Supplementary file

Projecting the impact of testing and vaccination on the transmission dynamics of the 2022 monkeypox outbreak in the United States.

Supplementary Methods

Epidemiological dynamical model: Our mathematical model describes the dynamics of the monkeypox disease through seven epidemiological compartments (Figure 1A). S: susceptible; V: protected by ring vaccination or routine vaccination, cannot be symptomatically infected; E: exposed and latent, but not infectious; I: infected and infectious, with symptoms, undetected; L: infected and infectious, with symptoms, detected (laboratory confirmed); R: recovered; D: dead.

The dynamical system describes the time evolution of the population fractions in the various compartments:

\[
\begin{align*}
\dot{S}_i &= -\beta I_i \frac{S_i}{N_i} - \beta' L_i \frac{S_i}{N_i} \\
\dot{E}_i &= \beta I_i \frac{S_i}{N_i} + \beta' L_i \frac{S_i}{N_i} - \alpha E_i \\
\dot{V}_i &= \alpha \cdot v \cdot VE \cdot E_i \\
\dot{I}_i &= \alpha (1 - v \cdot VE) E_i - \eta I_i - \gamma I_i - \sigma I_i \\
\dot{L}_i &= \eta I_i - \gamma L_i - \sigma L_i \\
\dot{R}_i &= \gamma I_i + \gamma L_i \\
\dot{D}_i &= \gamma I_i + \sigma L_i
\end{align*}
\]

where the subscript \( i \) represents the state \( i \) in the United States. Parameters \( \beta \) and \( \beta' \) are the transmission rates respectively due to undetected and detected infected subpopulations, where \( \beta' \) is 50 times smaller than \( \beta \) thanks to the isolation of detected cases [1 2]. The transmission rate \( \beta \) is estimated by combining the secondary attack rate and the average number of contacts of an infected individual [3]. The secondary attack rates of close contacts and general contacts were defined by [4], and the average number of persons exposed to an infected case was obtained from a surveillance study [5], of which 45% were household or sexual (close) contacts, others were general contacts.

The efficacy of smallpox vaccines against monkeypox is assumed to be 85%. Smallpox vaccines are employed in both routine and ring vaccination campaigns [6 7]. The delay between symptom onset and laboratory testing results is reflected through the diagnosis rate \( \eta \). It has been reported that the median time between
symptom onset and monkeypox virus testing was 7 days, while the turnaround time from monkeypox virus testing to result availability was 2 days at the early stage of the 2022 outbreak [8]. Therefore, the median confirmation delay in our retrospective simulation was assumed to be 9 days.

Before the outbreak, the total population $N_i$ is assumed to have been composed of susceptible subpopulation ($S$), constituting 70% of the total population, and vaccinated subpopulation ($V$), constituting 30% of the total population, to account for individuals born before 1980s who have been routinely vaccinated against smallpox [9] and are therefore protected against monkeypox with 85% vaccine efficacy [7].

Other parameters were also taken from verified sources [6 10].

**Scope, timeframe and data sources:** The reported monkeypox virus (MPVX) cases were obtained from an open-access database (https://github.com/globaldothealth/monkeypox) compiled from verified sources [11]. We investigated the MPXV epidemiology of the US states. The timeframe of epidemic recapitulation started from June 20 and ended on July 15, 2020. The time window of MPXV spread prediction is six months.
Table S1. Key parameters of the mathematical model.

| Parameter | Definition                                                         | Value                        | Source |
|-----------|--------------------------------------------------------------------|------------------------------|--------|
| $\beta$   | transmission rate due to undetected infections                     | 0.329 (95% CI 0.231-0.429)   | [4 5]  |
| $\beta'$  | transmission rate due to detected infections                       | 0.006                        | [1 2]  |
| $\nu$     | coverage of ring vaccination to exposed individuals               | 0%                           | Assumed |
| $VE$      | vaccine efficacy of ring vaccination                               | 85%                          | [6 7]  |
| $1/\eta$  | delay from symptom onset to diagnosis                             | 9                            | [8]    |
| $1/\alpha$| incubation period                                                 | 8.5                          | [12]   |
| $\gamma$  | recovery rate                                                      | 4.54%                        | [6 10] |
| $d$       | fatality rate for infected individuals with symptoms               | 0.22%                        | [13]   |
Figure S1. Graphical Scheme of the epidemiological model. In the mathematical model, the vaccinated subpopulation (compartment V) already includes individuals born before 1980s, who received the routine smallpox vaccination. Exposed individuals who are identified and ring vaccinated are transferred from compartment E to compartment V. The transmission rate of detected infections is assumed to be much lower than that of undetected infections, thanks to the isolation of detected cases.
Figure S2. The impact of rapid diagnosis on curbing monkeypox spread in different states of the United States
**Figure S3.** The impact of different coverage of ring vaccination on curbing monkeypox spread in different states of the United States
Figure S4. Model simulation to fit the monkeypox epidemic dynamics from 15 July to 15 August in the United States. The total coverage of vaccine of this simulation scenario is 30%, which is close to the aggregated data that 14% of persons reported receipt of pre-exposure smallpox vaccine and 14% of at-risk contacts receive vaccine [5 14]. The delay between onset and conformation was assumed to be 5 days, which is consistent with the observation from the open-access monkeypox database [15]. The reported data were obtained from US CDC [16].
Supplementary references

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