國立臺灣大學公共衛生學院流行病學與預防醫學研究所

碩士論文

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# 疫苗施打與高風險群風險意識對美國 2022-2023 M 痘疫情的防治效果：傳染病數理建模研究

# Impact of Vaccination and High-Risk Group Awareness on the Mpox Epidemic in the United States, 2022–2023: A Modelling Study

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# 國立臺灣大學碩士學位論文
# 口試委員會審定書

論文中文題目：疫苗施打與高風險群風險意識對美國 2022-2023 M 痘疫情的防治效果：傳染病數理建模研究

論文英文題目：Impact of vaccination and high-risk group awareness on the mpox epidemic in the United States, 2022–2023: a modelling study

本論文係林吟謙君（學號 R12849003）在國立臺灣大學流行病學與預防醫學研究所完成之碩士學位論文，於民國 114 年 6 月 17 日承下列考試委員審查通過及口試及格，特此證明。

口試委員：方啓泰

（簽名）

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# 摘要

**背景：**

2022 年開始的 M 痘（mpox）全球爆發流行帶來前所未有的公共衛生挑戰。因應 M 痘疫情，美國除推動全國 MVA-BN ( JYNNEOS®) 疫苗接種計畫外，亦有社區組織與公衛機構進行衛教宣導風險與隨後的高風險族群性行為風險降低之行為改變。本研究透過建構風險結構分層之 M 痘數理模型，估計上述兩項防疫介入措施對美國 M 痘疫情的防治效果，以及是否有協同作用。

**方法：**

本研究建構「易感-潛伏-症狀前期-有症狀感染期-無症狀-康復-接種（SEIARV）」確定性分室模型 (deterministic compartmental model)，並根據 M 痘傳播風險將模型人口分層為高風險群與低風險群，其中高風險為 13 歲以上，具有透過危險性行為而感染 M 痘風險的男男間性行為者 (men who have sex with men, MSM)。模型結構依據 M 痘傳播感染自然史以及 2 劑疫苗施打過程，區分為 11 個分室。模型參數依據文獻資料、CDC 通報數據、疫苗接種統計與行為問卷調查推估，並使用平方根轉換的最小平方法擬合 2022 年 5 月 22 日至 12 月 22 日間美國每日通報猴痘病例數來估計 3 項參數：M 痘傳播系數、具感染力之分室的初始人數、高風險群人口佔比。藉由模擬四種情境（無介入措施、只實施疫苗接種、只具備行為改變、兩者共同實施），本研究計算各情境下累積通報病例數與感染數之差異，以評估各措施的預防百分比成效。另外也進行單變項與多變項敏感度分析，以了解該參數之不確定性對預防百分比結果估計的影響。

**結果：**

模型估計高風險與低風險族群之基本再生數分別為 3.88 與 0.39，並成功重建疫情曲線，預測期間累積通報病例數為 29,559（28,081, 31,036），其中 71.8% 為高風險族群，與實際通報資料中 16–45 歲男性佔比（78.6%）相近。若無衛教，在緊迫時間內所能完成的疫苗接種劑數僅能預防 21.2%（10.2%–24.1%）病



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例；若無疫苗接種，僅靠衛教與高風險群危機意識導致的性行為改變只能預防 15.4%（14.3%–20.6%）病例；兩者同時實施時則可預防 64.0%（43.8%–69.0%）病例，顯示疫苗與行為改變間產生協同作用。敏感度分析結果顯示，疫苗保護力與通報率的高低對預防百分比估計值有較大的影響；然而，所有情境中疫苗與行為改變皆呈現協同作用而非單純累加效應。

**結論：**

本研究指出，儘管疫苗覆蓋率與行為改變程度皆有限，但兩者的共同實施在控制 2022–2023 年美國 M 痘疫情中發揮協同作用。高風險族群之風險意識提升和減少危險性行為，在群體層面可迅速降低傳播率，進而爭取時間讓疫苗施打的覆蓋率提高並帶來相對更持久的個體層級之免疫保護，兩者產生協同作用，成功防治美國 M 痘疫情。此結果也可望普遍應用於其他可透過疫苗預防和行為介入防治的傳染病，對未來新興傳染病防治策略提供重要參考。

**關鍵字：M 痘、美國 M 痘疫情、疫苗接種、行為改變、風險意識、傳染病數理模式**



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# Abstract

Background

The unprecedented global outbreak of mpox in 2022 posed a public health challenge. In addition to the mpox vaccine campaign in the United States (US), community organizations and public health agencies initiated educational efforts to promote sexual risk reduction. This modelling study estimated the impact of the two-dose vaccination campaign and sexual behavior changes coincident with high-risk group awareness on the mpox epidemic in the US.

Method

We constructed a deterministic, risk-structured "susceptible-exposed-infectious-asymptomatic-recovered-vaccinated" (SEIARV) model based on careful parameter estimations using results from survey studies, national-wide statistics on mpox cases, and data on vaccine administration, and fitted our model to the epidemic curve of reported mpox cases in the US between May 22, 2022 to December 22, 2022. We evaluated the putative effects of the two preventive responses in the US -- vaccination and sexual risk reduction -- at the population-level, by calculating the prevention percentages of cumulative cases compared to the counterfactual scenario without interventions. We performed sensitivity analyses with four parameters: case reporting fidelity, vaccine effectiveness, proportion of asymptomatic cases, and assortative mixing.

Result

Model fitting revealed a basic reproduction number of 3.88 and 0.39 for the high-risk



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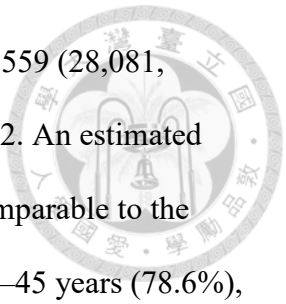

and low-risk populations, respectively. Model simulated a total of 29,559 (28,081, 31,036) mpox reported cases between May 22 and December 22, 2022. An estimated 71.8% of mpox cases was from the high-risk population, which is comparable to the actual distribution of cases in the United States among males aged 16–45 years (78.6%), a demographic most actively engaged in sexual activity. A two-dose vaccination campaign, solely, could prevent 21.2% (10.2%–24.1%) of cases, while behavior changes due to high-risk group awareness alone could prevent 15.4% (14.3%–20.6%). The combination of both measures were synergistic, with the model suggesting that 64.0% (43.8%–69.0%) of US cases were averted that would have otherwise occurred. In the sensitivity analyses, the proportion of mpox cases reported in the US and the proportion of asymptomatic cases had some effect on the estimates of prevention percentage for the preventive measures individually, and for the combination of both measures. However, in all scenarios, the vaccination campaign and high-risk group awareness demonstrated synergistic effects.

Conclusion

Our models suggest that the 2022-2023 mpox epidemic in the US was controlled by a combination of two-dose mpox vaccination campaign and high-risk group awareness and sexual risk reduction. Awareness-associated behavior adaptations can quickly reduce transmission across the population at risk, thus buy time for the vaccination campaign to catch up to provide more durable protection to maximize the prevention proportions. This principle can be applied to preparedness and response to other vaccine-preventable and behaviorally mediated infectious diseases.



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**Keywords: mpox, US outbreak, vaccination, sexual behavior changes, awareness, mathematical modelling**



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# Introduction

## Background

Mpox (monkeypox) is a viral zoonotic disease, causing smallpox-like symptoms, though less lethal, primarily rash, fever, and pain.[1] Mpox is transmitted through close contact with the blood, body fluid, skin lesions, or respiratory droplets of infected animals or humans.[1] It has been endemic in central and western African countries since the 1970s.[1] Since early May 2022, countries outside these endemic regions began reporting cases of mpox, quickly expanding into a global outbreak. Over 8.8 million incident cases and 150 deaths from 110 countries had been reported by July 2023.[2] Prior to 2022, there had been more isolated cases of mpox documented in non-endemic regions. In 2003, there was an autochthonous mpox infection cluster in the United States (US) suspected to have been introduced by pet store imports of African rodents, and during 2018-2019, there were clusters in locations such as the United Kingdom (UK) and Singapore, attributed to index cases from Nigeria.[1] However, the 2022-2023 mpox outbreak marked the first time that chains of person-to-person transmission of mpox virus occurred on a global scale, with most of the transmission happening through sexual contact; an estimated 86% of the cases occurred among men who have sex with men (MSM), based on case reporting to the World Health Organization (WHO).[2,3]

The first mpox case in the US was confirmed on 17 May, 2022 in Massachusetts; more than 30 000 incident cases and 32 deaths were reported in the US by January 2023.[4] Some jurisdictions initiated JYNNEOS® vaccine (Bavarian Nordic A/S, Hellerup, Denmark) campaigns at the beginning of the outbreak,[5] and the US Food and Drug



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Administration issued an emergency use authorisation (EUA) for the intradermal injection of JYYNEOS® vaccine on 9 August, 2022 to increase access to the vaccine.[4] JYNNEOS® vaccine, approved in 2019 for the prevention of smallpox and mpox infection in adults 18 years or older, has an effectiveness of 35.8-75.2% for 1-dose and 66.0-85.9% for 2-doses.[6] By January 2023, vaccination coverage among persons at risk in the US reached an estimated 37% for the first dose and 23% for the second dose.[4] In surveys, 40-60% of MSM reported reducing their number of sexual partners, one-time sexual encounters, and/or other high-risk sexual behaviors after learning about the outbreak.[7] The mpox epidemic in the US peaked on 1 August, 2022,[8] and then declined markedly.

## Research gap and aim of study

It is not known the extent to which limited vaccine coverage and effectiveness and/or behavior changes translated into a reduction in the number of mpox cases. The extent to which these two interventions may have been synergistic is also unknown. Estimating these effects in the 2022 US outbreak can guide priorities to prepare for subsequent mpox spread and may be relevant for other emerging or re-emerging infectious diseases. We used dynamic models to estimate the impact of the two-dose JYNNEOS® vaccination campaign and the behavior change consequent to high-risk group awareness on the 2022 mpox epidemic in the US, based on careful parameter estimations using surveys, national-wide statistics on mpox cases, and data on vaccine administration.



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# Methods

## Study design

This is a dynamic modelling study on the impact of mpox vaccination and high-risk group awareness on the mpox epidemic in the United States. We first constructed a mathematical model based on natural history and transmissibility of mpox infection as well as JYNNEOS® vaccine effectiveness, then fitted the model to actual daily reported mpox cases published by the US Centers for Disease Control and Prevention (CDC, Atlanta, GA, USA).

## Structure of mpox mathematical model

We constructed a deterministic, risk-structured "susceptible-exposed-infectious-asymptomatic-recovered-vaccinated" (SEIARV) compartmental model that considered high-risk and low-risk sub-populations, building upon an appropriate SEIARV model of hepatitis A disease by Lin KY et al.[9] We separated populations in each risk group into 11 compartments by stage of natural history and vaccination status (figure 1). The high-risk group consists of MSM 13 years or older and at risk of acquiring mpox through risky sexual behaviors. For model construction, we considered pre-symptomatic transmission to occur up to 4 days before symptom onset,[10] and decreased transmission after patients become ill. We also assumed substantially higher infectiousness of symptomatic patients compared with those who remained asymptomatic throughout the course of infection,[11-14] as well as the 14-day induction period after the first and second doses of vaccination. The supplemental material provides the differential equations applied to each compartment.



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## Model parameterization

We estimated real-world effectiveness of JYNNEOS® vaccine from large case control studies.[15,16] We estimated model parameters for the natural history of mpox infection from published empirical studies (table 1). Daily reported mpox cases came from US CDC reports.[8] We estimate the total at-risk population, N, based on the number of persons aged 13 years or older who have HIV or HIV pre-exposure prophylaxis (PrEP) prescription, adjusted for unknown persons and those who are at high risk but do not take PrEP by two folds.[17] We estimated the effective population size of the high-risk group, the transmission coefficients, and the initial numbers in the compartments that are or will be infectious for mpox (table 1 and table 2), by fitting the model to actual US mpox epidemic curve during the period between May 22, 2022 to December 22, 2022, using the least square method. We considered 10 May, 2022 as the first day of our model simulation, the date of illness onset for the first case of mpox in the US.[8]

## Statistical analysis

To stabilize the variance and mitigate the impact of the large values data on the fitting results, we first took the square root of the daily mpox reported cases and model simulated cases before applying the least square method. We used mean square error (MSE) as the goodness-of fit statistics to determine the performance of model fitting and selection of best-fit model with the smallest MSE under the base scenario as well as under the sensitivity analyses: MSE= $\frac{1}{n}\sum_{i=1}^{n}(\sqrt{Y_i}-\sqrt{\widehat{Y}_i})^2$ , where n is the number of days observed that was used in model fitting; $Y_i$ is the number of real-world US mpox reported cases for the i th day; $\widehat{Y}_i$ is the number of model simulated US mpox reported cases for the i th day.



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## Vaccination

We calculated the rate of vaccination for first and second doses of JYNNEOS® in the model based on daily JYNNEOS® doses administered and reported to the CDC.[5] Currently, the US CDC provides daily statistics on the number of vaccine doses administered. However, the precise proportion of high-risk MSM (with multiple sexual partners) among the vaccine recipients is not readily available. In our modelling approach, we have addressed this data gap by distributing the daily dose of vaccine administration in a 2:1 ratio between the high-risk and low-risk groups. This is equivalent to a 48-fold ( $\frac{\frac{2}{3} \,/\, 4\%}{\frac{1}{3} \,/\, 96\%}$ ) higher vaccination rate for the high-risk group because the high-risk group constitutes approximately 4% of the total at-risk population, as indicated by our fitting results. We assumed that all vaccines administered in the model were for pre-exposure prophylaxis, not for experimental therapeutic purposes. (supplemental figure 1).

## Behavior change in response to mpox epidemic

An estimated 50% of MSM in the US reported taking actions to reduce their risk of acquiring mpox by reducing engagement in risky sexual behaviors since they learned of the mpox outbreak, according to a CDC survey.[7] We therefore assumed that 50% of the high-risk group in our model reduced by 50% their previous risky sexual behaviors since they started to develop awareness on 22 May, 2022, when the first week of mpox vaccine administration was recorded by US CDC. This would yield an alteration of mpox transmission coefficient in the model from $\beta_{HH}$, $\beta_{HL}$, $\beta_{LH}$, to $0.75\beta_{HH}$, $0.75\beta_{HL}$, $0.75\beta_{LH}$ since 22 May, 2022.



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## Main outcome

We evaluated the preventive effect of current preventive responses in the US (vaccination and high-risk group awareness) at the population-level by calculating the prevention percentage of cumulative reported cases and cumulative infections (symptomatic and asymptomatic) compare to the numbers of cases or infections under the counterfactual scenario without any interventions between May 22, 2022 to December 22, 2022. The formula for calculating the prevention percentage is as follows:

$$\frac{\text{number of mpox cases averted through preventive response}}{\text{number of mpox cases under the scenario without any preventive response}}$$

## Sensitivity analysis

We performed a one-way sensitivity analysis by varying parameters with values of uncertainty, including the proportion of mpox cases reported in the US (*rp*), the proportion of asymptomatic cases (τ), JYNNEOS® vaccine effectiveness ($p_1$ and $p_2$), and assortative mixing ($\beta_{LL}$ vs. $\beta_{HL}, \beta_{LH}$); as well as a three-way sensitivity analysis on the combination of the first three aforementioned parameters, to assess their impact on the prevention percentages of cumulative reported cases and cumulative infections compare to those estimated under the counterfactual scenario without any interventions.

We conducted all analyses using STELLA® software version 3.3.0 (ISEE Systems, Lebanon, NH 03766, USA).



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# Results

## Model fit

Model simulation of mpox epidemic curve fitted to the real-world US outbreak data is illustrated in figure 2. The effective proportion of the population in the high-risk and low-risk groups, estimated by the best model simulation, was 4% (114931) and 96% (2758352) of the total population at risk (N), respectively. The fitted initial population were 20 each for the $I_{1H}$, $E_H$, $A_H$ compartment and 2 each for the $I_{1L}$, $E_L$, $A_L$ compartment. $\beta_{HH}$ was estimated at 8.93 $day^{-1}$, while $\beta_{HL}$, $\beta_{LH}$, $\beta_{LL}$ were each estimated at 0.04 $day^{-1}$ under the best-fitted model, yielding the basic reproduction number for the high-risk and low-risk population to be 3.88 and 0.39, respectively. Details for calculation of the basic reproduction numbers are provided in the supplemental material. The MSE of the best-fit model in the base scenario was 2.088. This low MSE (1.5% of 139, the mean number of daily reported mpox cases in the US between 22 May and 22 December, 2022) suggested that the model performed quite well against the variance-stabilized data, indicating a high level of accuracy in fittings.

In the context of the two-dose vaccine administration campaign and high-risk group awareness, daily reported mpox cases generated by the best-fitted model (figure 2) peaked on 6 August, 2022 with 505 cases reported that day, and declined to a very low level by the end of 2022. Number of cumulative cases estimated by the model during 22 May through 22 December, 2022 was 29559 (± 5%: (28081, 31036) ), which is similar to the actual reported number of 29918 cases.[8] Among the 29559 model-simulated cases, 71.8% (21227) were from the high-risk group. This is also comparable to the



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actual proportion of mpox cases in the US from males aged 16-45 years (78.6%),[18] an age group that is most actively involved in sexual activities (taking into account that the actual reported cases of males also include a portion that did not engage in risky sexual behaviors).

## Counterfactual scenarios and effects of the measures

Figure 3 presents the daily reported mpox cases simulated under some counterfactual scenarios without either campaign of vaccine administration or high-risk group awareness. The simulated epidemic curve in the absence of any preventive measures reach an extremely large peak on 31 July, 2022 with 1528 cases reported that day, and also yields a prolonged epidemic, producing 82160 cumulative reported cases between 22 May and 22 December, 2022. By incorporating only the vaccine administration, the simulated epidemic curve would peak at a slightly lower level compared to the scenario without any preventive measures, with 1365 cases reported on 27 July, 2022. On the other hand, with only the high-risk group awareness starting from 22 May, 2022, the simulated epidemic curve would peak at an apparently lower level, with 974 cases reported on 24 August, 2022. However, this high-risk group awareness alone scenario would endure a much longer period of epidemic compared to the three other scenarios (vaccination +/- awareness or no intervention).

By summing the simulated daily reported cases and daily infections under each scenario, we estimated that 2-dose vaccination administration, solely, could prevent 21.2% of reported cases or 21.2% of infections (symptomatic and asymptomatic) by the end of 2022, while high-risk group awareness could prevent 15.4% of reported cases or



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15.3% of infections, compared to the scenario without any preventive measures (table 3, table 4). With both the vaccine administration and high-risk group awareness, our model suggested how the mpox epidemic in the US was successfully controlled, preventing 64.0% of reported cases and 64.0% of infections.

## Sensitivity analysis

We further investigated the influence of varying parameters on the prevention percentage (table 3 and table 4). In the one-way sensitivity analysis (table 3), the proportion of mpox cases reported in the US and the proportion of asymptomatic cases had some effect on the estimates of prevention percentage for the preventive measures individually (12.9%-24.1% for vaccination, and 14.3-15.4% for high-risk group awareness), and for the combination of vaccination and awareness/risk reduction (47.4%-69.0%). Relaxing the relation between $\beta_{LL}$ and $\beta_{HL}, \beta_{LH}$ to two-fold ($2\beta_{LL} = \beta_{HL} = \beta_{LH}$) has more effects on the estimates of prevention percentage for high-risk group awareness (20.6%) than that of vaccination (22.7%). With a one-way sensitivity analysis with lower vaccine effectiveness, the vaccination campaign alone would only avert 10.2% of reported cases or 10.2% of infections. The preventive proportion for the combination of both preventive measures also dropped to 43.8% and 43.8% for reported cases and infections, respectively. The apparently lower estimates of prevention percentage under the lower vaccine effectiveness scenario are consistent in the three-way sensitivity analysis with the combination of different proportion of mpox cases reported and the proportion of asymptomatic cases. In all scenarios, the vaccination campaign and high-risk group awareness demonstrated synergistic effects (the joint effect, in terms of the percentages of prevented cases or infections, is larger than the



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sum of each individual effect) rather than merely addictive effects (the joint effect is only the same as the sum of each individual effect). The prevention percentage of cumulative infections had similar results to that of cumulative reported cases (table 3 and table 4).



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# Discussion

## Main findings

Our modelling study sought to parse the relative likely contributions of both the 2-dose mpox vaccination campaign and the awareness of the high-risk population for risk reduction. Using real-world data for parameter estimations, we found a synergistic effect with high effectiveness of the combination of both intervention measures in averting the number of mpox cases during the 2022-2023 mpox epidemic in the US. Our results indicate that the two-dose mpox vaccination campaign prevented 21.2% (sensitivity analysis: 10.2%–24.1%) of mpox cases, the high-risk group awareness prevented 15.4% (sensitivity analysis: 14.3%–20.6%) of mpox cases, and the combination of both measures prevented 64.0% (sensitivity analysis: 43.8%–69.0%) of mpox cases, compared to the counterfactual scenario in the absence of both measures.

## Model comparison with real-world US case distributions and behavior adaptations globally

The 2022-2023 global mpox outbreak, as well as the epidemic in the US, has the majority of infections observed to transmit among men through male-to-male sexual contact, with far fewer heterosexual sexual transmission, and skin-to-skin non-sexual transmission to children.[2] Our risk-structured mpox mathematical model successfully captured these distribution characteristics of cases among high- and low-risk populations. In the simulated results of our model, 71.8% of cases were from the high-risk group, a similar value to the actual distribution of mpox cases in the US among males aged 16-45 years (78.6%).[18] The epidemic curve for the low-risk group in our



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model exhibited a later onset and also peaked later compared to that of the high-risk group. This is also consistent with the real-world situation, where the proportion of cases in the US that reported other than male-to-male sexual contact (including women, and men with no known male-to-male sexual contact) accounted for nearly 0% of the total reported contacts in May 2022, gradually rose to about 10-15% in June and July, and comprised over 30% of the total reported contacts in late August 2022.[19]

Our model suggests that the US mpox epidemic may have been controlled due to the combination of 2-dose vaccination campaign and high-risk group awareness with risk reduction. The alarm raised by the 2022-2023 mpox outbreak motivated MSM to take action to reduce the risk of infection in the US. Results globally seem to support the impact of community messaging and risk reduction. A study from Australia found that participants recruited from a sexual health clinic and MSM communities reported reduced sexual activities during the outbreak.[20] This reduction included reduced sex with casual partners (53.9%), cessation of drug use proximate to sexual activity ("chemsex"; 49.8%), abstaining from group sex (45.3%), and an increase in condom use for anal sex (26.2%).[20] Additionally, most participants possessed correct knowledge of the mpox transmission route (94.7%), showed willingness toward vaccination (68.3%), and were concerned about the mpox epidemic.[20]

## Possible reasons for the synergistic effects

Either vaccination campaign or high-risk group awareness alone demonstrate limited prevention percentages (21.2% and 15.4%, respectively) in our study, given that the vaccine coverage for the at-risk population in the US only reached 37% for the first



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dose and 23% for the second dose by January 2023,[4] and the modest decrease in risky sexual behaviors associated with high-risk group awareness. That their combination exhibited such a synergistic effect (64.0%), nearly twice the sum of the effect of each intervention, sends a compelling public health message. From the modelling perspective, the high-risk group awareness rapidly reduced the transmission coefficients ($\beta_{HH}$, $\beta_{HL}$, $\beta_{LH}$) at the population level, while 2-dose vaccination campaign immunized the at-risk individuals and removed them from the susceptible pool, albeit with varying degrees of imperfect protection. The results of synergistic effects arise from the simultaneous implementation of population-level and individual-level control measures, which would likely be applied to other infectious disease risks when transmissibility is vaccine-preventable and behaviorally mediated. From the prevention policy perspective, awareness and vaccination campaign also act synergistically. When the high-risk MSM became aware of the mpox epidemic and changed their previous risky sexual behaviors, it was likely that they not only reduced the risk of contracting mpox, but also sought to obtain immunity against mpox through getting mpox vaccinations. On the other hand, the implementation of vaccination campaigns may raise public attention regarding mpox. These campaigns are often accompanied by public health education initiatives, encompassing information about the symptoms and transmission routes of mpox, as well as preventive measures. Such public health communications can enhance the understanding and knowledge of mpox for the public, thereby elevating the awareness and lead to behavior changes.

## Comparison with previous modelling studies

Owing to the shortages of vaccine supply at the early stage of this unprecedented global



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mpox outbreak, multiple countries opted to prioritize administering as many first doses as possible to the high-risk population until the supply were sufficient for full-dose administration.[21] Prior published modelling studies focused on exploring strategies to enhance the effect of vaccination campaign in situations of vaccine shortages, including dose-sparing strategies and prioritizing the vaccine for geographic networks with more initial infections and larger basic reproduction numbers.[22,23] A modelling study of the 2022 mpox outbreak suggested that the decline in mpox incidence in the UK was mainly attributed to immunity at the population level following infections and reduced exposure due to behavior changes, rather than to the single-dose vaccination.[24] Another modelling study in the UK that published later also came to corresponding conclusions that the downturn of the mpox outbreak in the UK possibly resulted from moderate reductions in sexual risk behavior of MSM in combination with the reduction of the effective infectious period. While the delayed initiation of vaccination only averted a small percentage of infections (9.8%), it helped to prevent the potential mpox resurgence.[25] However, the effectiveness of the first dose of the JYNNEOS® vaccine is substantially lower than that of full dose. Even with a 2-dose vaccination, titers of orthopoxvirus-neutralizing antibody were observed to wane by the 2-year mark.[26] A single dose immunization wanes even faster, indicating the need for boosters in the face of ongoing transmission and risk taking. As the subsequent vaccine supply gradually replenished, and an emergency use authorization (EUA) for the intradermal injection of JYNNEOS® vaccine was issued,[4] 5-fold increases were seen in the availability of the vaccine; incorporating full 2-dose vaccination into modelling will illuminate the potential of vaccination at the population level.



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## Strengths and limitations

Strengths of our study include our inclusion of up-to-date data on the US vaccination campaign, timely initiated in late May with expanded supplies after early July,[27] as well as high-risk group behavior changes in our risk-structured modelling. We suggest that both vaccination and awareness among MSM played roles in controlling the mpox epidemic in the US, with significant synergistic effects. These novel findings are highly relevant to countries facing the mpox epidemics and may apply to other vaccine-preventable and behaviorally mediated infectious diseases. Our study also has limitations. First, we postulated that the reduction in risky sexual activity within the high-risk population would be maintained at least until the end of 2022. There were possibilities that a reversion to risky sexual behaviors and a decrease in awareness to a lower level could occur, as the high-risk population might become fatigued with preventive measures. The lack of detailed sexual risk survey data throughout the study period makes it challenging to quantify fluctuations in these behaviors with time. The potential transience of protective effectiveness of behavior change highlights the synergism of the vaccination campaign with more durable protection. Second, we assumed a 10-fold difference in transmission potential between the high-risk and low-risk groups, based on currently obtainable informations.[2] The proportions of cases from the high-risk population simulated by our model align with the actual reports to the US CDC, supporting that the aforementioned assumptions should be reasonable, though we cannot be sure. Third, high-risk group awareness for mpox may theoretically increase the vaccination rate, and decrease the proportion of symptomatic patients who still engage in activity associated with transmission risk. However, our model did not incorporate these two theoretical component of awareness effects because vaccination



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rate was constrained by vaccine supplies, and there were no empirical studies that reported the actual decrease of the proportion of symptomatic patients who still engage in activity associated with transmission risk after the awareness initiation. Finally, our sensitivity analyses show that estimates of prevention percentages for the vaccination campaign are sensitive to uncertain estimates of vaccine effectiveness and the proportion of mpox cases reported in the US. Still, in all scenarios, the vaccination campaign and high-risk group awareness demonstrated synergistic effects.

# Conclusion

We conclude that our modelling evidence suggests that the JYNNEOS® mpox vaccine, highly effective among the at-risk population at the individual level (preventing against mpox infection and reducing severity of symptoms), is also highly effective at the population level (controlling mpox outbreaks), particularly when combined with high-risk group awareness and consequent changes in risky sexual behavior. The combination of these measures has a synergistic effect. Our findings on the effect of vaccination, behavior changes, and other control measures are highly relevant for countries facing the ongoing or reemerging threat of mpox. The model may also guide strategic preparedness for analogous epidemics of emerging or re-emerging infectious diseases.



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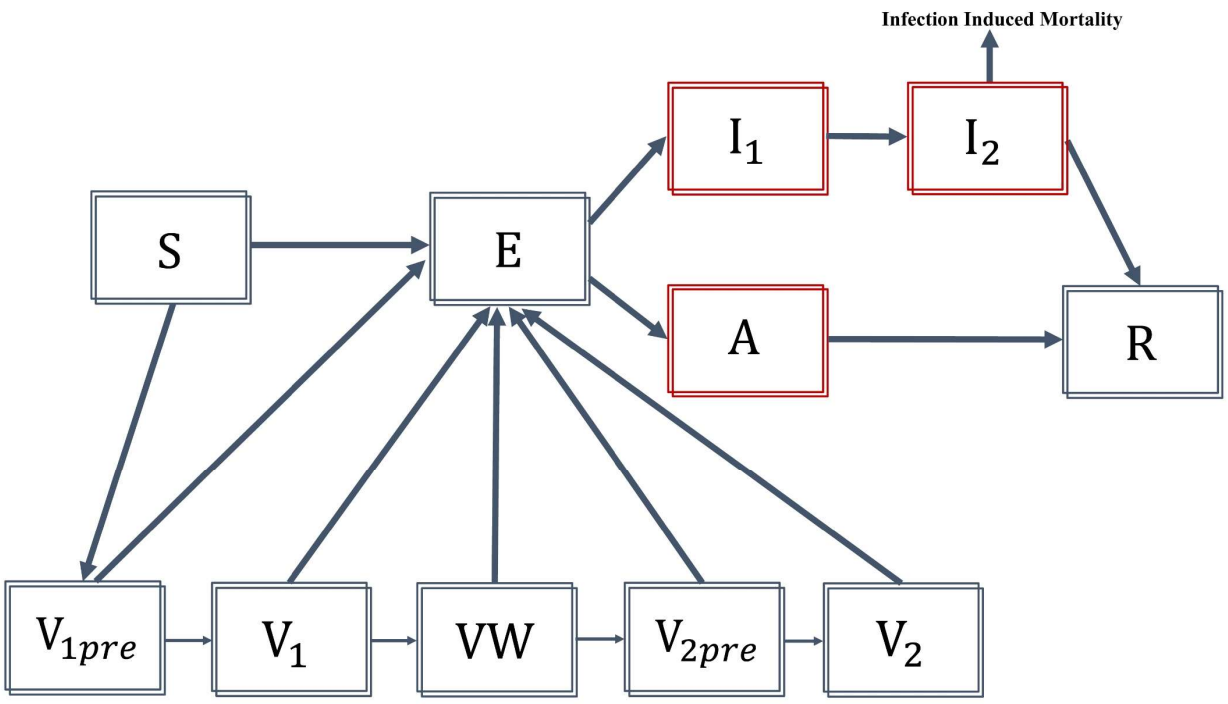
**Figure 1: Schematic diagram of SEIARV compartmental model**




The model population is classified into low-risk and high-risk group, illustrated by stacked compartments. The compartments are: S (susceptible), E (exposed), $I_1$ (pre-symptomatic), $I_2$ (symptomatic), A (asymptomatic), R (recovered), $V_{1pre}$ (less than 14 days since first dose vaccination, without complete first-dose efficacy), $V_1$(first dose vaccinated with complete first-dose efficacy), VW (more than 28 days since first dose vaccination, eligible for the second dose), $V_{2pre}$ (less than 14 days since second dose vaccination, without complete second-dose efficacy), $V_2$(second dose vaccinated with full efficacy). The compartments that are infectious are indicated with red frame.



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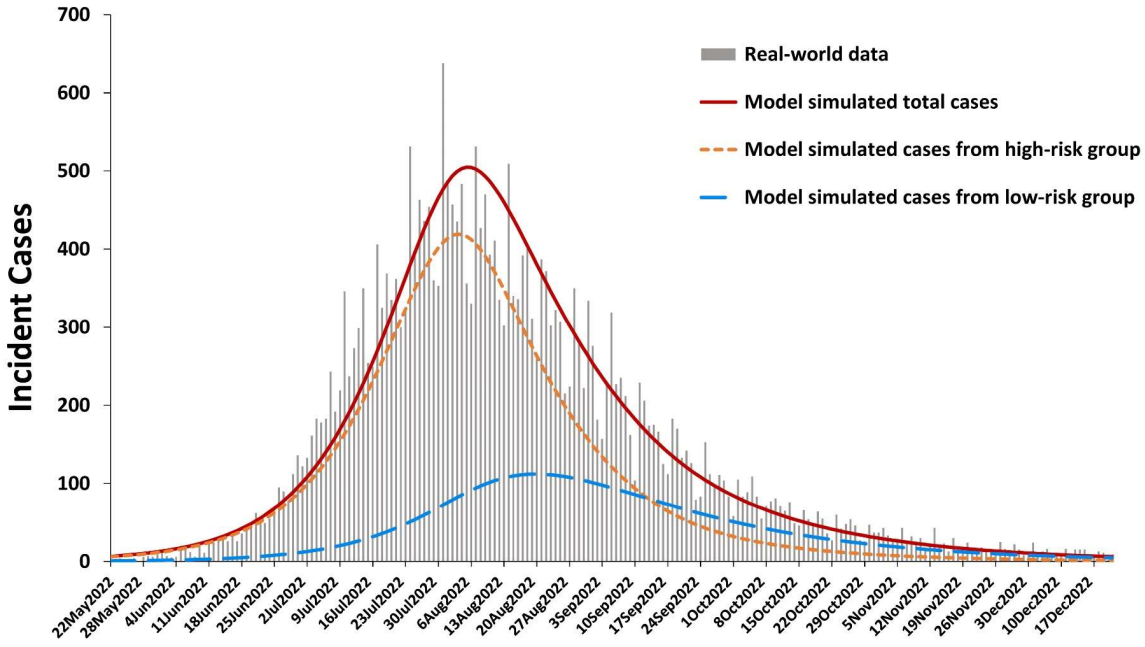
**Figure 2: Real-world daily reported cases and model predicted daily reported cases of mpox in the US from 22 May to 22 December, 2022**




Real-world data are presented in bar chart; model simulations are presented in line graphs.



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**Figure 3: Modelling results of daily reported mpox cases for different scenarios**

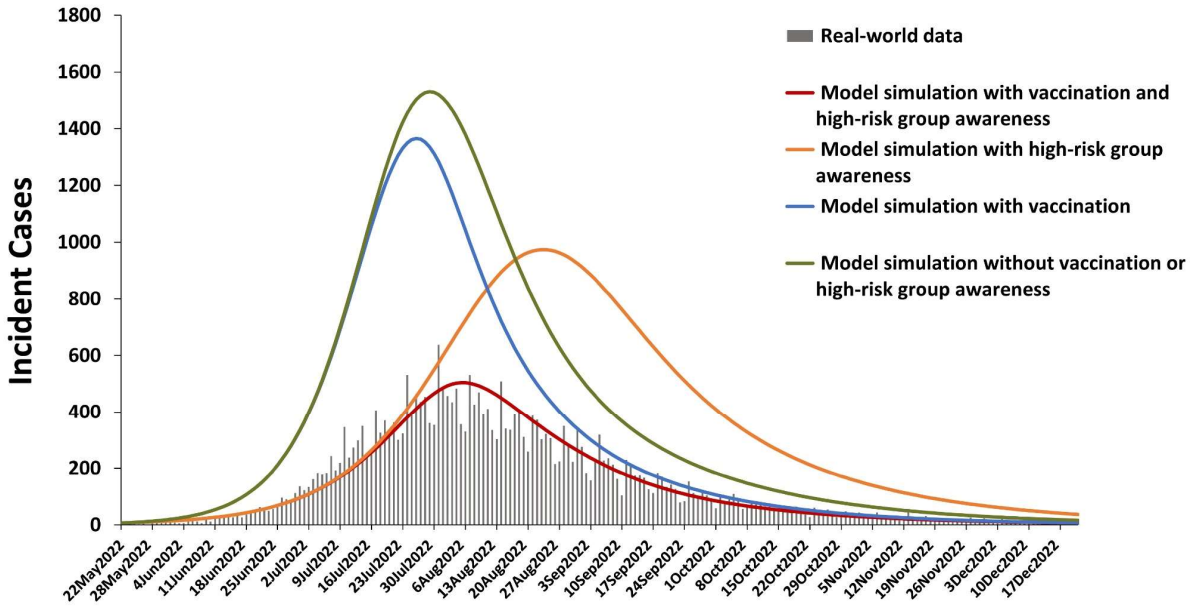




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**Table 1: Model parameters, values and data references.**

| Parameter | Description | Value (unit) | Source |
|---|---|---|---|
| $B$ | Transmission coefficient of mpox | $\beta_{HH}$: determined by fitting data $\beta_{LL} = \beta_{HL} = \beta_{LH}$: set at the level of a fraction of $\beta_{HH}$ to keep $R0_H = 10\ R0_L$¶ (sensitivity analysis: $2\beta_{LL} = \beta_{HL} = \beta_{LH}$: set at the level of a fraction of $\beta_{HH}$ to keep $R0_H = 10\ R0_L$) | Fitting real world epidemic curve Assume that the value of R0 of the high-risk group is 10-fold higher than that of the low-risk group |
| $\Theta$ | Proportion of symptomatic patients who still engage in activity associated with transmission risk | 0.3 | Lee YL et al[28] |
| $\delta$ | Relative risk of transmission of asymptomatic mpox patients, compared with that of symptomatic patients | 0.1 | Assumption |
| $\tau$ | Proportion of patients remained asymptomatic throughout the course of infection | 0.06 (sensitivity analysis: 0.2) | Reda A et al[29] (sensitivity analysis: assumption) |



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| | | | |
|---|---|---|---|
| $\sigma$ | Rate of progression from $E$ to $I_1$ or $A$ (reciprocal of incubation period minus pre-symptomatic period) | 1/(8.23-4) ($day^{-1}$) | Wei F et al[30] |
| $\gamma_{sym}$ | Rate of progression from $I_1$ to $I_2$ (reciprocal of pre-symptomatic period) | 1/4 ($day^{-1}$) | Miura F et al[10] |
| $\gamma_1$ | Rate of progression from $I_2$ to $R$ (reciprocal of infectious period for symptomatic patients) | 1/21 ($day^{-1}$) | WHO[1] |
| $\gamma_2$ | Rate of progression from $A$ to $R$ (reciprocal of infectious period for asymptomatic patients) | 1/(21+4) ($day^{-1}$) | Miura F et al[10], WHO[1] |
| $m$ | Infection-related mortality rate for symptomatic mpox | 0.0000611 ($day^{-1}$) † | WHO[2] |
| $p_1$ | Vaccine effectiveness of first dose JYNNEOS® vaccination against mpox | 75.2% (sensitivity analysis: 35.8%) | Dalton AF et al[15] (sensitivity analysis: Deputy NP et al[16]) |
| $p_2$ | Vaccine effectiveness of full dose (two dose) JYNNEOS® vaccination against mpox | 85.9% (sensitivity analysis: 66.0%) | Dalton AF et al[15] (sensitivity analysis: Deputy NP et al[16]) |
| $\mu$ | Rate of entry into (by arriving 13 years) and exit from | 1/365*64.5 ($day^{-1}$) | Life expectancy at 13 years |



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| | | | |
|---|---|---|---|
| | (through natural death) the model | | in the US: 64.5[31] |
| *rp* | Proportion of mpox cases reported in the US | 50%<br>(sensitivity analysis: 25% - 75%) | Assumption<br>(sensitivity analysis: assumption) |
| *N* | Total model population: high-risk and low-risk group in US | 1,436,642*2=2,873,284 | CDC AtlasPlus[17], adjusted for unknown HIV patients and high-risk people who did not take PrEP by multiplying the totoal number of HIV patients and people on PrEP prescription by two-fold. |
| $n_H$ | Proportion of the model population in the high-risk group | Determined by fitting data | Fitting real world epidemic curve |
| $n_L$ | Proportion of the model population in the low-risk group | Determined by fitting data | Fitting real world epidemic curve |

¶ $\beta_{HH}$: transmission coefficient for mpox transmission from high-risk individuals to high-risk individuals. $\beta_{HL}$: transmission coefficient for mpox transmission from low-risk individuals to high-risk individuals. $\beta_{LH}$: transmission coefficient for mpox transmission from high-risk individuals to low-risk individuals. $\beta_{LL}$: transmission coefficient for mpox transmission from low-risk individuals to low-risk individuals. We assumed the basic reproductive number for the high-risk group ($R0_H$) to be 10 times that of the low-risk group ($R0_L$) due to evidence on higher proportion of mpox transmission



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occurring through sexual contacts compare to non-sexual contacts during the current 2022-2023 outbreak according to WHO.[2]

† Case fatality ratio $\rho = 0.00128$ (111/86516),[2] $m = \rho(\mu + \gamma_1) / (1-\rho) = 0.0000611$



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**Table 2: Model compartments and their initial values. Compartments of the high-risk and low-risk group are indicated with subscript H for the high-risk group and subscript L for the low-risk group.**

| Status | Description | Initial Value |
|---|---|---|
| S | Population susceptible to mpox ($S_H$ and $S_L$) | $S_H: N \times n_H$; $S_L: N \times n_L$ |
| E | Population exposed to mpox but not yet infectious ($E_H$ and $E_L$) | $E_H$: determined by fitting data; $E_L$: $0.1E_H$* |
| $I_1$ | Population acquiring symptomatic mpox in their pre-symptomatic phase, infectious ($I_{1H}$ and $I_{1L}$) | $I_{1H} = E_H$; $I_{1L} = E_L$ |
| $I_2$ | Population acquiring symptomatic mpox in their symptomatic phase, infectious ($I_{2H}$ and $I_{2L}$) | $I_{2H}$: 1**; $I_{2L}$: 0 |
| A | Population with asymptomatic mpox, infectious ($A_H$ and $A_L$) | $A_H = E_H$; $A_L = E_L$ |
| R | Population recovered and immune to mpox ($R_H$ and $R_L$) | $R_H = R_L = 0$ |
| $V_{1pre}$ | Population with less than 14 days since first dose vaccination, without complete first-dose efficacy ($V_{1preH}$ and $V_{1preL}$) | $V_{1preH} = V_{1preL} = 0$ |
| $V_1$ | Population with more than 14 days but less than 28 days since first dose vaccination, with complete first-dose efficacy ($V_{1H}$ and $V_{1L}$) | $V_{1H} = V_{1L} = 0$ |
| $VW$ | Population with more than 28 days since first dose vaccination, eligible for the second dose ($VW_H$ and $VW_L$) | $VW_H = VW_L = 0$ |



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| | | |
|---|---|---|
| $V_{2pre}$ | Population with less than 14 days since second dose vaccination, without complete second-dose efficacy ($V_{2preH}$ and $V_{2preL}$) | $V_{2preH} = V_{2preL} = 0$ |
| $V_2$ | Population with more than 14 days since second dose vaccination, with full vaccine efficacy ($V_{2H}$ and $V_{2L}$) | $V_{2H} = V_{2L} = 0$ |

* We assumed the initial high-risk population in the status that are or will be infectious except for $I_2$ ($E_H$, $I_{1H}$, and $A_H$) status to be 10 times that of the low-risk population ($E_L$, $I_{1L}$, $A_L$) due to evidence on higher proportion of mpox transmission occurring through sexual contacts compare to non-sexual contacts during the current 2022-2023 outbreak according to WHO.[2]

** One case of mpox was reported to the US CDC on 10 May, 2022.[8]



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**Table 3: One-way sensitivity analysis of parameters with uncertainty on the impact of the prevention percentages of mpox reported cases and mpox infections for vaccination and high-risk group awareness.** Abbreviations: VE, vaccine effectiveness.

| | Vaccination percentage of prevented cases (percentage of prevented infections) | High-risk group awareness percentage of prevented cases (percentage of prevented infections) | Vaccination and high-risk group awareness percentage of prevented cases (percentage of prevented infections) |
|---|---|---|---|
| The base scenario | 21.2% (21.2%) | 15.4% (15.3%) | 64.0% (64.0%) |
| Reporting rate=25% | 12.9% (12.9%) | 14.3% (14.2%) | 47.4% (47.4%) |
| Reporting rate=75% | 24.1% (24.1%) | 15.4% (15.3%) | 69.0% (69.0%) |
| Asymptomatic rate=20% | 18.4% (18.4%) | 15.0% (14.9%) | 58.7% (58.8%) |
| First dose VE=35.8%, Second dose VE=66.0% | 10.2% (10.2%) | 17.3% (17.2%) | 43.8% (43.8%) |



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| | | | |
|---|---|---|---|
| $2\beta_{LL} = \beta_{HL} = \beta_{LH}$ | 22.7% (22.7%) | 20.6% (20.5%) | 65.4% (65.4%) |



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**Table 4: Three-way sensitivity analysis of parameters with uncertainty on the impact of the prevention percentages of mpox reported cases and mpox infections for vaccination and high-risk group awareness.** Abbreviations: VE, vaccine effectiveness.

| | | Vaccination percentage of prevented cases (percentage of prevented infections) | High-risk group awareness percentage of prevented cases (percentage of prevented infections) | Vaccination and high-risk group awareness percentage of prevented cases (percentage of prevented infections) |
|---|---|---|---|---|
| The base scenario: Reporting rate: 50%, Asymptomatic rate=6%, First dose VE=75.2%, Second dose VE=85.9% | | 21.2% (21.2%) | 15.4% (15.3%) | 64.0% (64.0%) |
| First dose VE=75.2%, Second dose VE=85.9% | Reporting rate: 25% - 75% Asymptomatic rate=6% | 12.9% - 24.1% (12.9% - 24.1%) | 14.3% - 15.4% (14.2% - 15.3%) | 47.4% - 69.0% (47.4% - 69.0%) |
| | Reporting rate: 25% - 75% Asymptomatic rate=20% | 12.8% - 21.3% (12.8% - 21.3%) | 14.2% - 15.1% (14.2% - 15.0%) | 46.8% - 64.4% (46.8% - 64.4%) |
| First dose VE=35.8%, | Reporting rate: 25% - 75% Asymptomatic rate=6% | 5.6% - 10.8% (5.6% - 10.9%) | 14.7% - 17.3% (14.6% - 17.2%) | 30.1% - 45.1% (30.1% - 45.1%) |



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| | | | | |
|---|---|---|---|---|
| Second dose<br>VE=66.0% | Reporting rate: 25% - 75%<br>Asymptomatic rate=20% | 4.6% - 8.8%<br>(4.6% - 8.8%) | 14.3% - 15.9%<br>(14.2% - 15.9%) | 26.1% - 39.5%<br>(26.1% - 39.5%) |



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# Supplemental material

## Model Equations

The following text presents the equations of the flows of each compartment in the mpox compartmental transmission model, along with explanations of the transmission dynamic.

*Susceptible Status* ($S_H$ and $S_L$)

Individuals in both the high-risk and low-risk population entered the model upon reaching an age of 13 at the rate of $\mu$. They left the susceptible status by getting infected by infectious individuals (from $I_1$, $I_2$, or $A$) of either the high-risk or low-risk population at a transmission rate $\beta$, by receiving first dose mpox vaccine at the pace of $v1speed$ ($v1speed_H$ and $v1speed_L$), or by natural death at the rate of $\mu$.

$$\frac{dS_H}{dt} = \mu N_H - \left(\beta_{HH} I_{1H} + \Theta\beta_{HH} I_{2H} + \delta\beta_{HH} A_H\right)\frac{S_H}{N} - \left(\beta_{HL} I_{1L} + \Theta\beta_{HL} I_{2L} + \delta\beta_{HL} A_L\right)\frac{S_H}{N} - \mu S_H - v1speed_H$$

$$\frac{dS_L}{dt} = \mu N_L - \left(\beta_{LL} I_{1L} + \Theta\beta_{LL} I_{2L} + \delta\beta_{LL} A_L\right)\frac{S_L}{N} - \left(\beta_{LH} I_{1H} + \Theta\beta_{LH} I_{2H} + \delta\beta_{LH} A_H\right)\frac{S_L}{N} - \mu S_L - v1speed_L$$

*Exposed status* ($E_H$ and $E_L$)

Susceptible ($S$) and vaccinated ($V_{1pre}$, $V_1$, $VW$, $V_{2pre}$, $V_2$) populations contracted mpox through close contact with infectious individuals from $I_1$, $I_2$, or $A$, and entered the exposed status. The exposed population left E status by becoming infectious after an incubation period ($1/\sigma$ day), or by natural death at the rate of $\mu$. The infectiousness of symptomatic ($I_2$) compartment was discounted by $\Theta$ due to a reduced level of activeness for mpox patients who were in their symptomatic period, suffering from mpox symptoms. The transmission rate for the asymptomatic ($A$) compartment was discounted by $\delta$, based on evidence that asymptomatic patients have a lower level of viral load



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compared to symptomatic patients. The risk of contracting mpox was reduced to varying degrees for the population in each of the vaccinated status, and this will be further interpreted in detail.

$$\frac{dE_H}{dt}=\left(\beta_{HH}I_{1H}+\Theta\beta_{HH}I_{2H}+\delta\beta_{HH}A_H\right)\frac{S_H}{N}+\left(\beta_{HL}I_{1L}+\Theta\beta_{HL}I_{2L}+\delta\beta_{HL}A_L\right)\frac{S_H}{N}+\left(\beta_{HH}I_{1H}+\Theta\beta_{HH}I_{2H}+\delta\beta_{HH}A_H\right)\frac{V_{1preH}}{N}$$
$$+\left(\beta_{HL}I_{1L}+\Theta\beta_{HL}I_{2L}+\delta\beta_{HL}A_L\right)\frac{V_{1preH}}{N}+(1-p1)\left[\left(\beta_{HH}I_{1H}+\Theta\beta_{HH}I_{2H}+\delta\beta_{HH}A_H\right)\frac{V_{1H}}{N}+\left(\beta_{HL}I_{1L}+\Theta\beta_{HL}I_{2L}+\delta\beta_{HL}A_L\right)\frac{V_{1H}}{N}\right]$$
$$+\left(1-p_1\right)\left[\left(\beta_{HH}I_{1H}+\Theta\beta_{HH}I_{2H}+\delta\beta_{HH}A_H\right)\frac{VW_H}{N}+\left(\beta_{HL}I_{1L}+\Theta\beta_{HL}I_{2L}+\delta\beta_{HL}A_L\right)\frac{VW_H}{N}\right]$$
$$+\left(1-p_1\right)\left[\left(\beta_{HH}I_{1H}+\Theta\beta_{HH}I_{2H}+\delta\beta_{HH}A_H\right)\frac{V_{2preH}}{N}+\left(\beta_{HL}I_{1L}+\Theta\beta_{HL}I_{2L}+\delta\beta_{HL}A_L\right)\frac{V_{2preH}}{N}\right]$$
$$+\left(1-p_2\right)\left[\left(\beta_{HH}I_{1H}+\Theta\beta_{HH}I_{2H}+\delta\beta_{HH}A_H\right)\frac{V_{2H}}{N}+\left(\beta_{HL}I_{1L}+\Theta\beta_{HL}I_{2L}+\delta\beta_{HL}A_L\right)\frac{V_{2H}}{N}\right]-\mu E_H-\sigma E_H$$

$$\frac{\mathrm{dE_L}}{\mathrm{dt}}=\left(\beta_{LL}I_{1L}+\Theta\beta_{LL}I_{2L}+\delta\beta_{LL}A_L\right)\frac{\mathrm{S_L}}{\mathrm{N}}+\left(\beta_{LH}I_{1H}+\Theta\beta_{LH}I_{2H}+\delta\beta_{LH}A_H\right)\frac{\mathrm{S_L}}{\mathrm{N}}+\left(\beta_{LL}I_{1L}+\Theta\beta_{LL}I_{2L}+\delta\beta_{LL}A_L\right)\frac{\mathrm{V_{1preL}}}{\mathrm{N}}$$
$$+\left(\beta_{LH}I_{1H}+\Theta\beta_{LH}I_{2H}+\delta\beta_{LH}A_H\right)\frac{V_{1preL}}{N}+(1-p1)\left[\left(\beta_{LL}I_{1L}+\Theta\beta_{LL}I_{2L}+\delta\beta_{LL}A_L\right)\frac{V_{1L}}{N}+\left(\beta_{LH}I_{1H}+\Theta\beta_{LH}I_{2H}+\delta\beta_{LH}A_H\right)\frac{V_{1L}}{N}\right]$$
$$+\left(1-p_1\right)\left[\left(\beta_{LL}I_{1L}+\Theta\beta_{LL}I_{2L}+\delta\beta_{LL}A_L\right)\frac{VW_L}{N}+\left(\beta_{LH}I_{1H}+\Theta\beta_{LH}I_{2H}+\delta\beta_{LH}A_H\right)\frac{VW_L}{N}\right]$$
$$+\left(1-p_1\right)\left[\left(\beta_{LL}I_{1L}+\Theta\beta_{LL}I_{2L}+\delta\beta_{LL}A_L\right)\frac{V_{2preL}}{N}+\left(\beta_{LH}I_{1H}+\Theta\beta_{LH}I_{2H}+\delta\beta_{LH}A_H\right)\frac{V_{2preL}}{N}\right]$$
$$+\left(1-p_2\right)\left[\left(\beta_{LL}I_{1L}+\Theta\beta_{LL}I_{2L}+\delta\beta_{LL}A_L\right)\frac{V_{2L}}{N}+\left(\beta_{LH}I_{1H}+\Theta\beta_{LH}I_{2H}+\delta\beta_{LH}A_H\right)\frac{V_{2L}}{N}\right]-\mu E_L-\sigma E_L$$

*Pre-symptomatic status ($I_{1H}$* and *$I_{1L}$)*

A proportion ($1-\tau$) of exposed population became infectious and first experienced a period of pre-symptomatic phase. The pre-symptomatic population left $I_1$ status by developing symptoms after a pre-symptomatic period ($1/\gamma_{sym}$day), or by natural death at the rate of $\mu$.

$$\frac{dI_{1H}}{dt}=(1-\tau)\sigma E_H-\left(\mu+\gamma_{sym}\right)I_{1H}$$

$$\frac{dI_{1L}}{dt}=(1-\tau)\sigma E_L-\left(\mu+\gamma_{sym}\right)I_{1L}$$



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*Symptomatic status ($I_{2H}$* and *$I_{2L}$)*

Population in the pre-symptomatic status entered the symptomatic ($I_2$) phase at the rate of $\gamma_{sym}$. They left $I_2$ status by recovering from mpox infection at the rate of $\gamma_1$, by dying of infection induced mortality at the rate of $m$, or by natural death at the rate of $\mu$.

$$\frac{dI_{2H}}{dt} = \gamma_{sym} I_{1H} - (\mu + \gamma_1 + m) I_{2H}$$

$$\frac{dI_{2L}}{dt} = \gamma_{sym} I_{1L} - (\mu + \gamma_1 + m) I_{2L}$$

*Asymptomatic status ($A_H$* and *$A_L$)*

A proportion ($\tau$) of exposed population became infectious but remained asymptomatic throughout the course of infection. The asymptomatic population left $A$ status by recovering from mpox infection at the rate of $\gamma_2$, or by natural death at the rate of $\mu$.

$$\frac{dA_H}{dt} = \tau\sigma E_H - (\mu + \gamma_2) A_H$$

$$\frac{dA_L}{dt} = \tau\sigma E_L - (\mu + \gamma_2) A_L$$

*Recovery status ($R_H$* and *$R_L$)*

Population from the $I_2$ and $A$ status entered the recovery phase after they recovered from mpox infection at the rate of $\gamma_1$ and $\gamma_2$, respectively. They left the $R$ status by natural death at the rate of $\mu$.



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$$\frac{dR_H}{dt} = \gamma_1 I_{2H} + \gamma_2 A_H - \mu R_H$$

$$\frac{dR_L}{dt} = \gamma_1 I_{2L} + \gamma_2 A_L - \mu R_L$$

$V_{1pre}$ *status* ($V_{1preH}$ and $V_{1preL}$, less than 2 weeks since first dose vaccination, without complete first-dose effectiveness)

Susceptible population entered the $V_{1pre}$ status after receiving first dose JYNNEOS vaccination. They left the $V_{1pre}$ status by getting infected by infectious individuals (from $I_1$, $I_2$, or $A$) at a transmission rate $\beta$, by acquiring complete first-dose effectiveness after a two-week induction period, or by natural death at the rate of $\mu$.

$$\frac{dV_{1preH}}{dt} = v1speed_H - \left(\beta_{HH} I_{1H} + \Theta\beta_{HH} I_{2H} + \delta\beta_{HH} A_H\right)\frac{V_{1preH}}{N} - \left(\beta_{HL} I_{1L} + \Theta\beta_{HL} I_{2L} + \delta\beta_{HL} A_L\right)\frac{V_{1preH}}{N} - \frac{1}{14} V_{1preH} - \mu V_{1preH}$$

$$\frac{dV_{1preL}}{dt} = v1speed_L - \left(\beta_{LL} I_{1L} + \Theta\beta_{LL} I_{2L} + \delta\beta_{LL} A_L\right)\frac{V_{1preL}}{N} - \left(\beta_{LH} I_{1H} + \Theta\beta_{LH} I_{2H} + \delta\beta_{LH} A_H\right)\frac{V_{1preL}}{N} - \frac{1}{14} V_{1preL} - \mu V_{1preL}$$

$V_1$ *status* ($V_{1H}$ and $V_{1L}$, first dose vaccinated with complete first-dose effectiveness)

Population from the $V_{1pre}$ status entered $V_1$ status after a two-week induction period. They left the $V_1$ status by getting infected by infectious individuals (from $I_1$, $I_2$, or $A$) at a transmission rate that is discounted by $1\text{-}p_1$ due to a complete first-dose vaccine effectiveness, by being eligible for the second dose after receiving the first dose for 4 weeks, or by natural death at the rate of $\mu$.

$$\frac{dV_{1H}}{dt} = \frac{1}{14} V_{1preH} - (1-p_1)\left[\left(\beta_{HH} I_{1H} + \Theta\beta_{HH} I_{2H} + \delta\beta_{HH} A_H\right)\frac{V_{1H}}{N} + \left(\beta_{HL} I_{1L} + \Theta\beta_{HL} I_{2L} + \delta\beta_{HL} A_L\right)\frac{V_{1H}}{N}\right] - \frac{1}{14} V_{1H} - \mu V_{1H}$$

$$\frac{dV_{1L}}{dt} = \frac{1}{14} V_{1preL} - (1-p_1)\left[\left(\beta_{LL} I_{1L} + \Theta\beta_{LL} I_{2L} + \delta\beta_{LL} A_L\right)\frac{V_{1L}}{N} + \left(\beta_{LH} I_{1H} + \Theta\beta_{LH} I_{2H} + \delta\beta_{HL} A_H\right)\frac{V_{1L}}{N}\right] - \frac{1}{14} V_{1L} - \mu V_{1L}$$



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*VW status* ($VW_H$ and $VW_L$, more than 4 weeks since first dose vaccination, with complete first-dose effectiveness and also eligible for the second dose)

Population from the $V_1$ status entered $VW$ status after staying in the $V_1$ status for 2 weeks, which was equivalent to 4 weeks after first dose vaccination. They left the $VW$ status by getting infected by infectious individuals (from $I_1$, $I_2$, or $A$) at a transmission rate that is discounted by $1\text{-}p_1$ due to a complete first-dose vaccine effectiveness, by receiving the second dose mpox vaccine at the pace of $v2speed$ ($v2speed_H$ and $v2speed_L$), or by natural death at the rate of $\mu$.

$$\frac{dVW_H}{dt} = \frac{1}{14}V_{1H} - (1\text{-}p_1)[(\beta_{HH}I_{1H} + \Theta\beta_{HH}I_{2H} + \delta\beta_{HH}A_H)\frac{VW_H}{N} + (\beta_{HL}I_{1L} + \Theta\beta_{HL}I_{2L} + \delta\beta_{HL}A_L)\frac{VW_H}{N}] - v2speed_H - \mu VW_H$$

$$\frac{dVW_L}{dt} = \frac{1}{14}V_{1L} - (1\text{-}p_1)[(\beta_{LL}I_{1L} + \Theta\beta_{LL}I_{2L} + \delta\beta_{LL}A_L)\frac{VW_L}{N} + (\beta_{LH}I_{1H} + \Theta\beta_{LH}I_{2H} + \delta\beta_{LH}A_H)\frac{VW_L}{N}] - v2speed_L - \mu VW_L$$

$V_{2pre}$ *status* ($V_{2preH}$ and $V_{2preL}$, less than 2 weeks since second dose vaccination, with complete first-dose effectiveness but without complete second-dose effectiveness)

Population from the $VW$ status entered the $V_{2pre}$ status after receiving second dose JYNNEOS vaccination. They left the $V_{2pre}$ status by getting infected by infectious individuals (from $I_1$, $I_2$, or $A$) at a transmission rate that is discounted by $1\text{-}p_1$ due to a complete first-dose vaccine effectiveness, by acquiring complete full-dose effectiveness after a two-week induction period, or by natural death at the rate of $\mu$.

$$\frac{dV_{2preH}}{dt} = v2speed_H - (1\text{-}p_1)[(\beta_{HH}I_{1H} + \Theta\beta_{HH}I_{2H} + \delta\beta_{HH}A_H)\frac{V_{2preH}}{N} + (\beta_{HL}I_{1L} + \Theta\beta_{HL}I_{2L} + \delta\beta_{HL}A_L)\frac{V2pre_H}{N}] - \frac{1}{14}V_{2preH} - \mu V_{2preH}$$

$$\frac{dV_{2preL}}{dt} = v2speed_L - (1\text{-}p_1)[(\beta_{LL}I_{1L} + \Theta\beta_{LL}I_{2L} + \delta\beta_{LL}A_L)\frac{V_{2preL}}{N} + (\beta_{LH}I_{1H} + \Theta\beta_{LH}I_{2H} + \delta\beta_{LH}A_H)\frac{V_{2preL}}{N}] - \frac{1}{14}V_{2preL} - \mu V_{2preL}$$



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$V_2$ *status* ($V_{2H}$ and $V_{2L}$, second dose vaccinated with full-dose effectiveness)

Population from the $V_{2pre}$ status entered $V_2$ status after a two-week induction period. They left the $V_2$ status by getting infected by infectious individuals (from $I_1$, $I_2$, or $A$) at a transmission rate that is discounted by $1-p_2$ due to a complete full-dose vaccine effectiveness, or by natural death at the rate of $\mu$.

$$\frac{dV_{2H}}{dt} = \frac{1}{14} V_{2preH} - (1-p_2)\left[(\beta_{HH} I_{1H} + \Theta\beta_{HH} I_{2H} + \delta\beta_{HH} A_H)\frac{V_{2H}}{N} + (\beta_{HL} I_{1L} + \Theta\beta_{HL} I_{2L} + \delta\beta_{HL} A_L)\frac{V_{2H}}{N}\right] - \mu V_{2H}$$

$$\frac{dV_{2L}}{dt} = \frac{1}{14} V_{2preL} - (1-p_2)\left[(\beta_{LL} I_{1L} + \Theta\beta_{LL} I_{2L} + \delta\beta_{LL} A_L)\frac{V_{2L}}{N} + (\beta_{LH} I_{1H} + \Theta\beta_{LH} I_{2H} + \delta\beta_{LH} A_H)\frac{V_{2L}}{N}\right] - \mu V_{2L}$$



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**Calculation of the basic reproduction numbers**

The formulae for calculating the basic reproduction numbers for the high-risk and low-risk group ($R0_H$ and $R0_L$) are as follows:

$$R0_H = \frac{(\beta_{HH}\frac{S_H}{N}\times\frac{(1-\tau)\sigma}{\sigma+\mu})}{(\mu+\gamma_{sym})} + \frac{(\Theta\beta_{HH}\frac{S_H}{N}\times\frac{(1-\tau)\sigma}{\sigma+\mu}\times\frac{\gamma_{sym}}{\mu+\gamma_{sym}})}{(\mu+\gamma_1+m)} + \frac{(\delta\beta_{HH}\frac{S_H}{N}\times\frac{\tau\sigma}{\sigma+\mu})}{(\mu+\gamma_2)} + \frac{(\beta_{LH}\frac{S_L}{N}\times\frac{(1-\tau)\sigma}{\sigma+\mu})}{(\mu+\gamma_{sym})} + \frac{(\Theta\beta_{LH}\frac{S_L}{N}\times\frac{(1-\tau)\sigma}{\sigma+\mu}\times\frac{\gamma_{sym}}{\mu+\gamma_{sym}})}{(\mu+\gamma_1+m)} + \frac{(\delta\beta_{LH}\frac{S_L}{N}\times\frac{\tau\sigma}{\sigma+\mu})}{(\mu+\gamma_2)}$$

$$R0_L = \frac{(\beta_{LL}\frac{S_L}{N}\times\frac{(1-\tau)\sigma}{\sigma+\mu})}{(\mu+\gamma_{sym})} + \frac{(\Theta\beta_{LL}\frac{S_L}{N}\times\frac{(1-\tau)\sigma}{\sigma+\mu}\times\frac{\gamma_{sym}}{\mu+\gamma_{sym}})}{(\mu+\gamma_1+m)} + \frac{(\delta\beta_{LL}\frac{S_L}{N}\times\frac{\tau\sigma}{\sigma+\mu})}{(\mu+\gamma_2)} + \frac{(\beta_{HL}\frac{S_H}{N}\times\frac{(1-\tau)\sigma}{\sigma+\mu})}{(\mu+\gamma_{sym})} + \frac{(\Theta\beta_{HL}\frac{S_H}{N}\times\frac{(1-\tau)\sigma}{\sigma+\mu}\times\frac{\gamma_{sym}}{\mu+\gamma_{sym}})}{(\mu+\gamma_1+m)} + \frac{(\delta\beta_{HL}\frac{S_H}{N}\times\frac{\tau\sigma}{\sigma+\mu})}{(\mu+\gamma_2)}$$



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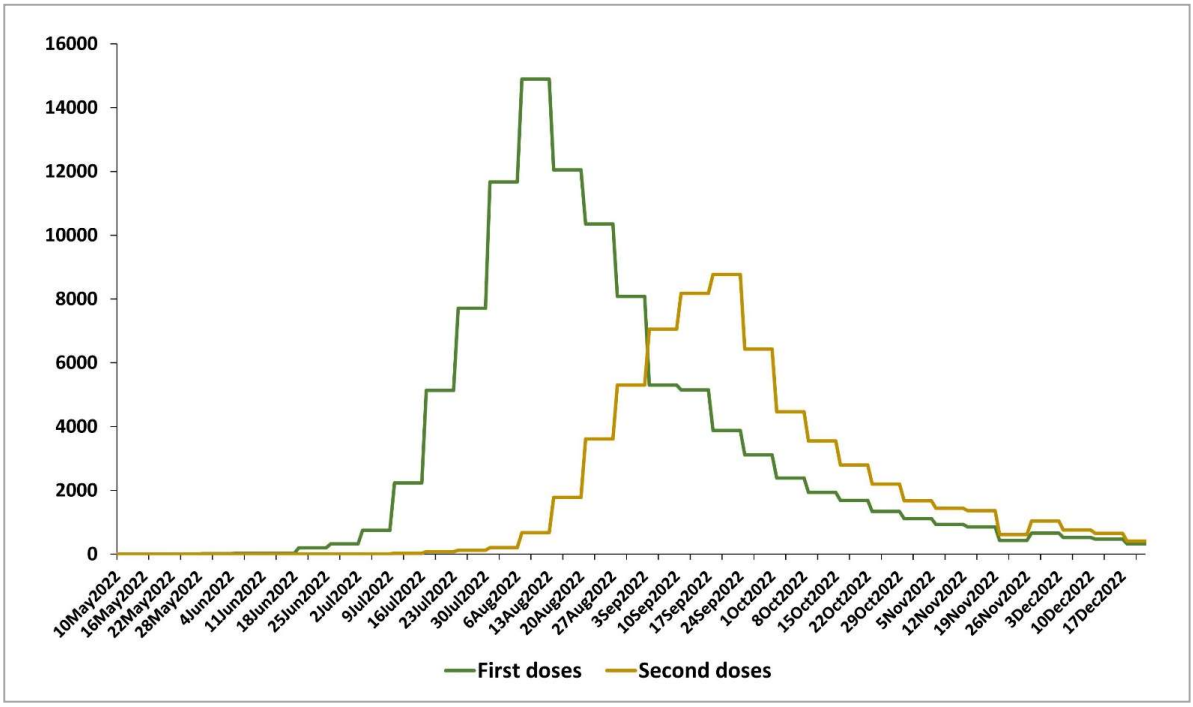
**Supplemental Figure 1. Vaccine Administration in the United States.**

(A) Total JYNNEOS vaccine first doses and second doses administered in the United States reported to US CDC.[1] (B) Vaccination pace of the model. The daily number of the first vaccine doses administrated to the high-risk (v1speed_H) and low risk group (v1speed_L), as well as the daily number of the second vaccine doses administrated to the high-risk (v2speed_H) and low risk group (v2speed_L), were assumed to have a 2-fold difference. Considering the probability that vaccine supplies for the high-risk population (4%, as indicated by our fitting results) may surpass the demand, we allowed reallocation of vaccines initially earmarked for the high-risk group to the low-risk group when such a situation arose.

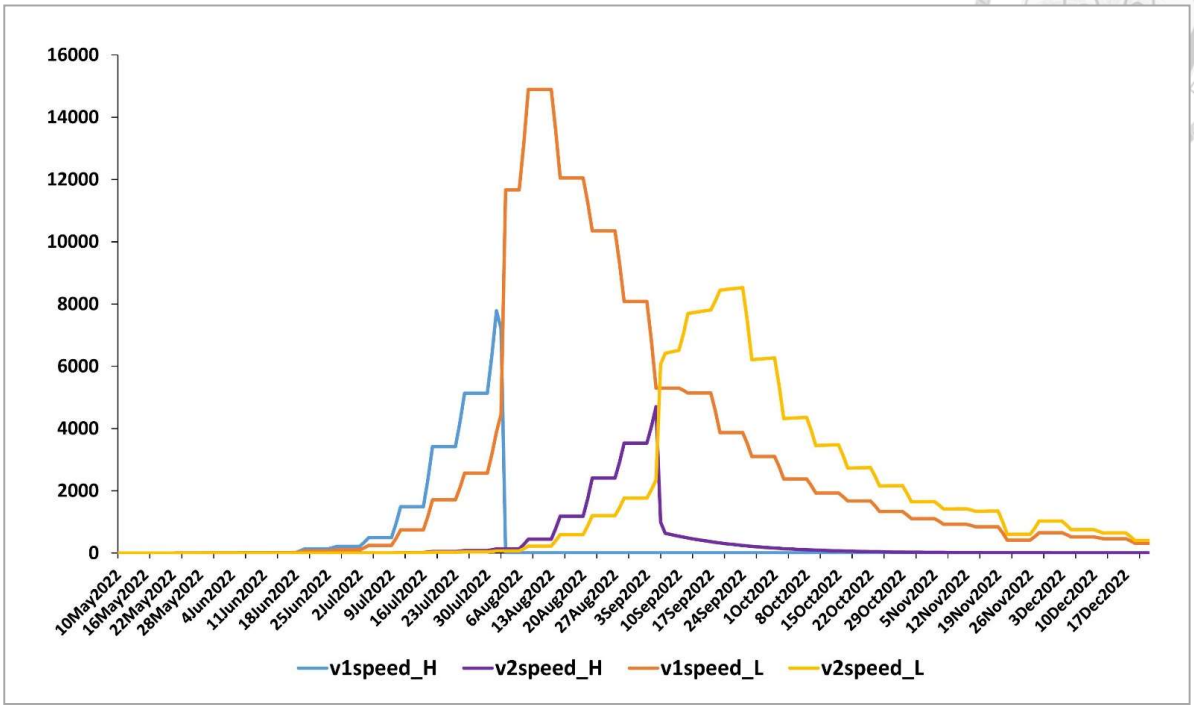
(A)






doi:10.6342/NTU202501270

(B)



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## Supplemental material references

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