Modeling the Spread of Tuberculosis in a Closed Population

Math 201

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Abstract

Disease prevention and control is a prevalent concern of human society. Current news reports provide ample evidence of the dramatic influence of infectious disease - the recent H1N1 influenza epidemic, for example, has had a variety of health care, behavioral, and economic consequences that impact millions of people. Because of this, an accurate understanding of the dynamics of disease proliferation across the human population is essential for the prevention and treatment of infectious illnesses. The ability to predict the trajectory of infection of a particular disease can aid in the planning of vaccination production, inpatient treatment, and various other health care initiatives. One such disease is tuberculosis, a common infectious disease that affects the lungs, predominantly causing chronic cough, and which, if left untreated, can be fatal (3). Nearly a third of the world's population is infected with tuberculosis, with millions of deaths as well as millions of new cases of infection each year. Infected individuals can also be asymptomatic, thereby significantly contributing to the spread of the illness without exhibiting its symptoms (1).

Thus, considering its global prevalence, it is clear that a model for the spread of tuberculosis has significant utility. Specifically, we model the spread of multi-drug-resistant tuberculosis, which is a strain resistant to the two mainstream drugs for tuberculosis, in a closed population (2). Herein we report our model of tuberculosis outbreak and conclude that, albeit a potent pathogen, it can be effectively contained in a human population with the exception of an highly virulent strain.

Problem Statement

We will investigate the effects of the introduction of multi-drug-resistant tuberculosis into a closed population over a period of 200 days. We first examine the spread of tuberculosis with the assumption that all people infected with the disease exhibit its symptoms. This model predicts changes in the levels of the susceptible population, the infected population, and the recovered population based on rates of recovery from the disease and the rate of contact among the population. We will then modify this model to include an additional population - asymptomatic carriers - that does not physically express the symptoms of tuberculosis, yet carries the disease and is capable of transmission to those in the susceptible population. We expect that the inclusion of the asymptomatic parameter will dramatically change the dynamics of each category of people in the population compared to the simpler model. We use documented rates of infection and recovery in order to estimate parameters, and explore the effects of changing these various rates. Finally, we briefly explore the effects of introducing a deceased class into the model.

We base our initial model on known recovery rates, the preponderance of asymptomatic versus infected individuals, rates of progression from asymptomatic to infected classes, and,

finally, the probability that both an infected/asymptomatic and a susceptible individual may come into contact in order to further spread the disease. In our model we explore the nature of these parameters and demonstrate their effect on the nature of a tuberculosis pandemic in a sparse as opposed to a localized population, or the potential danger of a new, more virulent strain of the disease.

Model Design and Implementation

We make the following assumptions:

(i) The entire susceptible population is healthy prior to the start of the outbreak;

(ii) the probability of disease transmission is identical for both infected and asymptomatic classes;

(iii) the incidence rate is constant for a given population.

We define *S(t)* to be the population of susceptible individuals, that is, individuals who have not yet contracted tuberculosis. *I(t)* refers to the population of individuals that are currently infected with tuberculosis and exhibit its symptoms. For simplicity, we assume that as long as a person is infected with the disease, the infected person is capable of transmitting the disease to a susceptible person. *R(t),* the removed population, represents the population of individuals who have been infected with tuberculosis and have either recovered from the illness or have died. We assume that once an individual has recovered, this person is immune to the disease and can no longer infect or be infected. The differential equations for the simple model are as follows:

$$S'(t) = -\beta S(t)I(t)$$
$$I'(t) = \beta S(t)I(t) - kI(t)$$
$$R'(t) = kI(t)$$

The constant β refers to the incidence rate, in units of people^{-1}days^{-1}. This represents the likelihood of an infected individual coming into contact with a susceptible individual and having this contact result in infection (5). Therefore, for S′(t), and *I′(t),* the terms $-\beta S(t)I(t)$ and $\beta S(t)I(t)$, respectively, refer to the rate at which individuals are moving out of the susceptible population and into the infected population. The constant *k* indicates the recovery rate of infected individuals, in units of days^{-1}. Since the disease spans weeks and even months and is not detectable immediately, k should be a relatively small number (1). Thus, we initially choose k=0.05. This represents the rate at which infected individuals will either recover from tuberculosis or die from the disease. For *I′(t)* and *R′(t)*, the terms $-kI(t)$ and $kI(t)$ represent the movement of the population of infected individuals into the recovered population.

Using MatLab, we will employ Euler's method for systems of differential equations in order to visualize the changes in each category of people over time. Applying Euler's method gives the following equations, which we investigate in MatLab in the following discussion:

$$S(n) = S(n-1) - \Delta t \beta S(n-1) I(n-1)$$
$$I(n) = I(n-1) + \Delta t [\beta S(n-1) I(n-1) - kI(n-1)]$$
$$R(n) = R(n-1) + \Delta t k I(n-1)$$

The parameter Δt refers to the step size, while n represents the recursion.

After having examined the traditional SIR model for the spread of a disease, we now introduce an additional parameter, *A(t)*, into our model. We define *A(t)* to be the population of asymptomatic carriers. Asymptomatic carriers have been infected with tuberculosis and are now capable of transmitting the disease, but unlike those that are infected, these carriers do not exhibit symptoms of the disease. The modified differential equations are shown as follows:

$$S'(t) = -\beta S(t)[I(t) + A(t)]$$
$$I'(t) = r\beta S(t)[I(t) + A(t)] - kI(t) + dA(t)$$
$$R'(t) = k[I(t) + vA(t)]$$
$$A'(t) = (1-r)\beta S(t)[I(t) + A(t)] - A(t)(d + vk)$$

Note that *S′(t)* has been modified to include *A(t)*; analogous to the *I(t)* term, this term indicates the rate at which susceptible individuals are moving into the asymptomatic population. Similarly, *I′(t)* has been modified to include a term for *A(t)*; this term indicates the rate of individuals becoming infected by asymptomatic carriers. The constant *r* is a unitless constant that indicates the fraction of exposed individuals who are symptomatic upon initial infection. Since tuberculosis is a disease defined by mostly asymptomatic infection, we assume *r* to be 0.1 (3). We therefore multiply *A(t)* and *I(t)* by *r* to indicate that the contact between the susceptible and asymptomatic or infected person resulted in an infection. The constant *d* refers to the rate at which asymptomatic individuals will become infected, that is, the probability of asymptomatic carriers moving into the infected population and exhibiting symptoms of tuberculosis. The final term in the equation for *I′(t)*, *dA(t)*, therefore refers to the movement of asymptomatic individuals into the infected population. The equation for *R′(t)* has also been modified to account for the possibility of those who are asymptomatic carriers being treated for the disease and thereby recovering. We introduce a new parameter, *v*, to indicate this possibility. Because this is a much less likely occurrence than for an infected individual recovering, we choose *v* to be constant at 0.1 throughout the discussion. The equation for *A′(t)* can be explained by analogy to the additional terms described above, with each term indicating the rate of movement of individuals to or from each respective category to or from the asymptomatic population.

We again use Euler's method for solving systems of differential equations, which gives rise to the following solutions:

$$S(n) = S(n-1) - \Delta t\beta S(n-1)[I(n-1) + A(n-1)]$$
$$I(n) = I(n-1) + \Delta tr\beta S(n-1)[I(n-1) + A(n-1)] - \Delta tkI(n-1) + \Delta tdA(n-1)$$
$$R(n) = R(n-1) + \Delta tk[I(n-1) + vA(n-1)]$$
$$A(n) = A(n-1) + \Delta t(1-r)\beta S(n-1)[I(n-1) + A(n-1)] - \Delta tA(n-1)(d + vk)$$

The parameter Δt refers to the step size, while n represents the recursion.

Again, we use a program in MatLab to visualize these equations. In doing so, we will now explore the ways in which the spread of tuberculosis through a population will change based on alterations in the incidence rate β, the rates of recovery k and d, and the rate of infection upon exposure, r. We find that variations in these constants have dramatic effects on the course of the spread of the disease.

We now modify the model a final time to include a deceased class in the population.

$$S'(t) = -\beta S(t)[I(t) + A(t)]$$
$$I'(t) = r\beta S(t)[I(t) + A(t)] - kI(t) + dA(t) - jI(t)$$
$$R'(t) = k[I(t) + vA(t)]$$
$$A'(t) = (1-r)\beta S(t)[I(t) + A(t)] - A(t)(d + vk)$$
$$D'(t) = jI(t)$$

Note that $S'(t)$, $R'(t)$, and $A'(t)$ have not been modified. $D'(t)$ represents the rate at which infected individuals die from tuberculosis. The parameter j indicates the mortality rate of tuberculosis, in units of days^{-1}. Thus, the term $jI(t)$ refers to the movement of infected individuals into the deceased population. The additional term in $I'(t)$, $-jI(t)$, can be explained similarly. Note also that $R(t)$ now only represents the population of individuals who have recovered from the disease.

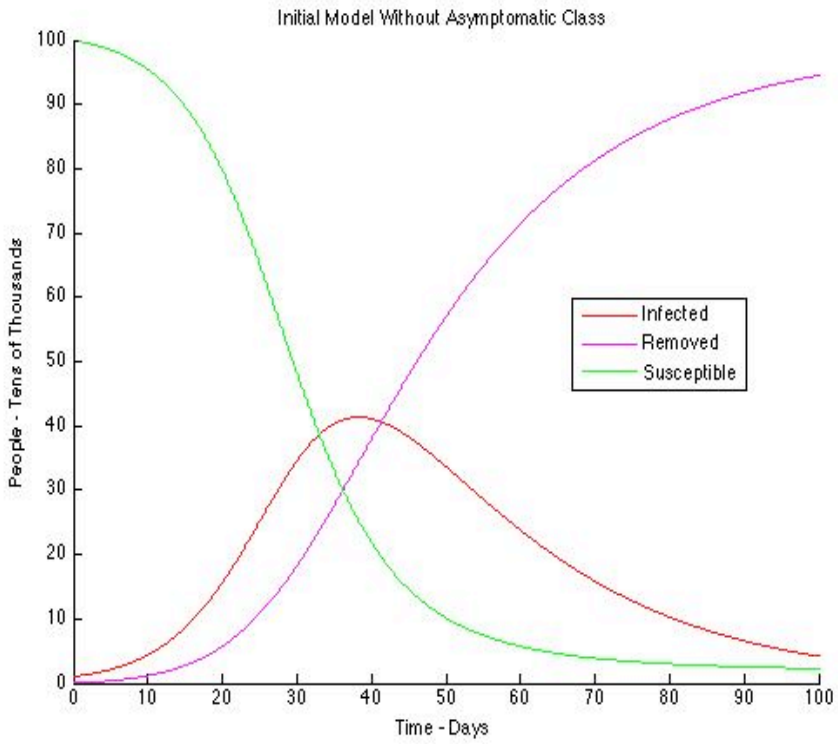
Euler's method yields the following equations, which were visualized in MatLab.

$$S(n) = S(n-1) - \Delta t\beta S(n-1)[I(n-1) + A(n-1)]$$
$$I(n) = I(n-1) + \Delta tr\beta S(n-1)[I(n-1) + A(n-1)] - \Delta tkI(n-1) + \Delta tdA(n-1) - \Delta tjI(n-1)$$
$$R(n) = R(n-1) + \Delta tk[I(n-1) + vA(n-1)]$$
$$A(n) = A(n-1) + \Delta t(1-r)\beta S(n-1)[I(n-1) + A(n-1)] - \Delta tA(n-1)(d + vk)$$
$$D(n) = D(n-1) + \Delta tjI(n-1)$$

This final model is used to examine whether extinction of an isolated population is possible with an abnormally high mortality rate.

Discussion

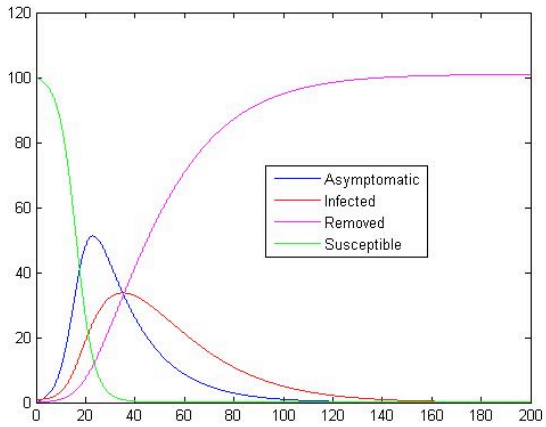
Figure 1. Graph of Initial Model; No Asymptomatic Carriers

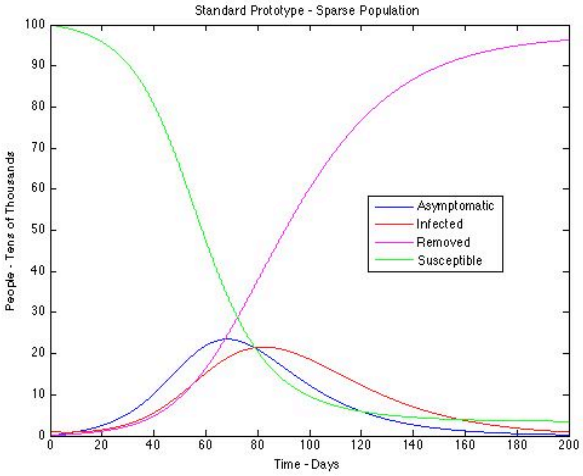


Graph of the basic model for the spread of tuberculosis, with constants $\beta = .002$ *and* $k = .05$.

Initially we sought to detail the standard SIR model for the spread of disease specific to tuberculosis in a moderately dense population. We note that without an asymptomatic class, the infected class spikes halfway through the duration of the outbreak, with eventual full recovery of all infected persons.

Figures 2 and 3.





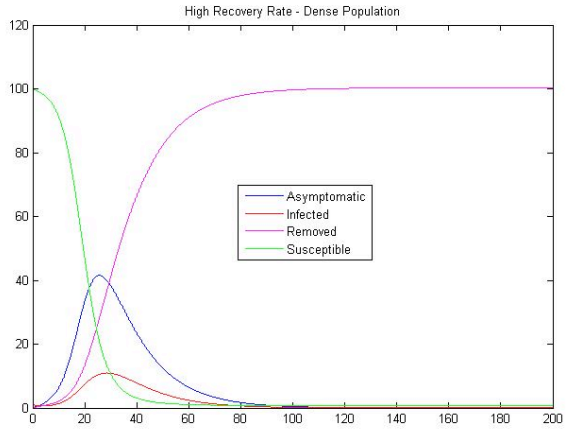
β=*.003 k=.05 r=.1 d=.05*

β=*.001 k=.05 r=.1 d=.05*

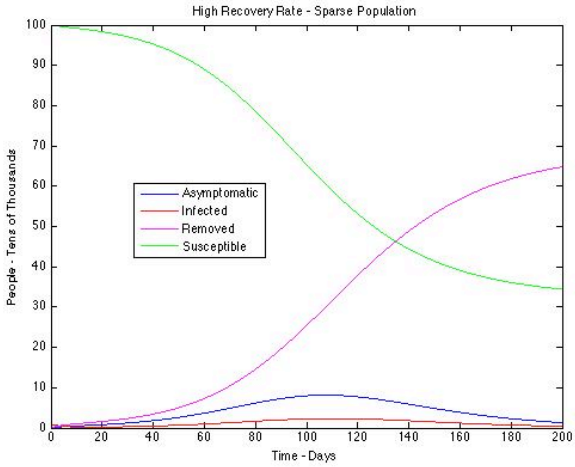
Effect of population-dependent incidence rates on tuberculosis outbreak with standard recovery and asymptomatic transmission rates.

The two above scenarios model the spread of a tuberculosis outbreak in densely and sparsely populated areas, respectively. We varied β from .003 to .001 people^{-1}day^{-1} in order to capture the difference in incidence rates from an urban to rural population. After 100 days, the infection is essentially eradicated in the dense population, whereas the same results require twice the time for the sparse population. These observations result from the sharper spike in infections in the dense class due to increased overall probability of person-to-person contact compared to those living in more rural areas, where we see a smaller percentage of infected individuals, yet the disease itself is able to linger for another 100 days. In both cases we note that the disease is eventually neutralized. Therefore, the current state of tuberculosis and the current recovery protocols indicate that tuberculosis does not pose a significant pandemic threat to human health.

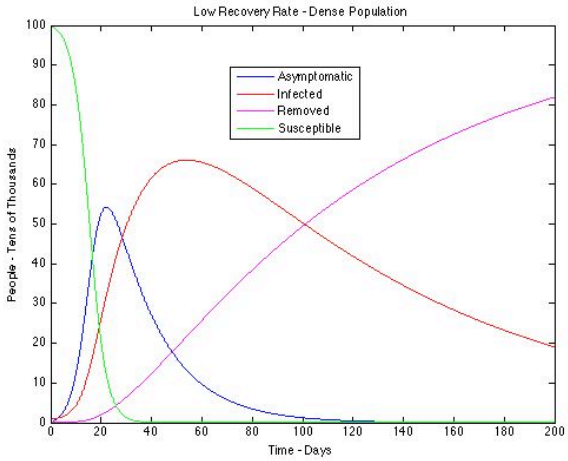
Figures 4, 5, 6, and 7.



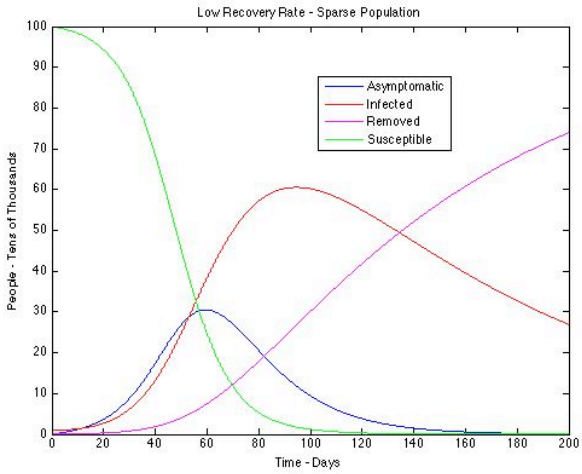
β=.003 k=.2 r=.1 d=.05



β=.001 k=.2 r=.1 d=.05



β=.003 k=.01 r=.1 d=.05



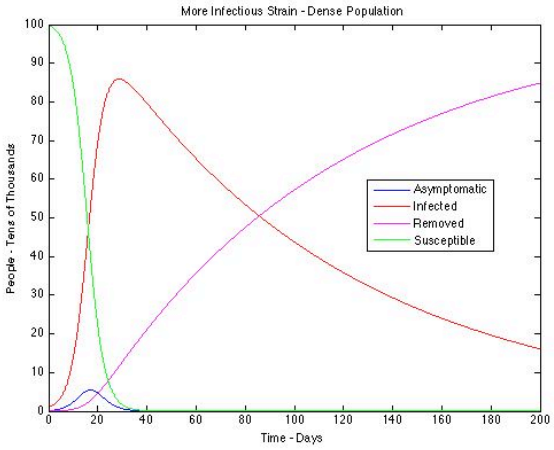
β=.001 k=.01 r=.1 d=.05

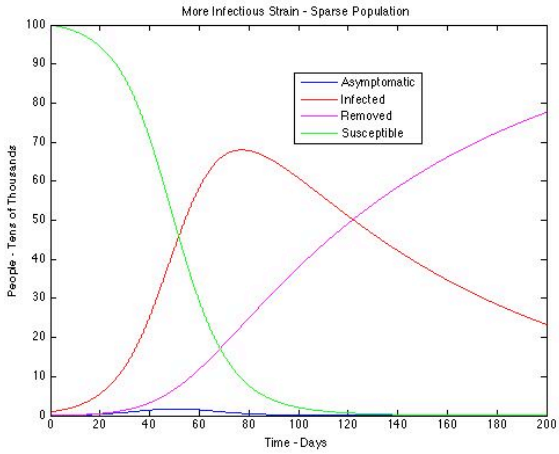
Effect of varied recovery rates on dense and sparse populations.

Here we experiment by increasing the recovery rate of a tuberculosis outbreak in both urban and rural regions. This model is most effective in describing a tuberculosis epidemic in more developed areas that have greater access to care and more sanitary conditions. We note that even after 200 days the infection has passed completely out of the sparse population, with still over thirty percent of individuals having never contracted the disease. However, in the dense condition we see the susceptible class drop quickly, coupled with a rise in the asymptomatic and removed classes. In both cases there is a relatively small infected class, indicating that the spread of tuberculosis in a developed area, regardless of population density, is a mild phenomenon. With regard to the low recovery rate scenarios, it is clear that a much larger infected class is present and lingers for a longer amount of time. The low recovery rate cases indicate that a tuberculosis outbreak in less developed countries could present a

significant problem to public health, since their access to care is significantly less than that of developed countries.

Figures 8 and 9.



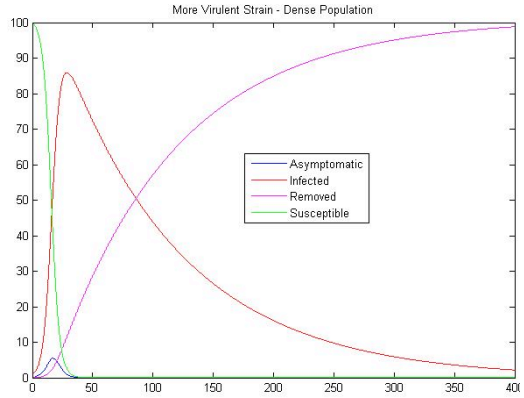


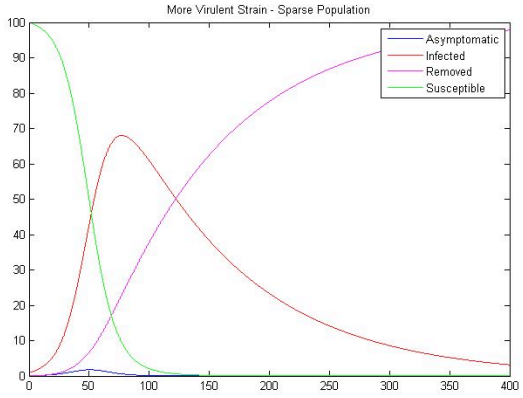
β=*.003 k=.01 r=.6 d=.5* β=*.001 k=.01 r=.6 d=.5*

Monitoring the spread of a highly infectious strain of tuberculosis.

We attempt to model the spread of a more virulent variant of tuberculosis in various populations that could possibly occur due to the introduction of a new strain of the bacterium. Therefore, recovery rates will be low because the strain is expected to be resistant to the most common anti-bacterial antibiotics. Furthermore, *r* increases because the strain is more virulent, and consequently the amount of asymptomatic carriers with a latent form of the disease drastically decreases. Finally, we would expect *d* to increase significantly because it would be more likely for an individual with a latent infection to progress to the disease stage. The only difference between the two above models is that we assume the rate of transmission to be lower because the disease is spreading in a less populated area. In the dense variant, we see a large and rapid spike in the infected class, consisted with the introduction of a highly infectious disease that is resistant to common therapeutics. However, in the sparsely populated model, we see a smaller spike in the infectious population since the disease is spreading less rapidly and there is more time for infected and asymptomatic individuals adjust to and recover from the infection. Consistent with a more infectious strain, the infection incubates longer in the population. Yet, we note that in both cases the magnitude of the infected class gradually diminishes, such that it will eventually become negligible. Therefore, we can say that, although a drug-resistant strain of tuberculosis could pose significant short term problems for a population, it is still possible to recover and move on from the disease.

Figures 10 and 11.





β=.003 k=.01 r=.6 d=.5

β=.001 k=.01 r=.6 d=.5

Extension of figures 8 and 9 over a longer time scale.

To look at what will occur to the population in the steady state, that is, after a long period of time, we set each differential equation equal to zero as follows:

$$S'(t) = -\beta S(t)[I(t) + A(t)] = 0$$
$$I'(t) = r\beta S(t)[I(t) + A(t)] - kI(t) + dA(t) = 0$$
$$R'(t) = k[I(t) + vA(t)] = 0$$
$$A'(t) = (1-r)\beta S(t)[I(t) + A(t)] - A(t)(d + vk) = 0)$$

$$k[I(t) + vA(t)] = 0$$
$$kI(t) = -kvA(t)$$
$$I(t) = -vA(t)$$

$$-\beta S(t)[I(t) + A(t)] = 0]$$
$$S(t)I(t) = -S(t)A(t)$$
$$I(t) = -A(t) = -vA(t) \Rightarrow A(t) = 0 = I(t)$$

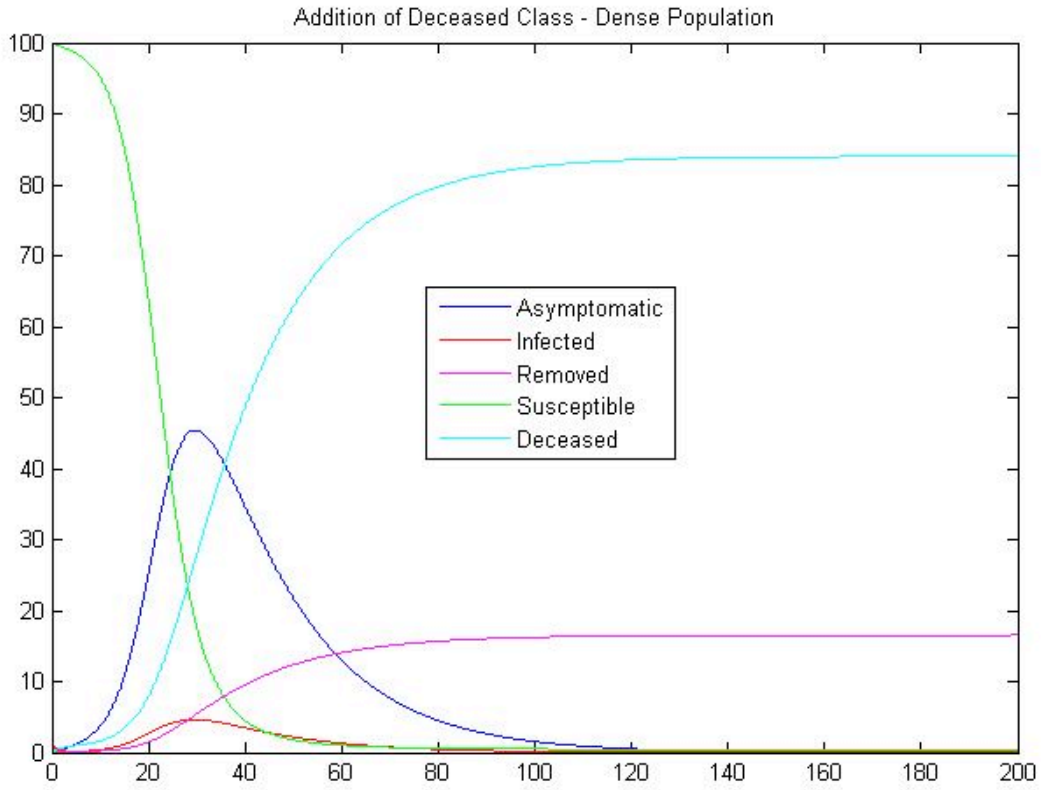
$$-\beta S(t)[I(t) + A(t)] = 0$$
$$\Rightarrow S(t) = -[I(t) + A(t)]/\beta = 0$$

$$R'(t) = 0$$
$$\Rightarrow R(t) = C_1$$

This demonstrates what occurs at equilibrium, when the population of each class is not changing. We observe that *I(t), S(t),* and *A(t)* all tend towards zero as t approaches infinity.

However, *R(t)* approaches the constant value C_1. To further confirm this finding, we show above in figures 10 and 11 how our model behaves as we lengthen the period of observation. Algebraic calculations correlate with the asymptotic behavior of each graph.

Figure 12.



β=.003 k=.05 r=.1 d=.05 j=0.5

Analyzing the introduction of a deceased class.

Here we report the addition of the deceased class and attempt to gauge the effect of death rate on our current model of tuberculosis in a dense population. Even setting *j* the death rate to fifty percent we still do not observe complete extinction of our model population. Given that a short-term death rate for a bacterial disease above fifty percent is rare in today's developed populations, we can say that even a particularly virulent strain of tuberculosis will not wipe out an entire population. Notably, however, we do observe under twenty percent survival, so a tuberculosis pandemic of this sort would severely challenge an isolated population.

We now determine the steady state behavior of the deceased class as time approaches infinity, that is, as the change in each respective class over time approaches zero. Using the same calculations shown above, we obtain the following:

$$S'(t) = -\beta S(t)[I(t) + A(t)] = 0$$
$$I'(t) = r\beta S(t)[I(t) + A(t)] - kI(t) + dA(t) - jI(t) = 0$$
$$R'(t) = k[I(t) + vA(t)] = 0$$
$$A'(t) = (1 - r)\beta S(t)[I(t) + A(t)] - A(t)(d + vk) = 0$$
$$D'(t) = jI(t)$$

$$I(t) = A(t) = S(t) = 0$$
$$R(t) = C_1$$

$$D'(t) = 0$$
$$\Rightarrow D(t) = C_2$$

We see that *D(t)*, like *R(t)*, approaches a constant value, C_2. This observation is in agreement with the plot shown above. The infected, asymptomatic, and susceptible populations all tend towards zero as t approaches infinity, while the recovered and deceased populations approach constant values.

Conclusion

We presented a functional model for the spread of tuberculosis in both urban and rural populations. We analyzed the impact of a variable recovery rate on the severity of the outbreak depending upon its localization – either in developed or developing countries. Finally, we determined the response of populations to the influx of a novel, highly infectious strain of tuberculosis. In light of our analyses and observations, we conclude that tuberculosis, although a potent pathogen, can be effectively dealt with and overcome in modern society. In addition, we showed that over time, both the recovered and deceased populations approach constant values whereas the susceptible, asymptomatic, and infected classes approach zero. This demonstrates that over a long enough period of time, the disease will be eradicated in an isolated population. These conclusions supplement our understanding of infectious disease behavior with the hope that intelligent decisions can be made in the management of its treatment, especially in the case of a new breakout of multi-drug-resistant tuberculosis. Further research could explore the application of this model to the spread of other infectious diseases.

Author Contribution

John Scotti – Computer modeling, discussion

Ashley Takahashi – Model Design, problem statement

Jackie Spreadbury – Abstract, research

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