Modelling transmission dynamics for the 1918-1919 influenza pandemic in Montreal and Winnipeg

Romarie Morales[1], Helene Nehrebecki[2], Carolina Pontones-Argueta[3], Jose M. Vega-Guzman[2], Anuj Mubayi[2] and Joaquin Rivera[2]

[1] Department of Mathematics, University of Puerto Rico

[2] Department of Mathematics and Statistics, Arizona State University, Tempe

[3] Department of Mathematics, Instituto Tecnológico Autónomo de México

1st August 2007

Abstract

In recent years, communicable diseases, such as The Avian Flu and SARS, have dominated the news, and in the process, they have had tremendous impact on public health policies. In this paper, we introduce a mathematical model that is used to study epidemics and pandemics. The work is motivated by data on the 1918-1919 influenza pandemic in two cities of Canada, Montreal and Winnipeg. We estimated model parameters for the two cities using 1918 fall wave epidemic data through non-linear least square fitting. We then explore the role of heterogeneity via a two-patch (city) model. For the two-patch version of the model, we derive a formula for a final size epidemic and the basic reproduction number (R_0). R_0 is found to be 9.9695 for Montreal and 5.5234 for Winnipeg. It is surprising to find that a decrease in infectivity of infected individuals in the region increases the final epidemic size. The number of asymptomatic cases in Montreal and Winnipeg were found to be approximately 19,000 and 60,000, respectively. We surmise that the low reporting and high number

of asymptomatic cases can be explained by a lack of public health facilities, and higher severity of the disease during that period.

1 Introduction

History tells us that influenza viruses have caused even larger amounts of morbidity and mortality than smallpox, malaria, and West Nile. Influenza rapidly mutates, increasing its potential ability to wipe out large portions of the human population. It takes five to eight months to develop partially-effective treatments to combat some influenza strains [10]. The aim of this paper is to quantify the impact of the associated outbreak in the cities of Winnipeg and Montreal, in terms of the effect of socioeconomic conditions on the final size epidemic of the disease.

The pandemic influenza discussed in this paper was a highly contagious viral disease which emerged in 1918. The disease was transmitted by direct contact via respiratory secretions. Individuals infected with this strain of influenza experienced common flu symptoms; that is body aches, muscle and joint pain, headache, sore throat, unproductive cough, and occasional harsh breathing [9]. These symptoms are common to many diseases and often lead to misdiagnosis. The 1918 flu often progressed into the secondary pneumonia (often fatal) bacterial infection. The World Health Organization estimates that about 40 to 50 million individuals died during 1918-1919 pandemic [5].

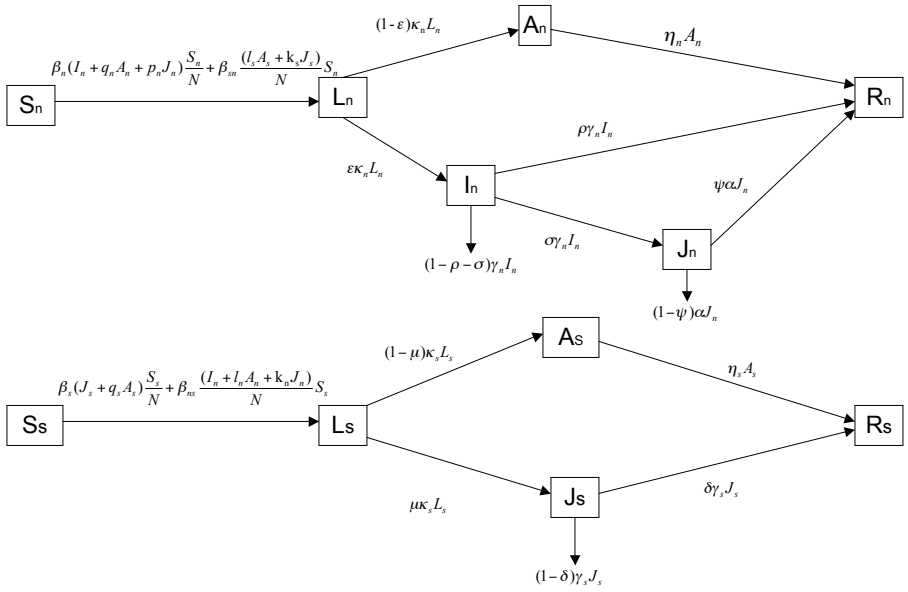
We have focused on studying two cities of Canada, Winnipeg (W) and Montreal (M). W ass not very dense, and it exhibited a large socioeconomic divide [16]. The northern area was mainly populated by immigrants holding blue collar jobs. The southern area was mainly populated by wealthier settlers. M was a port city, and the disease entered the city by soldiers passing through, since World War I was just ending.

We approximate some epidemiological parameters from data on daily reported cases and deaths during the fall wave of the influenza pandemic of 1918, in the two mentioned cities. To this end we study the 1918 influenza outbreak in Winnipeg and Montreal. We

assume that individuals in the poor region would be more susceptible and less aware of the disease.

In section 2, we describe the model and discuss model assumptions. Here, we define the model parameters. In section 3, we provide some mathematical analysis, including an R_0 expression, and the final epidemic size relation. In Section 4 we discuss our numerical results.

2 Model Description



The fall wave lasted 114 days in Winnipeg [7] and 38 days in Montreal [4]. Consequently, we do not include births and deaths, since the time scale of interest is short. During our investigation, we noticed that the population of Winnipeg was significantly divided by the

availability of health care [16]. We therefore decided to focus on the role of socioeconomic differences on this pandemic. The southern area of the city had more resources, and the northern zone was occupied by immigrants and working class citizens [16]. More cases per population were reported in the south than in the north [16].

Some individuals from the north went to work in the south, since the south was the center of the economy for the city [16]. Although the movement of the people from south to north was considered relatively low, both populations naturally interacted.

The population is stratified into the following classes: susceptible (S_i), latent (L_i), asymptomatic (A_i) who always recover, infected and not reported (I_i), reported (J_i), recovered (R_i), or dead (D_i), where the indices $i = n, s$ correspond to north and south, respectively. We assume no unreported infectives per unit of time in the south (no I_s). N is the total population; that is $N_s + N_n$.

We model the mixing as follows: $\frac{\beta_n(I_n+q_nA_n+p_nJ_n)}{N}S_n$ denotes the number of people per unit of time in the north infected by residents of the north, and $\frac{\beta_s(I_s+q_sA_s+p_sJ_s)}{N}S_s$ the number of people per unit of time in the south infected by residents of the south. We define q_i and p_i to be the reduction factors in the transmissibility of A_i and J_i, respectively, with $0 < q_i < 1$, and $0 < p_i < 1$ (see [8]).

The number of people of the south infecting people of the north is $\beta_{sn}S_n\frac{l_sA_s+k_sJ_s}{N}$, and the number of people of the north infecting people of the south is $\beta_{ns}S_s\frac{l_nA_n+k_nJ_n}{N}$. In this case, β_{ij} is the transmission coefficient of infectives from region i infecting susceptibles from region j. We define l_i to be a reduction factor in the transmissibility of A_i with $0 < l_i < 1$, and k_i a reduction factor in the transmissibility of J_i with $0 < k_i < 1$.

Setting β_{sn} and β_{ns} both equal to zero would represent the north and south each spreading the disease within their own group. If we consider a population stratified like the one in the north, we would have a reduced version of this model. In this model, individuals as classified as susceptible (S), latent (L), asymptomatic (A), infected and not reported (I), reported (J), recovered (R), or dead (D). N is the total population, and $N(t) = S(t) + L(t) + A(t) + I(t) + J(t) + R(t)$ at time t [8]. The new infection per unit

time is $\beta(I + qA + pJ)\frac{S}{N}$, where q and p are reduction factors in the transmissibility of A and J respectively, and $0 < q, p < 1$.

The reduced model is used for studying the dynamics of both cities, whereas the two-patch model is discussed in terms of conditions in Winnipeg.

Our model is given by

$$
\begin{aligned}
\dot{S}_n &= -[\beta_n(I_n + q_n A_n + p_n J_n)\frac{S_n}{N} + \beta_{sn} S_n \frac{(l_s A_s + k_s J_s)}{N}] \\
\dot{L}_n &= \beta_n(I_n + q_n A_n + p_n J_n)\frac{S_n}{N} + \beta_{sn} S_n \frac{(l_s A_s + k_s J_s)}{N} - \kappa_n L_n \\
\dot{A}_n &= (1-\epsilon)\kappa_n L_n - \eta_n A_n \\
\dot{I}_n &= \epsilon\kappa_n L_n - \gamma_n I_n \\
\dot{J}_n &= \sigma\gamma_n I_n - \alpha J_n \\
\dot{N}_n &= -(1-\rho-\sigma)\gamma_n I_n - (1-\psi)\alpha J_n \\
\dot{D}_n &= (1-\rho-\sigma)\gamma_n I_n + (1-\psi)\alpha J_n \\
\dot{S}_s &= -[\beta_s(J_s + q_s A_s)\frac{S_s}{N} + \beta_{ns} S_s \frac{(I_n + l_n A_n + k_n J_n)}{N}] \\
\dot{L}_s &= \beta_s(J_s + q_s A_s)\frac{S_s}{N} + \beta_{ns} S_s \frac{(I_n + l_n A_n + k_n J_n)}{N} - \kappa_s L_s \\
\dot{A}_s &= (1-\mu)\kappa_s L_s - \eta_s A_s \\
\dot{J}_s &= \mu\kappa_s L_s - \gamma_s J_s \\
\dot{N}_s &= -(1-\delta)\gamma_s J_s \\
\dot{D}_s &= (1-\delta)\gamma_s J_s
\end{aligned}
\tag{1}
$$

where n stands for the northern region, and s stands for southern region of Winnipeg.

Mixing between the north and south populations occurs when β_{sn} and β_{ns} are not equal to zero.

Table 1 displays the parameters, definitions, and values we use for the two-patch model, and Table 2 displays those for the one-patch model.

Parameter	Definitions	Values	Source
β_n, β_s	Transmission coefficient related to people in same group	8 per day, 5.75 per day	[8]
β_{sn}, β_{ns}	Transmission coefficient due to infectives in south (north) infecting susceptiples in north (south)	5.26 per day	[8]
q_n, q_s	Reduction factor of asymptomatic class from same section	0.5	[5]
p_n, p_s	Reduction factor of clinically diagnosed class	1.0	[5]
l_s, l_n	Reduction factor of asymptomatic class from other section	0.5	[5]
k_s, k_n	Reduction factor of clinically diagnosed class from other section	1.0	[5]
ϵ	Proportion of latent class who proceed to infective class in northern	0.667	[5]
μ	Proportion of latent class who proceed to clinically diagnosed class in southern	0.667	[5]
κ_n, κ_s	Rate of leaving latent class	0.526 per day	[18]
η_n, η_s	Rate of going to recovery class from asymptomatic class	0.244 per day	[18]
ρ	Proportion of infectives who recover in northern	0.4	estimated
σ	Proportion of infectives who get diagnosed in northern	0.58	estimated
γ_n, γ_s	Rate of leaving infective class (clinically diagnosed class)	0.244 per day	[18]
α	Rate of leaving clinically diagnosed class in northern	0.333 per day	estimated
ψ	Proportion of clinically diagnosed class who recover in northern	0.6635	estimated
δ	Proportion of clinically diagnosed class who recover in southern class	0.3318	data & estimated

Table 1: Model parameters and their values

Parameter	Definitions	Values	Sources
β	Transmission coefficient between people of Montreal	5.75 per day	[8]
q	Reduction factor of asymptomatic class	0.5	[5]
p	Reduction factor of subclinical class	1.0	[5]
ϵ	Proportion going from latent class to subclinical class	0.667	[5]
κ	Rate of leaving latent class	0.526 per day	[18]
η	Rate of leaving asymptomatic class	0.244 per day	[18]
ρ	Proportion recovering from infective class	0.4	estimated & [5]
σ	Proportion of entering clinically diagnosed class from infective class	0.58	estimated & [5]
γ	Rate of leaving infective class	0.244 per day	[18]
ψ	Proportion recovering from clinically diagnosed class	0.9953	data & [17]
α	Rate of leaving clinically diagnosed class	0.333 per day	estimated

Table 2: Parameters of the reduced model

3 Mathematical Analysis

3.1 Basic Reproductive Number

The basic reproductive number (R_0) is an essential concept in studying the dynamics of the spread of communicable diseases. As mentioned in [22] it is defined as the spatial radius of the next generation matrix operator. Since the disease-free state is not unique in our model, we use the method described in [3] for calculating R_0.

For the disease-free equilibria,

$$S_n = N_n,\ L_n = A_n = I_n = J_n = 0,\ S_s = N_s,\ A_s = J_s = 0.$$

Thus the R_0 for our model is given by

$$\begin{aligned} R_0 \quad = \quad & \left[\frac{\beta_n q_n(1-\epsilon)}{\eta_n}\frac{S_{n_0}}{N_0} + \frac{\beta_n p_n \epsilon\sigma}{\alpha}\frac{S_{n_0}}{N_0} + \frac{\beta_n\epsilon}{\gamma_n}\frac{S_{n_0}}{N_0}\right] + \left[\frac{\beta_{ns} l_n(1-\epsilon)S_{n_0}}{\eta_n N_0} + \frac{\beta_{ns}\sigma\epsilon\kappa_n S_{n_0}}{\alpha N_0} + \frac{\epsilon\beta_{ns}S_{n_0}}{\gamma_n N_0}\right] \\ & + \left[\frac{\beta_s(1-\mu)q_s S_{s_0}}{\eta_s N_0} + \frac{\beta_s\mu S_{s_0}}{\gamma_s N_0}.\right] + \left[\frac{\beta_{sn}(1-\mu)l_s S_{s_0}}{\eta_s N_0} + \frac{\beta_{sn}\mu\kappa_s S_{s_0}}{\gamma_s N_0}\right] \end{aligned}$$

where $N_0 = N_n(0) + N_s(0)$.

We consider the first bracketed term.

The first term of this,

$$\frac{\beta_n q_n(1-\epsilon)}{\eta_n}\frac{S_{n_0}}{N_0},$$

represents the total number of newly infected people generated by one person in the A_n class. The term

$$\frac{\beta_n p_n \epsilon\sigma}{\alpha}\frac{S_{n_0}}{N_0}$$

gives us the total number of newly infected people in the north generated by one individual of the J_n class. In a similar way, the term

$$\frac{\beta_n \epsilon}{\gamma_n}\frac{S_{n_0}}{N_0}$$

represents the total number of newly infected people in the north generated by an individual of the I_n class.

The three other bracketed terms represent the newly infected individuals generated by cross-infection from north to south, the newly infected individuals in the south, and the newly infected individuals generated by cross-infection from south to north, respectively.

Since almost everyone is susceptible at the beginning of the epidemic, we assume that $S_0 = N_0$ for Montreal, so that $\frac{S_0}{N_0} = 1$. Taking this case into account, we find that the basic reproduction number for our reduced model is given by

$$R_0 = \beta\Big(\frac{\epsilon}{\gamma} + \frac{q(1-\epsilon)}{\eta} + \frac{p\sigma\epsilon}{\lambda}\Big)$$

.

In this case, $\beta\frac{\epsilon}{\gamma}$, $\beta\frac{q(1-\epsilon)}{\eta}$, and $\beta\frac{p\sigma\epsilon}{\lambda}$ represent the total number of newly infected people generated by the I class, the A class, and the J class, respectively.

3.2 Final Size of Epidemic

We assume that $L_{n_0} = L_{s_0} = A_{n_0} = A_{s_0} = J_{n_0} = 0$ and $L_{n_\infty} = L_{s_\infty} = A_{n_\infty} = A_{s_\infty} = J_{n_\infty} = I_{n_\infty} = 0$.

The final epidemic size is given by

$$\begin{aligned} S_0(\ln S_{n_0} - \ln S_{n_\infty}) \quad &\leq \quad S_0\beta_n\Big[\Big(\frac{\epsilon}{\gamma_n} + \frac{q_n(1-\epsilon)}{\eta_n} + \frac{p_n\sigma\epsilon}{\alpha}\Big)(S_{n_0} - S_{n_\infty}) \\ &\quad + I_{n_0}\Big(\frac{1}{\gamma_n} + \frac{p_n\sigma}{\alpha}\Big)\Big] + S_0\beta_{sn}\Big(\frac{l_s(1-\mu)}{\eta_s} + \frac{k_s\mu}{\gamma_s}\Big)(S_{s_0} - S_{s_\infty}). \end{aligned} \tag{2}$$

If N were constant, we would be able to write (2) as an equality, with the right side divided by N (see appendix).

The total number of disease deaths in the model is given by

$$\begin{aligned} (1-\rho-\sigma)\gamma_n\hat{I}_n + (1-\psi)\alpha\hat{J}_n + (1-\delta)\gamma_s\hat{J}_s = (1-\rho-\sigma)[\epsilon(S_{n_0} - S_{n_\infty}) + I_{n_0}] \\ +(1-\psi)[\sigma(\epsilon(S_{n_0} - S_{n_\infty}) + I_{n_0}))] + (1-\delta)[\mu(S_{s_0} - S_{s_\infty}) + I_{s_0} \end{aligned}$$

The total number of asymptomatic cases is given by

$$\eta_n\hat{A}_n + \eta_s\hat{A}_s = (1-\epsilon)(S_{n_0} - S_{n_\infty}) + (1-\mu)(S_{s_0} - S_{s_\infty})$$

The total number of unreported or untreated cases is given by

$$\rho\gamma_n\hat{I}_n = \rho[\epsilon(S_{s_0} - S_{s_\infty}) + I_{n_0}].$$

Similarly, the final size epidemic relation for the reduced model under the assumption of constant population N and no one being infected at the end of the epidemic is given by

$$S_0(\ln S_0 - \ln S_\infty) \leq S_0R_0(S_0 - S_\infty) + \frac{S_0I_0}{\epsilon}\Big(R_0 - \frac{\beta q(1-\epsilon)}{\eta}\Big) \tag{3}$$

As described above, we can tabulate total number of disease deaths, asymtomatic cases and unreported cases for the reduced model.

4 Numerical Results

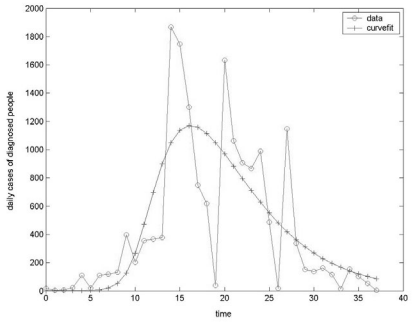
4.1 Parameter Estimation

Literature review was carried out to obtain point estimates of most of the parameters. The remaining parameters were obtained from our estimation procedure using the Matlab

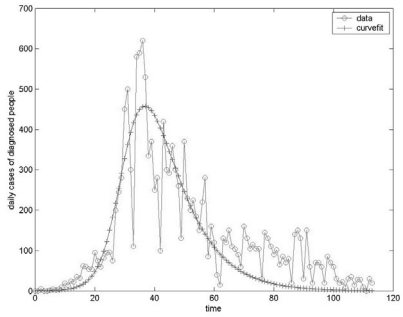
function lsqcurvefit for each of the two cities. The nonlinear best curve fit for daily reported cases is obtained for the reduced model based on the epidemiological data.

The duration for the fall wave was 38 days in Montreal, and 114 days in Winnipeg (given in Table 3). In 1918, the total population of Montreal was 640,000, and the total population in Winnipeg was 183,595 [17]. Since the north was occupied by more immigrants and poor people, we assume that the population in northern Winnipeg was larger than that of southern Winnipeg. For numerical simulations, we assume that 2/3 of the total population of Winnipeg lived in the north, and 1/3 lived in the south. The estimates of the parameters are shown in Table 4.1. The best curve fit for Montreal and Winnipeg are shown in Figure 1(a) and Figure 1(b), respectively.

The average infectious period of unreported cases is $\frac{1}{\gamma}$. We estimated the parameter γ to have a value of .1231 per day (infectious period of 8.12 days) and .1 per day (infectious period of 10 days) for Montreal and Winnipeg, respectively. Therefore, these values lie in the interval of 6 to 10 days, as reported by [13].



(a) Represents the fit curve of the model of Winnipeg in the epidemic data of 1918 in Winnipeg.



(b) Represents the fit curve of the model of Montreal in the epidemic data of 1918 in Montreal.

Figure 1: Best curve fit using simple model through lsqcurvefit funtion of MATLAB.

We estimated the total number of asymptomatic cases, unreported cases, and deaths for the fall wave of the 1918-1919 influenza pandemic in Montreal and Winnipeg. Matlab *ode45* solver was used to find the following numbers using their own estimated parameters

Parameters	Montreal	Winnipeg	Units
β	4.434	1.5	per day
q	0.2754	0.01	dimensionless
γ	0.1231	0.1	per day
η	0.1	0.4	per day
ρ	0.8992	0.9771	dimensionless
A_0	1	30	Individuals
I_0	3	7	Individuals
L_0	0	10	Individuals

Table 3: Table of Estimated Parameters using Reduced Model

given in Table 3. For Montreal these numbers were found to be 19000, 35000, and 3500, respectively. For Winnipeg the numbers are 60000, 47000, and 2300, respectively.

4.2 Final Size of the Epidemic

The analysis of the final size of the epidemic is carried out using a two-patch model where parameter values were taken from Table 1.

Since people in the north were mainly poor, we assumed that they are more susceptible and infective than people in the south. For the purpose of understanding the effect of socioeconomic status on the final epidemic size in Winnipeg, we introduced two variables: susceptibility (k_s) and infectivity (k_i) of an individual in the north relative to an individual in the south, where $k_s, k_i \geq 1$. Hence, we are able to find the relationship between different transmission coefficients in our model ($\beta_n = \beta_{nn} = k_i k_s \beta$, $\beta_{ns} = k_i \beta$, $\beta_{sn} = k_s \beta$, and $\beta_s = \beta_{ss} = \beta$). That is, β_{ij} represents the transmission coefficient which is due to an infective from i infecting a susceptible from j, where $i = n, s$. We also considered $\mu < \epsilon$ and $\eta_n < \eta_s$ by the same reasoning.

We calculated the proportion of final size of north (and south) under the above as-

sumptions. We use *ode45* solver in Matlab to solve the model system for different values of k_s and k_i.

We found that the proportion of the final size of epidemic of the north is approx. 0.6 (and hence, the proportion in the south is approx. $1 - 0.6 = 0.4$) for all values of k_s and k_i. There is a monotonic increase in the proportion of the final size of the epidemic in the north (south) with an increase in the value of parameter k_s . Moreover, the rate of increase is more for smaller values of k_s . The rate of change is large up to a point ($k_s = 1.5$). The proportion of the final size changes steadily if k_s is increased beyond this point. The proportion of final size changes steadily. It was surprising to find that reduction in the infectivity, up to a point, of infected individuals in the north increases the proportion of the final epidemic size (Figure 2).

The proportion of the final epidemic size in the north decreases with an increase in k_i for any fixed value k_s. The rate of change is large between zero and some critical value of k_i. For example, this value is approximately 2.2 for $k_s = 1.2$. The change seems negligible beyond this critical value.

5 Discussion

There are only a few studies on the influenza pandemic of 1918-1919. We decided to focus on this disease, particularly the 1918 pandemic, because more susceptible people were from younger generations, which is usually not seen in pandemic influenzas. We chose to focus on the Canadian cities of Winnipeg and Montreal, for various reasons. For one thing, these two cities had large populations for the time (Winnipeg had 183,595 and Montreal had 640,000). Secondly, Montreal is a port city on the coast, so more people were passing through during this time, especially since World War I ended in 1919. This may have caused more infection in this city. For Winnipeg, we were able to find information about the division of economic classes, divided by geographic location.

For our work, we used a compartmental epidemic model, where we divided the popu-

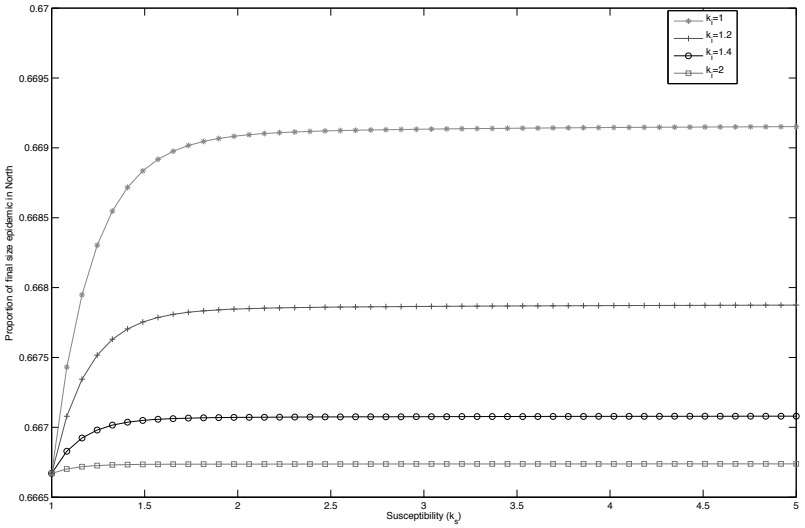


Figure 2: Proportion of final size epidemic in the north as a function of susceptibility k_s

lation of Winnipeg into two parts, rich (south) and poor (north). The model was reduced into a simplified version in order to compare the outcomes of the two cities. We considered the fall wave data of 1918-1919 from the Health Department of Canada for both of the cities.

We estimated the number of asymptomatic cases, unreported and undiagnosed cases, and deaths, using the simplified model. The model considers the homogeneous mixing population.

We found that the basic reproductive number, R_0, was 9.9695 for Montreal, and 5.5234 for Winnipeg. In pandemic influenza, R_0 ranges from 4 and 16 [13]. Our estimates lie between this range.

There are some limitations in our model, and it may be inappropriate to model future pandemic outbreaks in some cities using the model considered here. Although our aim here is to study the effect of susceptibility and infectivity on the final epidemic size, we can incorporate education and awareness into the population.

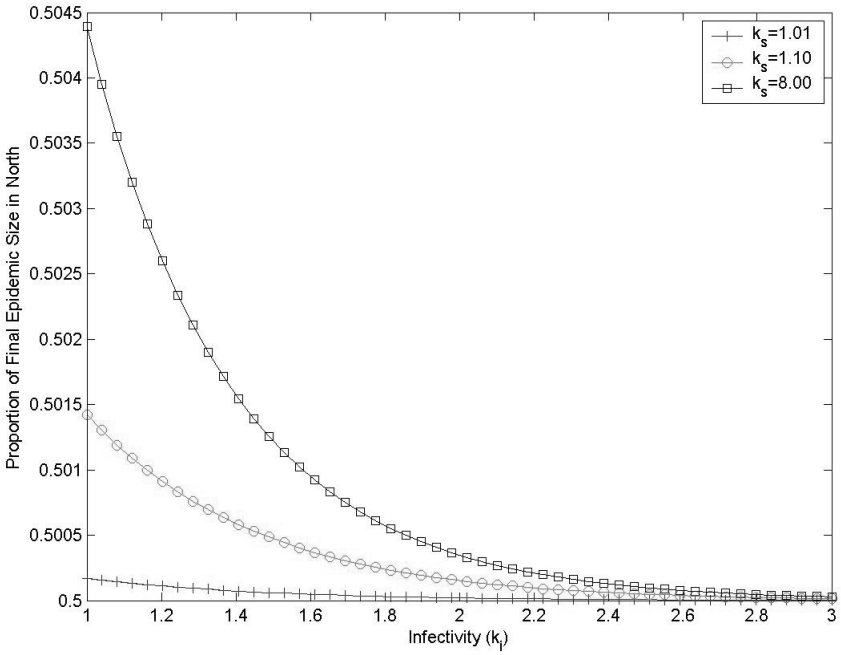


Figure 3: Proportion of final size epidemic in the north as a function of infectivity k_i

We should also study the way the population size influences the quantity of the population that acquires the disease. We must stress the fact that giving the higher economic society all the methods needed combat diseases will help them only temporarily. In the long run, the disease would be spread everywhere. For these reasons, medical procedures should be provided proportionally to all populations.

6 Acknowledgements

We would like to thank Carlos Castillo-Chavez, Christopher Kribs-Zaleta, and Fred Brauer for all their advice on how to do our project in the best possible way, and also for being supportive of our group. We would also like to thank Gerardo Chowell for providing us with the data for our two cities. The MTBI/SUMS Summer Undergraduate Research Program is supported by The National Science Foundation (DMS-0502349), The National Security Agency (DOD-H982300710096), The Sloan Foundation, and Arizona State University. We also thank Project 1000 for the support of students with ambitions and self-improving desires.

Appendix

Derivation of Basic Reproductive Number (R_0)

In this subsection we explain how we found the basic reproductive number for the complex version of the model corresponding to Winnipeg, and the basic reproductive number for the simple version of the model corresponding to the city of Montreal. We found the R_0 for both cities using a formula from [3].

$$R_0 = tr(\Pi DQy_0\beta(0, y_0, z_0)bV^{-1} = \beta(0, y_0, z_0)bV^{-1}\Pi DQy_0$$

For the calculation of the R_0 for Winnipeg, we use the following transformations:

$$\beta_s = p_1 a_1, \beta_n = p_1 a_2, \beta_{sn} = p_2 a_1, \beta_{ns} = p_2 a_2$$

and

$$q_n = q_s = \hat{q}, p_n = p_s = \hat{p}, l_s = l_n = \hat{l}, k_s = k_n = \hat{k}.$$

We also use the following matrices

$$\Pi = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}^T$$

$$D = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix},$$

$$Q = \begin{bmatrix} \frac{a_2}{N} & 0 \\ 0 & \frac{a_1}{N} \end{bmatrix},$$

$$y_0 = [S_n(0),\ S_s(0)]^T$$

$$\beta * b = \begin{bmatrix} 0 & 0 & p_1\hat{q} + p_2\hat{l} & p_2\hat{l} + p_1\hat{q} & p_1\hat{p} + p_2\hat{k} & p_2\hat{k} + p_1 & p_1 + p_2 \end{bmatrix},$$

$$V^{-1} = \begin{bmatrix} \frac{1}{\kappa_n} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{1}{\kappa_s} & 0 & 0 & 0 & 0 & 0 \\ \frac{(1-\epsilon)}{\eta_n} & 0 & \eta_n & 0 & 0 & 0 & 0 \\ 0 & \frac{(1-\mu)}{\eta_s} & 0 & \eta_s & 0 & 0 & 0 \\ \frac{\sigma\epsilon}{\alpha} & 0 & 0 & 0 & \frac{1}{\alpha} & 0 & \frac{\sigma}{\alpha} \\ 0 & \frac{\mu}{\gamma_s} & 0 & 0 & 0 & \frac{1}{\gamma_s} & 0 \\ \frac{\epsilon}{\gamma_n} & 0 & 0 & 0 & 0 & 0 & \frac{1}{\gamma_n} \end{bmatrix},$$

The R_0 for the complex model becomes

$$\begin{aligned} R_0 &= \left[\frac{\beta_n q_n(1-\epsilon)}{\eta_n}\frac{S_{n_0}}{N_0} + \frac{\beta_n p_n \epsilon\sigma}{\alpha}\frac{S_{n_0}}{N_0} + \frac{\beta_n\epsilon}{\gamma_n}\frac{S_{n_0}}{N_0}\right] + \left[\frac{\beta_{ns} l_n(1-\epsilon)S_{n_0}}{\eta_n N_0} + \frac{\beta_{ns}\sigma\epsilon\kappa_n S_{n_0}}{\alpha N_0} + \frac{\epsilon\beta_{ns}S_{n_0}}{\gamma_n N_0}\right] \\ &\quad + \left[\frac{\beta_s(1-\mu)q_s S_{s_0}}{\eta_s N_0} + \frac{\beta_s\mu S_{s_0}}{\gamma_s N_0}.\right] + \left[\frac{\beta_{sn}(1-\mu)l_s S_{s_0}}{\eta_s N_0} + \frac{\beta_{sn}\mu\kappa_s S_{s_0}}{\gamma_s N_0}\right] \end{aligned}$$

where $N_0 = N_n(0) + N_s(0)$.

For the calculation of R_0 for Montreal, we use the following matrices

$$\Pi = [1,\ 0,\ 0,\ 0]^T$$

$$D = [1]$$

$$Qy_0 = [1]$$

$$\beta * b = [0,\ q,\ 1,\ p]$$

$$V^{-1} = \begin{bmatrix} \frac{1}{\kappa} & 0 & 0 & 0 \\ \frac{1-\epsilon}{\eta} & \frac{1}{\eta} & 0 & 0 \\ \frac{\epsilon}{\gamma} & 0 & \frac{1}{\gamma} & 0 \\ \frac{\epsilon\sigma}{\alpha} & 0 & 0 & \frac{1}{\alpha} \end{bmatrix},$$

The basic reproduction number (R_0) for Montreal becomes

$$R_0 = \beta\Big(\frac{\epsilon}{\gamma} + \frac{q(1-\epsilon)}{\eta} + \frac{p\sigma\epsilon}{\lambda}\Big) \tag{4}$$

Derivation of Final size Epidemic Relation

Adding and integrating $\dot{S}_n$ and $\dot{L}_n$ from 0 to ∞, with respect to t gives

$$S_{n_0} - S_{n_\infty} + L_{n_0} - L_{n_\infty} = \kappa_n \hat{L}_n. \tag{5}$$

Similarly, when we add and integrate $\dot{S}_s$ and $\dot{L}_s$ from 0 to ∞, with respect to t, we get

$$S_{s_0} - S_{s_\infty} + L_{s_0} - L_{s_\infty} = \kappa_n \hat{L}_n \tag{6}$$

Integrating $\dot{A}_i$, $\dot{I}_i$, and $\dot{J}_i$ where $i = n, s$, we obtain

$$\eta_n \hat{A}_n = (1-p)\kappa_n \hat{L}_n + A_{n_0} - A_{n_\infty} \tag{7}$$

$$\gamma_n \hat{I}_n = p\kappa_n \hat{L}_n + I_{n_0} - I_{n_\infty} \tag{8}$$

$$\alpha \hat{J}_n = \sigma\gamma_n \hat{I}_n + J_{n_0} - J_{n_\infty}. \tag{9}$$

$$\eta_s \hat{A}_s = (1-\mu)\kappa_s \hat{L}_s + A_{s_0} - A_{s_\infty} \tag{10}$$

$$\gamma_s \hat{J}_s = \mu\kappa_s \hat{L}_s + J_{s_0} - J_{s_\infty}. \tag{11}$$

We now divide $\dot{S}_n$ by S_n and integrate from 0 to ∞ with respect to t. We get

$$\begin{aligned} \ln S_{n_0} - \ln S_{n_\infty} &= \beta_n \left[\int_0^\infty \frac{I_n(t)}{N(t)} dt + q_n \int_0^\infty \frac{A_n(t)}{N(t)} dt + p_n \int_0^\infty \frac{J_n(t)}{N(t)} dt \right] \\ &\quad + \beta_{sn} \left[l_s \int_0^\infty \frac{A_s(t)}{N(t)} dt + k_s \int_0^\infty \frac{J_s(t)}{N(t)} dt \right]. \end{aligned}$$

Since $N = (S_n + L_n + A_n + I_n + J_n + R_n) + (S_s + L_s + A_s + I_s + J_s + R_s)$, we get the inequality

$$\ln S_{n_0} - \ln S_{n_\infty} \leq \beta_n(\hat{I}_n + q_n \hat{A}_n + p_n \hat{J}_n) + \beta_{sn}(l_s \hat{A}_s + k_s \hat{J}_s).$$

Then

$$S_0[\ln S_{n_0} - \ln S_{n_\infty}] \leq S_0[\beta_n(\hat{I}_n + q_n \hat{A}_n + p_n \hat{J}_n) + \beta_{sn}(l_s \hat{A}_s + k_s \hat{J}_s)]. \tag{12}$$

Substituting (7), (8), (9), (10), and (11) into (12) gives

$$
\begin{aligned}
S_0[\ln S_{n_0} - \ln S_{n_\infty}] \;\leq\; & S_0\beta_n\Big[\Big(\frac{\epsilon}{\gamma_n} + \frac{q_n(1-\epsilon)}{\eta_n} + \frac{p_n\sigma\epsilon}{\alpha}\Big)(S_{n_0} - S_{n_\infty} + L_{n_0} - L_{n_\infty}) \\
& + \Big(\frac{I_{n_0} - I_{n_\infty}}{\gamma_n} + \frac{q_n(A_{n_0} - A_{n_\infty})}{\eta_n} + \frac{p_n\sigma(I_{n_0} - I_{n_\infty})}{\alpha} + \frac{p_n(J_{n_0} - J_{n_\infty})}{\alpha}\Big)\Big] \\
& + S_0\beta_{sn}\Big[\Big(\frac{l_s(1-\mu)}{\eta_s} + \frac{k_s\mu}{\gamma_s}\Big)(S_{s_0} - S_{s_\infty} + L_{s_0} - L_{s_\infty}) \\
& + \frac{l_s(A_{s_0} - A_{s_\infty})}{\eta_s} + \frac{k_s(J_{s_0} - J_{s_\infty})}{\gamma_s}\Big].
\end{aligned}
$$

This is our final size epidemic relation for Winnipeg. We now follow similar steps to find the final size epidemic relation for Montreal.

By adding and integrating $\dot{S}$ and $\dot{L}$ from 0 to ∞, with respect to t, we obtain

$$S_0 - S_\infty + L_0 - L_\infty = \kappa\hat{L}. \tag{13}$$

We add and integrate $\dot{A}$, $\dot{I}$, and $\dot{J}$, respectively, from 0 to ∞, with respect to t. We obtain

$$\eta\hat{A} = (1-\epsilon)\kappa\hat{L} + A_0 - A_\infty \tag{14}$$

$$\gamma\hat{I} = \epsilon\kappa\hat{L} + I_0 - I_\infty \tag{15}$$

$$\lambda\hat{J} = \sigma\gamma\hat{I} + J_0 - J_\infty. \tag{16}$$

We now divide $\dot{S}$ by S and integrate, getting

$$\ln S_0 - \ln S_\infty = \beta_[\int_0^\infty \frac{I(t)}{N(t)}dt + q\int_0^\infty \frac{A(t)}{N(t)}dt + p\int_0^\infty \frac{J(t)}{N(t)}dt]$$

Since N is not constant,

$$\ln S_0 - \ln S_\infty \leq \beta(\hat{I} + q\hat{A} + p\hat{J}).$$

Thus

$$S_0[\ln S_0 - \ln S_\infty] \leq S_0[\beta(\hat{I} + q\hat{A} + p\hat{J})]. \tag{17}$$

We substitute (4),(14),(15), and (16) into (17) and get

$$\begin{aligned} S_0[\beta(\hat{I} + q\hat{A} + p\hat{J})] &= S_0 R_0(S_0 - S_\infty + L_0 - L_\infty) \\ &\quad + S_0\beta\Big(\frac{I_0 - I_\infty}{\gamma} + \frac{q(A_0 - A_\infty)}{\eta} + \frac{p\sigma(I_0 - I_\infty)}{\lambda} + \frac{p(J_0 - J_\infty)}{\lambda}\Big) \end{aligned}$$

This implies we have

$$\begin{aligned} S_0(\ln S_0 - \ln S_\infty) &\leq S_0 R_0(S_0 - S_\infty + L_0 - L_\infty) \\ &\quad + \frac{S_0(I_0 - I_\infty)}{\epsilon}\Big(R_0 - \frac{\beta q(1-\epsilon)}{\eta}\Big) \\ &\quad + \frac{S_0(A_0 - A_\infty)}{1-\epsilon}\Big(R_0 - \beta\Big(\frac{\epsilon}{\gamma} + \frac{p\epsilon\sigma}{\lambda}\Big)\Big) \\ &\quad + S_0\beta p\frac{(J_0 - J_\infty)}{\lambda} \end{aligned}$$

for the final size relation of the epidemic in Montreal. Since β is not constant, the final size relation is an inequality [5]. Furthermore, we can assume that at start and end of the epidemic the number of individuals in the infected classes is zero.

Also, this shows that S_∞ is greater than zero, so not everyone in the city was affected by the pandemic [5]. This relation calculates $S_0 - S_\infty$, the total number of people infected by the pandemic. We can now find the total number of disease deaths, asymptomatic and symptomatic cases, and unreported and undiagnosed cases.

The total number of disease deaths is given by

$$\begin{aligned} (1-\rho-\sigma)\phi\hat{I} + (1-\psi)\lambda\hat{J} &= (1-\rho-\sigma)[\epsilon(S_0 - S_\infty + L_0 - L_\infty) + I_0] \\ &\quad + (1-\psi)[\sigma(\epsilon(S_0 - S_\infty + L_0 - L_\infty) + I_0) + J_0] \end{aligned}$$

The total number of asymptomatic cases is given by

$$\eta\hat{A} = (1-\epsilon)(S_0 - S_\infty + L_0 - L_\infty) + A_0 \tag{18}$$

The total number of unreported and undiagnosed cases is given by

$$\rho\gamma\hat{I} = \rho[\epsilon(S_0 - S_\infty + L_0 - L_\infty) + I_0] \tag{19}$$

Mixing

In this section, we discuss various ways that mixing population and contact process can be modeled. Restricted mixing (or segregation) is mixing of populations within the same group [20]. For instance, the mixing of people in the north only with other individuals from the north. Proportional (or random) mixing is when the entire population is randomly mixing, and there is the same probability of getting in contact with everyone [20]. Preferred mixing (also called Bernoulli Noise) is when there is a different probability of getting in contact with people from different groups [20].

Since proportional and restricted mixing are special cases of preferred mixing, we state the definition of preferred mixing. Preferred mixing can be thought of as an approximation to mixing that results from perfect knowledge of the other unmodeled attributes such as attractiveness and familiarity [19],[14],[15]. Let ρ_{ij} be the proportion of total contacts of a person in group i with a person in group j per unit of time [15]. Assume ρ_i is the proportion of contacts in group i by people of group i with the same group of people, per unit of time [15]. Then $(1-\rho_i)$ is the proportion of contacts, outside of group i, of people in group i with people in groups other than i, per unit of time. Let N_i be the total population of group i [15]. c_i is the average number of total contacts of a person in group i per unit of time [15]. These contacts can be inside or outside of the group. $c_i(1-\rho_i)$ is the average number of contacts of people in group i with people in group i, outside of group i, per unit of time [15].

We first discuss ρ_{ii}. This is equal to ρ_i plus $(1-\rho_i)$ times a reduction factor. The reduction factor is a fraction with $c_i(1-\rho_i)N_i$ in the numerator. $c_i(1-\rho_i)N_i$ is the total number of contacts of people in group i with people of other groups, in a different section, per unit of time. The denominator is $\sum_k c_k(1-\rho_k)N_k$, is the total number of contacts of people in any group with people of other groups, in a different section, per unit of time. Note this fraction is less than or equal to 1. This reduction factor explains the preference mixing of a particular group of individuals. Thus $\rho_{ii} = \rho_i + (1-\rho_i)\frac{c_i(1-\rho_i)N_i}{\sum_k c_k(1-\rho_k)N_k}$.

For ρ_{ij} where $i \neq j$, we do not take into account contacts between members in the same group, so we can ignore the ρ_i factor. So it is $(1-\rho_i)$ times a reduction factor with $c_j(1-\rho_i)N_j$ in the numerator and $\sum_k c_k(1-\rho_k)N_k$ in the denominator [15]. So it is $\rho_{ij} = (1-\rho_i)\frac{c_j(1-\rho_j)N_i}{\sum_k c_k(1-\rho_k)N_k}$.

For proportional mixing, we obtain ρ_{ij} in the same way, except with $\rho_i = 1$ Then for all i and j, $\rho_{ij} = c_j\frac{N_i}{\sum_j c_j N_j}$.

References

[1] Arino J., Brauer F., Van Den Driessche P., Watmough J.,Simple models for containment of a pandemic, J.R. Soc Interface, 2006 Jun 22;3(8):453-7. 2006

[2] Arino J., Brauer F., Van Den Driessche P., Watmough J.,Simple models for containment of a pandemic Supplementary Information, Mathematical Biosciences and Engineering Volume 4, Number 2, April 2007

[3] Arino J., Brauer F., Van Den Driessche P., Watmough J., Wu, J., A Final Size Relation of Epidemic Models, Mathematical Biosciences and Engineering Volume 4, Number 2, April 2007

[4] Boucher S.,The Epidemic Influenza, Canadian Medical Association.1918

[5] Brauer F., Modeling Influenza: Pandemics and Seasonal Epidemics (preprint).2007

[6] Burr T., Chowell G., Observation and model error effects on parameter estimates in susceptible-infected-recovered epidemiological models, Far East Journal of Theoretical Statistics vol.19, Issue 2, pg.163-183, July,2006

[7] Cadham M.F.T., The use of a vaccine in the recent epidemic of influenza, Canadian Medical Association Journal, June 1919

[8] Chowell G.,Ammonb C.E., Hengartena N.W.,Hymana J.M. Transmission dynamics of the great influenza pandemic of 1918 in Geneva, Switzerland: Assessing the effects of hypothetical interventions.2005

[9] Chowell G., Nishiura H., Bettencourt L.,Comparative estimation of the reproduction number for pandemic influenza from daily case notification data, Journal of Theoretical Biology.2006

[10] Del Valle S., The Impact of Changes in Behavior on the Spread of Pandemic Influenza (Pre-Print)

[11] Diekmann O., Heesterbeek J., Metz J., On the definition and the compuatation of the basic reproductive ratio R_0 in models for infectious diseases in heterogeneous populations, Journal of Mathematical Biology, vol 28, Number 4, June 1990

[12] Duncan K., Lessons from the 1918 Spanish Flu, A PERI Symposium.2006

[13] Dushoff, J., Plotkin, J., Levin, S., Earn, D., Dynamical resonance can account for seasonality of influenza epidemics, National Academy of Sciences of the USA 2004

[14] Hethcote, H.W., Van Ark, J.W., Epidemiological models for heterogenious populations: proportionate mixing, parameter estimation, and immunization programs, Mathematical Biosciences vol. 84, no1.1987

[15] Jacquez, J., Simon, C., Koopman, J., Sattenspiel, L. Perry, T., Modeling and Analyzing HIV Transmission: The Effect of Contact Patterns, Mathematical Biosciences 92.1988

[16] Jones E., Co-operarion in All Human Endeavour: Quarantine and Immigrant Disease Vectors in the 1918-1919 Influenza Pandemic in Winnipeg, Canadian bulletin of medical history.2005

[17] McCullough, J, The Control of Influenza in Ontario, Canadian Medical Association.1918

[18] Mills, C., Robins, J., Lipsitch, M., Transmissibility of the 1918 pandemic influenza, Nature vol:432 155:7019.2004

[19] Nold, A, Heterogeneity in disease-transmission modeling, Mathematical Biosciences Vol.S2, no.3-4.1980

[20] Simon, C., Jacquez, J., Reproduction Numbers and the Stability of Equilibria of SI Models for Heterogeneous Populations, Society of Industrial and Applied Math. 1992

[21] Taubenberger J., Morens D.,1918 Influenza: The Mother of All Pandemics, Armed Forces Institute of Pathology, Rockvill, Maryland, USA, and National Institutes of Health Bathesda Maryland, USA.2006

[22] van den Driessche P., Watmough J., Reproduction numbers and subthreshold endemic equilibria for compartmental models of disease transmission, Mathematical Biosciences vol:180 pg.29.2002

[23] Xu, Y., Allen, L., Perelson, A., Stochastic model of and influenza epidenmic with drug resistance, Journal of Theoretical Biology. 2007