**Epidemiological parameters related to the transmission and severity of the 2022-23 mpox outbreak: a systematic review**

**Authors**

 Cándida Diaz-Brochero1, Laura Cristina Nocua-Báez2, Jorge Alberto Cortes2, Kelly Charniga3, Adriana Buitrago-Lopez1, Zulma M. Cucunubá1

**Authors affiliation**

1Department of Clinical Epidemiology and Biostatistics. Faculty of Medicine. Pontificia Universidad Javeriana. 2Department of Internal Medicine, School of Medicine, Universidad Nacional de Colombia. 3Institute Pasteur, Paris.

**Corresponding author**

Zulma M. Cucunubá.  [zulma.cucunuba@javeriana.edu.co](mailto:zulma.cucunuba@javeriana.edu.co) Department of Clinical Epidemiology and Biostatistics. Faculty of Medicine. Pontificia Universidad Javeriana.  Cra. 7 No 40 - 62. San Ignacio Hospital Building, 2nd Floor. Bogota, Colombia.

**Introduction**

Mpox is a zoonotic disease that is endemic in Central and West Africa. The first case in humans was reported in 1970. Since then, intermittent cases of infection have been reported in endemic countries, characterized by a febrile prodrome followed by vesiculopustular skin eruptions. In 2022–2023, the world experienced the largest outbreak of mpox in history. As of October 2023, Mpox has spread across 115 countries with more than 90,000 confirmed cases and 157 deaths worldwide. Compared to previous mpox outbreaks, the current outbreak has shown some critical differences related to modes of transmission, clinical presentation, and population at risk (1, 2). The majority of cases include men who report male to male sexual contact, and the most common form of transmission is skin-to-skin contact during sexual encounters. Most cases reported globally are in the Americas and Europe, with more severe cases related to immunosuppressive conditions such as HIV (3), who may benefit from antiviral treatment in some cases. In 2019, the US Food and Drug Administration (FDA) approved the modified vaccinia Ankara vaccine to prevent mpox infection, but as for antivirals, their availability in many regions is scarce.

Because of the new mode of transmission and speed with which the outbreak spread, the Director-General of World Health Organization (WHO) declared mpox a Public Health Emergency of International Concern between July 2022 and May 2023 (4). In outbreaks of emerging or re-emerging infectious diseases, one of the main priorities is to establish and intensify epidemiological disease surveillance. It is also important to collect and analyze key epidemiological and clinical parameters related to the dynamics of transmission and severity of the disease (5, 6). Parameters, such as the incubation period, serial interval, generation time, infectious period, basic and effective reproductive numbers, and case fatality rate, among others, have been shown to be especially useful for assessing the trajectory of an epidemic and the impact of control strategies (7-9).

Although the number of mpox cases has diminished considerably since the beginning of 2023 (1), some lessons can be learnt from this outbreak that could be used in future outbreaks. Several studies of mpox epidemiology and transmission have been published during the current outbreak (10-13). Epidemiological parameters estimated from these studies can serve as input for statistical and mathematical models to retrospectively understand the 2022-23 outbreak and to be better prepared for future mpox outbreaks. In this way, summarizing the available evidence could help provide a comprehensive overview of parameter estimates from multiple studies, allowing modelers to derive robust and well-informed parameter values.

Here, we aim to identify and synthesize the key epidemiological parameters related to the transmission and severity of the 2022-23 mpox outbreak (incubation period, serial interval, generation time, infectious period, basic and effective reproductive number, and case fatality rate) through a systematic review and meta-analysis.

**Material and methods**

*Protocol*

We conducted this systematic review following the protocol of the International Prospective Registry of Systematic Reviews (PROSPERO): CRD42023404503.

*Search strategy*

A search strategy was developed to identify as many studies as possible (sensitive), including controlled vocabulary (Medical Subject Headings (MeSH), Emtree (EMB)) and free text terms (considering variant spellings, synonyms, acronyms and truncators), using field tags, boolean and proximity operators adapted for each search engine, without language restrictions, from May 2022 to September 10, 2023. The search strategy was adapted for the following electronic databases: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (Ovid Platform), EMBASE (Elsevier), Web of Science, Scopus, Latin American and Caribbean Literature in Health Sciences (LILACS) and Clinical Trials.

We also performed a semi-structured search in repositories of preliminary reports or preprints of scientific articles in the following sources: medRxiv, bioRxiv, arXiv, SSRN, Research Square, Virological. Additionally, we searched websites, institutional repositories, and electronic databases of the following institutions: the London School of Hygiene & Tropical Medicine (LSHTM), Imperial College London, the US Centers for Disease Control and Prevention (CDC), the European Centre for Disease Prevention and Control (ECDC), and UK Health Security Agency (UKHSA), given their involvement during the outbreak response work for mpox.

Additional references were requested from opinion leaders and clinical experts in infectious diseases via email and ResearchGate. Finally, a manual search was performed by reviewing the list of bibliographic references of the selected studies ("snowball"). Search strategies are available in Supplementary table 1.

*Studies selection*

Two authors (CDB and LNB) independently reviewed the studies identified with the search strategy. Initially, they performed it by title and abstract, later by full text. Disagreements were resolved by consensus or by involving a third review author (ABL).

*Eligibility Criteria*

The types of publications included were published or preprinted original articles, short reports, short communications, and epidemiological surveillance reports. The

types of studies included were descriptive or analytical observational studies, experimental or quasi experimental studies, statistical or mathematical modeling studies, and simulation studies. We excluded purely theoretical mathematical models (i.e., not fitted to data)

Types of participants: adults, categorized as suspected or confirmed cases of Mpox infection, or their contacts in follow-up.

Type of outcome measures:

* Basic reproduction number (𝑅0): Number of secondary infections from a primary case in a fully susceptible population.
* Effective reproduction number 𝑅(𝑡): Number of secondary infections from a primary case in a partially susceptible population.
* Incubation period: Period between the time of exposure to the pathogen and the time of symptom onset.
* Serial interval: Time from the onset of symptoms in the primary case to the onset of symptoms in the secondary case.
* Generation time: Time from infection in the primary case to infection in the secondary case.
* Infectious period: Time during which an infected host, with or without symptoms, can transmit an infectious agent to susceptible persons.
* Case Fatality Ratio (CFR): Proportion of confirmed cases that result in death.
* Infection Fatality Ratio (IFR): Proportion of all infections (confirmed, symptomatic, asymptomatic) that result in death.

*Data extraction*

Two review authors (CDB and LNB) independently extracted the following data from each of the included studies, using a previously tested data extraction form: 1) General information about the study, such as: type of publication, type of study, country or region, inclusion and exclusion criteria, sample size; 2) Baseline characteristics of study participants/population/patients, such as: age, sex, race, sexual orientation, gender identity, HIV status, other non-HIV immunosuppressive conditions, baseline CD4 count, concomitant antiretroviral treatment, HIV viral load, history of smallpox vaccine, history of smallpox vaccine in the current outbreak (JYNNEOS, ACAM2000); 3) Aspects related to viral transmission dynamics (for suspected or confirmed cases), such as: sexual or intimate contact in the 21 days prior to symptom onset, suspected source of transmission, type of sexual or intimate contact, close contact with suspected or confirmed case, when available; 4) Description of the disease and its severity: signs and symptoms, total duration of symptoms, location of lesions, concomitant diagnosis of another sexually transmitted disease (STD), treatment administered, hospital or intensive care unit (ICU) admission, and final outcome of last contact, when available; and 5) Information related to the estimation of the parameters. For all parameters, we extracted information about the definition used by the authors, sample size to fit the distribution (when applicable), study period and availability of code and data. For the incubation period, infectious period, serial interval, and generation time, we collected information about measures of central tendency and dispersion (mean or median, range, interquartile range, coefficient of variation, among others), uncertainty (confidence intervals or credible intervals), probability distribution (e.g., Weibull, beta, gamma), and recorded whether authors adjusted for bias (e.g., censoring or truncation). Investigators of included studies were contacted by e-mail to request missing data when necessary.

*Assessment of quality of included studies*

For mathematical models, we designed a checklist, considering the following aspects: 1) The availability of code and data; 2) The report of central and/or dispersion tendency measures (e.g., mean, standard deviation, median, range, IQR) with their respective uncertainty values (95% or 90% confidence or credible intervals, according to the method used: frequentist vs Bayesian analysis, respectively); 3) The description of the type of distribution fitted (e.g., Weibull, Gamma , Log-normal, etc.), sample size used to fit the distribution and the parameters of the distribution; and 4) If methods to adjust the model for bias were used (e.g., censored or truncated data or the application of other statistical methods for adjustment).

For the remaining study designs, we implemented the tools of the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Series (14), Cross Sectional Studies and Cohort studies (15) included in our analysis, with minor modifications according to a preliminary analysis of the included studies and their objectives and methods.

*Analysis*

We used descriptive tables and figures to present the collated data. Unless otherwise specified, uncertainty intervals in tables and figures (e.g., 95% confidence intervals (CI) or credible intervals (CrI)) were extracted from the papers or computed from reported central estimates and standard errors.

For the incubation period, serial interval and generation time, meta-analyses were performed using the meta R package (16) through a calculation of an overall mean from studies reporting a single mean using the inverse variance method for pooling. Random effects models were calculated. A subgroup analysis was performed dividing the studies into mathematical models or primary studies, when applicable.

For the CFR, a meta-analysis was performed by calculating an overall proportion from studies reporting a single proportion using a generalized linear mixed model (GLMM) for pooling, given the expected low frequency of the outcome. Both common effect and random effects models were estimated, with 95% CI and statistics on heterogeneity in CFR across studies.

For the infectious period, we could not present pooled results through a meta-analysis due to scarcity of information obtained (the only one study found is presented (17)).

Likewise, for the basic and reproduction numbers, we decided not to perform an aggregated analysis of estimates because of difficulties in the interpretation of the results, given heterogeneity in the times, locations, and methods used to calculate these parameters. Instead, we present the findings in forest plot.

When analyses of aggregated results were performed, statistical heterogeneity was assessed by visual inspection of forest plots and the , and statistical tests.

A subgroup analysis was performed for incubation period and CFR according to the geographical distribution of the estimates and type of study (parameters obtained by mathematical models vs other study designs). Although we planned to perform a subgroup analysis of estimates according to sex assigned at birth, mechanism of transmission, HIV status and type of vaccine strategy used (pre- and post-exposure prophylaxis), these were not possible due to limited data. Analyses were conducted using R (version 4.2.2) (18).

**Results**

*Search Results*

A total of 6110 references were identified from the electronic search in databases and other mentioned sources. After removing duplicates and performing an initial screening by title and abstract, 157 references were eligible for full-text evaluation. Of these, a total of 109 studies were excluded: 77 for failing to evaluate epidemiological parameters of interest, 24 for being theoretical models only (not fitted to data), two for wrong study design, two for not corresponding to the study period of interest and four for no full-text availability (only poster abstracts). Finally, 47 studies were identified and included in the present systematic review as shown in the PRISMA flow diagram (Figure 1). Table 1 shows the characteristics of the included studies. The characteristics of the excluded studies are found in Supplementary Table 2.

*Included studies.*

Forty-seven references were included in the analysis. The predominant study designs were mathematical models n=24 (51%), followed by case series n=13 (28%), cross sectional studies/surveillance reports n=8 (17%) and cohort studies n=2 (4%). Regarding the epidemiological parameters estimated by the studies, incubation period was the main parameter reported (n=26 references), followed by basic reproductive number (n=9), effective reproductive number (n=8), serial interval (n=5), CFR (n=5), generation time (n=2) and infectious period (n=1). The proportion of each study design and epidemiological parameters evaluated in the included references is visualized in Figure 2.

The main characteristics of the studies included in this review are detailed in Table 2. The studies were carried out in different countries and locations worldwide, but most of the evidence comes from Spain, United States of America, and United Kingdom, respectively. A map of the number of articles selected per country is represented in Figure 2.

*Assessment of quality of included studies*

The results of the quality assessment are summarized in Figure 3 and a detailed description of the decision of each study is available in supplementary table 3.

For mathematical models, most of the studies reported the fitted distribution used and their parameters, the time frame, and central or dispersion tendency measures with their respective uncertainty intervals. Nevertheless, more than 25% of the studies failed to perform model adjustments to overcome critical aspects, such as phase bias when the outbreak was in an ascending or descending phase or did not account for censoring or truncated data when necessary. Additionally, 21% of the studies did not explicitly report the code and data used for their reported parameter’s estimations (Figure 3a).

For case series, 84% of the studies reported clear eligibility criteria and provided information about case definition of mpox disease, including a detailed description of demographics of patients and the setting where the patients were identified (i.e., clinic, residence). Seven percent of the studies had limitations in the inclusion of consecutives patients and their contacts at risk, and clear reporting of clinical information (Figure 3b).

In the case of cross-sectional and surveillance reports, all included studies had clear criteria for inclusion of participants, offered a detailed description of subjects and the setting where the patients were identified, demonstrating reliability in the measurement of the outcomes evaluated (Figure 3c).

Lastly, the two cohort studies included in this review demonstrated adequate standardization of the processes and diagnostic tests performed in the cohort; however, they failed to provide detailed information about the follow-up of the patients and the reasons for loss to follow up (Figure 3d).

*Epidemiological parameters*

*Incubation period:* twenty-six studies (see Table 1) reported estimates of this parameter, combining data on a total of 2034 confirmed or suspected mpox cases. Pooling these estimates yielded a mean incubation period of 7.56 days (95% CI: 7.13-8.02) using a random effect model, = 15%, = 0.0047, p 0.24. (Figure 4a). The most common fitted distributions across the studies that were used by the authors to estimate the parameter were in order gamma, log-normal, and Weibull.

We performed a subgroup analysis according to the type of study design (mathematical model vs other study designs). For mathematical models, we analyzed estimates of 10 studies, obtaining a pooled mean incubation period of 7.67 (95% CI: 7.13-8.25) for both common and random effect models, = 0%, = 0, p 0.51. (Supplementary Figure 1a). As for non-mathematical models, we analyzed estimates of 16 studies, obtaining a pooled mean of incubation period of 7.46 (95% CI: 6.87-8.10) using a random effect model, = 30%, = 0.0079, p = 0.13. (Supplementary Figure 1b).

*Serial interval:* five mathematical models (19-23) reported estimates of this parameter, combining data on a total of 225 confirmed or suspected mpox cases. Pooling these estimates yielded a mean serial interval of 8.25 days (95% CI: 6.45-10.55) using a random effect model, = 90%, = 0.06, p <0.01. (Figure 4b). Four of the studies fitted a gamma distribution to the data, and one study fitted a normal distribution.

*Generation time:* two mathematical models (17, 24) reported estimates of this parameter, obtaining a pooled mean generation time of 10.83 days (95% CI: 8.11-14.46) using a random effect model, = 0%, = 0, p 0.60 (Figure 1d). A gamma distribution was fitted to the data in both studies.

*Infectious period:* only one study (17) reported estimates of this parameter. It was an analysis and prediction system for epidemics based on a general SEIR model fitted to data of confirmed mpox cases from the US CDC and the WHO. For the USA, the mean infectious period was 4.01 days (95% CI 1.6-11.6); for Europe, it was estimated as 3.89 days (95% CI 1.6-12.1); and globally, the mean infectious period was 3.7 (95% CI 1.5-11.7).

*Case fatality rate:* Twenty-five studies (Table 1) reported the proportion of deaths related to mpox in its study populations, for a total of 67395 suspected or confirmed mpox cases. Pooling these estimates, we obtained a CFR of 0.0003 (95% CI: 0.0000-0.0024) using a random effect model, = 94%, = 6.9665, p <0.01 (Figure 4d).

It is important to notice that some of these studies could be overlapped (VER FOREST)

**Discussion**

Maybe compare your pooled estimates of IP and SI (they were similar) to comment on the idea of pre-symptomatic transmission. There were a few papers (including Madewell 2023, Ward 2023, and Miura 2023) that were debating whether pre-symptomatic transmission occurs and if so, to what extent. Pre-symptomatic transmission has implications for the controllability of an outbreak (Fraser 2004 PNAS).

Si el periodod e incubación es mas corto que ek interval serial significa que hay transmisión presintomática sustancial.

Maybe comment on why so few estimates of generation time (not observable, difficult to estimate). Que tan diferente gi vs serial interval 8 vs 10.

I think it will be important to put these estimates in context i.e. how are they different or similar to estimates for mpox before 2022? What did we learn and what do we still need to research/understand?

Limitation: your assessment of bias for the modeling studies was pretty superficial I think

**Conclusion**

Figure 1: PRISMA flow diagram

**Identification of studies via other methods**

**Identification of studies via databases and registers**

Records identified from electronic databases: n = 5962

Medline: n= 1714

Embase: n= 1351

Scopus and Web of Science: n= 2897

Records identified from preliminary references repositories, websites, organizations, and citation searching (n = 148)

Records removed *before screening*:

Duplicate records removed (n =2808)

**Identification**

Records screened.

(n =3154)

Records excluded.

(n =3000)

Reports not retrieved.

(n = 0)

Reports sought for retrieval.

(n =3)

Reports sought for retrieval.

(n =154)

Reports not retrieved.

(n = 1)

**Screening**

Reports excluded: (n = 109)

Failing to evaluate epidemiological parameters of interest (n =77)

Wrong study design (n = 2)

Not study period of interest (n=2)

Theoretical model only (n=24)

Poster abstract (no full text) (n=4)

Reports excluded: (n = 0)

Reports assessed for eligibility.

(n = 3)

Reports assessed for eligibility.

(n =153)

**Included**

Studies included in review (n =47)

Case fatality rate: n= 24

Incubation period: n = 26

Basic reproduction number: n = 9

Effective reproduction number: n = 8

Serial interval: n = 5

Generation time: n = 2

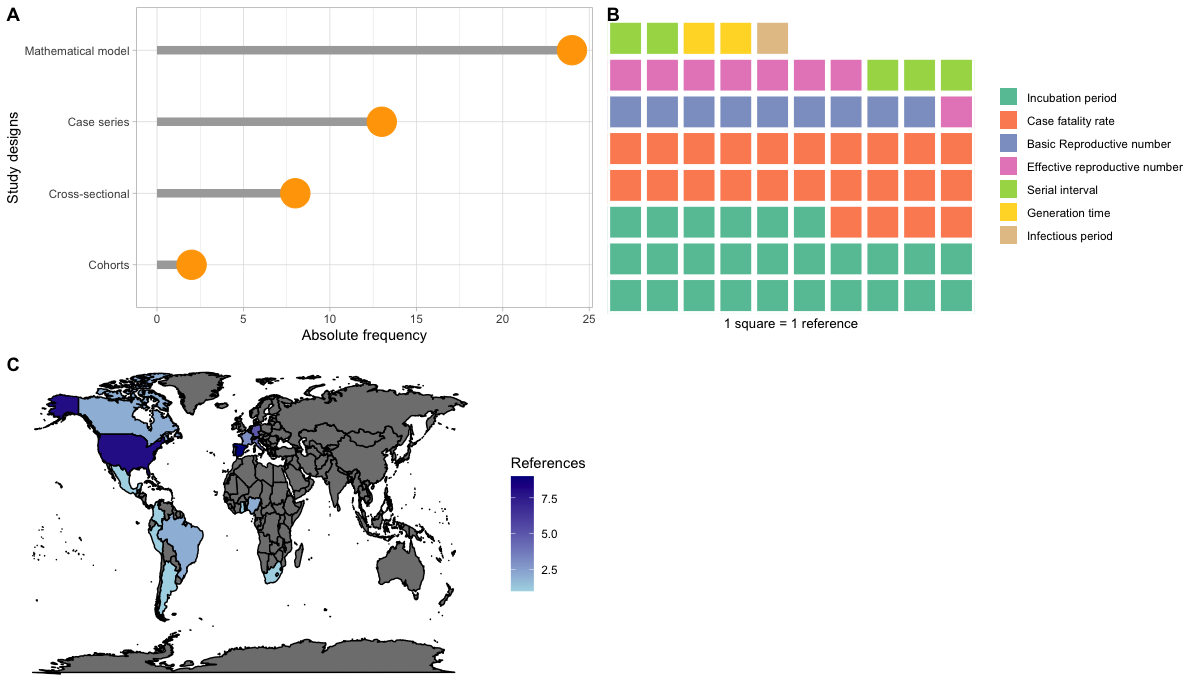
Infectious period: n = 1

**Table 1: Main characteristics of the studies included in the analysis.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **First author (year)** | **Study design** | **Region** | **Parameters evaluated** | **Study period** | **Sex (n, %)** | **Age** | **Sexual orientation and gender identity** | **People living with HIV (n, %)** |
| UKHSA (2022) Technical briefing 1 | Surveillance report | United Kingdom | Incubation period, serial interval | May 6 to June 8, 2022 | Female (3/314,0.9)  Male (311/314,  99.1) | Median 38 (IQR 32-44) | 151/152 men identified as GBMSM\* | NA\*\* |
| UKHSA (2022) Technical briefing 2 | Surveillance report | United Kingdom | Incubation period | May 6 to June 22, 2022 | Female (5/810,0.6)  Male (805/810,  99.4) | Median 37 (IQR 31-43) | 308/321 (96%) men identified as GBMSM\* | 90/321 (28) |
| Alvarez-Moreno (2023) | Cross-sectional study | Colombia | Case fatality rate | June 29 to  November 16, 2022. | Female (25/521, 4,8)  Male (496/521, 95.2) | Median 32.6 (IQR 28-38.3) | NA\*\* | 367/521 (70.4) |
| Angelo (2023) | Cross-sectional study | North America, Europe, Argentina, South Africa | Incubation period | May 1 to July 1, 2022 | Male (226/226,100) | Median 37 (IQR 32-43) |  | 92/209 (44) |
| Betti (2022) | Mathematical model | Canada and global | Basic reproduction number | May to Aug, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Bragazzi (2023) | Mathematical model | Canada | Basic reproduction number | May 19 to July 25, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Branda (2022) | Mathematical model | Europe | Basic reproduction number | May to Aug, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Català (2022) | Prospective cross-sectional study | Spain | Incubation period | May 28 to July 14, 2022 | Male (185/185,  100) | Mean 38.7 (SE 8.2) | 184/185 (99%) men identified as GBMSM\* | 78/185(42) |
| Charniga (2022) | Mathematical model | United States of America | Incubation period | May 17 to June 6, 2022 | Male 22/22 (100) | Range 28 to 61 | 22/22 (100) men identified as GBMSM\* | NA\*\* |
| Chitwood (2023) | Mathematical model | United States of America | Effective reproduction number | May to Nov, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Choudhury (2022) | Case series | Germany | Incubation period | May to September, 2022 | Male 179/179 (100) | Mean 38 (Range 20-67) | 164/169 (97) men identified as GBMSM\* | 55/131 (42) |
| Cobos (2023) | Case series | Spain | Incubation period | May 19 to June 7, 2022 | Male 30/30 (100) | Mean 33 | 30/30 (100) men identified as GBMSM\* | 14/30 (47) |
| Diaz-Brochero (2023) | Mathematical model | Argentina, Chile, Colombia, Mexico, Peru, Brazil | Effective reproduction number | June to November, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Du (2022) | Mathematical model | United States America, France, Germany, Spain, England, Portugal | Effective reproduction number | May to July, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Endo (2022) | Mathematical model | Global | Basic reproduction number | Up to May 31, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Eustaquio (2023) | Surveillance report | United States of America | Case fatality rate | May 10, 2022, to May 17, 2023 | NA\*\* | 2,909/29,984 (9.7%) were aged >50 | -Cisgender men 28,475/29,984 (94.9)  -Cisgender women 897/29,984 (2.9)  -Transgender men 55/29,984 (0.2)  -Transgender women 229/29,984 (0.8)  -Other gender identity 236/29,984 (0.8) | 4,798 (55.4) among 18–50 yrs  552 (66.2) among >50 yrs |
| Gao (2023) | Mathematical model | Global | Basic reproduction number | January to August,2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Garcia-Garcia (2023) | Mathematical model | Spain | Effective reproduction  number | April to August 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Gaspari (2022) | Case series | Italy | Incubation period | June 20 to August 10, 2022 | Male 30/30 (100) | Mean 37.5 (Range 21-65) | 30/30 (100) men identified as GBMSM\* | 12/30 (40) |
| Gomez-Garberi (2022) | Case series | Spain | Incubation period | May to August 2022 | Male 14/14 (100) | Median 42 (Range 20-56) | 10/14 (71) men identified as GBMSM\* | 8/14 (57) |
| Guo (2022) | Mathematical model | Global | Serial interval | January to August, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Guzzetta (2022) | Mathematical model | Italy | Incubation period, generation time, and reproduction number | May to June, 2022 | Female (2/255,0.8)  Male (253/255,  99.2) | Median 37 (range 20–71) | 190/200 (95) men identified as GBMSM\* | NA\*\* |
| Kroger (2023) | Case series | Germany | Incubation period | May 22 to October 30, 2022 | Female (1/368,0.3)  Male (367/368,  99.7) | Median 41 (range 12-80) | 247(67) men identified as GBMSM\* | 143/368 (39) |
| Kwok (2022) | Mathematical model | England, Portugal, and Spain | Basic reproduction number | May 18 to June 18, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Liao (2023) | Mathematical model | United States of America, Brazil, United Kingdom,Democratic Republic of the Congo | Effective reproduction number | May to September, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Madewell (2023) | Mathematical model | United States of America | Incubation period, serial interval | May to August, 2022 | Female (5/112,5)  Male (106/112,  95) | Median 35 (Range 1-76) | NA\*\* | NA\*\* |
| McFarland (2023) | Mathematical model | Germany | Incubation period | May to June 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Mailhe (2023) | Case series | France | Incubation period | May to July, 2022 | Female (1/263, 0.3)  Male (262/263, 99.7) | Median 35 (Range 30-41) | 245/262 (93.5) men identified as GBMSM\* | 73/256 (29) |
| Maldonado (2023) | Case series | Peru | Incubation period | July 1 to September 3, 2022. | Female (3/205, 1.5)  Male (202/205, 98.5) | Median 32 (Range 28-38) | 192/205 (94) men identified as GBMSM\* | 136/205 (66) |
| Miura (2022) | Mathematical model | Netherlands | Incubation period | Up to May, 2022 | Male 18 pairs (100) | NA\*\* | NA\*\* | NA\*\* |
| Miura (2023) | Mathematical model | Netherlands | Incubation period, serial interval, basic reproduction number | May to September, 2022 | Male 109 pairs (100) | NA\*\* | 109 pairs (100) men identified as GBMSM\* | NA\*\* |
| Mitjà (2023) | Case series | Global | Case fatality rate | May 11, 2022, and  January 18, 2023, | NA\*\* | Median 35 (Range 30–43) | -Cisgender women 4 (1)  -Transgender women 10 (3)  -Cisgender men 367 (96)  -Non-binary  Individual 1 (0) | 382/382 (100) |
| Moschese (2023) | Case series | Italy | Incubation period | May to June, 2022 | Male (32/32, 100) | Median 38 (Range 34-42) | 32 (100) men identified as GBMSM\* | 16/32 (50) |
| Núñez (2023) | Surveillance-based study | Mexico | Incubation period | May 1 to September 10, 2022 | Female (16/565, 2.8)  Male 549/565 (97.2) | Median 34 (Range (30–41) | 327/565 (59.6) men identified as GBMSM\* | 299/565 (52.9) |
| Musa (2022) | Mathematical model | Nigeria | Effective reproduction number | January to September, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Ogoina (2023) | Cohort study | Nigeria | Case fatality rate | February 1, 2022, to January 30, 2023 | Female 46/160 (29)  Male 114/160 (71) | <18 years 26/160 (16%)  18–35 years 82/160 (51%)  >35 years 52/160 (33%) | NA\*\* | Advanced HIV disease 11/160 (7)  Stable HIV 14/160 (9)  No HIV 69/160 (43)  Unknown HIV status 66/160 (41) |
| Okyere (2023) | Mathematical model | Ghana | Basic reproduction number | May to October, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| O’Laughlin (2022) | Case series | United States of America | Incubation period | May to August, 2022 | Female 12/549 (2.3)  Male 515/549 (97.7) | Median 36.5 (IQR 31.4–43.9) | NA\*\* | 254/549 (46.3) |
| Riser (2023) | Surveillance report | United States of America | Case fatality rate | May 10, 2022, to March 7, 2023 | NA\*\* | Median 34 (Range 0–89) | Survivors (n = 30,183)  Cisgender man 24,759 (94.9)  Cisgender woman 806 (3.1)  Transgender man 55 (0.2)  Transgender woman 227 (0.9)  Another gender identity 235 (0.9)  Decedents (n = 38)  Cisgender man 36 (94.7)  Cisgender woman 1 (2.6)  Transgender man 0 (—)  Transgender woman 1 (2.6) | Survivors: HIV positive 5,186 (38.3)  Decedents: HIV positive 31 (93.9) |
| Saldaña (2022) | Mathematical model | Spain, France, Germany, the United Kingdom, the Netherlands, Portugal, and Italy | Effective reproduction number | May to September, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Schrarstzhaupt (2022) | Mathematical model | Brazil | Effective reproduction number | June to August 22, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |
| Suárez Rodríguez (2022) | Case series | Spain | Incubation period | May to June, 2022 | Female 14/1256 (1.1) Male 1242/1256 (98.9) | Median 37 | 290/332 (87.3) men identified as GBMSM\* | NA\*\* |
| Tarín-Vicente (2022) | Multicentre, prospective, observational cohort study | Spain | Incubation period | May 11 to June 29, 2022 | Female 6/181 (3)  Male 175/181 (97) | Median 37, (IQR 31-42) | 166/175 (95) men identified as GBMSM\*, 9/175 (5) men identified as heterosexual, 6/6 (100) women identified as heterosexual | 72/181 (40) |
| Thornhill (2022) | Case series | 16 countries from  Europe, Americas, Western Pacific, and Eastern Mediterranean | Incubation period | April to June, 2022 | Female 0  Male 527/528 (99.8)  Trans or nonbinary 1/528 (<1) | Median 38 (Range 18–68) | Heterosexual 9/528 (2), Homosexual 509/528 (96), Bisexual 10 (2) | HIV positive 218 (41)  HIV negative or status unknown 310 (59) |
| Thornhill (2022) | Case series | 15 countries from North and South America, Europe, and Africa | Incubation period | September 10 to October 4, 2022. | All female sex at birth | Median 34 (IQR 28–40; range 19–84) | 62 trans women, 69 cis women, and five non-binary individuals. 121/136 (89) reported sex with men. | 37/136 (27) |
| Ward (2022) | Mathematical model | United Kingdom | Incubation period, serial interval | May 6 to August 1, 2022. | NA\*\* | Mean 37.8 (SE 9.1) | 1160/1213 (95) men identified as GBMSM\* | NA\*\* |
| Wei (2022) | Mathematical model | United States, Europe, Global | Infectious period, generation time, basic reproduction number, incubation period | May to October, 2022 | NA\*\* | NA\*\* | NA\*\* | NA\*\* |

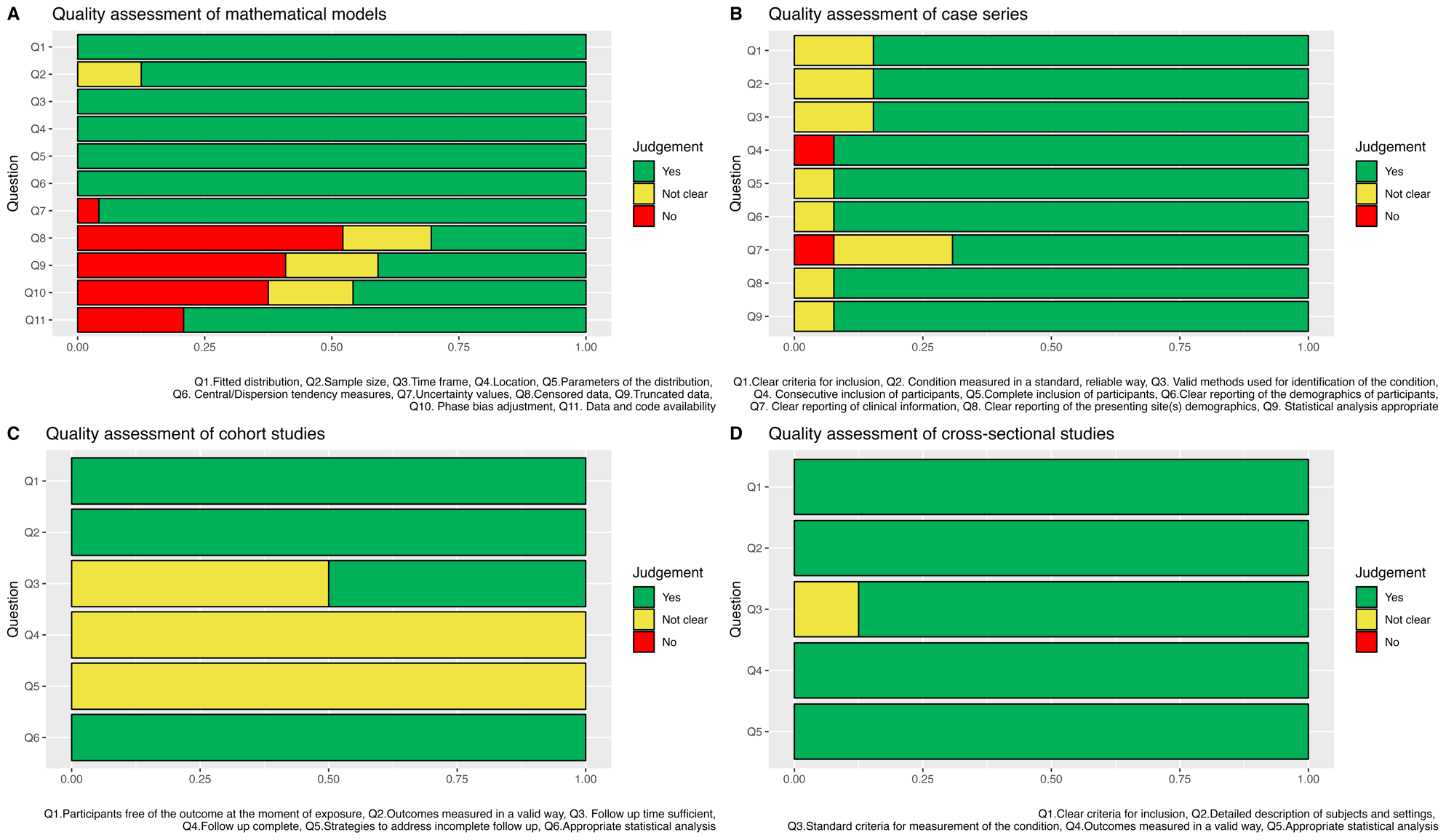
\*GBMSM: gay, bisexual, and other men who have sex with men, \*\*NA: not available or applicable, IQR: interquartile range.

**Figure 2: Visual representation of study characteristics included in the systematic review.**



**A:** Lollipop plot of the distribution of the included study designs by reference number; **B**: Waffle plot of the distribution of the number of references by epidemiological parameter evaluated in the analysis (one reference may report more than one parameter); **C:** Map of the number of references included per country

**Figure 3: Quality assessment of included studies**



**Figure 4: Pooled analysis of epidemiological parameters for mpox during the 2022-2023 global outbreak**

**analisis subgrupos por region, multiples regiones**

Note: The blue diamonds correspond to the pooled estimates, and the gray shaded boxes to the 95% uncertainty around the mean.

**References**

1. 2022-23 Mpox (Monkeypox) Outbreak: Global Trends. (<https://worldhealthorg.shinyapps.io/mpx_global/> , accessed 19 September, 2023).

2. Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, et al. The changing epidemiology of human monkeypox-A potential threat? A systematic review. PLoS Negl Trop Dis. 2022;16(2):e0010141.

3. Callaby H, Gordon NC. Mpox: evidence for strengthening and sustaining global surveillance. Lancet Glob Health. 2023;11(7):e983-e4.

4. Organization. PPAH. **WHO declares end of mpox emergency, calls for sustained efforts for long-term management of the disease** 2023 [November, 1 2023]. Available from: <https://www.paho.org/en/news/11-5-2023-who-declares-end-mpox-emergency-calls-sustained> efforts-long-term-management disease#:~:text=May%2011%2C%202023%2D%20The%20Emergency,General%20accepted%20the%20Committee%27s%20advice.

5. Second meeting of the International Health Regulations (2005) (IHR) Emergency Committee regarding the multi-country outbreak of monkeypox. Geneva: World Health Organization; 2022 (<https://www.who.int/> news/item/23-07-2022-second-meeting-of-the- international-health-regulations-(2005)-(ihr)- emergency-committee-regarding-the-multi- country-outbreak-of-monkeypox, accessed 19 September 2023).

6. Fifth meeting of the International Health Regulations (2005) (IHR) Emergency Committee on the Multi-Country Outbreak of mpox (monkeypox). Geneva: World Health Organization; 2023 (https:// <www.who.int/news/item/11-05-2023-fifth-> meeting-of-the-international-health-regulations- (2005)-(ihr)-emergency-committee-on-the-multi- country-outbreak-of-monkeypox-(mpox), accessed 19 September 2023).

7. Biggerstaff M, Cowling BJ, Cucunuba ZM, Dinh L, Ferguson NM, Gao H, et al. Early Insights from Statistical and Mathematical Modeling of Key Epidemiologic Parameters of COVID-19. Emerg Infect Dis. 2020;26(11):e1-e14.

8. Boelle PY, Ansart S, Cori A, Valleron AJ. Transmission parameters of the A/H1N1 (2009) influenza virus pandemic: a review. Influenza Other Respir Viruses. 2011;5(5):306-16.

9. Heesterbeek H, Anderson RM, Andreasen V, Bansal S, De Angelis D, Dye C, et al. Modeling infectious disease dynamics in the complex landscape of global health. Science. 2015;347(6227):aaa4339.

10. Thornhill JP, Barkati S, Walmsley S, Rockstroh J, Antinori A, Harrison LB, et al. Monkeypox Virus Infection in Humans across 16 Countries - April-June 2022. N Engl J Med. 2022.

11. Moritz U G Kraemer HT, David M Pigott, Abhishek Dasgupta, James Sheldon, Eduan Wilkinson, Marinanicole Schultheiss, Aimee Han. Tracking the 2022 monkeypox outbreak with epidemiological data in real-time. Lancet Infect Dis 2022;S1473-3099(22)00359-0.

12. Akira Endo HM, Sam Abbott, Ruwan Ratnayake, Carl A. B. Pearson, W. John Edmunds, Elizabeth Fearon, Sebastian Funk. Heavy-tailed sexual contact networks and the epidemiology of monkeypox outbreak in non-endemic regions, May 2022. medRxiv 2022061322276353. 2022.

13. Philpott D, Hughes CM, Alroy KA, Kerins JL, Pavlick J, Asbel L, et al. Epidemiologic and Clinical Characteristics of Monkeypox Cases - United States, May 17-July 22, 2022. MMWR Morb Mortal Wkly Rep. 2022;71(32):1018-22.

14. Munn Z, Barker TH, Moola S, Tufanaru C, Stern C, McArthur A, Stephenson M, Aromataris E. Methodological quality of case series studies: an introduction to the JBI critical appraisal tool. JBI Evidence Synthesis. 2020;18(10):2127-2133.

15. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, Currie M, Qureshi R, Mattis P, Lisy K, Mu P-F. Chapter 7: Systematic reviews of etiology and risk . In: Aromataris E, Munn Z (Editors). Joanna Briggs Institute Reviewer's Manual. The Joanna Briggs Institute, 2017. Available

from <https://reviewersmanual.joannabriggs.org>.

16. Balduzzi S, Rücker G, Schwarzer G (2019), How to perform a meta-analysis with R: a practical tutorial, Evidence-Based Mental Health; 22: 153-160.

17. Wei F, Peng Z, Jin Z, Wang J, Xu X, Zhang X, et al. Study and prediction of the 2022 global monkeypox epidemic. J Biosaf Biosecur. 2022;4(2):158-62.

18. R Core Team (2022). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>.

19. (UKHSA) TUHSA. Investigation into monkeypox outbreak in England: technical briefing 1. 2022.

20. Guo Z, Zhao S, Sun S, He D, Chong KC, Yeoh EK. Estimation of the serial interval of monkeypox during the early outbreak in 2022. J Med Virol. 2023;95(1):e28248.

21. Madewell ZJ, Charniga K, Masters NB, Asher J, Fahrenwald L, Still W, et al. Serial Interval and Incubation Period Estimates of Monkeypox Virus Infection in 12 Jurisdictions, United States, May-August 2022. Emerg Infect Dis. 2023;29(4):818-21.

22. Miura F, Backer JA, van Rijckevorsel G, Bavalia R, Raven S, Petrignani M, et al. Time scales of human mpox transmission in the Netherlands. J Infect Dis. 2023.

23. Ward T, Christie R, Paton RS, Cumming F, Overton CE. Transmission dynamics of monkeypox in the United Kingdom: contact tracing study. BMJ. 2022;379:e073153.

24. Guzzetta G, Mammone A, Ferraro F, Caraglia A, Rapiti A, Marziano V, et al. Early Estimates of Monkeypox Incubation Period, Generation Time, and Reproduction Number, Italy, May-June 2022. Emerg Infect Dis. 2022;28(10):2078-81.