Approximations of Stochastic Household Models for Comparing Antiviral Allocation Schemes

Michael Lydeamore

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While not explicitly listed, all code used to generate the data throughout this thesis is made available at

`https://github.com/MikeLydeamore/AntiviralAllocationSchemes`.

Signed Statement

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Commonly Used Notation

Rate governing internal infection	β
Rate governing external infection	α
Rate governing progression	σ
Rate governing recovery	γ
Reduction in susceptibility due to antivirals	ρ
Reduction in infectivity due to antivirals	τ
Mean delay until antivirals arrive into household	ζ
Mean effective duration of antivirals	κ
Number of households	N
Household size	k
Mean household size	$\bar{k}$
Household size distribution	$\mathbf{h}$
Size-biased distribution	$\boldsymbol{\pi}$
Amount of available antivirals	M

Abstract

From the first recorded influenza pandemic in 1890, there have been new strains of influenza which have caused pandemics approximately every 30 years including recent events such as the H5N1 Avian 'Flu pandemic and the 2009 H1N1 Swine 'Flu pandemic. Although the 2009 pandemic was mild in nature, if events of the past are any indication then control of future pandemics is of utmost importance.

Vaccination is commonly looked at to help control the spread of a pandemic, however, vaccinations are strain-specific. While developing a new vaccine is possible, the World Health Organisation estimates that this process would take four to five months. This means that vaccination cannot be used to help control the spread of influenza early on in a pandemic. An alternative are *antivirals* which are not strain-specific, meaning that they can potentially be used to help control the spread of influenza early on in a pandemic. Antivirals are, however, not as effective at reducing the spread of disease when compared to vaccination.

In the 2009 Swine 'Flu pandemic, many countries worldwide utilised antiviral medication, with the aim to assist in controlling the spread of influenza. The most common method in which these antivirals were utilised we refer to as dynamic allocation. In dynamic allocation, when the first person in a household experiences influenza-like symptoms, they report to a health professional. Then, a sample is sent for laboratory testing. If the individual is confirmed to have influenza, the entire household is allocated a course of antivirals and every member of the household begins taking them. The potential weakness in this strategy is the delay between becoming infectious and a household receiving antivirals.

We consider an alternative antiviral allocation scheme which we call preallocation. In a preallocation scheme, instead of waiting for antivirals to be delivered after the first confirmed infection, as is the case with dynamic allocation, the antivirals are delivered to households at the beginning of the pandemic. When the first person experiences symptoms, they contact a health professional via a telephone hotline. The professional then decides if it is likely that the individual has influenza. If the individual is likely to have influenza then the entire household starts taking antivirals immediately, just as is the case in dynamic allocation. The advantage of this scheme is that the delay is essentially zero, but there is the potential for the antivirals to be wasted in at least two ways. First, this type of identification of infection is clearly less precise than laboratory testing. Second, it is possible that antivirals will be preallocated to a household who will never experience infection and so those antivirals will essentially be wasted. It is this tradeoff that is the focus of this thesis.

The stochastic households epidemic model which is detailed and developed in this work incorporates the household structure of a general population. This allows us to incorporate the stronger mixing of individuals who share a household compared to individuals in the general population, as well as the fact that antivirals are allocated to an entire household when infection is first detected. To analyse this model, we develop two approximations:
(i) A branching process approximation, and
(ii) a deterministic approximation,
that assist us in calculating quantities associated with a pandemic.

The branching process is very fast to compute, but due to required assumptions in the derivation, it is only able to describe the early stages of the pandemic. The branching process is able to rapidly compute quantities such as the Malthusian parameter, r, and the household reproductive ratio, R_*, but is unable to calculate quantities such as the *final epidemic size*, that is, the total number of people infected over the course of the pandemic.. The deterministic approximation does not allow for as rapid evaluation as the branching process approximation, but is able

to approximately reproduce the entire expected pandemic curve, giving access to quantities such as the expected final epidemic size. Both of these approximations are fast to compute so we can explore a range of parameters and compare the two allocation schemes—dynamic allocation and preallocation.

We show that preallocation of antivirals often leads to a smaller final epidemic size than dynamic allocation for a *severe* pandemic outbreak, while a dynamic allocation scheme often gives a lower Malthusian parameter, r, and household reproductive ratio, R_*. We provide a justification for this behaviour and demonstrate that the results are relatively robust across the parameters controlling the pandemic. We also consider a number of extensions to the deterministic approximation such as the incorrect use of antivirals, a hybrid allocation scheme, and the production of antivirals during the pandemic. Under these extensions, the general behaviour of the two schemes—preallocation yielding a lower final epidemic size but dynamic allocation yielding superior early-time quantities—is unchanged.