Modeling the impact of screening algorithms and prisoner turnover levels on TB transmission in South African prisons

Zachary Chen Liao

A thesis

submitted in partial fulfillment of the

requirements for the degree of

Master of Public Health

University of Washington

2018

Committee:

Scott Barnhart

Susan M. Graham

Joseph Heim

Program Authorized to Offer Degree:

Department of Global Health

University of Washington

Abstract

Modeling the impact of screening algorithms and prisoner turnover levels on TB transmission in South African prisons

Zachary Chen Liao

Chair of the Supervisory Committee:

Scott Barnhart

Department of Global Health

Controlling transmission of *Mycobacterium tuberculosis* (TB) within prisons is a key component of the overall effort against TB in South Africa. In this study, a Monte Carlo discrete event simulation model was used to compare instances of TB transmission occurring in a hypothetical prison cell under different conditions of prisoner turnover, cell ventilation and TB screening. High prisoner turnover rates substantially increased TB transmission. Furthermore, when assuming baseline conditions of no TB screening and poor cell ventilation (1 air change per hour), improved screening with chest radiography and Xpert testing yielded equal or better results compared to improved ventilation (12 air changes per hour) at every level of turnover modeled. This study suggests that the number of prisoners in high-turnover environments should be reduced in order to decrease TB transmission. Directions for future studies include simulating different combinations of TB screening and improved cell ventilation to determine their efficacy in preventing transmission, as well as analysis of the financial and logistical feasibility of implementing these measures.

Introduction

Prisons are a high-risk environment for transmission of *Mycobacterium tuberculosis* (TB). For example, data from European countries show that the risk of active TB infection for prisoners ranges from 4 to 180 times that of the general population.[1] Though reliable national estimates for TB prevalence in South African prisons are not available, a 2010 study conducted in the country's largest prison found the prevalence of undiagnosed active TB among inmates to be 3.5 percent, more than 3 times the estimated prevalence in the general population.[2] TB in prisons is a particularly salient issue for South Africa, which in 2016 had the world's 11th largest prison population (161,984 people) despite ranking just 25th in overall population.[3,4] As such, controlling TB transmission within prisons is a key component of the overall effort against TB in South Africa.

TB transmission occurs via inhalation of aerosolized TB bacilli. In adults, initial exposure and infection typically results in latent TB infection, during which the bacilli are isolated within granulomas without causing symptoms or making the infected individual contagious. Progression from latent TB infection to active TB disease occurs in up to 10 percent of infected individuals over their lifetime, with half of these cases occurring in the first 18 months following initial infection. The majority of active TB cases include pulmonary TB disease, in which individuals cough up aerosolized bacilli and can transmit the infection to others.[5]

Guidelines on preventing the spread of TB in healthcare facilities have included detailed discussions of engineering controls such as airborne infection isolation rooms, cell ventilation rates, and filtration methods such as high efficiency particulate air (HEPA) filters and ultraviolet germicidal irradiation (UVGI).[6] Indeed, previous modeling has suggested that poor cell ventilation and overcrowding contribute substantially to TB transmission in South African prisons.[7] However, improving cell ventilation in resource-limited settings is difficult, as mechanical ventilation systems are expensive to maintain and UVGI still faces technical and regulatory obstacles to widespread adoption.[8] Furthermore, while the architectural design of a facility can help achieve better natural ventilation,[9] rebuilding the country's existing prisons could be prohibitively costly. In light of these constraints, administrative controls may offer more feasible approaches to reducing TB transmission in South African prisons. Indeed, the CDC guidelines on TB place administrative measures at the top of the control hierarchy, above engineering controls and respiratory protection.[6]

Active screening, identification of positives and isolation and treatment are one way to put administrative controls into use. The South African Department of Health has published guidelines on TB screening in correctional facilities, recommending symptom screening for all prisoners, followed by chest X-ray (CXR) and Xpert (a nucleic acid amplification test for TB detection) for those suspected to have TB. However, the guidelines also acknowledge that these testing resources are not available at all prisons.[10] The choice of TB screening method upon prisoner entry may influence the likelihood of transmission between inmates. For example, per a 2013 meta-analysis, screening by asking about a prolonged cough is only 49% sensitive in settings with high HIV prevalence, meaning that most prisoners with active TB would be missed by this method.[11] By modeling the effects of different screening algorithms, it is possible to

quantify the potential benefits of these algorithms, which may help guide decisions about how best to allocate limited resources for medical and laboratory equipment.

A second application of administrative controls is to modify turnover rates to limit the number of people exposed to someone with unidentified active TB. Turnover rate is defined as the total number of prisoners entering a facility within a given time frame, divided by the average inmate population of the facility during that time. In 2006, un-sentenced prisoners (awaiting sentencing by a court and/or temporarily detained) comprised roughly 30 percent of the country's inmates, and their annual turnover rate was 6.5, which corresponds to an average length of stay of less than 2 months.[12] Such rapid turnover may facilitate TB transmission by exposing a greater number of individuals to infectious particles. Understanding the effect of rapid turnover rates on TB transmission within prisons may help inform administrative policies to prevent new infections.

This study aimed to quantify the effect that prisoner turnover, screening method and cell ventilation have on TB transmission. To do this, I used a combined Wells-Riley and Monte Carlo discrete event simulation approach to model the number of new TB infections arising within a hypothetical prison cell over 1 year, taking into account environmental factors such as cell capacity and overcrowding. The Wells-Riley model is a convenient method for estimating the risk of infection for susceptible individuals exposed to airborne pathogens. First fully elucidated by Riley et al. in 1978 to model a measles outbreak, it has also found use in TB modeling, including a prior study of TB in South African prisons.[7,13,14] The Wells-Riley model assumes that the population in question is static: the infectious individuals and susceptible individuals must remain the same throughout the timeframe being modeled. It is a deterministic model; the relevant equations are described below in the methods section.

Monte Carlo discrete event simulation allows for the modeling of probabilistic events using a random number generator (RNG). In the context of TB modeling, this approach allows for incorporation of probability distributions governing outcomes of key events such as new prisoner arrival and TB screening. For instance, to simulate the screening of a prisoner with active TB infection, the RNG will produce a random number n with a value between 0 and 1. If the sensitivity of the TB screening algorithm is 0.8, the prisoner will test positive if $0<n\leq 0.8$ and negative if $0.8<n\leq 1$. By using the RNG to simulate probabilistic events, and repeating the simulations a large number of times, it is possible to estimate the number of new infections resulting from different screening and turnover parameters. The Monte Carlo model used in this study is described in more detail below.

Specific aims:

1. To model the impact that prisoner turnover rates have on the number of new TB infections arising within a prison cell.
2. To compare the impact of improved TB screening and improved cell ventilation on the number of new TB infections arising within a prison cell.

Methods

Modeling risk of TB infection for an individual susceptible prisoner

To calculate the risk that a prisoner in a prison cell will be infected with TB, I estimated the concentration of infectious TB particles in each cell. To do so, I used the concept of an infectious quantum first developed by Wells. A quantum is defined as an infectious particle that, when inhaled, is sufficient to cause infection. Based on the Poisson distribution with $\lambda=1$, for a group of susceptible individuals breathing in an average of 1 quantum per person, infection is expected to occur in $(1 - e^{-1})$, or approximately 63 percent, of individuals.

Using the Wells-Riley model,[13] the steady-state concentration of TB quanta in a cell is given by the following equation:

Equation 1.

$$C = \frac{Iq}{Q}$$

where

$C = concentration\ of\ TB\ quanta\ (quanta/m^3)$
$I = number\ of\ infectious\ sources\ (no\ unit)$
$q = quantum\ production\ rate\ per\ infectious\ source\ (quanta/hour)$
$Q = ventilation\ rate\ of\ cell\ (m^3/hour)$

The ventilation rate of the cell, in turn, is given by the following equation:

Equation 2.

$$Q = V * ACH$$

where

$Q = ventilation\ rate\ of\ cell\ (m^3/hour)$
$V = volume\ of\ cell\ (m^3)$
$ACH = air\ changes\ per\ hour\ (no\ unit)$

After calculating the steady-state concentration of TB quanta in the cell, I used the Wells-Riley model to estimate the risk of infection to a susceptible prisoner.[13] The risk is described by the following equation:

Equation 3.

$$R = 1 - e^{-Cpt}$$

where

$R = risk\ of\ infection\ (no\ unit)$
$C = concentration\ of\ TB\ quanta\ (quanta/m^3)$
$p = pulmonary\ ventilation\ rate\ (m^3/hour)$
$t = duration\ of\ exposure\ (hours)$

Modeling number of total new TB infections within a prison cell using Wells-Riley

Before incorporating prisoner turnover and screening methods into the model, I used the Wells-Riley approach to estimate TB transmission over time for a static prison cell population with 1 infectious prisoner:

Equation 4.

$$N = S * R = S(1 - e^{-Cpt})$$

where

$N = number\ of\ newly\ infected\ prisoners\ (prisoners)$
$S = initial\ number\ of\ susceptible\ prisoners\ (prisoners)$
$R = risk\ of\ infection\ (no\ unit)$
$C = concentration\ of\ TB\ quanta\ (quanta/m^3)$
$p = pulmonary\ ventilation\ rate\ (m^3/hour)$
$t = duration\ of\ exposure\ (hours)$

The outcome of interest was number of instances of TB transmission over time. This was modeled for each hypothetical level of cell ventilation (1, 6, and 12 ACH; see Table 2 for justification of and references for parameters).

Modeling number of total new TB infections within a prison cell using discrete event simulation

A Monte Carlo discrete event simulation approach was used to model the overall number of instances of TB transmission occurring in a single prison cell over a 365-day time frame. It was assumed that at the start of the year, there are an initial number of prisoners in the cell, all of whom are susceptible to TB infection and none of whom have active TB.

Each repetition of the simulation represented a 365-day period in the prison cell, with simulated events occurring on each of those 365 days as part of the model. The simulated events in the model are depicted in Figure 1.

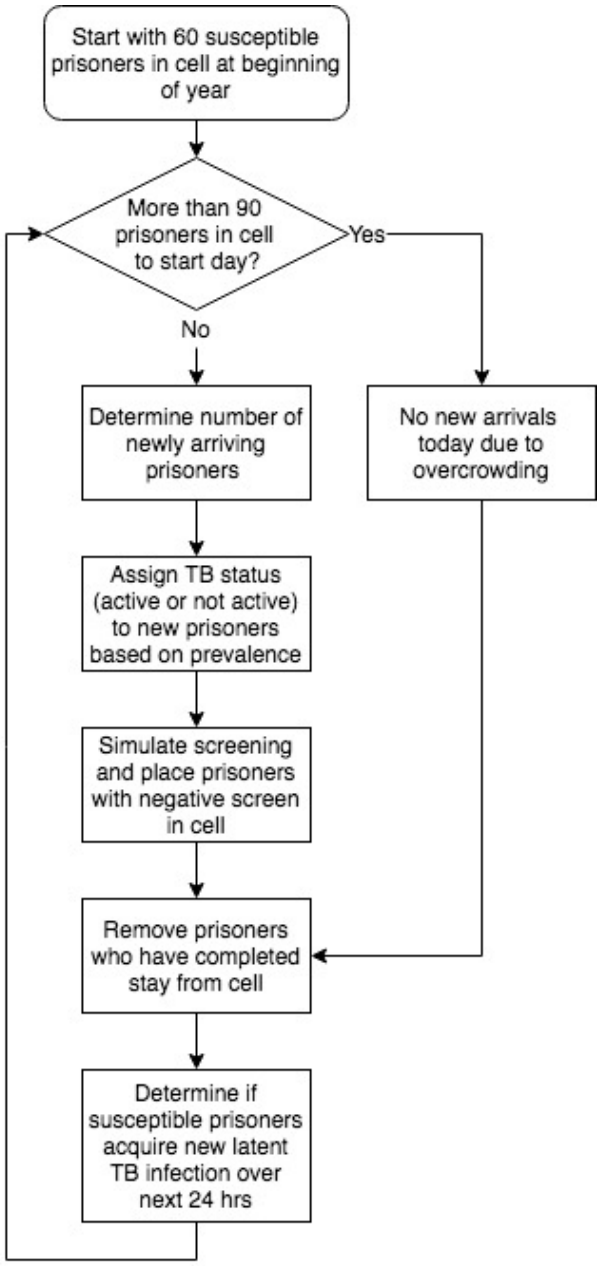

Figure 1. Flow diagram of simulated events in model

As part of the model, the following occurrences were simulated on a daily basis:

- **New prisoners arriving at the cell**

This was modeled using a Poisson distribution based on the average rate of arrival of new prisoners, based on Table 2 parameters. It was assumed that the rate of arrival of new prisoners does not vary during the year. The rate of arrival is given by the following equation:

Equation 5.

$$\lambda = T * n_i * \frac{1\ year}{365\ days}$$

where

λ = *average daily rate of arrival of new prisoners (prisoners/day)*
T = *annual turnover rate (year^{-1})*
n_i = *initial number of prisoners in cell at start of year (prisoners)*

Although the initial number of prisoners in the cell at the start of the year was held constant in all simulations, the total number of prisoners in the cell was allowed to fluctuate from day to day during each simulation, as a variable number of new arriving prisoners entered the cell each morning and prisoners who had finished their stay left the cell. The probability of new prisoners arriving on a given day is derived from the Poisson distribution:

Equation 6.

$$P(k) = \frac{\lambda^k e^{-\lambda}}{k!}$$

where

k = *number of new prisoners arriving in 1 day (no unit)*
λ = *average daily rate of arrival of new prisoners (prisoners/day)*

For instance, assuming a turnover rate of 12 and an initial prison cell population of 60, equation 5 gives an average daily rate of arrival of 1.97 prisoners per day. Given λ=1.97, Equation 6 indicates that on any given day, the probability of exactly 0 new prisoners arriving is approximately 13.9%, 1 new prisoner 27.4%, 2 new prisoners 27.1%, and so on.

- **Length of imprisonment/prisoners leaving the cell**

In the absence of complete data showing the true distribution of incarceration length, it was assumed for the purposes of the model that all prisoners stay in the prison cell for the same amount of time, given by the following equation:

Equation 7.

$$L = \frac{1}{T} * \frac{365\ days}{year}$$

where

L = *expected length of prison cell stay (days)*
T = *annual turnover rate (year^{-1})*

In the simulation, each morning all prisoners whose duration of stay was equal to or greater than the expected length of stay were released from the cell. The prisoners initially in the cell were assumed to have arrived at randomly staggered times prior to the beginning of the year; at the start of each simulation, they were assigned a random duration of stay between 0 and L.

- **New prisoners having active TB**

The probability of new prisoners having active TB was assumed to be equal to the prevalence of active TB in the overall population. For modeling purposes, all new prisoners with active TB

were assumed to have pulmonary disease and to be equally contagious. All prisoners without active TB were assumed to be susceptible to new latent TB infection.

- **Prisoners screening positive for active TB**

It was assumed that all newly arrived prisoners in a given simulation underwent equivalent TB screening, that prisoners screening positive were isolated, and that prisoners screening negative were placed in the prison cell. For prisoners with active TB, the probability of a positive screening test result was equal to the sensitivity of the screening test. For patients without active TB, the probability of a positive result was equal to 1 minus the specificity of the screening test.[a]

This study compared two different screening algorithms described in 2013 WHO guidelines, as well as a no-screening scenario; the algorithms are summarized in Table 4.[15] Both algorithms consist of an initial screening test (TB symptom questionnaire or CXR) followed by a second confirmatory test for those screening positive (sputum smear microscopy or Xpert). In the model, arriving prisoners screening positive on both tests were prevented from entering the cell. Arriving prisoners screening negative on the initial test, as well as those screening positive on the initial test but negative on the confirmatory test, were allowed to enter the cell.

- **Susceptible prisoners acquiring latent TB from another prisoner with active TB**

The probability of newly acquired latent TB infection was calculated on a daily basis using equation 3 for each day of the year. Susceptible prisoners who become infected on a particular day were no longer considered susceptible on subsequent days. It was assumed that newly infected prisoners did not progress to active TB during their prison stay, and that no prisoners died prior to release.

Simulation steps:

First, to verify and validate the simulation model, I sought to reproduce the Wells-Riley results given by equation 4. I did this by simulating the number of instances of TB transmission in a prison cell with a static population of 1 infectious prisoner and 60 initially susceptible prisoners, mimicking the assumptions of the Wells-Riley equation. The validation model differed from the full model described above in the methods section in that there were no prisoners entering or leaving the cell; however, it was identical to the full model in other respects. The validation model was used to simulate different lengths of exposure (31 days, 61 days, 365 days) and air changes per hour (1, 6, 12), corresponding to the lengths of stay and ACH levels to be simulated in the full model. For each combination of parameters (length of exposure and ACH level), 10,000 replications of the validation model were run, and the model results were compared to the Wells-Riley results from equation 4. The number of replications was chosen to obtain narrow confidence intervals; the half-with (i.e. the difference between the mean and the 95% CI boundary) was less than 0.1 instances of transmission for each combination of parameters. This allowed for more precise determination of agreement between the model results and the Wells-Riley equation.

[a] Sensitivity is defined as the probability of a positive test given that the individual is positive for disease. Specificity is defined as the probability of a negative test given that the individual is negative for disease.

Next, I used the full model to simulate the number of new infections occurring over 1 year, incorporating prisoner arrivals and prisoner departures as described in equations 6 and 7. I performed simulations for each of the different turnover rates (annual turnover of 1, 6 and 12, corresponding to lengths of stay of 365 days, 61 days and 31 days, respectively). For each of the three turnover levels, I modeled 5 scenarios: a baseline scenario with no prisoner screening upon entry and minimal ventilation of the prison cell, as well as additional scenarios with either improved screening or improved cell ventilation. These scenarios are outlined in Table 1 below.

Table 1. Modeled scenarios

Turnover rate	Scenario	Screening	ACH
1	Baseline	None	1
	Basic screening	Symptoms, microscopy	1
	Enhanced screening	CXR, Xpert	1
	6 ACH	None	6
	12 ACH	None	12
6	Baseline	None	1
	Basic screening	Symptoms, microscopy	1
	Enhanced screening	CXR, Xpert	1
	6 ACH	None	6
	12 ACH	None	12
12	Baseline	None	1
	Basic screening	Symptoms, microscopy	1
	Enhanced screening	CXR, Xpert	1
	6 ACH	None	6
	12 ACH	None	12

For each unique combination of parameters and screening algorithms, the Monte Carlo simulation was run 5,000 times, and the mean results were reported. After 5,000 simulations, the difference between the mean and the 95% confidence interval boundary was either less than 5 percent of the mean or less than 1 instance of transmission for all 15 modeled scenarios. This was felt to be sufficiently precise and further simulations were not run.

The parameters used in the simulation and references for their sources are shown below in Table 2. The primary outcome of interest is the number of instances of TB transmission. Secondary outcomes included number of prisoners with active TB passing through a cell, and the number of true and false positives on TB screening. Discrete event simulations were performed using Simio version 9.158 (http://www.simio.com).

Table 2. Parameters used in simulations

Variable	Value(s)	Comments
Inner volume of cell	351.75 m^3	Based on cell capacity of 30 prisoners. HRW 1994 observed 58 prisoners in a 1200-sq-ft cell, which roughly corresponds to a cell designed for a capacity of 30 prisoners functioning at 200 percent occupancy.[16] Assuming 3.5 m^2 of floor area per prisoner in accordance with South African national standards.[12,16] Assuming ceiling height of 3.35 m based on dimensions at Pollsmoor prison.[7]
Quantum production rate of source TB patient	1 quanta/hr	Same value used by Johnstone-Robertson et al. in their model.[7] Extrapolated from Riley et al., 1962.[17]
Air changes per hour in cell	1, 6, 12	Study of hospitals without mechanical ventilation of patient rooms showed 1.5 ACH with all windows closed.[9] Recommended minimum for mechanically ventilated hospital rooms is 12 ACH.[6]
Pulmonary ventilation rate	0.36 m^3/hr	Equivalent to minute ventilation of 6 L (12 respirations per minute with tidal volume of 500 mL). Also used by Johnstone-Robertson et al.[7]
Annual prisoner turnover rate	1, 6, 12	Unsentenced prisoners have an annual turnover rate of 6.5, which corresponds to an average stay of just under 2 months. Most sentenced prisoners serve multiple-year sentences, equivalent to a turnover rate less than 1.[12]
Duration of daily TB exposure	23 hrs	Inmates typically stay in their cells for 23 hours per day.[12]
Initial number of prisoners in cell at start of year	60	Based on cell capacity of 30 and occupancy level of 200 percent.
Number of prisoners in cell needed to trigger diversion	90	Based on cell capacity of 30 and occupancy level of 300 percent. Reported occupancy levels have been as high as 353 percent.[12] In the model, if there are 90 or more prisoners in the cell on a given day, no new arrivals will be accepted the following morning.
Prevalence of active TB among newly admitted prisoners	696 per 100,000 population	Nationwide prevalence of active TB disease in South Africa, per 2015 UN Global TB Report.[18]

Table 3. Sensitivity and specificity of TB screening and diagnostic methods

Method	Sensitivity	Specificity	Source
CXR, any abnormality	0.978	0.754	[11]
TB symptom screen	0.842	0.740	[11]
Sputum smear microscopy	0.61	0.98	[15]
Xpert MTB/RIF	0.92	0.99	[15]
No screening	0	1	

Table 4. Screening algorithms to be compared

Method	Source
No screening	
TB symptom screen followed by sputum smear microscopy if positive	Dept. of Health guidelines mandate screening for 4 symptoms.[10] Algorithm described in WHO guidelines.[15]
CXR followed by Xpert if positive	Algorithm described in WHO guidelines.[15]

Results

Verifying and validating the model using Wells-Riley

First, the Wells-Riley equation (Equation 4) and the discrete event model were used to predict the number of new infections in a prison cell with 1 infectious prisoner, 60 susceptible prisoners, no screening, and no prisoners entering or leaving the cell. Different lengths of exposure and different ACH levels were simulated. Table 4 shows the results of the Wells-Riley equation and the discrete event model. For each scenario, 10,000 simulations were run to produce an estimate of the mean; the difference between the mean and the 95% CI boundary was less than 0.1 instances of transmission for all scenarios. The model results closely reproduce the results of the Wells-Riley equation, with the Wells-Riley figures falling within the 95% CI of the model results for every scenario.

Table 5. Results of Wells-Riley equation and discrete event model after 10,000 simulations

Air changes per hour (ACH)	Days	Mean instances of TB transmission, Wells-Riley	Mean instances of TB transmission, model	95% CI of mean, model	
1	31	31.077	31.073	30.997	31.148
1	61	45.726	45.762	45.698	45.827
1	365	59.989	59.988	59.986	59.990
6	31	6.871	6.851	6.802	6.900
6	61	12.770	12.733	12.670	12.797
6	365	45.670	45.661	45.596	45.726
12	31	3.540	3.514	3.479	3.551
12	61	6.767	6.736	6.687	6.785
12	365	30.678	30.650	30.573	30.726

Following reproduction of the Wells-Riley equation results with the validation model, the full model was used to simulate the prison cell scenarios previously described in Table 1. A summary of the results is given in Table 6 below.

Table 6. Mean instances of TB transmission in 1 year under different simulated parameters.

Annual prisoner turnover rate	Screening algorithm: CXR, Xpert	Screening algorithm: Symptoms, microscopy	Screening algorithm: No screening	Cell ventilation (air changes per hour)
12	16.93	78.97	149.03	1
	-	-	33.41	6
	-	-	17.28	12
6	13.10	58.13	109.62	1
	-	-	29.38	6
	-	-	15.60	12
1	2.68	12.86	25.32	1
	-	-	11.94	6
	-	-	7.30	12

Modeling a high-turnover prison cell

Table 7 shows the results of the model with an annual turnover of 12, corresponding to a length of stay of 31 days for each prisoner. In the baseline scenario (no screening and 1 ACH), a mean of 5 prisoners with active TB infection entered the cell in one year, leading to 149 instances of transmission to other prisoners. Enhanced screening with CXR/Xpert and improved cell ventilation with 12 ACH yielded the fewest instances of transmission, with a mean of roughly 17 in both scenarios. The screening scenarios reduced the number of prisoners with active TB entering the cell, but also produced false positives on screening.

Table 7. Results of high-turnover model after 5,000 simulations

Scenario	Screening	ACH	Mean instances of transmission (Ratio)		Active TB prisoners entering cell	True positive on screening	False positive on screening
Baseline	None	1	149.03	1	4.95	0	0
Basic screening	Symptoms, microscopy	1	78.97	0.53	2.49	2.56	3.73
Enhanced screening	CXR, Xpert	1	16.93	0.11	0.51	4.49	1.77
6 ACH	None	6	33.41	0.22	5.02	0	0
12 ACH	None	12	17.28	0.12	5.06	0	0

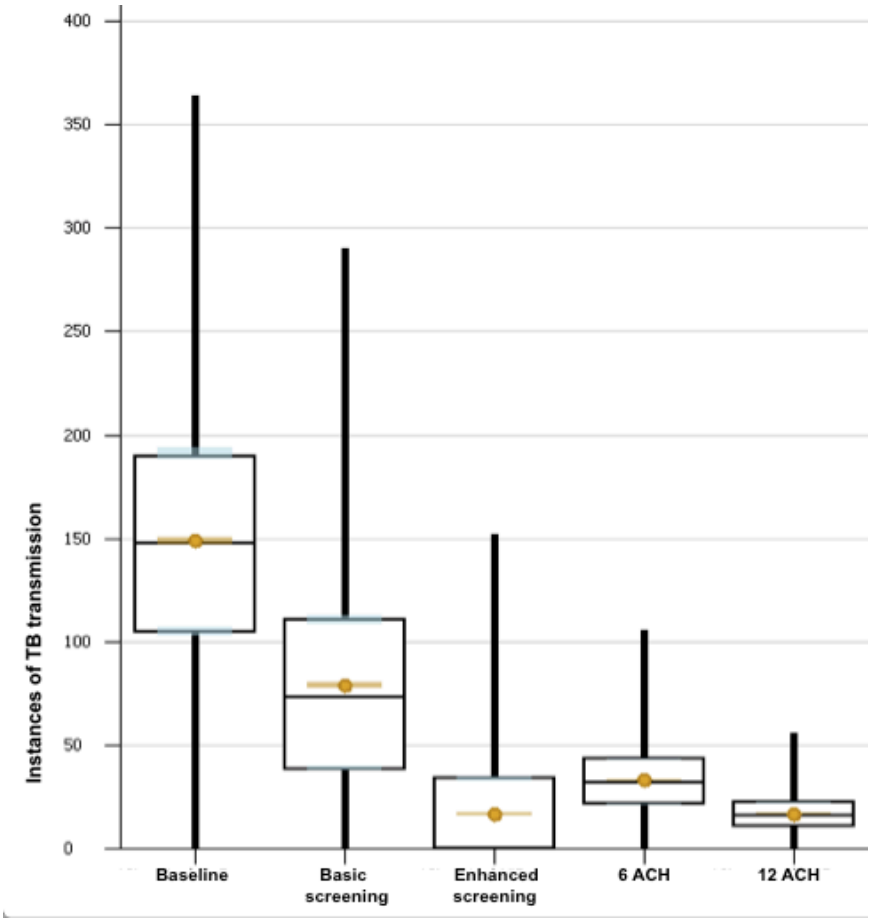

Figure 2. High-turnover model results. Yellow dot and shaded area represent mean and 95% confidence interval, respectively. Blue shaded area represents confidence interval of 25th and 75th percentile values.

Modeling a medium-turnover prison cell

Table 8 shows the results of the model with an annual turnover of 6, corresponding to a length of stay of 61 days for each prisoner. In this case, the baseline scenario (no screening and 1 ACH) produced a mean of 110 annual instances of TB transmission, a 26% decrease compared to the high-turnover model. Enhanced screening with CXR/Xpert produced the least TB transmission, with 13 annual instances of transmission.

Table 8. Results of medium-turnover model after 5,000 simulations

Scenario	Screening	ACH	Mean instances of transmission (Ratio)		Active TB prisoners entering cell	True positive on screening	False positive on screening
Baseline	None	1	109.62	1	2.50	0	0
Basic screening	Symptoms, microscopy	1	58.13	0.53	1.23	1.28	1.84
Enhanced screening	CXR, Xpert	1	13.10	0.12	0.26	2.27	0.91
6 ACH	None	6	29.38	0.27	2.52	0	0
12 ACH	None	12	15.60	0.14	2.53	0	0

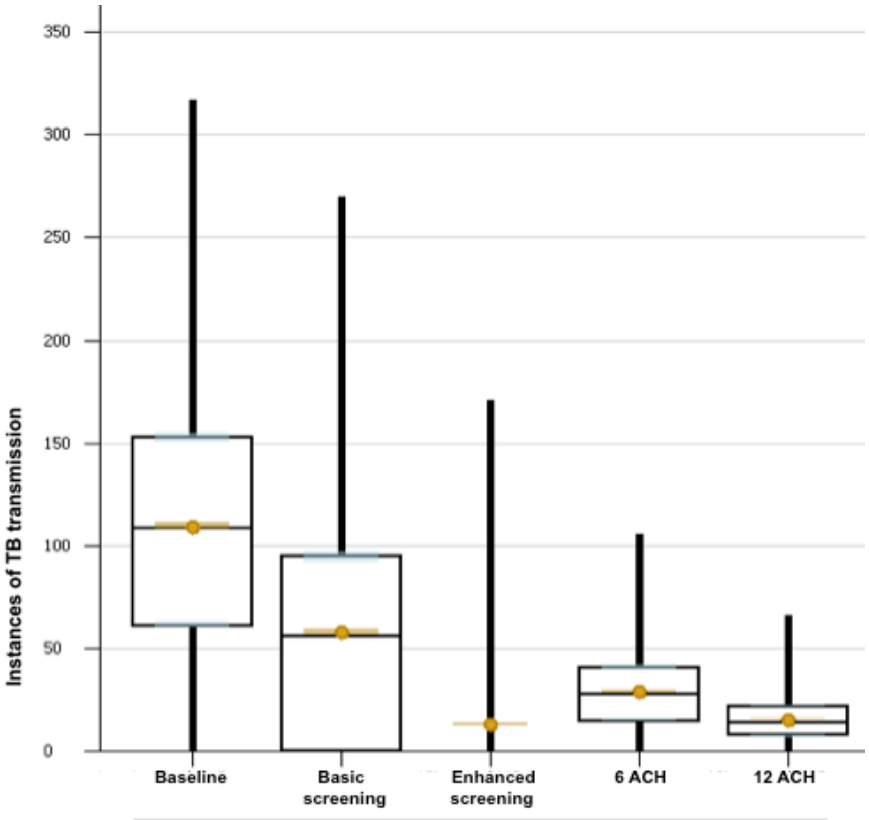

Figure 3. Medium-turnover model results. Yellow dot and shaded area represent mean and 95% confidence interval, respectively. Blue shaded area represents confidence interval of 25th and 75th percentile values.

Modeling a low-turnover prison cell

Table 9 shows the results of the model with an annual turnover of 1, corresponding to a length of stay of 365 days for each prisoner. In this case, the baseline scenario (no screening and 1 ACH) produced a mean of 25 annual instances of TB transmission, an 83% decrease compared to the high-turnover model. Enhanced screening with CXR/Xpert was again the best performer in the low-turnover model, with just 3 annual instances of TB transmission.

Table 9. Results of low-turnover model after 5,000 simulations

Scenario	Screening	ACH	Mean instances of transmission (Ratio)		Active TB prisoners entering cell	True positive on screening	False positive on screening
Baseline	None	1	25.32	1	0.41	0	0
Basic screening	Symptoms, microscopy	1	12.86	0.51	0.20	0.22	0.31
Enhanced screening	CXR, Xpert	1	2.68	0.11	0.04	0.37	0.15
6 ACH	None	6	11.94	0.47	0.42	0	0
12 ACH	None	12	7.30	0.29	0.42	0	0

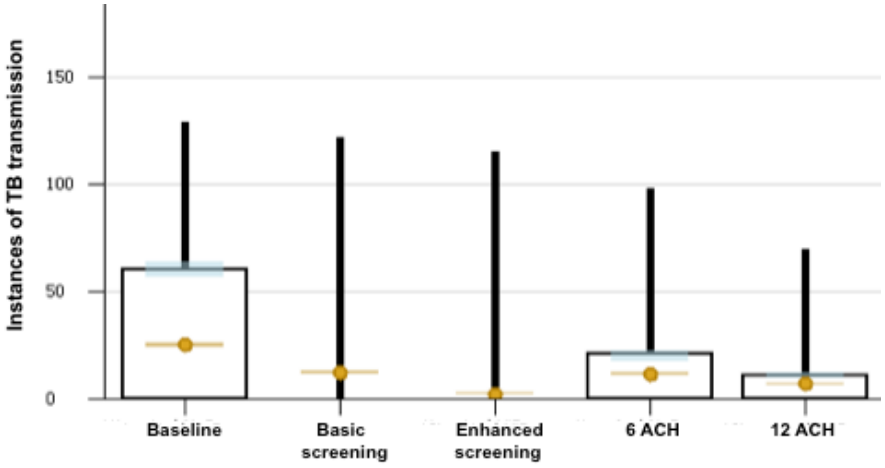

Figure 4. Low-turnover model results. Yellow dot and shaded area represent mean and 95% confidence interval, respectively. Blue shaded area represents confidence interval of 25th and 75th percentile values.

Discussion

This study used a Monte Carlo discrete event simulation approach to model TB transmission in a prison cell under conditions similar to those found in South African prison facilities. The primary contributions of this study to the literature are twofold. First, this model quantifies the effect of prisoner turnover on instances of TB transmission. Second, it compares the effectiveness of different screening and cell ventilation strategies at different levels of turnover. Prior modeling by Johnstone-Roberston et al. used a deterministic Wells-Riley approach, which described the effects of overcrowding and poor ventilation on TB transmission but did not address prisoner turnover or screening.[7]

The three "baseline" scenarios (no screening and 1 ACH) illustrate the dramatic effect of turnover rates on TB transmission, with 149 annual instances of transmission in the high-turnover scenario compared to just 25 in the low-turnover scenario. This suggests that efforts to reduce transmission in prisons ought to be focused on high-turnover settings, such as facilities housing unsentenced prisoners. Prisoner turnover rate is a complex phenomenon, influenced by legal and judicial policy as well as the role of an individual facility in the broader corrections system.[12] The extent to which a prison facility is able to influence its own turnover rate is likely limited. However, larger-scale changes to reduce the number of people imprisoned for 2 months or less could reduce the number of new infections arising from high-turnover settings.

Perhaps the more immediately relevant question is the comparison between TB screening and cell ventilation improvements. In the high-turnover model, enhanced screening with CXR/Xpert and improved ventilation of 12 ACH were about equally effective in reducing the instances of transmission, with both lowering the transmission by nearly 90 percent. However, in the medium and low-turnover models, CXR/Xpert screening was more effective than ventilation of 12 ACH in reducing cases of transmission; this can be attributed to longer prisoner length of stay

counteracting the reduction in infectious quanta achieved with greater cell ventilation. These results suggest that, for a prison facility with poor ventilation and no preexisting screening system, implementing screening with CXR/Xpert would be equivalent or superior to increasing cell ventilation to the 12 ACH standard at both high and low turnover rates.

Even with similar outcomes in TB transmission, as is the case with CXR/Xpert and 12 ACH ventilation in the high-turnover model, enhanced screening does offer an important benefit over cell ventilation improvements: the ability to isolate and treat those prisoners who already have active TB before releasing them from prison back into the community. In the high-turnover model, roughly 5 prisoners with active TB entered the cell each year in scenarios with no screening; using CXR/Xpert screening reduced that number by 90 percent, to 0.5 prisoners per year on average. Interestingly, the "moderate screening" scenario using symptom screening and sputum smear microscopy did not perform nearly as well, missing nearly half of prisoners with active TB. The symptoms/microscopy screening combination also had more false positives than true positives. Thus, this screening approach, though less technologically intensive than CXR/Xpert, could create added costs through unnecessary isolation and treatment for false-positive prisoners, while failing to detect many active TB cases.

The number of undetected active TB cases entering the prison cell may also impact another element of TB prevention: isoniazid preventive therapy (IPT). Current Department of Health guidelines stipulate that all prisoners with HIV should receive IPT for TB prophylaxis while incarcerated.[10] However, if prisoners with active TB not detected by screening are started on IPT instead of the appropriate multi-drug treatment regimen, this could potentially create isoniazid resistance and foster the development of multidrug-resistant TB strains (i.e. those resistant to both isoniazid and rifampicins). Although evidence regarding the existence of this phenomenon is equivocal,[19] this may be another reason to emphasize screening over cell ventilation as a means of curbing TB transmission.

Limitations

The model used in this study has substantial limitations, some of which are the result of a lack of detailed information regarding the South African prison population. Due to a lack of data on the distribution of prisoner length of stay, for the model all prisoners were assumed to have an equivalent length of stay; thus, the simulation results may not correspond to actual conditions within prison cells. Similarly, the true prevalence of active TB amongst arriving prisoners is likely higher than that of the general population due to socioeconomic factors. Thus, using the nationwide prevalence rate may underestimate the number of prisoners arriving with active TB. The sensitivity and specificity data used for the screening tests were not specifically derived from South African studies, so the performance of these tests in a South African context may differ.

Other limitations of this study are due to assumptions that were made in order to simplify the model. For instance, I assumed that no newly infected prisoners go on to develop active TB during their incarceration. While this may be a reasonable assumption for immunocompetent individuals over the short time frames modeled, progression from initial infection to active TB may occur much more rapidly in HIV-positive individuals.[5] Given the high HIV prevalence in

South Africa, this decision may affect the applicability of the results. Furthermore, because I assumed no progression from latent to active TB, no active case finding was included in the model. However, active case finding for TB in prisons should occur at least twice a year according to South African government guidelines.[10]

Finally, the Wells-Riley equation used by the model to estimate infectious risk has its own limitations in modeling TB transmission, as it assumes a steady-state equilibrium of TB quanta. Since it takes some time to reach a new steady-state concentration after infectious individuals enter or leave the cell, the Wells-Riley equation may inaccurately predict infectious risk over short time frames. However, over time frames longer than a few hours, the impact of this difference is minimal.[20]

Conclusion

In this study, a Monte Carlo discrete event simulation model was used to compare instances of TB transmission occurring in a hypothetical prison cell under different conditions of prisoner turnover, cell ventilation and TB screening. High prisoner turnover rates substantially increased TB transmission. Furthermore, when assuming baseline conditions of no TB screening and poor cell ventilation, improved screening with CXR/Xpert yielded equal or better results compared to improved ventilation of 12 ACH at every level of turnover modeled.

This study suggests that the number of prisoners in high-turnover environments should be reduced in order to decrease TB transmission. While turnover throughout the criminal justice system may be difficult to change immediately through administrative policy, simpler tactics such as preventing inmates from switching cells while detained/imprisoned would help to reduce turnover at the cell level. Directions for future studies include simulating different combinations of TB screening and improved cell ventilation to determine their efficacy in preventing transmission, as well as analysis of the financial and logistical feasibility of implementing these measures.

References

1. World Health Organization (WHO). *Global TB Report: Spotlight on TB in Prisons*.; 2013.
2. Telisinghe L, Fielding KL, Malden JL, et al. High Tuberculosis Prevalence in a South African Prison: The Need for Routine Tuberculosis Screening. 2014;9(1). doi:10.1371/journal.pone.0087262.
3. Highest to Lowest - Prison Population Total. World Prison Brief, Institute for Criminal Policy Research. http://www.prisonstudies.org/highest-to-lowest/prison-population-total?field_region_taxonomy_tid=All. Accessed February 18, 2017.
4. *Total Population - Both Sexes*. https://esa.un.org/unpd/wpp/DVD/Files/1_Indicators (Standard)/EXCEL_FILES/1_Population/WPP2015_POP_F01_1_TOTAL_POPULATION_BOTH_SEXES.XLS. Accessed February 18, 2017.
5. Raviglione MC. Tuberculosis. In: Kasper D, Fauci A, Hauser S, Longo D, Jameson JL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine, 19e*. New York, NY: McGraw-Hill Education; 2015. http://accessmedicine.mhmedical.com/content.aspx?aid=1120799793.
6. Jensen PA, Lambert LA, Iademarco MF. Guidelines for preventing the transmission of Mycobacterium tuberculosis in health-care settings, 2005. *MMWR Recomm Rep*. 2005;54(RR-17):1-141. doi:10.2307/42000931.
7. Johnstone-Robertson S, Lawn SD, Welte A, Bekker L, Wood R. Tuberculosis in a South African prison – a transmission modelling analysis. *South African Med J*. 2011;101(11):809-813. doi:10.1016/j.ygyno.2014.12.035.Pharmacologic.
8. Nardell EA. Indoor environmental control of tuberculosis and other airborne infections. *Indoor Air*. 2016;26:79-87. doi:10.1111/ina.12232.
9. Escombe AR, Oeser CC, Gilman RH, et al. Natural ventilation for the prevention of airborne contagion. *PLoS Med*. 2007;4(2):0309-0317. doi:10.1371/journal.pmed.0040068.
10. *Guidelines for the Management of Tuberculosis, Human Immunodeficiency Virus and Sexually-Transmitted Infections in Correctional Centres*. Pretoria: Department of Health; 2013. https://www.health-e.org.za/wp-content/uploads/2014/06/DCS-TB-HIV-and-STI-Guidelines-2013.pdf.
11. van't Hoog AH, Langendam MW, Mitchell E, et al. *A Systematic Review of the Sensitivity and Specificity of Symptom- and Chest-Radiography Screening for Active Pulmonary Tuberculosis in HIV-Negative Persons and Persons with Unknown HIV Status*.; 2013. doi:10.1890/09-2296.1.Abrams.
12. Erasmus NC. *Annual Report for the Period 1 April 2006 to 31 March 2007*. Cape Town; 2007. http://judicialinsp.dcs.gov.za/Annualreports/ANNUAL REPORT 2007.pdf.
13. Riley EC, Murphy G, Riley RL. Airborne spread of measles in a suburban elementary school. *Am J Epidemiol*. 1978;107(5):421-432.
14. Ko G, Thompson KM, Nardell EA. Estimation of Tuberculosis Risk on a Commercial Airliner. *Risk Anal*. 2004;24(2):379-388. doi:10.1111/j.0272-4332.2004.00439.x.
15. World Health Organization (WHO). *Systematic Screening for Active Tuberculosis: Principles and Recommendations*.; 2013. doi:WHO/HTM/TB/2013.04.
16. Human Rights Watch. *Prison Conditions in South Africa*. New York; 1994. https://www.hrw.org/reports/pdfs/s/safrica/safrica942.pdf.
17. Riley RL, Mills CC, O'Grady L, Sultan LU, Wittstadt F, Shivpuri DN. Infectiousness of air from a tuberculosis ward. *Am J Respir Dis*. 1962;85:511-525.

18. World Health Organization (WHO). *Annex 2: Country Profiles for 22 High-Burden Countries*.; 2015. http://www.who.int/tb/publications/global_report/gtbr15_annex02.pdf?ua=1.
19. Balcells ME, Thomas SL, Godfrey-Faussett P, Grant AD. Isoniazid Preventive Therapy and Risk for Resistant Tuberculosis. *Emerg Infect Dis*. 2006;12(5):744-751. doi:10.3201/eid1205.050681.
20. Beggs CB, Noakes CJ, Sleigh PA, Fletcher LA, Siddiqi K. The transmission of tuberculosis in confined spaces: an analytical review of alternative epidemiological models. *Int J Tuberc Lung Dis*. 2003;7(11):1015-1026.