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Role of community and sexual contacts as drivers of MPXV clade I

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Initial investigation into the emerging mpox outbreak caused by novel monkeypox virus (MPXV) clade Ib in the eastern Democratic Republic of the Congo has identified signs of sustained human-to-human transmission and epidemiological links to sexual contacts involving female sex workers (FSWs), which have not been observed in previous clade Ia outbreaks. Using mathematical models incorporating age-dependent contact patterns, we quantified the role of frequent sexual interactions as opposed to community contacts in clade Ib's dynamics and found that this additional mode of transmission could explain its increased outbreak potential compared with clade Ia. As with the globally circulating clade IIb, which is transmitted predominantly among men who have sex with men, our findings reinforce the importance of protecting key population groups—specifically FSWs for clade Ib—in controlling ongoing mpox outbreaks.

Since September 2023, sustained local transmission of a novel subclade of monkeypox virus (MPXV), classified as clade Ib, has been observed in the Democratic Republic of the Congo (DRC), along with its spread to multiple other countries[1]. In response to the escalating situation, the World Health Organization declared a public health emergency of international concern on 14 August 2024[2]. Clade Ib was first identified from a cluster of cases in the Kamituga health zone of the South Kivu province in the eastern DRC, where an initial investigation found epidemiological links to sexual contacts and an outstanding proportion of female sex workers (FSWs) among reported cases[3]. Genetic analyses have indicated a distinct profile from clade Ia circulating in other parts of the DRC, characterized by the accumulation of mutations associated with apolipoprotein B messenger RNA editing enzyme catalytic subunit 3 (APOBEC3)[3]. These mutations suggest sustained human-to-human transmission and were also observed in the globally circulating MPXV clade IIb, which primarily affected men who have sex with men (MSM)[4]. Over the summer of 2024, clade Ib showed steady growth within many health zones in the North and South Kivu provinces and introductions to other provinces of the DRC[5]. Additionally, international spread to neighbouring countries (Burundi, Uganda, Rwanda, Kenya, Zambia and Zimbabwe) and beyond the African continent (Sweden, Thailand, India, Germany and the UK) had been confirmed by October 2024[6], of which Burundi had reported the largest number of cases (1,509 as of 27 October 2024[7]). Thereafter, the mpox (formerly known as monkeypox) outbreak has continued to expand predominantly within Africa, with nearly 20,000 cases in 2025 alone as of May[8]. The numbers of countries ever reporting clade Ib cases have increased to 12 within Africa and 29 globally, including sporadic suspected local transmission events outside of Africa[8].

MPXV clade Ia has been circulating in the DRC and other Central African countries for over 50 years[9] via zoonotic transmission followed by self-limiting chains of human-to-human transmission through close contact, mostly within households[10]. Since cessation of the smallpox vaccination programme in 1980, which had provided cross-protection against mpox[11,12], the DRC has seen a consistent rise in suspected mpox cases[13], from 3.0 per 100,000 people in 2010 to 11.5 per 100,000 people in 2023[14]. Despite this increase, zoonotic spillover has remained the primary driver of outbreaks[15,16], and there has been no evidence of large clade I outbreaks solely sustained by human-to-human transmission before the emergence of clade Ib in 2023. In contrast, the clade Ib

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outbreak in South Kivu province has shown a clear exponential growth trend, suggesting human-to-human contact as the primary mode of transmission[17,18]. The rapid rise of clade Ib cases with a potential increase in the contribution of human-to-human transmission relative to clade Ia is of growing global concern, especially given that the outbreak is not restricted to specific at-risk populations but is affecting broader groups, including children[19].

The extensive clade Ib case profiles, including both children and adults, along with documented occupational risks among FSWs, may reflect its mixed transmission routes through regular contacts in the community and through sexual contacts. Sexual contact as a novel route of transmission has also been documented in the ongoing global mpox outbreak caused by clade IIb since 2022 and was suggested to have contributed to the rapid spread among MSM[20,21]; meanwhile, sustained transmission of clade IIb through community or heterosexual contact routes has not been observed and cases were mostly restricted to the MSM group[22]. If clade Ib, transmissible through heterosexual contact, continues to grow into another international mpox outbreak following clade IIb, the potentially more emphasized role of community contacts in its transmission compared with clade IIb may enable it to affect a larger susceptible population and pose challenges for control. Although the involvement of sexual contacts among FSWs and their clients has been well documented in the initial spread of clade Ib in the Kamituga health zone in South Kivu[19], little is currently understood about the relative contribution of community and sexual contacts to subsequent clade Ib dynamics in broader settings not limited to Kamituga, and how they may explain the distinct epidemiological features of clade Ib compared with clade Ia. With the gradual expansion of clade Ib within the DRC and beyond borders, analytical efforts to identify its plausible transmission mechanisms and priority groups for prevention should leverage the best available evidence, if limited, to inform and support effective control policies.

In this study, we hypothesized that the rapid growth of the clade Ib outbreak could be explained by its entry into a key population group with a high rate of sexual contact. We developed a mathematical model for MPXV transmission dynamics, incorporating both a community contact route and a sexual contact route involving FSWs. We first used a model incorporating only a community contact route, to replicate the age profiles of the current and historical clade Ia outbreak datasets (Extended Data Table 1). We then expanded the model to include a sexual contact route, to quantify the contribution of each route to the overall clade Ib transmission dynamics.

Community contact transmission patterns for clade Ia

The age-dependent contact matrix, whose entries represent the average number of contacts (typically defined as either conversational or physical contacts) that an individual of specific age group has with other age groups per unit time, is a common tool for modelling the transmission dynamics of directly transmitted infections across multiple age groups. Assuming that the risk of transmission is proportional to the frequency of relevant types of contacts one experiences with infectious individuals, the contact matrix is associated with the so-called next-generation matrix, a matrix that is multiplied by a vector containing the number of cases by age group in one generation to produce a vector for the next generation[23]. During the exponential phase of an outbreak, the age distribution of cases would quickly converge to the dominant eigenvector of the next-generation matrix and the dominant eigenvalue would define the effective reproduction number[23]. We modelled the next-generation matrix by combining a contact matrix informed by empirical contact survey data from Zimbabwe[24] and age-dependent susceptibility that we assumed to reflect potentially higher susceptibility among children aged 0–4 years[25] and lower susceptibility among smallpox-immunized birth cohorts born in or before 1980[11,12].

This simple model, validated by hold-out data (empirical Kullback–Leibler divergence < 0.01; Extended Data Table 2 and Supplementary Fig. 1), well described the age distribution for both the historical clade Ia cases in the Tshuapa province (from a well-documented clade Ia outbreak between 2011 and 2015[26]) of the DRC and the recent cases in six provinces of the DRC where clade Ia has been endemic, with a decade's shift in the age of smallpox-immunized cohorts from 34 years and above to 45 years and above (Fig. 1a,b). Our model employed four contact matrices with different contact definitions; since all four models were overall similar in goodness of fit, we used model averaging[27] to pool the model outputs (Table 1). The estimated susceptibility among children aged 0–4 years (model averaging estimate = 1.5; 95% credible interval = 1.05–2.1) and the smallpox-immunized cohort (model averaging estimate = 0.26; 95% credible interval = 0.17–0.38) relative to other age groups was consistent with the literature: ratios of 1.3–1.6 between the historical secondary attack risk estimates for clade Ia among ages 0–4 and 5–14 years[25] and the estimated effectiveness of past smallpox vaccines against clade IIb of around 70–75%[12,28], combined with high historical coverage in the DRC (89–97%)[29].

Modelling sexual contact transmission for clade Ib outbreaks

Assuming that the community contact transmission patterns relevant to clade Ia would also apply to clade Ib transmission, we modelled a sexual contact transmission route among heterosexual individuals with high sexual activity (who we assume primarily represent FSWs and clients) alongside the community contact matrix to represent the transmission dynamics of clade Ib outbreaks. We considered simple proportionate mixing between age groups, where sexual partners are chosen randomly among those in the high-activity group of the opposite sex. We parameterized the age-dependent proportion of male and female high-activity individuals (aged 15–19, 20–29, 30–39 and 40–49 years) and their mean neighbour degrees[30] over the infectious period of mpox to construct the age-, sex- and transmission route (community versus sexual contact)-dependent next-generation matrix. We fitted our model to the age–sex distribution of clade Ib cases in multiple geographical settings: the North and South Kivu provinces (referred to as the Kivus hereafter), the Kamituga health zone, other health zones of South Kivu, and Burundi. Across these geographical settings, we assumed that age-dependent relative susceptibility was identical to what we estimated from clade Ia datasets.

Our model reproduced the observed age–sex distributions of clade Ib cases generally well, including age groups not assumed to be involved in high-activity sexual contact (Fig. 1c–f). This supports the hypothesis that the transmission dynamics of clade Ib could be explained by a combination of community contact transmission patterns similar to those of clade Ia and additional sexual contact transmission among the high-activity group. Meanwhile, the model fit to a few data points in other health zones of South Kivu and Burundi was slightly suboptimal, potentially due to reporting bias or limitations in empirical contact matrix data. The estimated role of transmission through sexual contact varied between geographical settings, potentially reflecting different sexual behaviours among high-activity individuals. The estimated relative contribution of sexual contact to the overall effective reproduction number was higher in the Kivus (model averaging estimate = 42%; 95% credible interval = 37–47%), which is probably attributable to the dynamics in the Kamituga health zone (62%; 55–68%) (Table 1). In the other health zones of South Kivu (14%; 6–21%) and Burundi (16%; 11–20%), sexual contact was suggested to play a smaller (although non-negligible) role. A recent study on the Kamituga outbreak associated clade Ib spread in the region with a high number of bars serving as places for commercial sex services in the context of the local gold mining industry[31]. Frequent engagement in commercial sex associated with mining work[32] in Kamituga, and potentially other nearby mining areas[31], may account for the distinct epidemiological characteristics of clade Ib

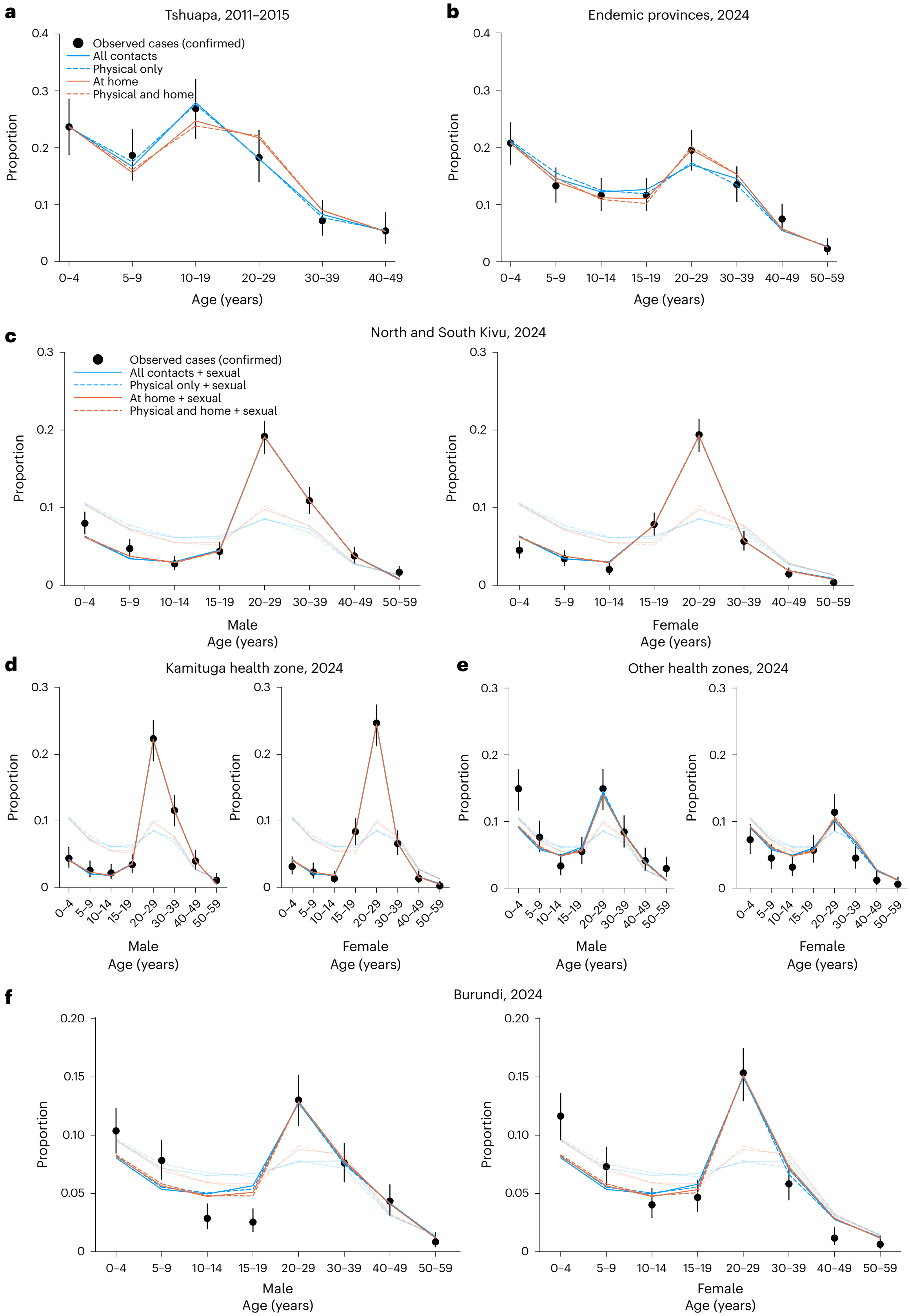

Fig. 1 | Observed and modelled age distributions of mpox cases. a, Clade Ia cases with suspected human-to-human exposure from the Tshuapa province of the DRC from 2011 to 2015 (*n* = 279 cases). Those aged 34 years and older were assumed to be smallpox immunized. **b**, Cases from clade Ia-endemic provinces in the DRC from January to mid-August 2024 (*n* = 482). Those aged 45 years and older were assumed to be immunized. **c**–**f**, Clade Ib cases from multiple settings in the DRC (North and South Kivu (**c**), the Kamituga health zone (**d**) and other health zones (**e**)) from January to mid-August 2024 (*n* = 1,377, 725 and 510, respectively) and in Burundi from mid-September to October 2024 (**f**; *n* = 945). Those aged 45 years and older were assumed to be immunized. Half-transparent lines represent the model fit without assuming transmission through sexual contact. Dots and whiskers represent the observed age distributions among cases and their 95% confidence intervals.

Table 1 | Relative contribution of sexual contacts to the transmissibility of clade Ib in the DRC and Burundi

Model	Contact type	Model weight[a]	Estimated relative susceptibility[b]		Estimated fraction of R_{eff} attributable to sexual transmission (%)[c]			
			Children aged 0–4 years	Immunized cohort	North and South Kivu	Kamituga health zone	Other health zones in South Kivu	Burundi
1	All contacts[d]	0.21	1.9 (1.6–2.2)	0.27 (0.18–0.38)	41 (36–45)	60 (54–66)	14 (9–21)	16 (12–20)
2	Physical contacts only	0.33	1.6 (1.4–1.9)	0.30 (0.21–0.42)	42 (37–46)	61 (55–66)	15 (9–21)	16 (13–20)
3	All contacts at home	0.29	1.3 (1.1–1.6)	0.22 (0.15–0.32)	43 (38–47)	63 (57–69)	12 (5–19)	15 (11–20)
4	Physical contacts at home	0.17	1.2 (0.96–1.4)	0.25 (0.17–0.36)	42 (38–47)	63 (57–68)	12 (4–19)	15 (11–19)
Model average	–	–	1.5 (1.05–2.1)	0.26 (0.17–0.38)	42 (37–47)	62 (55–68)	14 (6–21)	16 (11–20)

Posterior median estimates and 95% credible intervals are shown. [a]Based on Watanabe–Akaike weights[75]. [b]Referenced to the pre-immunization cohort aged 5 years or older. [c]Defined as the relative reduction in effective reproduction number R_{eff} when sexual contacts were excluded from the next-generation matrix. [d]Physical and conversational contacts. Physical contacts are defined as any skin-to-skin contact and conversational contacts are defined as in-person contacts with a two-way exchange of at least three words.

in the Kivus. These differences in the relative roles between community and sexual contacts could shape contrasting age-dependent transmission patterns between regions. We reconstructed the frequency of transmission across age groups from our modelled next-generation matrix, assuming proportionate mixing (Fig. 2a). Compared with clade Ia in the endemic provinces, clade Ib in the Kivus was estimated to be more frequently transmitted among sexually active age groups (Fig. 2a; left versus middle). Such excess in estimated transmission among the sexually active age groups was also present, but less pronounced, in Burundi (Fig. 2a; right).

Linking clade I transmission patterns and outbreak potential

Our models allowed us to project the time-evolving effective reproduction numbers (R_y) of MPXV clades Ia and Ib (Fig. 2b). We constructed R_y to reflect the transmission potential in a hypothetical pre-outbreak state (that is, accounting for immunity from the historical smallpox immunization, but not from infections or mpox vaccination), to focus on the effect of a changing smallpox immunity landscape associated with demographic shift. The projection suggested a 9.8% increase in R_y of clade Ia over the past decade in the DRC, reflecting the ageing of the smallpox-immunized cohorts. When assuming an R_y of 0.82 for clade Ia in the DRC in 2015[15], this increase translates into an R_y of 0.90 in 2024, which aligns with our estimates from the pre-Ib mpox incidence data in the DRC (Supplementary Fig. 2). As R_y gradually approaches 1, the expected final size of an outbreak initiated by a single zoonotic infection, given as $1/(1-R_y)$[33], would increase from 5.6 in 2015 to 10.0 in 2024, which may also explain the recent rise in clade Ia cases in the endemic areas in the DRC[34].

If the same community contact transmission patterns estimated for clade Ia also apply to clade Ib, the overall R_y in the Kivus, combining both community and sexual contact routes, would be around 1.5 in our projection. This is similar to our estimate of the initial reproduction number from suspected clade Ib cases in South Kivu (Supplementary Fig. 2). The increase in R_y attributable to sexual contact, resulting in an overshoot of the epidemic threshold of 1, could explain the stable exponential growth of clade Ib cases observed in the Kivus over the summer of 2024. In Burundi, our model projected that R_y for clade Ia would be 4% higher than in the DRC in 2024, reflecting a slightly different population age distribution. With an additional sexual contact transmission route, R_y for clade Ib in Burundi may have also exceeded the epidemic threshold of 1 (with a point estimate of 1.08), which explains the major spread of clade Ib in Burundi, observed the earliest among the countries neighbouring the DRC.

Focused and mass vaccination strategies

Using the Kivus as a case study, we compared the possible impact of FSW-focused and mass vaccination strategies (Fig. 2c). Given the age eligibility for vaccines (18 years and above for JYNNEOS[35]) and the previously smallpox-immunized cohort, we considered adults aged 20–39 years as the primary group for mass vaccination—our results also suggested that this group is more likely to contribute to onward transmission in the Kivus (Fig. 2a). Under current global vaccine shortages, prioritizing FSWs, typically accounting for <1% of the total population[36], may allow for the efficient use of available supply. In the Kivus, where sexual contact was estimated to play a substantial role in the overall dynamics, achieving high vaccine uptake among FSWs would reduce the doses required among general adults for control (Fig. 2c). Realistically, both strategies may be pursued in tandem, considering uncertainty and a possible shift in the relative role of sexual and community contact transmission, as well as challenges in approaching FSWs facing social barriers and stigma[37]. Regardless of the vaccine target population, clear and supportive communication and de-stigmatization are essential[38]. Existing community support networks for FSWs and other populations at risk, including human immunodeficiency virus and acquired immune deficiency syndrome programmes, could play a key role in public health outreach[38,39].

Discussion

This study quantified the role of community and sexual contacts in MPXV clade I outbreaks. The results suggest that past and current clade Ia outbreaks are primarily driven by community contacts, whereas clade Ib is additionally transmitted through contacts among individuals with high sexual activity, such as FSWs and their clients. This additional transmission route may be responsible for the increased effective reproduction number of clade Ib in the Kivus compared with clade Ia in other endemic regions. The estimated relative contribution of sexual contact was particularly pronounced in the Kamituga health zone and less so elsewhere, suggesting that the epidemiology of clade Ib in the Kivus in 2024 may be largely attributable to sexual contact patterns specific to Kamituga, and that generalizability to other settings should be explored in conjunction with the local sociobehavioural contexts. Our results also suggest that, with the ageing of smallpox-immunized cohorts over decades, the reproduction number of MPXV clade I has already been approaching the epidemic threshold of 1, even without additional involvement of sexual contact. In this regard, a small increment in transmission pathways, including but not limited to sexual contact, may sustain a clade I outbreak, particularly in countries with lower historical vaccine coverage.

The current MPXV clade Ib outbreak has exhibited an epidemiological pattern that is distinct from past clade Ia outbreaks, characterized as more rapid spread involving a novel mode of human-to-human transmission through sexual contact. A similar sudden emergence of sustained human-to-human transmission was the nature of the global clade IIb outbreak in 2022 onwards, which was primarily (if not exclusively) transmitted through sexual contacts among MSM[40]. Our previous modelling work offered a plausible explanation for this

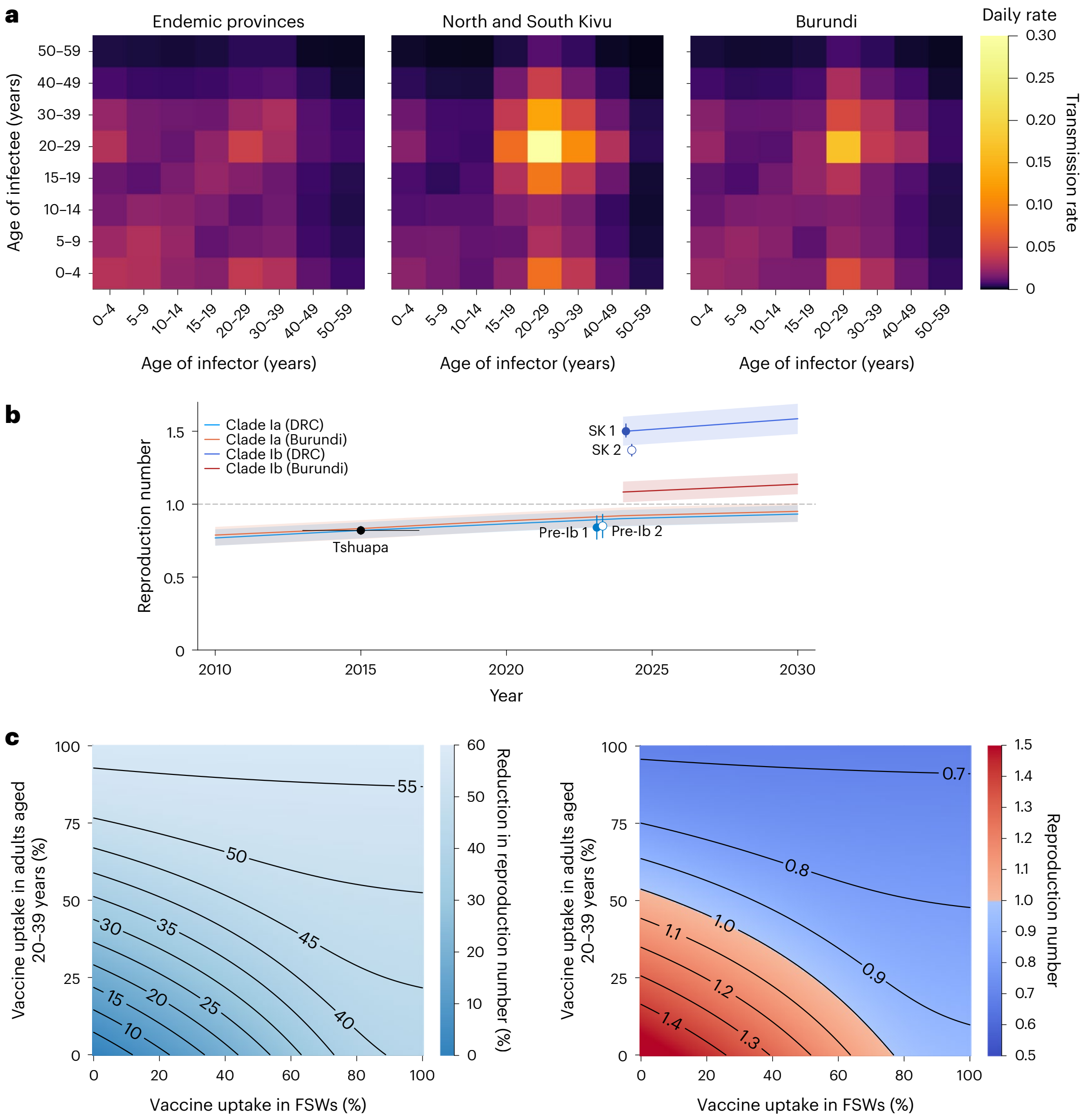

Fig. 2 | Transmission dynamics of MPXV clade I outbreaks. **a**, Age-specific transmission patterns inferred for clade Ia in endemic provinces of the DRC and clade Ib in North and South Kivu and Burundi. The colours represent daily transmission rates between infector–infectee pairs in given age groups according to the estimated next-generation matrices. **b**, Projected time-evolving effective reproduction numbers (R_y) for clades Ia and Ib in the DRC (blue lines) and Burundi (red lines) from 2010 to 2030. The lines and shaded areas represent median estimates and 95% credible intervals of R_y, respectively. The estimated reproduction number of 0.82 (95% confidence interval = 0.79–0.85) from the clade Ia case data between 2013 and 2017 in Tshuapa province in the DRC[15] was used as a reference value for 2015 (the midpoint of the study period), denoted by horizontal whiskers. The empirical estimates of the effective reproduction number from the DRC incidence data in the pre-clade Ib period in 2023 (pre-Ib) and from the South Kivu incidence data (SK) in 2024, as proxy data for clades Ia and Ib, respectively, are displayed as dots (medians and 95% credible intervals) for comparison. Paired dots (jittered horizontally for visual aid) denote the different serial interval distributions used, which were estimated elsewhere from two separate sets of infector–infectee pairs (distribution 1: mean = 17.5 days; distribution 2: mean = 11.4 days)[77]. The dashed horizontal line denotes the epidemic threshold value of 1. **c**, Contour plots for the estimated impact (percentage reduction in reproduction number (left) and reproduction number (right)) of different combinations of FSW-focused and mass vaccination strategies on the effective reproduction number in the Kivus. Note that the axes represent very different scales in the absolute number of doses, reflecting population sizes for FSWs and general adults.

transition that clade IIb had established itself in a densely connected portion of the MSM sexual network, allowing for the rapid spread that was not sustained elsewhere[20]. Likewise, the emergence of clade Ib may be another example of MPXV's entry into a key population group where it can sustain itself. Although extensive transmission among FSWs and their clients was not specifically reported in the clade IIb global outbreak, sexual transmission of clade II involving FSWs had already been reported from 2017[41], and the potential risk has been discussed since the initial phase of the global outbreak[42,43]. It remains unclear whether only clade Ib is able to be readily transmitted within FSW-related networks, or if it was just the first to have an opportunity among the clades with similar potential. Recent studies on co-circulating clades Ia and Ib in Kinshasa, DRC[44] and on the clade IIb outbreak in Sierra Leone[45] both report over-representation of sexually active age groups of both sexes among cases, as was typically observed in clade Ib outbreaks, although without direct evidence of transmission through sexual contacts. Further investigation is warranted to assess and monitor the potential shift in the role of sexual contacts in broader mpox outbreak settings. Regardless, investigation and control efforts for mpox continue to require a tailored and inclusive approach, with a particular focus on the most vulnerable groups, including children, MSM, FSWs and other key populations at risk for sexually transmitted infections[46,47].

This study holds several limitations. First, we assumed that contact survey data sufficiently represented community contacts relevant to MPXV transmission. Some forms of transmission, including fomite or nosocomial routes, may not be fully captured by existing contact data from population samples. Contact matrices also represent the mean contact rates between age groups and neglect possible heterogeneity beyond this. However, we believe our eigenvector approach with hold-out validation (Supplementary Fig. 1c,e) helped to ensure robustness. We used the empirical contact data from a different country (Zimbabwe) as a proxy, since empirical contact data were not available from the DRC or Burundi. Nevertheless, the model using Zimbabwe contact data outperformed the model using a synthetic contact matrix for the DRC (Extended Data Table 2 and Supplementary Fig. 1), and our findings remain overall consistent between these models (Supplementary Fig. 6).

Second, our model of the sexual contact route for clade Ib was simplistic due to limited sexual behaviour data; for example, proportionate mixing with age-invariant contact rates. However, the estimated relative contributions of the community and sexual contact routes—the primary interest of this study—would be relatively robust to these assumptions as long as our model can capture the excess in mixing patterns attributable to sexual contacts (Supplementary Fig. 7). We assumed that sexual contacts outside of the high-activity groups were captured by contact survey data and had limited contributions to the difference in dynamics between clades Ia and Ib. Despite our sensitivity analyses, additional data on local sexual behaviours, including the detailed distribution of sexual engagement rates in FSWs and their clients, could further inform the analysis. We also limited our analysis to heterosexual contacts and did not consider MSM networks. The reported clade Ib case profile with near-even sex balance as of the time of analysis (Supplementary Table 1) does not suggest pronounced transmission within the MSM group[48], and our additional analysis also suggests that infection- or vaccine-derived immunity in this group may lower the risk of sustained clade Ib transmission in populations previously affected by the global clade IIb outbreak (Supplementary Fig. 9). However, this does not exclude the future possibility of clade Ib outbreaks among MSM; for example, in countries without previous clade IIb circulation (including the DRC and Burundi[49]) or after herd immunity is lost[50].

Third, our model primarily focused on a few epidemiological variables (age, sex and sexual activity) as key population attributes; other potential risk factors, including malnutrition[51], co-infection with other sexually transmitted infections (particularly human immunodeficiency virus[52]) and living conditions, were not explicitly considered. Although some of these factors may be indirectly accounted for by the modelled components, such as age-dependent susceptibility and sexual or community contact matrices, future studies are required to better characterize the role of those risk factors in mpox outbreaks. Biological factors have not been considered either, including possible viral adaptation that might breach our assumption of the same community transmission patterns between clades Ia and Ib. Although our model suggested that the increase in the estimated reproduction number for clade Ib can be explained without requiring evolutionary changes, this does not necessarily exclude their potential role in the clade Ib dynamics.

Finally, case data used for the analysis may have been subject to uncertainty and biases due to challenges in healthcare access, testing or reporting in an outbreak, especially when coinciding with civil conflict and natural disasters[53,54]. Differential case ascertainment between age groups (for example, reflecting child healthcare policies[55]) could lead to biases. Most importantly, the potential under-reporting of cases among FSWs, who are facing criminalization and stigma[56], may have resulted in an underestimation of the relative contribution of sexual contacts to the clade Ib dynamics. Our estimation of the effective reproduction number from incidence data may also have been affected by time-varying ascertainment or spatially aggregated data[57] (particularly for clade Ia in 2024, estimated from national-level data).

Methods

Data sources

We used the numbers of confirmed mpox cases by age and sex in both historical and current outbreaks from public sources[7,26,58,59]. We used reported cases from 1 January to 18 August 2024 for the current outbreak in the DRC for its stable growth trend and data availability at the sub-provincial level (Kamituga and other health zones of South Kivu) during that period. For Burundi, which only reported cases from late July 2024 onwards, we used case data from 16 September to 27 October, roughly corresponding to the second half of the stable growth phase until its peak, to exclude potential influences of reporting bias or initial transients. Further details of the datasets are available in Extended Data Table 1. Weekly incidence data for the DRC and South Kivu were collected from public reports[17,18,60]. Empirical contact survey data from Manicaland, Zimbabwe[24] were retrieved via the socialmixr R package[61]. Population age distributions in the DRC, Burundi and Manicaland from relevant years were collected from censuses (where available)[62,63] and *World Population Prospects 2024*[64]. We also used synthetic contact matrix data published by Prem et al.[65].

Model structure

We assumed that the observed number of mpox cases by age or by age and sex follows a multinomial distribution with probabilities proportional to the elements of the dominant eigenvector of the next-generation matrix.

$$\mathbf{i} \sim \text{Multinom}\left(\sum \mathbf{i}, \upsilon(K)\right) \tag{1}$$

where $\upsilon(K)$ is the normalized dominant eigenvector of the next-generation matrix K. We constructed the next-generation matrix as a product of transmissibility, β, age-dependent relative susceptibility, σ_a, and a contact matrix, C. We used age-disaggregated case data and contact matrices for the analysis of clade Ia (that is, $C = \{c_{ab}\}$), where c_{ab} represents the mean number of community contacts (conversational and/or physical, depending on the type of contact matrix used) an individual from age group b has per unit time with those from age group a. We used multiple contact matrices potentially relevant to mpox transmission (Extended Data Table 2). For each contact matrix, β was adjusted so that the dominant eigenvector of the next-generation matrix estimated for the historical Tshuapa dataset was equal to the previously estimated reproduction number of 0.82 (ref. 15).

For the analysis of clade Ib, we used age- and sex-disaggregated case data and expanded the contact matrix to account for heterosexual transmission dynamics in addition to community contacts. We stratified male and female populations into groups with high and low sexual activity. Following the approach described by Endo et al.[20], we further stratified cases in the high-activity groups by their route of exposure (community- versus sexually associated exposures) and allowed sexually acquired cases to have higher risks of onward sexual transmission because of a substantial variance in sexual behaviour[66]. Namely, in a highly heterogeneous sexual network, transmissions through sexual contact tend to concentrate among individuals with the highest rates of sexual activity; this renders sexual exposure an indicator of even higher contact rates than the average among the high-activity groups. We assumed that this variance effect is negligible among low-activity groups (such that stratification by exposure route can be disregarded) and that their sexual contacts are reflected in the existing contact matrices, whose definition of contacts includes sexual contacts. Despite its simplicity, our approach of stratifying sexual contacts by two activity classes and two exposure routes could well capture the stationary growth pattern of mpox transmission (see Supplementary Tables 2 and 3 and Supplementary Figs. 10–12 for a proof-of-concept network model).

Let subscripts H and L denote high- and low-activity groups and M/m and F/f represent male and female cases with sexual (upper case) and community exposures (lower case), respectively. Vectors $\mathbf{i}_\text{X}$

represent the age-stratified number of mpox infections in category X. The generation-wise reproduction process of $\mathbf{i}_{\mathrm{X}}$ is then described in a block matrix format (with each block an 8-by-8 matrix accounting for age group stratification) as:

$$\begin{bmatrix} \mathbf{i}^{t+1}_{\mathrm{M_H}} \\ \mathbf{i}^{t+1}_{\mathrm{m_H}} \\ \mathbf{i}^{t+1}_{\mathrm{m_L}} \\ \mathbf{i}^{t+1}_{\mathrm{F_H}} \\ \mathbf{i}^{t+1}_{\mathrm{f_H}} \\ \mathbf{i}^{t+1}_{\mathrm{f_L}} \end{bmatrix} = B_\sigma \begin{bmatrix} O & O & O & S_{\mathrm{MF}} & \Sigma_{\mathrm{MF}} & O \\ PC_{\mathrm{MM}} & PC_{\mathrm{MM}} & PC_{\mathrm{MM}} & PC_{\mathrm{MF}} & PC_{\mathrm{MF}} & PC_{\mathrm{MF}} \\ (I-P)\,C_{\mathrm{MM}} & (I-P)\,C_{\mathrm{MM}} & (I-P)\,C_{\mathrm{MM}} & (I-P)\,C_{\mathrm{MF}} & (I-P)\,C_{\mathrm{MF}} & (I-P)\,C_{\mathrm{MF}} \\ S_{\mathrm{FM}} & \Sigma_{\mathrm{FM}} & O & O & O & O \\ QC_{\mathrm{FM}} & QC_{\mathrm{FM}} & QC_{\mathrm{FM}} & QC_{\mathrm{FF}} & QC_{\mathrm{FF}} & QC_{\mathrm{FF}} \\ (I-Q)\,C_{\mathrm{FM}} & (I-Q)\,C_{\mathrm{FM}} & (I-Q)\,C_{\mathrm{FM}} & (I-Q)\,C_{\mathrm{FF}} & (I-Q)\,C_{\mathrm{FF}} & (I-Q)\,C_{\mathrm{FF}} \end{bmatrix} \begin{bmatrix} \mathbf{i}^{t}_{\mathrm{M_H}} \\ \mathbf{i}^{t}_{\mathrm{m_H}} \\ \mathbf{i}^{t}_{\mathrm{m_L}} \\ \mathbf{i}^{t}_{\mathrm{F_H}} \\ \mathbf{i}^{t}_{\mathrm{f_H}} \\ \mathbf{i}^{t}_{\mathrm{f_L}} \end{bmatrix} \qquad (2)$$

where O and I are zero and unit matrices, respectively. S_{MF} and S_{FM} are block contact matrices representing heterosexual transmission from sexually acquired high-activity individuals. Similarly, Σ_{MF} and Σ_{FM} represent community-acquired transmission from high-activity heterosexual individuals. Again, note that we expect S_{X} to be larger than Σ_{X} because sexually acquired cases are more likely to have more sexual partners than the population average. $P = (p_a)$ and $Q = (q_a)$ are diagonal matrices representing the age-dependent proportions of high-activity individuals for males and females, respectively. C_{X} is a sex-specific contact matrix and is assumed to be half of the sex-aggregated contact matrix hereafter for simplicity. We define B_σ as a diagonal block matrix whose diagonal blocks are an 8-by-8 diagonal matrix of the age-specific susceptibility σ_a multiplied by transmissibility β.

Noting that for $t \geq 1$, $\mathbf{i}_{\mathrm{m_H}} = P(\mathbf{i}_{\mathrm{m_H}} + \mathbf{i}_{\mathrm{m_L}})$ and $\mathbf{i}_{\mathrm{f_H}} = Q(\mathbf{i}_{\mathrm{f_H}} + \mathbf{i}_{\mathrm{f_L}})$, the above relationship can be simplified into

$$\begin{bmatrix} \mathbf{i}^{t+1}_{\mathrm{M_H}} \\ \mathbf{i}^{t+1}_{\mathrm{m}} \\ \mathbf{i}^{t+1}_{\mathrm{F_H}} \\ \mathbf{i}^{t+1}_{\mathrm{f}} \end{bmatrix} = B_\sigma \begin{bmatrix} O & O & S_{\mathrm{MF}} & \Sigma_{\mathrm{MF}}Q \\ C_{\mathrm{MM}} & C_{\mathrm{MM}} & C_{\mathrm{MF}} & C_{\mathrm{MF}} \\ S_{\mathrm{FM}} & \Sigma_{\mathrm{FM}}P & O & O \\ C_{\mathrm{FM}} & C_{\mathrm{FM}} & C_{\mathrm{FF}} & C_{\mathrm{FF}} \end{bmatrix} \begin{bmatrix} \mathbf{i}^{t}_{\mathrm{M_H}} \\ \mathbf{i}^{t}_{\mathrm{m}} \\ \mathbf{i}^{t}_{\mathrm{F_H}} \\ \mathbf{i}^{t}_{\mathrm{f}} \end{bmatrix} \qquad (3)$$

where $\mathbf{i}_{\mathrm{m}} = \mathbf{i}_{\mathrm{m_H}} + \mathbf{i}_{\mathrm{m_L}}$ and $\mathbf{i}_{\mathrm{f}} = \mathbf{i}_{\mathrm{f_H}} + \mathbf{i}_{\mathrm{f_L}}$.

We assumed proportionate mixing to model $S_{\mathrm{MF}}, S_{\mathrm{FM}}, \Sigma_{\mathrm{MF}}$ and Σ_{FM}; further details on parameterization are described in the next section.

We constructed a multinomial likelihood for the observed number of male and female cases by age group:

$$\mathbf{i} \sim \mathrm{Multinom}\left(\sum \mathbf{i}, \left[\mathbf{i}_{\mathrm{M_H}} + \mathbf{i}_{\mathrm{m}}; \mathbf{i}_{\mathrm{F_H}} + \mathbf{i}_{\mathrm{f}}\right]\right) \qquad (4)$$

where $[\mathbf{i}_{\mathrm{M_H}} + \mathbf{i}_{\mathrm{m}}; \mathbf{i}_{\mathrm{F_H}} + \mathbf{i}_{\mathrm{f}}]$ is a vector obtained by sex-wise aggregation of the normalized dominant eigenvector of the next-generation matrix in equation (3).

Model fitting

Our model fitting process was twofold. We first fitted and validated the model of community contact transmission using the age distributions of cases from the historical and current clade Ia outbreaks in the DRC. We used this model to estimate age-dependent susceptibility parameters σ_a for the community contact matrix. We then constructed an expanded contact matrix including sexual contacts and calibrated it to the age–sex distributions of cases from clade Ib outbreaks in the DRC and Burundi to estimate additional parameters that describe transmission dynamics of clade Ib through community and sexual contact routes. All of the parameters used in the model are summarized in Extended Data Table 3.

Analysis of clade Ia outbreaks. As in the 'Model structure', we defined the next-generation matrix $K = \{k_{ab}\} = \beta\sigma_a c_{ab}$. The contact matrix c_{ab} was constructed from existing datasets (Extended Data Table 2), with adjustment for age structures between the source and modelled populations where different (using the density correction method described by Arregui et al.[67]). Based on data availability, we used six age groups (0–4, 5–9, 10–19, 20–29, 30–39 and 40+ years) for the 2011–2015 Tshuapa data and eight age groups (0–4, 5–9, 10–14, 15–19, 20–29, 30–39, 40–49 and 50+ years) for the 2024 DRC endemic provinces data. When the age groups in the case data were coarser than the contact matrix, the elements were merged accordingly[68]. Transmissibility β is a nuisance scaling parameter and was not estimated. We assumed that children aged 0–4 years may have potentially higher susceptibility to infection and that adults born before cessation of the smallpox vaccine in 1980[11] may have lower susceptibility. To account for this, we parameterized σ_a as

$$\sigma_a = \begin{cases} \sigma_0 & \text{(aged 0 – 4 years)} \\ 1-\varepsilon & \text{(smallpox immunized)} \\ 1 & \text{(otherwise)} \end{cases} \qquad (5)$$

Here, ε represents the net vaccine protection among the vaccinated cohorts (that is, the product of the vaccine effectiveness and coverage in the historical campaign, also referred to as the effective vaccine coverage). The susceptibility for the age group that contains both vaccinated and unvaccinated cohorts (ages 30–39 years in the historical Tshuapa dataset and ages 40–49 years in the 2024 outbreak datasets) was specified as the weighted average between $1-\varepsilon$ and 1, based on the proportion of individuals born in or before 1980 in those age groups[64] as of 2013 (the midpoint of the Tshuapa dataset period) or 2024. Given the high historical vaccination coverage in the DRC (89–97%)[29], the estimated vaccine protection ε would provide an approximation (or at least a reasonable lower bound) for the effectiveness against clade I mpox. We estimated σ_0 and ε using the Bayesian importance sampling method[69], based on the multinomial likelihood in equation (1), and obtained median estimates and 95% credible intervals.

Exploratory model development was done using the historical Tshuapa dataset. The resulting model, described above, was then validated using the 2024 DRC endemic provinces dataset. We estimated two parameters, σ_0 and ε, from the historical Tshuapa dataset alone and compared the model outputs (after accounting for a decade's shift in the age of the vaccinated cohort) with the age distribution from the (hold-out) 2024 DRC endemic provinces dataset (Supplementary Fig. 1). The model outputs showed good overall concordance with the validation data. We obtained final parameter estimates from the joint estimation using both datasets for the subsequent analyses.

Analysis of clade Ib outbreaks. We parameterized the block components representing sexual contacts among high-activity individuals $\Sigma_{\mathrm{MF}}, \Sigma_{\mathrm{FM}}, S_{\mathrm{MF}}$ and S_{FM} in equation (3) as follows. We assumed that the age groups 15–19, 20–29, 30–39 and 40–49 years potentially contain high-activity populations (that is, $p_a = q_a = 0$ outside these age groups). We assumed a simple proportionate mixing assumption (that is, no age assortativity) where each high-activity individual makes sexual contacts at a specified rate over the infectious period of MPXV, which are randomly assigned to other high-activity individuals of the opposite sex, irrespective of age. We denote the mean sexual contact rates among high-activity females and males infected through community contact as υ_F and υ_M; similarly, we denote the mean sexual contact rates among those infected through sexual contact as w_F and w_M. Note that υ_F, υ_M, w_F and w_M are defined to have the same scale as the community contact matrix in relation to onward transmission (that is, one unit of υ_F, υ_M, w_F or w_M represents the amount of sexual contact that contributes to the transmission equivalent of one daily community contact). The entries of Σ_MF, Σ_FM, S_MF and S_FM are then modelled as:

$$\begin{aligned}(\Sigma_\mathrm{MF})_{ab} &= \upsilon_\mathrm{F}\frac{n_a p_a}{\sum_a n_a p_a}\\ (\Sigma_\mathrm{FM})_{ab} &= \upsilon_\mathrm{M}\frac{m_a q_a}{\sum_a m_a q_a}\\ (S_\mathrm{MF})_{ab} &= w_\mathrm{F}\frac{n_a p_a}{\sum_a n_a p_a}\\ (S_\mathrm{FM})_{ab} &= w_\mathrm{M}\frac{m_a q_a}{\sum_a m_a q_a}\end{aligned} \tag{6}$$

where n_a and m_a are the relative population sizes for males and females by age group (we assumed even sex distribution[70,71]; that is, $\sum_a n_a = \sum_a m_a = 1/2$). Note that S_X and Σ_X are proportional, with a ratio of w_X:υ_X. We assumed that infection through community contact has no association with one's sexual contact rate (that is, υ_F and υ_M represent the mean sexual contact rates among the high-activity groups). Reciprocity of heterosexual contacts then requires:

$$\upsilon_\mathrm{F}\sum_a m_a q_a = \upsilon_\mathrm{M}\sum_a n_a p_a \tag{7}$$

We estimated the ratio between w_F and υ_F assuming that the sexual network among high-activity groups is represented by a configuration network (that is, no degree assortativity; an alternative scenario is discussed in Supplementary Fig. 7), in which υ_X corresponds to the mean degree and w_X to the mean neighbour degree (or degree-weighted average of degree)[30]. We assumed that FSWs represent the behaviour of the majority of high-activity female individuals and used FSW survey data from the DRC[72]. Since both the mean degree and mean neighbour degree can be characterized by the mean μ and standard deviation, σ, of the sexual contact degree distribution, $\pi(x)$, their ratio is estimated as:

$$\frac{w_\mathrm{F}}{\upsilon_\mathrm{F}} = \frac{\int_0^\infty x^2\pi(x)\,\mathrm{d}x}{\left(\int_0^\infty x\pi(x)\,\mathrm{d}x\right)^2} = 1 + \frac{\sigma^2}{\mu^2} \tag{8}$$

We used the reported mean and s.d. for the weekly number of clients (mean = 17.61; s.d. = 12.0) and non-paying partners (mean = 5.51; s.d. = 22.0) per FSW[72] to derive $w_\mathrm{F}/\upsilon_\mathrm{F} = 2.17$. Here we assumed that the numbers of clients and non-paying partners are uncorrelated (an alternative scenario is discussed in Supplementary Fig. 7); the sexual contact degree as a sum of these two numbers would then have a mean of 17.61 + 5.51 = 23.12 and a variance of $12.0^2 + 22.0^2 = 628$, which were supplied to equation (8). This and the reciprocity requirement in equation (7) assure that υ_M and υ_F are derived from w_F, $\{p_a\}$ and $\{q_a\}$. We also set boundary conditions for the total number of high-activity individuals (that is, $\sum_a n_a p_a$ and $\sum_a m_a q_a$). Namely, we assumed that high-activity males account for 10% of the male population among the sexually active age groups and high-activity females account for 1% of the total female population (translated into ~2.2% among the sexually active age groups), based on engagement data on commercial sex in Africa (the proportion reporting paid sex in the past 12 months among males aged 15–59 years in Mozambique[73] and the estimated number of FSWs per capita in the DRC[36]).

Assuming the community transmission patterns are similar between clades Ia and Ib, we used the same σ_a estimated for clade Ia throughout the clade Ib analysis. This implicitly assumes uniform smallpox vaccine coverage across geographical settings (see Supplementary Fig. 7 for a sensitivity analysis). The rest of the parameters, $\{p_a\}$, $\{q_a\}$, w_F and w_M, were estimated using the Markov chain Monte Carlo method (No-U-Turn Sampler[74]). We obtained 2,000 Markov chain Monte Carlo samples while ensuring an effective sample size of at least 500 for every parameter; most parameters achieved an effective sample size of ~1,000 or larger. Using these posterior samples, we estimated the proportion of R_eff attributable to sexual transmission as a measure of the relative contribution of sexual contacts to mpox transmission. We defined it as the relative reduction in the effective reproduction number (R_eff) by excluding sexual contacts from the next-generation matrix. Namely, this proportion was given as $1 - \lambda_\mathrm{C}/\lambda_\mathrm{SC}$, where λ_SC and λ_C are the dominant eigenvalues of the next-generation matrix (equation (3)) with and without the sexual contact blocks (S_X and Σ_X), respectively.

Model averaging and outputs

We used model averaging over candidate models using different contact matrix data (Extended Data Table 2) with Watanabe–Akaike weights[75] based on the combined likelihood for datasets 2, 3 and 4 in Extended Data Table 1. We did not include the likelihood for sub-provincial datasets (datasets 5 and 6) or Burundi (dataset 7) in the weights for the main analysis due to overlapping cases and potentially different data collection and contexts, respectively. Alternatively, weights also using these likelihoods were included in our sensitivity analysis (see Supplementary Fig. 7). Models 5 and 6 using synthetic contact matrices had substantially worse likelihood than other models, resulting in effectively zero weights, and were therefore not included in the main analysis.

Frequency of transmission between age groups. We estimated the relative frequency of infector–infectee age pairs at equilibrium using the next-generation matrix and normalized dominant eigenvector:

$$M = B_\sigma \begin{bmatrix} O & O & S_\mathrm{MF} & \Sigma_\mathrm{MF}Q \\ C_\mathrm{MM} & C_\mathrm{MM} & C_\mathrm{MF} & C_\mathrm{MF} \\ S_\mathrm{FM} & \Sigma_\mathrm{FM}P & O & O \\ C_\mathrm{FM} & C_\mathrm{FM} & C_\mathrm{FF} & C_\mathrm{FF} \end{bmatrix} \mathrm{diag}\left[\begin{bmatrix} \mathbf{i}^t_{\mathrm{M_H}} \\ \mathbf{i}^t_\mathrm{m} \\ \mathbf{i}^t_{\mathrm{F_H}} \\ \mathbf{i}^t_\mathrm{f} \end{bmatrix}\right] \tag{9}$$

We then aggregated the block elements of M to obtain a sex- and transmission-route-aggregated frequency matrix.

Projection of time evolution of the reproduction numbers. We projected the effective reproduction number (R_y) of mpox in the DRC and Burundi by shifting the age of the smallpox-immunized cohorts and modifying the contact matrices[67] according to the population projection[64]. Referring to the previous estimate[15], we assumed that the effective reproduction number of clade Ia in the Tshuapa province was 0.82 (95% confidence interval = 0.79–0.85) in 2015 (the midpoint of the estimation period 2013–2017). We then projected the effective reproduction number for clade Ia between 2010 and 2030 as the dominant eigenvalue of the next-generation matrix for each year, accounting for the following two factors. First, the relative susceptibility of age groups that include the immunized cohorts was adjusted according to the estimated net protection, ε (model averaging weights from Table 1), and the proportion of immunized cohorts (those born in or before 1980, per the population projection[64]) within the age groups. Second, the community contact matrices were also adjusted to the projected population age distribution using the density correction method[67]. For clade Ib, we projected the effective reproduction number in 2024 onward assuming that patterns of community contact transmission are shared between clades Ia and Ib. Namely, the R_y for clade Ib was projected by incorporating the additional sexual contact contributions described in equation (3) (estimated for the Kivus and Burundi) into the projected next-generation matrices for clade Ia, assuming time-invariant sexual contact patterns. Here we assumed a hypothetical pre-outbreak state and neglected potential infection- or mpox-vaccination-derived immunity, as well as any future interventions. To yield an uncertainty range for these projections, we considered uncertainty in the reference estimate[15] (both the confidence interval and the estimation period being for 2013–2017 instead of the midpoint, assuming normally and uniformly distributed errors, respectively) in addition to the uncertainty in our parameter estimation.

Effective reproduction numbers under focused and mass vaccination scenarios. We modelled the change in the effective reproduction number of clade Ib under a combination of FSW-focused and mass vaccination scenarios. We used an mpox vaccine effectiveness estimate of 86%[76], which we assumed to protect against infection but not against onward transmission in the case of breakthrough infections. FSW-focused vaccination was assumed to be offered to female high-activity individuals of 20–39 years of age. For mass vaccination, all individuals aged 20–39 years, regardless of sexual activity level, were included. The baseline effective reproduction numbers without vaccines were matched to the projected values reflecting the ageing of the smallpox-immunized cohorts for each population setting.

Ethics and inclusion

This study used publicly available data only and did not require ethics approval. Per the Global Code of Conduct for Equitable Research Partnerships, local researchers were included in the study design, study implementation, data ownership and authorship of publications. The local relevance of the research has been discussed with and guided by local researchers.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

All of the data supporting the results of this study are publicly available. The data files used for analysis are available from the GitHub repository at https://github.com/akira-endo/mpoxclade1_eigen.

Code availability

All analyses were conducted using Julia (version 1.9.3) and R (version 4.3.1). Source codes are available from the GitHub repository at https://github.com/akira-endo/mpoxclade1_eigen.

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Author contributions

A.E. conceived of the article idea. H.M., T.R.A., K.P. and A.E. developed the methodology. H.M., T.R.A, D.B. and A.E. performed the investigation, visualized the data and wrote the original draft of the manuscript. T.R.A., J.H.F., S.J., K.P. and A.E. curated the data. A.E. and A.N. acquired funding. B.L.D., D.B., J.H.F., S.J., P.K.M., K.E., S.-m.J., A.N., K.P., A.M.W., D.S.-N. and D.N. reviewed and edited the paper.

Competing interests

The authors declare no competing interests.

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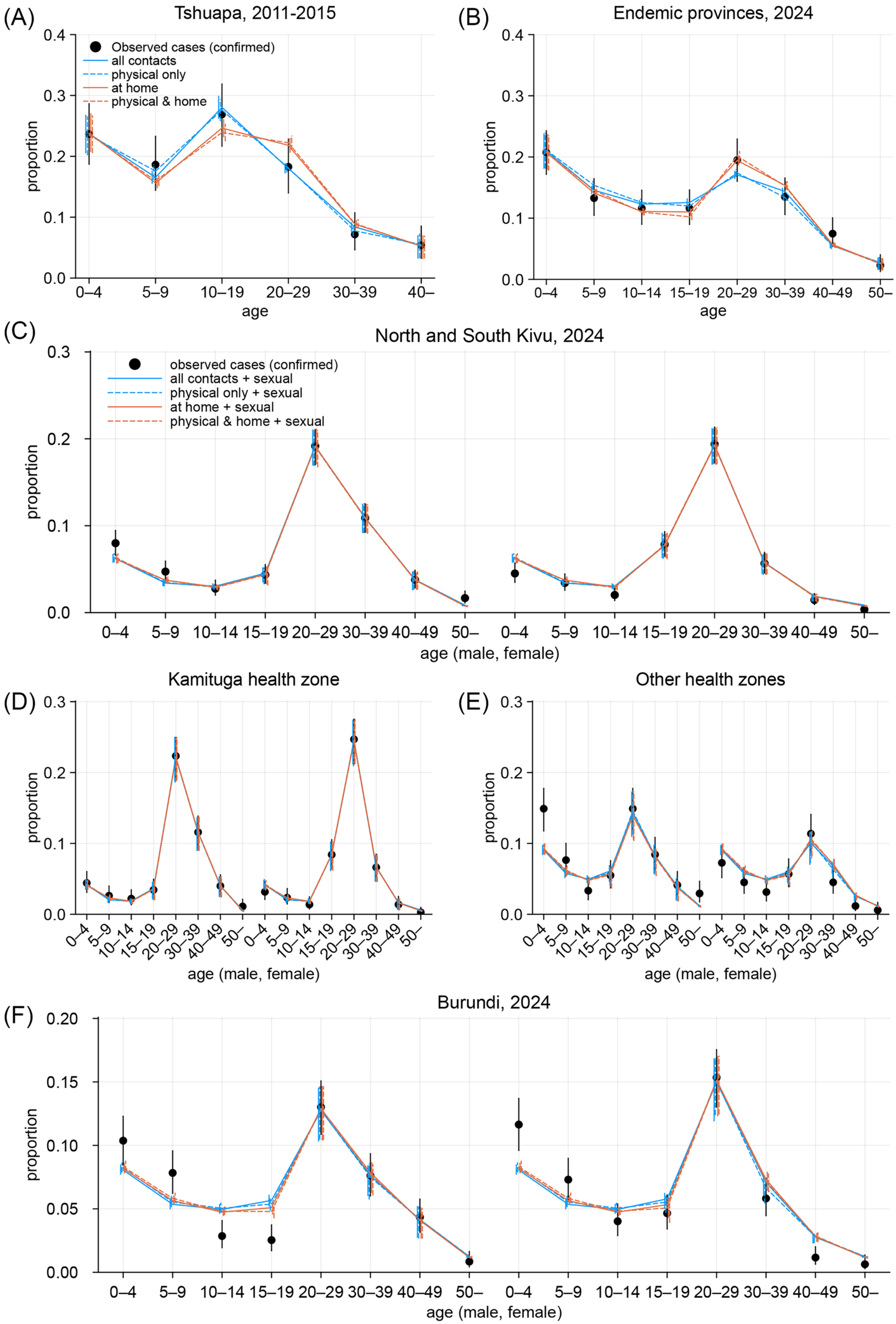

Extended Data Fig. 1 | See next page for caption.

Extended Data Fig. 1 | Observed and modelled age distributions of mpox cases with uncertainty ranges. **a**, Clade Ia cases with suspected human-to-human exposure from the Tshuapa province of the DRC from 2011–2015 (*n* = 279 cases). Those aged 34 years and older were assumed to be smallpox immunized. **b**, Cases from clade Ia-endemic provinces in the DRC from January to mid-August 2024 (*n* = 482). Those aged 45 years and older were assumed to be immunized. **c**–**f**, Clade Ib cases from multiple settings in the DRC (North and South Kivu (**c**), the Kamituga health zone (**d**), other health zones (**e**)) from January to mid-August 2024 (*n* = 1,377, 725 and 510, respectively) and Burundi from mid-September to October 2024 (**f**; *n* = 945). Those aged 45 years and older were assumed to be immunized. Black dots and whiskers represent the observed age distributions among cases and their 95% confidence intervals. Coloured whiskers represent the 95% credible intervals for the modelled age distributions (horizontally offset for visual aid).

Extended Data Table 1 | MPXV clade I outbreak datasets

ID	Location	Year	Clade	Exposure type	N	Reference
1	Tshuapa province, DRC	2011-2015	Ia	Zoonotic[*]	308	[26]
2	Tshuapa province, DRC	2011-2015	Ia	Human-to-human[**]	279	[26]
3	Six endemic provinces[***], DRC	2024[†]	Ia	Not classified	482	[58]
4	North and South Kivu provinces, DRC[††]	2024[†]	Ib	Not classified	1,377	[58]
5	Kamituga health zone, South Kivu[††]	2024[†]	Ib	Not classified	725	[58]
6	Other health zones, South Kivu[††]	2024[†]	Ib	Not classified	510	[58]
7	Burundi	2024[†††]	Ib	Not classified	945	[7,59]

[*] Defined by reporting only exposure to an animal within 3 weeks before onset. [**] Defined by reporting only exposure to a human with a rash illness only within 3 weeks before onset. [***] Equateur, South and North Ubangi, Sankuru, Tshopo and Tshuapa. [†] As of 18 August 2024. [††] North and South Kivu province data also contain cases in Kamituga and other health zones of South Kivu. [†††] 16 September–27 October 2024.

Extended Data Table 2 | Community contact matrices used for analysis

ID	Contact type	Contact setting	Data type	Country	Reference	Hold-out validation loss*	Hold-out empirical KLD**
1	All	All	Empirical	Zimbabwe	[24]	47.23	0.009
2	Physical only	All	Empirical	Zimbabwe	[24]	47.18	0.009
3	All	Home	Empirical	Zimbabwe	[24]	44.37	0.006
4	Physical only	Home	Empirical	Zimbabwe	[24]	46.40	0.008
5	All	All	Synthetic	DRC	[65]	79.60	0.04
6	All	Home	Synthetic	DRC	[65]	62.68	0.03
7	All	Home	Synthetic	Burundi	[65]	NA***	NA***
8	All	All	Synthetic	Burundi	[65]	NA***	NA***

*Mean negative log-likelihood multiplied by 2 for the validation dataset (dataset 3; Extended Data Table 1) not used in training. **Kullback–Leibler divergence[78] from the empirical distribution of the validation dataset to the mean modelled distribution. ***Not used for validation; only for the sensitivity analysis (Supplementary Fig. 6).

Extended Data Table 3 | Model parameters

Notation	Dimension*	Description	Reference
σ_0	1	Relative susceptibility of children aged 0–4	Estimated Prior: Unif(0,1)
ε	1	Net vaccine protection among immunised cohorts (born in or before 1980)	Estimated Prior: Unif(0,1)
C	6×6 or 8×8	Community contact matrix	[24]
β	1	Transmissibility	Nuisance parameter (not explicitly estimated)
p_a	4	Proportion of high-activity individuals among males of age group *a*: (aged 15–19, 20–29, 30–39, and 40–49 years)	Estimated Prior: LogNorm(0, 5) truncated on [0, 1]
q_a	4	Proportion of high-activity individuals among females of age group *a*: (aged 15–19, 20–29, 30–39, and 40–49 years)	Estimated Prior: LogNorm(0, 5) truncated on [0, 1]
v_F	1	Mean sexual contact rate of high-activity females (mean degree)	Derived
v_M	1	Mean sexual contact rate of high-activity males (mean degree)	Derived
w_F	1	Mean sexual contact rate of high-activity females with sexually-acquired infection (mean neighbour degree)	Estimated Prior: LogNorm(0, 2)
w_M	1	Mean sexual contact rate of high-activity males with sexually-acquired infection (mean neighbour degree)	Estimated Prior: LogNorm(0, 2)
n_a	8	Relative population size for males of age group *a*	[63,64]
m_a	8	Relative population size for females of age group *a*	[63,64]

*Number of free parameters represented by each notation.

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Software and code

Policy information about availability of computer code

Data collection	No software was used for data collection.
Data analysis	All the analysis was conducted in Julia v.1.9.3 and R v.4.3.1. Source codes are available on a GitHub repository: https://github.com/akira-endo/mpoxclade1_eigen.

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All data used in this study are publicly available (https://github.com/akira-endo/mpoxclade1_eigen).

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Reporting on sex and gender	We reported and conducted the analysis on the data separated by sex.
Reporting on race, ethnicity, or other socially relevant groupings	N/A
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Recruitment	N/A
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Life sciences study design

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Sample size	This study was a retrospective analysis of multiple publicly available datasets on all comfirmed mpox cases in the Democratic Republic of the Congo and Burundi rather than a sample.
Data exclusions	No data were excluded.
Replication	The datasets and analysis code used in this study are provided in a GitHub repository, which enable all the analysis to be replicated.
Randomization	Randomisation was not applicable as this study was a retrospective analysis of case data.
Blinding	Randomisation was not applicable as this study was a retrospective analysis of case data.

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