

# **Estimating the Prevalence of Monkeypox Among Men Who Have Sex with Men in Chengdu, China, Since 2023 Using Capture-Recapture Methods**

Jingpei Xu, Junfan Li, Zhen Dai, Xiaodong Wang, Liang Wang

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# Estimating the Prevalence of Monkeypox Among Men Who Have Sex with Men in Chengdu, China, Since 2023 Using Capture-Recapture Methods

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## Abstract

**Background:** Monkeypox (mpox) is a zoonotic disease caused by the mpox virus, which was previously observed primarily in west-central Africa. Since May 2022, mpox outbreaks have emerged in several non-endemic countries around the world and have continued to spread, mainly through close contact (including sexual contact) in the population of men who have sex with men (MSM). Since June 2, 2023, when the first indigenous case of mpox in mainland China was reported in Beijing, the mpox epidemic in China has lasted for more than a year, and is still showing delayed transmission, with the total number of reported cases in 2023 ranking tenth in the world. With the gradual increase of the total number of indigenous cases, cases among females have been found to be infected via sexual contact, and there is a risk of further spread of the epidemic to the general population. MSM are a high-risk group for mpox infection and are central to prevention and control efforts aimed at halting the spread of the virus.

**Objective:** The aim of this study is to ascertain the prevalence of mpox infection among MSM in Chengdu and to provide a scientific basis for predicting the mpox epidemiological situation and formulating prevention and control strategies.

**Methods:** A capture-recapture method was applied to estimate the size of mpox cases in MSM populations residing or active in Chengdu City since May 1, 2023. The first capture and tagging were conducted at offline activity sites of the MSM population, and the second capture was carried out through peer network snowball sampling. Capture was accompanied by a questionnaire survey covering mpox diagnosis history, suspected mpox symptoms, risk exposure in the 21 days prior to symptom onset, and HIV and sexually transmitted infection (STI) status.

**Results:** The first capture tagged 1501 individuals, of whom 31 were mpox cases, and the second capture recruited a total of 1538 individuals, of whom 18 were mpox cases. A total of 21 people had been tagged in the second capture, of whom 1 was a mpox case. The capture-recapture method estimated the number of mpox cases among MSM in a provincial capital city to be 303 (95% CI: 48~ 618 ), and the size of the MSM population in Chengdu city to be 105,070 (95% CI: 62,751 ~ 147,391), and the prevalence rate of mpox infection to be 2.88 per 1,000 (95% CI: 0.33 ~ 9.85 per 1,000).

**Conclusions:** The capture-recapture method can estimate the size of the MSM population and the number of mpox cases, providing essential data for mpox prevention and control. Mpox infection among the MSM population in Chengdu is of notable proportion, and behavioral intervention targeting this population are necessary to control the transmission of mpox.

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## Original Manuscript

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### Abstract

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**Conclusion:** The capture-recapture method can estimate the size of the MSM population and the number of mpox cases, providing essential data for mpox prevention and control. Mpox infection among the MSM population in Chengdu is of notable proportion, and behavioral intervention targeting this population are necessary to control the transmission of mpox.

**Keywords:** monkeypox; population size; men who have sex with men; capture-recapture; infections

## Introduction

Monkeypox (mpox) is a zoonotic disease caused by mpox virus (MPXV) that had been steadily emerging in Africa until a global outbreak occurred in 2022-2023, when an unprecedented number of cases in non-endemic countries[1]. On 23 June 2022, the World Health Organization (WHO) declared mpox a “public health emergency of international concern”. Although the highest level of alert has since been lifted, mpox continues to spread globally. On August 14, 2024, WHO Director-General once again declared the mpox outbreak a public health emergency of international concern(PHEIC), highlighting the potential for further spread across countries in Africa and beyond[2]. This marks the second PHEIC declaration related to mpox within two years. Surveillance, diagnostics, risk communication and community engagement remain crucial to halting the outbreak and eliminating human-to-human transmission in all contexts[3].

As of 31 March 2024, China was among the ten countries with the highest cumulative number of reported mpox cases totally 2034[4]. In response to the rising number of cases, mpox was classified as a Category B infectious disease in China under the Law of the People's Republic of China on Prevention and Control of Infectious Diseases as of September 20, 2023, with corresponding preventive and control measures implemented[5]. The first indigenous mpox case in mainland China was confirmed on June 1, 2023, following only one previously reported imported case in September 2022[6]. In July 2023, Sichuan Province, whose capital city is Chengdu, reported 49 confirmed cases of mpox[7]. Notably, Sichuan Province is among the top five regions in China for mpox cases, with Chengdu accounting for more than 70% of the province's total cases [8].

Mpox outbreaks have predominantly affected men who have sex with men(MSM) due to their high exposure of sexual behavior and relative frequent engagement in risky sexual activities, making this



group particularly vulnerable to MPXV transmission [9]. In China, over 90% of mpox cases have been identified among MSM [7]. As the country with the largest MSM population globally, China faces unique challenges in managing this outbreak[10]. Chengdu, the capital city of Sichuan province and a major economic and cultural center in southwest China, has a resident population exceeding 20 million [11]. And in 2018, the upper estimate of active MSM in Chengdu reached approximately 120,000[12]. Given their heightened risk, the MSM population is a critical focus for mpox prevention and control efforts.

Despite lasting for more than a year, the mpox epidemic in China shows signs of delayed transmission [13]. However, no comprehensive report has yet estimated the true prevalence of mpox in mainland China, partly due to uncertainties about the extent of asymptomatic infections [3]. Even if asymptomatic cases are prevalent, not all infections are likely to be diagnosed, leaving the true number of cases unknown. Some studies suggest that the actual number of mpox cases in several countries could be more than three times the observed number[14]. This raises the question: what is the true situation in a megacity like Chengdu? The objective of this study is to determine the true prevalence of mpox infection among MSM in Chengdu using the classic capture-recapture survey method. The results will provide policymakers with critical information about undetected cases and the overall magnitude of the epidemic, enabling health systems to better prepare for and respond to the needs of this population[14]. Furthermore, the study will offer the most up-to-date estimation of the size of the MSM population in Chengdu, providing a foundation for addressing other public health challenges relevant to this key group.

## Method

### 1. Research team

The researchers, mainly from the Chinese Centre for Disease Control and Prevention (CDC) and Chengdu CDC, were responsible for the design and quality control of the study. The largest local

community-based organization in Chengdu was responsible for the implementation of the survey and data collection.

## 2. Capture-recapture surveys

The capture-recapture method is considered the gold standard for estimating populations when it is impossible to identify each case individually and significant undercounts are expected [15]. To estimate the true scale of mpox infection among the MSM population in Chengdu since May 1, 2023, we employed a two-source capture-recapture fieldwork method. This method involved two phases of data collection: capture and recapture.

The definition of a mpox case is based on the *Monkeypox Prevention and Control Program* issued by the National Bureau of Disease Control and Prevention and the National Health Commission of China in 2023[16]. According to this program, mpox cases are categorized into the following types:

1. **Mpox-like cases:** Individuals exhibiting mpox-like symptoms such as unexplained acute rash (facial or oral mucous membranes, extremities, genital or perineal area, perianal area, etc.) accompanied by fever ( $>37.3^{\circ}\text{C}$ ) or enlarged lymph nodes.
2. **Suspected cases:** Individuals with mpox-like symptoms and any of the following within 21 days prior to onset: (1) travel history to an area with reported mpox cases; (2) exposure to confirmed or suspected mpox cases; (3) engagement in homosexual behavior or sexual partners with a history of such behavior; (4) suspected contact with animals in an endemic area.
3. **Confirmed cases:** Mpox-like or suspected cases that test positive for mpox virus nucleic acid or have positive virus isolation results from laboratory tests.

### First Capture Phase:

The initial capture and tagging were conducted at offline MSM activity venues in Chengdu. Eight staff members, selected by CBO, conducted the survey at selected venues. These venues were chosen based on criteria such as a high number of active MSM gatherings, cooperative venue owners, and location diversity (including central Chengdu and suburban areas). A total of 21 venues

were surveyed, including bars, tearooms, public outdoor places, mahjong complexes, baths and saunas, and youth salon activity centers.

During this phase, individuals were identified and tagged using two unique markers: a printed image of a panda in a tree under the moon (generated by an AI-powered drawing tool) and an eight-word slogan related to the investigation (printed on the back of the panda image).

The eight staff members conducted the capture from May 24 to May 31, 2024, explaining the study's purpose and obtaining informed consent. Participants meeting the inclusion criteria (at least 18 years old, having engaged in penetrative sexual intercourse with another man in the past year, and having resided or been active in Chengdu since May 1, 2023) were asked to complete an e-questionnaire. Responses not meeting these criteria were automatically excluded. Valid questionnaires were considered upon completion, with each respondent receiving a uniformly labeled image of the panda and being instructed to remember the eight slogans. The questionnaire collected data on basic information, mpox diagnosis history, suspected mpox symptoms, risk exposure, and HIV and sexually transmitted infection (STI) status. Respondents were also compensated with a RMB 19.80 survey subsidy.

#### Second Capture Phase:

Two weeks after the first phase, 17 MSM volunteers with broader social networks, selected by the CBO, conducted the second round of captures from June 14 to June 24. This phase utilized peer social networks primarily through online platforms and to a lesser extent through offline networks, employing a snowball sampling technique. To minimize selection bias, the volunteers covered a wide geographical area including urban, suburban, and peripheral regions. They represented a diverse age range, from younger individuals to the elderly. Participants from this phase were also required to complete the same questionnaire.

To verify previous tagging, two questions were added at the end of the original questionnaire: one about memorizing the slogan and another about seeing the panda picture. If respondents answered

affirmatively to both, additional verification was conducted through a supplementary survey comprising four questions. Correct answers to at least three of these questions confirmed tagging and recapture: (1) whether a survey with similar content was conducted in the previous month; (2) the route and format of the aforementioned survey; (3) the format of the slogan that the staff requested to be memorized at the time of the aforementioned survey; (4) and the amount of subsidy received for the aforementioned survey after its completion.

By comparing the number of tagged individuals in both phases, we estimated the total number of MSM and mpox cases within the MSM population in Chengdu. This dual-phase approach allowed us to cross-verify the data and improve the accuracy of population size estimation.

### **3.Quality Control**

To ensure the exclusivity of captured subjects, the survey site implemented equipment limitations, stipulating that each cell phone could complete the questionnaire only once per capture round. Furthermore, to guarantee the integrity of the data collected, respondents are required to complete the questionnaire in its entirety before submission. During the first capture round, only the investigator provided the e-questionnaire's QR code, avoiding the use of fixed display boards to ensure face-to-face recruitment and prevent duplication. The e-questionnaire was configured to a password upon scanning the code, ensuring only authorized individuals could complete it.

### **4.Sample Size and Sampling**

The sample size was calculated according to the formula for determining the sample size required for transect surveys,  $n=400*(1-p)/p$ , where  $p$  represents the hypothetical infection rate[17]. Reports indicated a total population infection rate of 70.7 per million after several months of the outbreak[18]. Multiplying this rate by Chengdu's population of 20 million and dividing by the estimated MSM population size of 68,258 [12], resulted in a  $p$ -value of approximately 0.02. The extrapolated sample size was approximately 1,600, which was the target for recruitment.

### **5.Data Management**

Data were exported from the e-questionnaire application to password-protected Microsoft Excel sheets. Daily data cleaning procedures included deduplication and consistency checks. When duplicate IP addresses were identified, the quality control staff contacted the CBO survey leader on the same day to investigate the issue. If the IP duplicates were due to a volunteer not using the peer network but instead randomly selecting MSM individuals for offline surveys, then the sampling is considered incorrect and the questionnaire is judged to be invalid and would be excluded.

Additionally, any questionnaire completed using a computer browser rather than a cell phone was also deemed invalid and excluded.

## 6. Statistical Analysis

Data analysis was performed using R v.4.4.1 software for Windows. Capture-recapture formulae were used to estimate population size with 95% confidence intervals. The Chapman

estimator[19] was employed for population size calculation  $N = \frac{(M+1)(C+1)}{R+1} - 1$ , where N represents the estimated total population size, M denotes the total number of individuals “captured” and “tagged”, C represents total number of people “captured” during the second phase, and R indicates the number of individuals “captured” on both phases. Confidence intervals (CI) were constructed as

$N \pm 1.96 \sqrt{\text{Var}(N)}$ , where Var (N) is calculated as follows:

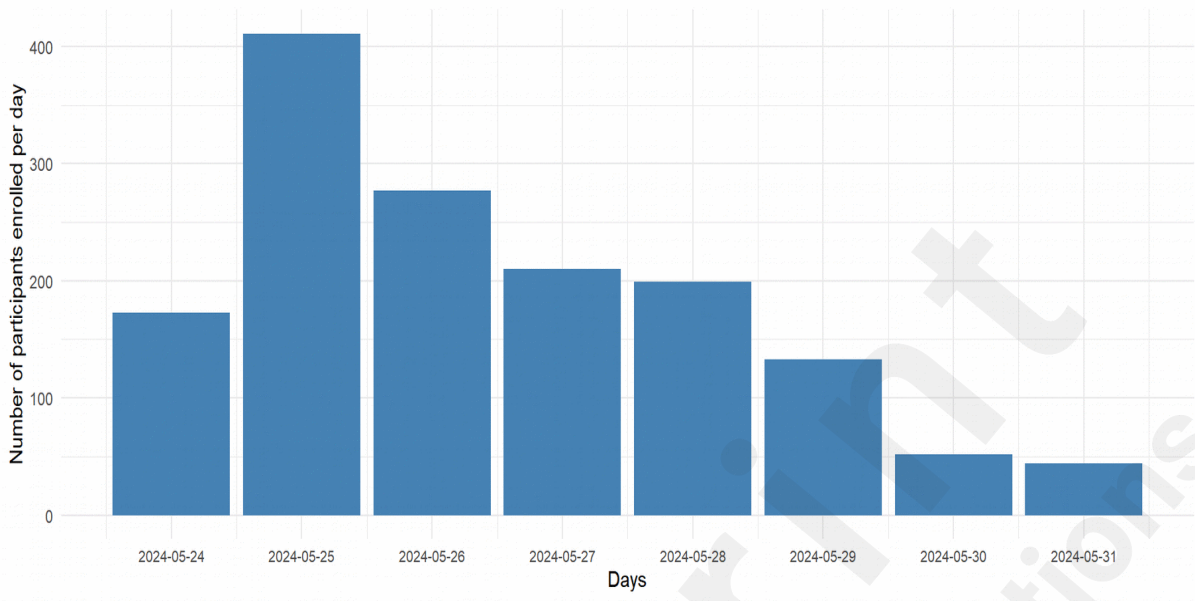
$$\text{Var}(N) = \frac{[(M+1)(C+1) * (M-R) * (C-R)]}{[(R+1)^2 (R+2)]}$$

## Results

### MSM captured

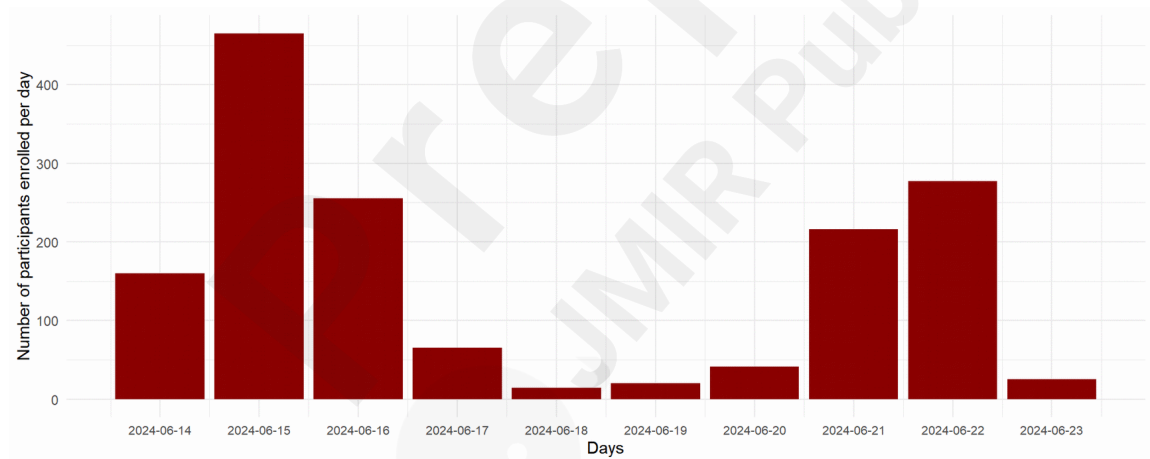
A total of 1,501 MSM respondents were captured in the first round, while 1,538 qualified questionnaires were identified in the second round. Figure 1 illustrates the number of participants enrolled each day during the first capture phase, and Figure 2 depicts the data from the second capture phase.

**Figure 1.** Number of respondents per day for the first capture survey in Chengdu, China



**Figure 2.** Number of

respondents per day for the second capture survey in Chengdu, China



In the second round of captures, 46

individuals indicated positive responses to both questions regarding the recall of the project slogan and the presentation of project-related images from the previous month. Following an additional investigation, 21 of these 46 individuals were confirmed to have been successfully tagged during the initial round of captures. Based on these statistics, with  $M=1501$ ,  $C=1538$ , and  $R=21$  the estimated MSM population size is 105,070, with a 95% confidence interval (CI) of 62,750 to 147,390. The estimated proportion is 1.14%, with a 95% CI of 0.68% to 1.60%. Proportion estimates for men were

based on data from 2023 provided by the Institute of Statistics of Chengdu. Although our survey focused on individuals aged 18 and older, the publicly available age data is in 5-year intervals, so we used the male resident population aged 15 years and above, totaling 9,226,025, as a rough denominator for proportion calculations.

### Mpox captured

The captured cases of mpox from the two phases are shown in Table 1.

According to the above statistics,  $M=31$ ,  $C=18$ ,  $R=1$ . The estimated number of mpox cases,

calculated	<b>Table 1</b>	Number of different types of monkey(mpox) cases in the two captures					using
the		<b>Type of mpox cases</b>					
specified				<b>Confirmed</b>			
formula, is	<b>Round</b>	<b>Mpox-like cases</b>	<b>Suspected cases</b>	<b>d</b>	<b>Total</b>		303,
with a 95%				<b>cases</b>			
confidence	<b>Capture one</b>	11	6	14	31		
interval	<b>Capture two</b>	6	5	7	18		
	<b>Total</b>	17	11	21	49		(CI) of
-12 to 618.							The

initial lower limit of the CI was negative, which is unreasonable. To correct this, we refer to relevant literature [20], and adjust the lower bound to  $(M + C - R)$ , ensuring that the population size is meaningful. The final confidence interval obtained after correction is (95% CI: 48~618). The prevalence rate of mpox infection is 2.88 per 1,000 (95% CI: 0.33 ~ 9.85 per 1,000).

Out of the 49 total cases, 21 underwent nucleic acid testing. Among the 33 individuals with symptoms consistent with mpox, five sought medical attention. Despite 18 of these symptomatic individuals reporting complications, only three sought hospital care for diagnosis and treatment.

Among the 21 confirmed cases, only five had a rash or typical symptoms of mpox, such as fever and swollen lymph nodes. Eight cases continued sexual activity despite experiencing symptoms.

## Discussion

To date, no estimates exist for the size of the mpox-infected population in China. The most recent estimate for the MSM population and other key prevention and control groups in Chengdu, a prefecture-level city in Sichuan Province, was made six years ago[21]. Chengdu, the fourth-largest city in China after Beijing, Shanghai, and Chongqing, was the focus of this study, which is pioneering in its use of the capture-recapture method to estimate both the MSM population size and the number of monkeypox infections since 2023. According to CDC data, Chengdu reported 140 confirmed monkeypox cases between 2023 and May 2024. The ratio of the estimated total number of cases to observed cases was approximately 2.16, closely aligning with estimates reported for Italy [14]. Despite Chengdu's comprehensive mpox surveillance and early warning program initiated in 2023, the actual number of infections detected was less than half of the expected figure. This discrepancy may be due to asymptomatic infections and incomplete diagnostic coverage [14]. Mpox cases must be confirmed through real-time PCR, next-generation sequencing, or MPXV isolation from a clinical specimen [22]. In our survey, fewer than half of mpox cases had undergone nucleic acid testing. Despite some symptomatic individuals reporting complications, most chose not to seek hospital care, likely due to the stigma associated with mpox, especially within the MSM community [23]. This suggests that, despite efforts to improve testing accessibility, high-risk MSM populations may benefit from more convenient and private rapid test kits to enhance diagnostic rates [24]. Notably, some cases were confirmed despite individuals denying symptoms consistent with mpox, indicating that our expanded surveillance efforts successfully detected a portion of asymptomatic infections. Furthermore, some mpox cases continued to engage in high-risk sexual contact during their symptomatic period, highlighting the critical need for health education targeting both mpox cases and the general population. Contact tracing and isolating individuals with mpox remain essential for curbing the disease's spread, and these, alongside enhanced national surveillance, are currently our primary tools for managing the epidemic [25]. Additionally, it is vital to focus on de-



stigmatizing individuals in public health communications and educational efforts to address concerns among those who might otherwise avoid seeking help due to fear of being labeled.

The estimated MSM population size has increased by nearly 54% compared to the 2018 estimate of 68,258 using the multiplier method [12]. In contrast, the Chengdu Municipal Bureau of Statistics reported a 28% increase in resident males over the age of 15, from 7,191,484 in 2018 to 9,226,025 in 2023. It is evident that the MSM population in Chengdu has grown more significantly than other groups over the past 5-6 years. This trend may be attributed to Chengdu's reputation as a city with a relatively tolerant atmosphere, widely recognized across China [26].

From a methodological perspective, the decision to use the classical capture-recapture method for estimating population size was based on several factors. Various approaches exist for estimating the size of hidden populations, each with its own strengths and limitations [27]. Given the initial lack of data and the goal of obtaining preliminary size estimation, along with the practical challenges associated with other methods, we ultimately opted for the classical two-source capture-recapture approach.

Based on guidelines from the definitive guide [28], it is crucial that the two captures in a "capture-recapture" approach be conducted independently to avoid interference. Therefore, we used different locations, volunteers, or recruitment methods compared to the first capture. Additionally, to ensure independence, the staff involved in the initial capture were distinct from those conducting the second. A key prerequisite for implementing capture surveys is that the target population should be closed, meaning the population remains relatively constant over time. To meet this condition, we avoided major Chinese holidays to reduce population mobility during the survey period.

Furthermore, a sufficient time gap between the two captures is essential to prevent interference between sampling sources and to ensure that tagged individuals are dispersed throughout the population. We set a two-week interval between the captures, referencing similar literature with distinct recruitment methods [29]. Given the acute nature of mpox, each capture round was designed

to be completed within the incubation period of mpox, which is 21 days [3], to avoid confounding results with new cases arising during the survey. As a result, we did not use the Respondent-Driven Sampling (RDS) method for the second capture, despite its effectiveness for obtaining representative samples of hidden populations[30], due to the limitation on the number of MSM populations required and the capture time constraints.

A graph depicting the temporal distribution of survey respondents recruited during the two capture phases shows that the first capture, conducted in offline venues, exhibited a more uniform temporal distribution of recruitment. In contrast, the second capture, which relied on peer-to-peer network recruitment, displayed a more random temporal distribution, likely due to the primary dissemination of recruitment through the Internet.

There are some limitations in our research. While the two-sample capture-recapture methods are straightforward to use, they can sometimes produce biased estimates because truly independent sources are rare [31]. This approach offers no additional degrees of freedom to model or test for independence or additional heterogeneity [32], and the data are insufficient for estimating dependence unless additional information or covariates are available [33].

According to the study [19], when applying Chapman's parameter, to ensure that  $R \geq 1$ ,  $M + C$  should be equal to or exceed  $R$  theoretically. However, it does not address whether this condition must still be met if  $R$  already satisfies  $R \geq 1$ , which in our study, is met with  $R = 1$ . Nevertheless, a small  $R$  value introduces another issue. Initially, we employed Chapman's original formula to directly calculate the confidence interval for the number of mpox cases. The resulting lower limit was negative, which is clearly unreasonable. The literature offers guidance on how to handle such situations [20]. Regarding potential bias in the estimated total size of mpox cases from the current sample size, some literature suggests corresponding correction methods. Specifically, the bias in  $N$  is approximately  $100e^{-MC/N}$  percent, which becomes negligible only when the product of the two sample sizes ( $M * C$ ) exceeds the population size ( $N$ ) by a factor of 3 or 4 [19]. By applying the

correction formula from the literature, we estimate that N is underestimated by about 15.86 percent. Thus, the estimated number of mpox cases would be approximately 360, which is 2.5 times the number of reported cases.

## Conclusions

This study provides the first estimate of Chengdu's mpox-infected and MSM populations using capture-recapture methods, offering critical insights for optimizing resource allocation for mpox prevention and treatment. The findings can inform both local and national public health strategies, particularly given the ongoing global mpox outbreaks. Despite the study's limitations, future research should explore the use of multiple capture methods or alternative estimation techniques to improve accuracy. These refinements represent a promising direction for enhancing public health interventions.

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## Declaration of competing interest

The authors have no competing interests or conflict of interest to declare.

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The study was funded by Chinese Center for Disease Control and Prevention.

## Ethical Approval statement

The survey received ethical approval from the Institutional Review Board of the Chinese Center for Disease Control and Prevention on November 30, 2023, and the number of the approval notice is 202335. Although no personally identifiable information was collected, the questionnaire involved the collection of sensitive information related to sexual behavior history, mpox symptoms, and treatment history. An informed consent form was included at the beginning of the questionnaire,

requiring respondents to read and acknowledge understanding of the study's risks and benefits before participating .

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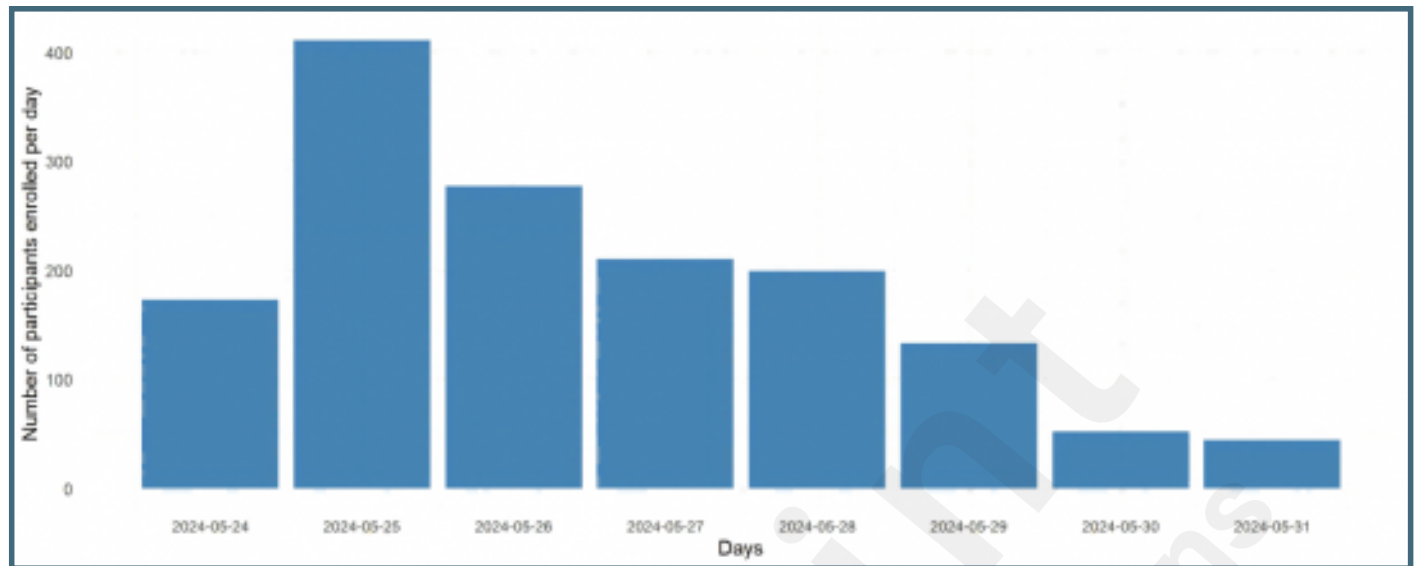
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## Supplementary Files

## Figures



Number of respondents per day for the first capture survey in Chengdu, China.



Number of respondents per day for the second capture survey in Chengdu, China.

