developed to evaluate the effectiveness of CT and relevant interventions such as random screening for HIV (Hyman, Li, & Stanley, 2003), treatment for early latent TB infection (Ziv et al., 2001), and derivation of important thresholds and outbreak likelihood for sexually transmitted disease (Mueller, Kretzschmar, & Dietz, 2000). The authors previously contributed a system dynamics (SD) study of the effectiveness of the speed and

¹University of Saskatchewan, Saskatoon, Saskatchewan, Canada

²Saskatchewan Tuberculosis Control Program, Saskatoon, Saskatchewan, Canada

Corresponding Author:

Yuan Tian, Department of Computer Science, College of Arts and Science, University of Saskatchewan, 110 Science Place, Saskatoon, Saskatchewan, Canada S7N 5C9.
Email: yut473@mail.usask.ca

scope contact tracing for TB control and noted that CT efficiency can be self-limiting (Tian et al., 2011).

An agent-based model (ABM) is a computational dynamic model composed of interacting agents representing individual actors (e.g., people, institutions) within one or more environments (Gilbert, 2007; Railsback & Grimm, 2012). Supported by increasing computational power, ABMs are particularly attractive due to their capacity to capture individual context (localized network or spatial position), history, and heterogeneity (Osgood, 2004); to represent more complex behavior patterns (e.g., those involving learning; Gilbert, 2007); and to characterize multilevel systems in a natural fashion. Use of ABMs in health science has gained momentum in recent years (Epstein, 2009; Newman, 2003), with infectious disease being a key application area. Earlier contributions have noted the desirability of formulating ABMs to simulate CT (Hyman et al., 2003). Such an individual-level representation is an important enabler for—among other factors—evaluating prioritization schemes that take into account individual network position, history, and diverse attributes (Osgood, 2004) and for accurate simulation of the queue of those awaiting tracing (Tian et al., 2011).

The work described here arose in the context of a TB research effort making use of a methodologically diverse and complementary suite of models. This effort included not only ABMs—such as that presented here—but also models applying compartmental SD (Lich, 2010; Lich, Osgood, & Dyck, 2009; Tian et al., 2011) and social network analysis (Al-Azem, Hoepfner, & Osgood, 2010a, 2010b) techniques. For the study described here, several considerations recommended the application of agent-based rather than compartmental modeling. The first was the capacity to represent important processes with sufficient detail to reliably capture their impacts on intervention trade-offs. For example, an aggregate model is poorly suited to capturing the network percolation effects associated with both infection spread and CT processes. Capturing such effects was judged important for not only the localized spread of TB in the network but also the fact that CT process in effect “pursues” the spread of TB across the same network—a characteristic that was both hard to capture within an aggregate model and also likely (in light of aggregate modeling experience) to be important in shaping trade-offs between distinct CT regimens. A second advantage of an agent-based approach was the ability to more naturally and flexibly capture history dependence in individual evolution and diverse dimensions of heterogeneity in risk factors (Osgood, 2004), including here age, ethnicity, and past CT history. Third, an individual-based approach supported the ability to calibrate and validate the model results against certain types of detailed empirical data possessed by the research team. For instance, we sought to compare model findings to longitudinal, individual-level data, which is challenging to leverage with an aggregate model (Meng & Osgood, 2012)—and to investigate the consistency

between empirical case-contact network data and comparable synthetic network structure emerging from simulated CT. The final motivation for ABM reflected the fact that persistent patterns of contact are an important feature of many human institutions, and the position of individuals within contact networks can be the key to understanding their vulnerability and intervention effectiveness. The capacity of ABMs to characterize such networks can allow for detailed study of both network-informed and network-shaping interventions and enrich understanding of determinants of specific epidemiological patterns and intervention trade-offs.

A Real-World Example: TB Contact Tracing in Saskatchewan

The burden of TB in Saskatchewan falls far more heavily among the predominantly Aboriginal communities of Saskatchewan’s north (Irvine & Stockdale, 2004). CT investigation of TB in Saskatchewan is currently limited to two target categories: those with infectious TB (with a focus on identifying persons who might have been infected) and those with primary TB (with a focus on identifying the infecting individual). Figure 1 illustrates a hypothetical investigation of an infectious active TB case and provides statistics collected from Saskatchewan TB Control regarding tracing procedures and loss of contacts to follow-up. Starting from an infectious TB case—diagnosed either actively through previous CT or passively through presentation with symptoms—a number of potential contacts will be identified by interviewing the case. Contacts with a history of previously positive skin tests (also known as a Mantoux test) will usually not be reexamined unless they are the contacts of a primary TB case, since they are known tuberculin reactors. The remaining contacts are typically summoned via mail for examination. The objective set—but rarely met—by Saskatchewan TB Control is to have 95% of contacts examined within 30 days following case identification and to maintain a low level of follow-up loss across the skin test and clinical review stages. Data collected from CT investigation suggest roughly 30% to 40% loss to follow-up in the skin test and clinical review stages, and only 16% of contacts are examined within 30 days.

Scenario Definitions

Derived from the empirical data regarding the Saskatchewan TB CT process, we formulated a set of scenarios to explore how the incidence of active TB and TB infection would respond to changes focused on four leverage points:

1. Scope of CT
2. Degree of loss to follow-up
3. Prioritization scheme for contacts awaiting tracing
4. Timeliness of CT

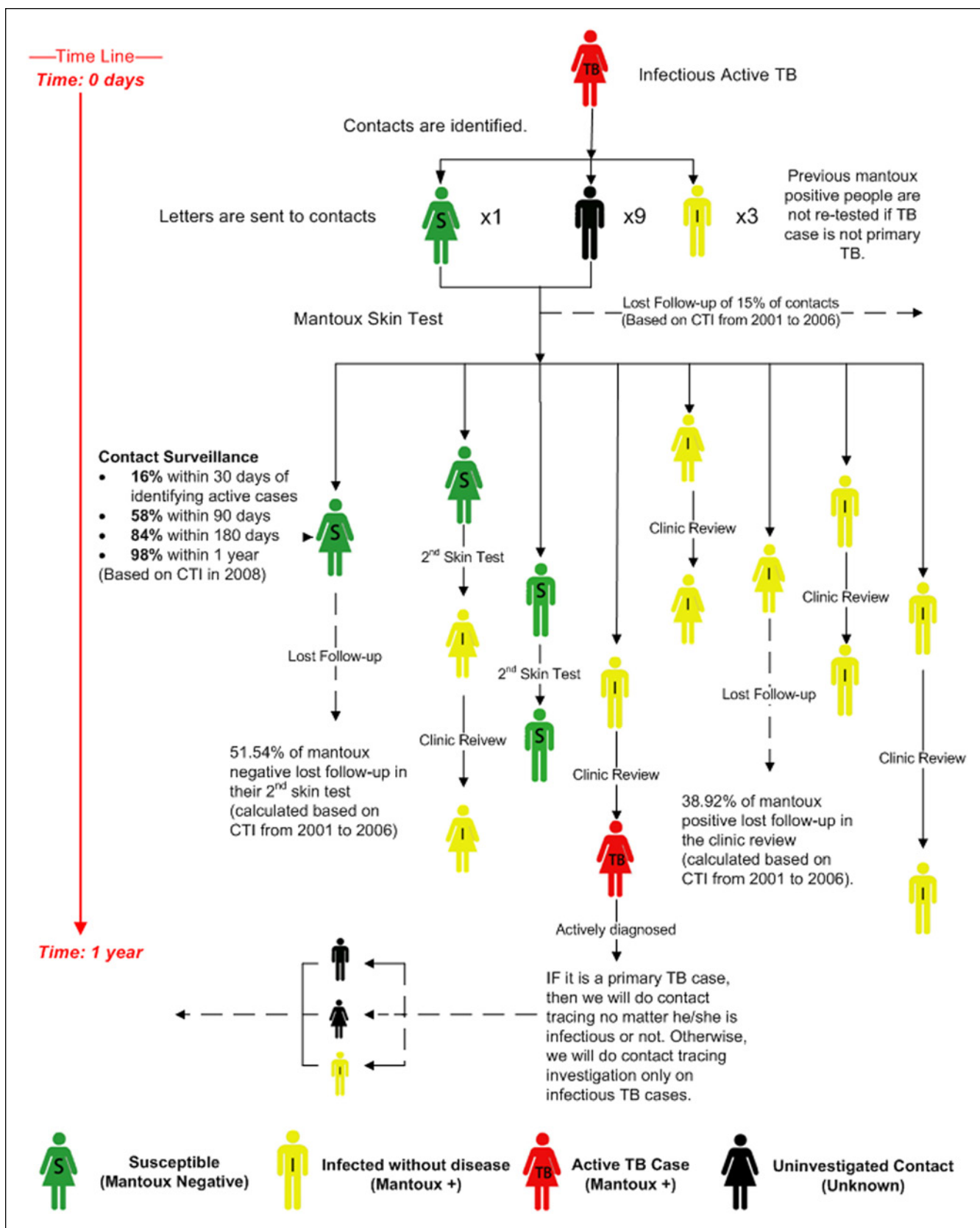


Figure 1. Saskatchewan tuberculosis (TB) contact tracing investigation (CTI) procedure and statistics.

Table 1. Scenario Definitions.

ID	Contact Tracing	Tracing Target	Loss to Follow-Up (%)	Priority	Tracing Fraction (%)
S0	Disabled	NA	NA	NA	NA
S1	Enabled	Infectious and primary tuberculosis	30-40	None	90
S2	Enabled	Infectious and primary tuberculosis	10	None	90
S3	Enabled	Infectious and primary tuberculosis	10	None	45
S4	Enabled	Infectious and primary tuberculosis	10	Age	45
S5	Enabled	Infectious and primary tuberculosis	10	Ethnicity	45
S6	Enabled	Infectious and primary tuberculosis	10	Reported times	45
S7	Enabled	Infectious and primary tuberculosis	10	Age and ethnicity	45
S8	Enabled	Infectious and primary tuberculosis	10	None	90 (Fast contact tracing)

Each intervention scenario is associated with a corresponding reference scenario from which it differs only with respect to a single attribute (e.g., the presence of faster CT, prioritization by age). By comparing the difference between the intervention scenario and the associated reference scenario, it is possible to gain some understanding as to how a given change affects TB outcomes. Table 1 shows the parameters associated with different CT scenarios.

To address Leverage Point 1 (the scope of CT), we created a distinguished baseline scenario (S0) without CT. Comparing the TB outcomes for S0 (on one hand) and all other scenarios (on the other) reveals health gains secured by distinct variants of CT compared to a situation lacking CT. Scenarios S2 and S3 are particularly notable, as each depicts successively greater fractions of contact names being elicited from cases for CT (considered relative to current practice), and successively more extensive CT.

S1 and S2 address Leverage Point 2 by focusing on the impact of loss to follow-up (in the absence of CT prioritization). S2 posits a greatly reduced level of loss to follow-up (10%) relative to a reference scenario (S1) that assumes the historic level (between 30% and 40%) of loss to follow-up.

By contrast, S4 (age prioritization—children younger than 9 years old are traced first), S5 (ethnicity prioritization—First Nations [FN] individuals are traced first), S6 (individuals who have been named as a contact a greater number of times are traced first), and S7 (prioritization based on both age and ethnicity) seek to address Leverage Point 3 by evaluating the impact of various CT prioritization schemes against a reference scenario (S3) that simulates CT using identical assumptions but lacks prioritization.

S8 is designed to investigate Leverage Point 4 (timeliness of CT), by evaluating the impact of assuming expedited CT—where 90% of contacts are skin tested within 30 days of diagnosis—relative to reference scenario S2 where the current speed of CT (Figure 1) is used.

Method

This contribution built atop insights from two previously contributed aggregate SD TB models (Osgood et al., 2011; Tian et al., 2011). Firstly, we reconstructed the well-calibrated

aggregate model of TB dynamics for Saskatchewan population (Osgood et al., 2011) at an individual level, and then extended it to a network-based ABM by adding network features and CT. The model is implemented with the simulation software AnyLogic® for Windows Version 6.2.2. This software—which leverages the trend toward model-driven software development (Beydeda, Book, & Gruhn, 2005) and object-oriented application frameworks (Fayad & Schmidt, 1997)—offers graphical modeling toolboxes of commonly needed model abstractions, support for various types of experiments (e.g., single-realization scenarios, Monte Carlo ensembles), libraries, and other interfaces for extension of the model with Java code.

Our ABM of TB and CT has a 20-year time horizon of sufficient duration to observe the longer term outcomes of CT. The time unit of the model is a year. The model runs atop AnyLogic's continuous-time discrete event scheduler, so no fixed-time step is used; events may be scheduled with whatever temporal resolution is required to simulate the processes of interest. The following sections describe essential elements of our ABM. Readers seeking additional information concerning model design are referred to the supplemental material online at <http://heb.sagepub.com/supplemental>. Starting from a global view of the model, the demographic settings of the simulated population and the network initialization are first introduced. This is followed by explanation of agent structure and characteristics.

Population

In the model we assume a hypothetical Aboriginal community with a population size of 15,000, where FN individuals constitute 90% of the population. The ABM follows a previous TB model findings of Osgood et al. (2011) by treating younger age-groups as experiencing a higher risk of TB infection given exposure and FN people as subject to a relatively higher likelihood of TB infection and progression—the latter partly a reflection of adverse conditions involving housing and other social determinants of health. When the model is initialized, the model imposes ethnicity-specific age structure on the population in accordance with Saskatchewan demographics (Osgood et al., 2011); a network environment

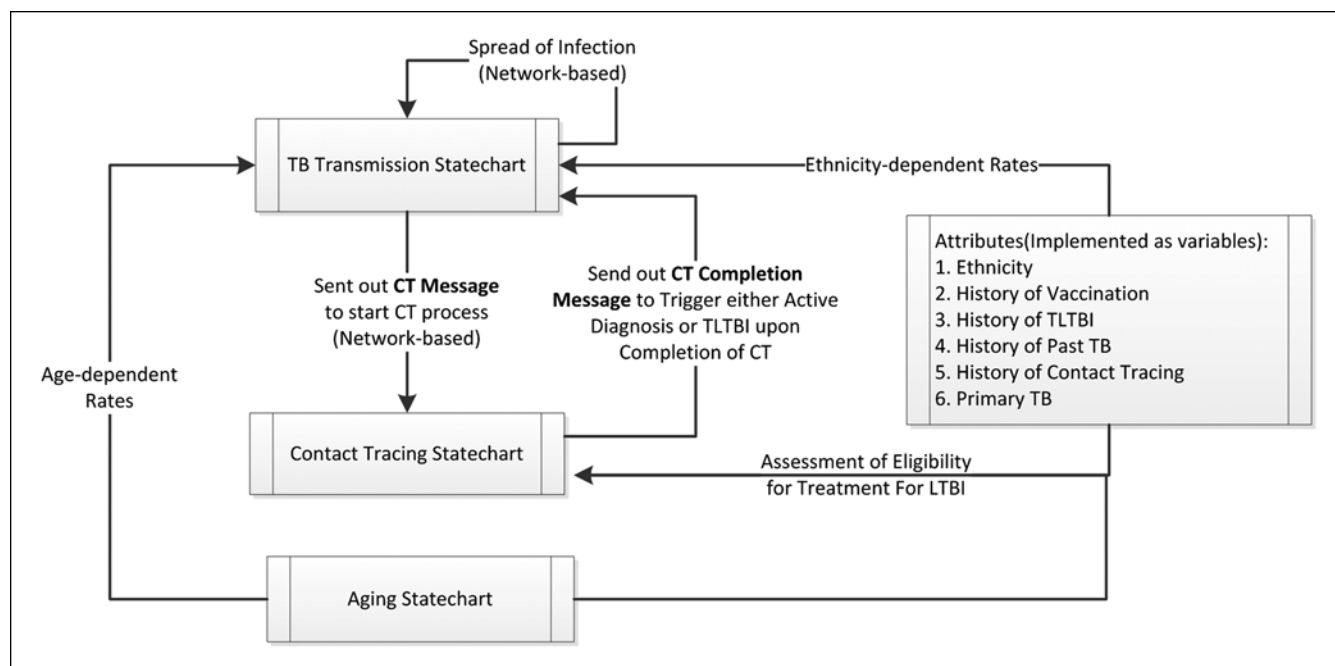


Figure 2. Macro structure of the agent and the interactions among different components.

Note. TB = tuberculosis; CT = contact tracing; TLTI = treatment of latent tuberculosis infection.

is then established on the population. To reflect the persistence of many relationships underlying contact patterns in smaller and remote communities, each individual will have static connections with others for the duration of the simulation. As a result, his or her contacts evolve only with the death of contacts (disconnection) or arrival of newborns (new connection). Newborn individuals are added into the model according to Saskatchewan empirical ethnicity-specific birth rates. Such individuals are subsequently assigned random connections with existing individuals in the population; the death of individuals is driven by the historical death rate stratified by age and ethnicity. Past investigations by the researchers suggest significant complexities associated with gender and intergenerational mixing within Saskatchewan's TB case-contact population; as a simplifying assumption, the model does not seek to specifically represent an agent's gender or family structures within the model contact network.

Environment and Network

TB case-contact networks are layered atop an underlying contact network structure about which there is limited knowledge. Past investigations of network structure in Aboriginal communities within the neighboring province of Manitoba by a research team member suggested that both TB case-contact networks and underlying contact networks may exhibit scale-free properties (Al-Azem, 2007). Our investigations using ubiquitous sensing in small Saskatchewan populations have also suggested scale-free elements of contact patterns

(Hashemian, Stanley, Knowles, Calver, & Osgood, 2012; Hashemian, Stanley, & Osgood, 2010). For our analysis presented here, we assumed a scale-free underlying network, with both TB transmission and CT procedure taking place over this network. The initial network structure is generated using the algorithm of Barabasi and Albert (1999), which is implemented as a part of the ABM, and handled by the built-in network-specific features of AnyLogic libraries, which allow alternative network structures (e.g., ring lattice, distance-thresholded, small world, random) with specified network parameters. We additionally inserted code to maintain the scale-free character of this network in the presence of a dynamic population.

Although this article focuses on CT in the presence of a hypothesized scale-free network, we further conducted Monte Carlo intervention simulations with random and small world network assumptions to assess the sensitivity of the relative effectiveness of CT regimens to assumptions concerning the class of network (see supplemental material online).

Agent Attributes and Behavior

The population is constructed by initializing each agent with attributes (e.g., ethnicity and history information), a list of network contacts, and three state charts representing status with respect to TB infection and disease, aging, and CT. Figure 2 illustrates the macro structure of an agent and dependency relationships between different components.

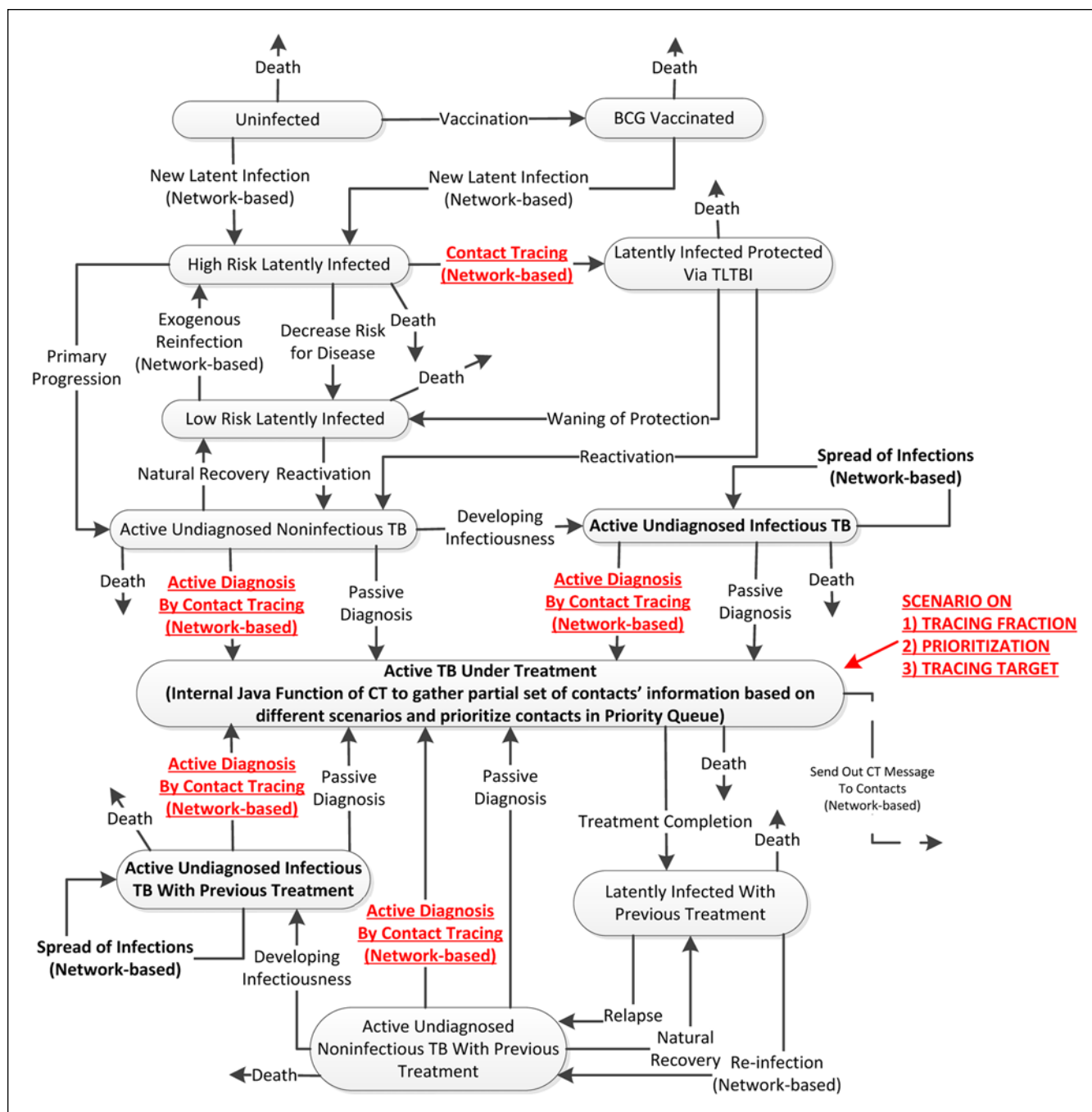


Figure 3. TB transmission state chart of the agent.

Note. Contacts retrieval, prioritization, and notification procedure occur in the “Active TB Under Treatment” state. Scenarios on tracing fraction, prioritized CT, and tracing target are coded in an associated function (additional implementation details can be found in the supplemental material online). TB = tuberculosis; CT = contact tracing.

TB transmission state chart. Figure 3 shows the TB transmission state chart, which includes the same 11 states used in our previously contributed SD TB model (Osgood et al., 2011). Individuals are born into the “Uninfected” state. Such individuals can subsequently either remain there or transition to the “BCG Vaccinated” state via vaccination or to the “High-Risk Latently Infected” state via acquiring a

new TB infection from a contact. People who remain in the “BCG Vaccinated” state are treated as remaining susceptible to TB infection but carry a lower probability of infection given exposure compared to those without vaccine. Individuals in the “High-Risk Latently Infected” state can develop active TB via primary progression (within 2 years of being infected), receive treatment of latent tuberculosis

infection, or transit automatically to the “Low-Risk Latently Infected” state on average 2 years following infection. Those in the “Low-Risk Latently Infected” state can return to the “High-Risk Latently Infected” state via reinfection. Persons who are protected by treatment of latent tuberculosis infection can either progress to active TB or return to the “Low-Risk Latently Infected” state following waning of protection. States associated with active TB are stratified (dichotomously) by infectiousness, diagnosis, and treatment. In addition, people who were previously treated for active TB but lack current disease will remain in the “Latently Infected With Previous Treatment” state. Those transitions noted with “Network-based” in Figure 3 are either associated with sending out “exposure” messages or triggered by receiving such messages via the network. TB transmission risk is simulated in the model as agents with undiagnosed infectious TB send out exposure messages to their contacts on the network. When an agent (a contact) receives an exposure message, that contact might acquire a new TB infection or become reinfected.

With respect to CT, contacts retrieval, prioritization, and notification are incorporated in the “Active TB Under Treatment” state. When a contact enters into this state, a partial set of the contacts of that case is added to a prioritized queue. Ongoing CT serves to process the queue, and when a contact reaches the head of the queue (based on different scenario settings), a CT notification message will be sent to that contact. When considering prioritized CT protocols, this priority queue will automatically order the contacts, taking into account the prioritization criteria (e.g., age, ethnicity, and number of times an individual has been reported as a contact).

Contact tracing state chart. Figure 4 depicts the CT state chart, which includes a detailed representation of the contact investigation protocol. Individuals can be in one of five states with regard to their CT status. Initially, individuals are present in the “Unknown or Previous Skin Negative” state. On receiving a CT notification message, the contacts will go to the “Notified by Contact Tracing” state, where they await their first skin test. The “Mantoux 1st Skin Test” state represents a situation where people are undergoing skin testing or awaiting a second skin test. The “Potential 2nd Skin Test & Clinical Review” state denotes a transient clinical review procedure for those positive in the first skin test; for those who are negative in the first skin test, it represents the occurrence of the second skin test and an immediate potential clinical review. According to the historical data, 4.4% contacts were lost between the second skin test and clinical review; for simplicity, we assumed no loss. Since the loss is modest, we simplified the implementation by assuming that there is no loss between the second skin test and clinical review. “Previous Skin Positive” is a state for past TB cases and those previously investigated with positive skin test results.

Both TB transmission and CT procedure are performed via messaging on the network. Figure 5 illustrates a

summary possible agent messaging and the interactions between state charts within or between agents.

Parameterization

Data for our ABM (e.g., birth, death rate, population stratified by age and ethnicity) were primarily drawn from our previous contributed SD model (Osgood et al., 2011) and obtained from updated calibration of that model, Saskatchewan Anti-TB League reports, the Saskatchewan TB Control database and reports, vital statistics for the Saskatchewan population, and the secondary literatures (Colditz et al., 1994; Vynnycky & Fine, 1997; Ward, 2004). Key TB-related parameters applied in our model are summarized in Tables 2 and 3. CT parameters drew on estimates from Saskatchewan TB Control (Figure 1).

Analysis Methods

Given the stochastic character of the ABM, 100 realization Monte Carlo ensembles (which vary the random number seeds used both for initial tasks—such as building model structure—and for stochastics) were conducted for each scenario. A total of 900 realizations were analyzed to evaluate the effectiveness of CT. As the cumulative cases over 20 years were highly positively skewed (Figure 6), we used bivariate nonparametric tests to assess the significance of differences in results across pairs of scenarios. Specifically, we used the Mann–Whitney *U* test (Wackerly, Mendenhall, & Scheaffer, 2007) at a 5% level of significance, with a null hypothesis that both scenarios share the same distribution for the count of cumulative TB cases. To compare successive CT scenarios to the no-CT case (S0), the one-tailed test was used to test the alternative hypothesis that the count of cumulative TB cases for the no-CT case tended to be larger than (i.e., were shifted to the right of) those for the CT scenario. When comparing all scenarios to each other, we used a two-sided Mann–Whitney test to test the alternative hypothesis that the cumulative counts of TB cases are different between the two scenarios.

Results

Contact Tracing Extent

In the absence of any CT, the average cumulative incidence is 411.08 active TB cases (Table 4)—the highest across all the—and the gap regarding the total number of incident TB cases between baseline S0 and all other scenarios (Table 5) is statistically significant ($p < .0001$).

In addition to reducing TB cases, CT also significantly lowers prevalence of TB infection. Figures 7 and 8 show that the baseline scenario (involving no CT) leads to notably higher average prevalence of TB infection than any scenario with CT. In short, CT significantly reduces the average prevalence of TB infection in the population.

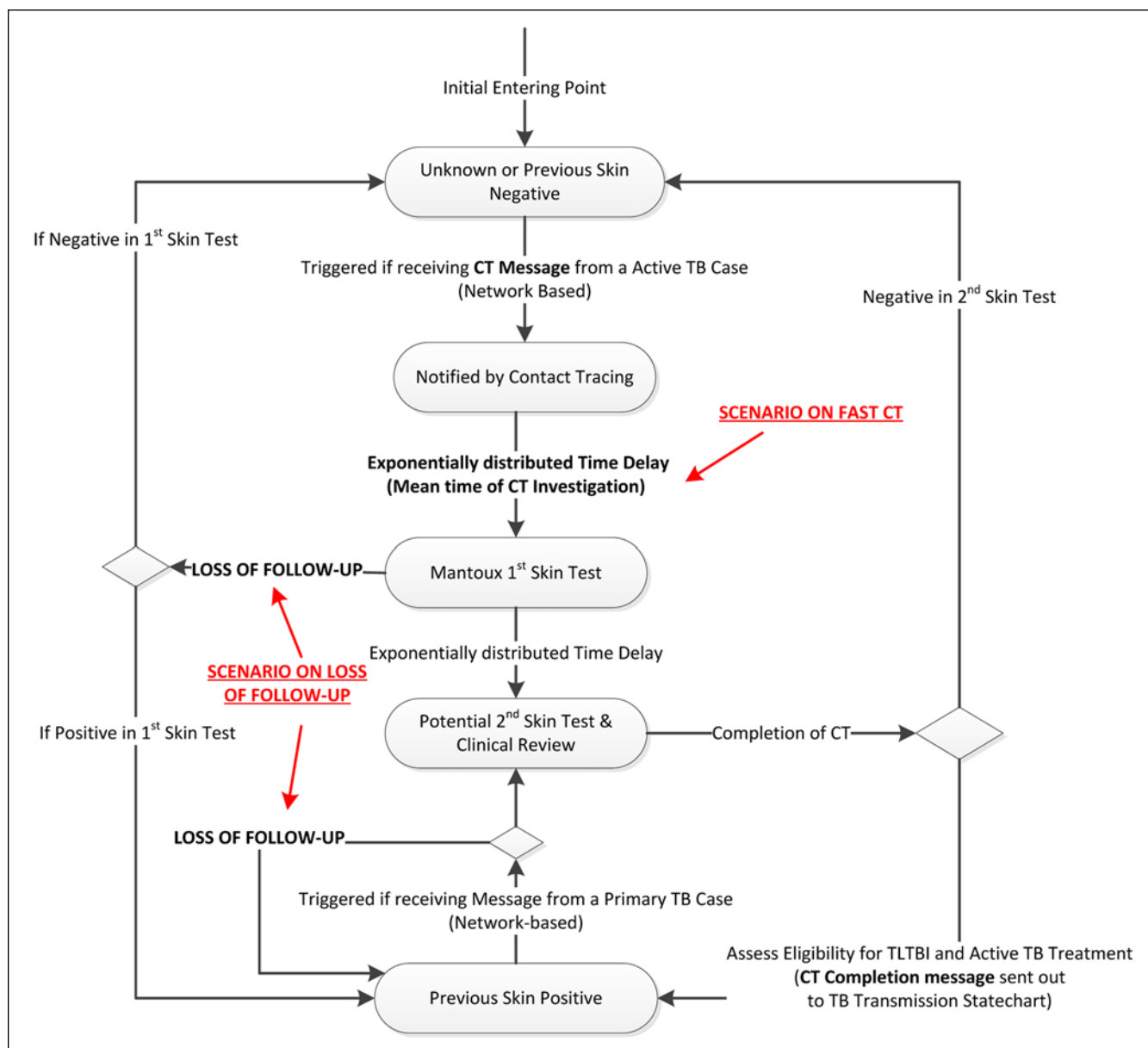


Figure 4. Contact tracing state chart of the agent.

Note. The transitions in the state charts involving implementation of scenarios (e.g., loss of follow-up and faster CT) are highlighted. Greater details on the CT process or implementation can be found in Tian (2012). TB = tuberculosis; CT = contact tracing; TLTB = treatment of latent tuberculosis infection.

Echoing results from our SD model (Tian et al., 2011), a diminishing returns phenomenon is observed with respect to both cumulative active TB cases (Table 4) and prevalence of TB infection (Figure 8), with the benefit of tracing the first 45% of contacts (S3 vs. S0) being notably larger than that from tracing the second 45% of contacts (S2 vs. S3).

Loss to Follow-up

For situations where 90% of contacts are investigated, reducing loss to follow-up from the historic level of 30% to 40% (S1) to 10% (S2) can eliminate 15.7 TB cases on average, a

reduction of 5.4% ($p = .02$). Figure 7 shows how the average TB infection prevalence is affected over time by altering assumptions regarding loss to follow-up. It can be appreciated that, regardless of CT target, reducing loss to follow-up has little effect on the short-term prevalence of TB infection but reduces it notably in the medium and long term.

Prioritization

Gains from prioritizing CT are recognized by comparing S4, S5, S6, and S7 against reference S3. Compared to the reference scenario S3 using unprioritized CT, significant

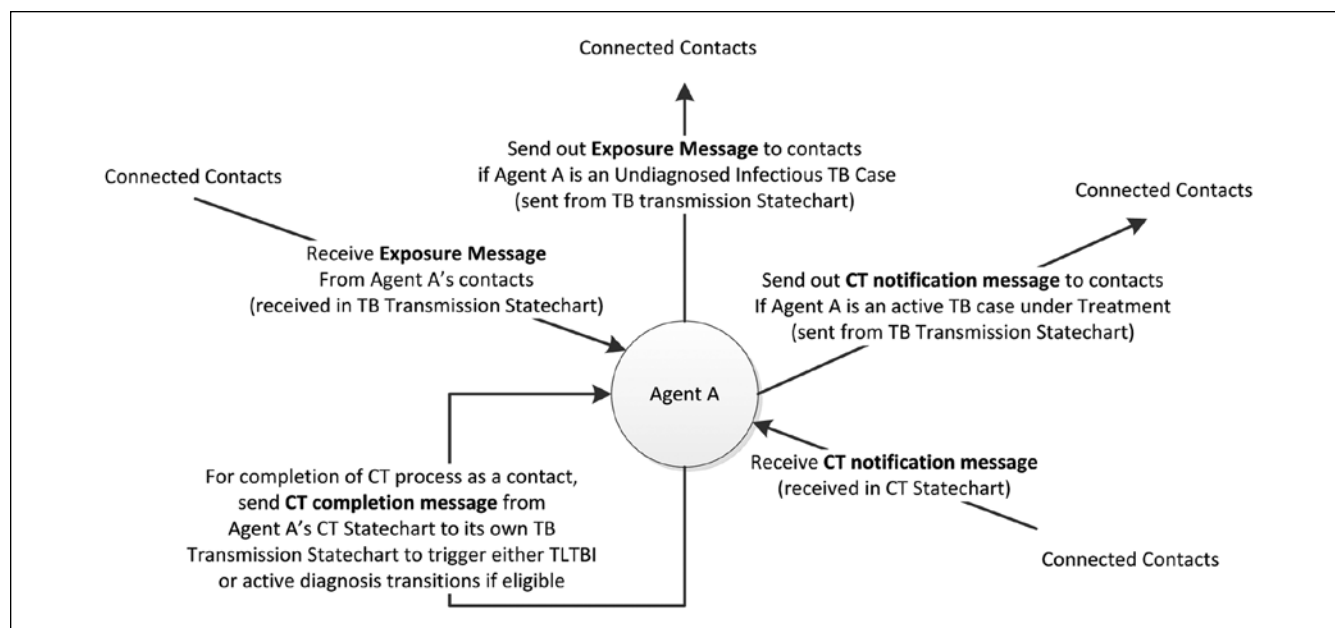


Figure 5. Messaging interactions internally in the agents and externally with other agents.

Note. TB = tuberculosis; CT = contact tracing.

Table 2. Selected Relative Risk Parameters and Estimates in Our Model.

Relative Risk (RR)	Values	Data Source or Reference
RR of TB infection for age 0-4	11.1094	Calibrated ^a
RR of TB infection for age 5-9	14.7316	Calibrated ^a
RR of primary progression for age 0-4	2.3495	Calibrated ^a
RR of primary progression for age 5-9	1	Calibrated ^a
RR of primary progression for age 10 to 14	1.0444	Calibrated ^a
RR of TB infection while being reported as a contact 2 times	2.1481	Al-Azem (2007)
RR of TB infection while being reported as a contact 3 times	2.7396	Al-Azem (2007)
RR of TB infection while being reported as a contact 4 or more times	3.9381	Al-Azem (2007)

^a Those "calibrated" parameters are obtained from an updated calibration on the aggregate system dynamics model (Osgood et al., 2011).

Table 3. Key Model Parameters and Estimates.

Parameters	Value		Data Source or Reference
	Registered Indian	Nonregistered Indian	
β_c	38.0299	28.9106	Calibrated ^a
Relapse to active TB rate	0.0062	0.001	Calibrated ^a
Natural recovery rate	0.1	0.1638	Calibrated ^a
Mean time until discovery of undiagnosed infectious TB	0.2221	0.1	Calibrated ^a
Primary progression rate	0.0142	0.0109	Calibrated ^a
Mean time until developing infectious TB		1.29	Saskatchewan TB Control
Mean time until discovery of undiagnosed noninfectious TB		2.9012	Calibrated ^a
Reactivation rate		0.001562	Calibrated ^a
Previously treated death rate coefficient		5	Calibrated ^a
Average connections per person in the network		60	Assumed

Note. β_c denotes average number of infections per year an infectious person causes in a fully susceptible population.

^a Those "calibrated" parameters are obtained from an updated calibration on the aggregate system dynamics model (Osgood et al., 2011). Space constraints prevent further inclusion of dozens of additional model input parameters that could not be listed here.

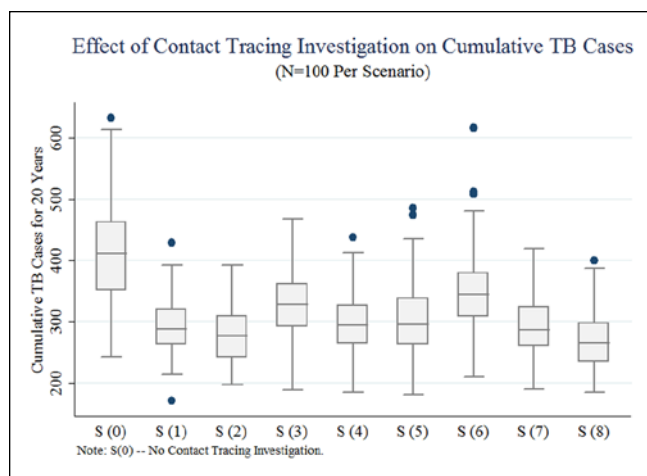


Figure 6. Box plot of cumulative TB cases over 20 years per scenario.

Note. The bottom and top of the box are the 25th percentile and 75th percentile, respectively, and the line in the box shows the median cumulative TB cases. The whiskers are the maximum and minimum values of the cumulative TB cases, excluding outliers; outliers are depicted by solid circles. TB = tuberculosis.

reductions in average cumulative incident cases (Table 5) can be achieved by prioritizing CT by age (S4; $P < .001$), ethnicity (S5; $p = .002$), or a combination of age and ethnicity (S7; $p < .001$). As shown in Figure 8, such schemes also notably reduce average TB infection prevalence. Reflecting the vulnerabilities of children and Saskatchewan's FN population to TB infection, age and ethnicity prioritized CT yields 11% reduction in mean cumulative incident cases, which is the largest observed improvement. Surprisingly, in light of the strong observed association between the number of times a contact has been named and risk of TB infection and of active TB (Al-Azem, 2007; Al-Azem et al., 2010b), prioritizing CT by the count of times a contact has been previously named triggers adverse outcomes, yielding an mean increase of 26.22 (8%; $p = .02$) incident TB cases (S6) compared to the reference unprioritized CT scenario. Broadly similar results can be seen in Figure 8 for prevalence of TB infection.

Contact Tracing Speed

The gains from improving CT speed in reducing active TB cases can be observed by comparing scenario S8 with its corresponding normal-speed reference scenario S2 (Table 5). At the level explored, faster CT does not secure statistically significant improvements in the preventing active TB cases over the course of 20 years; as shown in Figure 9, faster CT (S8) also achieves only very modest reduction in the prevalence of TB infection compared with normal-speed CT (S2). Although the far higher level of detail considered in the current investigation yields added confidence in the robustness

Table 4. Scenarios Results.

Scenario ID	Cumulative Incident Cases (Active Tuberculosis)			
	Median	M	SD	p
S0	411	411.08	76.5	
S1	288	292	47.1	<.0001
S2	277	276.3	44.6	<.0001
S3	328	326.79	53.4	<.0001
S4	294	294.52	50.6	<.0001
S5	295	304.56	57.7	<.0001
S6	344.5	353.01	67.1	<.0001
S7	286	291.04	48.7	<.0001
S8	265	265.7	41.9	<.0001

Note. The statistical tests are Mann-Whitney *U* tests (one-tailed).

of the assessment, these results concerning the speed of CT are broadly consistent with the findings of our previously SD model of CT (Tian et al., 2011).

Discussion and Future Work

This work has investigated the impacts on TB outcomes of CT scope, speed, loss to follow-up, and prioritization. The detailed simulation of CT protocols at an individual level supports quantification of trade-offs associated with diverse alternatives.

Investigation suggests that CT confers strong benefits for TB outcomes but secures diminishing returns as program scope expands. Our results further suggest that reducing loss to follow-up as a whole can yield significant reduction in TB burden over time; the detailed character of our CT simulation leaves open the possibility of extending such findings by conducting stage-specific analyses of loss to follow-up.

Most significantly, our investigation of CT prioritization effectiveness suggests that use of age- and ethnicity-prioritized schemes can significantly improve the effectiveness of CT relative to an unprioritized approach. Such gains are especially important given the tight limits on human resources and funding confronting many TB control efforts, and both vindicate and underscore the importance of maintaining the emphasis historically placed by Saskatchewan TB Control on young contacts.

Given the strong reported association between the count of times an individual has been named in CT and his or her risk of TB infection and TB cases, the adverse impacts associated with prioritization according to this metric require study. We believe this metric retains promise, and we plan to examine promising variants (e.g., those controlling for the effects of age) and conduct further social network analysis to identify additional important associations that might support competitive prioritization strategies.

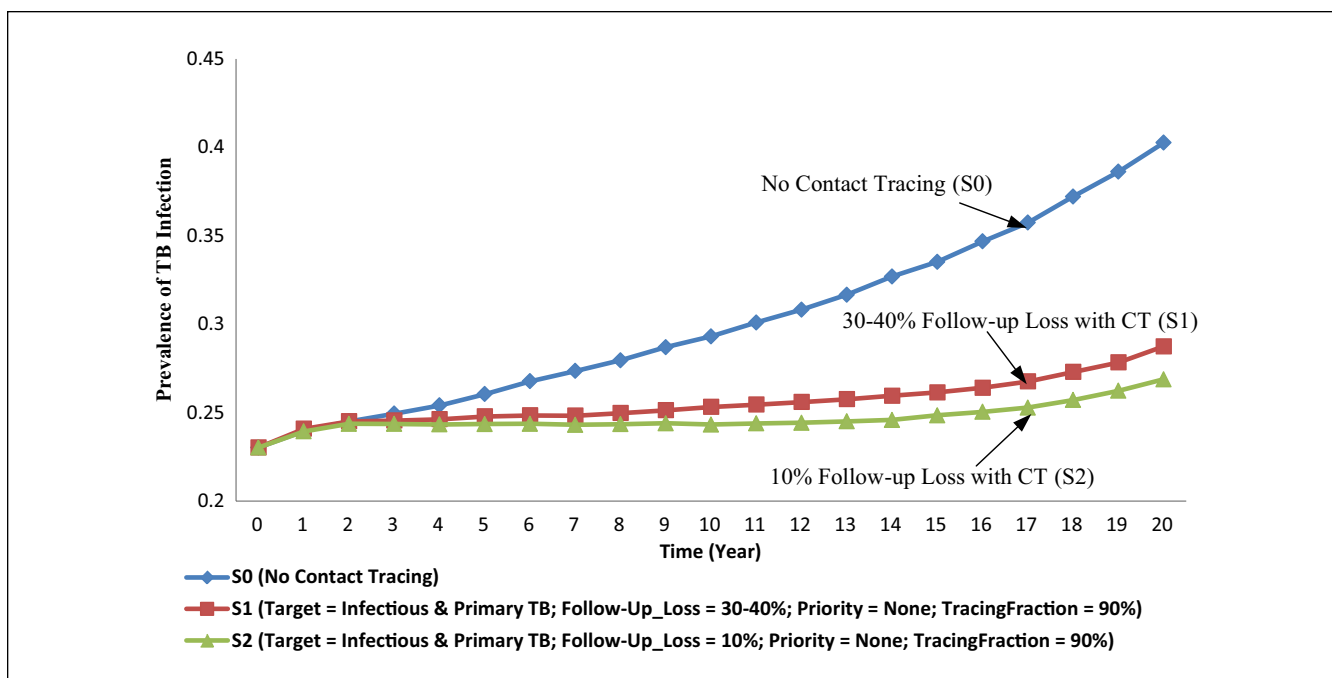


Figure 7. Average prevalence of TB infection for scenarios regarding loss to follow-up in the scale-free network.
 Note. TB = tuberculosis; CT = contact tracing.

Table 5. Difference in Mean of Cumulative Tuberculosis Cases for 20 Years Across All the Scenarios.

Reference ID	S1	S2	S3	S4	S5	S6	S7	S8
S0	-119.08**	-134.78**	-84.29**	-116.56**	-106.52**	-58.07**	-120.04**	-145.38**
S1	0	-15.7*	34.79**	2.52	12.56	61.01**	-0.96	-26.3**
S2		0	50.49**	18.22**	28.26**	76.71**	14.74*	-10.6
S3			0	-32.27**	-22.23**	26.22*	-35.75**	-61.09**
S4				0	10.04	58.49**	-3.48	-28.82**
S5					0	48.45**	-13.52	-38.86**
S6						0	-61.97**	-87.31**
S7							0	-25.34**
S8								0

Note. Mann-Whitney *U* tests (two-tailed) are used for statistical tests.

p* < .05. *p* < .01.

From a methodological perspective, ABM has proven a powerful vehicle for examining CT policy design. The greater flexibility of ABM in representing the detailed operation of the CT process and in representing and investigating prioritization strategies based on individual history, network position, and heterogeneous attributes makes it a particularly valuable and versatile tool for shedding light on the key TB control policy of CT. We note that the general strategy followed here will readily support adaptation to CT efforts for diverse notifiable pathogens, including—but not limited to—HIV and many sexually transmitted and blood-borne infections. Most important, we hope that this contribution will aid policy analysts in identifying high-leverage strategies to address diverse communicable illnesses, thus both improving the health of the population and relieving health system burdens.

This study also suffers from some important limitations. Most notably, we extended the existing mechanisms drawn from a previously calibrated model by adding CT procedure, which might appreciably alter the dynamics of the original model. Further calibration work is needed to verify that our enriched TB model with CT can reproduce the historical patterns among the Saskatchewan communities.

Acknowledgment

NDO gratefully acknowledges the support of the Saskatchewan Health Research Foundation via the Research Alliance for the Prevention of Infectious Disease Network, and the National Science and Engineering Research Council's Discovery Grant RGPIN-327290-20, and the contributions of A. Mahamoud, MPH, for her work with an earlier TB model from which the model described here drew insights.

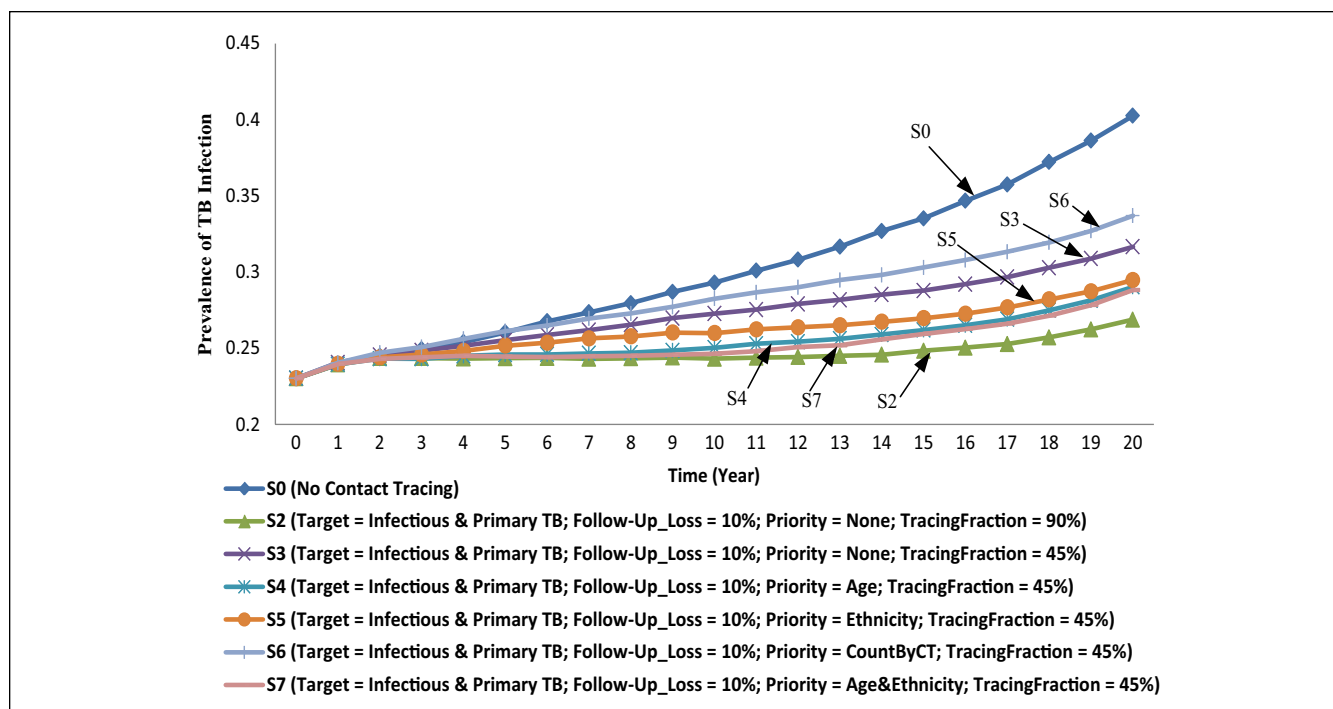


Figure 8. Average prevalence of TB infection for scenarios regarding prioritized contact tracing in the scale-free network.
Note. TB = tuberculosis; CT = contact tracing.

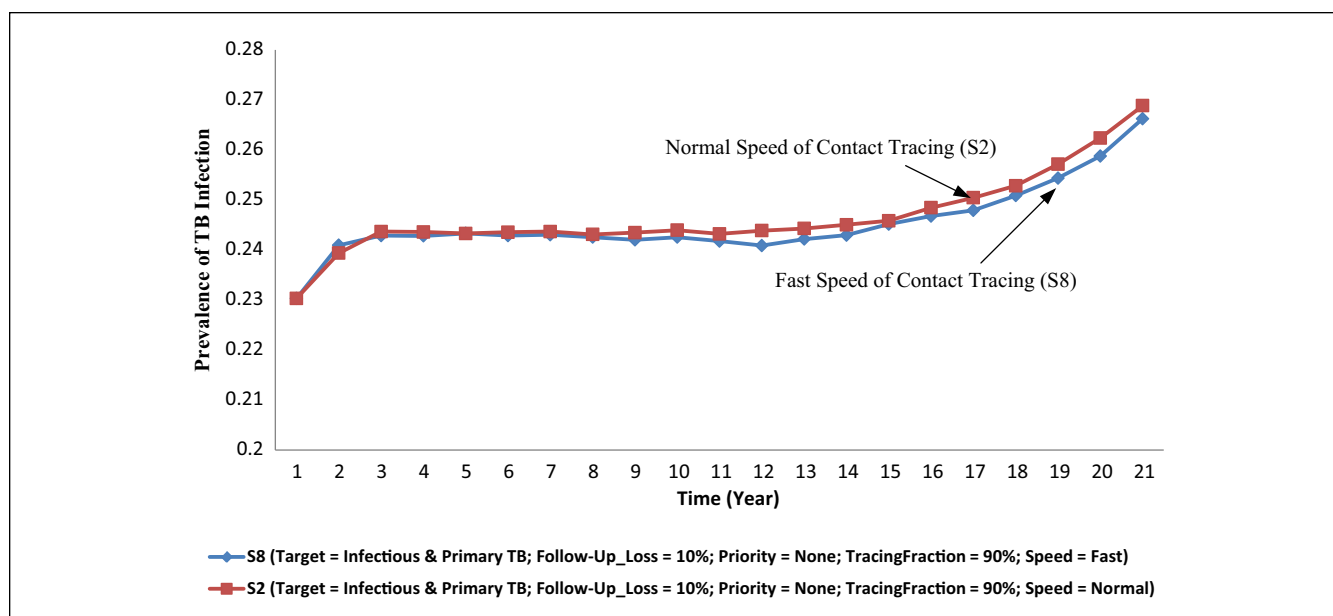


Figure 9. Average prevalence of TB infection for scenarios regarding the speed of contact tracing in the scale-free network.
Note. TB = tuberculosis.

Authors' Note

The supplemental material can be found online at <http://heb.sagepub.com/supplemental>

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Support of the Saskatchewan Health Research Foundation via the Research Alliance for the Prevention of Infectious Disease Network, and the National Science and Engineering Research Council's Discovery Grant RGPIN-327290-20.

Supplement Note

This article is published in the *Health Education & Behavior* supplement, Systems Science Applications in Health Promotion and Public Health, which was supported under contract HHSN276201200329P by the National Institutes of Health Office of Behavioral and Social Sciences Research, the Fogarty International Center, the National Cancer Institute, the National Institute on Dental and Craniofacial Research, and the National Institute on Aging.

References

- Al-Azem, A. (2007). Social network analysis in tuberculosis control among the aboriginal population of Manitoba (Unpublished doctoral dissertation). University of Manitoba, Winnipeg, Manitoba, Canada.
- Al-Azem, A., Hoepfner, V., & Osgood, N. D. (2010a, March). *Advantage of using INH as network-informed prophylaxis treatment among TB contacts in a high TB incidence Saskatchewan community*. Poster presented at STOP TB 2010, Edmonton, Alberta, Canada.
- Al-Azem, A., Hoepfner, V., & Osgood, N. D. (2010b, June). *Social network analysis (SNA) advantages in tuberculosis (TB) control in high TB incidence community in Saskatchewan*. Paper presented at Sunbelt XXX, Trento, Italy.
- Aparicio, J. P., & Hernandez, J. C. (2006). Preventive treatment of tuberculosis through contact tracing. *Contemporary Mathematics*, 410, 17-29. Retrieved from <http://www.suagm.edu/umet/pdf/preventive.pdf>
- Barabasi, A. L., & Albert, R. (1999). Emergence of scaling in random networks. *Science*, 286, 509-512.
- Beydeda, S., Book, M., & Gruhn, V. (2005). *Model-driven software development*. New York, NY: Springer.
- Colditz, G. A., Brewer, T. F., Berkey, C. S., Wilson, M. E., Burdick, E., Fineberg, H. V., & Mosteller, F. (1994). Efficacy of BCG vaccine in the prevention of tuberculosis: Meta-analysis of the published literature. *Journal of the American Medical Association*, 271, 698-702.
- Epstein, J. M. (2009). Modelling to contain pandemics. *Nature*, 460, 687.
- Fayad, M. E., & Schmidt, D. C. (1997). Object-oriented application frameworks. *Communications of the ACM*, 40(10), 32-38.
- Gilbert, N. (2007). *Agent-based models*. Thousand Oaks, CA: Sage.
- Hashemian, M., Stanley, K. G., Knowles, D. L., Calver, J., & Osgood, N. D. (2012, January). *Human network data collection in the wild: The epidemiological utility of micro-contact and location data*. Paper presented at 2nd ACM SIGHIT International Health Informatics Symposium, Miami, FL.
- Hashemian, M., Stanley, K., & Osgood, N. D. (2010, May). *Flunet: Automated tracking of contacts during flu season*. Paper presented at the 6th International Workshop on Wireless Network Measurements, Avignon, France.
- Hyman, J. M., Li, J., & Stanley, E. A. (2003). Modeling the impact of random screening and contact tracing in reducing the spread of HIV. *Mathematical Biosciences*, 181, 17-54.
- Irvine, J., & Stockdale, D. (2004). *Northern Saskatchewan Health Indicators Report 2004*. La Ronge, Saskatchewan, Canada: Athabasca Health Authority, Keewatin Yatthe Regional Health Authority, Mamawetan Churchill River Regional Health Authority, Population Health Unit.
- Lich, K. H. (2007). *The impact of smoking on population-level tuberculosis outcomes* (Unpublished doctoral dissertation). University of Michigan, Ann Arbor.
- Lich, K. H. (2010). Using system dynamics tools to gain insight into intervention options related to the interaction between tobacco and tuberculosis. *Global Health Promotion*, 17(1 Suppl.), 7-20.
- Lich, K. H., Osgood, N. D., & Dyck, R. (2009, December). *Why we must care about the effects of diabetes and smoking on TB and what else we most need to learn*. Paper presented at the 40th Union World Conference on Lung Health, Cancun, Mexico.
- Meng, A., & Osgood, N. D. (2012, July). *Design of the system dynamics longitudinal analysis system: Quantifying the hidden trajectories of system dynamics models*. Paper presented at the 30th International Conference of the System Dynamics Society, St. Gallen, Switzerland.
- Mueller, J., Kretzschmar, M., & Dietz, K. (2000). Contact tracing in stochastic and deterministic epidemic models. *Mathematical Biosciences*, 164, 39-64.
- Newman, M. E. J. (2003). The structure and function of complex networks. *Siam Review*, 45, 167-256.
- Osgood, N. D. (2004, July). *Representing heterogeneity in complex feedback system modeling: Computational resource and error scaling*. Paper presented at the 22nd International Conference of the System Dynamics Society, Oxford, England.
- Osgood, N. D., Mahamoud, A., Lich, K. H., Tian, Y., Al-Azem, A., & Hoepfner, V. H. (2011). Estimating the relative impact of early-life infection exposure on later-life tuberculosis outcomes in a Canadian sample. *Research in Human Development*, 8, 26-47.
- Railsback, S. F., & Grimm, V. (2012). *Agent-based and individual-based modeling: A practical introduction*. Princeton, NJ: Princeton University Press.
- Tian, Y. (2012). *Agent-based modeling and system dynamics modeling on transmission of tuberculosis in Saskatchewan* (Unpublished master's thesis). University of Saskatchewan, Saskatoon, Saskatchewan, Canada.
- Tian, Y., Alawami, F., Al-Azem, A., Osgood, N. D., Hoepfner, V., & Dutchyn, C. (2011, December). *A system dynamics model of tuberculosis diffusion with respect to contact tracing investigation*. Paper presented at the 2011 Winter Simulation Conference, Phoenix, AZ.
- Vynnycky, E., & Fine, P. E. M. (1997). The natural history of tuberculosis: the implications of age-dependent risks of disease and the role of reinfection. *Epidemiology & Infection*, 119, 183-201. doi:10.1017/s0950268897007917
- Vynnycky, E., & Fine, P. E. M. (2000). Lifetime risks, incubation period, and serial interval of tuberculosis. *American Journal of Epidemiology*, 152, 247-263.
- Wackerly, D., Mendenhall, W., & Scheaffer, R. L. (2007). *Mathematical statistics with applications* (7th ed.). Pacific Grove, CA: Duxbury Press.
- Ward, H. (2004). *Risk factors in the progression from tuberculosis infection to disease* (Unpublished master's thesis). University of Saskatchewan, Saskatoon, Saskatchewan, Canada.
- Ziv, E., Daley, C. L., & Blower, S. M. (2001). Early therapy for latent tuberculosis infection. *American Journal of Epidemiology*, 153, 381-385.