****

**ISARIC Data Platform Statistical Analysis Plan (DRAFT VERSION)**

ALL APPLICATIONS MUST BE COMPLETED AND SUBMITTED VIA: [data@isaric.org](mailto:data@isaric.org)

All data contributors who generated the data you are requesting will be invited to participate in the analysis by reviewing and providing input on the statistical analysis plan and the resulting publication. The findings from this work will be widely disseminated to inform patient care and public health policy, including submission to an international, peer-reviewed journal. ISARIC aims to recognise all the names of data contributors as cited collaborators in the resulting publication, in accordance with ISARIC's publication policy.

# Part 1: General Information and Research team

## 1. Study Title

The title of the study should be clear, concise, and should accurately convey the primary purpose of the study.

| Describing clinical presentation, treatments and disease severity of patients hospitalised with mpox, across multiple clades |
| --- |

## 2. Study version and date

List the study version and date of the SAP.

| Version | 1.0 (draft) |
| --- | --- |
| Date (DD/MM/YYYY) | 22/08/2024 |

## 3. Analysis Lead

List the full name, institution and country, and e-mail address for correspondence of the Analysis Lead.

| Full name | Esteban Garcia-Gallo |
| --- | --- |
| Institution and country | ISARIC, Pandemic Sciences Institute, University of Oxford, UK |
| Email address | [esteban.garcia@ndm.ox.ac.uk](mailto:esteban.garcia@ndm.ox.ac.uk) |
| ORCID ID | 0000-0002-8030-9985 |

## 4. Other investigators/Working Group Members

List the full name, institution and country, and e-mail address for other working group members working on the proposed analysis.

| Full name | Elise Pesonel |
| --- | --- |
| Institution and country | ISARIC, Pandemic Sciences Institute, University of Oxford, UK |
| Email address | [elise.pesonel@ndm.ox.ac.uk](mailto:elise.pesonel@ndm.ox.ac.uk) |
| ORCID ID | 0009-0009-0133-5009 |

| Full name | Leonardo Bastos |
| --- | --- |
| Institution and country | ISARIC, FIO CRUZ, Brazil |
| Email address | [lslbastos@tecgraf.puc-rio.br](mailto:lslbastos@tecgraf.puc-rio.br) |
| ORCID ID | 0000-0002-1406-0122 |

| Full name | Igor Peres |
| --- | --- |
| Institution and country | ISARIC, FIO CRUZ, Brazil |
| Email address | [igor.peres@puc-rio.br](mailto:igor.peres@puc-rio.br) |
| ORCID ID | 0000-0001-9863-4690 |

| Full name | Tom Edinburgh |
| --- | --- |
| Institution and country | ISARIC, Pandemic Sciences Institute, University of Oxford, UK |
| Email address | [tom.edinburgh@ndm.ox.ac.uk](mailto:tom.edinburgh@ndm.ox.ac.uk) |
| ORCID ID | 0000-0002-3599-7133 |

| Full name | Sara Duque Vallejo |
| --- | --- |
| Institution and country | ISARIC, Pandemic Sciences Institute, University of Oxford, UK |
| Email address | [sara.duque@ndm.ox.ac.uk](mailto:sara.duque@ndm.ox.ac.uk) |
| ORCID ID |  |

## 5. Members requiring access to data

List the full name, institution and country, and e-mail address for correspondence of all the Members of the research team who will be analysing the data. Anyone who will have access to data must have signed an Oxford Researcher Agreement.

| Full name |  |
| --- | --- |
| Institution and country |  |
| Email address |  |
| ORCID ID |  |

# Part 2: Research Plan

## 5. Background, Research Objectives, and Scientific Value

This section should explain the rational for the research aim and objectives and support this with relevant information from scientific or other literature. All supporting statements should be referenced in this section with the full reference included in the “Reference” section of the form.

| This prospective observational study aims to describe and characterise patients hospitalised with mpox, focusing on their clinical presentation, illness severity, transmission route, treatments, and outcomes. Additionally, the study seeks to identify risk factors that predict both in-hospital and 28-day mortality among patients with confirmed mpox cases. This research will also compare disease severity and characteristics across different clades or variants of mpox, and analyse how the presentation of the disease changes over time during the course of study. |
| --- |

## 6. Proposed Target Population

This section should describe the specific target population that the study will focus on.

| Patients diagnosed with suspected or confirmed mpox, admitted to a participating site and providing informed consent. |
| --- |

## 7. Clinical Questions

This section should outline the key clinical questions that the statistical analysis aims to address. These questions should be clearly defined and directly related to the objectives of the study.

| * What are the characteristics and clinical presentation of patients with mpox at hospital admission? * What are the outcomes within 28 days of presentation, and what are the risk factors associated with outcomes and complications? * What treatments are administered to patients with mpox during their observation period? * What are the results from pathogen testing of patients with suspected or confirmed Mpox? * How do mpox CRF variables evolve during the course of the study, and how reliably are these data captured at sites? |
| --- |

## 8. Statistical Analysis and Methodology

This section should detail the planned data analysis. Specify the analytical methods to be used, such as calculating measures of central tendency (e.g., mean, median), and any statistical tests that will be conducted. Additionally, outline the strategies that will be implemented to handle potential issues related to missing data.

| Primary endpoints:   * Describe the demographic and clinical characteristics of patients with mpox at hospital presentation, including co-morbodities and risk factors, vital signs, symptoms and clinical assessment, such as skin and mucosa assessment. * Investigate sources of mpox exposure, where known. * Characterise pregnancy status where applicable and the clinical presentation of infants less than 12 months old at the time of hospital presentation. Assess pregnancy outcomes by disease severity and transmission route. * Describe medical history, including vaccination history and medication use in 14 days prior to hospital admission. * Characterise laboratory results for samples taken at the time of hospital presentation. * Determine the percentage of patients with any complication during the observation period and within 28 days from presentation, as well as the percentage of patients with each specific complication. * Determine the all-cause mortality within 28 days from presentation and in-hospital all-cause mortality. * Characterise associations between all-cause mortality within 28 days from presentation and co-infection, and all-cause mortality and any complication. * Explore the relationship between disease severity and transmission route, adjusted for key covariates.   Secondary endpoints:   * Identify the percentage of patients receiving specific drug types, including steroids, antivirals, antibiotics, immunosuppressant agents, and specific medications within these. * Describe results from pathogen testing, including the percentage of patients tested for pathogens with a breakdown of the percentage for each specific pathogen among those who tested positive. * Estimate risk factors for prediction of all-cause mortality or complications within 28 days from presentation, and for prediction of in-hospital all-cause mortality.   Exploratory endpoints:   * Describe how primary and secondary endpoints evolve during the course of the study, with analysis divided into distinct time periods, e.g. weekly. * Assess how mpox CRF variables are being captured by different sites, in terms of proportion of missing values and consistency errors.   Analysis will be performed for the overall population, and for subpopulations with laboratory confirmed mpox of each clade: Ia, Ib, I sub-type unknown, IIa, IIb, II sub-type unknown, other/unknown.  Variables will be summarised as follows:   * Numerical/quantitative: the number of non-missing/number of missing values (n/nmiss), the mean and standard deviation (SD) for approximately normally distributed variables, or the median and interquartile range (IQR) for non-normally distributed variables, and the minimum and maximum values. * Categorical: the number of non-missing/number of missing values (n/nmiss), frequencies and percentages (out of total number of non-missing values).   When applicable, two-sided tests will be conducted at a 5% significance level. Since no inferential statistics are planned for the primary, secondary, or exploratory endpoints, no adjustments for multiplicity will be made. Instead, the analysis will be descriptive, focusing on summarising and characterising the data without making broader inferences.  Cox proportional hazards models will be fitted to predict outcomes for risk factor identification and to estimate hazard ratios, after adjusting for potential confounders. Schoenfeld residuals will be used to assess the proportional hazards assumption. Logistic regression will be used to analyse binary outcomes.  The study's main and secondary objectives are descriptive, and a formal sample size calculation is not needed and has not been performed. Since this is an ongoing study, there is no set end date, and there is no overall limit on the total sample size.  While efforts will be made to minimise missing data through careful data management, some data may still be unavailable. Missing data will be documented, and the reasons for their absence will be identified where possible. Patterns of missingness, and whether the data are likely missing at random, will be investigated. Multiple imputation may be used for relevant variables if the data are assumed to be missing at random and if the missing data do not exceed 30%. If multiple imputation is performed, any differences between analyses of complete data sets and those using multiple imputation will be reported, and the reasons for these differences will be examined. |
| --- |

## 9. References

This section should list all sources cited throughout the statistical analysis plan.

|  |
| --- |

## 10. Appendices

Please provide all appendices related to this research.

|  |
| --- |