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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☒	☐ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☒	☐ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐ A description of all covariates tested
☒	☐ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☒	☐ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection

The basic descriptive data was collected from the hospital database, and in the provincial surveillance database. Geographic and epidemiological data were processed using the R programming language. For the geographical maps cases and sexworkers were scaled by population density and aggregated by health area defined by the shapefiles provided by national health ministry in Democratic Republic of the Congo available online: https://data.humdata.org/dataset/drc-health-data. .

Data analysis

Mapping of mpox cases
Geographic and epidemiological data were processed using the R programming language. The epidemiological curve was plotted using the "ggplot2" package (Pebesma, 2018). For the geographical maps cases and sexworkers were scaled by population density and aggregated by health area defined by the shapefiles provided by national health ministry in Democratic Republic of the Congo available online: https://data.humdata.org/dataset/drc-health-data. Map plots were made by using the "sf" and "ggmap" R packages (Pebesma, 2018; Kahle and Wickham, 2013).
Data analysis and generation of sequences
The code used for data analysis is available on GitHub: https://github.com/dnieuw/mpox-south-kivu-mapping-manuscript. Briefly, reads were trimmed using fastp v0.23.2 (https://github.com/OpenGene/fastp) and cutadapt (https://github.com/marcelm/cutadapt). Amplicon primers were trimmed with Ampliclip v1 (https://github.com/dnieuw/Ampliclip) and mapped to the reference genome NC_003310.1. Consensus sequences were generated using Samtools v1.10. Sequences with >85% genome coverage (n=58) were included in the phylogenetic analysis.

All available Clade I sequences on NCBI and GISAID on the 31st of August 2024 were merged and a maximum likelihood phylogenetic tree was generated using IQ-Tree v2.2.0.3 using the K3Pu+F+I model as best predicted model (GISAID acknowledgment is present in Extended Data Table 1). The maximum likelihood phylogenetic tree was visualized using a custom R script making use of mainly the ggtree, tidytree, ape, and

patchwork packages. APOBEC3 mutations were identified as described by O'Toole and colleagues (27). Based on the tree and the specific mutations, we identified clusters with arbitrarily assigned numbers that were subsequently added as a field to the metadata file for testing of possible associations with potential exposure routes (specific bars, households, etc).

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Consensus sequences are available on GenBank under the accession numbers: PQ305763-PQ30582 and GISAID under the accession ID: ENA under the accession numbers: EPI_ISL_18886301, EPI_ISL_18886467, EPI_ISL_18886588, EPI_ISL_18886634, EPI_ISL_18886635, EPI_ISL_18886639, EPI_ISL_19357138, EPI_ISL_19357623, EPI_ISL_19357654, EPI_ISL_19361815, EPI_ISL_19361896, EPI_ISL_19361897, EPI_ISL_19363685, EPI_ISL_19363686, EPI_ISL_19364035, EPI_ISL_19364149, EPI_ISL_19364369, EPI_ISL_19364511, EPI_ISL_19364948, EPI_ISL_19365441, EPI_ISL_19365466, EPI_ISL_19365506, EPI_ISL_19365507, EPI_ISL_19365542, EPI_ISL_19365543, EPI_ISL_19365544, EPI_ISL_19365545, EPI_ISL_19366314, EPI_ISL_19367803, EPI_ISL_19381268, EPI_ISL_19382151, EPI_ISL_19382354, EPI_ISL_19382355, EPI_ISL_19382807, EPI_ISL_19382808, EPI_ISL_19382908, EPI_ISL_19382942, EPI_ISL_19382949, EPI_ISL_19382965, EPI_ISL_19422968, EPI_ISL_19422969, EPI_ISL_19429464, EPI_ISL_19429465, EPI_ISL_19429466, EPI_ISL_19431759, EPI_ISL_19431760, EPI_ISL_19431761-63, EPI_ISL_19433147, EPI_ISL_19434036-38, EPI_ISL_19434063, EPI_ISL_19434064, EPI_ISL_19439694-97, EPI_ISL_19460816, EPI_ISL_19460883, EPI_ISL_19460954, EPI_ISL_19461017, EPI_ISL_19462380, EPI_ISL_19462381.
Reference genome: NC_003310.1

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	The majority of patients were aged between 15 -24 years old. In total, 646/670 (96.1%) were confirmed by PCR. There were slightly more female than male cases (351/670 [52,4%] versus 319/670, [47,6%]. In contrast to other outbreaks in the DRC, only 15,5 % (104/670) of suspected cases were children under 16 years of age. Of these, 45 were less than 5 years old. Four of the seven fatalities were young adults (between 20 and 30 years), with three females and one male patient
Population characteristics	A total of 670 hospitalized mpox case records were listed as confirmed, probable, or suspected (Figure 1A) between September 29th, 2023 and June 30th, 2024. Three of these were health care workers, and seven deaths occurred during the study period (1%). In contrast to other outbreaks in the DRC, only 15,5 % (104/670) of suspected cases were children under 15 years of age. Of these, 45 were less than 5 years old. The majority of patients were aged between 16 -26 years old. In total, 646/670 (96.1%) were confirmed by PCR. There were slightly more female than male cases (351/670 [52,4%] versus 319/670, [47,6%], and cases were reported from 17 of the 23 health areas (Table I).Of the 670 hospitalized mpox cases, 83.4% (559/670) reported recent sexual contact in bars among which 44,6 % were female and 38.8% were male. Only a few cases reported to not have had sexual contact in bars: in total 16.6% (111/670) with 8.8% (59/670) males and 7.8 % (52/670) females.
Recruitment	Basic descriptive data as part of routine public health surveillance was collected for all patients hospitalised during the study period,. For patients who consented, additional information on possible exposures was collected.
Ethics oversight	The ethical clearance to conduct these studies was obtained from the Ethical Review Committee of the Catholic University of Bukavu (Number UCB/CIES/NC/022/2023.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	The study included all consenting patients admitted to a hospital in South Kivu province. A total of 670 hospitalized mpox case records were listed as confirmed, probable, or suspected between September 29th, 2023 and June 30th, 2024. Following the initial observation of the contribution of sex workers driving transmission, and the mentioning of specific bars as possible places of exposure, we carried out a census of bars and professional sex workers (PSW) of Kamituga health zone.
Data exclusions	No data were excluded
Replication	The first author worked in the provincial public health office to validate the findings.
Randomization	Not applicable
Blinding	Not applicable

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	N/A
Study protocol	N/A
Data collection	N/A
Outcomes	N/A