Contents lists available at ScienceDirect







journal homepage: www.keaipublishing.com/idm

The need for pre-emptive control strategies for mpox in Asia and Oceania



Gregory Gan^a, A. Janhavi^a, Guan Tong^a, Jue Tao Lim^{b, **}, Borame L. Dickens^{a, *}

^a Saw Swee Hock School of Public Health, National University of Singapore, Singapore ^b Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore

ARTICLE INFO

Article history: Received 23 August 2023 Received in revised form 19 December 2023 Accepted 19 December 2023 Available online 28 December 2023 Handling Editor: Dr Daihai He

Keywords: Monkeypox virus Modelling Network model Mpox Contact matrix Sexual contact

ABSTRACT

Introduction: The transmission dynamics of the recent mpox outbreak highlights the lack of infrastructure available to rapidly respond to novel STI outbreaks, of which Asia and Oceania remains particularly susceptible. Here, we simulate outbreaks in this setting and propose the use of pre-emptive vaccination within the men who have sex with men (MSM) community before the arrival and establishment of the virus.

Materials and methods: Using data driven heterogeneous sexual contact networks, we simulated outbreaks of mpox in Singapore, Hong Kong, and Sydney. An individual based SEIR compartmental model was used to simulate epidemic trajectories and the impact of different vaccination uptakes was assessed in their ability to avert or suppress outbreaks upon the arrival of mpox within the MSM populations.

Results: The highly dense sexual networks of Singapore and Sydney experience rapid outbreaks, with infection peaks occurring at day 41 and 23 respectively, compared to Hong Kong which occurs at day 77. Across the simulations with no vaccination, 68.2%–89.7% of the MSM community will become infected with mpox across the different cities, over a simulation period of 1 year. By implementing vaccination strategies, the infection rate across the cities can be reduced to as low as 3.1% of the population (range: 3.1%–82.2%) depending on the implementation and uptake of the vaccine. Vaccination is also extremely effective in slowing the start of the epidemic, delaying the epidemic peak by 36–50 days in Hong Kong, or even preventing the outbreak of mpox.

Discussion: With extremely dense and well-connected sexual contact networks, where 65.2%–83.2% of the population are connected to a super-spreader in the different contact networks, pre-emptive or immediate vaccination upon identification of the first case is strongly recommended to help better manage the outbreak of mpox and prevent potential straining of healthcare systems.

© 2024 The Authors. Publishing services by Elsevier B.V. on behalf of KeAi Communications Co. Ltd. This is an open access article under the CC BY-NC-ND licenses (http://creativecommons.org/licenses/by-nc-nd/4.0/).

* Corresponding author.

** Corresponding author.

E-mail addresses: juetao.lim@ntu.edu.sg (J.T. Lim), ephdbsl@nus.edu.sg (B.L. Dickens). Peer review under responsibility of KeAi Communications Co., Ltd.

https://doi.org/10.1016/j.idm.2023.12.005

2468-0427/© 2024 The Authors. Publishing services by Elsevier B.V. on behalf of KeAi Communications Co. Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Monkeypox (mpox) is a zoonotic orthopoxvirus endemic to Central and Western Africa that is clinically indistinguishable from other poxlike viruses and gaining global public health importance due to an increasing number of outbreaks being recorded in non-endemic regions (World Health Organizationa). Historically, two known distinct clades of mpox exist: Clade I, and Clade IIa, both primarily zoonoses with mortality rates of up to 10% and less than 1% respectively (Americo et al., 2023). In 2003, Clade IIa cases were reported outside Africa across 6 US states, primarily associated with contact events around infected prairie dogs who themselves had been infected by imported small mammals from Ghana (Reed et al., 2004), leading to the banning of the importation of African Rodents into the US (Di Giulio & Eckburg, 2004). Following this outbreak, sporadic cases were rare but have been reported over the years, in the US (CDC, 2022a), Israel (Erez et al., 2019), Singapore (Ng et al., 2019) and the UK (Vaughan et al., 2018). There was a significant change in the transmission dynamics for the recent outbreak, with the detection of a new mpox Clade IIb in London on 6 May 2022, which exhibited extensive human-to-human spreading capability (Fink et al., 2022). Unlike the prior outbreaks of mpox and of particular concern is that many of the cases in the recent outbreak have no travel-related link to an endemic country (Monkeypox).

Close contact with infected individuals has been identified as the most significant risk factor in the recent mpox outbreak through direct contact with rashes or bodily fluids from an infected individual, or indirect contact through bodily secretions left on objects (Peir'o-Mestres et al., 2022). By March 2023, over 86 000 mpox cases had been reported in over 113 countries, many of which were men who have sex with men (MSM)(Guarner et al., 2022). Although self-limiting and largely mild with estimates of ~1% cases presenting asymptomatic illness (De Baetselier et al., 2022), 119 deaths have been reported to date (World Health Organizationb). With the availability of two smallpox vaccines JYNNEOS and ACAM2000 (CDC, 2022b) which demonstrate ~85% effectiveness against mpox, it is likely a substantial proportion of these deaths could have been avoided.

While the initial wave of the epidemic has subsided, there has been a recent resurgence of 55 cases in Japan in March 2023 (Nishiura et al., 2022). Previous sporadic cases in Japan were from individuals who travel, or were in contact with travellers, but the recent resurgence shows signs of sustained local transmission. The exponentially increasing epidemic in Japan (Endo et al., 2023) demonstrates the imperative need for the better understanding of mpox outbreaks in susceptible cities and implementation of control measures, especially within Asia and Oceania with their large susceptible populations that were the least affected regions by the initial wave. With the potential introduction of new clades or variants, many of these cities will therefore be at substantial risk of receiving infected travellers with outbreaks occurring within the region and should therefore have strategies in place to effectively respond and curb infection sizes.

To support policymaking, this study thus aims to simulate the trajectories of MSM mpox outbreaks and effectiveness of vaccination control strategies for three cities in the two continents where sexual contact studies or data has been made available: Singapore, Hong Kong, China and Sydney, Australia. The MSM communities within these three cities have reported different community sizes, and sexual behaviours in terms of partner distributions and frequency of sex with their partners, that may be biased due to cultural or social aspects, which may lead to underestimation of the data (Singapore, 2020; C&SD, 2021; Greater Sydney, 2021; Chapin-Bardales et al., 2019; Wong & Tang, 2004; Hui et al., 2015; Wall et al., 2013; Crawford et al., 2006; Wong et al., 2012; The Kirby Institute, 2013; Rich et al., 2018). We created sexual contact networks and micro-simulations of outbreaks post case introduction based on the aforementioned factors and estimate the efficacy of different vaccination strategies according to vaccine uptake. By providing estimations on the change in outbreak size and outbreak duration from the deployment of vaccines for the MSM community, we aim to assist in policymaking for outbreak preparedness with the introduction of mpox from travellers into susceptible populations.

2. Material and methods

Data and parameters on mpox have been collected from available literature to construct the models (Table 1) for Singapore (a; Chapin-Bardales et al., 2019; Wall et al., 2013; Wong et al., 2012), Hong Kong, China (hereby referred to as Hong Kong), and Sydney, Australia (hereby referred to as Sydney) (b; Greater Sydney, 2021; Wong & Tang, 2004; Hui et al., 2015; Crawford et al., 2006; The Kirby Institute, 2013). We simulate transmission in each city through the construction of sexual contact networks within Susceptible-Exposed-Infectious-Recovered (SEIR) individual based models where disease spread can be moderated by vaccination strategies. The model tracks the sexual activity of each individual as well as their infection status over time.

A schematic of the SEIR model and how it works can be seen in Fig. 1 below.

To construct the contact network, individuals are assumed to be partaking in intimate sexual contact such as oral sex or anal sex with their respective partners where the direct contact with infectious sores or lesions on mucous membranes acts as the primary mode of transmission (Peir'o-Mestres et al., 2022). We assumed that non-sexually associated contact did not result in transmission. We fitted a gamma distribution to the estimates of the number of partners (to account for the heavy-tailed nature of sexual contact networks), and a log-normal distribution to the amount of sex individuals have with their last partner, except for Sydney, where a normal distribution was used. These distributions were developed to fit to the mean number of partners and mean frequency of sex with last partner over a period of time obtained from literature, while ensuring that the distribution shape stay consistent with prior research findings. More information on how the distributions were determined can be found in the Supplementary Information. For the size of the networks in each city, the number of MSM were estimated to be 3% of the working population of men in the city (Rich et al., 2018). Further details on the generation of

G. Gan, A. Janhavi, G. Tong et al.

Table 1

Parameters used within the model.

Model Parameters	Value	Source
mpox Incubation Period ^a	8.75 ± 1.09 days	Rich et al. (2018)
Mpox Recovery Period ^b	17.5 ± 1.05 days	Rich et al. (2018)
MSM Population		
Singapore	35 767	Singapore (2020)
Hong Kong	50 383	C&SD (2021)
Sydney	37 943	Greater Sydney (2021)
Mean number of partners (Yearly) ^c		
Singapore	8 (95% CI: 7.0–8.5)	Chapin-Bardales et al. (2019
Hong Kong	3	Wong and Tang (2004)
Sydney	30 (Range: 1–60)	Hui et al. (2015)
Reconstructed median number of part	ners (Yearly) ^c	
Singapore	5	_
Hong Kong	3	-
Sydney	19	_
Mean frequency of sex with partner (I	Monthly) ^c	
Singapore	6.72	Wall et al. (2013)
Hong Kong	6.92	Wong and Tang (2004)
Sydney	8.00 (Range: 6.40–9.60)	Crawford et al. (2006)
Condom Usage with Partner		
Singapore	15.7%	Wong et al. (2012)
Hong Kong	39.0%	Wong and Tang (2004)
Sydney	37.0%	The Kirby Institute (2013)

^a Refers to length of time between infection and experiencing of symptoms.

^b Refers to length of time for infected individual to fully recover.

^c Refer to Supplementary Information for detailed derivation of number of partners and frequency of sex with partner.

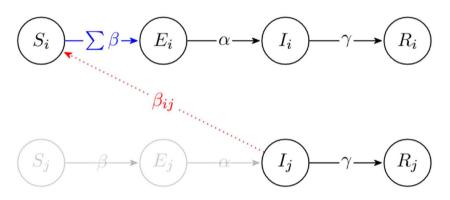


Fig. 1. Schematic of the transmission model with 2 connected individuals, 1 infected and 1 susceptible. The circles represent specific state of the individual, susceptible S, exposed E, infected I and recovered R. The red dotted line represents the connection an individual has with an infected individual. The blue line represents the transition probability of an individual per day, $\sum \beta$, after accounting for every sexual encounter he has, which would be the sum of all red lines. Black lines represent the transition from an exposed state to an infectious state after α days and from an infectious state to a recovered state where they cannot infect others after γ days.

the distribution for both number of partners, and number of times each individual has sex with their partner can be found in the Supplementary Information. Using these data, we created a simulated MSM population of the three cities, which randomly paired sexually active individuals together based on the distribution of the number of partners.

These individuals were then taken to have a chance of having sex with their respective partner daily, generating the unique transmissibility of mpox per day between two individuals as

$$\beta_{ij} = \frac{X_{ij}}{30} \bullet p \bullet (1 - (CE \bullet CU))$$
⁽¹⁾

where β_{ij} is the transmissibility of mpox per day for individual *i* after having sex with individual *j*, X_{ij} the random draw of number of sex events occurring over the last month between the partner-pair of individual *i* and individual *j*, *p* the chance of getting mpox after a sex event between individuals (taken to be 1 if the sex event is with an infectious individual, or 0 if sex event is with a non-infectious individual), *CE* the effectiveness of condom in preventing spread of mpox, and *CU* the probability of using of condoms when having sexual encounters in the country. If there is sexual activity between individuals where nobody is infectious, then the transition probability is $\beta_{ij} = \beta_{ii} = 0$.

The model then determines if the individual acquires mpox by checking across all sexual encounters the individual has for that time step. If an individual acquires mpox, they will move into the exposed state in the next time step. An update of individual SEIR states is conducted at every time step. For Singapore, we assumed that sexual behaviours largely follow findings from USA based on local expertise (unpublished data).

Within the SEIR, we utilised epidemiological data of mpox from literature (Moore et al., 2023). Representing a significant importation event (Koh et al., 2022), we seeded 5 infected individuals and 5 exposed individuals. Individuals engage in sexual activity where multiple individuals may engage in sexual activity together. Due to the large proportion of people in each city with 1 partner, a sizeable amount of exposed and infected individuals is required to ensure that spread occurs. If the exposed and infected individuals chosen only have 1 partner, or are in a closed network among few members, the spread of mpox will be contained. We have conducted additional simulations with 1 exposed and 1 infected individual, and 3 exposed and 3 infected individuals, and the results of these simulations can be found in the Supplementary Information. We also assumed that condoms were 80% effective at reducing the transmission (Weller et al., 1996), seasonality in sexual behaviour did not exist and the virus only spread between individuals after the incubation period has passed where exposed individuals cannot infect others until the virus has fully incubated and lesions appear. As the current outbreak of mpox has a very low case fatality rate of 0.08% (Multi-Country Outbreak of mpox), we assumed no fatalities occurred and that individuals would not be reinfected within our simulation.

No vaccination was assumed for baseline estimations with outbreak sizes compared to intervention strategies. To estimate the efficacy of early adoption of vaccines, we simulated the introduction of a vaccination program, prior to the start of the epidemic, at 3 different vaccine uptakes: (1) 25%, (2) 50%, and (3) 80%, representing low, medium and high uptake depending on the level of community engagement or policies. Using the JYNNEOS vaccine, which has an 85% efficacy (CDC, 2022b), a proportion of susceptible individuals are transferred to the recovered compartment. To account for recent studies on different vaccine effectiveness, the simulations were repeated for a more conservative vaccine effectiveness of 66.0% (Deputy et al., 2023), and the results can be found in the supplementary information.

As there is uncertainty in the epidemiological parameters and MSM contact parameters (Table 1), we used a Monte Carlo approach for 1000 simulations of each scenario for 1 year. We report their medians, together with their 95% uncertainty intervals (UI) representing the 5th and 95th percentiles of the simulations. The effective reproduction number at the start of the epidemic was also calculated for each city, and can be found in the Supplementary Information.

3. Results

Simulation results on the spread of mpox are presented for Singapore, Hong Kong, and Sydney (Table 2, Figs. 2–4) with differing levels of vaccination uptakes for mass vaccination. With no vaccination, a total of 24 393 (95% UI: 24 119–24 634) infections were estimated for Singapore, 39 415 (95% UI: 37 487–39 976) for Hong Kong and 34 030 (95% UI: 33 907–34 150) for Sydney. This resulted in a total of 68.2% (67.4%–68.9%), 78.2% (74.9%–79.3%) and 89.7% (89.4%–90.0%) of the respective MSM community becoming infected with lengths of the epidemic waves being 156 days, 232 days and 146 days. Daily infection peaks occurred at day 41 with 1030 cases, day 77 with 1015 cases, and day 23 with 4925 cases respectively.

With vaccination, total mpox case numbers can be lowered by 22.3%–96.1%, as a function of vaccine uptake and the sexual behaviour of the population. Vaccine uptake of 80% will suppress the epidemic wave substantially by 77.8% in Singapore, and 71.4% in Sydney, and can be suppressed altogether in Hong Kong due to the lower mean number of partners; 3 for Hong Kong versus 8 for Singapore and 30 for Sydney. For Singapore, at 25% and 50% vaccination uptake, a peak of 720 cases (30.1% reduction) at day 44 and 509 cases (50.6% reduction) at day 43 was observed. The equivalent for Hong Kong was a peak of 545 cases (46.3% reduction) at day 116 and 286 cases (71.8% reduction) at day 127. For Sydney, we observed peaks of 2086 cases

Table 2

Simulation results for Mass Va	ccination over 1 year.
--------------------------------	------------------------

Simulation	Total Vaccinated (median, 95%UI)	Total Cases (median, 95%UI)	% Infected
Baseline			
Singapore	_	24 393 (24 119-24 634)	68.2%
Hong Kong	_	39 415 (37 487-39 976)	78.2%
Sydney	-	34 030 (33 907-34 150)	89.7%
25% Vaccine Uptake			
Singapore	7368 (7217-7523)	18 300 (17 994–18 545)	51.2%
Hong Kong	12 208 (12 008-12 408)	27 819 (25 941-28 544)	55.2%
Sydney	8948 (8793-9125)	26 443 (26 251-26 635)	69.7%
50% Vaccine Uptake			
Singapore	14 736 (14 560-14 936)	12 247 (11 954-12 509)	34.2%
Hong Kong	24 429 (24 207-24 653)	15 967 (14 209–16 758)	31.7%
Sydney	17 905 (17 702–18 092)	18 819 (18 617–19 026)	49.6%
80% Vaccine Uptake			
Singapore	23 585 (23 397–23 771)	5404 (5172-5616)	15.1%
Hong Kong	39 090 (38 883-39 289)	1545 (15-3159)	3.1%
Sydney	28 647 (28 480-28 816)	9738 (9540-9938)	25.7%

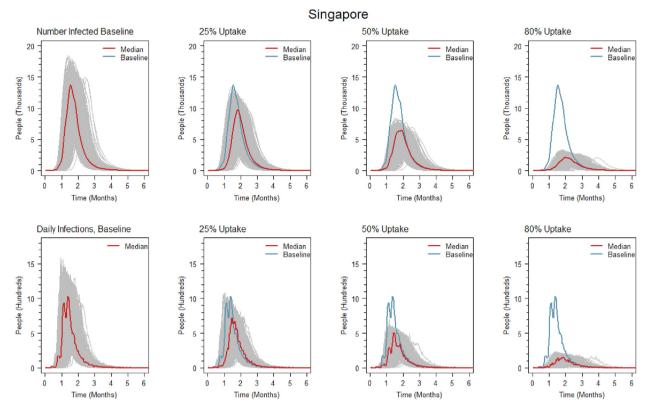


Fig. 2. Row 1) Simulations of the epidemic curve of mpox in Singapore across the different vaccination uptakes over the period of 6 months, under the Mass Vaccination approach. Every simulation is plotted in grey, and the red line represents the median simulation run. The blue line is the median simulation run of the baseline scenario, with no vaccination. Row 2) Simulations of the Daily Infections of mpox in Singapore across the different vaccination uptakes over the period of 6 months, under the Mass Vaccination approach.

(57.6% reduction) occurring at day 28 and 1370 cases (72.1% reduction) at day 39 respectively. At the 3 locales, vaccination at 25–50% uptake delayed the outbreak by 2–3 days, 39–50 days and 5–16 days. Overall, the cumulative infections peaked at around 13 730 cases after 46 days, 9701 cases after 54 days, 6428 cases after 57 days, and 2117 cases after 60 days for Singapore, 15 757 cases after 88 days, 8085 cases after 126 days, 3876 cases after 140 days, and 105 cases after 329 days for Hong Kong, 25 365 cases after 34 days, 21 198 cases after 42 days, 13 408 cases after 46 days, and 5573 cases after 45 days for Sydney, at 0%, 25%, 50%, and 80% vaccine uptake respectively.

While vaccination can suppress epidemic waves by an average of 25.5%, 51.3% and 82.0% at 25%, 50% and 80% uptake, substantial vaccine stockpiling is necessitated. At 25% uptake 7368 (7217-7523), $12\ 208$ ($12\ 008-12\ 408$) and 8948 (8793-9125) vaccines are needed for Singapore, Hong Kong, and Sydney. At 50% uptake, this increases to $14\ 736$ ($14\ 560-14\ 936$), $24\ 429\ (24\ 207-24\ 653)$ and $17\ 905\ (17\ 702-18\ 092)$; At the highest uptake of 80%, $23\ 585\ (23\ 397-23\ 771)$, $39\ 090\ (38\ 883-39\ 289)$ and $28\ 647\ (28\ 480-28\ 816)$ is required. By targeting high-risk individuals as a vaccination strategy, vaccine stockpiling requirements can be reduced by 64.9%, 64.8% and 63.4% for Singapore, Hong Kong and Sydney; $2586\ (2495-2681)$, $4300\ (4185-4416)$ and $3280\ (3173-3391)$ at 25% uptake, $5173\ (5037-5304)$, $8595\ (8437-8767)$ and $6561\ (6420-6710)$ at 50% uptake, and $8274\ (8122-8423)$, $13\ 758\ (13\ 563-13\ 952)$ and $10\ 495\ (10\ 314-10\ 663)$ at 80% uptake.

Simulation results of the spread of mpox are presented for Sydney, Hong Kong, and Singapore (Table 3, Supplementary Figs. 1–3) with differing levels of vaccination uptakes for high-risk vaccination. With the high-risk vaccination strategy, total mpox case numbers can be lowered by 8.4%–66.9%. At 25% vaccination uptake, peaks of 835 daily cases (18.9% reduction) at day 52, 606 daily cases (40.3% reduction) at day 122 and 2402 daily cases (51.2% reduction) at day 31 can be seen for Singapore, Hong Kong, and Sydney. Likewise, at 50% vaccination uptake, peaks of 607 cases (41.1% reduction) at day 50, 426 cases (58.0% reduction) at day 128 and 1875 cases (61.9% reduction) at day 44 can be observed. With a vaccination uptake of 80%, we observe a suppression of the epidemic wave of 32.1% in Singapore, 66.9% in Hong Kong and 26.5% in Sydney with peaks of 395 daily cases (61.7% reduction) at day 75, 109 daily cases (89.3% reduction) at day 281 and 1480 daily cases (69.9% reduction) at day 41 for Singapore, Hong Kong, and Sydney respectively. This resulted in cumulative infection peaks of 11 851 cases after 61 days, 9543 cases after 63 days, and 5724 cases after 85 days for Singapore, 9519 cases after 49 days, and 16 402 cases after 50 days for Sydney, at 25%, 50%, and 80% vaccine uptake respectively.

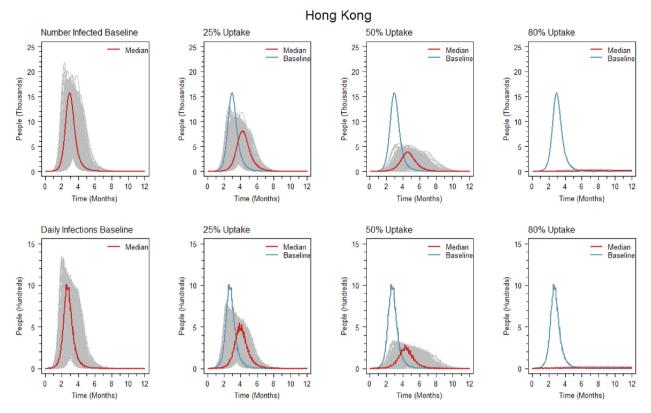


Fig. 3. Row 1) Simulations of the epidemic curve of mpox in Hong Kong across the different vaccination uptakes over the period of 12 months, under the Mass Vaccination approach. Every simulation is plotted in grey, and the red line represents the median simulation run. The blue line is the median simulation run of the baseline scenario, with no vaccination. Row 2) Simulations of the Daily Infections of mpox in Hong Kong across the different vaccination uptakes over the period of 12 months, under the Mass Vaccination approach.

There was an average of 0.82, 0.96 and 0.85 cases averted per vaccine in Singapore, Hong Kong and Sydney for the mass vaccination strategy, compared to the average of 0.92, 1.47 and 0.86 cases averted per vaccine in Singapore, Hong Kong, and Sydney for the targeted vaccination strategy.

4. Discussion

Here we studied mpox in three different contexts at current risk of outbreak; Singapore, Hong Kong and Sydney, where different sexual behaviours in terms of the number of partners and frequency of sexual encounters are observed. While models have been created to estimate outbreaks in the EU and Americas (Liu et al., 2023; Overton et al., 2023; Van Dijck et al., 2023; Yang et al., 2023), limited research exists for outbreak preparation in Asia and Oceania. The susceptible population is large in Western Pacific and South-east Asia, which has 0.38% and 0.05% of all reported cases (World Health Organizationb). As such, with the rising mpox cases in Japan (Endo et al., 2023; Nishiura et al., 2022), it is likely that more cases will occur in these regions, due to the increase in travel within these regions post COVID-19.

Outbreak sizes differ by 1.5% (67.4%–68.9%), 4.9% (74.4%–79.3%) and 0.6% (89.4–90.0%) respectively, but in all contexts, when a superspreader is infected, an outbreak size of around 24 393 (24 119–24 634), 39 415 (37 487–39 976) or 34 030 (33 907–34 150) is expected with no vaccination plan in place. The introduction of vaccination of 25%, 50%, and 80% of the population however causes an average reduction of 25.6%, 51.3% and 81.8% in total outbreak size, with a much higher efficacy in Hong Kong compared to the other two cities, due to its less dense sexual contact network. Prior mpox modelling studies have shown that cases will continue to grow rapidly, if no intervention is implemented (Multi-Country Outbreak of mpox), which corroborate with our simulation findings leading up to the peak of the epidemic. The delay and reduction in the peak of the epidemic when vaccination is implemented shows the importance of policy planning and rapid responses via vaccination deployment upon the notification of imported cases, which will help for easier management of mpox cases, preventing healthcare resource strain (Morris et al., 2021). We also simulated an epidemic outbreak with vaccine implementation after 21 days, and results can be found in the Supplementary Information. Any form of vaccination will help to reduce the size of the epidemic, but pre-emptive vaccination before the outbreak is shown to have much greater efficacy in dampening the epidemic curve.

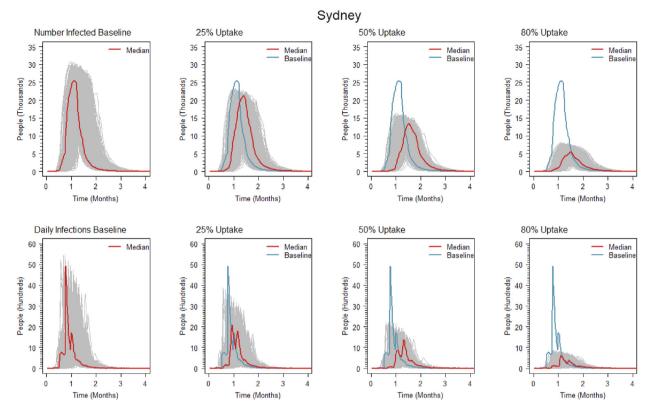


Fig. 4. Row 1) Simulations of the epidemic curve of mpox in Sydney across the different vaccination uptakes over the period of 4 months, under the Mass Vaccination approach. Every simulation is plotted in grey, and the red line represents the median simulation run. The blue line is the median simulation run of the baseline scenario, with no vaccination. Row 2) Simulations of the Daily Infections of mpox in Sydney across the different vaccination uptakes over the period of 4 months, under the Mass Vaccination approach.

Superspreaders typically support 20–120 partner connections for all three cities: Singapore, Hong Kong and Sydney (Supplementary Figs. 4–6). Given the relatively small size of the MSM community, 65.2%–83.2% across the networks are connected to at least one super-spreader. This interconnection makes outbreak control particularly challenging with the high level of ongoing contact. Fewer MSM in Singapore are connected to a super-spreader, compared to Hong Kong, where the clusters are less dense, which could be due to the presence of multiple smaller connected networks in Hong Kong rather than one largely connected network (Supplementary Fig. 7-9). Our model structure accommodates for the heavy-tailed sexual partner distribution with heterogenous mixing (Endo et al., 2022) and contextualises the heterogeneous sexual behaviour within the different MSM networks (Molla et al., 2022). With few studies conducted on sexual contact degrees (Multi-Country Outbreak of mpox), and the lack of mpox modelling in non-endemic countries (Sewell et al., 2020), our study aims to build on available data to assist in policy making in countries with large susceptible populations, such as Asia and Oceania. The current mpox models also do not consider the different sexual behaviours in different countries (Multi-Country Outbreak of mpox), fail to account for super-spreading events (Yang et al., 2023), or are built using confirmed case data (Multi-Country Outbreak of mpox; Yang et al., 2023; Van Dijck et al., 2023; Liu et al., 2023), which will limit its usefulness in estimating and forecasting novel outbreaks. By using location specific sexual behaviour data to create the model, our model will be more useful in simulating mpox outbreaks (Sewell et al., 2020). While mpox modelling has been done in a college campus setting, it was not a network model and used simplified mixing patterns, which will limit the influence of super-spreaders (Savinkina et al., 2023), the primary drivers of the epidemic (Endo et al., 2022).

High-risk sexual behaviours and the lack of vaccination have contributed to the outbreak of mpox (Beer; Jezek et al., 1987). With vaccination being an effective intervention in managing the mpox outbreak (Yang et al., 2023), more emphasis should be placed on encouraging vaccination in the MSM community. Analysis of the network structure of the population is also important in determining efficiency and effectiveness of interventions, for use in infectious disease policy making (Kao & Enns, 2020), especially in times of vaccine shortages. With recommendations to lower sexual contact between individuals, and high vaccination uptake in the community, it is possible to prevent the epidemic, as seen in the simulation for Hong Kong.

Although our study highlights the importance of pre-emptive or immediate vaccination upon the notification of the first case, many policy challenges exist. The identification of superspreaders or individuals at risk of transmission within the MSM can be met with substantial resistance in many local contexts where stigmatisation of MSM or mpox is rampant and can cause

Table 3

Simulation results for Targeted Vaccination over 1 year.

Simulation	Total Vaccinated (median, 95%UI)	Total Cases (median, 95%UI)	% Infected
Baseline			
Singapore	_	24 393 (24 119-24 634)	68.2%
Hong Kong	_	39 415 (37 487-39 976)	78.2%
Sydney	_	34 030 (33 907-34 150)	89.7%
25% Vaccine Uptake			
Singapore	2586 (2495-2681)	22 058 (21 806-22 299)	61.7%
Hong Kong	4300 (4185-4416)	34 440 (33 007-35 203)	68.4%
Sydney	3280 (3173-3391)	31 187 (31 030-31 348)	82.2%
50% Vaccine Uptake			
Singapore	5173 (5037-5304)	19 638 (19 330–19 878)	354.2%
Hong Kong	8595 (8437-8767)	28 041 (26 094-29 163)	55.7%
Sydney	6561 (6420-6710)	28 385 (28 207-28 568)	74.8%
80% Vaccine Uptake			
Singapore	8274 (8122-8423)	16 564 (16 239–16 835)	46.3%
Hong Kong	13 758 (13 563–13 952)	13 052 (3563–16 378)	25.9%
Sydney	10 495 (10 314-10 663)	25 023 (24 819-25 205)	65.9%

individuals to not seek protective measures or medical care (Dsouza et al., 2023). This additionally makes contact tracing measures difficult as individuals may be unwilling to divulge information of their sexual partners or be unaware of their identity entirely in casual hook-ups. Solutions to this include the use of anonymous vaccination centres, and high levels of community engagement to increase awareness of the risks and publicise the availability of vaccines for the MSM community. Although the MSM community has been primarily affected with most cases (84.1%)(World Health Organizationb), the vaccine could also be offered to female partners of MSM who may be at risk of transmission should they seek protective measures.

Our study has several limitations, including only accounting for the primary form of transmission for mpox, and lack of importation of mpox into the MSM communities. While most reported cases (82.2%)(World Health Organizationb) have skin and mucosal contact be the reported mode of transmission, there are other forms of transmission which was not considered in the model. The model is also built around surveys conducted regarding sexual behaviours of people living in the USA (assumed to be parallel to Singapore based on local expertise), Hong Kong, and Sydney. These data were gathered before the COVID-19 outbreak, which may have changed the sexual behaviour dynamics (Gleason et al., 2023; Lehmiller et al., 2021). Additionally, the sexual behaviour of the MSM community is dynamic, and changes over time, which makes our simulation useable as an estimation of the trajectory of mpox based on the best understanding we have on sexual contact patterns. There may however be overestimation of the epidemic curve, due to an overestimation of the number of sexual partners and frequency of sex with each partner should the MSM community reduce sexual contacts rates due to concerns on mpx transmission. More recent contact and behavioural data is required to estimate the sexual behaviours and dynamics of the MSM community, and accurately model the spread of the disease and provide better resolution to how a novel outbreak may look like. There was also no differing of importation rates of mpox carriers in the model across time, as we explored the impact of one seeding event instead of continual importation, which may occur with the resumption of international travel post COVID-19 pandemic (Chen & Williamson, 2022). With increasing globalisation and frequent migration, more emphasis on awareness and pre-emptive measures need to be implemented to limit the impact of a new outbreak (Sklenovská & Van Ranst, 2018). While countries had reported less than 1% of their estimated MSM population size being infected (Murayama et al.), our model assumes that the sexual behaviour of individuals do not change with time, even if they are infected with mpox. Together with the high transmission probability of mpox in the model if condom is not used, the number of cases simulated by the model will be drastically higher than reported cases. There is also a possibility that there is an underreporting of cases, as most cases are mild, and recovery is possible without medical treatment.

Funding

This work was supported by the NUS Saw Swee Hock School of Public Health's Start Up Fund [22-5118-A0001] and the Singapore Ministry of Health's National Medical Research Council under its National Epidemic Preparedness and Response R&D Funding Initiative (MOH- 001041) Programme for Research in Epidemic Preparedness And REsponse (PREPARE).

CRediT authorship contribution statement

Gregory Gan: Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **A. Janhavi:** Writing – review & editing, Methodology, Investigation, Formal analysis. **Guan Tong:** Writing – review & editing, Visualization, Validation. **Jue Tao Lim:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Borame L. Dickens:** Writing – review & editing, Visualization, Validation, Supervision, Project administration, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.idm.2023.12.005.

References

- Greater Sydney, Census All persons QuickStats | Australian Bureau of Statistics [Internet]. Available from: https://abs.gov.au/census/find-census-data/ quickstats/2021/1GSYD.
- Americo, J. L., Earl, P. L., & Moss, B. (2023). Virulence differences of mpox (monkeypox) virus clades I, IIa, and IIb. 1 in a small animal model. Proceedings of the National Academy of Sciences, 120(8), Article e2220415120.
- Beer EM, Rao VB A systematic review of the epidemiology of human monkeypox outbreaks and implications for outbreak strategy. PLoS Neglected Tropical Diseases 13(10): e0007791.
- C&SD: 2021 population census. Available from: https://www.censtatd.gov.hk/en/scode600.html.
- CDC. (2022a). Mpox in the U.S [Internet]. Centers for Disease Control and Prevention. Available from: https://www.cdc.gov/poxvirus/mpox/outbreak/usoutbreaks.html.
- CDC. (2022b). Mpox in the U.S. Centers for disease control and prevention. Available from: https://www.cdc.gov/poxvirus/monkeypox/clinicians/vaccines/ vaccine-considerations.html.
- Chapin-Bardales, J., Rosenberg, E. S., Sullivan, P. S., et al. (2019). Trends in number and composition of sex partners among men who have sex with men in the United States, National HIV behavioral surveillance, 2008–2014. *Journal of Acquired Immune Deficiency Syndromes*, 81, 257, 1999.
- Chen, M. Y., & Williamson, D. A. (2022). Sexually transmitted outbreaks and genomic surveillance. The Lancet Infectious Diseases, 22, 1409-1411.
- Crawford, J. M., Kippax, S. C., Mao, L., et al. (2006). Number of risk acts by relationship status and partner serostatus: Findings from the HIM cohort of homosexually active men in Sydney, Australia. AIDS and Behavior, 10(3), 325–331.
- De Baetselier, I., Van Dijck, C., Kenyon, C., et al. (2022). Retrospective detection of asymptomatic monkeypox virus infections among male sexual health clinic attendees in Belgium. *Nature Medicine*, 1–5.
- Deputy, N. P., Deckert, J., Chard, A. N., Sandberg, N., Moulia, D. L., Barkley, E., Dalton, A. F., Sweet, C., Cohn, A. C., Little, D. R., & Cohen, A. L. (2023). Vaccine effectiveness of JYNNEOS against mpox disease in the United States. *New England Journal of Medicine*.

Di Giulio, D. B., & Eckburg, P. B. (2004). Human monkeypox: An emerging zoonosis. The Lancet Infectious Diseases, 4(1), 15-25.

- Dsouza, V. S., Rajkhowa, P., Mallya, B. R., et al. (2023). A sentiment and content analysis of tweets on monkeypox stigma among the LGBTQ+ community: A cue to risk communication plan. *Dialogues Health*, *2*, Article 100095.
- Endo, A., Jung, S., & Miura, F. (2023). Mpox emergence in Japan: Risks of establishment in Asia and the global resurgence. https://doi.org/10.21203/rs.3.rs-2548920/v3
- Endo, A., Murayama, H., Abbott, S., et al. (2022). Heavy-tailed sexual contact networks and monkeypox epidemiology in the global outbreak, 2022. *Science*, 378(6615), 90–94.
- Erez, N., Achdout, H., Milrot, E., et al. (2019). Diagnosis of imported monkeypox, Israel, 2018. Emerging Infectious Diseases, 25(5), 980.
- Fink, D. L., Callaby, H., Luintel, A., et al. (2022). Clinical features and management of individuals admitted to hospital with monkeypox and associated complications across the UK: A retrospective cohort study. *The Lancet Infectious Diseases*.
- Gleason, N., Conroy, K., Taylor, S., et al. (2023). Sex seems less important when you are worried about a deadly virus. A content analysis of reported reasons for changes in sexual behavior and satisfaction during the COVID-19 pandemic. *Journal of Sex & Marital Therapy*, 49(1), 17–40.
- Guarner, J., del Rio, C., & Malani, P. N. (2022). Monkeypox in 2022-what clinicians need to know. JAMA, 328, 139-140.
- Hui, B., Fairley, C. K., Chen, M., et al. (2015). Oral and anal sex are key to sustaining gonorrhoea at endemic levels in MSM populations: A mathematical model. Sexually Transmitted Infections, 91, 365–369.
- Jezek, Z., Khodakevich, L. N., & Wickett, J. F. (1987). Smallpox and its post-eradication surveillance. *Bulletin of the World Health Organization*, 65(4), 425. Kao, S. Y. Z., & Enns, E. A. (2020). Follow the sex: Influence of network structure on the effectiveness and cost-effectiveness of partner management strategies for STI control. *Sexually Transmitted Diseases*, 47, 71.
- Koh, X. Q., Chio, M. T., Tan, M., et al. (2022). Global monkeypox outbreak 2022: First case series in Singapore. Annals Academy of Medicine Singapore, 51(8), 462–472.
- Lehmiller, J. J., Garcia, J. R., Gesselman, A. N., & Mark, K. P. (2021). Less sex, but more sexual diversity: Changes in sexual behavior during the COVID-19 coronavirus pandemic. *Leisure Sciences*, 43(1–2), 295–304.
- Liu, T., Yang, S., Luo, B., et al. (2023). Anticipating the transmissibility of the 2022 mpox outbreak. Journal of Medical Virology.
- Molla, J., Sekkak, I., Ortiz, A. M., et al. (2022). Mathematical modeling of mpox: A scoping review. medRxiv.
- Monkeypox. Available from:: https://www.who.int/news-room/fact-sheets/detail/monkeypox.
- Moore, M. J., Rathish, B., & Zahra, F. (2023). *Mpox (Monkeypox)* [Updated 2022 Nov 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. Available from: https://www.ncbi.nlm.nih.gov/books/NBK574519/.
- Morris, D. H., Rossine, F. W., Plotkin, J. B., & Levin, S. A. (2021). Optimal, near-optimal, and robust epidemic control. Communications Physics, 4(1), 78.
- Multi-country outbreak of mpox. External Situation Report#12- 14 December 2022. Available from: https://www.who.int/publications/m/item/multicountry-outbreak-of-mpox-external-situation-report-12-14-december-2022.
- Murayama, H., Pearson, C.A., Abbott, S., et al. Accumulation of immunity in heavy-tailed sexual contact networks shapes mpox outbreak sizes. The Journal of Infectious Diseases, p.jiad254.
- Ng, O. T., Lee, V., Marimuthu, K., et al. (2019). A case of imported Monkeypox in Singapore. *The Lancet Infectious Diseases*, *19*(11), 1166.
- Nishiura, H., Hayashi, K., Anzai, A., et al. (2022). Upcoming major epidemic of mpox in Japan. https://doi.org/10.13140/RG.2.2.34892.08327, 23.
- Overton, C. E., Abbott, S., Christie, R., et al. (2023). Nowcasting the 2022 mpox outbreak in England. arXiv preprint arXiv:2302.09076.
- Peiró-Mestres, A., Fuertes, I., Camprubi-Ferrer, D., et al. (2022). Frequent detection of monkeypox virus DNA in saliva, semen, and other clinical samples from 12 patients, Barcelona, Spain, May to June 2022. Euro Surveillance, 27, Article 2200503.
- Reed, K. D., Melski, J. W., Graham, M. B., et al. (2004). The detection of monkeypox in humans in the Western Hemisphere. *New England Journal of Medicine*, 350(4), 342–350.
- Rich, A. J., Lachowsky, N. J., Sereda, P., et al. (2018). Estimating the size of the MSM population in Metro Vancouver, Canada, using multiple methods and diverse data sources. *Journal of Urban Health*, 95, 188–195.
- Savinkina, A., Chitwood, M., Kwon, J., et al. (2023). Planning for mpox on a college campus: A model-based decision-support tool. *Annals of Internal Medicine*, 176(3), 340–347.

Sewell, D. K., & Miller, A., for the CDC MInD-Healthcare Program. (2020). Simulation-free estimation of an individual-based SEIR model for evaluating nonpharmaceutical interventions with an application to COVID-19 in the District of Columbia. PLoS One, 15(11), Article e0241949. https://doi.org/10. 1371/journal.pone.0241949

Singapore census of population 2020. Base. Available from: http://www.singstat.gov.sg/publications/reference/cop2020/cop2020-sr1.

Sklenovská, N., & Van Ranst, M. (2018). Emergence of monkeypox as the most important orthopoxvirus infection in humans. Frontiers in Public Health, 6, 241.

The Kirby Institute. (2013). HIV, viral hepatitis and sexually transmissible infections in Australia Annual Surveillance Report 2013. Sydney, NSW: The Kirby Institute, the University of New South Wales.

Van Dijck, C., Hens, N., Kenyon, C., & Tsoumanis, A. (2023). The roles of unrecognized mpox cases, contact isolation and vaccination in determining epidemic size in Belgium: A modeling study. Clinical Infectious Diseases, 76(3), e1421–e1423.

- Vaughan, A., Aarons, E., Astbury, J., et al. (2018). Two cases of monkeypox imported to the United Kingdom, September 2018. Euro Surveillance, 23(38), Article 1800509.
- Wall, K. M., Stephenson, R., & Sullivan, P. S. (2013). Frequency of sexual activity with most recent male partner among young, Internet-using men who have sex with men in the United States. *Journal of Homosexuality*, 60, 1520–1538.
- Weller, S. C., Davis-Beaty, K., & Group, C. H. (1996). Condom effectiveness in reducing heterosexual HIV transmission. Cochrane Database of Systematic Reviews, 2012.

Wong, M. L., Sen, P., Wong, C. M., et al. (2012). Human immunodeficiency virus (HIV) prevention education in Singapore: challenges for the future. Annals Academy of Medicine Singapore, 41, 602–609.

Wong, C., & Tang, C. S. (2004). Sexual practices and psychosocial correlates of current condom use among Chinese gay men in Hong Kong. Archives of Sexual Behavior, 33, 159–167.

World Health Organization (13 April 2023). Emergency situational updates; Multi-country outbreak of mpox. External situation report #20 -13 April 2023. Available at: https://www.who.int/publications/m/item/multi-country-outbreak-of-mpox-external-situation-report-20-13-april-2023.

World Health Organization (21 May 2022). Disease Outbreak News; Multi-country monkeypox outbreak in non-endemic countries. Available at: https:// www.who.int/emergencies/disease-outbreak-news/item/2022-DON385.

Yang, S., Guo, X., Zhao, Z., et al. (2023). Possibility of mpox viral transmission and control from high-risk to the general population: A modeling study. BMC Infectious Diseases, 23(1), 119.