

# The Incubation Periods of Mpox Virus Clade Ib

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**Background:** Mpox virus (MPXV) clade Ib, first detected in the Democratic Republic of the Congo (DRC) in September 2023, spread internationally within months, prompting an emergency declaration from the World Health Organization. Data on its incubation period, which both shapes outbreak dynamics and informs epidemic response strategies, remain limited.

**Objective:** To estimate the incubation periods of mpox clade Ib, examining evidence for differences by route of exposure and demographic factors.

**Design:** Bayesian analysis of clinical surveillance data collected between June and October 2024.

**Setting:** South Kivu, DRC, the epicenter of the current mpox clade Ib global outbreak.

**Participants:** Clinically attended persons with confirmed mpox clade Ib infection.

**Measurements:** Demographic characteristics, exposure history, symptom onset, and transmission route.

**Results:** Among 37 polymerase chain reaction-confirmed cases with high viral load (cycle threshold values <34), the median incubation period from exposure to rash was 13.6 days (95% credible interval [CrI], 9.6 to 19.0 days). Five percent of cases are expected to develop a rash within 3.1 days (CrI, 1.3 to 5.5 days) and 95% within 32.3 days (CrI, 22.4 to

45.8 days). The incubation period seemed to differ by putative transmission route: Sexual transmission had a shorter median (10.3 days [CrI, 3.1 to 20.3 days]) than nonsexual transmission (13.5 days [CrI, 9.5 to 19.1 days]), although the CrIs overlapped.

**Limitation:** Surveillance data lacked detailed exposure histories and a lower bound for exposure periods, but models accounted for these uncertainties, yielding robust median estimates.

**Conclusion:** Evidence from this study suggests that clade Ib may have a longer incubation period than other MPXV clades, and this may vary by transmission route. The shorter incubation for sexual transmission mirrors patterns seen in the predominantly sexually transmitted clade IIb outbreak, highlighting the potential role of exposure route in disease progression. These findings have implications for global recommendations on postexposure monitoring periods and prophylaxis.

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The Democratic Republic of the Congo (DRC) is the epicenter of the current multicountry outbreak of clade I mpox virus (MPXV) (1). Mpox cases in South Kivu, eastern DRC, have been linked to a new MPXV subclade, clade Ib, estimated to have emerged in September 2023 (2). Early transmission chains of clade Ib were primarily attributed to sexual exposures (3). A shift to broader, nonsexual, community transmission has since been seen in parts of eastern DRC where young children are now predominantly affected (4). Community transmission of clade Ib has since been reported in 11 additional African countries (as of August 2025), including Uganda, Burundi, and Kenya (5). Although recent evidence has suggested fire-footed rope squirrels as a potential natural reservoir of MPXV (6), the current clade Ib epidemic in DRC seems to be driven by transmission in humans, with little evidence of frequent spillover events.

The differences between the natural history of clade Ib and other variants of MPXV remain unclear. The incubation period is the time between infection

and symptom onset, which is linked to the speed of outbreaks and determines the feasibility and impact of control interventions (7). Estimates of the incubation period have typically ranged from 1 to 2 weeks, although most estimates come from the predominantly sexually transmitted clade II (8, 9). On the basis of these estimates, the World Health Organization (WHO) recommends a 21-day "observation period" for risk reduction precautions and for epidemiologic studies (10). Furthermore, postexposure vaccination is recommended by the WHO for up to 14 days after exposure, which is based on estimates of the incubation period for non-clade Ib MPXV and historical data on

## See also:

*Web-Only*

Supplemental material

smallpox vaccination. Changes in the incubation period of MPXV as the virus evolves may undermine these recommendations, yet we know of no peer-reviewed and published estimates of the incubation period for clade Ib. This gap may limit our ability to tailor efficient responses to the ongoing MPXV clade Ib epidemic.

Here, we present estimates of the incubation period of MPXV clade Ib based on case data from South Kivu, DRC, focusing on its variability across demographic characteristics and putative transmission routes.

## METHODS

### Study Setting and Population

This analysis is based on surveillance data from the Mpox Treatment Center (MTC) in the Uvira health zone in South Kivu province, eastern DRC. The Uvira health zone has about 460 000 inhabitants, 65% of whom reside in the city of Uvira, on the shore of Lake Tanganyika, bordering Burundi. The Uvira health zone is one of the DRC's mpox clade Ib hotspots, prioritized for interventions such as vaccination. It reported its first mpox case on 2 May 2024, eight months after the outbreak was declared in Kamituga, a remote mining town 360 km away. Initially, suspected cases, mostly adults, were managed in outpatient or community settings. However, as cases increased, an MTC was established on 8 June 2024, within the Uvira General Hospital. With support from Médecins Sans Frontières, mpox care, including essential medicines and meals for patients and caregivers, became free at the Uvira MTC on 17 June 2024.

Two small-scale vaccination campaigns took place in Uvira by August 2025. A 2-dose vaccination campaign targeting adults perceived to be at highest risk (sex workers, health workers, and contacts of cases) was conducted in October 2024 (round 1) and December 2024 (round 2), with a total of approximately 14 000 doses of the Modified Vaccinia Ankara-Bavarian Nordic vaccine available, followed by a single-dose campaign in May and June 2025 with 2000 doses available. No other smallpox or mpox vaccination campaigns have been conducted in eastern DRC since the late 1970s (11).

### Case Definitions and Data Collection

The official DRC Ministry of Health case definition for mpox during the time of this study included 3 criteria: sudden high fever followed by a vesiculopustular rash, primarily on the face, palms, and soles; the presence of at least 5 smallpox-type scars; or fever greater than 38.3 °C, severe headache, lymphadenopathy, back pain, myalgia, and severe asthenia, followed within 1 to 3 days by a progressive rash spreading from the face to other body parts, including the palms and soles (12). The community case definition is broader, classifying any person with fever and a skin rash as a suspected case. At the Uvira MTC, after outbreak confirmation, a simplified case definition was applied: Anyone

presenting with a skin rash or papulovesicular or pustular eruptions was considered a suspected mpox case.

Starting from June 2024, the clinical staff at the Uvira General Hospital's MTC conducted structured interviews with suspected cases. Data were collected on demographic characteristics, exposure history, and clinical manifestations, using forms on the KoboCollect platform (Kobo). A suspected case contact was defined as someone with a rash, lesions, and/or similar symptoms to the patient or a confirmed mpox case, contacted in the 3 weeks before symptom onset or diagnosis of the clinical case. For each reported contact with a suspected case, we collected information on whether a single or multiple exposures occurred, the types of exposure (physical nonsexual contact, sexual contact, respiratory contact, or contact with contaminated material) (see **Supplement Section 1**, available at [Annals.org](https://annals.org)), and the date of most recent exposure.

Staff at the MTC collected skin lesion secretions of suspected cases using a dry swab, whereas oropharyngeal secretions were taken with a swab that was soaked into a viral transport medium. Although lesion swabs were meant to be collected and tested from all suspected cases, only a subset had test results due to stockouts of materials and reagents during this phase of the outbreak. The subset of suspected cases that were tested had dry lesion swabs tested by quantitative polymerase chain reaction (qPCR) with GeneXpert (Xpert Mpox; Cepheid) or the Radi Fast Mpox Kits (KH Medical). The choice of PCR test was based on the availability of reagents and laboratory testing capacity during the study period and was not based on patient characteristics.

On the basis of previous reports of potential misclassification of patients with high PCR cycle threshold (Ct) values, we defined a subset of cases who had Ct values below a conservative threshold for positivity (<34) to reduce the risk for false positives (13). We refer to these persons as "high-confidence confirmed cases," those with a Ct value below 39 as "confirmed cases," and all clinical cases as "suspected cases."

Due to the deletion of the *OPG032* gene in clade Ib viruses, amplification of the GeneXpert MPXV PCR target is inhibited (2). Clade Ib viruses therefore test negative for MPXV by GeneXpert assay but positive for orthopoxvirus (based on the *E9L* target). This result is specific to clade Ib viruses and was seen for all GeneXpert tests done in Uvira. In addition, a subsample of 49 cases from Uvira from the same period were clade-typed using the TIB Molbiol qPCR kit, which confirmed that all cases tested belonged to clade Ib (14, 15).

### Statistical Inference of the Incubation Period

The aim of the statistical modeling framework was to infer the distribution of the incubation periods of MPXV clade Ib for different definitions of symptom onset (fever, rash, earliest symptom) and its variability

across key factors, including demographic characteristics and transmission routes. To do so, we used Bayesian methods to obtain a robust estimate of the incubation period distribution accounting for the limitations of the data and known sources of bias in the estimation of epidemiologic delay distributions (16).

Our modeling framework accounted for multiple reported contacts per case; censored times from exposure to symptom onset, as only time to most recent contact was reported; and right-truncation of the time from exposure to symptom onset, as only contacts in the previous 21 days were recorded. When case contacts were also enrolled in our study, we used the date of rash onset of contacts to bound the exposure window and assumed a uniform probability of exposure within that window. When the exposure time was unknown and contact pair information unavailable, we used a maximum exposure window of 35 days before symptom onset up to the time of most recent contact, consistent with published estimates of the incubation period for clades I and II (8). We used published estimates of the time to clade Ib lesion resolution (17) to set priors on the date of exposure within possible exposure windows. We compared across multiple distributional assumptions typically used for incubation period estimation (log-normal, gamma, and Weibull) and across different assumptions on the probability of unreported exposures in the community based on the observed epidemic curve (no additional community exposures vs. exposures as a function of the epidemic curve). We set priors on the mean incubation period based on published estimates of the clade Ib 2022 epidemic and historical clade I and clade II outbreaks by Ponce and colleagues (8). A full model description is given in **Supplement Section 2** (available at [Annals.org](https://annals.org)).

We produced separate incubation period estimates for different symptom types: fever, rash, and earliest symptom. In addition, we produced stratified estimates by demographic characteristics (age group and sex), exposure type (sexual vs. nonsexual) (see definitions in **Supplement Section 1.1**, available at [Annals.org](https://annals.org)), epidemic period (before vs. after 1 September 2024) (**Supplement Figure 2**, available at [Annals.org](https://annals.org)), and hospitalization status (inpatient vs. outpatient). As multiple exposure types could be reported for the same contact, we defined the exposure to be "sexual" if any of the exposure types was sexual for that contact, and "nonsexual" otherwise. Given that all cases were not tested and current diagnostics are imperfect, we conducted all analyses using 3 sets of outcomes: all suspected cases, all cases with positive PCR result (confirmed cases), and all confirmed cases with a Ct value less than 34 (high-confidence confirmed cases) (see previous Case Definitions and Data Collection section). Inference was drawn using a Hamiltonian Monte Carlo sampler as implemented in the Stan programming language (18). Model comparison was done using

estimated leave-one-out cross-validation log predictive density (19).

The data used in this study were collected with the Uvira health zone team for public health surveillance. Ethical approvals were obtained from the institutional review boards of the Johns Hopkins Bloomberg School of Public Health (reference number IRB00030442) and the Université Catholique de Bukavu (UCB/CIES/NC/019/2024) to use those data.

**Table 1.** Mpox Patient Demographic Characteristics and Exposure Details for All Cases ( $n = 243$ ), PCR-Confirmed Cases (Ct Value  $<39$ ), and High-Confidence Confirmed Cases (Ct Value  $<34$ )

Characteristic	All Cases ( $n = 243$ ), $n$ (%)	PCR-Confirmed Cases ( $n = 92$ ), $n$ (%)	High-Confidence Confirmed Cases ( $n = 37$ ), $n$ (%)
<b>Age group</b>			
<1 y	17 (7)	8 (9)	5 (14)
1-4 y	56 (23)	21 (23)	10 (27)
5-14 y	90 (37)	33 (36)	12 (32)
15-44 y	75 (31)	28 (30)	9 (24)
$\geq 45$ y*	5 (2)	2 (2)	1 (3)
<b>Male sex</b>	117 (48)	48 (52)	18 (49)
<b>Hospitalized</b>	107 (44)	52 (57)	20 (54)
<b>Number of suspected case contacts</b>			
1	192 (79)	68 (74)	28 (76)
2	33 (14)	13 (14)	4 (11)
>2	18 (7)	11 (12)	5 (13)
<b>Exposure type†‡</b>			
Physical	230 (95)	87 (95)	32 (86)
Respiratory	203 (84)	78 (85)	32 (86)
Sexual	20 (8)	7 (8)	6 (16)
Materials	9 (4)	2 (2)	1 (3)
Health care worker	3 (1)	1 (1)	0 (0)
<b>Exposure location†</b>			
Within household	175 (72)	67 (73)	29 (78)
Other residence§	49 (20)	18 (20)	7 (19)
Health care setting	10 (4)	3 (3)	0 (0)
Work	6 (2)	1 (1)	0 (0)
Bar	4 (2)	2 (2)	2 (5)
Other	12 (5)	5 (5)	2 (5)

Ct = cycle threshold; PCR = polymerase chain reaction.

\* The age group  $\geq 45$  y represents persons who were alive during the last country-wide smallpox vaccination initiative and therefore potentially eligible for smallpox vaccination.

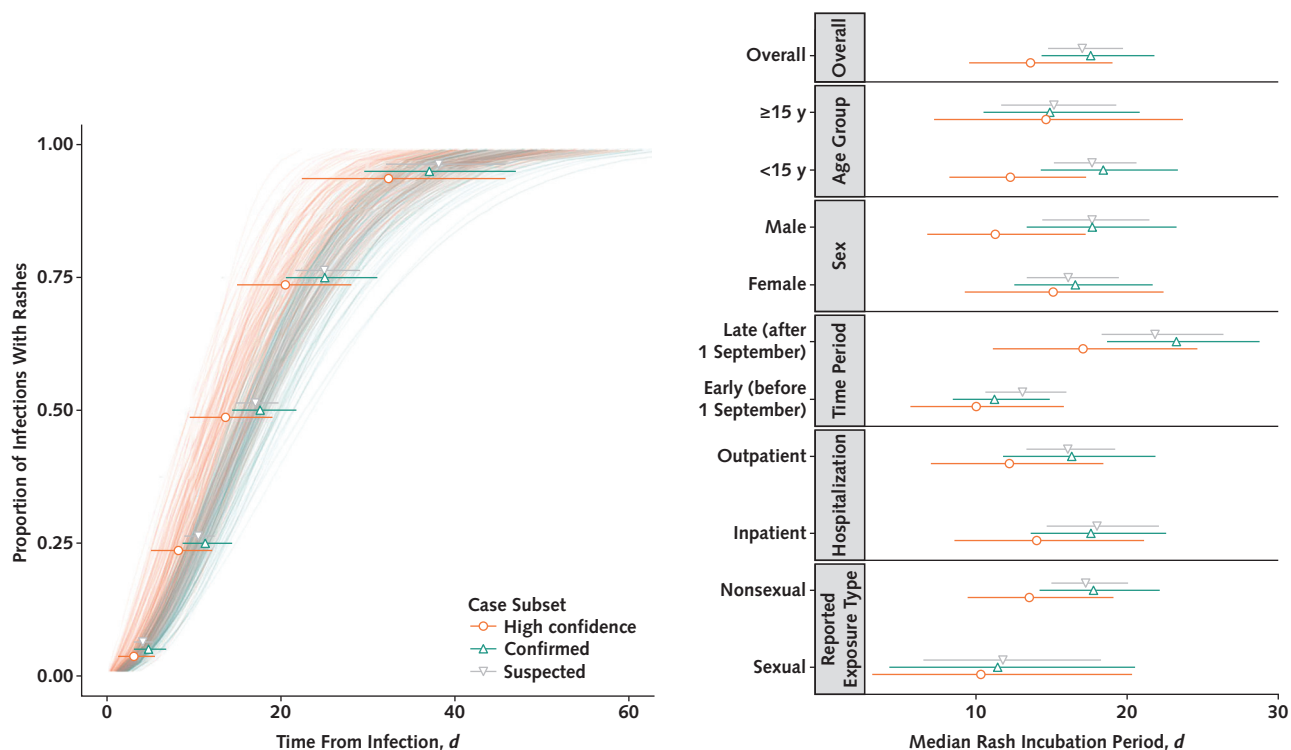
† Multiple exposure types and locations could be reported per case. This field represents whether each person reported at least 1 of each exposure type.

‡ Physical exposure was defined as having physical touch with the suspected case; respiratory exposure was defined as being near the suspected case; sexual exposure was defined as having any sexual contact with the suspected case; materials was defined as having contact with shared materials of the suspected case; and health care worker was defined as contact with a health care worker.

§ Other residence is defined as exposure within a place of residence with a nonhousehold member.

|| Other exposure locations reported included a restaurant ( $n = 1$ ), a nightclub ( $n = 1$ ), an outdoor sports venue ( $n = 1$ ), and a school or nursery ( $n = 2$ ).

**Figure.** Estimates of mpox clade Ib rash incubation period.



CrI = credible interval. **Left.** Posterior draws of the incubation period cumulative distribution function (lines, 100 draws) and estimates of quantiles of interest (points: mean, bars: 95% CrI) by mpox case definition. Estimates are shown for the Weibull distribution assumption and the main model (no community infections), which was retained in model comparison. **Right.** Estimates of the median incubation period (dots: mean, bars: 95% CrI) by strata for the overall estimates (first facet) and across analysis stratifications.

**Role of the Funding Source**

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

**RESULTS**

**Clinical Surveillance and Reported Exposures of Mpox Cases**

Of the 973 cases recorded between June and October 2024, a total of 35.6% (346 of 973) of suspected mpox cases reported having contact with a suspected mpox case, with 70% (243 of 346) of them reporting temporal information of these contacts. Of the 243 suspected cases with reported contacts, 48% (117 of 243) were male, 30% (73 of 243) were children younger than 5 years, and 2% (5 of 243) were 45 years and older and thus likely to have been eligible for smallpox vaccine through routine vaccination (11) (Table 1). Only 1% (3 of 243) reported having received a smallpox vaccine. The dates of vaccination were not reported, but all 3 persons were older than 48 years; therefore, they could have been vaccinated as children during smallpox eradication efforts. Two had a positive PCR result, and 1 had a Ct value less than 34. A total of 44% (107 of 243) of cases with reported

contacts were hospitalized, and 3% (8 of 243) were tested for HIV, all of which were negative, with 1 receiving preexposure prophylaxis. Among the cases with both complete contact information and valid laboratory results (123 of 243), 72% (92 of 123) were PCR-positive (confirmed cases), 25% (31 of 123) were negative, and the rest had indeterminate results. Among confirmed cases, 40% (37 of 92) were considered high-confidence confirmed cases based on their low Ct values (13). The distribution of cases by age, sex, and self-reported exposure types were similar across these 3 case definitions (Table 1).

The 243 suspected cases with complete contact information reported contact with 320 suspected mpox cases. Seventy-nine percent (192 of 243) reported contact with a single suspected case, and 21% (51 of 243) reported contact with more than 1 suspected case (Table 1). Most suspected cases reported nonsexual physical contact with a case (95% [230 of 243]) and/or respiratory contact (84% [203 of 243]), with most exposures reported to have occurred within the household. Only 8% (20 of 243) of cases reported sexual exposures. Exposure types among suspected and confirmed cases were similar, although sexual exposure was more frequent among high-confidence confirmed cases (16% vs. 8% in suspected and confirmed cases) (Table 1).

### Incubation Period Estimation

We estimated the incubation period on the basis of data from 92 confirmed cases with complete data on reported exposure to suspected cases, with a focus on 37 high-confidence confirmed cases (see Methods). We performed secondary analyses on all 243 suspected cases with contact information, as not all cases were tested and the field sensitivity of current PCR assays is not well understood. Among confirmed cases, the median time from most recent contact (before symptoms) to rash onset was 10 days (IQR, 3 to 14 days), 9 days (IQR, 3 to 14 days) to fever onset, and 9 days (IQR, 2 to 13 days) to any symptoms, with similar times for high-confidence and suspected cases (Supplement Figure 3, available at [Annals.org](#)). However, these numbers do not account for biases because the last reported exposure may not have been the one that led to infection.

When restricting analyses to high-confidence confirmed cases, we estimate that the median time from exposure to rash onset is 13.6 days (95% credible interval [CrI], 9.6 to 19.0 days) (Figure and Table 2), with 5% of infections expected to develop rash within 3.1 days of exposure (CrI, 1.3 to 5.5 days), and 95% within 32.3 days (CrI, 22.4 to 45.8 days). Estimates of the median time to onset of fever were similar (14.5 days [CrI, 9.7 to 20.5 days]) and shorter for the onset of any symptom (11.6 days [CrI, 7.7 to 16.3 days]) (Table 2). Estimates based on alternative models, including those with different distributional assumptions, were similar to those with the best fitting model (Supplement Tables 1 and 2, available at [Annals.org](#)).

We found evidence of differences in the incubation period by transmission route (Figure, right, and Table 3). The median rash incubation period was shorter for putative sexual versus nonsexual transmission (median, 10.3 days [CrI, 3.1 to 20.3 days] vs. 13.5 days [CrI, 9.5 to 19.1 days]) (Table 3), although the 95% CrIs overlapped.

We estimate a shorter rash incubation period in the early phase of the epidemic (before 1 September; median, 10.0 days [CrI, 5.7 to 15.8 days]) versus the later phase (after 1 September; median, 17.1 days [CrI, 11.1 to 24.7 days]). Incubation periods among those younger than 15 years seemed shorter than those aged 15 years and older (10.0 days [CrI, 6.0 to 15.4 days] vs. 13.7 days [CrI, 6.7 to 22.3 days]) (Supplement Tables 3 and 4, available at [Annals.org](#)), although this trend reversed when considering alternative case definitions. We found similar differences between groups in stratified estimates for time to fever and any symptom onset (Supplement Figure 4 and Supplement Tables 3 to 5, available at [Annals.org](#)).

### Sensitivity Analyses

Estimates of the median incubation period using confirmed (17.6 days [CrI, 14.3 to 21.8 days]) and suspected cases (17.0 days [CrI, 14.8 to 19.7 days]) were longer than our main estimates from high-confidence confirmed cases. The median incubation period was similar for self-reported sexual exposure across case definitions (confirmed: 11.5 days [CrI, 4.3 to 20.5 days]; suspected: 11.8 days [CrI, 6.5 to 18.3 days]) but was consistently longer for nonsexual exposure (confirmed: 17.8 days [CrI, 14.2 to 22.1 days]; suspected: 17.3 days [CrI, 15.0 to 20.1 days]) (Supplement Tables 3 to 5). Our median incubation period estimates for high-confidence confirmed cases was robust to the choice of Ct thresholds when these were smaller than or equal to 34 (used for our main results) but increased with increasing Ct thresholds above 34 (Supplement Figure 5, available at [Annals.org](#)).

We further refined our analysis to 50 contact pairs for which symptom onset dates were available for both case and contact, all but one of which reported nonsexual exposures (Supplement Table 8, available at [Annals.org](#)).

**Table 2.** Estimated Quantiles of Incubation Period Distribution by Symptom Type\*

PCR Confirmation and Symptom Type	Patients, n	Mean Incubation Period Quantile (95% CrI)				
		5%	25%	50%	75%	95%
<b>High-confidence cases</b>						
Any symptom	37	1.9 (0.7-3.8)	6.2 (3.4-9.7)	11.6 (7.7-16.3)	19.0 (13.6-25.8)	33.2 (22.9-46.5)
Fever	28	3.8 (1.3-7.2)	9.1 (5.1-14.0)	14.5 (9.7-20.5)	21.0 (15.4-28.8)	31.9 (22.7-45.0)
Rash	37	3.1 (1.3-5.5)	8.2 (5.0-12.1)	13.6 (9.6-19.0)	20.5 (15.0-28.1)	32.3 (22.4-45.8)
<b>Confirmed cases</b>						
Any symptom	92	3.2 (1.8-4.9)	8.9 (6.5-11.8)	15.1 (12.0-19.0)	23.0 (18.6-28.7)	36.8 (28.7-47.5)
Fever	77	3.4 (2.0-5.2)	9.1 (6.6-12.1)	15.3 (12.0-19.5)	22.9 (18.4-29.2)	36.1 (27.9-47.1)
Rash	92	4.8 (3.0-6.8)	11.3 (8.7-14.4)	17.6 (14.3-21.8)	25.0 (20.5-31.1)	37.1 (29.6-47.0)
<b>Suspected cases</b>						
Any symptom	243	2.9 (2.0-3.8)	8.6 (7.1-10.3)	15.2 (12.9-17.9)	23.7 (20.3-28.1)	38.9 (32.5-47.7)
Fever	195	3.9 (2.8-5.1)	9.9 (8.1-11.9)	16.0 (13.7-18.8)	23.4 (20.0-27.8)	35.7 (29.6-44.0)
Rash	243	4.1 (3.1-5.3)	10.5 (8.9-12.4)	17.0 (14.8-19.7)	24.9 (21.6-29.1)	38.1 (32.1-45.8)

CrI = credible interval; Ct = cycle threshold; PCR = polymerase chain reaction.

\* Main model estimates (Weibull distribution, without community infections) shown for high-confidence cases (PCR-positive with Ct <34, main result, n = 37), confirmed cases (PCR-positive with Ct <39, n = 92), and suspected cases with reported contacts (n = 243) by symptom type. Estimates for all distributional assumptions are provided in the Supplement (available at [Annals.org](#)).

**Table 3.** Estimated Quantiles of Incubation Period Distribution to Rash Onset by Exposure Type\*

PCR Confirmation and Exposure Type	Patients, <i>n</i>	Mean Rash Incubation Period Quantile (95% CrI)				
		5%	25%	50%	75%	95%
<b>High-confidence cases</b>						
Sexual	6	1.7 (0.1–6.1)	5.5 (0.9–13.4)	10.3 (3.1–20.3)	17.6 (8.5–29.3)	32.9 (20.5–48.6)
Nonsexual	31	3.4 (1.4–6.3)	8.4 (5.1–12.7)	13.5 (9.5–19.1)	19.8 (14.2–27.5)	30.4 (19.9–43.9)
<b>Confirmed cases</b>						
Sexual	7	2.1 (0.1–6.4)	6.3 (1.4–13.5)	11.5 (4.3–20.5)	18.8 (10.0–29.8)	33.4 (21.3–48.7)
Nonsexual	85	5.0 (3.1–7.1)	11.5 (8.7–14.7)	17.8 (14.2–22.1)	25.0 (20.4–31.1)	36.8 (29.2–47.1)
<b>Suspected cases</b>						
Sexual	19	1.7 (0.4–4.1)	6.1 (2.6–10.6)	11.8 (6.5–18.3)	20.1 (13.2–28.4)	36.8 (25.2–51.3)
Nonsexual	224	4.5 (3.3–5.7)	10.9 (9.2–12.8)	17.3 (15.0–20.1)	24.8 (21.5–28.9)	37.0 (31.4–44.6)

CrI = credible interval; Ct = cycle threshold; PCR = polymerase chain reaction.

\* Main model estimates (Weibull distribution, without community infections) are shown for high-confidence cases (PCR-positive with Ct <34, main result, *n* = 37), confirmed cases (PCR-positive with Ct <39, *n* = 92), and all suspected cases with reported contacts (*n* = 243). Stratified estimates are provided by self-reported exposure pathway. Estimates for all distributional assumptions and stratifications are provided in the Supplement (available at [Annals.org](https://annals.org)).

org). Median incubation period estimates based on all contact pairs were similar to our main estimates for nonsexual exposure (*n* = 50; median, 12.4 days [CrI, 9.2 to 16.5 days]) but shorter for high-confidence cases (*n* = 7; median, 9.8 days [CrI, 2.7 to 20.3 days]) and slightly longer for confirmed cases (*n* = 19; median, 15.5 days [CrI, 9.3 to 23.1 days]), although these case definitions had limited sample sizes (Supplement Figure 6 and Supplement Table 9, available at [Annals.org](https://annals.org)). We could not perform stratified analyses on exposure type within this subset due to the limited sample size of reported sexual exposures.

## DISCUSSION

We estimate the median incubation period for MPXV clade Ib in Uvira, DRC, to be 13.5 days. This is longer than estimates for MPXV clades Ia or IIb (9 to 10 days) (20) and slightly longer than, but not inconsistent with, historical estimates of the incubation period of smallpox (21). We find evidence of differential incubation period by route of transmission.

The incubation period from sexual contact was lower (10.5 days) than for nonsexual exposure (13.5 days), although the uncertainty intervals overlapped. Our estimates of clade Ib incubation periods align with those in a preprint from a clade Ib outbreak in Kamituga, another region of the DRC, where transmission was predominantly heterosexual and in adults (22), and were similar to estimates for the predominantly sexually transmitted MPXV clade IIIb 2022 outbreak (8) (Supplement Figure 6). By contrast, our median incubation period estimates from nonsexual exposures are longer than the reported range of 5 to 13 days for nonsexual human-to-human transmission events during a clade Ia outbreak in 2013 in central DRC (9) but are compatible with earlier studies reporting clade Ia nonsexual human-to-human incubation periods in the country, ranging between 1 and 3 weeks (23, 24). Comparison with clade IIa zoonotic exposures

in the 2003 U.S. outbreak (median, 12 days [range, 1 to 41 days]; mostly adults) further shows that both host age and exposure route are important determinants of incubation period (25).

The fact that previous MPXV clade IIb incubation period estimates align closely with our clade Ib results for sexual contacts, but less with the longer overall estimates, may be at least in part attributable to biological factors. Higher infectious doses are known to shorten the incubation periods of viral infections (26), and route of exposure (mucosal vs. epidermal) may also affect the timing of rash onset, as mpox lesions preferentially appear at anatomical sites correlating with site of exposure (27). Taken together, our exposure-stratified clade Ib results and previous clade IIb estimates thus support the hypothesis that MPXV incubation periods are shorter after sexual exposures due to higher viral infectious doses and differential exposure routes than for nonsexual contacts.

In Uvira, we find that the mode of transmission seems to have changed over the course of the epidemic, from predominantly sexual in the early weeks to mainly nonsexual later on (4). These shifts in transmission may therefore explain our longer overall incubation period estimates, as most cases for which we had contact information were recruited in the later phase of the epidemic. Our longer estimates may also stem from methodological differences, as we here correct for common sources of downward bias (16), including censoring due to unknown exact contact dates, and right truncation, as we asked only about exposures in the past 21 days following WHO recommendations (28).

Our incubation period estimates were sensitive to PCR-based case definitions, which may have implications for MPXV clade Ib epidemiologic studies and control. The fact that suspected and confirmed cases had similarly longer incubation periods with respect

to our high-confidence confirmation definition may indicate low test specificity when using higher Ct value thresholds to define positivity. These findings echo challenges in defining positive cases during the clade Ib outbreak in the United States (13). Taken together, these elements warrant careful investigations of Ct value distributions in suspected MPXV clade Ib cases and their implication for defining positivity thresholds.

Our results have implications for both surveillance and control of mpox clade Ib. Around one fifth of cases (23.2% [CrI, 7.2% to 43.6%]) (Supplement Table 5) developed rash after the WHO's recommended 3-week monitoring period for exposed persons and recall period for epidemiologic investigations. As detailed below, this finding is subject to limitations in our study and is to be interpreted with care, especially given the wide uncertainty intervals. Nevertheless, these results suggest that locally adapted time bounds could improve our ability to both understand and ultimately contain this virus. In addition, our observation that the median incubation period may be longer than previous estimates for MPXV suggests the possibility that the time window for postexposure prophylactic vaccination could be longer than current recommendations, although evidence on the effectiveness of this use of the vaccine is needed.

These results come with several limitations. First, we attribute these estimates to clade Ib, yet cases were not all clade typed. However, all 45 samples from Uvira that were clade typed with TIB Molbiol qPCR clade typing kits were clade Ib, as were all samples in the province of South Kivu that were clade typed at the Institut National de Recherche Biomédicale. Second, data were collected during routine surveillance activities, allowing for limited descriptions of contacts and exposures. We asked only about the date of most recent exposure to a suspected mpox case and do not have the lower bound on the exposure period. We accounted for these sources of uncertainty in the models, and results were robust to various assumptions about this lower bound. Third, our analyses implicitly assume that transmission is from person-to-person, with no zoonotic infections. We have no data suggesting a major role for zoonotic infections in this clade Ib outbreak, and it is unclear how these might influence our estimates of the incubation period. Finally, our estimates of the right tails of the incubation period have more uncertainty than the median because of their sensitivity to distributional assumptions.

Our results show that the incubation period of MPXV clade Ib may be longer than previously characterized MPXV variants and may vary by transmission route, which has important implications for outbreak management. The observed shorter incubation periods for sexual versus nonsexual exposures suggest that dose and exposure site may have a major influence on the timeline of disease, underscoring the need for

flexible and locally adapted public health responses. Our estimates suggest that the current 3-week monitoring period recommended by the WHO may be insufficient for a nonnegligible fraction of clade Ib nonsexually transmitted infections, potentially leading to missed cases and ongoing transmission, although this finding should be confirmed by future MPXV clade Ib studies. Strengthened surveillance, extended monitoring periods, and targeted interventions based on dominant transmission routes could improve containment efforts in South Kivu, DRC, and other clade Ib-affected countries. Future research should aim to confirm these findings in other regions and further explore the ways in which viral dose and exposure site may influence the natural history of disease.

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