



Department of Mathematics and Statistics

**An investigation of Agent based models for
Monkeypox Virus spread**

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Abstract

This thesis explores two agent based models for the spread of monkeypox virus (MPXV) in the population and in MSM communities. Some of the parameter choices and assumptions are changed to see what affect they have on the model's output. The assumption of a fixed rate of regular sexual contact between couples is examined by replacing the fixed parameter with a distribution of sexual contact rates sourced from survey data. The affect of changing the number of main partners per year and the relationship length is also examined.

Acknowledgements

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Lastly I would like to thank my family and friends for their constant support.

Declaration

I, Dara Corr, declare that this thesis titled, *An Investigation of Agent based models for Monkeypox Virus spread* and the work presented in it are my own. I confirm that:

- This work was done wholly or mainly while in candidature for a degree at this University.
- Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated.
- Where I have consulted the published work of others, this is always clearly attributed.
- Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work.
- I have acknowledged all main sources of help.
- Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself.

Signed:

Date:

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1 Introduction

Epidemiology can be described as “the study (scientific, systematic, and data-driven) of the distribution (frequency, pattern) and determinants (causes, risk factors) of health-related states and events (not just diseases) in specified populations (neighborhood, school, city, state, country, global)” [11]. The very first epidemiological studies can be traced back to Ancient Greece where Hippocrates, now known as the Father of Medicine, began to think about disease spread in a more scientific way than the supernatural beliefs that existed circa 400 BC. John Snow conducted studies on the transmission of Cholera in the mid-1800s. He hypothesised that water was the medium that transmitted the disease and used a spot map of recorded deaths from Cholera in London to locate the water pump with the Cholera infection. Snow’s data driven epidemiological studies proved significant to understanding how Cholera was transmitted in a population which then prompted a public health reaction. Snow’s work led to him being known as the “Father of Field Epidemiology” [11].

The dynamics of infectious disease spread can be described as a complex system, one which is difficult to model. There are many parameters and events that influence disease transmission including a person’s age, sex, ethnicity and the disease reproduction speed. In the early 19th century, scientists began to turn to mathematics to model phenomena in the life sciences following the growth of probability theory and statistics from the 19th century [12]. The mathematical lens of disease modelling allows scientists to model some of the complex environmental, biological and human behavioural elements and parameters that influence disease transmission and severity.

Mathematical disease modelling plays a crucial role in disease monitoring and informing health authorities so that health officials can make the best, informed decisions regarding controlling and managing disease outbreaks and trying to prevent them. Mathematical models mainly consist of agent based modelling and differential equation based compartment models. The compartment based models (also known as SEIR-

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based models) divide the population into compartments e.g. susceptible population, exposed population, infected population and recovered population. Agent based modelling generates models from the ground up, where each agent is a node in a network. Each agent can have its own traits and properties and agents interact with each other in a stochastic manner, much like how individuals in a population interact with each other somewhat randomly. There are pros and cons to these different modelling approaches which will be discussed further later in this thesis.

Monkeypox, also known as mpox, is an infectious disease caused by the mpox virus (MPXV). People infected with monkeypox usually experience symptoms of skin rash or mucosal lesions which can last for 2-4 weeks [10]. These symptoms are often accompanied by fever, headache, muscle aches, back pain, low energy and swollen lymph nodes.

A monkeypox outbreak began in early May 2022, where most monkeypox infections were reported from countries in North America and Europe where monkeypox was not endemic. Monkeypox is endemic in central and western Africa where monkeypox infections occur regularly [13].

In this thesis I will investigate the application of an agent based model used to model monkeypox in the population and in the MSM (men who have sex with other men) community. A major advantage of using ABMs is that they allow for modelling of micro-simulations of scenarios which may lead to an outbreak and are thus quite useful. For monkeypox ABMs are quite useful in this way as one can simulate superspreader events.

2 Monkeypox

Monkeypox (mpox) is an infection caused by the monkeypox (MPXV) virus, a species of the genus Orthopoxvirus of the Poxviridae family. Smallpox and Cowpox are similar to mpox. Two clade of mpox currently exist, clade I and clade II [10]. In 2022 there was a rapid increase in cases in Ireland and across several other countries - mostly in North America and Europe. The disease spread to all 6 WHO regions with 110 countries reporting 87,000 cases and 112 deaths [10]. The strain that caused this global outbreak is known as clade IIb.

Symptoms of mpox infection are usually seen within one week of exposure but in some cases they can start 1-21 days after exposure [10]. A monkeypox infection is usually characterised by the common symptoms of rash, fever, sore throat, headache, muscle aches, back pain, low energy and swollen lymph nodes. For many the first symptom of mpox is a rash, this rash begins as a flat sore, develops into a fluid-filled blisters which can be painful or itchy. As the rashes heal, the blisters dry up into crusty scabs and then these fall off [10]. The rash normally appears 1-5 days after the onset of symptoms and in some cases the rash can be the only symptom someone infected with mpox will experience [14].

Mpox is spread through very close contact between people. Mpox can be transmitted during sexual contact and close contact including hugging, kissing or cuddling. It can also be spread by touching clothing or towels used by someone with mpox rash, touching mpox rash or blisters and it can also be transmitted from respiratory droplets from talking or breathing or prolonged close contact [14] [10].

Mpox is often compared to sexually transmitted diseases such as HIV when comparing how the diseases spread from person-to-person. However, mpox is not classified as a sexually-transmitted disease, but it often tends to be transmitted by those who engage in sexual activities with one another because of the close contact nature of

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sexual activity. This is why when modelling mpox, researchers are interested in peoples' sexual contacts. If someone is diagnosed with mpox then using a contact tracing method based on the individuals sexual contacts is a good method to identify where the disease may have spread.

2.1 Diagnosis

There can be some difficulty in diagnosing monkeypox infections as the symptoms of monkeypox infection can be quite similar to other infections and conditions that produce a rash or hives in infected individuals. It is important to differentiate mpox from diseases that produce similar rashes e.g. chickenpox, herpes, measles, scabies, allergic reactions to medication and other bacterial skin infections or sexually transmitted diseases. There may also be cases where an individual infected with mpox also has a sexually transmitted disease or cases where children with suspected mpox actually have chickenpox. It is important to test people who are suspected to have mpox to remove ambiguity surrounding similar rashes from other infections and allergies [10].

Mpox diagnoses are determined by using polymerase chain reaction (PCR) tests which detect DNA of the mpox virus DNA in the test sample. Samples are taken from people suspected to have mpox by swabbing some of the rashes on the person's skin, this is the best method for collecting mpox test samples. In the absence of rashes or lesions on the skin then oropharyngeal, anal or rectal swabs can be used to obtain a swab for PCR testing [10]. Blood and semen testing are also used to detect the virus in people [15] [10].

The Centre for Disease Control (CDC) states it takes several days for results to be available following testing [16]. In the UK mpox diagnostic testing is offered in UK Health Security Agency laboratories and in some NHS and private laboratories [15].

2 Monkeypox

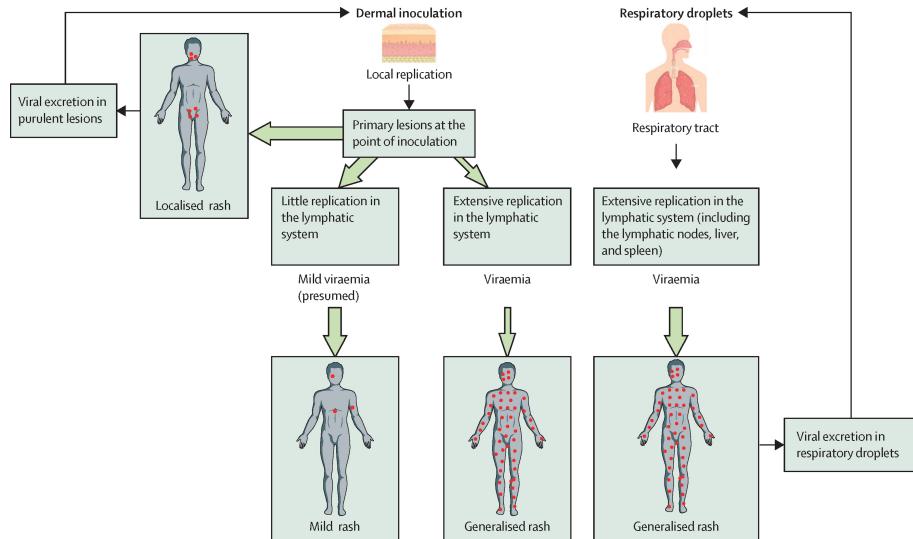


Figure 1: Proposed mechanism for the spread of the mpox virus throughout the body. Figure from the paper of Mitjà et al. [1].

2.2 Treatment

The severity of an mpox infection is highly dependent on the individual's immune response. People with a good immune system showing a strong response to the virus may only need some pain relief and some supportive care.

People with more severe cases of mpox including people with hemorrhagic diseases, a large number of lesions or people with difficulty swallowing due to lesions on the pharynx for example. Treatment is also considered for high risk individuals including those with weak autoimmune systems (e.g. people diagnosed with HIV), pregnant people, very young children with particular attention paid to children under the age of 1 year, and people with skin conditions like eczema, burns or psoriasis for example [17].

Existing treatments for mpox are supportive care and pain control treatments as no specific approved treatment exists for mpox yet [18]. Several antiviral medications are used to treat mpox including tecovirimat, brincidofovir and cidofovir. Intravenous vaccinia immune globulin (VIGIV) is licensed for the treatment of complications

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from smallpox vaccination and can also be used to treat mpox during outbreaks. NIAID is currently conducting two clinical trials of tecovirimat on treating patients with mpox.

2.3 Spread

Mpox is spread through very close contact from person-to-person. The disease is endemic in areas in West and Central Africa, but in 2022 an outbreak of the clade IIb strain worldwide raised global concern. Homosexual and bisexual men and men who have sex with other men (MSM) make up a large majority of the number of reported cases of mpox in the 2022-2023 outbreak. This group appears to be at a much higher risk of mpox exposure and becoming infected with mpox.

Some studies suggest that mpox is spread through sexual interactions [19]. It is already established that Mpox is transmitted through close contact with someone who is already infected with mpox. Since sexual contact involves prolonged person-to-person contact, it is likely that sexual activity spreads mpox from person to person because close contact between individuals occurs during sexual activity. Initial studies of Mpox spread in the MSM community in 2022 showed that men with more than one partner in the preceding 3 weeks had 1.8–6.9 times the risk for acquiring monkeypox as men with only one partner had [20]. This indicates that people having an increased number of sexual contacts/partners is a big reason for the rapid spread of mpox in 2022-2023. Members of the MSM community who have several sexual partners are deemed the group most at risk to smallpox [21].

It is believed that dating apps and “sex on premises” venues like saunas and sex clubs were a large factor in driving the spread of mpox in the 2022 global outbreak. People from the MSM community who have multiple partners and go to events like sex clubs or sex parties are considered high risk individuals and are believed to be

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“superspreaders” who cause the disease to spread rapidly from person-to-person [21].

At present it is unknown if semen can transmit monkeypox virus from person-to-person or not [15]. Reports have shown that there is evidence that RNA and DNA can be detected in semen after acute viral infection for a range of different viruses [22]. Of the 27 viruses tested, many cause chronic infections after being transmitted by semen, such as HIV. Several have been found to cause only acute infections through seminal transmission such as Lassa fever, Zika and Ebola [22]. One study has shown that MPXV DNA has been detected in semen up to 11 days after acute infection with mpox in Italian men [23]. Since it is unknown whether mpox can be transmitted via semen, the UK Health Security Agency advises that men who have a probable or confirmed mpox diagnosis should wear condoms during sexual interactions for 12 weeks after complete recovery from mpox infection [15].

2.4 Prevention and Vaccination

Public health advice following the mpox outbreak in 2022 is to avoid close contact with other people who may have mpox. People limited the number of sexual partners they had and avoided going to sex clubs and meeting people through dating apps after mpox outbreak in 2022-2023 [21].

Because smallpox belongs to the same family of poxviruses, this means that smallpox shares some similarities with mpox. Smallpox vaccinations can be used to induce immunity to mpox virus in people [24], which means that vaccinated people will be less likely to be infected with the virus as their body will fight off the infection more quickly and symptoms should not be as severe if a vaccinated person becomes infected with the virus. When a smallpox vaccine is used to protect against mpox it is called a mpox vaccine. Vaccine trials of the smallpox vaccine against mpox infection in the USA showed 66.0 % effectiveness (95% confidence interval, 47.4 to

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78.1) for fully vaccinated people (2 doses) and 35.8 % effectiveness (95% CI, 22.1 to 47.1) for partially vaccinated people (1 dose) [25].

The CDC have stated that the efficacy of the JYNNEOS Vaccine in preventing mpox infections is 85.9% (95% CI: [73.8%,92.4%]) effective for full vaccination and 75.2% (95% CI: [61.2%, 84.2%]) effective for partial vaccinations [26].

3 Epidemiological Modelling

3 Epidemiological Modelling

The University of Auckland describes mathematical Epidemiological models as “simplified representations of real-world processes expressed in mathematical language” [27].

An epidemiological model takes inputs related to the characteristics of the virus (e.g. incubation period and symptoms), characteristics of the population (e.g. age structure, level of immunity in population) and estimates of other rates and structures e.g. rate of contact between people and estimates of the population network structure.

Some of the inputs are easily obtainable from data and they are normally gathered from multiple data sources such as population demographics from census data, disease surveillance by world and government-led health authorities and health service data from hospital admissions and vaccination programmes. However, many parameters are difficult or even impossible to measure exactly so these parameters and values can be estimated in epidemiological models.

3.1 Types of models

There are two main types of epidemiological modelling - Deterministic modelling and Stochastic modelling [2].

Deterministic modelling approaches usually consist of dividing the population of interest into several compartments and then defining a set of difference equations or differential equations which determine the rate at which individuals move from one compartment to the next. Deterministic models are used to describe what happens on average in a population. The most simple example of this kind of compartment model is the SI model, where healthy individuals are placed in the Susceptible compartment (S) and when they get infected they move into the Infected compartment (I).

3 Epidemiological Modelling

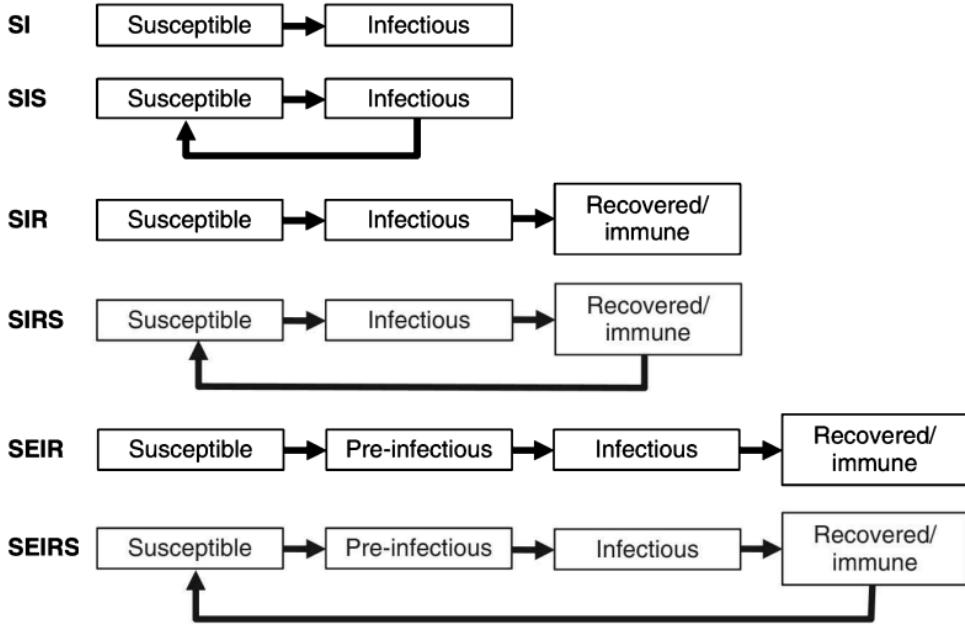


Figure 2: Examples of compartmental model setups from An Introduction to Infectious Disease Modelling page 16 [2].

Data is used to determine the rates at which members of the population move from one compartment to the next. More compartments can be added to include more information for more complex scenarios.

Stochastic modelling allows individuals to move between compartments in a random manner governed by pre-defined probabilities instead of at given rates like in deterministic modelling. Stochastic modelling adds an element of randomness to the model which aims to capture the randomness of human behaviour and decision making.

There are pros and cons to using Deterministic models and Stochastic models, which will be discussed in more detail in the following subsections of this chapter.

3 Epidemiological Modelling

3.2 Differential Equation-based Models

When trying to model an infectious disease using a compartment model, it is important to decide on what compartments are important to include in the model. Some of the basic compartment model setups are displayed in figure 2. The most basic form of compartment model is the Susceptible-Infectious (SI) model, where individuals become infected and they remain infectious forever until they die. The SI model can be used to model HIV, since individuals infected with HIV remain infected with the disease for life [2].

Some other configurations allow for individuals to be reintroduced to compartments over time such as the SIS model where a susceptible individual becomes infected with a disease, they recover from the disease but can become infected with the disease again in the future and are reintroduced to the susceptible compartment. This kind of model can be used for certain types of common sexually transmitted diseases such as gonorrhoea [2].

One of the most widely used compartment model configurations is the SIR or SEIR configuration. The SIR model consists of Susceptible, Infected and Removed/Recovered compartments. Once an infected person recovers from the disease, they develop immunity to the disease and are placed in the removed/recovered compartment. The SEIR configuration is a slight modification to the SIR model which also includes an ‘Exposed’ compartment which consists of individuals who have been exposed to the virus but cannot yet infect others [2].

Influenza is commonly modelled using a SEIR/SIR model structure as seen in Vynnycky’s book [2]. Figure 3 gives a general idea of how the compartments are related to one another and the rates that members of the population move from being susceptible to pre-infectious to infectious to being immune. For example, in figure 2, we see that susceptibles become pre-infectious at a rate $\lambda(t)S(t)$. Then in

3 Epidemiological Modelling

the table in figure 4, we see that the rate of decrease of the susceptible population is defined as:

$$\frac{dS(t)}{dt} = -\lambda(t)S(t)$$

which means that the susceptible population is declining at a rate $-\lambda(t)S(t)$, where $\lambda(t)$ is a parameter to be determined from data which describes the risk that a susceptible person becomes infected in a time step.

One assumption used when creating compartment models is that all members of the population are equally as likely to mix with one another. This assumption certainly is not true in real life but is a simplification made when creating models on a large population scale.

There are ways to implement different mixing rates between groups in a population. One example of this is by introducing what is called a Who Acquires Infection from Whom (WAIFW) matrix. A WAIFW matrix can be useful for describing different rates of transmission between two groups [2] of different ages such as between children and adults for example.

Compartmental based modelling usually has parameters determined from aggregated data and because of this, compartmental models tend to look at the average behaviour of an entire population.

There are some limitations associated with differential equation-based modelling. To create more complex models, more data and assumptions are needed to create additional parameters. Real-world circumstances often make it difficult to obtain reliable data to specify parameters, which creates errors in some of these models [28]. This problem applies to all kinds of disease modelling also. SEIR models still play

Differential equations model:

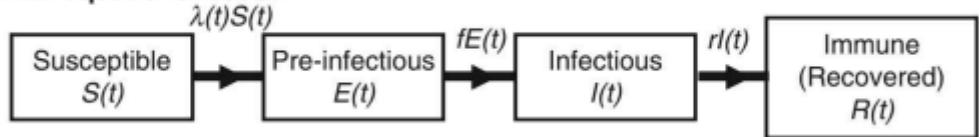


Figure 3: Typical setup of an SEIR model from Vynnycky's An Introduction to Infectious Disease Modelling [2]

Differential equations which describe the rate of change in the number of susceptible, pre-infectious, infectious, immune individuals at time t

$$\frac{dS(t)}{dt} = -\lambda(t)S(t)$$

$$\frac{dE(t)}{dt} = \lambda(t)S(t) - fE(t)$$

$$\frac{dI(t)}{dt} = fE(t) - rI(t)$$

$$\frac{dR(t)}{dt} = rI(t)$$

Figure 4: Table describing the differential equations which govern the rates at which members of the population move between compartments. Taken from Vynnycky's An Introduction to Infectious Disease Modelling [2]

3 Epidemiological Modelling

an important role in forecasting a disease's evolution and investigating the impact of applying control measures at the beginning of an epidemic, even in the absence of reliable, accurate data. Biases and poor assumptions and data can lead to models which make bad predictions such as the UK modellers over-estimating the effect of rapid herd-immunity at the beginning of the COVID-19 pandemic [28] [29].

3.3 SIR models for Mpox

Compartment models such as SIR/SEIR models are very useful in describing the state of an epidemic on a population level and can be very beneficial for epidemic planning in the future. There have been many attempts at constructing different models for mpox, such as compartmental models, branching models, network models, Monte Carlo models and agent based models. Branching processes and Compartmental models are the most frequently used models to model mpox [30].

Basic compartmental models are relatively straightforward to construct and to run (determining model parameters can be a difficult process involving inverse-problems, regression models and Bayesian estimation methods for example), which is a big reason for why they are quite popular for disease modellers to use, and why they were one of the most popular models used to model COVID-19 during the COVID-19 pandemic. SEIR differential equation models became the model of choice by IEMAG and NPHEP when modelling COVID-19 in 2020 [31]. Advancements in computing power in the previous few decades make computing derivatives a very quick process using difference equations and optimised Runge-Kutta simulations. These techniques are used to fit parameters to the models and to run the models [3]. Studies have shown that mpox can be transmitted in some animals such as rodents like squirrels [32]. This has been incorporated in some models, but this thesis will focus only on the human-to-human transmission of mpox.

Several approaches to mpox modelling use variations of an SIR compartmental model

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approach [33] [3] [30]. Al Raeei's mpox model uses a SIR model with mortality (also known as an SIRD model with a fourth compartment for Death) [3].

The model consisted of the following Equations:

Equation 1 describes the rate that Susceptible individuals become infected and enter the infected compartment. The susceptible population flows into the infected compartment at a rate of $\frac{\theta_1}{N}$ where N is the total number of individuals in the population of interest:

$$\frac{dS(t)}{dt} = -\theta_1 I(t) N^{-1} S(t). \quad (1)$$

Equation 2 describes the rate of the infected compartment $I(t)$ with respect to time. Susceptible individuals flow into this department and the total number of infected decreases over time due to member of the population either recovering or dying from the disease:

$$\frac{dI(t)}{dt} = \theta_1 I(t) N^{-1} - \theta_2 I(t) - \theta_3 I(t). \quad (2)$$

The third equation 3 describes the rate which infected individuals recover from mpox virus infection:

$$\frac{dR(t)}{dt} = \theta_2 R(t). \quad (3)$$

The final equation describes the rate of the mortality compartment $D(t)$ with respect to time:

$$\frac{dD(t)}{dt} = \theta_3 I(t). \quad (4)$$

The three parameters θ_1 , θ_2 and θ_3 used in AL Raeei's model can be used to calculate the basic reproduction number of the 2022 human mpox disease as follows:

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$$R_0 = \frac{\theta_1}{\theta_2 + \theta_3}. \quad (5)$$

Values for herd immunity can be derived from R_0 values as follows:

$$H_0 \equiv 1 - \frac{1}{R_0} = \frac{\theta_1 - \theta_2 + \theta_3}{\theta_1} \quad (6)$$

Using data from the USA and Spain from the 2022 mpox outbreak, it was possible to obtain estimates for the three parameters. For the model of mpox in the USA, it was found that the infectious coefficient θ_1 is 0.1022 per day, the recovery coefficient θ_2 is 0.659 per day and the mortality coefficient θ_3 is less than 0.0001 per day [3]. When the model was applied to Spanish data, they obtained $\theta_1 = 0.0507$ per day, $\theta_2 = 0.0338$ per day and $\theta_3 \approx 0.0001$ per day.

AL Raeei's mpox model found herd immunity occurs for $H_0 = 0.3552$ and the basic reproduction number R_0 equals 1.5508 in the USA [3]. They also found that for Spain, Herd immunity occurs at a value of 0.309 and the basic reproduction number is 1.4490. This indicates that for the entire population to be effectively protected against mpox infections through immunization, 35.52 % of the population must be vaccinated against mpox in the USA and 30.99 % of the population of spain must be vaccinated against mpox [3] to reach herd immunity.

A Bayesian SIR model using a directed acyclic graph method found that the basic reproduction number R_0 and effective reproduction number R_e reached maximum values of 1.16 (1.15–1.17), 1.20 (1.20–1.20), 1.34 (1.34–1.35), 1.33 (1.33–1.33) and 2.52 (2.41–2.66) for United States, Spain, Brazil, the United Kingdom and the Democratic Republic of the Congo, respectively [33]. Values for R_0 and R_e were below 1 after August 2022.

Since R_0 was less than 1 in after August 2022, this meant that the outbreak began

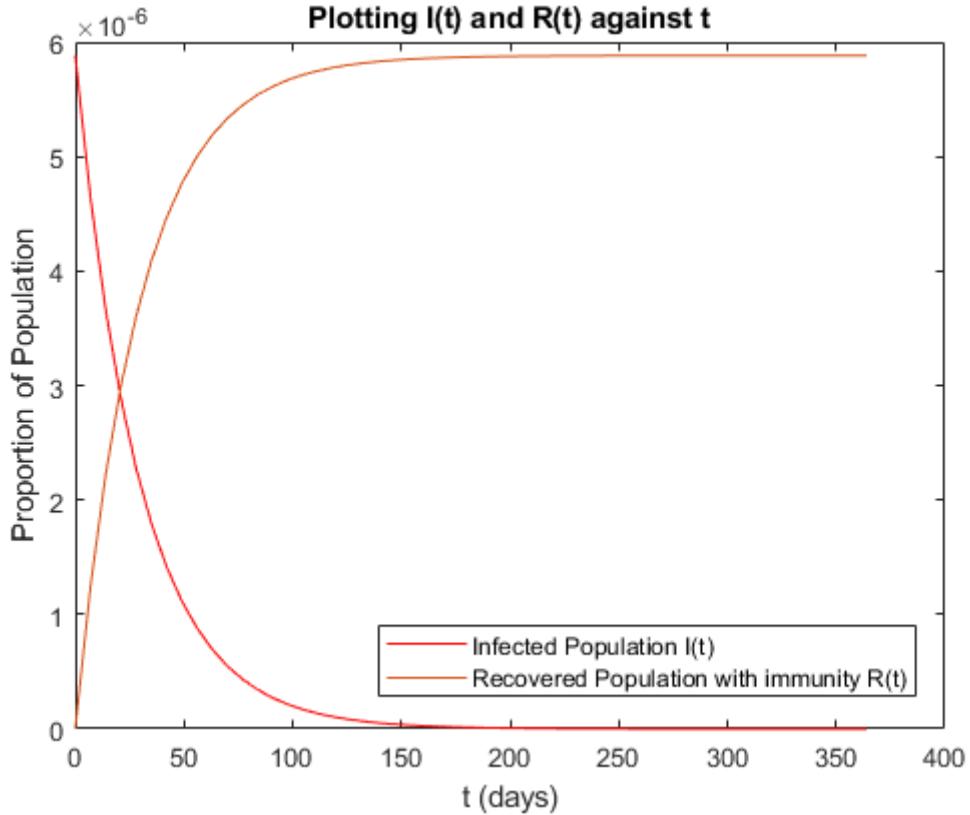


Figure 5: Plots of Infected and Recovered compartments using Al Raeei's mpox SIR model with Spanish parameters, 50 initial infected and total population size of 8.5 million [3]. The plot was generated in MATLAB.

to die out since on average, each person was infecting less than one person. More modelling is necessary to determine the cause of the change in infectiousness of the virus. Perhaps herd-immunity was reached in MSM communities, MSM communities began to limit sexual contact because of fear of contracting the virus or perhaps it is down to a combination of factors.

From the plot in figure 5, we can see that only a small number of the total population become infected with mpox. Because mpox clade IIb predominantly affected the MSM community, some population level models fail to show the true impact of the virus. This is a big factor leading to the development of a MSM mpox ABM model as well as a population level ABM model by Hamda Ajmal to closer investigate how the virus behaves within MSM communities.

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Al Raeei's mpox model is an example of a simple SIR model for mpox. More complicated models with more compartments require more parameters , data and more assumptions to be made.

The virus dies out in the population after approximately 5 or 6 months which again is consistent with what has been seen in the real world as well as the results from Hamda's model [9] [7].

The USA parameters predict an average recovery time of 15.17 days and the Spanish parameters predict an average recovery time of 29.58 days, both of these are consistent with the infectious period of 2-4 weeks stated by the CDC [17].

3.4 Agent Based Models (ABMs)

An Agent Based Model (ABM) is a type of stochastic model. Unlike compartment based deterministic models, Agent based models are built from the ground up. Each agent in the model represents an individual from the population, each with its own traits described by parameters in the model.

ABMs used in epidemiological modelling typically use network structures to determine which agents are in contact with other agents in the model. These networks normally consist of nodes (agents) who are connected to other agents via links in the model. Links can represent friendships, social contacts or sexual relationships for example. Often agents will make new relationships or social contacts in ABMs. Random events like entering a relationship or 2 agents meeting each other normally occur through pseudo random number generation in ABMs.

Pseudo random number generation is a way for a computer to simulate a random event such as rolling a die and obtaining a number. A computer cannot generate

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random numbers in a completely random manner, so it uses pseudo random number generating techniques instead. Usually, pseudo random number generation algorithms consists of passing the current time through a function which outputs a random number based on the time executed.

Since the user can define the network structure of agents in an agent based model and how they interact, it is possible to create micro-simulations with agents to see what happens in certain situations of interest. For example there are examples of ABMs which investigated how COVID-19 spread in school classrooms and supermarkets during the COVID-19 pandemic [34].

Some downsides to agent based modelling are that since the models are stochastic in nature, many repetitions of the models are needed to see the mean behaviour of the model. These models are much more computationally expensive to run compared to differential-equation based models since the computer running the simulation has to keep track of all the individual agents in the model. Because of this, computation times for ABMs are much larger than that for differential-equation-based models.

Agent based models lack the generality that analytical models provide, when studying agent based models, there is no reference solution to compare results with when dealing with ABMs, unlike in analytical models where it is very easy to obtain a solution from a set of equations to compare all other results with. This has caused some criticisms of agent based models in some academic circles [35].

One major advantage of ABMs is that they allow you to specify how the population mixes with each other, which is much harder to do in compartmental models. ABMs allow for the modelling of individual and collective behaviour of a population in the model, whereas differential equation based models normally only allow for insights into the collective behaviour of a population.

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Since ABMs are built from the ground up, changing the parameters in the model can provide very valuable insights into what drives the disease to spread. It is less obvious what may cause outbreaks when using differential equation based models. ABMs are very useful for testing scenarios and the effect of implementing certain strategies such as vaccination strategies, lockdowns with COVID-19 or condom use for sexually transmitted diseases for example.

ABMs are usually set up using social contact data including contact tracing data and epidemiological data to set up model parameters. Examples of contact data may include the average number of partners someone has in a given month, how many people/friends a person meets each day, how long an average relationship lasts, etc.

ABMs are becoming increasingly popular and have been used to model multiple infectious diseases including COVID-19 [34] [36] [37], Measles [38], HPV [39] , Tuberculosis [40] and influenza [41]. Agent Based Models are becoming quite popular for pandemic planning since they simulate human behaviour better than traditional compartmental methods due to the stochastic nature of the models and the ability to specify individuals' traits and behaviours [42].

3.5 Networks and Vaccination strategies

Many epidemiological studies of mpox, look at mpox in a similar lens to how sexually transmitted diseases are transmitted even though mpox itself is not classified as a sexually transmitted disease. This is because very close contact is necessary for sexual encounters and mpox is known to spread from prolonged skin-to-skin contact between people.

When looking at diseases that are spread through sexual contact, researchers are

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particularly interested in sexual networks. A network consists of points called nodes which are connected to each other by links or edges that represent connections between the links in the network.

Sexual networks have been a focus of study for many social scientists for years, particularly in the last 2 decades [43] [44] [4] [5]. The study of sexual networks allows researchers to understand who has sex with whom, which is crucial in understanding how diseases spread. The first big study of sexual networks was the study of the “Sex Web” conducted through questionnaires and surveys in Sweden [44] [6]. By asking participants to estimate the number of sexual partners they had in their lifetime it was possible to generate a degree distribution of the sexual network which is estimated by a power law distribution [4] - this is a well-known distribution also known as a scale free network distribution [6]. A scale -free/power law distribution is characterised by the probability distribution $P(k) k^{-\alpha}$, where k denotes the degree of each node - in this case k denotes the number of sexual partners someone has had. Poisson distributions are often used to approximate scale-free distributions [6].

The study by F. Lilijeros et al. showed that human sexual networks do indeed follow a power-law distribution with $\alpha = 2.31 \pm 0.2$ for males in the range $k > 5$ and $\alpha = 2.54 \pm 0.2$ in the range $k > 4$ for females, when participants responded with how many sexual partners they had in the past year. The scale-free distribution of peoples’ sexual contacts was confirmed Schneeberger A. et al. [5] where they also found that heterosexual men had values of α (γ) around 2.5, heterosexual women had α value of around 3.1, homosexual women had α value of 3.1.

The study found that the sexual network of heterosexual men could be described by a scale-free degree distribution with a α value in the region between 1.5 and 2, which is quite different to the distributions for heterosexual males and females and homosexual females [5]. Smaller values of the α (γ) parameter in scale-free networks

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indicate accelerated growth in these networks, i.e. as individuals are added to the network, the number of links between nodes in the network increases very quickly. This means that on average, the number of sexual contacts a MSM man has will tend to increase as the size of the MSM population increases [5].

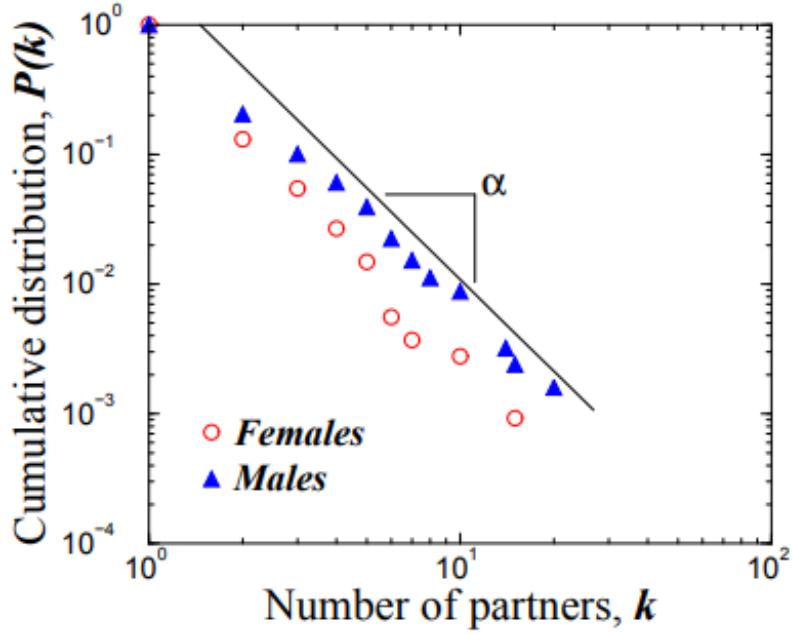


Figure 6: Scale-free distribution of number of sexual partners for males and females in the previous year. Taken from article by Liljeros et al. [4]

Smaller values of α (also denoted by γ) in scale-free networks mean that the network is far much more connected and the mean distance between any 2 nodes $\langle d \rangle$ decreases as γ decreases. Small values of $\gamma < 3$ lead to ultra-small world networks where on average, there is only a small number of ‘hops’ between links in the network required to reach any nodes in the network. This is normally because of the presence of large ‘hubs’ in the network with many links to other nodes. The small world phenomenon is well studied in network sciences [45] and is commonly seen in social network and travel networks such as airport networks for example [6].

It is believed that large hubs in these networks act as super-spreaders in the network because of the large number of links they have to other people in the network as well as the small path lengths in small and ultra-small networks, they have the potential to infect a large amount of people in the network, with the potential to cause large outbreaks.

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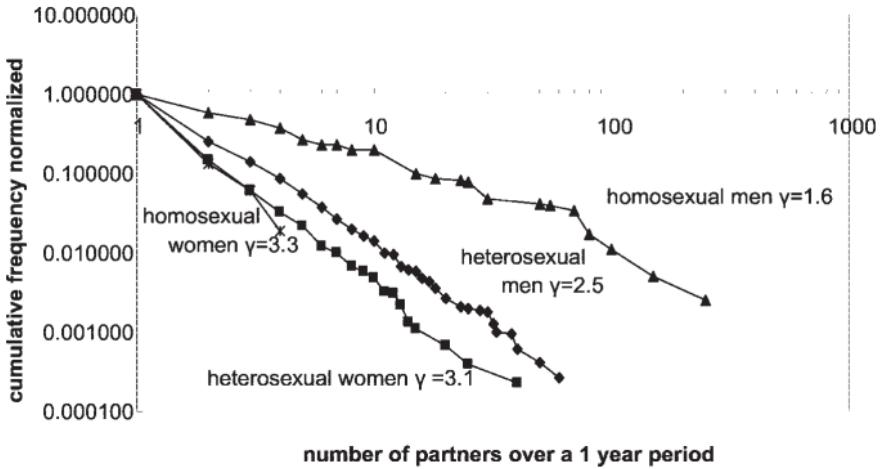


Figure 7: Scale-free distribution of number of partners in the past year for both heterosexual males and females as well as homosexual males and females. Taken from Schneeberger A. et al. [5].

$$\langle d \rangle \sim \begin{cases} \text{const.} & \gamma = 2 \\ \ln \ln N & 2 < \gamma < 3 \\ \frac{\ln N}{\ln \ln N} & \gamma = 3 \\ \ln N & \gamma > 3 \end{cases}$$

Figure 8: Barabasi's book outlines how average distance $\langle d \rangle$ depends on the size of the network N and the degree exponent γ . $\gamma \approx 3$ gives way to small worlds, values of $\gamma \approx 2 - 3$ give way to ultra small worlds. Taken from Barabási's book Network Science [6].

In the case of many infectious diseases such as diseases transmitted through airbourne droplets or sexually transmitted diseases, the social/sexual network structure is very important when considering vaccination strategies. Generally, the most common kind of vaccination is random vaccination where individuals from the population are vaccinated at random. If the population of interest can be modelled as a scale-free distribution with a low value of γ then it may be of interest to use a targeted vaccination strategy to vaccinate groups at greater risk (e.g. MSM community in case of mpox) or to prioritise vaccinating super-spreader “hub” nodes instead of a random vaccination approach. Selective vaccination has been shown to be more effective than random vaccination even for networks with larger values of $\gamma > 3$.

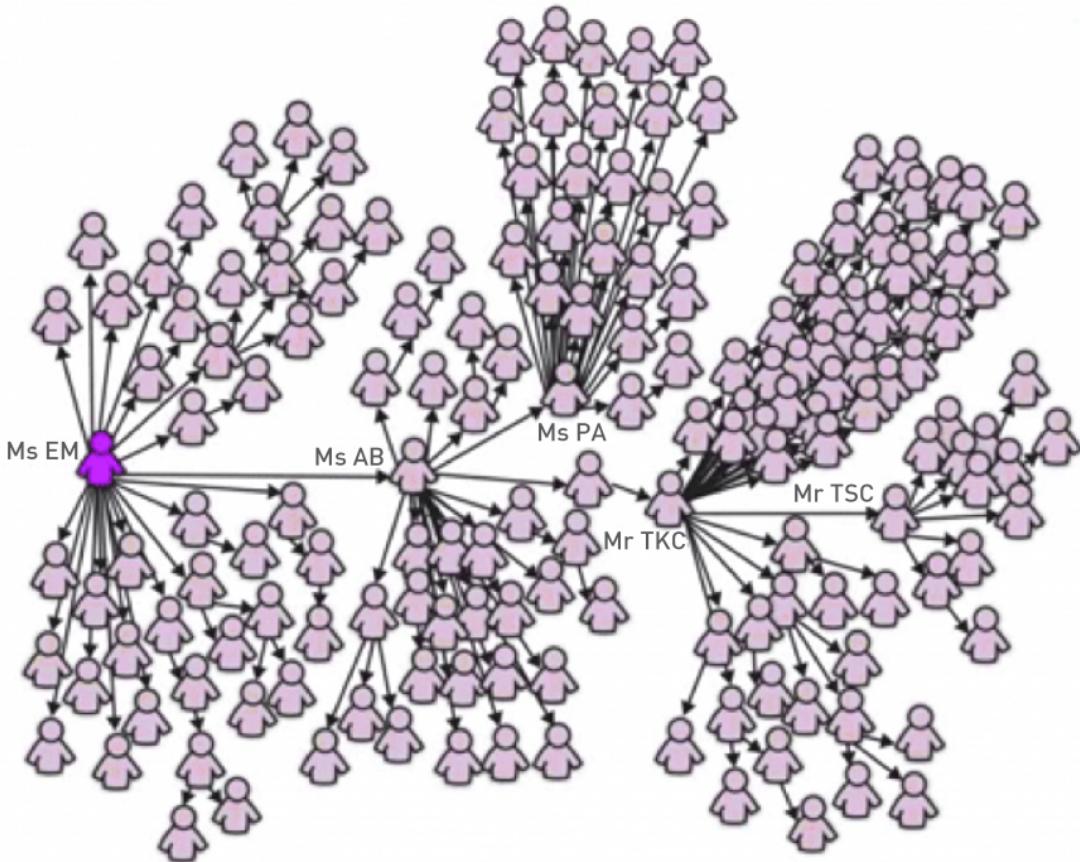


Figure 9: Image visualising the potential effect of hub nodes becoming superspreaders in a network epidemic. Taken from Barabási's book Network Science [6]

where hubs are less prominent [6]. Extensive contact tracing is required in order for targeted vaccination programmes to be possible and effective.

The study of network structure can suggest other effective ways to vaccinate members of the population - for example, during the COVID-19 pandemic healthcare workers were one of the first cohorts to be vaccinated because of the high number of patients that health care staff were in contact with [46]. Other vaccination strategies may rely on health-data more than network theory. For example, it might be of interest to vaccinate those who are more at risk to the virus because of existing health conditions or subsets of the population who are known to be more exposed or more

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at risk to the virus.

3.6 Models used

In this thesis I used an Agent Based Models developed by University of Galway post-doctorate researcher Hamda Ajmal [7]. Hamda developed two agent-based models for mpox, one population model and one model which only modelled mpox within the MSM community. Both agent based models were created in the modelling software called Netlogo [47].

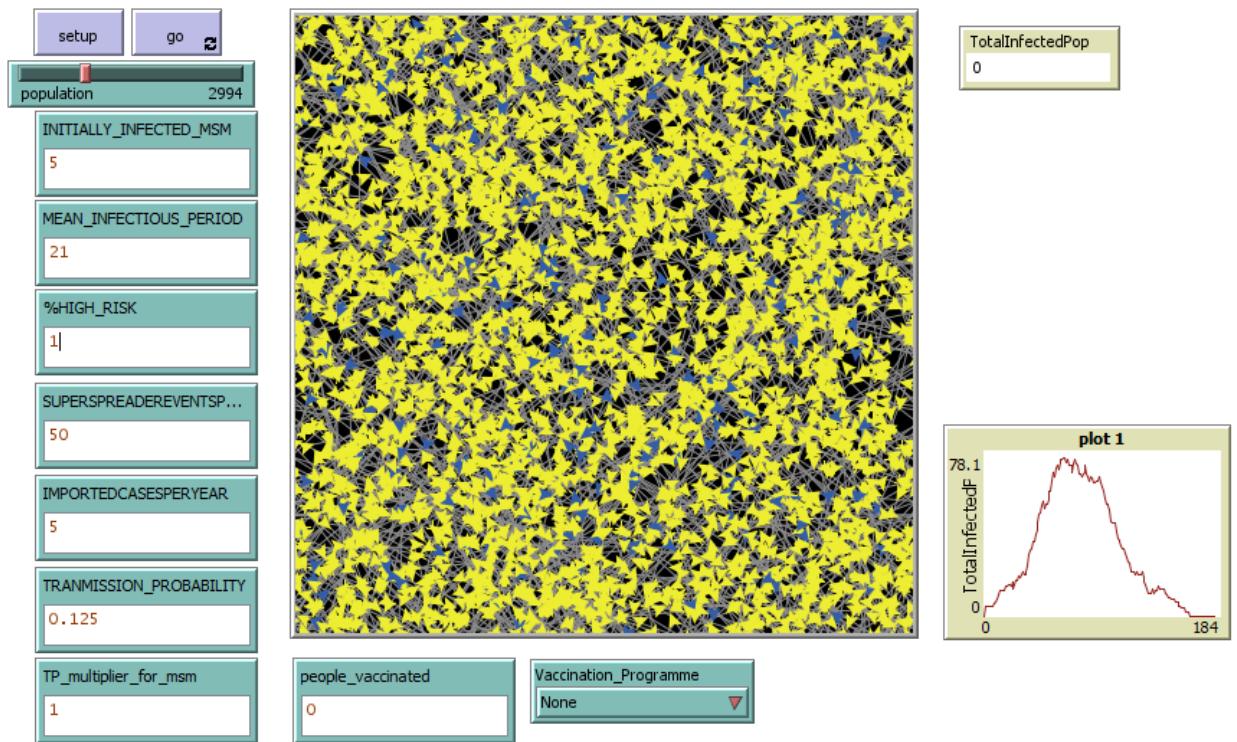


Figure 10: MSM agent based model setup in Netlogo [7].

The interface of this model allows the user to specify parameters in the model e.g. the size of the population, number of initially infected agents , % of high risk agents, mean infectious period etc. The software provides a window where you can watch as changes occur in the model at each time step (Netlogo refers to each time step as a ‘tick’). The yellow/blue nodes are individual members of the population with

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yellow indicating uninfected/susceptible, red indicating an infected agent and blue indicating an agent that was infected and has recovered from mpox infection. Links between agents show that there is a sexual relationship between the two linked nodes. This sexual relationship can be long term or short term in nature.

Each simulation runs for 180 ticks (1 tick = 1 day) or for approximately 6 months. The software records what happens in each simulation and can report it back to the user in plots or monitors. The user can save these plots and other values of interest as .txt or .csv files. The model can report:

- Effective reproduction number R_e which represents the average number of new infections caused by each individual in a population (which is made up of susceptible and non-susceptible individuals). R_e is calculated at the end of the simulation.
- The time varying reproduction number R_t which is the average number of secondary infections generated by an infected individual at each day in the simulation
- Total number of active mpox cases and new mpox cases in the entire population or in subgroups of the population e.g. age groups, sex or by sexual-preferences.

The NetLogo interface allows the user to monitor values and plots in real-time as the model runs and allows the user to export results into a .txt or .csv file for further analysis in another programme. Most plots and analysis in this thesis were carried out in Microsoft Excel.

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4.1 Parameters

The population model is comprised of the following parameters found in table 1 [7].

Table 1: Parameters for the population model. Parameters determined by Hamda Ajmal [7].

Variable	Description	Value	Source
Minimum Age	Minimum age of agent in model	16	NATSAL-3
Maximum Age	Maximum age of agent in model	74	NATSAL-3
Total Population	Size of population in model	10,000	-
Homosexual Males (%)	Percentage of homosexual males in population	1.144%	NATSAL-3
Bi-sexual Males (%)	Percentage of bi-sexual males in population	3.92%	NATSAL-3
Homosexual Females (%)	Percentage of homosexual females in population	0.30%	NATSAL-3
Bi-sexual Females (%)	Percentage of bi-sexual females in population	6.04%	NATSAL-3
Initially Infected MSM	Number of infected MSM agents at start of model	5	-
Size of a super spreader event	Number of people that attend an event where there are multiple short term sexual partners	30	-
Transmission Probability (TP)	Probability of acquiring infection after sexual contact	$\frac{1}{8}$	-
Weekly contact rate (WC)	Number of sexual encounters per week for agents in long-term relationships	$\frac{3}{7}$	-
Exposed Period	Number of days an agent is exposed to disease but not infectious	Weibull distribution with scale parameter $\eta = 8.4$ and shape parameter $\beta = 1.5$	Ward et al. (2022) [48]

Many of the population parameters found in the model in table 1 are derived from the NATSAL-3 dataset (National Survey of Sexual Attitudes and Lifestyles) [49]. The model creates a population of 10,000 agents with uniformly distributed ages

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between 16 and 74 years. Each agent is also assigned one of 15 age cohorts, each consisting of 4 years, i.e. first age cohort is from 16-20 years. The upper and lower limits of agents' ages in this model correspond to the youngest and oldest respondents in the NATSAL-3 dataset [49].

The model is based on an SEIR model framework, with susceptible agents vulnerable to infection following sexual contact. Exposed agents are those who have been exposed to the virus by making contact with an infected individuals. Infected agents are agents infected with the virus who are displaying symptoms and recovered agents are those who have had the virus and are now immune to contracting the virus in the future.

Mpox is not classified as a sexually transmitted disease as mentioned earlier in this thesis, however there is evidence that shows it is transmitted primarily through sexual contact in the MSM community [19]. In the model, the Transmission Probability parameter is assumed to be $\frac{1}{8}$, meaning that there is a one in eight chance that mpox will be transmitted after a sexual encounter between agents in the model. The model also assumes that agents in sexual partnerships will have sex 3 times a week, leading to the fixed weekly contact rate value of $\frac{3}{7}$. This can be interpreted as a 3 in 7 chance of a sexual encounter happening on a given day between a couple in a long-term relationship. The variables TP and WC can be varied to investigate their impact on the size of the outbreak.

We can write the daily probability that a susceptible partner in a long-term relationship with an infected agent becomes exposed as $P(S \rightarrow E_L)$. Then $P(S \rightarrow E_L)$ is calculated as follows:

$$P(S \rightarrow E_L) = TP \times WC = \frac{1}{8} \times \frac{3}{7} = 0.0535, \quad (7)$$

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Where TP is the transmission probability assumed to be $1/8$ and WC is the weekly contact rate assumed to be $3/7$. Each time step in the simulation is considered to be one day. A random floating point number is chosen from uniform distribution $U(0, 1)$ each day, if the number drawn is less than $P(S \rightarrow E_L)$, the susceptible agent enters the exposed state. For one-time short-term sexual encounters during superspread events, equation 7 no longer contains the WC term. The probability that the susceptible partner of a short-term sexual encounter becomes exposed to the disease can then be written as:

$$P(S \rightarrow E_S) = WC. \quad (8)$$

The incubation period is taken from Ward et al. [48]. An agent is in the incubation period from the moment they are exposed to the virus until symptoms begin to emerge. According to Ward et al. [48], an individual can be infectious for up to 4 days before symptoms emerge. This delay in the onset of symptoms is implemented by drawing a random number from a uniform distribution $U(0, 4)$ and subtracting it from the incubation period. We take Inc to represent the incubation period for an exposed agent, then $Inc - U(0, 4)$ represents the time an agent is in the exposed period before they become infectious. This subtraction only occurs when the incubation period for the agent is less than 6 days, otherwise issues can arise where the ‘exposed’ state becomes very close to zero or takes on a negative value.

In the model an infected agent stays infected for 2 to 4 weeks. This infectious period is taken from the CDC [16]. This number is chosen from a normal distribution centred on 21 with a standard deviation of 3 days. Infected agents spread the disease through sexual contact with other agents. Vaccination efficacy is assumed to be 85 % based on estimates in several studies [50] [26].

Once an agent recovers from the infection they are placed in the ‘recovered state’. For simplicity, permanent immunity to the disease after recovery is assumed. This

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assumption is made as mpox tends to induce long-term immunity in recovering patients [1] and there are very few recorded cases of reinfection [51].

All agents are assigned a sex of being male or female with 50% probability. Each agent is also assigned a sexuality with probabilities of being given a sexuality outlined in table 1. The three possible sexualities an agent can have are heterosexual, homosexual or bi-sexual. The percentage of heterosexual men/women in the model is found from the proportion of men/women who reported only having sexual encounters with members of the opposite sex in the NATSAL-3 dataset. Similarly, the percentage of homosexual men/women in the model is found from the number of men/women who reported only having sexual encounters with those of the same sex in the NATSAL-3 dataset and the percentage of bi-sexual men/women is found from the percentage of men/women who reported having had sexual encounters with both the same sex and opposite sex in their lifetime [7].

There are two kinds of sexual relationships for agents in this model - long term and short term. In long-term relationships sexual encounters occur on a regular basis between agents. Short term sexual contact is a once-off event between agents to mimic transmission through superspread events and travel [7].

Each agent has a “number of new partners each year” denoted by k . This is based on each agent’s age, sex and sexual preference. The number k is generated randomly from a Poisson distribution using inputs for age a , sex s , and sexual preference p derived from the NATSAL-3 dataset. The probability mass function used to derive the probabilities for values of k is as follows:

$$f(k, \lambda_{s,a,p}) = PR(X = k) = \frac{\lambda_{s,a,p}^k \cdot e^{-\lambda_{s,a,p}}}{k}. \quad (9)$$

Here k denotes the number of sexual partners each year, e is Euler’s constant, $\lambda_{s,a,p}$ is the average number of partners of sex $s = [male, female]$, age-cohort $a = [0, 1, \dots, 15]$

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and sexual preference $p = [\text{homosexual}, \text{bi-sexual}, \text{heterosexual}]$ calculated from the NATSAL-3 survey data. There are 90 mean values for k since there are 15 age cohorts, 3 sexual preferences and 2 sexes.

Bisexual agents have a probability of choosing a partner of the same sex which is determined by the relative frequency of same-sex partners out of all the partners chosen by bisexual agents the previous year. This calculation is done for each sex and for each age cohort of the bi-sexual group of the population in the model. The probabilities of a bi-sexual individual choosing someone of the same-sex or opposite sex can be written as:

$$P(\text{SameSexPartner}, a, s) = \sum_{i \in C_{\text{bi-sexual}, a, s}} \frac{N_{\text{SameSexPartners}}}{N_{\text{AllPartners}}} \quad (10)$$

$$P(\text{OppositeSexPartner}, a, s) = 1 - P(\text{SameSexPartner}, a, s), \quad (11)$$

Where $N_{\text{SameSexPartners}}$ represents the number of same sex partners and $N_{\text{AllPartners}}$ represents the total number of all partners of agents in the bi-sexual cohort $C_{\text{bi-sexual}, a, s}$ in the last 12 months. The sum term here sums over all 16 age cohorts in a and the 2 sexes in s .

The formulae governing the choice of sexual partners is outlined above. If an agent already has a long-term partner they must break up with them before they can choose a new long-term partner. The probability that an agent will breakup on a given day is modelled by an exponential distribution:

$$P_{\text{BreakupToday}} = 1 - e^{-1 \cdot \frac{k+0.1}{365}}. \quad (12)$$

Where k is the Poisson number drawn from a Poisson distribution of mean $\lambda_{s,a,p}$. A small number $\frac{0.1}{365}$ is added to avoid a small number of agents having probability 0 of finding a new partner. At each timestep/day a random number between 0 and

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1 is generated for each agent. If the random number is less than $P_{BreakupToday}$ then the link connecting an agents to its partner in the network is broken and the agent seeks a new partner now.

Agents in the model are also permitted to start short term casual relationships with other agents. There is limited data concerning casual and concurrent relationships in the NATSAL-3 dataset so parameters relating to short-term relationships in this model are estimates based on assumptions we make about short-term links between agents. The way that short-term sexual relationships occur in the model is by agents attending events where there are multiple one-time short term sexual contacts made. These contacts only occur during the event and do not last after the event has ended.

In the population model the only people who attend these events are MSM agents aged between 16 and 32 years old. These individuals who go to these events are the “high risk” agents in the model. The number of people who attend the events is set to 35 agents for simplicity. The number of events per year is a variable in the model that can be changed to see how it affects simulation outcomes. The high risk events are implemented in the model to model events and establishments which historically have a high risk of STI spread within MSM communities such as Saunas, sex clubs, dating apps and sex parties [21]. These events will be referred to as “Superspreader events” in this paper.

4.2 Population mixing

One major reason to opt for using an Agent-Based model over other epidemic models is the ability to specify how agents mix in the model. The mpox agent-based models examined in this thesis use an age-mixing matrix which uses data from the NATSAL-3 dataset [8] to determine the probabilities that someone from one age cohort begins a relationship with someone from another age-cohort. In the paper of Datta et al. [8] the authors investigate the distributions of the rate of new partners that

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involve condomless sex, which contributes to the spread of STIs. Condomless sex is not an important assumption in these mpox models since it is not yet known whether mpox can be spread through semen [15].

Each cell in the age-mixing matrix states the probability that an agent from an age-cohort C_i begins a relationship/sexual partnership with someone from a particular age cohort C_j . Each time an agent seeks a new partner, the age-cohort their partner belongs to is determined by the age-mixing matrix. The probability that an Agent in age cohort C_i will seek a sexual partnership with an agent in cohort C_j is determined by relative frequency counts obtained from the NATSAL-3 dataset. This leads to the following formula which generates the probabilities for each cell of the age-mixing matrix:

$$P(P_{C_i, C_j}) = \frac{\sum \theta_{i,j}}{\theta_i}. \quad (13)$$

$\sum \theta_{i,j}$ is the sum of the weights of all the respondents in the NATSAL-3 survey in cohort (row) i who had a sexual partnership or relationship with a person in age cohort j . Then $\sum \theta_i$ is the sum of weights of all the respondents in age cohort i who reported having any sexual relationship with any of the age cohorts surveyed. The matrix can be written as follows:

$$P_{AGEMIXING} = \begin{bmatrix} P_{C_1, C_1} & P_{C_1, C_2} & \cdots & P_{C_1, C_N} \\ \vdots & \ddots & & \vdots \\ P_{C_N, C_1} & & & P_{C_N, C_N} \end{bmatrix}$$

$$P_{AGEMIXING} = \begin{bmatrix} \frac{\sum \theta_{C_1, C_1}}{\sum \theta_{C_1}} & \frac{\sum \theta_{C_1, C_2}}{\sum \theta_{C_1}} & \dots & \frac{\sum \theta_{C_1, C_N}}{\sum \theta_{C_1}} \\ \vdots & \ddots & & \vdots \\ \frac{\sum \theta_{C_N, C_1}}{\sum \theta_{C_N}} & & & \frac{\sum \theta_{C_N, C_N}}{\sum \theta_{C_N}} \end{bmatrix} \quad (14)$$

The resulting age-mixing matrix can then be visualised as it was by Hamda Ajmal

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using the results from Datta et al.'s work on the NATSAL-3 dataset [7] [8].

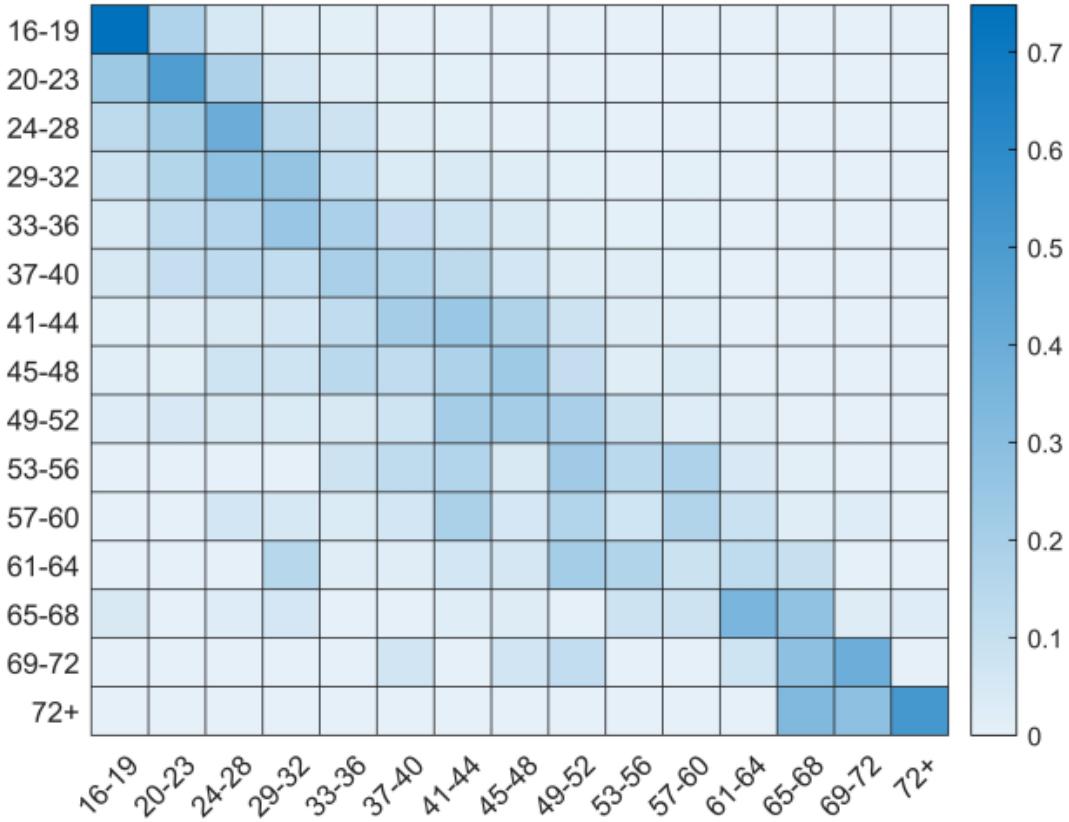


Figure 11: Age-mixing matrix derived from NATSAL-3 dataset using code provided in Datta et al.'s paper [8]. Visualisation done by Hamda Ajmal [7]

In figure 11, each row r represents the age cohort of a respondent from the NATSAL-3 survey. Each column c represents the age cohorts of respondents' sexual partners in the last 12 months. Each cell is a probability value in the range from 0 to 1, with a white cell representing low probability values and dark blue cells representing high probability values close to 1.

4.3 MSM model

Since the mpox outbreak in 2022/2023 disproportionately affected members of the MSM community with little spillover to other groups - both from recent mpox case

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Table 2

Variable	Description	Value	Source
Homosexual Males (%)	Perc-entage of Homosexual men	63.6 %	NATSAL-3
Bi-sexual Males (%)	Percentage of bi-sexual men	36.3%	NATSAL-3
% High-Risk	Percentage of MSM at high-risk behaviour	1% (variable)	

data and from population model results -, it made sense to create a version of the mpox model which focused specifically on the MSM community subset of the entire population.

There are some differences between the MSM model and the population model. The main difference is that the MSM model has a population that consists mostly of just homosexual men and bi-sexual men with the percentage of homosexual and bi-sexual men determined from the NATSAL-3 dataset. Women only feature in this model if a bi-sexual male agent enters a relationship with a woman. If a relationship between a bi-sexual male and a female agent begins, then a female agent is added to the model, and if that relationship ends, then the female agent is removed from the MSM model population. There are no heterosexual men in this model.

4.4 Population Model

Hamda's results [7] for running the population model show that when there are no superspread events or imported cases due to travel, the infection does not persist within the society and the infection dies out after 50 days. The time varying reproductive number R_t remains close to zero after these 50 days.

When there are 30 imported cases per year the amount of mpox cases is still low but the infection is still sustained throughout the population. R_t remains close to zero but above 0 after the 50 days.

In the scenario where there are 30 superspread events per year, there is a trend of higher disease incidences and increased R_t values. R_t exceeds 1 sometimes. R_t frequently exceeds 1 when the population is not vaccinated or the MSM population is not vaccinated. The number of cases peak after several weeks and after the peak the infection begins to die out. The number of cases and R_t reach 0 values after about 3 months on average.

Imported cases due to travel and superspread events are modelled to occur exclusively within the MSM subset of the population in the population model, specifically members of the MSM population aged between 16-40 years old.

There are close to zero cases of mpox recorded in heterosexual men, homosexual women and bisexual women from running the model multiple times under different situations. In most situations modelled, homosexual and bi-sexual men make up the majority of the infections in the model, with heterosexual women being the third most effected group. This is consistent with recorded mpox data where MSM males are disproportionately affected by mpox compared to heterosexual males and females of all sexualities [52] [53]. There are very few recorded cases of mpox in females compared to the number of recorded mpox cases in males [52] [53]. The

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model does tend to over-estimate the number of hetero-sexual women infected with mpox, which is close to the number of homosexual men infected with mpox in several simulations of the model.

Because the MSM population are disproportionately affected by mpox, a second version of the model was created by Hamda which only models mpox within the MSM community.

Hamda's models and results show that randomly vaccinating the population provides little to no benefit against mpox outbreaks. Randomly vaccinating 100 MSM agents notably reduces R_e , thus limiting mpox spread.

4.5 MSM Model

The MSM model is very similar to the original population model, but models only MSM individuals i.e. homosexual males and bi-sexual males. Female agents are added into the model whenever a bi-sexual male enters a relationship with a female partner and the female agent is removed once that relationship ends. The proportion of homo-sexual and bi-sexual males in the model is referenced in table 2.

When running the model we can change parameters between simulations to investigate what happens under changes in the population, the environment or the disease of study.

I ran several simulations of the MSM model, replicating Hamda's results. All simulations had a population of 10,000 and 30 replicates of each simulation were carried out to produce the average results. The simulations carried out are found in table 3.

Running the MSM model with 5 initial infected, 30 superspreader events per year, 0 travel related cases and no vaccination appeared to produce results which most

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Table 3: Simulations carried out

% Vaccinated	No. of Superspreader events	No. of Imported Cases	Weekly Contact rate (WC)
0	0	0	$\frac{3}{7}$
0	30	0	$\frac{3}{7}$
0	0	30	$\frac{3}{7}$

resembled the mpox outbreak in 2022.

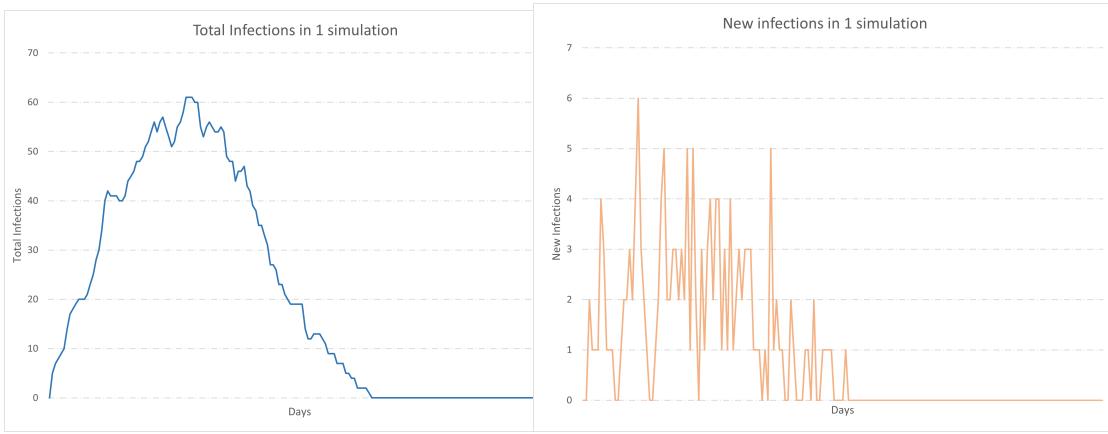


Figure 12: Plots showing number of total infections and number of daily infections on each day for one 180-day long simulation of the MSM model.

Because of the stochastic nature and the sensitivity to initial conditions of the mpox agent based model, it is not sufficient to run the model once and make conclusions from a single simulation of the model. Agent based models require repeated simulations, then observations can made from the average of the simulations.

Running the simulations described in table 3, I generated the following plots, with error bars $\pm 1.96 \frac{\sigma}{\sqrt{n}}$, for 95 % Confidence interval, where $n = 30$ for the 30 replicate simulations done for each scenario.

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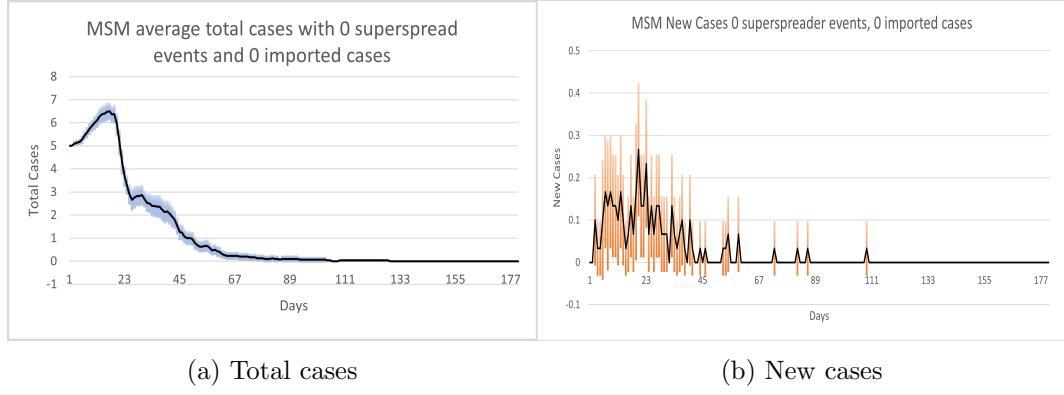


Figure 13: Plots showing mean total cases and mean new cases for 30 simulations with no superspread events and no imported cases.

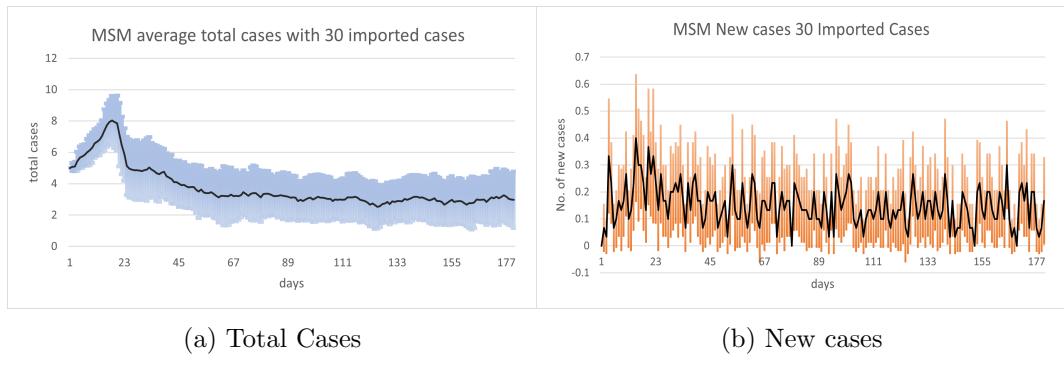


Figure 14: Plots showing mean total cases and mean new cases for 30 simulations of the model with 30 imported cases due to travel and 0 superspread events.

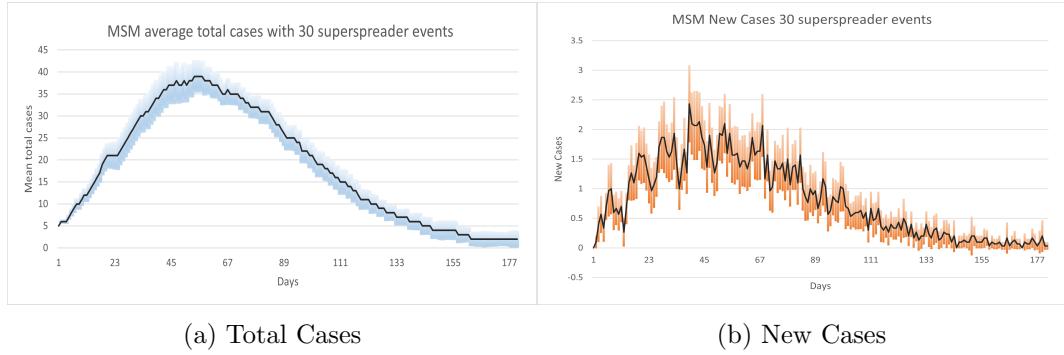


Figure 15: Plots showing mean total infections and mean new infections from 30 runs of the model with 30 superspread events per year and no imported travel cases.

4 Model

The plots with 30 superspread events most resemble the shape of the plots from recorded mpox case data in the 2022-2023 outbreak [9].

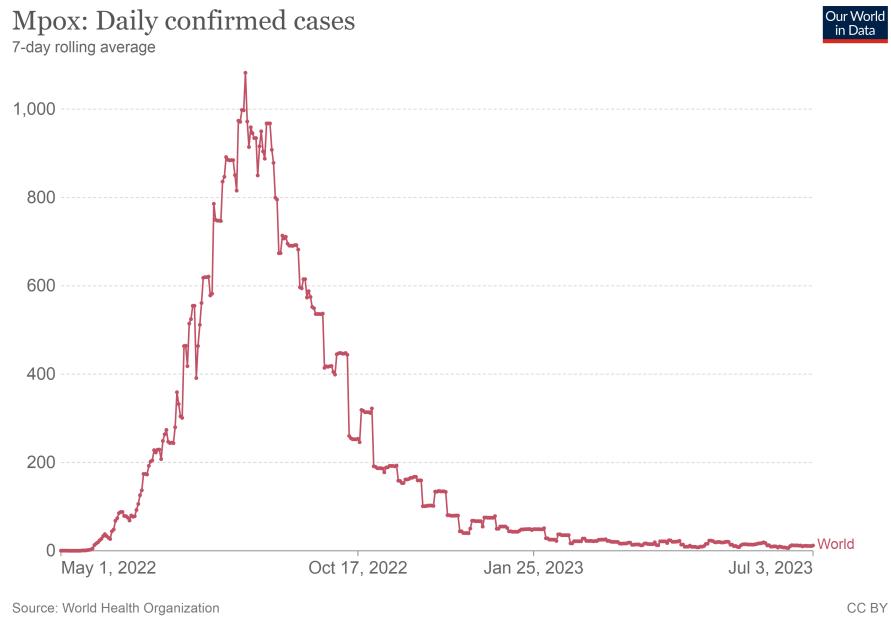


Figure 16: Plot of Daily recorded mpox cases worldwide on a 7-day rolling average. Plot created by Our World in Data [9] using mpox case data gathered by the WHO [10].

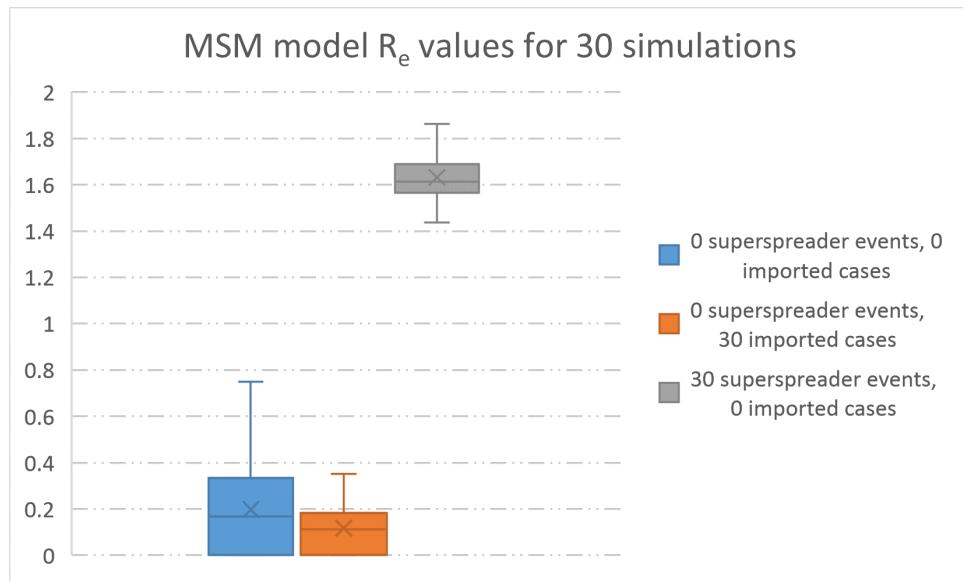


Figure 17: Effective R values from 3 the MSM model used in 3 different scenarios. Each scenario of the model was run 30 times.

4 Model

In figure 13, when there are no superspread events or imported cases, the infection dies out within approximately 50 days and few infections are seen after this point. When travel cases are introduced in 14 the number of cases stabilises around 2-5 cases each day and the infection does not die out in many instances. The effective R number R_e is still quite low when travel cases are introduced as seen in figure 17. When superspread events are introduced, we see the shape of the plot resembles the plot of recorded mpox outbreaks from 2022 to date [9]. There is a peak in the number of new and active cases, with the rate of new cases reducing after the first 40 days. New cases are close to zero with little variance after 5/6 months, which again agrees with the data from the outbreak in 2022, which saw a huge reduction in reported cases after 6 months [9].

At the very start of the outbreak, R_t can reach values between 2 and 4. The effective R number of the disease R_e is found in the range 1.44 and 1.86. R_t seldom went below 1 in simulations run with 30 superspread events.

The results generated in these simulations, verify the results generated in Hamda's simulations of the MSM model [7]. Hamda found a median R_e value of 0.12 and 0.14 in the scenarios where there are 0 superspread events and 0 travel cases and the scenario where there are 0 superspread events and 30 travel cases for an unvaccinated MSM population. In the case where there are 30 superspread events per year, her simulations found a median R_e value of 1.72 which ranged from a minimum value of approximately 1.5 to a maximum value of about 2.0. This is very consistent with the range of 1.44 to 1.86 which I found in my simulations.

In figure 17, we see in the cases where there were no superspread events, the effective R number value does not exceed 1. In the cases where there were superspread events, the effective R number has a median value of 1.61 with upper and lower quartiles of 1.69 and 1.56. The minimum value recorded for R_e in the superspread

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case was 1.44 which is above the threshold of 1 required to sustain a prolonged outbreak. The two scenarios with no superspreader events fail to attain an effective R_e value of 1 which means a prolonged outbreak will not last in these cases. This shows that superspreader events is one of the main driving causes of the spread of mpox in 2022-2023.

4.6 Time to run the model

To compare the mpox ABM model to other models and mpox case data, it is necessary to repeat simulations multiple times and aggregate the simulations to see what the average behaviour of the model is like. For each set of parameters, I ran the model 30 times to generate plots of total cases and daily cases over the 180 days the model runs for.

This process of creating replicate simulations can be quite time consuming, I ran a number of simulations with different population sizes N to see how the time taken to run the simulation scales with the population size. I ran 5 simulations for each population size and plotted the average time taken against population size N .

For smaller populations, the model's time complexity scales quadratically as $O(N^2)$, which is undesirable if this trend continues for large N as increasing population size will mean very large computation times. The computation times are very manageable when $N < 3000$ with the average simulation taking 9.25 seconds when $N = 3000$.

In figure 19a, we notice that as $N > 3000$, the time complexity of the model changes and time begins to scale linearly with population size. Time complexity of $O(N)$ is much more desirable than $O(N^2)$, but still not as desirable as one would like as it still means lengthy computation times for larger population sizes. The largest

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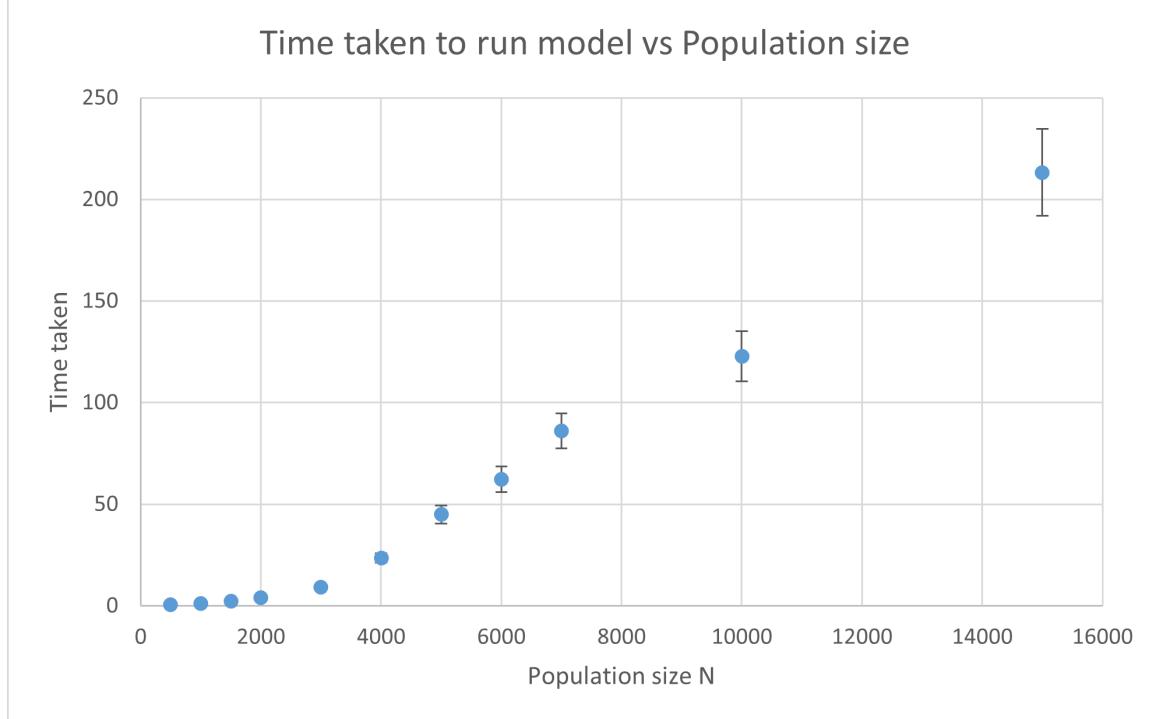
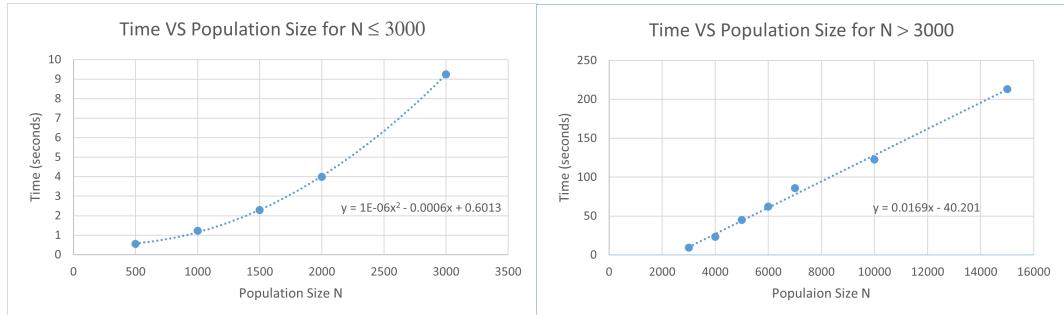


Figure 18: Plotting the average time taken over 5 simulations for each population size N with 10 % error bars.



(a) Plotting elapsed times for the model for population sizes $N \leq 3000$ (b) Plotting elapsed times for the model for population sizes $N > 3000$

Figure 19: Plots showing how time elapsed scales with population size for small values of N ($N \leq 3000$) and large values of N ($N > 3000$). A 2nd order polynomial is fitted to the plot with small N and a linear fit is fitted to the plot with large N .

population size tested here was for $N = 15000$ which saw an average computation time of 213 seconds using my computer with an Intel Core i5 5200U processor with maximum clock speed of 2.20 Ghz. Due to the stochastic nature of agent based modelling, it is necessary to replicate simulations multiple times to obtain average results that we can compare with other models and real-world case data. In this

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thesis I replicated all simulations 30 times. To replicate the simulation 30 times with a population size of 15000, this would take 1 hour and 46 minutes to compute the 30 simulations.

Hamda's model focuses on using procedures rather than loops, which is good for computational efficiency. There is only one loop in the programme used to store time dependent reproduction number R_t values and there are no nested loops used. Simple loops have computation complexity of $O(N)$, whereas nested loops have computation complexity of $O(N^2)$ which is significantly more computationally expensive to run.

From the NATSAL-3 dataset, we assume that the population is comprised of 1.144 % Homosexual males and 3.92 % bisexual males, meaning we can assume that the total population is comprised of approximately 5 % MSM individuals. An article from 2007, used dating apps and dating website traffic in Germany to estimate the postal code distribution of the MSM population in Germany and found that large MSM communities are often found in the larger German cities such as Munich and Berlin [54]. If we consider a small-sized city with a population of 200,000 then we would expect a MSM population of approximately 10,000 under these assumptions. A population size of 10,000 gives a decent balance in terms of accuracy and trying to achieve lower computation times.

We could choose to model a smaller population so that the computation times would be more manageable, and we could produce more replicates of simulations. A larger population size, allows for a more accurate view of the disease dynamics within a real-world population. A larger number of replicates of model simulations reduces the error associated with the aggregated results since the error I used in generating plots is $\pm 1.96 \frac{\sigma}{\sqrt{n}}$ where n is the number of replicate simulations carried out for each scenario simulated and σ is the standard distribution of the results across all the

replicates.

5 Investigating changing model parameters

The models used in this thesis involve many parameters, most derived from data and other academic papers but the models also rely on many assumptions and some of the parameters themselves are formed on assumptions.

While it is favourable to have every parameter and variable backed by data and scientific evidence, it is not feasible for every aspect of a model to be driven by reliable data in most cases. Modelling relies on intelligent guesses and assumptions to create models; these assumptions can later be tested by validating model results with actual results. It is important to note the quote from George Box : “All models are wrong, some are useful.” While some of the parameters may be inaccurate and not reflect the real world as precisely as one may like, as long as the model provides a good insight into what is being modelled. Assumptions in the model are not inherently bad as long as they do not interfere with the model’s ability to model the problem of interest.

In this section I will be investigating some of the assumed parameters in the model and seeing what happens upon changing some of these parameters.

One parameter of interest is the Weekly Contact rate WC which governs the probability that agents in a relationship have sex in each time-step.

5.1 Sex-frequency parameter

The Weekly Contact parameter WC governs the number of times an agent in a long term sexual relationship/partnership (sometimes referred to as a main-relationship to differentiate between casual relationships) has a sexual encounter with their

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partner each week. Hamda assumed the weekly contact (WC) parameter to be $\frac{3}{7}$, assuming that most couples in relationships have sex 3 times every week. A paper from Kristin M. Wall et al. [55] used online surveys to estimate the frequency MSM men in the United States had sexual encounters with other men. They asked respondents how many times in the past year had they had sexual encounters with their main partner as well as how many times they had sexual relations with casual partners. Using the data collected in this paper, I replaced the value of $WC = 3$ in the model with a distribution of weekly contact rates for all MSM agents in the model.

Table 4: Annualised sex frequency in previous years with last male partner in Main relationship [55]

Frequency	%	Cumulative %	Frequency in Model	Weekly value
1 time per year	0.9	0.9	1/yr	0.019/week
2-5 times per year	5.8	6.7	5/yr	0.096/week
6-11 times per year	5.7	12.4	11/yr	0.2115/week
12-23 times per year	7.9	20.3	23/yr	0.4423/week
24-35 times per year	20.3	40.6	35/yr	0.673/week
36-51 times per year	20.9	61.5	51/yr	0.9807/week
52-155 times per year	18.9	80.4	156/yr	2.981/week
>156 times per year	19.7	100	200/yr	3.846/week

I used this data in the model by creating a new variable for every MSM agent called `contact-rate`. The contact rate of each agent was assigned by generating a random float from 0 to 1 for each agent and assigning a contact-rate value based on what value from 0 to 100 (0-1 in code) the random number falls on. The contact-rate value assigned to each agent is based off of the cumulative % distribution of sex frequencies in table 4. For simplicity WC is kept equal to 3 for female agents. These simulations were carried out in the MSM version of the model.

I ran the model with $WC = 3$ and another simulation with the sex frequency distribution from table 4 included. For these simulations I used the scenario with 30

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superspreader events per year and 0 imported cases per year as the reference model, all other parameters remained unchanged. 30 simulations of each scenario of the model were carried out to keep consistent with previous simulations.

Simulating the model with 30 superspreader events per year and keeping the Weekly Contact rate $WC = 3$, resulted on average 147.8 new cases of mpox emerging in the 180 days of the simulation. When the model had WC replaced with the sex frequency distribution from table 4, the average number of new cases dropped to 127.4. This is to be expected, as a higher rate of sexual contact in relationships makes the chance of transmitting the virus between partners higher. The updated model has 61.5 % of the population engaging in sex less frequently than in the reference model with WC fixed to a value of 3. 18.9 % of the population retained a WC value of $2.981 \approx 3$ and only 19.7 % of the population had a larger value of $WC = 3.846$ in the updated model.

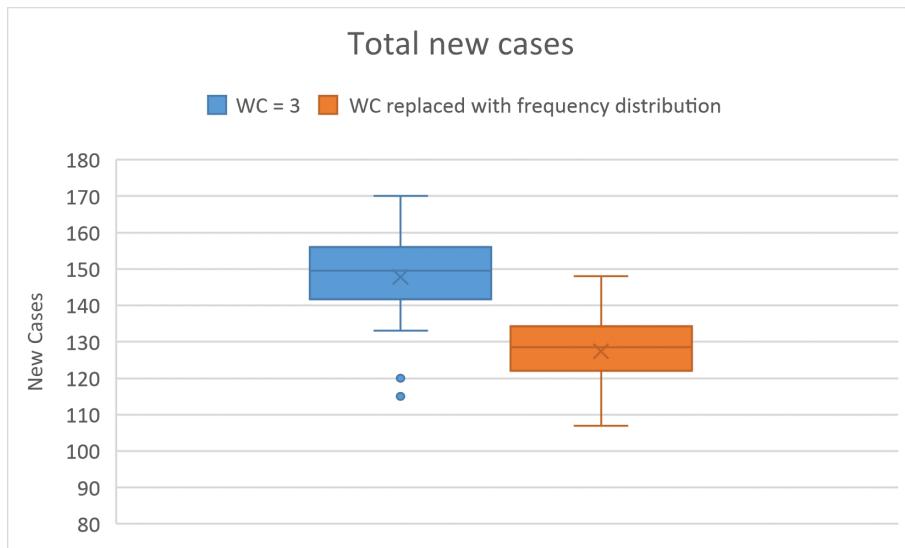


Figure 20: Plots showing difference in total new cases between keeping the weekly contact rate fixed and using the contact rate distribution from table 4

By replacing the fixed weekly contact rate with the contact rate distribution seen in table 4, there is a clear reduction in the number of cases seen in most simulations.

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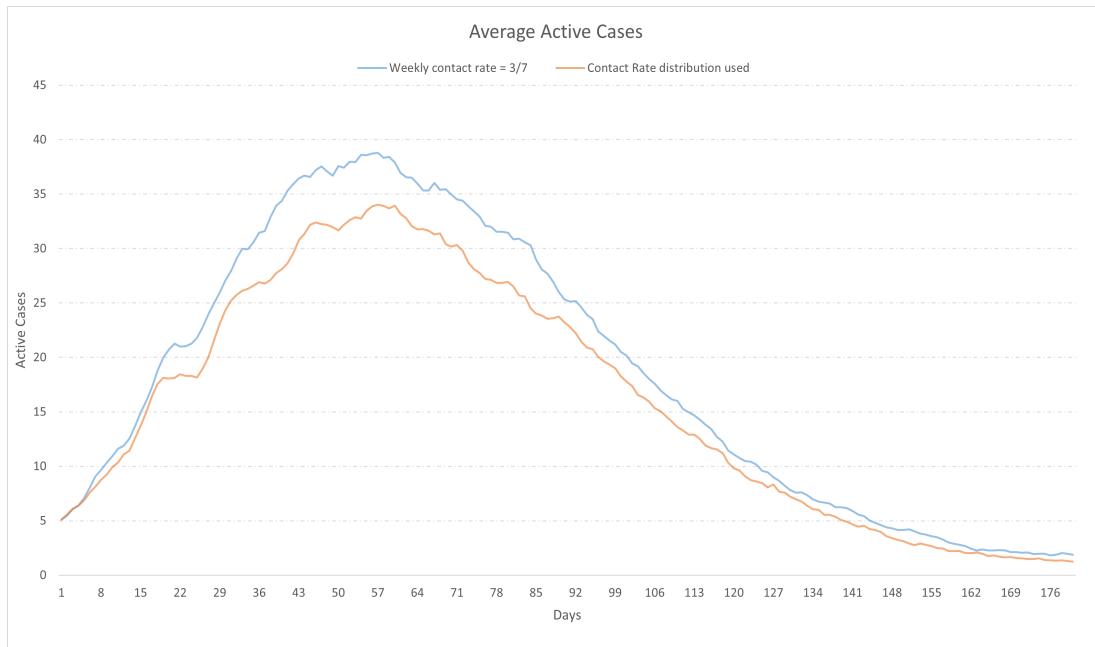


Figure 21: Plots comparing average active case numbers for fixed weekly contact rate versus using the contact-rate distribution in table 4.

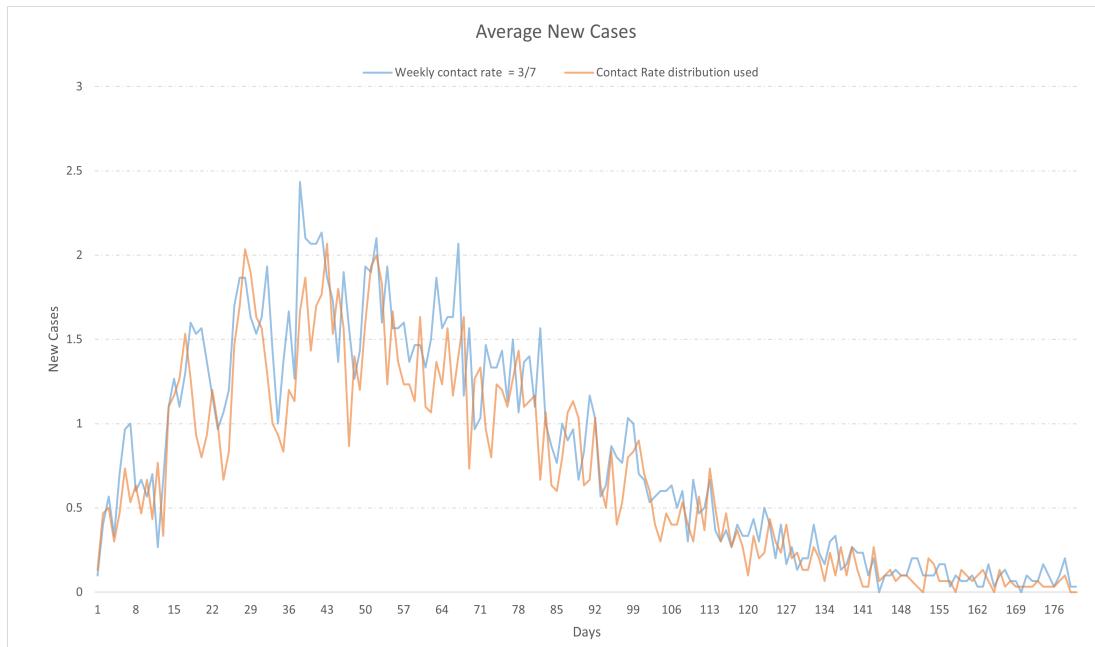


Figure 22: Plots comparing average new case numbers for fixed weekly contact rate versus using the contact-rate distribution in table 4.

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Figure 20 shows that replacing the assumption that WC has a fixed value of $3/7$ with the frequencies and probabilities in the table, results in the mean value of the total new cases dropping from 147.8 to 127.4.

In figures 21 and 22, we see from the traces of the average active cases and new cases that changing the frequency of sexual encounters in partnerships does not affect the shape of the infection curve and the infection peaks at the same time in both scenarios that were tested. The number of peak active mpox cases is seen when WC is set to a fixed value of $3/7$. For fixed WC , the infection peaks with 38 active cases versus 34 cases when the contact frequency distribution is applied to the model. The model with WC fixed tends to have higher spikes of new cases than with the frequency distribution applied, which in turn leads to increased cases when WC is let fixed as $3/7$.

From these results, it appears that regularly having regular sex with multiple partners without regular testing and checking for symptoms can lead to spread of mpox. Unlike HIV, most of the transmission does not occur through ‘main’ partners (boyfriends or husbands or significant-others) as suggested in several studies about HIV transmission [56], but instead through casual partners as shown by the inclusion of 30 superspread events into the model.

Decreasing the frequency of sex between agents in mid/long-term relationships does appear to reduce the spread of mpox as seen by introducing the distribution of sex frequency into the MSM population in the MSM ABM model developped by Hamda Ajmal [7] where the average number of new cases reduced by 13.8 %. The assumption of a fixed $\frac{3}{7}$ weekly contact rate is a reasonable assumption, but it tends to overestimate the number of new cases by about 13.8 % as found from the simulation results.

5 Investigating changing model parameters

It appears that the frequency of sex in relationships is an important parameter in the model for the spread of mpox. In the next section I will investigate changing the average number of main partners (long-term partnerships/relationships) homosexual male MSM agents have each year.

5.2 Changing number of partners

The number of partners each agent has in the model each year is governed by a Poisson distribution with parameter $\lambda_{s,a,p}$, which is the number of partners each sex, age and sexual preference group has per year on average according to the NATSAL-3 dataset. As mentioned in the Networks section, the Poisson distribution is a good approximation for scale-free networks in practice, which makes it a good choice of distribution to use here.

The rate at which couples in long-term partnerships breakup to form new relationships is also governed by this parameter $\lambda_{s,a,p}$ in an exponential distribution, which is a distribution which describes the rate at which Poisson events take place.

A study by Vanden Berghe et al. on sexual behaviour of MSM men in Belgium indicates that ‘sexually mobile men’ - Belgian residents who had sex with a casual partner abroad in the previous 12 months - had a higher number of non-steady partners compared to Belgian men who did not have sex abroad [57]. Sexually mobile men are reported to have on average 11 to 20 non-steady sex partners compared to 2 for Belgians who did not have sex with someone abroad. To attempt to capture the two extremes, I wanted to try increasing and decreasing the number of average partners each agent has sexual contact within the model.

To investigate the effect of changing the number of partners, I simulated the model with values of $\lambda_{s,a,p}$ increased by +50 % for homosexual MSM agents and I also simulated the model with $\lambda_{s,a,p}$ decreased by 50 % for homosexual MSM agents in

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the MSM model. These simulations are done 30 times per each scenario and each simulation has 30 superspreader events per year with all other parameters kept same as before. Bisexual MSM and homosexual female lambda values remain unchanged in these simulations.

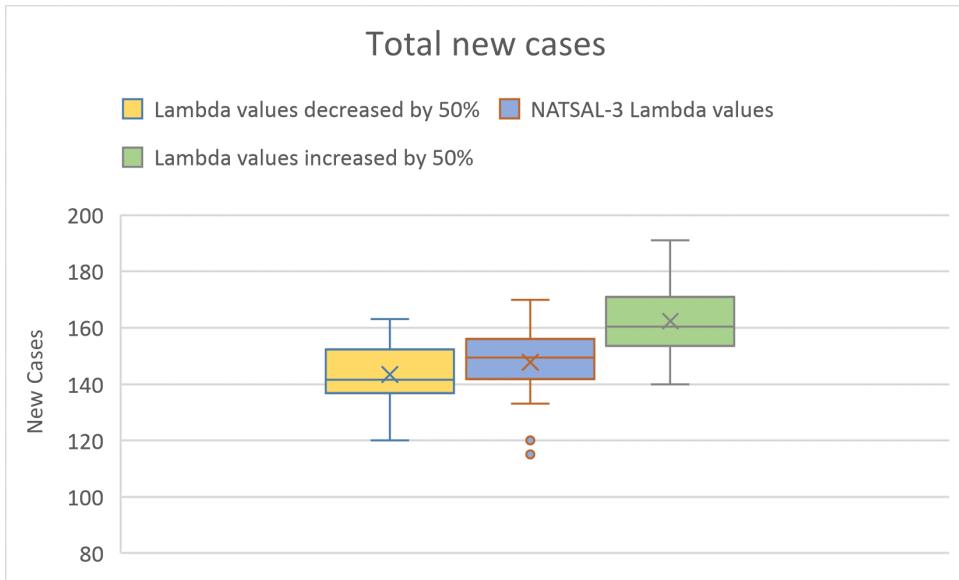


Figure 23: Boxplots of total of new cases for three scenarios: average number of homosexual MSM partners decreased by 50%, number of average partners remaining unchanged from NATSAL-3 data and average number of homosexual MSM partners increased by 50%

In figure 23 there appears to be a trend of the total number of new cases increasing on average as the number of average partners is increased and also as the total number of average partners is decreased the number of new mpox cases was observed to decrease on average. From the results of these simulations the average number of new cases from the reference model (Lambda values unchanged from NATSAL-3 data) was 147.8. Reducing the average contacts for homosexual men resulted in a decrease in the total new cases by 4.26 % to 143.4 cases. An increase in the average contacts of homosexual males by 50 % led to a 9.86 % increase in new cases to 162.4 new cases. As expected, an increase in average number of partners leads to an increase in number of cases.

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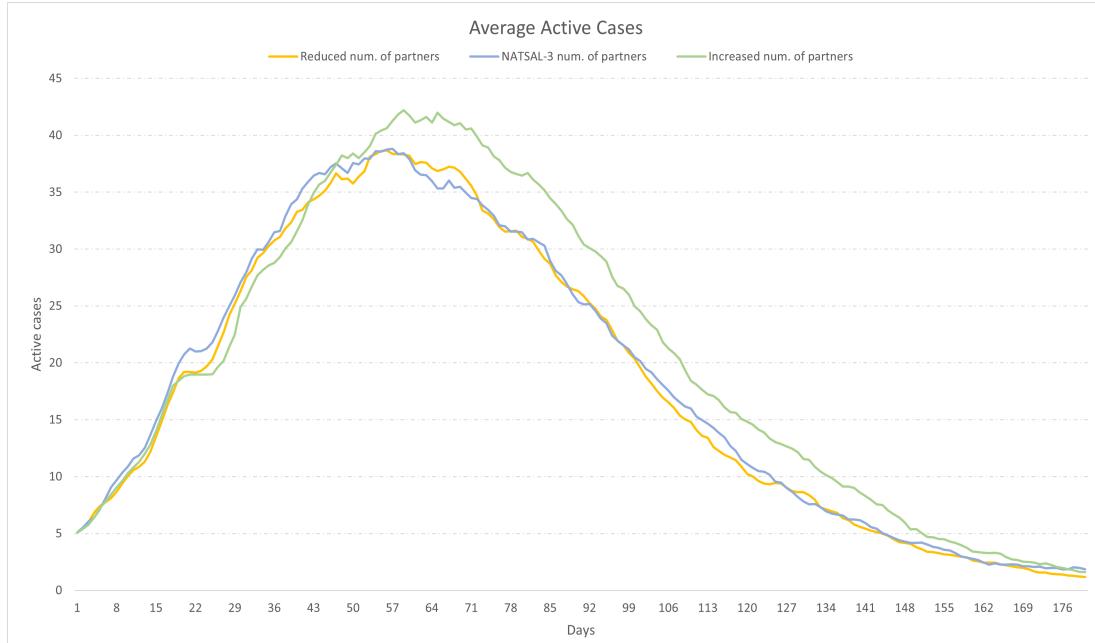


Figure 24: Average active cases over 30 simulations of the MSM model with the number of average main/long-term partners per year for homosexual MSM agents increased by 50 % and decreased by 50 %, compared with unchanged NATSAL-3 values for $\lambda_{s,a,p}$

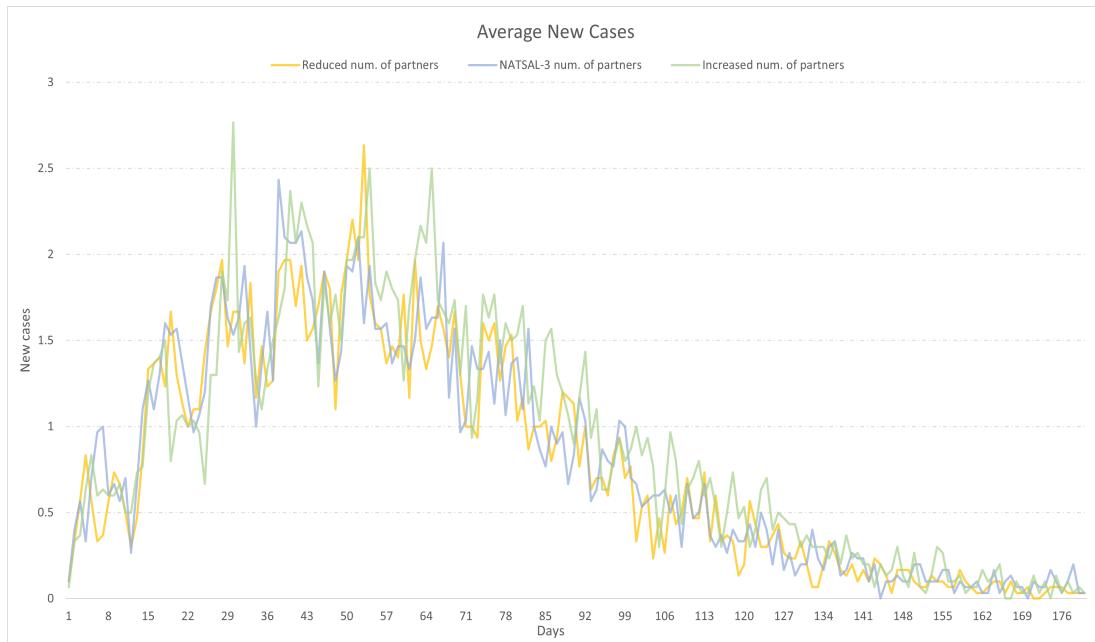


Figure 25: Average new cases over 30 simulations of the MSM model with the number of average main/long-term partners per year for homosexual MSM agents increased by 50 % and decreased by 50 %, compared with unchanged NATSAL-3 values for $\lambda_{s,a,p}$

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We can see in figure 24 and 25, that reducing the number of partners has only a minor effect on the number of cases and the total number of cases peaks at approximately 38 cases on average both when $\lambda_{s,a,p}$ is increased and when using the unchanged $\lambda_{s,a,p}$ values from the NATSAL-3 dataset. Increasing the number of partners per year by 50 % leads to an increase in the total amount infected and the amount of active cases reaches a higher peak of 42 cases. The peak of the infection appears to occur about 1-2 weeks later on average from observing figure 24. In figure 25, spikes in the plot show days where more “superspread” events took place leading to a large increase in case numbers. The spikes observed for keeping the number of partners constant or decreasing them by 50 % are of a similar magnitude on the plot. When the average number of partners is increased, the spikes of new cases are greater in magnitude than for the other 2 scenarios on the plot.

This result also shows that the number of main partners a homosexual agent has throughout the year has an effect on the propagation of mpox throughout the MSM population. A decrease in the number of partners has little effect on mpox spread, whereas an increase in the number of partners in the population leads to an almost 10 % increase in the total number of mpox cases on average from 30 simulations of the model for each $\lambda_{s,a,p}$ value. Superspread events and having several concurrent partners still appear to be the main cause of mpox spread in the MSM community and increasing the number of main/long-term partners throughout the year has a comparatively small effect on the number of new cases.

5.3 Superspread event parameters

In the model the number of individuals attending superspread events is fixed at an assumed value of 35. There is a scarce amount of data available to estimate this parameter. Relevant data could be obtained to get a better estimate on the number of superspread events per year through use of extensive contact tracing methods. However, there may be data privacy concerns regarding this kind of data.

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The number of superspreader events per year is also a difficult value to estimate for similar reasons as there is a mixture of these types of events such as ones organised through dating apps in private homes or ones organised in official venues such as saunas [21].

5.4 Model restrictions

Time to run the models can be very long, many of the simulations with population size of 10,000 took approximately 3-5 minutes to run, meaning 30 simulations could take a total of 90-130 minutes. The computational complexity of the model becomes tedious when there are many scenarios that one wishes to model. Because of this restriction, it is difficult to model large population sizes, since computational complexity scales linearly with population size for populations of size $N > 3000$. A combination of ABMs and other modelling approaches may be more suitable for attempting to model larger population sizes, e.g. examining how the model behaves for smaller populations (what R_e value is achieved for example) and then applying the results to a SEIR model.

Since an Agent based model is built from the ground up, it relies on many parameters to describe disease dynamics. Some parameters are very difficult (or even impossible) to measure or observe in real life, such as the transmission probability of the virus. Other parameters are very difficult to measure accurately due to ethical concerns or impracticalities regarding data collection (e.g. recording the number of people who attend superspreader events) and because of this, we often rely on data from online surveys and traffic on dating apps to try to determine some of the models' parameters. This approach to data collection may be biased towards younger generations as older generations are less likely to be involved in online forums and dating sites. Another problem with regards surveying people is depending on truthful, honest answers from respondents, which can be a problem when asking

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sensitive questions such as the number of sexual partners someone had in the previous month for example. People may not want to give an honest answer to a sensitive and personal question like this and in some cases like asking about the frequency of sex in the last 12 months, it can be difficult for respondents to rely on their memory to give a reliable response.

By applying the data on sex frequency in relationships between MSM men in the United States to the model, I made the assumption that the sex frequency in MSM groups is the same in the UK as it is in the USA. While in reality, it is quite likely that there are cultural and behavioural differences between countries that are ignored when applying the data from the USA to the NATSAL-3 based MSM model.

The uncertainty in the model's outputs can be remedied somewhat by applying confidence interval bounds on the output values, such as in figures 13, 14 and 15 where 95 % confidence intervals are displayed using error bars using the standard error as the error metric.

Agent-based models are met with a lot of criticism in some academic circles. A paper by Roberto Leonbruni and Matteo Richiardi in 2005 deems ABMs fit only for explorative purposes due to a lack of generality and the inability of ABMs to provide descriptions of models to the same level as analytical mathematical models [35]. They make some valid points in their paper, but in Epidemiology it is very important to explore different possibilities and ABMs provide a unique framework to explore simulating models with population mixing and other complex scenarios where it is important to assign different parameters to individual agents.

6 Conclusions

In this thesis I have examined differential equation based models and agent based models for mpox disease. The SEIR equation based approach gives an analytical result which can be fast to compute, is easily replicated and R_0 can be easily changed to investigate the trajectory of virus spread. Differential equation models assume a population which is homogeneously mixed.

Agent based models allow the modeller to specify how communities in the population mix, which is important as real-world social networks are formed of smaller communities and cliques which tend to mix with one-another more than outside of their own communities. Moving away from the homogeneously mixed population assumption allows the modeller to investigate the dynamics of the MSM community in further detail, which is crucial to understanding how mpox is spread and why mpox clade IIb predominantly affects members of the MSM community. The stochastic based nature of the agent based model approach models the random sense of events in the real world better, but at the cost of large computation times for larger populations.

The agent based models provide a good framework to investigate how different behavioural changes, relationships and events can shape a disease outbreak. The agent based approach to modelling is very applicable in the case of mpox since the mpox virus predominantly affects groups of people in the MSM community. It does not make sense to use a model for mpox spread that assumes that the population is homogeneously mixed given that the disease is predominantly spread in MSM populations and affects MSM men a disproportionate amount.

The Agent based model shows that superspreader events, where many short-term sexual encounters occur between MSM men, are the main cause of mpox spread in 2022. The effective reproductive number R_e ranged from 0 to 0.75 in the absence of superspreader events. Since $R_e < 1$, the outbreak is not sustained in the absence of

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superspread events. When the model was carried out simulating 30 superspread events per year, the effective R number was recorded to be between 1.44 and 1.86, leading to a simulated mpox outbreak similar to the observed world-wide mpox outbreak of 2022.

This thesis investigated the rate of sexual contact of MSM males in mid/long-term partnerships. The creator of the MSM models used in this paper, Hamda, assumed a weekly contact rate of 3 times per week in these partnerships. This value was replaced with a distribution of sex frequency rates taken from data from the USA. This resulted in a decrease in the average total cases by 13.8 % over 30 simulations with 30 superspread events compared to using the assumed rate of $\frac{3}{7}$.

The average number of main partnerships per year was increased and decreased by 50 % for homosexual men in the MSM community to investigate if this had any effect on the results. The results showed that increasing the average number of main partners by 50 % resulted in a 9.86 % increase in the total number of cases and decreasing the average number of main partners by 50 % led to a 4.26 % decrease in the total number of cases when the model was simulated with 30 superspread events.

The results show that the frequency of sex and number of partners per year that homosexual and bisexual men have per year impact the spread of the virus. This impact is minor in comparison to the effect of having concurrent casual partners and having sex with casual partners at superspread events like saunas or events arranged through dating apps which appears to be the main cause of mpox clade IIb spread from the results.

6 Conclusions

6.1 Further Study

Future applications of this model could include tuning the model parameters to Irish data from the HPSC and Irish Census data or using data from Belgium [57] to simulate mpox outbreaks in the Belgian population. Further research could include modelling more robust scenarios, e.g. including diagnosis delays into the model and using contact tracing data to estimate the number of attendees and frequency of superspreadер events.

Hamda's mpox models which were investigated in this thesis are very versatile models which can easily be adapted to model other populations or even different sexually transmitted diseases by changing parameters in the model to suit data of other populations or diseases.

These ABMs are very sensitive to network structure and NATSAL-3 data. In order to improve these models further, using contact tracing to better understand the network structure of the MSM community is vital. The publication of mpox data by public health bodies such as the HPSC would also be very beneficial in fine tuning model parameters. A better understanding of the parameter values and the network structure in the model would lead to more accurate predictions by the model which could play an important role in managing outbreaks of infectious diseases like mpox or other sexually transmitted diseases in the future.

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Appendix: NetLogo Code

Appendix: NetLogo Code

Modified MSM model code:

```
; exposed = pre symptomatic
breed [female-partners female-partner]
breed [msms msm]
extensions [matrix]
undirected-link-breed [lt-homo-links lt-homo-link]
undirected-link-breed [lt-het-links lt-het-link]
undirected-link-breed [st-links st-link]
msms-own
[
  contact-rate
  sexual-preference
  high-risk
  age
  age-days
  new_partners_per_year
  vaccinated?

  disease-status
  days_sick
  days_exposed
  sick-period
  incubation_period
  isTravelCase

  age-cohort ; from 0 to 15 , min age 16, max age 75
  brokenUp? ; set to true if just borken up and has to find new
               immediately

  infected_by
  day_I_got_sick
  day_infecto_got_sick

  numinfected
]
female-partners-own
[
  contact-rate
  disease-status
  days_sick
  days_exposed
  sick-period
  incubation_period
  vaccinated?
  infected_by
  day_I_got_sick
```

Appendix: NetLogo Code

```
day_infector_got_sick
numinfected

]

globals
[
    age-mix-agg

    lambda-homo
    lambda-bi-same-sex
    lambda-bi-opp-sex
    bi_prob_same_sex

    max-partners
    min-partners

    min-age
    max-age

    weekly_contact

]

to set-global-vars
    set min-age 16
    set max-age 74
    set weekly_contact 3

end

to load-age-mix ; all categories, male, females, hetero, homo, bi
    ; 0 row is age-cohort 16-19
    ; 1 row is age-cohort 20-23 and so on
    set age-mix-agg matrix:from-row-list [
        [ 0.747831829 0.177305409 0.049992136 0.014708313 0.007019141
            0.001151133 0.001095006 0.00041946 0.000476774 0 0 0 0 0 0 ]
        [ 0.231047208 0.490546778 0.185653325 0.057908237 0.022356877
            0.007148993 0.003917986 0.001317601 0 0.000102724 0 0 0 0 0 0 ]
        [ 0.127933614 0.21435767 0.4001897 0.14443666 0.078122539
            0.019691981 0.009961396 0.002309779 0.002996109 0 0 0 0 0 0 ]
        [ 0.076001244 0.16038241 0.280802333 0.262387001 0.116114574
            0.034741706 0.037985451 0.021671947 0.003505733 0.000852436
            0.005555166 0 0 0 0 ]
        [ 0.040796399 0.122034949 0.156768675 0.249481921 0.192635573
```

Appendix: NetLogo Code

```

    0.106408415 0.071892102 0.038002785 0.011678285 0.003363232
    0.00496565 0.001972014 0 0 0 ]
[ 0.046525192 0.10283495 0.130889686 0.115870047 0.192866939
    0.161486445 0.133942873 0.064003387 0.024135176 0.019019923
    0.003787471 0.002642426 0 0 0.002660646 ]
[ 0.006346823 0.019760219 0.03678893 0.064084986 0.117526889
    0.210149343 0.247059086 0.173584578 0.07977703 0.023804868
    0.016404244 0 0.002626774 0 0.002781639 ]
[ 0.012645278 0.01132567 0.075765226 0.07082388 0.13859355
    0.117767443 0.180830415 0.22852376 0.108886271 0.021504307
    0.0333342 0 0 0 0 ]
[ 0.026439486 0.042959568 0.036182116 0.03214682 0.046332086
    0.071440982 0.208081498 0.20870304 0.193550598 0.086363269
    0.027714186 0.020086352 0 0 0 ]
[ 0 0 0 0 0.077041259 0.12508842 0.160885877 0.045030504 0.225861297
    0.137573529 0.178896382 0.042103777 0.007518954 0 0 ]
[ 0 0 0.061103034 0.050863023 0.032146605 0.063440383 0.188836193
    0.055444896 0.164926323 0.070105275 0.172241693 0.09067874
    0.021798034 0.028415801 0 ]
[ 0 0 0 0.150701142 0.018506024 0.019569801 0.063931694 0.058109094
    0.211889124 0.16732933 0.087347778 0.125179978 0.097436034 0 0 ]
[ 0.045594308 0 0.026424301 0.052848602 0 0 0.023079258 0.023580197
    0 0.081017046 0.0779076 0.351577669 0.27334111 0.024811683
    0.026424301 ]
[ 0 0 0 0 0.064995283 0 0.066197868 0.115064423 0 0 0.073991064
    0.286523556 0.393227806 0 ]
[ 0 0 0 0 0 0 0 0 0 0 0 0.324660919 0.283416828 0.522563003 ]

]

end
to load-lambda

    set lambda-homo matrix:from-row-list ; replace NAN by 0
    [
[ 1.7 1.7 ]
[ 1.3 0.75 ]
[ 0.625 0.4286 ]
[ 3 0 ]
[ 7.3333 0 ]
[ 4.6667 0 ]
[ 4.5 0 ]
[ 6.6667 0 ]
[ 0 1 ]

```

Appendix: NetLogo Code

```
[ 0 0 ]
[ 1.3333 0 ]
[ 0 0 ]
[ 0 0 ]
[ 0 0 ]
[ 5 0 ]

]

set lambda-bi-same-sex matrix:from-row-list
[[ 0.9375 0.4444 ]
[ 1.5238 0.5679 ]
[ 0.6522 0.1667 ]
[ 2.9231 0.1789 ]
[ 1.05 0.1167 ]
[ 9.3636 0.3077 ]
[ 0.2727 0.1212 ]
[ 1.375 0.2059 ]
[ 0.2143 0.0714 ]
[ 0.0588 0.2105 ]
[ 0.7368 0.1 ]
[ 0.5417 0 ]
[ 0 0 ]
[ 0.25 0 ]
[ 0 0 ]
]

set lambda-bi-opp-sex matrix:from-row-list
[
[0.6250 1.4889]
[0.9524 1.5926]
[ 1.1304 0.7619]
[0.3077 0.6526]
[1.0500 0.5833]
[0.8182 0.5000]
[2.0000 4.9091]
[0.5000 0.7647]
[0.2143 0.2143]
[0.2941 0.1053]
[0.2632 0]
[0.5417 0.1818]
[ 0 0.4286]
[0.1250 0]
```

Appendix: NetLogo Code

```
[ 0 0]

]

set bi_prob_same_sex matrix:from-row-list
[
  [ 0.6000 0.2299]
  [0.6154 0.2629]
  [0.3659 0.1795]
  [0.9048 0.2152]
  [0.5000 0.1667]
  [0.9196 0.3810]
  [0.1200 0.0241]
  [0.7333 0.2121]
  [0.5000 0.2500]
  [0.1667 0.6667]
  [0.7368 1.0000]
  [0.5000 0]
  [ 0.5 0]
  [0.6667 0.5]
  [0.5 0.5] ; changing some NAN to 0.5

]

end

to create-population
  ; 36.3% bi men and 63.6% homo men
  let homo-men round population * 63.6 / 100
  let bi-men round population * 36.3 / 100

  create-msms population
  [
    set infected_by nobody
    set brokenUp? FALSE
    set age min-age + (random (max-age + 1 - min-age))
    set age-days 1 + random 365
    set age-cohort cohort-from-age age
    set vaccinated? FALSE
```

Appendix: NetLogo Code

```
ifelse random-float 1 < .363
[
  set sexual-preference 3
]
[
  set sexual-preference 2
]
setxy random-xcor random-ycor

set-disease-status(1)
set high-risk FALSE

let num random-float 1

ifelse num < 0.009 [
  set contact-rate 0.01923
]
[ifelse num > 0.009 and num < 0.067 [
  set contact-rate 0.09615
]
[ifelse num > 0.067 and num < 0.124 [
  set contact-rate 0.2115
]
[ifelse num > 0.124 and num < 0.203 [
  set contact-rate 0.4423
]
[ifelse num > 0.203 and num < 0.406 [
  set contact-rate 0.673
]
[ifelse num > 0.406 and num < 0.615 [
  set contact-rate 0.9807
]
[ifelse num > 0.615 and num < 0.804 [
  set contact-rate 2.981
]
[if num > 0.804 [
  set contact-rate 3.846
]
]]]]]]]

ask msms
[
```

Appendix: NetLogo Code

```
update-lambda

]

update-risk

end

to update-risk
; take top 5% msms with highest number of new partners
; set them as high-risk

let number %high_risk * count msms / 100
ask max-n-of number msms [new_partners_per_year] [ set high-risk
TRUE]

end

to SuperSpreaderEvent ; function to model random events where
intimate contact increases
; output-print "party today"
; let total_partygoers count turtles with [partygoer? = TRUE]
let partypeople1 no-turtles
let n count msms with [high-risk = TRUE]
let p 35
if (n < p)
[set p n]
set partypeople1 n-of p msms with [high-risk = TRUE ]

output-print p
output-print "people going to party today"

let joinset (turtle-set partypeople1)

output-print "People going to party today who are infected: "
output-print count joinset with [disease-status = 3]

; output-print count joinset with [disease-status = 3]
ask joinset with [disease-status = 3]
[
  create-st-links-with other joinset
```

Appendix: NetLogo Code

```
]

ask st-links
[
  set color pink
; stop
]
;stop
end
to party-end

ask st-links
[die]
end
to-report cohort-from-age [my-age]
  let cohort floor ((my-age - 16) / 4)
  report cohort
end

to go

go-age
ask msms; with [count link-neighbors > 0]
[
  change-relationship-status
]

ask msms with [brokenUp? = TRUE]
[
  get-partners
]

if (SuperspreadEventsPerYear > 0)
[
  if (ticks mod (floor ( 364 / SuperspreadEventsPerYear)) = 0)
  [
    SuperSpreaderEvent
  ]
]

if (ImportedCasesPerYear > 0)
[
  if (ticks mod (floor ( 364 / ImportedCasesPerYear)) = 0)
  [
    ; output-print ticks
  ]
]
```

Appendix: NetLogo Code

```
    TRAVEL
]
]

SEIR

party-end

if ticks >= 180
[
  print CalculateR
  stop

]

tick

end
to women-die
  ask female-partners with [ count lt-het-link-neighbors = 0]
    [die]
end
to TRAVEL
; if random-float 1 < (TravelRelatedCasesPerYear / 365)
; [
  if any? msms with [high-risk = TRUE]
  [
    output-print "New Travel Related Case"

    ask one-of msms with [high-risk = TRUE]
    [
      if (disease-status = 1 and vaccinated? = FALSE)

      [
        set-disease-status(2) ; exposed after travel
        set isTravelCase TRUE ; new change (2/05/2023)
      ]
    ]
  ]
;
]
```

Appendix: NetLogo Code

```
end
to stay-sick
  set days_sick days_sick + 1
end

to contract-disease-normal [digs infector]
  let prb 1

  ifelse breed = female-partners ;and mybreed = msms ;mysex = 1 and
  sex = 1
  [
    set prb Transmission_probability * (weekly_contact / 7) ;
    retain weekly contact rate assumption for female-partners
    for simplicity
  ]

  [ifelse vaccinated? = FALSE
  [
    set prb Transmission_probability * (contact-rate / 7) ; old
    assumption was assuming a couple comes in contact 3 times
    a week
  ]
  [
    set prb 0
  ]
]

  if breed = msms ;and mybreed = msms ;mysex = 1 and sex = 1
  [
    set prb prb * TP_multiplier_for msm ; if increase
    transmission in msm
  ]

  if random-float 1 < prb
  [
    set day_infector_got_sick digs
    set infected_by infector
    set-disease-status(2) ; expose link neighbors
  ]
end

to contract-disease-through-party [digs infector]
  let prb 1
  ifelse vaccinated? = FALSE
```

Appendix: NetLogo Code

```
[  
  set prb Tranmission_probability  
]  
[  
  set prb 0;attack_rate * (1 - vaccine_efficiency) ; assuming a  
  couple comes in contact 5 times a week and force of attack  
  is 80% and vaccine is 85% effective ;; check  
]  
  
; if mysex = 1 and sex = 1  
; [  
if breed = msms  
[  
  set prb prb * TP_multiplier_for msm ; increase transmission  
  in msm  
  
]  
  
; let pr1 random-float 1  
;output-print pr1  
  if random-float 1 < prb  
  [  
    set infected_by infector  
    set day_infector_got_sick digs  
    set-disease-status(2) ; expose link neighbors  
  ]  
end  
to SEIR  
; output-print count turtles with [disease-status = 3 and partygoer?  
= TRUE]  
ask turtles with [disease-status = 3]  
[  
  let ds day_I_got_sick  
  let infector self  
  
; let mysex sex  
; let sex 1  
if breed = msms  
[  
  ask lt-homo-link-neighbors with [disease-status = 1] ; only  
  susceptible to be exposed  
  [  
    contract-disease-normal ds infector  
  ]  
  ask lt-het-link-neighbors with [disease-status = 1] ; only  
  susceptible to be exposed
```

Appendix: NetLogo Code

```
[  
  contract-disease-normal ds infector  
]  
ask st-link-neighbors with [disease-status = 1] ; only  
  susceptible to be exposed  
[  
  
  contract-disease-through-party ds infector  
]  
]  
  
ifelse days_sick <= sick-period  
[  
  stay-sick  
]  
[  
  set-disease-status (4)  
]  
  
]  
ask turtles with [disease-status = 2]  
[  
  ifelse days_exposed <= incubation_period  
  [  
    stay-exposed  
  ]  
  [  
  
    set-disease-status (3)  
  ]  
  
]  
;  
;; check party people  
  
end  
  
to stay-exposed  
  set days_exposed days_exposed + 1  
end  
  
to update-lambda ; turtle procedure since only dealing with msms so  
  sex is always 1  
  
  let cohort cohort-from-age age
```

Appendix: NetLogo Code

```
let lambda 0
let sex 1
if sexual-preference = 2
[
  set lambda matrix:get lambda-homo cohort (sex - 1)
]
if sexual-preference = 3
[
  set lambda matrix:get lambda-bi-opp-sex cohort (sex - 1) +
    matrix:get lambda-bi-same-sex cohort (sex - 1)
]
set new_partners_per_year random-poisson lambda
end

to change-relationship-status ; basically break up first

let prob 1 - exp( -1 * ((new_partners_per_year / 365) + (0.1 / 365)
)) ; daily probability
if random-float 1 < prob
[
  breakup
  set brokenUp? TRUE

]

end

to breakup
ask lt-het-link-neighbors
[
  if breed = female-partners
  [
    ; output-print "agent dying"

    ; die
  ]
]

if count my-links > 0
[
  ask my-links
  [
```

Appendix: NetLogo Code

```
; output-print "breakup"
die

]
]

end
to setup
  clear-all
  reset-ticks
  set-global-vars
  load-lambda
  load-age-mix
  create-population
  initial-infection
  initial-relationships
  initial-vaccination
end
to initial-vaccination

  let really_vaccinated People_vaccinated
  if (Vaccination_Programme = "None")
  [
    ;output-print "no one vacc"
    set People_vaccinated 0
    ; do nothing.
    stop
  ]
  if (Vaccination_Programme = "RandomAll")
  [
    set really_vaccinated round (vaccine_efficiency *
      People_vaccinated)
    ask n-of really_vaccinated msms with [disease-status = 1] ; leave
      already infected alone
    [
      set vaccinated? TRUE
      set color green

    ]
  ]

  if (Vaccination_Programme = "RandomHighRisk")
  [
    let n count msms with [high-risk = TRUE and disease-status = 1];
    if n < People_vaccinated
    [
      set People_Vaccinated n
```

Appendix: NetLogo Code

```
]
ask n-of People_vaccinated msms with [disease-status = 1 and
high-risk = TRUE]
[
  set vaccinated? TRUE
  set color green

]
]

end

to set-disease-status [status]
  set disease-status status
  if disease-status = 1
  [
    set color yellow
    get-susceptible

  ];susceptible]

  if disease-status = 2
  [
    set color orange
    get-exposed

  ];exposed]
  if disease-status = 3
  [
    set color red
    get-sick
  ]
  if disease-status = 4
  [
    set color blue ; recovered help
  ];recoverd

end

to initial-infection
  ask n-of initially_infected MSM msms with [high-risk = TRUE];
  [age-cohort >= 2 and age-cohort <= 5 ] ;and sex = 1 and
  sexual-preference > 1]
  [
    set-disease-status 3
```

Appendix: NetLogo Code

```
    set infected_by nobody
]

end

to get-susceptible

    set days_sick 0
    set days_exposed 0
    set sick-period 0
    set incubation_period 0
end

to get-exposed
    set incubation_period (round (random-weibull 1.5 8.4)) ;
    set days_exposed 1
    set days_sick 0
end

to get-sick
; set-disease-status 3
    set days_sick 1
    set days_exposed 0
    set sick-period round(random-normal mean_infectious_period 2) ;
        2 - 4 weeks
    output-print sick-period

    set day_I_got_sick ticks; + random 4 ; because here being sick
        means being infectious

    let ser_int day_I_got_sick - day_infector_got_sick
end

to recover

    set days_sick 0
    set days_exposed 0
    set sick-period 0
    set incubation_period 0
    set isTravelCase FALSE
end

to find-partner [potential-partners]
```

Appendix: NetLogo Code

```
let my-age age
let my-cohort cohort-from-age my-age
; let mysex sex
let selected-partner-cohort partner-age my-age

let found? false
let new-partner no-turtles
if any? potential-partners with [age-cohort =
    selected-partner-cohort and count link-neighbors = 0]
[
  breakup
  ask n-of 1 potential-partners with [age-cohort =
      selected-partner-cohort and count link-neighbors = 0]
  [
    ifelse breed = msms
    [create-lt-homo-link-with myself]
    [create-lt-het-link-with myself]
  ]
  set brokenUp? FALSE
]

]
end

to-report age-from-cohort [cohort]
let this-age cohort * 4 + 16 + random 4
report this-age
end

end
to initiate-homo-relationship ; have to add age mixing matrices here
later
let my-age age

let potential-partners no-turtles

if any? other msms ;with [sex = 1 and (sexual-preference = 2 or
sexual-preference = 3)];and count link-neighbors = 0]
[
  set potential-partners other msms; with [sex = 1 and
  (sexual-preference = 2 or sexual-preference = 3)]; and count
  link-neighbors = 0]
]
```

Appendix: NetLogo Code

```
find-partner potential-partners

; ]
end

to initiate-bi-relationship ; have to add age mixing matrices here
  later
  let my-age age
  let cohort cohort-from-age my-age
  let same-sex? TRUE
  let same-sex_prob matrix:get bi_prob_same_sex cohort 1; always
    msms now(sex - 1)
  ifelse random-float 1 < same-sex_prob
  [
    set same-sex? TRUE
  ]
  [
    set same-sex? FALSE
  ]

let potential-partners no-turtles

ifelse same-sex? = TRUE ; men to men
[
; output-print "bi and hom"
  if any? other msms; with [sex = 1 and (sexual-preference = 2
    or sexual-preference = 3)] ; look at homo and bi men
  [
    set potential-partners other msms; with [sex = 1 and
      (sexual-preference = 2 or sexual-preference = 3)]
  ]
  find-partner potential-partners
]

]

[

  create-new-female-partner
]

end

to create-new-female-partner
```

Appendix: NetLogo Code

```
breakup
hatch-female-partners 1
[
  set color pink
  set shape "bug"

  create-lt-het-link-with myself
  set-disease-status(1)
]
set brokenUp? FALSE

end
to initial-relationships
  ask msms ; lets assume 80% are currently in a relationship
  [
    if random-float 1 < 0.5 ; reduce to 0.4 because they are in pairs
    [
      ; output-print count link-neighbors
      if count link-neighbors = 0
      [
        get-partners
      ]
    ]
  ]
]

end

to get-partners
; output-print count link-neighbors
  if sexual-preference = 2
  [initiate-homo-relationship]
  if sexual-preference = 3
  [initiate-bi-relationship]

end

to go-age
  let dead 0
  ask msms
  [
    ;output-print age
    set age-days age-days + 1
    if age-days > 365
    [
      set age-days 1
    ]
  ]
]
```

Appendix: NetLogo Code

```
set age age + 1
set age-cohort cohort-from-age age
ifelse age <= max-age
[
  update-lambda
]
[
  set dead dead + 1
  die
]
]
create-msms dead
[
  ifelse random-float 1 < .363
  [
    set sexual-preference 3
  ]
  [
    set sexual-preference 2
  ]
  set age min-age
  set age-days 1
  setxy random-xcor random-ycor
  set color yellow
  set-disease-status 1
  set vaccinated? FALSE
]

end

to-report partial-sums [lst]
report butfirst reduce [[result-so-far next-item] -> lput (next-item
+ last
result-so-far) result-so-far] fput [0] lst
end

to-report partner-age [my-age]
let prob random-float 1
let cohort cohort-from-age my-age
let probabilities matrix:get-row age-mix-agg cohort
let cum-pmf partial-sums probabilities
let n random-float 1
report length filter [ [?1] -> ?1 < n ] cum-pmf ; indexing starts
at 0
```

Appendix: NetLogo Code

```
end

to-report TotalInfectedPop
  report count turtles with [disease-status = 3]
end
to-report TotalNewInfectedPop
  report count turtles with [disease-status = 3 and days_sick = 1 ]
end

to-report NewInfectedMSM
  report count msms with [disease-status = 3 and days_sick = 1]
end

to-report AllInfectedMSM
  report count msms with [disease-status = 3]
end

to-report NewInfectedFemales
  report count female-partners with [disease-status = 3 and
    days_sick = 1]
end

to-report AllInfectedFemales
  report count female-partners with [disease-status = 3]
end

to-report NewInfectedAge [c]
  report count msms with [disease-status = 3 and days_sick = 1 and
    age-cohort = c]
end

to-report AllInfectedAge [c]
  report count msms with [disease-status = 3 and age-cohort = c]
end

to-report AllInfectedHighRisk
  report count msms with [disease-status = 3 and high-risk = TRUE]
end

to-report NewInfectedHighRisk
  report count msms with [disease-status = 3 and high-risk = TRUE
    and days_sick = 1]
```

Appendix: NetLogo Code

```
end

to-report AllInfectedLowRisk
  report count msms with [disease-status = 3 and high-risk = FALSE]
end

to-report NewInfectedLowRisk
  report count msms with [disease-status = 3 and high-risk = FALSE
    and days_sick = 1]
end

to-report weibull-test [shp scl]
  let n 0
  let sum_ 0
  while [n < 1000000]
    [ set sum_ sum_ + random-weibull shp scl
    set n n + 1 ]

  report sum_ / 1000000

end

to-report random-weibull [shp scl]
  let result round ( scl * (-1 * ln (random-float 1)) ^ (1 / shp))

  report result
end

to TimeVaryingR
  let timeVaryingRt []
  let time_stamps []
  let i 1
  loop [
    ifelse i = ticks
    [
      file-open "Rt_MSModel.txt"
      file-print behaviorspace-run-number
      file-print timeVaryingRt
      file-close
      stop
    ]
    [
      ; output-print i
    ]
  ]

```

Appendix: NetLogo Code

```
let Rt_today []  
  
ifelse count turtles with [disease-status = 4 and day_i_got_sick  
= i and infected_by != nobody] > 0  
[  
  ask turtles with [disease-status = 4 and day_i_got_sick = i  
  and infected_by != nobody] ;Rt should only be calculated  
  for msms because theres no mechanism for women to transmit  
  inf  
  [  
    set Rt_today lput numinfected Rt_today  
  ]  
  set Rt_today mean Rt_today  
  set timeVaryingRt lput Rt_today timeVaryingRt  
  set time_stamps lput i time_stamps  
]  
]  
[  
  set Rt_today lput 0 Rt_today  
  set timeVaryingRt lput Rt_today timeVaryingRt  
  set time_stamps lput i time_stamps  
]  
set i i + 1  
]  
]  
  
end  
  
to-report calculateR  
let R_est -1  
ask turtles with [ disease-status = 4 ] ;and infected_by != nobody  
[  
  set numinfected count turtles with [  
    infected_by = myself  
  ]  
]  
;  
;; If there are any agents who have recovered and were not the  
initially infected agents creates a list of count of agents
```

Appendix: NetLogo Code

```
infected by each of the recovered agents and then finds the
average of the list.

if count turtles with [ disease-status = 4 and infected_by != nobody] > 0
[
  let infectedbycase []
  ask turtles with [ disease-status = 4 and infected_by != nobody]
  [
    set infectedbycase lput numinfected infectedbycase
  ]
  set R_est mean infectedbycase
]
report R_est

end

to-report NewTravelCases
  report count msms with [disease-status = 3 and isTravelCase = TRUE
    and days_sick = 1 ]
end

to-report InfectedPop
  report count turtles with [disease-status = 3 ]
end

to-report RecoveredPop
  report count turtles with [disease-status = 4 ]
end

to-report TotalNewInfectedMSM
  report count msms with [disease-status = 3 and days_sick = 1]
end

to-report TotalNewInfectedMSMSexPref [sp]
  report count msms with [disease-status = 3 and sexual-preference =
    sp and days_sick = 1]
end

to-report PercentageNewInfectedMSM
  let n count msms with [disease-status = 3 and days_sick = 1]
  ifelse n = 0
  [report n]
  [report count msms with [disease-status = 3 and days_sick = 1] / n
  ]
end

to-report TotalInfectedAge [ac]
  report count msms with [disease-status = 3 and age-cohort = ac]
```

Appendix: NetLogo Code

```
end

to-report TotalNewInfectedAge [ac]
  report count msms with [disease-status = 3 and age-cohort = ac and
    days_sick = 1 ]
end

to-report PercentageNewInfectedMSMSexPref [ sp]
  let n count msms with [disease-status = 3 and days_sick = 1 ]
  ifelse n = 0
  [
    report 0
  ]
  [
    report count msms with [disease-status = 3 and sexual-preference
      = sp and days_sick = 1 ] / n
  ];
end

to-report TotalNewInfectedFemales
  report count female-partners with [disease-status = 3 and
    days_sick = 1]
end
```