Clinical characterization of mpox including monitoring the use of therapeutic interventions

statistical analysis plan

13 October 2023

World Health Organization

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WHO/MPX/Clinical/Analytic_plan/2023.1

Suggested citation. Clinical characterization of mpox including monitoring the use of therapeutic interventions: statistical analysis plan, 13 October 2023. Geneva: World Health Organization; 2023 (WHO/MPX/Clinical/Analytic_plan/2023.1). Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.

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Acknowledgements

Data contributors

Individual facilities contributing clinical data are acknowledged on the following WHO web page:

https://cdn.who.int/media/docs/default-source/health-care-readiness---post-covid-19-condition/sep-acknowledgements.pdf?sfvrsn=7872dad1_5

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- Firdavs Kurbonov (Department of Sexual and Reproductive Health and Research)
- Rosamund Lewis (Technical lead for mpox, Epidemic and Pandemic Prevention and Preparedness Department, Health Emergencies Programme)
- Bernadette Mirembe (Alert and Response Coordination Department, Health Emergencies Programme)
- William Probert (Department of Global HIV, Hepatitis and STI Programmes)
- Mateo Prochazka Nunez (Department of Global HIV, Hepatitis and STI Programmes)
- Matthieu Rolland (Department of Country Readiness Strengthening, Health Emergencies Programme)
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- Dominik Stelzle (Department of Global HIV, Hepatitis and STI Programmes)
- Soe Soe Thwin (Department of Sexual and Reproductive Health and Research)
- Julie Viry (Department of Country Readiness Strengthening, Health Emergencies Programme)

Clinical Advisory Group

- Rashan Haniffa, University College Hospital, United Kingdom
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- Shabina Ariff, Department of Pediatrics & Child Health, Ministry of Health, Pakistan
- Tim Uyeki, Centres for Disease Control and Prevention, United States of America
- Yaseen Arabi, King Saud University, Saudi Arabia
- Yee Sin Leo, National Centres of Infectious Diseases, Ministry of Health, Singapore
- Yinzhong Shen, Fudan University, China

Abbreviations

ALT	alanine aminotransferase
ART	antiretroviral therapy
AST	aspartate transaminase
BMI	body mass index
CI	confidence interval
CRP	c-reactive protein
HIV	human immunodeficiency virus
HSV	herpes simplex virus
IQR	interquartile range
MEURI	monitored emergency use of unregistered and experimental interventions
mpox	infectious disease caused by the monkeypox virus, previously monkeypox
MPXV	monkeypox virus
MSM	men who have sex with men
RCT	randomized control trial
STI	sexually transmitted infection
ULN	upper limit of normal
WCC	white cell count
WHO	World Health Organization

1. Introduction

1.1 Background

In May 2022, a multi-country outbreak of mpox began and rapidly spread around the world. Healthcare workers, epidemiologists and health planners need to understand the specifics of this outbreak, which requires systematic collection of data on new cases.

Mpox is an infectious disease caused by a double-stranded DNA *Orthopoxvirus* (within the *Poxviridae* family). Since 1970, human cases of mpox have been reported in 9 countries in the World Health Organization (WHO) African region: Cameroon, Central African Republic, Republic of the Congo, Côte d'Ivoire, Democratic Republic of the Congo, Gabon, Liberia, Nigeria, and Sierra Leone.*(1)* Prior to the 2022 outbreak, there has been an increase in human mpox incidence associated with the declining population immunity to orthopoxviruses after cessation of worldwide smallpox vaccination. Transmission from person to person has been known in the past to generally require prolonged close contact, such as face-to-face contact in close proximity, or skin-to-skin physical contact. Such exposure can occur in a range of settings including at home, in social or sexual networks, or in the health care setting.*(2-4)*

The incubation period is usually between 3 and 21 days, while symptoms and signs generally last 2 to 4 weeks, and may be longer in persons who are immunosuppressed.*(5)* Initially, the illness is dominated by non-specific signs of infection including myalgia and lymph node swelling, followed by a variable rash which can affect the face, body, genitalia, and limbs. The mucosa of the mouth, eyes and genitals may also become inflamed. Skin lesions develop from macular-papular form into vesicles, and resolve by crusting.*(6)*

Mpox is usually self-limiting, and most people recover within a few weeks. Severe disease, which can be life threatening, can occur particularly in immunosuppressed persons, young children, and pregnant women.*(7, 8)* Reinfection is an ongoing area of investigation.*(9)*

The 2022-2023 mpox outbreak has been more frequent among men who have sex with men (MSM), mostly diagnosed after healthcare seeking within primary care and sexual health clinics or through contact-tracing for cases.*(2, 10)*

A WHO strategic preparedness, readiness and response plan was put in place in 2022.*(11)*

1.2 Aim

To gather information on the clinical characteristics of mpox, the WHO has created data collection tools in paper and electronic format. These are designed to support clinicians and Member States to systematically generate and share new knowledge on mpox. This includes aggregate statistics on presenting conditions, morbidity and mortality, and subgroup analysis in key populations thought to be at risk of poor outcomes. The

statistical analysis plan will be used for analysis by the WHO Global Clinical Platform. The reports generated and published from the proposed analyses will help clinicians and national programmes to optimize management and response strategies.

Consistent with the terms of use, data contributors own the data they submit and may wish to use and/or adapt the SAP as required for regional, country or facility-level analysis according to their needs.

1.3 Rationale

The use of a single standardized clinical data tool enables clinical data from multiple sites to be aggregated and analyzed together. It also allows localized and comparative analysis to inform actions at national and regional levels.

This is particularly important during health emergencies when unproven clinical interventions can be used within the *Monitored emergency use of unregistered and experimental interventions (MEURI)* framework. Ethical use within MEURI respects individual health needs, autonomy and beneficence in the context of an existential threat to large populations which requires collective action. All such interventions must record sufficient information to help understand the potential patient harms and benefits in a way which does not interfere with clinical trials which are required to categorically define the safety and risk profiles. The proposed data collection and analysis plan ensures that this information is available and accessible.

Where possible, the analysis is aligned with proposed outcomes for therapeutic trials of mpox, including the most common primary endpoint (time to active lesion resolution, up to 28 days).

Overall, these data will improve understanding of the disease, inform the public health response, and prepare key data to support the design of large-scale clinical trials.

1.4 Summary of objectives of the analysis

1. **Describe the clinical characteristics of patients:** To describe the demographic features, clinical features, pre-existing medical conditions, smallpox/mpox vaccination status, therapeutic interventions, laboratory markers (hereafter, collectively called clinical characteristics) among:
   1.1. the general population with suspected, probable and confirmed mpox
   1.2. specific subpopulations expected to be at risk of poor outcomes (including pregnant people, people living with HIV, those with immunosuppression of any origin, children)
2. **Describe therapeutic interventions given, and reported adverse events.** Specific sub-group analysis of interventions given within MEURI protocols will be performed.
   2.1. Summarise therapeutic interventions given for mpox

2.2. Describe adverse events as reported through the platform

3. **Describe patient outcomes and assess potential determinants and risk factors:** To identify patterns of outcomes within the overall dataset, including severity, extent of lesions and their time to resolution:
   3.1. all patients
   3.2. within pre-defined clinical sub-groups (children, pregnant people, people living with HIV and other forms of immunocompromise)
   3.3. within patients given therapeutic interventions within the MEURI framework

2. Methods

2.1 Case definition

Data are collected in the platform on the basis of a clinical suspicion of mpox, but no further case definition is applied. Confirmatory testing may be available depending on local circumstances. Analysis will be carried out for all cases and for confirmed cases separately.

2.2 Study design

The WHO Global Clinical Platform is an open platform where Member States and individual facilities are invited to contribute patient data.

The design is passive clinical surveillance which aims to capture cases of mpox, whether treated in the community or in a healthcare facility. The surveillance platform does not require sample size estimation. The platform works with existing and new partners to maximise the data available, which will improve precision around point estimates and statistical power.

2.3 Standardized data collection tool

Case report forms can be found at https://www.who.int/tools/global-clinical-platform/monkeypox.

2.4 Analytic sample

All patients with laboratory-confirmed or clinically suspected mpox will be included in the analytic sample. There are no age restrictions to inclusion. Results will also be analyzed by laboratory test confirmation (yes/no).

2.4.1 Missing data

For each analysis, the denominator will represent data that is available, with narrative explanation of the number of missing datapoints given. While imputation may be considered on a case-by-case basis, it is not likely to be widely employed due to expected heterogeneity.

2.5 Analytical approach

2.5.1 Descriptive statistics

According to the variable type, descriptive statistics will be:

- Quantitative criteria: number of observations (N), mean, standard deviation (SD), median, interquartile range (IQR, first and third quartiles), and ranges as applicable.
- Qualitative criteria: number of observations (N), absolute frequency (n), and relative frequency (%).

Percentages will be calculated on the number of participants with available data.

2.5.2 Comparisons

Statistical tests used for groups comparisons will be chosen based on underlying distributions of variables of interest and on the nature of the comparison, for example paired vs un-paired comparisons. Parametric and non-parametric tests to be used include, but is not limited to, Fisher and Chi-squared tests for categorical variables, Student's t-test, Mann Whitney-U and Kruskal Wallis for continuous variables.

Descriptions of patient outcomes will be given for each therapeutic intervention given, and specifically those given withing the MEURI framework (see specific objectives for details).

2.6 Sample size

No formal prospective power calculation is possible as the precision of estimates will be defined by the available data, according to:

$$N = \frac{z_{\alpha/2}^2 \cdot p' \cdot (1-p')}{MOE^2}$$

Where p' = true proportion, MOE = margin of error (precision).

2.7 Limitations

Subgroup analysis may be limited in interpretability by the size of each group. Some groups may be recombined (see chapter 3) as required. Bias and confounding by intervention are likely: universal data capture is not possible, sites uploading data may not be more broadly representative, and treatments are allocated on the basis of the opinion of the treating physician.

It is important to recognize the limitations of the inference which can be drawn for interventions, including for those within the MEURI framework; high quality evidence is likely to come from clinical trials over time. Given this caveat, a limited analysis of determinants of outcomes will be performed. The accuracy of determining true risk factors for rarer endpoints (e.g. mortality) is likely to be low.

2.8 Software

All analyses will be conducted in SAS (SAS Institute Inc., United States of America) or R (R Foundation for Statistical Computing, Vienna, Austria).

3. Objectives

Definitions of categorical classification of numeric data, and pre-defined group are described in *Annex A: Definitions*.

3.1 Objective 1: Describe the clinical characteristics of patients

Primary descriptions of the population and prespecified subgroups will be conducted for demographic data, signs/symptoms and laboratory features on admission, presence of chronic diseases, therapeutic interventions received (including specifically those given within the MEURI framework). Primary analysis will include those prioritized in Table 1, although all variables collected within the CRF will be examined. Subgroups will include those based on individual characteristics, WHO region, and country.

Note that the tests used for descriptive statistics (parametric vs. non-parametric) will be determined by the distribution of the variable.

Table 1 Variable summaries informing objective 1

Variable	Statistical method
Demographics	
Age[1] < 28 days (uncorrected for gestation)* ≥ 28 days and <1 year* ≥ 1 and <5 years † ≥ 5 and <18 years † ≥ 18 and <45 years ≥ 45 and <65 years ≥ 65 years	N (%) * / † may be collapsed where denominators are small
Sex at birth Male Female Intersex Not specified	N (%)
For females: pregnant, breastfeeding	N (%)
Vaccinated using ACAM2000, MVA-BN, LC16m8 or other vaccine number of vaccines received previous smallpox scar	N (%) median (IQR) time since last vaccine

[1] Further disaggregation will be performed where data in individual strata are sufficient, including for alignment with commonly used age bands e.g. for HIV indicators, 15-24, 24-49 and 50+ are used.

Healthcare worker	N (%)
Pre-existing conditions	
Hypertension, diabetes mellitus, chronic kidney disease; chronic heart disease; chronic liver disease; chronic pulmonary disease; chronic neurological condition; malignancy or chemotherapy, HIV, tuberculosis, smoker, alcohol use, prior herpes simplex infection, specific STIs (*Neisseria gonorrhoea*, syphilis, HSV, *Chlamydia trachomatis*)	N (%)
Specific to HIV taking ART, cotrimoxazole, isoniazid prophylaxis	N (%)
Exposure history Known contact with a case Contact with possible animal source Sexual activity within preceding 21 days Travel within preceding 21 days	N (%)
Symptoms and signs	
Symptoms at presentation and at 28 days (or last available), including fever, fatigue, weakness, malaise, myalgia, sore throat, rectal pain, discharge, tenesmus, urethral pain or discharge, ocular symptoms, pain/difficulties with swallowing, nausea, vomiting, diarrhea; chest pain, dizziness, joint pain, psychological disturbance	N (%)
Extent and type of skin lesions (at baseline and follow-up as recorded, up to 28 days, or last available) Location: face, mouth, trunk, perianal, external genitalia, limbs, palms, soles of feet Type: macule, papule, vesicle/pustule, ulcer, crusting, healed Presence and location of lymphadenopathy Number of lesions *(continuous measure where possible)*	N (%) median (IQR)
Vital signs (at baseline and 28 days, or last available) *Reported according to age group* Temperature, systolic blood pressure, pulse pressure, heart rate, respiratory rate, BMI	 mean (SD) median (IQR)
Laboratory tests	
monkeypox virus PCR (subdivided by source of sample)	N (%)
… first recorded hemoglobin, platelets, total WCC, neutrophils blood glucose, ALT, AST, sodium, potassium, creatinine, CRP, procalcitonin, bicarbonate	mean (SD)
…most extreme value of hemoglobin (lowest), ALT, AST (highest), potassium (lowest), creatinine (highest), bicarbonate (lowest)	mean (SD)
…difference from baseline at day 14 of hemoglobin, bicarbonate, potassium, creatinine	mean (SD)
Specific interventions	
Which intervention (tecovirimat, specified other)	

Access through RCT / MEURI / standard care	N (%)
Received supportive care: Analgesia, with breakdown by type; antibacterial; antifungal	N (%)
Outcome	
Final diagnosis • Confirmed mpox / Suspected / Probable • Concurrent diagnosis of a sexually transmitted infection	N (%)
Vital outcome • Dead / alive / lost to follow-up • Hospitalized	N (%) median (IQR) and mean (SD)
Additional outcomes, including complications: received renal support therapy, mechanical ventilation; symptoms persisting at last follow-up, including: pain (site), ocular symptoms, malaise, dysphagia, dysuria, psychological sequelae; visible lesions healed (yes/no) time to resolution number of residual lesions at day 14	N (%) median (IQR) and mean (SD)

3.2 Objective 2: Describe therapeutic interventions given, and reported adverse events

These will be described overall and by intervention received, and stratified by sex at birth, age group, HIV status, pregnancy, intervention delivery framework (MEURI, other)

Table 2 Variable summaries informing objective 2

Variable	Statistical summary method
Therapeutic interventions administered, tecovirimat (and others as available)	N (%)
Time from symptom onset to initiation (days)	median (IQR)
Adverse events Specified adverse events which relate to mpox therapeutics (AST or ALT >5x ULN)	N (%) and narrative summary

3.3 Objective 3: Describe patient outcomes and assess potential determinants and risk factors

These will be described by sex, age group, healthcare worker status, and according to each intervention patients have been given (tecovirimat and any others).

Table 3 Variable summaries informing objective 3

Variable	Statistical summary method
Overall outcome	
Time to clinical resolution, defined as the first day on which all skin lesions are scabbed, desquamated or healed, and visible mucosal lesions are healed (up to 28 days)	N (%)
Complication, defined as one of: mechanical ventilation, renal replacement therapy or admission to intensive care	
Hospitalized within 14 days of diagnosis	
Treated for infection (antibiotic or antifungal) within 14 days of diagnosis	
Vital outcome: dead / alive / lost to follow-up	
Specific outcomes of interest	
Persistent symptoms at 14 day and 28 days (or last available), expected to be divided as: pain, ulcerated skin lesions, ocular symptoms, malaise, psychological sequelae	N (%)
Number of active lesions at 14 days	Mean (SD) and median (IQR)
Pregnancy outcomes at 14 days (or last available): live birth, miscarriage, stillbirth, did not deliver	N (%)

3.3.1 Outcome variables

- Categorical outcomes of interest include
  - treatment with antibiotics for infection (yes/no)
  - persistent symptoms (any symptom [in "specific outcomes of interest" list, above]) still present at days 14 and 28 from diagnosis (yes/no). This may be broken down by individual symptom, depending on data availability.
  - vital outcome (dead or alive at last known follow-up) [by number of lesions (as category); initial severity of symptoms; HIV status; concomitant STIs]
  - pregnancy outcome ([miscarriage or stillbirth] vs. all others)
  - Number of lesions at days 14 and 28

3.3.2 Specific analysis methods

1. **Bivariate analysis:** pre-specified predictor variables will be tested for their association with outcomes of interest using statistical tests or regression models and correlation coefficients appropriated to the distribution of the variables. These

include variables described in Table 1 sections relating to demographics, pre-existing conditions, symptoms and signs at initial presentation, laboratory tests and specific interventions. Results of these assessments will inform multivariate analysis.

2. **Multivariate analysis:** Using each categorical outcomes of interest as the dependent variable, we will construct a log-binomial Generalized Linear Model (GLM) or Cox proportional hazards regression model for time-to-event data at 14 and 28 days. Random effects will be included for each facility. Predictors considered *a priori* of clinical importance (age, sex, HIV status, prior vaccination for smallpox, mpox or other orthopoxvirus) will be considered irrespective of bivariate analysis. For all others, only predictor variables with a p-value <0.10 on bivariate analyses and not highly correlated with other variables, using a correlation matrix threshold of a >0.8, will be considered for addition to the model. Among those, a backward stepwise selection using -2Log Likelihood (-2LogL) and p-value < 0.05 will be performed to obtain the final model, and the final set of risk factors. Predictors will be described by adjusted and unadjusted risk ratios (RRs) or hazard ratios (HRs) with 95% confidence intervals.

4. Additional considerations

4.1 Publication plan

WHO reports will be made available on the WHO website.

All sites/ data contributors have full access to their dataset and are given instructions and training on setting up R-Studio and R-code to generate descriptive reports.

Interim analysis will be provided on request from ministries of health or other contributors. Global reporting, where relevant, will describe the data across all countries submitting data.

Peer-reviewed publications generated from the above-mentioned analysis in certain instances may be published in peer-reviewed journals using standard authorship criteria. The SAP for these publications may be reviewed in discussion with data contributors.

Trial design: the reports serve as an important information source to inform the endpoints and core data set in trials of novel or repurposed therapeutics for mpox.

5. References

1. Yinka-Ogunleye A, Aruna O, Dalhat M, Ogoina D, McCollum A, Disu Y et al. Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report. Lancet Infect Dis. 2019;19:872-9. doi: https://doi.org/10.1016/S1473-3099(19)30294-4.
2. Li P, Li J, Ayada I, Avan A, Zheng Q, Peppelenbosch MP et al. Clinical Features, Antiviral Treatment, and Patient Outcomes: A Systematic Review and Comparative Analysis of the Previous and the 2022 Mpox Outbreaks. The Journal of Infectious Diseases. 2023;228:391-401. doi: https://doi.org/10.1093/infdis/jiad034.
3. Beeson A, Styczynski A, Hutson CL, Whitehill F, Angelo KM, Minhaj FS et al. Mpox respiratory transmission: the state of the evidence. The Lancet Microbe. 2023;4:e277-e83. doi: https://doi.org/10.1016/S2666-5247(23)00034-4.
4. Safir A, Safir M, Henig O, Nahari M, Halutz O, Levytskyi K et al. Nosocomial transmission of MPOX virus to health care workers –an emerging occupational hazard: A case report and review of the literature. American Journal of Infection Control. 2023;51:1072-6. doi: https://doi.org/10.1016/j.ajic.2023.01.006.
5. Chenchula S, Ghanta MK, Amerneni KC, Rajakarunakaran P, Chandra MB, Chavan M et al. A systematic review to identify novel clinical characteristics of monkeypox virus infection and therapeutic and preventive strategies to combat the virus. Archives of Virology. 2023;168:195. doi: https://doi.org/10.1007/s00705-023-05808-4.
6. Petersen E, Kantele A, Koopmans M, Asogun D, Yinka-Ogunleye A, Ihekweazu C et al. Human Monkeypox: Epidemiologic and Clinical Characteristics, Diagnosis, and Prevention. Infectious Disease Clinics of North America. 2019;33:1027-43. doi: https://doi.org/10.1016/j.idc.2019.03.001.
7. Ogoina D, Dalhat MM, Denue BA, Okowa M, Chika-Igwenyi NM, Yusuff HA et al. Clinical characteristics and predictors of human mpox outcome during the 2022 outbreak in Nigeria: a cohort study. The Lancet Infectious Diseases. 2023. doi: https://doi.org/10.1016/S1473-3099(23)00427-9.
8. D'Antonio F, Pagani G, Buca D, Khalil A. Monkeypox infection in pregnancy: a systematic review and metaanalysis. Am J Obstet Gynecol MFM. 2023;5:100747. doi: https://doi.org/10.1016/j.ajogmf.2022.100747.
9. World Health Organisation. Multi-country outbreak of mpox: External situation report 23. 2023 (https://www.who.int/docs/default-source/coronaviruse/situation-reports/20230526_mpox_external-sitrep-23.pdf.
10. Pan D, Nazareth J, Sze S, Martin CA, Decker J, Fletcher E et al. Transmission of monkeypox/mpox virus: A narrative review of environmental, viral, host, and population factors in relation to the 2022 international outbreak. J Med Virol. 2023;95:e28534. doi: https://doi.org/10.1002/jmv.28534.
11. World Health Organization. Strategic preparedness, readiness and response plan to end the global COVID-19 emergency in 2022. World Health Organization; 2022 (https://iris.who.int/bitstream/handle/10665/352861/WHO-WHE-SPP-2022.1-eng.pdf?sequence=1.

Annex: Definitions

Pre-specified subgroups

- Age[2]
  - < 28 days (uncorrected for gestation)
  - ≥ 28 days and <1 year
  - ≥ 1 and <5 years
  - ≥ 5 and <18 years
  - ≥ 18 and <45 years
  - ≥ 45 and <65 years
  - ≥ 65 years
- Sex: male; female
- Pregnancy
  - Currently pregnant or recently pregnant ≤ 21 days
  - Not currently pregnant or recently pregnant
- Healthcare worker: yes; no
- HIV status
  - Positive, already prescribed antiretroviral medications
  - Positive, not already antiretroviral medications
  - Negative
  - Unknown (no previous test result)
- Within the subpopulation with HIV infection
  - CD4 < 200
  - CD4 200 – 499
  - CD4 ≥ 500
- Other immunosuppression (including iatrogenic causes such as steroids and immunomodulators for autoimmune disease)
- Likely mode of transmission (based on exposure history)
  - direct contact with infectious lesions of the skin or mucosa
  - direct contact with body fluids
  - direct contact with sexual fluids
  - contact with contaminated clothing or linens
  - prolonged face-to-face respiratory exposure in close proximity
  - respiratory exposure
  - contact with contaminated materials

[2] Further disaggregation will be performed where data in individual strata are sufficient, including for alignment with commonly used age bands e.g. for HIV indicators, 15-24, 24-49 and 50+ are used.

    - sexually active ≤21 days prior to symptom onset
    - international travel ≤21 days prior to symptom onset
    - contact with possible animal source ≤21 days prior to symptom onset
- Comorbidity
    - Any of: Chronic cardiac disease (not hypertension); hypertension; asthma, chronic pulmonary disease; chronic kidney disease; chronic liver disease; chronic neurological condition; epilepsy ; diabetes type 1/type 2; malignancy (if yes, therapy), tuberculosis (active/previous); asplenia; acute/chronic skin disease; sexually transmitted infection; smoking; alcohol use; others
    - None of the above
- WHO region and country

For more information, please contact:

Global Clinical Platform
World Health Organization
Avenue Appia 20
CH-1211 Geneva
Switzerland

Email:
global_clinical_platform@who.int