**Methods**

We used a previously described dynamic network model of sexually associated monkeypox virus transmission in MSM [2,4,5], with parameters updated based on nationally distributed surveys of sexual behavior among MSM from 2017-2019 (the ARTnet study) [6]. This model simulates the 167,000 MSM living in NYC, and a changing network of sexual partnerships between them. We model three types of sexual partnerships: individuals in our model can have 0 or 1 ‘Main’ partners (defined as enduring sexual partners who took priority over others), between 0 and 3 ‘Casual partners’ (defined as enduring sexual partners besides the main partner), and 0 or 1 ‘one-time’ partners per timestep (defined as partners without repeat sexual contact). For each timestep in the model, enduring partnerships have a probability of forming and dissolving, and individuals have a probability of engaging in one-time partnerships based on their assignment to one of 6 sexual activity groups, with activity group 1 representing the lowest sexual activity level (40% of the population, < 0.1% chance of engaging in one-time partnerships) and activity group 6 representing the highest sexual activity level (1% of the population, 37% chance of engaging in a one-time partnership per day). All network parameters can be found in Table S1.

We used an SEIR (susceptible, exposed, infectious, resistant) natural history in our model, expanded to account for pre-symptomatic transmission and multi-dose vaccination [7]. Individuals start in the susceptible () class. An infectious individual has a probability of infecting a susceptible partner given by the probability of sexual contact per timestep multiplied by the probability of infection per sexual exposure . Upon acquiring infection, individuals enter a pre-symptomatic non-infectious state , after which they have a probability per day of entering the pre-symptomatic and infectious state (), then the symptomatic and infectious state , and finally the recovered and resistant state . Individuals can also be vaccinated with 1 () or 2 () doses of the vaccine, with effects described below. Symptom onset reduces sexual contact rate with ‘main’ and ‘casual’ partners by 50% and causes individuals to move to one lower sexual activity level until they recover. A proportion of individuals, , will test for mpox days after they develop symptoms, with based on the date-varying time between reported symptom onset and mpox tests in case data. After a positive mpox test, individuals become aware of their infection status, and no longer transmit the virus through sexual activity. Individuals who learn their infection status sustain contact with their ‘main’ partner such that they have a 10% chance of infecting their ‘main’ partner over the duration of the infection, reflecting prior estimates of household transmission [8]. Infected individuals who seek medical care are reported as diagnosed cases, hereafter referred to as *cases*.

We initiated the model by introducing 5 newly exposed individuals into the three highest sexual activity groups (most active 15% of population) on May 14th. This produced a median of 5 cumulative cases in the model on May 31st, matching case data from NYC.

Our network does not account for potential periods of increased sexual activity associated with the high frequency of MSM gatherings (e.g., pride festivals) throughout the summer. Additionally, we assume that importation of mpox cases from countries impacted by mpox prior to the outbreak in the United States may have fed the initial surge of mpox cases. Thus, we model a ‘surge period’ for the initial period of our simulations during which we add extra-network transmission to the model to represent transmission occurring during MSM gatherings and import additional infections into the network to represent travel related infection. The duration of the surge period is determined by our fitting process, below. For extra-network transmission, we assume an additional number of infections per day equal to

Where is the number of high activity individuals (activity groups 4-6), and are the number of pre-symptomatic and symptomatic infectious high activity individuals, respectively, is the total number of high activity individuals, and is the extra network transmission rate. For importation, we randomly select individuals in the top three sexual activity groups to enter the state at a constant rate, . , , and the length of the surge period are determined by our fitting procedure, described below.

Over the course of each simulation, individuals decrease their probability of one-time partnerships and their rate of sexual contact with casual partners as a function of perceived risk of mpox [9]. We parameterize this perceived risk based on frequency of mpox discussion on online LGBT+ discussion forums over time, as discussed by Clay et al. [5], and fit the magnitude of this behavioral adaptation to incident case report data (see fitting procedure below).

*Vaccination*

We ran a scenario where first and second doses administered per week matched those reported by NYC through March 18, 2023.

While MSM, transgender, gender non-conforming and non-binary adults (TGNCNB) with multiple sexual partners were all initially eligible for mpox vaccination, we only model MSM due to availability of sexual network data [6]. According to a 2020 citywide population-based survey, MSM made up 82% of MSM and TGNCNB adults in NYC with 2+ sexual partners over a 12-month period [10]. Thus, we assume that 82% of mpox vaccines administered in NYC were administered to MSM in our model.

As vaccines were originally intended for selected groups, including individuals with multiple recent sexual partners [11], we only vaccinate individuals in the top three sexual activity groups for the first four weeks of vaccination, only vaccinate individuals in the top four sexual activity groups for the next two weeks of vaccination, and only vaccinate individuals with a non-zero probability of engaging in one-time sexual partnerships for the rest of the simulation. In our model, susceptible and pre-symptomatic individuals are eligible for vaccination. However, vaccination does not prevent individuals in the or class from becoming infectious. Individuals are eligible for second doses of the vaccine if they have received their first dose at least four weeks in the past. In the case of breakthrough infections (i.e. infections of vaccinated individuals), we assume these individuals enter the pre-symptomatic class, i.e., prior vaccination has no effects on subsequent contagiousness or pathogenicity.

Several studies have estimated the effectiveness of the JYNNEOS vaccine, i.e., the proportional reduction in infection probability due to vaccination over a given period of time [e.g. 12]. However, vaccination in our model is implemented as vaccine *efficacy*, i.e. the per-exposure reduction in transmission probability due to vaccination. We thus rely on values of vaccine efficacy estimated by fitting mathematical models to vaccine administration and case data from X U.S. counties [13]. This method estimates values of 75% for first-dose efficacy and 89% for second-dose efficacy. We assume that doses become effective two weeks after administration.

*Fitting Process*

Our model has five free parameters whose values were informed via fitting: (1) the duration of the surge period (‘surge duration’), (2) the importation rate of infections during the surge period (‘importation rate’), (3) the transmission rate during extra-network MSM gatherings during the surge period (‘surge transmission’), (4) the probability of transmission per exposure (‘transmission probability’), and (5) the maximum percent reduction in probability of one-time or casual sexual contact per day in response to perceived risk of mpox (‘behavioral adaptation’). We fit these parameters to incident daily cases in NYC using a 5-step process.

First, we used Latin Hypercube Sampling (LHS) to generate 1,000 unique parameter sets of our five fit values (see Table 1 for prior ranges). Second, we simulated a single run of outbreak dynamics under the baseline ‘first-dose priority’ strategy employed by NYC for each LHS-generated parameter set from May 14, 2022 to January 18, 2023 (250 simulated days). Third, we filtered out parameter sets which predicted a final cumulative case incidence outside of that observed in NYC +/- 50%. Fourth, for each remaining parameter set, we calculated the likelihood that the simulated number of incident daily cases could generate the observed number of incident daily cases through Jan 18 using a negative binomial probability distribution. Finally, we drew 100 parameter sets (with replacement) with the calculated likelihood used as the relative draw probability for each parameter set. These 100 drawn parameter sets represent the posterior distributions of our fit parameters.

For each of these 100 parameter sets, we ran each of our vaccine model scenarios from May 14, 2022 to May 14, 2023 and compared median and interquartile ranges of cumulative cases over time for each vaccine administration strategy. We additionally ran a counterfactual model scenario where no vaccines were administered to measure the total percent of cases averted by vaccination compared to the ‘first-dose priority’ strategy (baseline model).

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Table 1: Model parameters. Values marked ‘Prior’ represent the prior range of values for our fitting procedure. Values marked ‘Posterior’ represent the median and interquartile range of values fit to case data.

|  |  |  |
| --- | --- | --- |
| **Parameter Description** | **Value** | **Source** |
| Initial Conditions | | |
| Population size | 167,000 | EpiQuery - Community Health Survey 2020: NYC Department of Health and Mental Hygeine. |
| Initial number infectious individuals | 5 | Model Assumption |
| Date seeded with initial infections | May 14th | Selected to align date of 5 cases in median model output and case reports |
| Surge Period Parameters | | |
| Surge Duration (days) | Prior: [45 – 130]  Posterior: 82 [65 – 106] | Fit to case report data |
| Importation Rate (importation rate of infections during the surge period) | Prior: [0 – 3]  Posterior: 2.0 [1.4 – 2.5] | Fit to case report data |
| Surge Transmission (transmission rate due to extra-network MSM gatherings during the surge period) | Prior: [0 – 0.5]  Posterior: 0.17 [0.13 – 0.23] | Fit to case report data |
| Natural History Parameters | | |
| Transmission Probability (Probability of transmission per sexual contact) | Prior: 10% – 90%  Posterior: 57% [47% – 78%] | Fit to case report data |
| Mean duration of post-exposure, pre-symptomatic period | 7.6 days | Charniga K, Masters NB, Slayton RB, et al. Estimating the incubation period of monkeypox virus during the 2022 multi-national outbreak. medRxiv. **2022** |
| Mean duration of pre-symptomatic infectious period | 4 days | Brosius I, Dijck C Van, Coppens J, et al. Presymptomatic viral shedding in high-risk mpox contacts: A prospective cohort study. J Med Virol [Internet]. **2023** |
| Mean duration of infectious period | 27 days | Spicknall IH, Pollock ED, Clay PA, et al. Modeling the impact of sexual networks in the transmission of Monkeypox virus among gay, bisexual, and other men who have sex with men — United States, 2022. MMWR. **2022** |
| Treatment Seeking and Vaccine Parameters | | |
| Probability of seeking treatment | 0.8 | Farley TA, Cohen DA, Elkins W. Asymptomatic sexually transmitted diseases: the case for screening. Prev Med. **2003** |
| Duration of infectious period if seeking treatment (time until medical attention post-symptoms) | 15 days on first day of simulation, linearly decreases to 5.0 days on day 42 of simulation, stays at 5.0 days for rest of simulation. | Case Report Data |
| First dose per-exposure vaccine efficacy | 75% | Saldarriaga et al. |
| Second dose per-exposure vaccine efficacy | 89% |
| Minimum time between first and second dose | 28 days | JYNNEOS Vaccine | Mpox | Poxvirus | CDC [Internet]. |
| Behavior Change Parameters | | |
| Behavioral Adaptation (Maximum percent reduction in daily probability of forming one-time sexual partnerships.) | Prior: 0% – 90%  Posterior: 47% [28% – 70%] | Fit to case report data |