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Genomics reveals zoonotic and sustained human Mpox spread in West Africa

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1 Genomics reveals zoonotic and sustained 2 human Mpox spread in West Africa

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48 Five years before the 2022 multi-country mpox outbreak, Nigeria and Cameroon
49 reported their first cases in over three decades.^{1,2} While Nigeria's outbreak is
50 recognized as an ongoing human epidemic, the drivers of Cameroon's resurgence
51 remain unclear.^{3,4} The rate of zoonoses remains uncertain in both countries, and
52 gaps in genomic data obscure the timing, zoonotic and geographic origin of mpox
53 virus (MPXV) emergence in humans. To address these uncertainties, we generated
54 118 MPXV genomes from Nigeria and Cameroon from 2018-2023. Our findings
55 show that, in contrast to Nigeria, cases in Cameroon are the result of repeated
56 zoonoses, with two distinct zoonotic lineages circulating across the Nigeria-
57 Cameroon border. Our findings suggest that shared animal populations in the
58 cross-border forest ecosystems drive virus emergence and spread. Accordingly,
59 we identify the closest zoonotic outgroup to the Nigerian human epidemic lineage
60 (hMPXV-1) in a southern Nigerian border state. We estimate that the shared
61 ancestor of the zoonotic outgroup and hMPXV-1 circulated in animals in southern
62 Nigeria in late 2013. We estimate that hMPXV-1 emerged in humans in August 2014
63 in the southern Rivers State and circulated undetected for three years. Rivers State
64 acted as the main source of viral spread across the human epidemic. Our study
65 sheds light on MPXV's recent establishment in the human population and
66 highlights the risk of persistent zoonotic emergence of MPXV in the complex
67 border regions of Cameroon and Nigeria.

68

69 Main

70 Mpox is a viral zoonosis caused by infection with the *Orthopoxvirus* mpox virus (MPXV)
71 transmitted from an as-yet unknown animal reservoir.^{5,6} MPXV diversity is partitioned into
72 two major clades. Clade I was historically googldafg restricted to animal populations in
73 Central Africa, and Clade II with its subclades IIa and IIb to Western Africa.^{5,6} From first
74 identification in humans in 1970 to 2017, mpox cases were largely infrequent, in rural
75 endemic regions, and had limited human-to-human transmission.^{1,7,8} However, a
76 significant increase in cases has been observed in both endemic and non-endemic
77 countries in recent years.⁹ Notably, Nigeria and Cameroon reported their first cases in
78 over three decades in 2017 and 2018 respectively.^{1,2,4,10}

79 In May 2022, a Clade IIb lineage termed B.1 rapidly disseminated around the world to
80 cause the multi-country mpox outbreak.¹¹ The apparent human-to-human transmission of
81 the B.1 lineage raised the possibility of a new MPXV transmission route. B.1 showed
82 significant divergence from the closest Clade IIb genome sampled in Nigeria in 2018, with
83 an evolutionary rate elevated above the expected rate for Orthopoxviruses.¹² The multi-
84 country outbreak was characterized by enrichment of mutations in a dinucleotide context
85 associated with the cytosine deaminase activity of the APOBEC3 (apolipoprotein B
86 mRNA editing enzyme, catalytic polypeptide 3) host antiviral mechanism.^{3,13} This
87 mutational signature has not been observed in sequences from zoonotic infections,
88 suggesting that APOBEC3 genomic editing was a characteristic feature of sustained
89 transmission in the human population.³

90 In light of this new evolutionary dynamic, several studies confirmed that the ongoing mpox
91 epidemic in Nigeria was driven by sustained human-to-human transmission.^{3,14} It is
92 estimated that MPXV emerged in the human population in Nigeria in 2016, circulating and
93 diversifying cryptically into multiple distinct lineages.^{3,14} Contrastingly, Cameroon's recent
94 increased incidence was most likely driven by sporadic cases and limited outbreaks
95 resulting from zoonotic transmission.⁴ The contiguous Cameroonian Highlands forest
96 belt, spanning Nigeria and Cameroon, provides suitable habitats for animal reservoirs.^{15,16}
97 Agriculture, hunting and human settlements in forested areas of this region increases
98 interaction at the human-animal interface and the risk of zoonotic transmission.^{2,4}
99 Significant human movement across the porous border can also facilitate viral spread,
100 especially as outbreaks in both countries intensify.²

101 Limited availability of full-length MPXV genomes from the region, however, means that
102 there are currently several unanswered questions about the zoonotic- and human-
103 transmission dynamics of MPXV.¹⁴ The extent of human-to-human transmission in
104 Nigeria and Cameroon, as well as the role of zoonotic spillover events in both countries
105 remain unclear. The drivers and patterns of the sustained human epidemic in Nigeria are
106 also unknown. Enhancing our understanding of the cross-border MPXV zoonotic
107 transmission dynamics is essential to assess the risk of recurrent spillover events and
108 bidirectional transmission. Concurrently, a deeper insight into MPXV transmission within
109 human epidemics is needed to inform public health interventions that reduce local cases,
110 and limit viral export. To support these goals, we established a Pan-African consortium
111 to compile the largest MPXV dataset to date.

112 **Zoonoses drove resurgence in Cameroon**

113 To elucidate the relative contributions of sustained human-to-human and zoonotic
114 transmission in the two countries, we generated 118 near-complete MPXV genomes
115 sampled from Nigeria (n=109) and Cameroon (n=9) between 2018 and 2023. The
116 majority of our Cameroonian sequences were sampled from the rural South-West and
117 North-West Regions bordering Nigeria, which accounts for the second and third highest
118 number of mpox cases in Cameroon respectively (Figure 1A). Our Nigerian sequences
119 were predominantly sampled from the South South, South East, and South West Regions
120 (Figure 1 B). Southern states were the epicenter of the epidemic from 2017 onwards,
121 reporting the earliest cases (Figure 1 C). From 2022 onwards, both northern and southern
122 Nigeria experienced a substantial resurgence of cases after a period of low incidence

123 (Figure 1 C). Our Nigerian dataset largely encompasses the resurgence from 2022
124 onwards (Figure 1C). All of our sequences belonged to Clade IIb.

125 To quantify the relative extent to which sustained human transmission and zoonotic
126 spillover events contribute to ongoing mpox cases in both countries, we reconstructed the
127 Clade IIb phylogeny with all available Clade IIb sequences. We found that 105 of our 109
128 Nigerian sequences were interspersed throughout six divergent, co-circulating sub-
129 lineages of the human-to-human transmitting lineage in Nigeria termed hMPXV-1 (Figure
130 1D, E).¹⁴ The divergence of the sub-lineages suggests that hMPXV-1 has cryptically
131 circulated and diversified, largely driven by APOBEC3 activity, in the human population
132 in Nigeria for a prolonged period after initial spillover (Figure 1D).^{3,14} Within hMPXV-1,
133 distinct lineages are designated according to a system similar to the SARS-CoV-2 Pango
134 nomenclature.^{17,18} Under this nomenclature hMPXV-1 is referred to as Lineage A, with its
135 descendants designated as e.g. A.1 and second subdivision descendants designated as
136 e.g. A.1.1.^{3,14,18} The majority of our 105 sequences belonged to sub-lineage A.2.3 (Figure
137 1E). None of our 105 sequences were from lineage A.1.1 from which the B.1 multi-country
138 outbreak lineage descended (Figure 1D). Only four of the 109 sampled cases in Nigeria
139 were identified as probable zoonotic infections (~3.7%), as their sequences did not fall
140 within the hMPXV-1 lineage (Figure 1D). Collectively, these findings indicate that
141 sustained human transmission is the primary driver of mpox cases in Nigeria.

142 Conversely, we found that all nine Cameroonian sequences form a divergent basal sister
143 lineage to hMPXV-1 and its zoonotic outgroup KJ642617 (Figure 1D). This suggests that
144 the sampled cases in Cameroon were the result of zoonotic transmission and not linked
145 to hMPXV-1. To confirm this, we quantified the APOBEC3 mutational bias characteristic

of human-to-human transmission across our phylogeny (see Methods). We observed a significant proportion of mutations consistent with APOBEC3 activity across the internal and terminal branches of hMPXV-1, including our new sequences (Figure 1D, F). Approximately 74% of reconstructed SNPs in hMPXV-1 were indicative of APOBEC3 editing, consistent with previous work.³ This APOBEC3 enrichment confirms that 105 of our 109 Nigerian sequences are a result of the sustained human transmission. In contrast, we found that only 9% of reconstructed SNPs across the remaining parts of the tree were APOBEC3-type mutations (Figure 1D, F). This includes all nine Cameroonian sequences and the four probable zoonotic infections from Nigeria. Overall, we sampled 13 zoonotic infections (~11%) in our total dataset. Our findings suggests that all (100%) of the sampled Cameroonian cases resulted from zoonotic transmission, confirming that the recent surge in cases was not driven by sustained human-to-human transmission as observed in Nigeria.^{3,4} Our findings also corroborate the continued if minor role of zoonotic transmission in the epidemiology of mpox in Nigeria (~3.7% of cases sampled).

Distinct zoonotic lineages cross the border

The Nigeria-Cameroon border is covered by a complex forest belt extending into both countries that hosts many animal populations susceptible to MPXV infection that can freely move across borders (Figure 1A).^{15,16} The forest belt also hosts a substantial amount of subsistence hunting and wild game trade across borders, alongside high levels of trans-border human movement that may potentially drive viral spread between the two countries.^{2,19–21} Leveraging our dataset encompassing both countries, we sought to investigate cross-border zoonotic transmission to elucidate the potential drivers of bidirectional spread.

169 In our phylogeny (Figure 1D), we found that two of the four Nigerian zoonotic sequences
170 clustered with Cameroonian sequences in the newly sampled sister lineage to hMPXV-1
171 (Figure 1D).^{3,14} This indicates that the new zoonotic lineage likely disseminated across
172 the border. The two Nigerian sequences were from the southern Akwa Ibom state
173 adjacent to Cross River state, which shares a border with the regions from where our
174 Cameroonian cases were sampled (Figure 1A). The Akwa Ibom sequences were most
175 closely related to a sequence we sampled in Mbongue in the South-West Region of
176 Cameroon, though they substantially diverged (separated by 25 and 29 SNPs
177 respectively from the Mbongue sequence) (Figure 1D). Taken together, the phylogeny
178 suggests that this new lineage, with its long internal branches, represents independent
179 zoonotic transmissions from a viral population that must have diverged over a long period
180 of time in a shared animal population driving bidirectional transmission from the cross-
181 border forest ecosystem. Additionally, prior to this study the only high quality zoonotic
182 Clade IIb sequence was hMPXV-1's closest zoonotic outgroup, KJ642617 (Figure 1A).
183 KJ642617 was sampled in 1971 in Abia province in southern Nigeria (Figure 1A, B, D).
184 KJ642617 and the novel lineage, predominantly sampled in Cameroon, share a common
185 ancestor that must have circulated within the animal population of the cross-border
186 ecosystem several decades ago as well (Figure 1D).

187 As KJ642617's relationship to the new zoonotic lineage and the nested Akwa Ibom
188 sequences support historic and recent viral dissemination across the border, we
189 performed Bayesian phylogenetic reconstructions to investigate the timing of the cross-
190 border dissemination.³ In our reconstructions, we found that the Cameroonian lineage
191 and KJ642617 shared a common ancestor that circulated in the animal reservoir around

192 February 1966 (median time to the most recent common ancestor or tMRCA, 95% HPD
193 February 1963 to November 1968) (Figure 2A). There is also evidence of more recent
194 cross-border viral spread, as the Akwa Ibom sequences diverged from the Mbongue
195 sequence in July of 2009 (95% HPD June 2006 to June 2013, Figure 2A). Sparse
196 sampling limits our ability to definitively resolve the geographic origin of the common
197 ancestor of all of Clade IIb. However, the country of origin and direction of spread is less
198 meaningful for a virus in a freely moving animal population in a cross-border ecosystem
199 where wild game sources and markets are often shared across the borders. Taken
200 together, our zoonotic sequences support both recent and historic viral spread across a
201 porous Nigeria-Cameroon border, likely originating in a shared animal population hosting
202 significant diversity in the cross-border forest ecosystem.^{5,22–26}

203 **Zoonotic ancestor traced to South Nigeria**

204 Building on our previous findings of a dynamic reservoir in the cross-border forest
205 ecosystem, we aimed to identify the potential zoonotic ancestor of hMPXV-1 by
206 leveraging our dataset from the forested border regions. The genomic data supports a
207 single zoonotic origin for hMPXV-1.³ However, no closely related zoonotic ancestor has
208 been identified for hMPXV-1 to date, with the closest known zoonotic outgroup
209 (KJ642617) sampled in Nigeria in 1971 (Figure 1A, B, D). Notably, we found that our two
210 remaining Nigerian zoonotic sequences formed a sister lineage to hMPXV-1 (termed “Zx”
211 in Figure 1D), breaking up the long stem branch from KJ642617 to hMPXV-1 (Figure 1D).
212 As our new Zx sequences share a direct common ancestor with hMPXV-1, they represent
213 the closest zoonotic outgroup to hMPXV-1.

214 The Zx sequences reduced the stem branch from a zoonotic ancestor to hMPXV-1 from
215 27 to 8 SNPs. The more recent divergence between our new Zx outgroup and hMPXV-
216 1 provides a narrow timeframe for when hMPXV-1's zoonotic ancestor was circulating in
217 animals as well as when hMPXV-1 first emerged in humans. To estimate these timings
218 with our newly identified outgroup, we adopted the partitioned two-epoch model of
219 O'Toole *et al.* implemented in the BEAST software package, which models APOBEC3-
220 mediated evolution by allowing for a transition from a polymerase error driven
221 evolutionary rate to an APOBEC3 driven rate across the tree in a partitioned alignment
222 (see Methods).³ In our Bayesian reconstructions, we estimated that the Zx outgroup
223 shared a common ancestor with hMPXV-1 that circulated in an animal population in late
224 November 2013 (95% HPD July 2012 - March 2015) (Figure 2B).

225 With this additional phylogenetic information of the Zx outgroup, we also estimated that
226 the transition to sustained human transmission, representing the time of emergence in
227 the human population, occurred in August 2014 (95% HPD 3 December 2013 - 25 March
228 2015) (Figure 2B). Our estimate is ~13.5 months earlier than previous reports, though the
229 credible intervals overlap.³ When the highly informative Zx sequences are excluded from
230 the phylogeny, our estimate for the transition to sustained human-to-human transmission
231 shifts to mid-September 2015 [95% HPD: January 2015 to May 2016], aligning closely
232 with the estimates from O'Toole *et al.* We estimated that the tMRCA of hMPXV-1 was
233 August 2015 (95% HPD 95% HPD 12 December 2014 - 18 March 2016), representing
234 the time at which hMPXV-1 started to diversify in humans (Figure 2B). Our estimate is
235 ~seven months earlier than previous, though credible intervals overlap.³

236 Notably, our new Zx sequences were sampled in southern Abia State close to Cross River
237 and Akwa-Ibom State bordering Cameroon, where the previous zoonotic outgroup
238 KJ642617 was also sampled in 1971. As both zoonotic outgroups were sampled in Abia
239 over a fifty year time span, this suggests that the precursor lineage of hMPXV-1 may have
240 circulated in an animal population in the south for decades before the recent emergence.
241 In our Bayesian reconstructions, we found that the Zx zoonotic outgroup diverged from
242 KJ642617 in early 1968 (95% HPD January 1966 - March 1970) (Figure 2A). This
243 suggests that the hMPXV-1 precursor lineage circulated in an animal population in Abia
244 or southern Nigeria for around 50 years.

245 Taken together, our findings indicate that the ancestor of hMPXV-1 circulated in animals
246 in the southern state Abia for less than a year before emergence. This is consistent with
247 the epidemiological data, which shows that the southern states were the epicenter of the
248 early stages of the Nigerian mpox outbreak (Figure 1C). On emergence, hMPXV-1
249 circulated cryptically in the human population in Nigeria for approximately three years
250 before detection in September 2017, and more than seven years before disseminating
251 globally during the B.1 multi-country outbreak in 2022.

252 **Southern Nigeria drove viral spread**

253 Our results support that the zoonotic progenitor of hMPXV-1 likely circulated in southern
254 Nigeria, in the forested border regions. Nevertheless, the precise geographic origin of
255 hMPXV-1's emergence and the subsequent outbreak remains undetermined. Towards
256 investigating this, we used discrete and continuous phylogeographic reconstructions on
257 a state and regional level. We found that both the reconstructions support that hMPXV-1
258 likely originated in Rivers State in the South South Region (Figure 3A, Posterior = 0.97,

259 Extended Data Figure 1). Notably, this is consistent with our sampling of the closest
260 zoonotic outgroup in the neighboring southern Abia state and the epidemiological data
261 (Figure 1A, C).

262 The epidemiological data indicates that Nigeria's southern states were the early epicenter
263 for the mpox epidemic, with the northern states only reporting a significant number of
264 cases after the resurgence in 2022 (Figure 1A). However, it is not known whether there
265 was under-ascertained and unsampled transmission outside of the southern states before
266 the resurgence. It is also not clear which states contributed to interstate viral
267 dissemination and how these patterns may have shifted across the different epidemic
268 phases. We used our phylogeographic reconstructions to investigate these
269 spatiotemporal dynamics of hMPXV-1 within Nigeria. We found that Rivers State was
270 also the primary source of interstate viral exports across the epidemic, with an estimated
271 75 viral introductions originating in Rivers (95% HPD: 70-84) (Figure 3 B, Extended Data
272 Figure 1). The highest number of viral exports from Rivers spread to other South South
273 states, followed by the South East and South West (Figure 3B, Extended Data Figure 2).
274 Overall, neighboring Imo, Bayelsa and Lagos in the South West had the highest number
275 of introductions from Rivers. The remainder of the South South states as well as the South
276 East and South West states were all equivalently the second highest source of viral
277 exports overall.

278 We found that all introductions in the early epidemic originated in Rivers State (Figure
279 3C). Viral spread from Rivers into neighbouring South South states such as Bayelsa and
280 Imo, as well as Lagos in the South West, occurred as early as 2016 (Figure 3C, Extended
281 Data Figure 3). This is consistent with the epidemiological data, with the first case

282 reported in southern Bayelsa on 11 September 2017 (Figure 1C). All save one sampled
283 introductions into northern states occurred in the later phase of the epidemic, after the
284 resurgence towards 2022 (Figure 3C, Figure 1C). This spatiotemporal pattern was
285 consistent across our discrete and continuous phylogeographic reconstructions on both
286 a regional and state level (Figure 3D, Extended Data Figures 1-3).

287 To investigate how widespread hMPXV-1 transmission was by the time the outbreak was
288 declared on 22 September 2017, we performed a continuous phylogeographic
289 reconstruction. We found that the virus had spread more than 500 km beyond Rivers
290 State into Bayelsa, Imo, Delta, Edo, FCT, and Lagos before the first case was detected
291 on 11 September 2017 (Figure 3D). Collectively, this suggests that the human epidemic
292 originated in Rivers State, with early spread of the virus to neighboring South South and
293 South East states and Lagos before outbreak declaration, and with delayed dispersal to
294 the north.

295 Though our findings suggest that River state was the dominant source of viral exports, it
296 is not clear whether cases across Nigerian states were continuously seeded by re-
297 introduction from Rivers, or whether there were also locally persistent transmission chains
298 in other regions sustaining local epidemics. Towards understanding the respective
299 contribution of persistence and introductions, we investigated the persistence of
300 transmission chains in each state. We found that hMPXV-1 has persistently circulated in
301 Rivers from emergence onwards (Figure 4 A, B). hMPXV-1 diversified in Rivers State for
302 more than two years before the first case was reported in Bayelsa on 11 September 2017
303 (Figure 4A, Extended Data Figure 4).^{1,10} When the outbreak was declared, transmission
304 chains had already been established in 11 states outside of Rivers (Figure 4A). Delta in

305 the South South had the second longest persistence of a transmission chain at
306 approximately four and a half and three years, followed by the earliest chain established
307 in Lagos (Figure 4 A, B). Outside of Rivers State and the early chains in Delta and Lagos,
308 the longest persistence was estimated for lineages introduced during the period of low
309 reported incidence in 2018-2021, when sampling was sparse (Figure 4B, 1C).

310 We found that persistence was the primary driver of the epidemic in Rivers State, relative
311 to repeat introductions (Figure 4A, C). However, the percentage of transmission chains
312 persistently circulating was dynamic over time in other South South states (Figure 4 D).
313 Transmission chains seeded by Rivers State early in the epidemic in the South South,
314 South West and South East only persisted locally for less than two years, excluding the
315 first transmission chains established in Bayelsa, Delta and Enugu (Figure 4 A, B). There
316 was a significant increase in the number of transmission chains circulating during the
317 resurgence of cases towards 2022 (Figure 4C). This is consistent with the increased viral
318 exports during this period (Figure 3C), seeding new transmission chains that drove local
319 surges across Nigeria (Figure 1C, 4A). Transmission chains from the later stage of the
320 epidemic were predominantly introduced from Rivers, and persisted for less than two
321 years (Figure 4A). However, it is unclear whether this pattern persists past the end of our
322 sampling frame. There was no evidence for significant persistence in Northern states prior
323 to the later phase of the epidemic, which is consistent with the low reported incidence and
324 delayed viral spread observed (Figure 4 A, 3D, 1C). Altogether, this further supports that
325 Rivers State acted as the persistent source for the epidemic, while local epidemics in
326 other states were largely driven by repeat introductions.

327 To account for uneven sampling across states, we also performed our phylogeographic
328 analyses at the regional level. We observed a consistent pattern to our state-level
329 analyses: early and predominant spread from the South South, with initial spread to the
330 South East and South West. There was strong evidence of persistent circulation in the
331 South South, with local epidemics in all other regions driven by repeated introduction from
332 the South South (Extended Data figures 1-4).

333 **Rivers State was main source of spread**

334 Our phylogeographic reconstructions consistently support a spatiotemporal pattern of
335 early viral spread between and then from southern states. To identify potential drivers of
336 this pattern, we used a phylogeographic generalized linear model that integrates
337 covariates of spatial spread to determine what factors were associated with hMPXV-1
338 dispersal. We incorporated covariates in our model including epidemiological,
339 demographic, geographic and economic variables, as well as location-specific predictors
340 that capture a pairwise binary transition across different states (see Extended Data table
341 1).

342 Of the 19 covariates analyzed, we found that the main predictor that positively affected
343 viral dispersal was whether the lineage originated in Rivers State ($BF > 50$) (Figure 5A, B).
344 There was no support for the residual covariates that assessed the deviations of sampling
345 numbers relative to epidemiological cases (Figure 5A). This suggests that the out-of-
346 Rivers pattern is robust and was not due to sampling heterogeneity across locations. This
347 finding supports our previous analyses highlighting Rivers' early and dominant role in the
348 spread of hMPXV-1 from emergence onwards (Figure 5B). The population density in the

349 destination was also positively associated with hMPXV-1 dispersal ($BF > 15$), which is
350 consistent with the principles of a gravity model in epidemiology (Figure 5A).^{27,28}

351 Discussion

352 The ongoing zoonotic transmission in the forested border regions of Nigeria and
353 Cameroon identified in this study underscores the continuous risk of MPXV emergence
354 and/or re-emergence. Furthermore, this risk is likely still significantly underestimated
355 owing to under-ascertainment of cases and sparse genomic data. Concurrently,
356 consensus evidence now strongly supports that MPXV Clade IIb is no longer solely a
357 zoonotic disease but is sustained in a human subpopulation in Nigeria, where it has been
358 circulating cryptically for nearly a decade. The drivers behind this emergence in humans
359 remains uncertain, however. It is not clear why the initial zoonotic transmission event did
360 not simply result in a self-limiting case or transmission chain as all previous zoonotic
361 infections. It is most likely that the zoonotic transmission occurred in a more
362 interconnected, mobile subpopulation with greater connectivity to densely populated
363 urban areas and more probable onward transmission driven by behavioral or
364 demographic factors as observed in the multi-country B.1 outbreak and the recent
365 outbreak in the eastern DRC.^{11,29}

366 In this study, all of our Cameroonian sequences were sampled from individuals living in
367 rural areas in the South-West and North-West regions, whereas our four zoonotic
368 sequences from Nigeria were sampled in the southern states of Akwa Ibom and Abia.
369 The North-West and South-West of Cameroon is dominated by the Cameroonian
370 Highlands and Guinean Lower forest ecosystems, which extends into southern Nigeria.¹⁵

371 These cross-border forest ecosystems are areas of high biodiversity, hosting a wide
372 range of potential hosts susceptible to MPXV.^{5,22–26} In these regions, agricultural
373 activities, subsistence hunting, the consumption and trade of wild game, as well as human
374 settlements and movement in forested areas owing to internal displacement associated
375 with conflict heightens exposure at the human-animal interface.^{2,4} Our findings support
376 that the cross-border forest ecosystems likely hosts the shared reservoir driving viral
377 dispersal between the countries. It is also likely that extant Clade IIb originated in this
378 region. In light of this, we need improved surveillance in the wildlife population in the forest
379 systems to better understand the transmission and maintenance of MPXV in animal
380 hosts. Additional sampling is likely to reveal significant unsampled viral diversity in the
381 reservoir, as observed in the deep divergences just in the sampled tree. It is also likely
382 that enhanced surveillance in the human population in border-adjacent communities at
383 the animal-human interface will reveal more zoonotic transmission events. Our results
384 should therefore be interpreted within the limits of our sample, which only represents 4.2%
385 and 7.5% of all suspected mpox cases in Nigeria and Cameroon respectively.

386 Our study provides critical insights to facilitate strategic public health interventions in the
387 human epidemic in West Africa. Across our phylogeographic reconstructions, we found
388 that Rivers State and other South South states in Nigeria served as early, dominant and
389 persistent sources of viral export. Interventions should accordingly be targeted to these
390 regions. Notably, we found evidence of prolonged cryptic circulation and geographic
391 expansion before detection in these regions, emphasizing the need for enhanced
392 surveillance and improved diagnostic and surveillance infrastructure in these regions.
393 Enhanced surveillance of cases is required to characterize the underlying transmission

394 network and associated risk factors, allowing for targeted interventions before the
395 epidemic becomes more generalized.

396 However, controlling ongoing mpox epidemics in Africa is impeded by inequities of access
397 to resources such as diagnostics, vaccines and therapeutics.^{30,31} Without access to
398 therapeutics and vaccines, transmission cannot be reduced in either the sustained human
399 epidemic or in populations at high risk for recurrent spillovers from the reservoir. Ongoing
400 zoonotic and human transmission in Africa does not only increase the probability of re-
401 emergence and future multi-country outbreaks but, vitally, results in preventable morbidity
402 and mortality in endemic countries. The global community can no longer afford to neglect
403 mpox in Africa or perpetuate inequities in therapeutic access in our vulnerably connected
404 world.

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471 **Figure 1 Drivers of mpox cases in Cameroon and Nigeria:** **A)** Map of Nigeria and Cameroon
472 showcasing the ecological setting of zoonotic MPXV in Nigeria and Cameroon. The forest cover is
473 highlighted in green. The border between Nigeria and Cameroon is annotated in red, with the Rivers Niger
474 in Nigeria and Sanaga in Cameroon highlighted in light blue. Our sampling sites in Cameroon are annotated
475 in orange, and states of interest annotated with highlighted borders. Sampling sites of zoonotic Nigerian
476 sequences are annotated in blue. **B)** Geopolitical regions of Nigeria, with Abia and Rivers State highlighted
477 with red borders. **C)** Epidemiological incidence of mpox cases in Nigeria coloured by geopolitical region
478 (top panel), relative to our Nigerian genomic dataset's temporal and geographic distribution (bottom panel).
479 **D)** Clade IIb phylogeny with reconstructed SNPs mapped onto branches. We performed ancestral state
480 reconstruction across our Clade IIb phylogeny to map SNPs to their relevant branches. We annotated
481 APOBEC3 characteristic mutations i.e. CT or GA in the correct dimer context along branches and calculated
482 their relative proportion across internal branches (Figure 1F). APOBEC3 mutations along the branches are
483 annotated in yellow and red, with the remainder in gray and black. The hMPXV-1 Clade (Lineage A) is
484 highlighted in the light blue box, with lineage annotation in text. Our new zoonotic outgroup sequences are
485 annotated as "Zx". Our sequences (N=118) are highlighted as enlarged tips. The lineage sampled from
486 Cameroon and Akwa Ibom in Nigeria is annotated in orange. **E)** Lineage distribution of our hMPXV-1
487 sequences. **F)** The number of APOBEC3 SNPs out of all mutations for the zoonotic lineage from Cameroon
488 and Akwa Ibom, the remaining zoonotic subtree (KJ642617 and Zx annotated in Figure D) and the hMPXV-
1 subtree (highlighted and annotated in Figure D).

489 **Figure 2: Time-resolved global phylogeny of Clade IIb** **A)** The time-resolved global phylogeny of Clade
490 IIb. Our new zoonotic outgroup from Abia is annotated as "Zx". Distributions on the x-axis represent the
491 tMRCA of the color matching node as annotated. Sublineages of Lineage A in hMPXV-1 are collapsed for
492 visualization. **B)** Detailed view of Zx outgroup and hMPXV-1, with timing of outgroup circulation, transition
493 to sustain human transmission and tMRCA(hMPXV-1) indicated on x-axis and in text.

494 **Figure 3 Spatiotemporal spread of hMPXV-1 in Nigeria:** **A)** Phylogeographic reconstruction of the
495 spatiotemporal spread of Clade IIb in Nigeria. The branches of the Maximum Clade Credibility tree (MCC)
496 are coloured by source region, as per legend. SS: South South; SW: South West; SE: South East; NW:
497 North West; NE: North East' NC: North Central. **B)** Distribution of total number of introductions by state
498 from each start location summarised across the posterior of 10 000 trees, annotated as per legend in colour,
499 to each end location on the y-axis. Distribution represents the 95% highest posterior density. The regions
500 of the end location state on the y-axis are highlighted in colour in the plot background as per the legend. **C)**
501 The distribution of the number of introductions across time by state summarised across the posterior of 10
502 000 trees. The end location state is coloured by region, as per legend. The start location is highlighted by
503 transparency: all introductions originating from Rivers State are presented with no transparency, whereas
504 introductions originating from other states are more transparent. **D)** Continuous phylogeography of hMPXV-
505 1 spatiotemporal spread across Nigeria, with timing of viral dissemination highlighted by colour range as
506 per legend.

507 **Figure 4 Transmission dynamics of hMPXV-1 in Nigeria:** **A)** Persistence of transmission chains across
508 all Nigerian states sampled. Individual chains are coloured by region, with the boundary of each individual
509 state highlighted by a filled background and annotated in text on the right. The start of each transmission
510 chain is coloured by its state of origin. The red line indicates the date of report for the first case in Bayelsa
511 on 17 September 2017. **B)** The persistence in years of each transmission chain across its time of origin
512 summarised across the posterior of 10 000 trees, coloured by region. **C)** The number of transmission chains
513 circulating across all regions across time, calculated by a month-sliding window. The red line indicates the
514 date the outbreak was declared on 22 September 2017. SS: South South; SW: South West; SE: South
515 East; NW: North West; NE: North East' NC: North Central. **D)** The percentage of transmission chains
516 persisting across time for South South states excluding Rivers. Colour bands represent 95% HPD.

517 **Figure 5 Drivers of spatiotemporal patterns of hMPXV-1 in Nigeria:** **A)** The Generalized Linear Model
518 (GLM) coefficients for spatial spread covariates, with corresponding Bayes Factors. Significant covariates
519 are highlighted in purple. **B)** Phylogeographic reconstruction of the migratory pattern of hMPXV-1 showing
520 Rivers State as the origin (highlighted in purple) and other Nigerian states in grey in accordance to the
521 posterior probability of location.

522 **Methods:**

523 **Ethics declaration**

524 No ethical approval was required for this study as it is based on data from Nigeria's
525 national surveillance program, collected by the Nigeria Centre for Disease Control and
526 Cameroon's national surveillance program, for which Centre Pasteur du Cameroun (CPC)
527 is the National Reference Laboratory (NRL). Under both programs, individual written or
528 oral informed consent was obtained from all suspected mpox cases. Informed consent
529 for children was obtained from their parents or recognized guardians.

530 **Sampling**

531 Samples from Nigeria were collected by laboratory personnel and Local Government
532 Area (LGA) Disease Surveillance and Notification Officers (DSNOs) equipped with
533 appropriate personal protective equipment (PPE), adhering to the guidelines outlined in
534 the Nigeria Centre for Disease Control and Prevention (NCDC) National Monkeypox
535 Public Health Response Guidelines.³² Samples comprised: swabs from the exudate of
536 vesicular or pustular lesions, lesion crusts obtained during the acute rash phase, whole
537 blood collected in ethylenediaminetetraacetic acid (EDTA) or plain/non-anticoagulated
538 tubes. All samples were labeled with case information and stored at 2-8°C during
539 transport to either the NCDC National Reference Laboratory (Gaduwa-Abuja) or the
540 Central Public Health Laboratory (Yaba-Lagos). On arrival, the crusts and swabs were

541 eluted, while the serum/plasma was separated from the red blood cells. Subsequently,
542 these components were stored at ultralow temperatures of $\leq -70^{\circ}\text{C}$ at the NCDC
543 biorepository. Our samples are predominantly collected from the South South and South
544 East regions, and do not include the period closer to the estimated emergence or the start
545 of the epidemic in 2017. However, as Southern regions represented the highest number
546 of cases throughout the epidemic from 2017 to the 2022 resurgence, it is unlikely that the
547 geographic distribution of samples represents a strong sampling bias.

548 From 2018 to 2022, a total of 28 human mpox cases were identified by the national
549 surveillance program in Cameroon. Suspected cases were identified by community health
550 workers (CHWs) or clinicians and samples collected by a Rapid Response and
551 Investigation Team (RRIT) equipped with appropriate personal protective equipment
552 (PPE) under the guidance of Regional Centers for Epidemic Prevention and Control
553 (CERPLE) and following the national guidelines for surveillance and response to mpox
554 outlined by the the Department for the Control of Disease, Epidemics and Pandemics
555 (DLMEP) of the Cameroonian MoH. Cases were confirmed by standard and genotyping
556 real-time PCR at the CPC which host the NRL for mpox in Cameroon.⁴ From the total
557 cases, we selected ten for sequencing based on Clade genotyping by rtPCR, cycle
558 threshold (value < 30) and sample availability. Samples were screened for DNA
559 concentration and quality (total DNA $> 500 \text{ ng}$ and absorbance ratio > 1.8 260/230 and
560 260/280). Samples represented maculopapular vesicles, skin crust or blood samples.

561 **Genome Sequencing**

562 Enrichment bead-linked transposomes was used to fragment the extracted DNA and
563 enriched using the Illumina- rna -prep enrichment with the VSP panel. Libraries were
564 quantified using dsDNA BR Assay, normalized to a concentration of 0.6nM and
565 sequenced on the Illumina NovaSeq 6000 platform with a read length of 151 base pair
566 paired end at the African Centre of Excellence for Genomics of Infectious Diseases
567 (ACEGID), based at Redeemer's University, Ede, Nigeria.

568 **Genome Assembly**

569 We performed initial *de novo* assembly with the viral-ngs pipeline, followed by reference
570 based assembly with an in-house pipeline (<https://github.com/broadinstitute/viral-pipelines>).³³ Briefly, we mapped reads against a Clade IIb reference genome
571 (NC_063383, an early hMPXV-1 genome from Nigeria) with *bwa-mem*³⁴, and called
572 consensus using samtools³⁵ and iVar.³⁶

574 **Genomic dataset curation**

575 We combined our 118 genomes with all high-quality, publicly available Clade IIb MPXV
576 genomes from Genbank (as of August 2023). We included a single representative of the
577 multi-country outbreak lineage B.1, as it was not our primary focus. We also included a
578 Clade IIA outgroup (DQ011153) to root the tree.In total, our dataset consists of 199
579 sequences.

580 **Phylogenetic Analysis**

581 We aligned our dataset to the Clade IIb reference genome (NC_063383) using the
582 'squirrel' package (<https://github.com/aineniamh/squirrel>) developed by O'Toole *et al.*³

583 The alignment was trimmed, and the 3' terminal repeat region and regions of repetition
584 or low complexity were masked. We also masked clustered mutations as identified with
585 the quality control mode of the squirrel package.

586 We investigated the preliminary placement of our sequences in a phylogeny of all
587 available mpox genome sequences from Genbank across clades. We reconstructed the
588 complete MPXV phylogeny with IQ-TREE v2.0, under the Jukes-Cantor substitution
589 model.³⁷ We identified three B.1 lineage sequences in our dataset. To investigate whether
590 these sequences represented re-importations to Nigeria, we reconstructed a phylogeny
591 with 769 B.1 genomes from Genbank. We confirmed the sequences represented re-
592 importations of B.1 into Nigeria and excluded them from subsequent analyses (data not
593 shown).

594 We reconstructed a phylogeny for Clade IIb alone under the same parameters as the
595 global phylogeny. We rooted to DQ011153, a Clade IIA outgroup and removed it from the
596 tree. We collapsed all zero branch lengths. We performed ancestral state reconstruction
597 with IQ-TREE2 across the Clade IIb phylogeny.³⁷ We mapped all nucleotide mutations
598 that occurred across the phylogeny to internal branches using tree traversal, excluding
599 missing data. Additionally, we catalogued the dimer genomic context of all C→T or G→A
600 mutations, as described by O'Toole *et al.*³ We classified our sequences into lineages
601 under the nomenclature developed in Happi *et al.*¹⁸ using Nextclade.³⁸

602 Prior to Bayesian analyses we performed temporal regression to evaluate the temporal
603 signal at APOBEC and non-APOBEC sites (Extended Data Figure 5). We also assessed
604 the rate of APOBEC3 mutations accumulation per year across hMPXV-1 using a

605 Bayesian regression on the root-to-tip data of the sequences as per O'Toole *et al*
606 (Extended Data Figure 6A).³

607 **Modeling APOBEC3-mediated evolution**

608 We adopted a similar approach described by O'Toole *et al.*³ to analyze the evolutionary
609 dynamics of hMPXV-1 in the software package BEAST³⁹ with the BEAGLE high-
610 performance computing library.⁴⁰ First, we partitioned the Clade IIb alignment into two
611 distinct partitions, with a custom script by O'Toole *et al.*³ The first partition comprised
612 sites with potential APOBEC3 modifications (specifically C→T and G→A substitutions in
613 the dinucleotide context TC and GA), along with target sites (e.g. C and G) that were
614 conserved. In this partition, we masked all other sites as ambiguous nucleotides. This
615 partition represents APOBEC3 mutations relative to the target APOBEC3 sites. The
616 second partition inversely contained sites with the APOBEC3 target sites masked. The
617 APOBEC3 alignment comprised 24 680 unmasked sites, whereas the non-APOBEC3
618 alignment comprised 172 529 sites. We used the standard nucleotide GTR+G substitution
619 model with four distinct rate categories for the non-APOBEC3 partition. For the APOBEC3
620 partition, we developed a substitution process where we categorize the nucleotides as
621 modified (T) and unmodified (C). We used a two-state continuous-time Markov chain with
622 an asymmetric rate to permit C→T mutations but not the reverse.

623 We used a two-epoch model to estimate the time of MPXV's emergence in the human
624 population. Under this model, the evolutionary rate transitions from the background rate
625 (i.e. non-APOBEC3 rate, driven by polymerase error rate) to the APOBEC3 rate at a
626 specific time point tp for the APOBEC3 partition. We parameterized this transition time as
627 $tp = t\text{MRCA}(\text{Lineage A}) + x$, where x is a free parameter in BEAST representing the pre-

628 sampled transmission history before the most recent common ancestor (MRCA) of
629 sampled Lineage A viruses.³ We incorporated a local clock to scale the mutation
630 proportion attributed to APOBEC3 activity across the branches up to the transition time.
631 We allowed the non-APOBEC3 partition to evolve under the background evolutionary rate
632 across the entire phylogeny (See Extended Data Figure 6B for rate estimates). We
633 additionally used a two-phase coalescent model: the tree from the MRCA (Lineage A)
634 onward was modeled with an exponential growth model, with the earlier phase modeled
635 as a constant-population size coalescent model. For each model, we ran three
636 independent chains of 100 million states to ensure convergence, discarding the initial
637 10% of each chain as burn-in. The chains were then combined with LogCombiner. For all
638 subsequent analyses, we assessed convergence using Tracer, and constructed a
639 maximum clade credibility (MCC) tree in TreeAnnotator 1.10.⁴¹

640 **Geographic history of hMPXV-1 in Nigeria**

641 **Discrete phylogeographic analysis**

642 To investigate the spread of hMPXV-1 across Nigeria, we reconstructed the timing and
643 pattern of geographic transitions across Nigerian states under an asymmetric discrete
644 trait analyses.⁴² We used Bayesian stochastic search variable selection (BSSVS) to infer
645 non-zero migration rates and identify statistically supported migration routes. We used a
646 non-parametric skygrid coalescent tree prior, with 12 change points distributed over 10
647 years as described above.⁴³ We combined three independent MCMC runs of 50 million
648 states each, sampling every 2000 states and discarding the respective initial 10% of trees
649 as burn-in. We confirmed all ESS values are above 200.

650 We used a Markov jump counting procedure to investigate the timing and origin of
651 geographic transitions, or Markov jumps, across the full posterior to account for
652 uncertainty in phylogeographic reconstruction.⁴⁴ We used the
653 TreeMarkovJumpHistoryAnalyzer from the pre-release version of BEAST 1.10.5 to obtain
654 the Markov jumps from posterior tree distributions.⁴⁵ Using the tree distribution annotated
655 with Markov jumps, we performed the persistence analysis on a month-to-month interval
656 to calculate the percentage of lineages that persisted in their ancestral state for each
657 Nigerian state and region.⁴⁵ We used the PersistenceSummarizer from the pre-release
658 version of BEAST 1.10.5.

659 We also performed all phylogeographic analyses on a regional level, to account for the
660 uneven distribution of sequences across Nigerian states. We categorized the states into
661 the six geopolitical zones of Nigeria.⁴⁶ We have a limited number of sequences from
662 Northern Nigeria, which had very low epidemic incidence from 2017 - 2022. To account
663 for this, we combined the North West and North East zones into a single North category.
664 All trees were visualized using baltic (<https://github.com/evogytis/baltic>).

665 **Continuous phylogeographic analysis**

666 We performed a continuous phylogeographic analysis to quantify the dispersal of hMPXV-
667 1 across Nigerian states. We assigned each sequence a latitude and longitude that
668 matched the local government area or village of collection. We used the two-epoch and
669 skygrid coalescent model described above, with a Cauchy distribution to model the
670 among-branch heterogeneity in dispersal velocity.⁴⁷ We ran two independent MCMC
671 chains of 50 million states, sampling every 2000 states. We combined the chains after
672 discarding 10% of the states as burn-in.

673 **Discrete phylogeographic analysis using a sparse General Linear
674 Model (GLM)**

675 To investigate the drivers of the transmission dynamics of the hMPXV-1 epidemic, we
676 used a sparse generalized linear model (GLM) in a continuous-time Markov chain
677 (CTMC) diffusion framework.⁴⁸ We considered 19 covariates in the model, including
678 epidemiological case counts relative to the numbers of sampled genomes per locations,
679 demographic data, and geographic and economic factors (Extended Data Table 1).
680 Besides the location-specific predictors, which were encoded as binary variables to reflect
681 migration patterns, we log-transformed and standardized all other predictors. This
682 standardization involved adding a pseudo-count to each entry to ensure a robust
683 analysis.¹⁹ We ran two independent MCMC chains of 50 million iterations, sampling every
684 2000 iterations. We combined the resulting posterior distributions after removing the initial
685 10% as burn-in.

686 **Covariate collation**

687 Covariates (Extended Data table 1) included in the GLM were collected from the following
688 sources: Epidemiological data was obtained from the Nigerian CDC; Economic covariates
689 were sourced from Okeowo el al.⁴⁹; Population covariates were sourced from the Bulletin
690 of the National Bureau of Statistics⁴⁶³; HIV prevalence was obtained from the PEPFAR
691 program⁵⁰; Drug use statistics were obtained from the National Bureau of Statistics.⁵¹ The
692 distance by road travel between each states was calculated from Google Maps.

693 **Geographical metadata**

694 Administrative level 2 (admin2) metadata for the sampling location of sequences in the
695 dataset were mapped to official admin2 as found in the Global Administrative Database

696 (GADM, <https://gadm.org>). All shapes files were obtained from the FAO geoNetwork
697 (<https://www.fao.org/land-water/databases-and-software/geonetwork/en/>)

698 Data availability

699 All sequences are available on Genbank under Accession numbers PP852943 -
700 PP853055. All other data are available at <https://github.com/andersen->
701 lab/Mpox_West_Africa, excluding shape files which are available at
702 <https://www.fao.org/land-water/databases-and-software/geonetwork/en/>

703 Code availability

704 All code to run the analyses is available in <https://github.com/andersen->
705 lab/Mpox_West_Africa, excluding shape files which are available at
706 <https://www.fao.org/land-water/databases-and-software/geonetwork/en/>

707 Methods References

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785 Competing interest declaration

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789 **Extended Data Figure 1: Phylogeographic analyses of Clade IIb in Nigeria.** The branches of the MCC
790 are coloured by source state, as per legend. Non-Rivers state were grouped by region. SS: South South;
791 SW: South West; SE: South East; NW: North West; NE: North East' NC: North Central.

792 **Extended Data Figure 2: Total number of introductions by region from each start region**, summarised
793 across the posterior of 10 000 trees, annotated as per legend in colour, to each end location on the y-axis.

794 **Extended Data Figure 3: The distribution of the number of introductions across time by region**,
795 summarised across the posterior of 10 000 trees. Distribution represents the 95% highest posterior density.
796 The end location state is coloured by region, as per legend. The start location is highlighted by transparency:
797 all introductions originating from the South-South region are presented with no transparency, whereas
798 introductions originating from other regions are transparent.

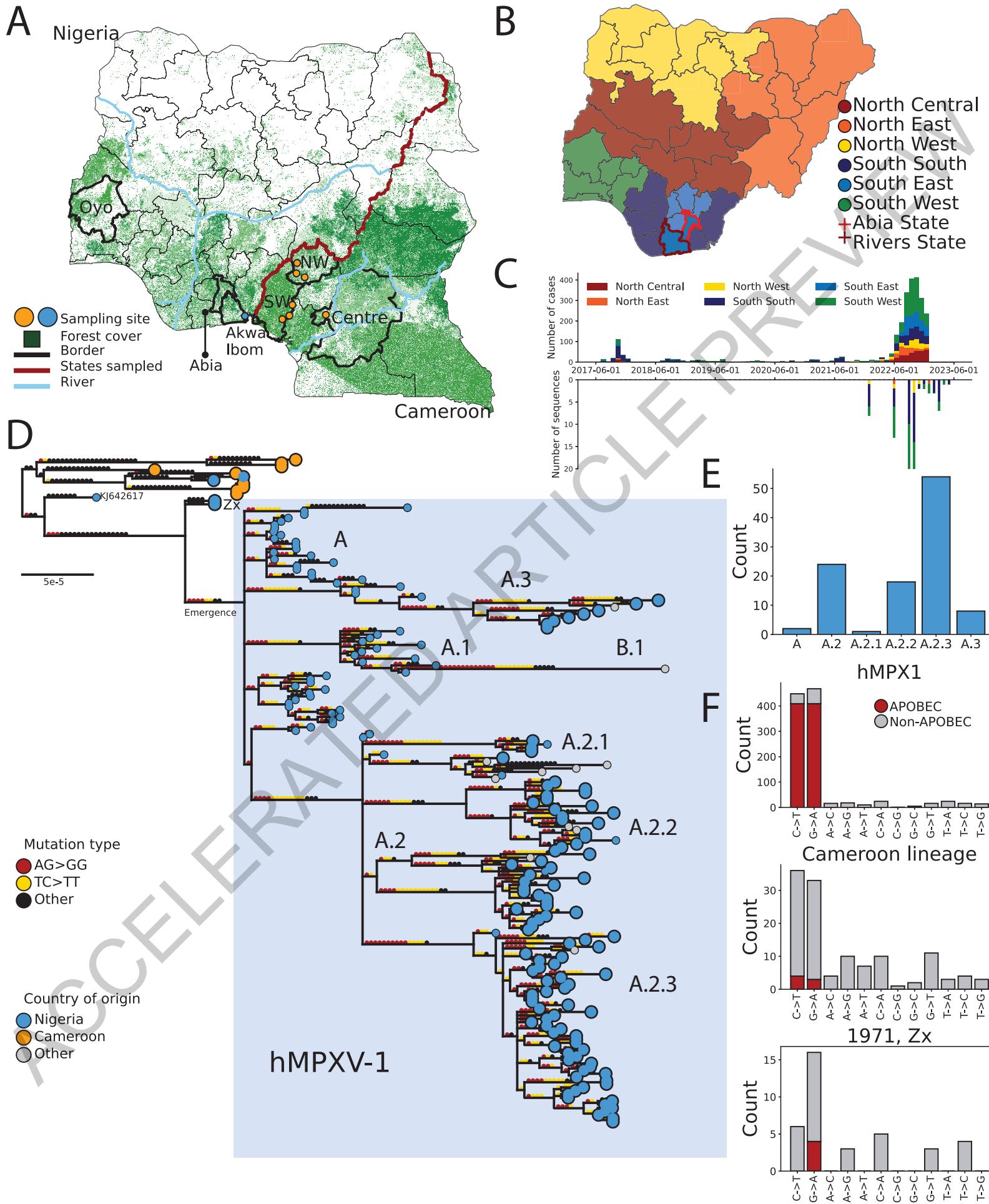
799 **Extended Data Figure 4: Persistence of transmission chains across all regions**, as annotated in text.
800 The start of each transmission chain is coloured by its region of origin. The red line indicates the date of
801 report for the first case in Bayelsa.

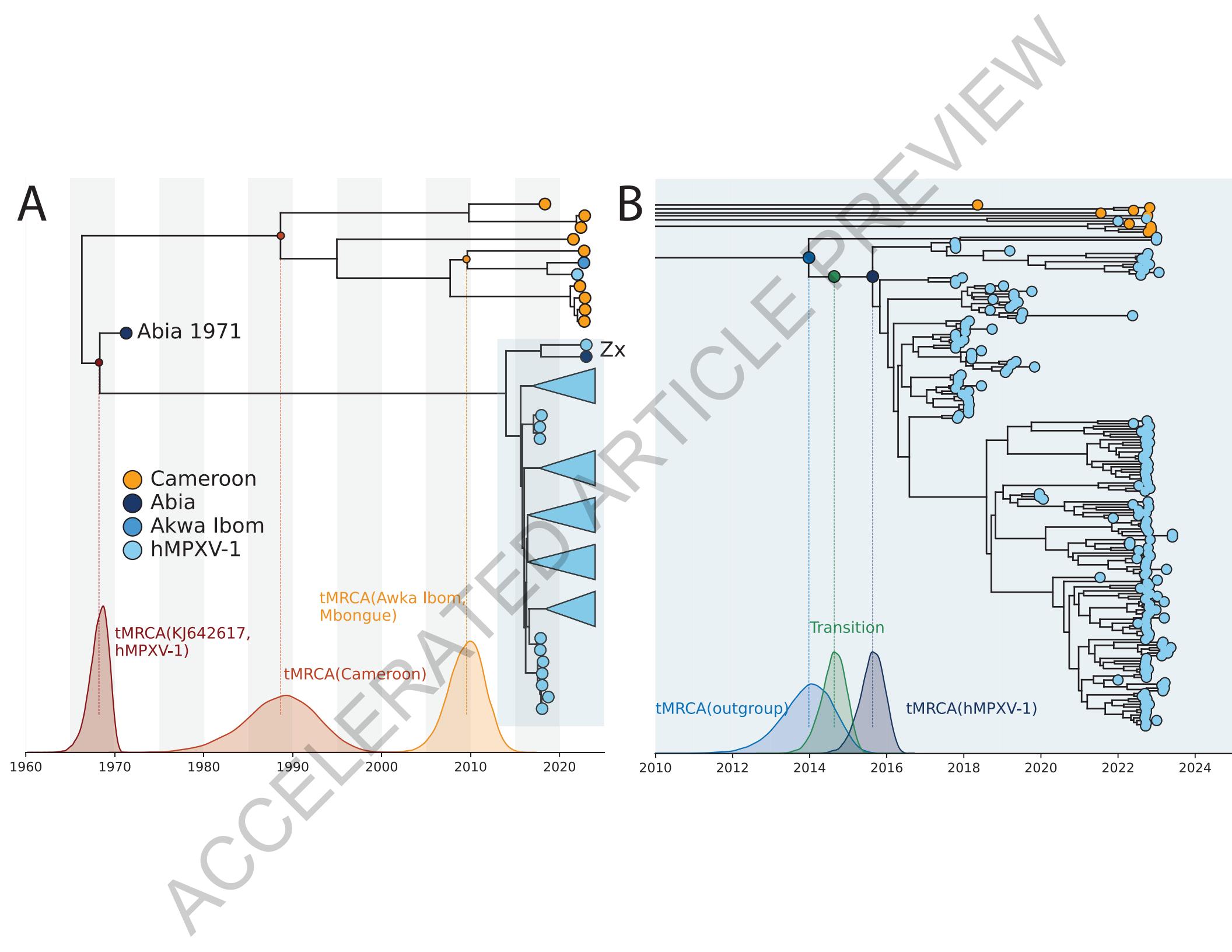
802 **Extended Data Figure 5: Root-to-tip regression of the accumulation of 1) non-APOBEC 2) APOBEC
803 and 3) all mutations (APOBEC and non-APOBEC combined) across the human epidemic (hMPXV-
804 1) and the zoonotic parts of the tree.** Each data point represents a sequence in the tree. The hMPXV-1
805 subtree's sequences are displayed in blue, and the zoonotic sequences in green. Lines represent the linear
806 model fitted to the respective (hMPXV-1 and zoonotic) data.

807 **Extended Data Figure 6: APOBEC and non-APOBEC driven clock rates. A)** Root-to-tip regression of the
808 accumulation of APOBEC3 mutations across the human epidemic. Line represents mean and error bands represent
809 the 95% highest posterior densities **B)** Comparison of the evolutionary rates under the two-epoch partitioned model
810 summarised across the posterior of 10 000 trees. Distribution represents the 95% highest posterior density,
811 and boxplot represents 25th, 50th and 75% percentile.

812 **Extended Data Table 1: Covariates for GLM analyses**

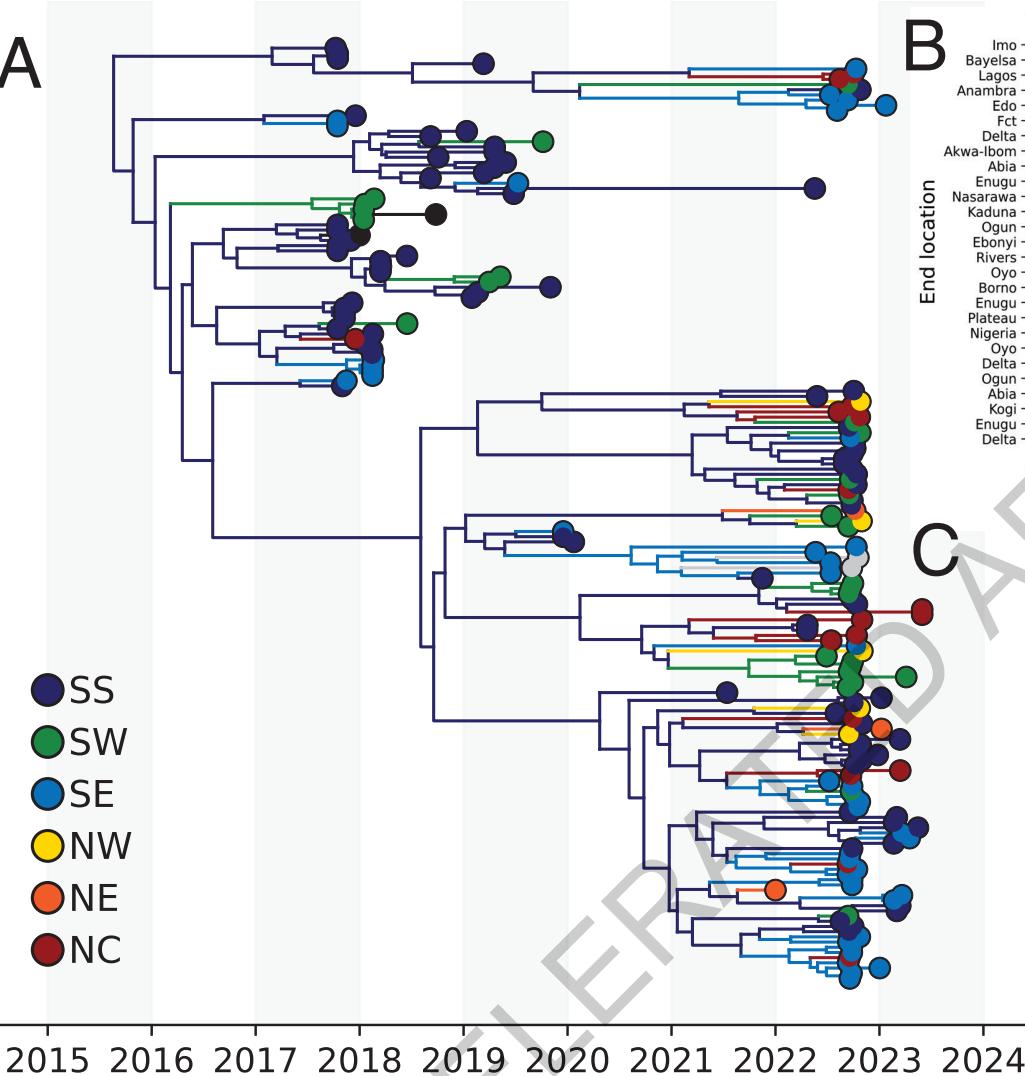
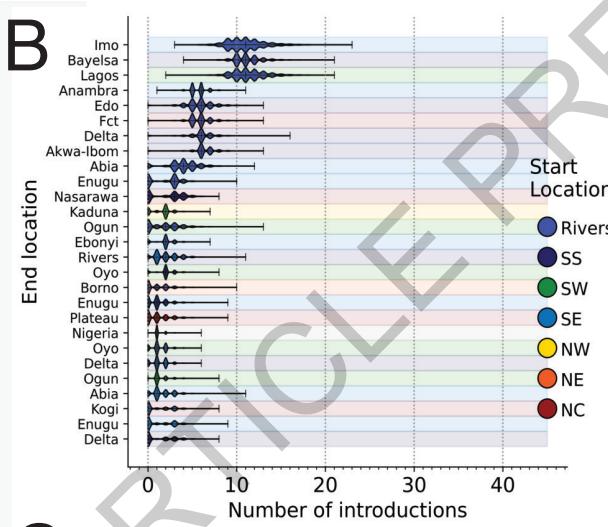
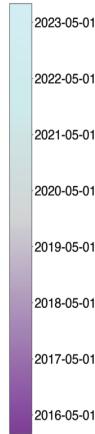
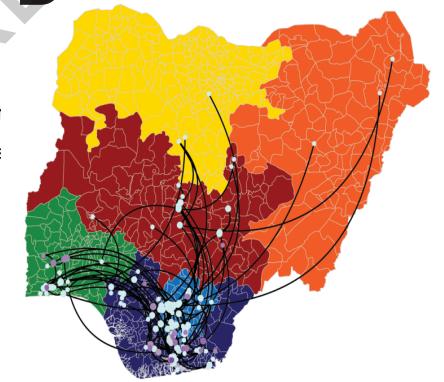
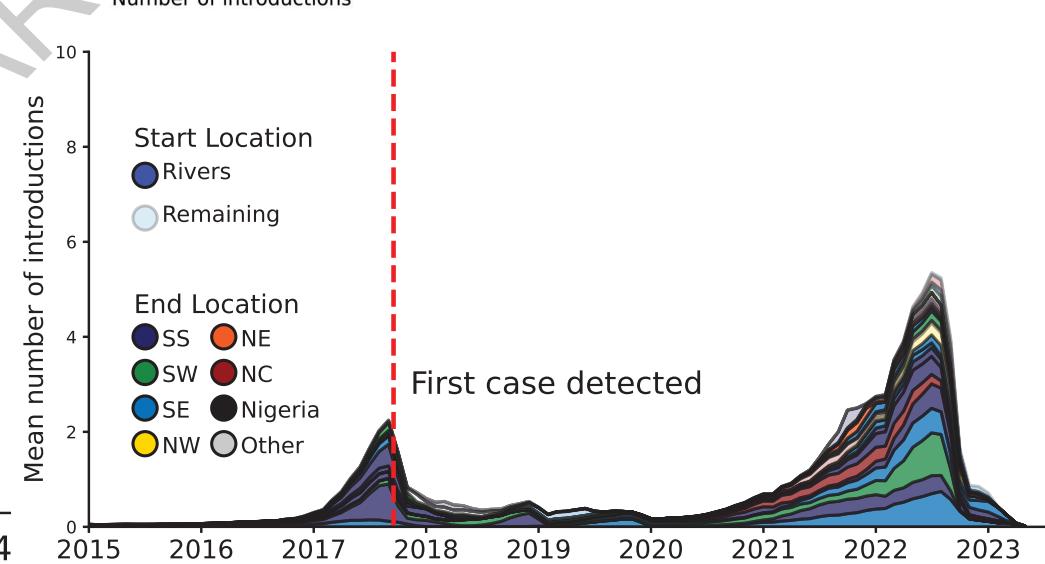
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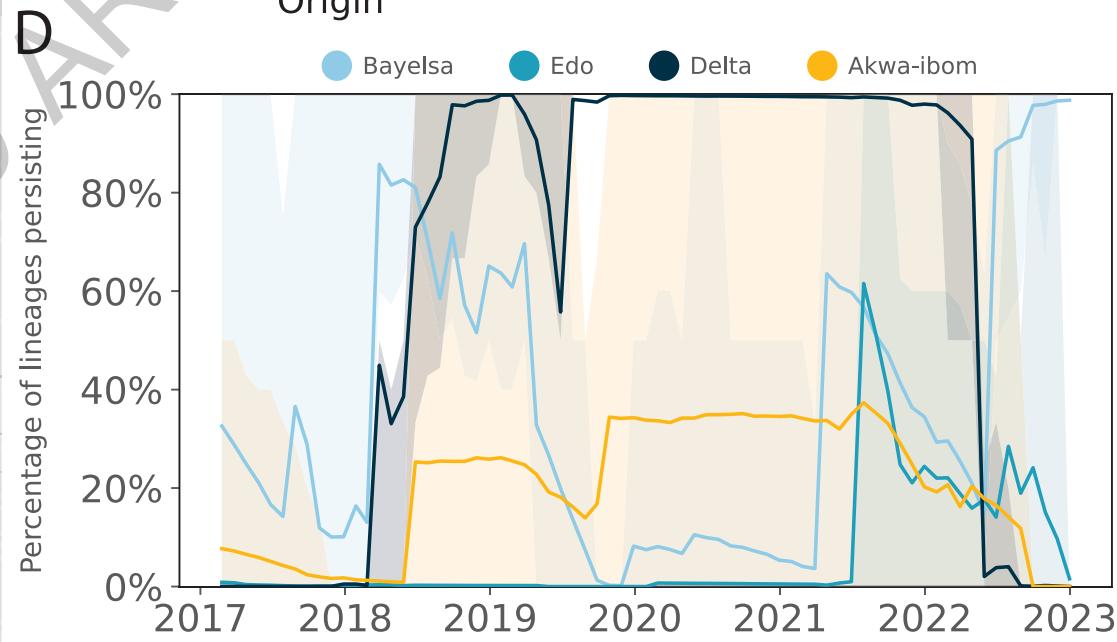
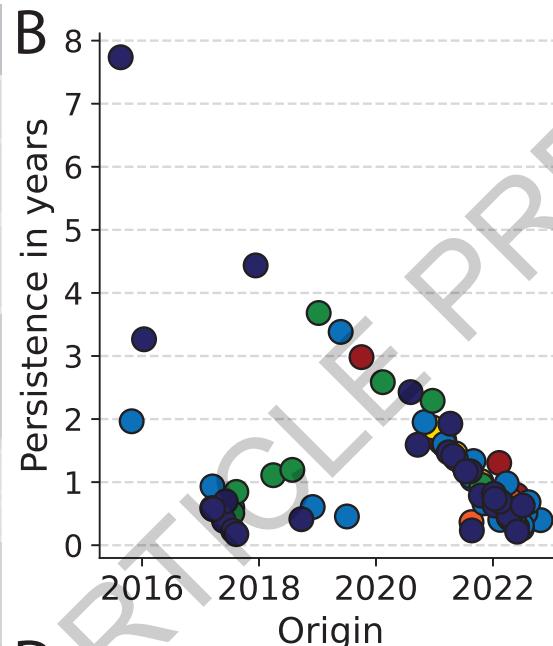
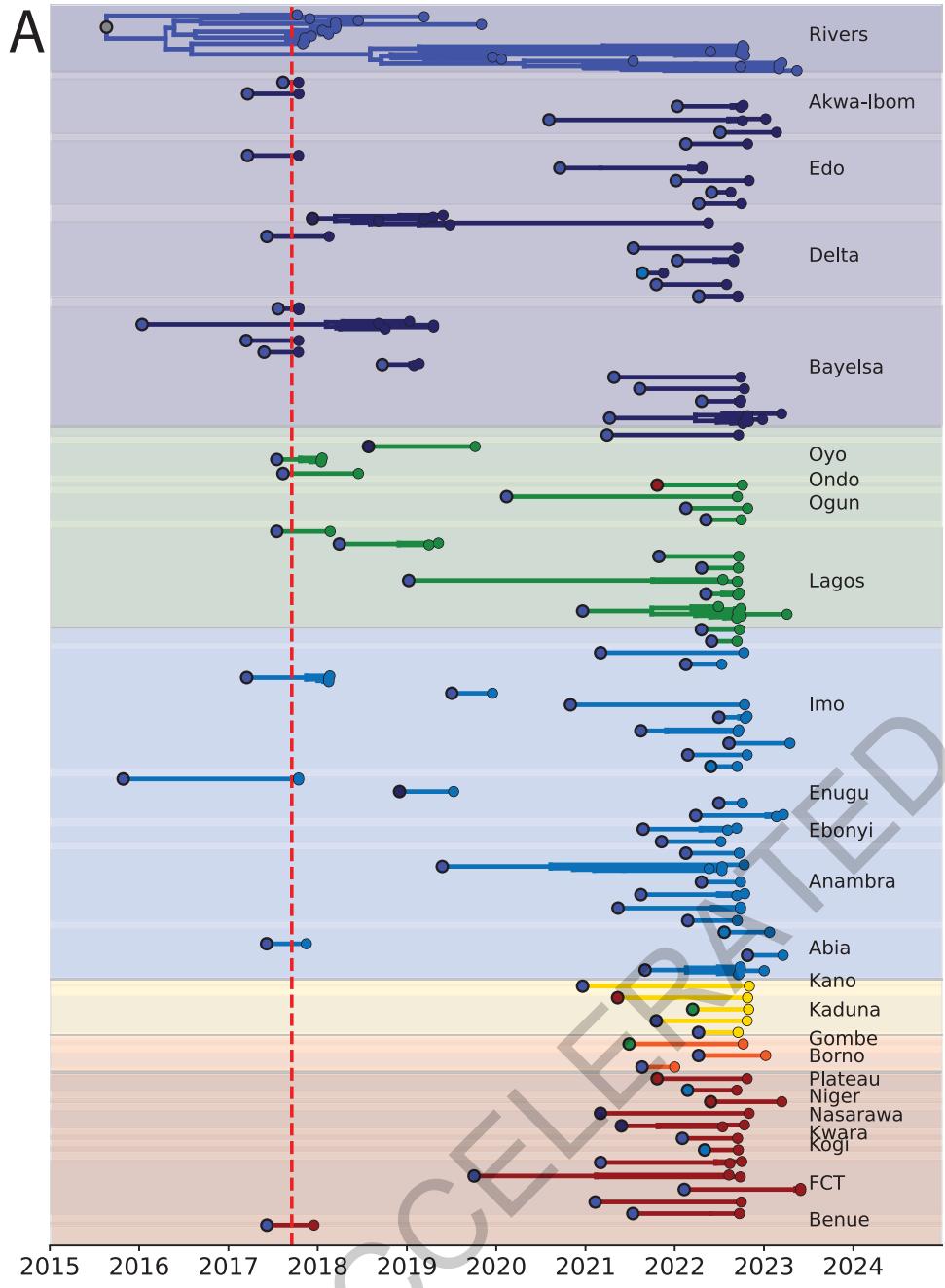


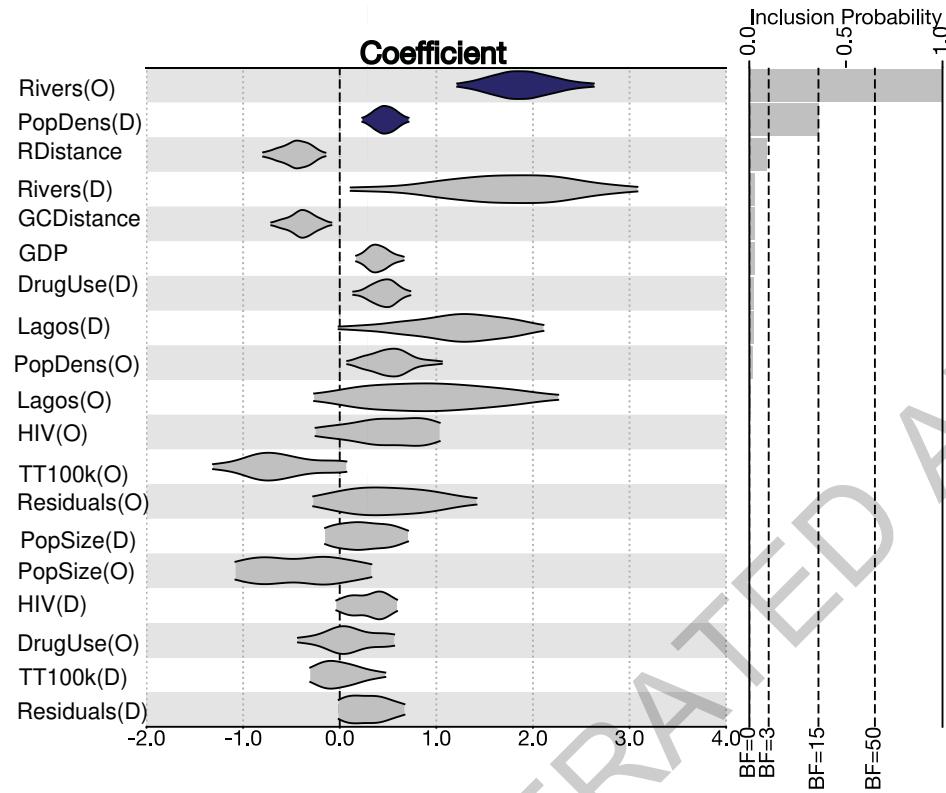
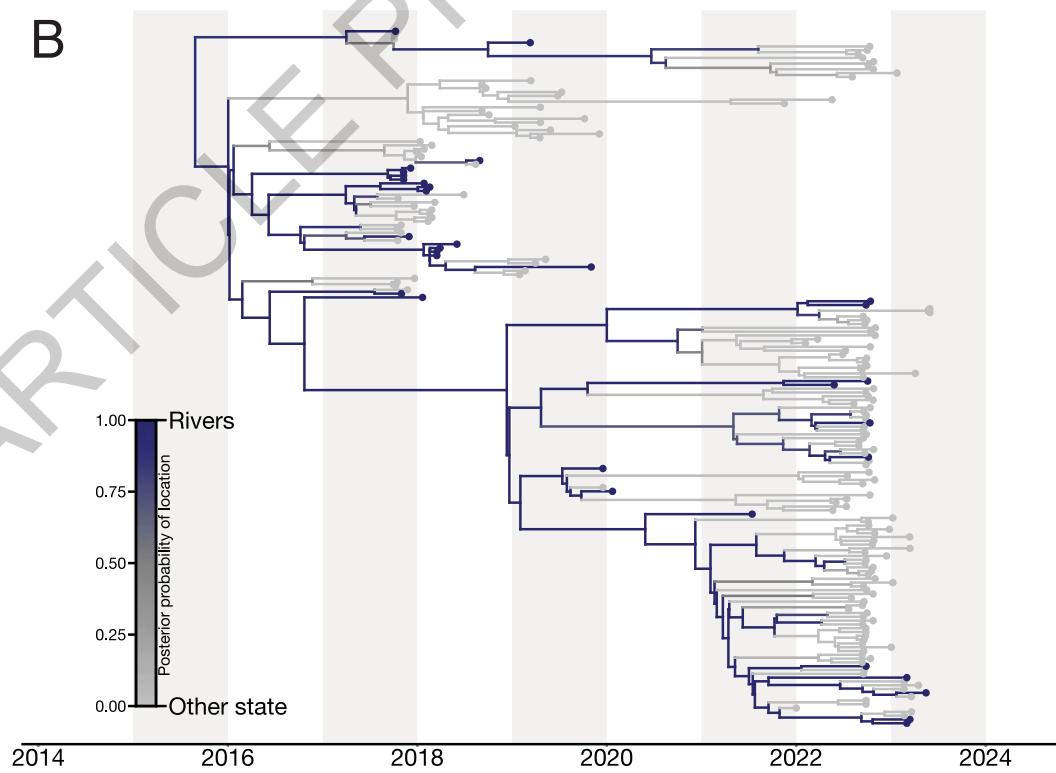


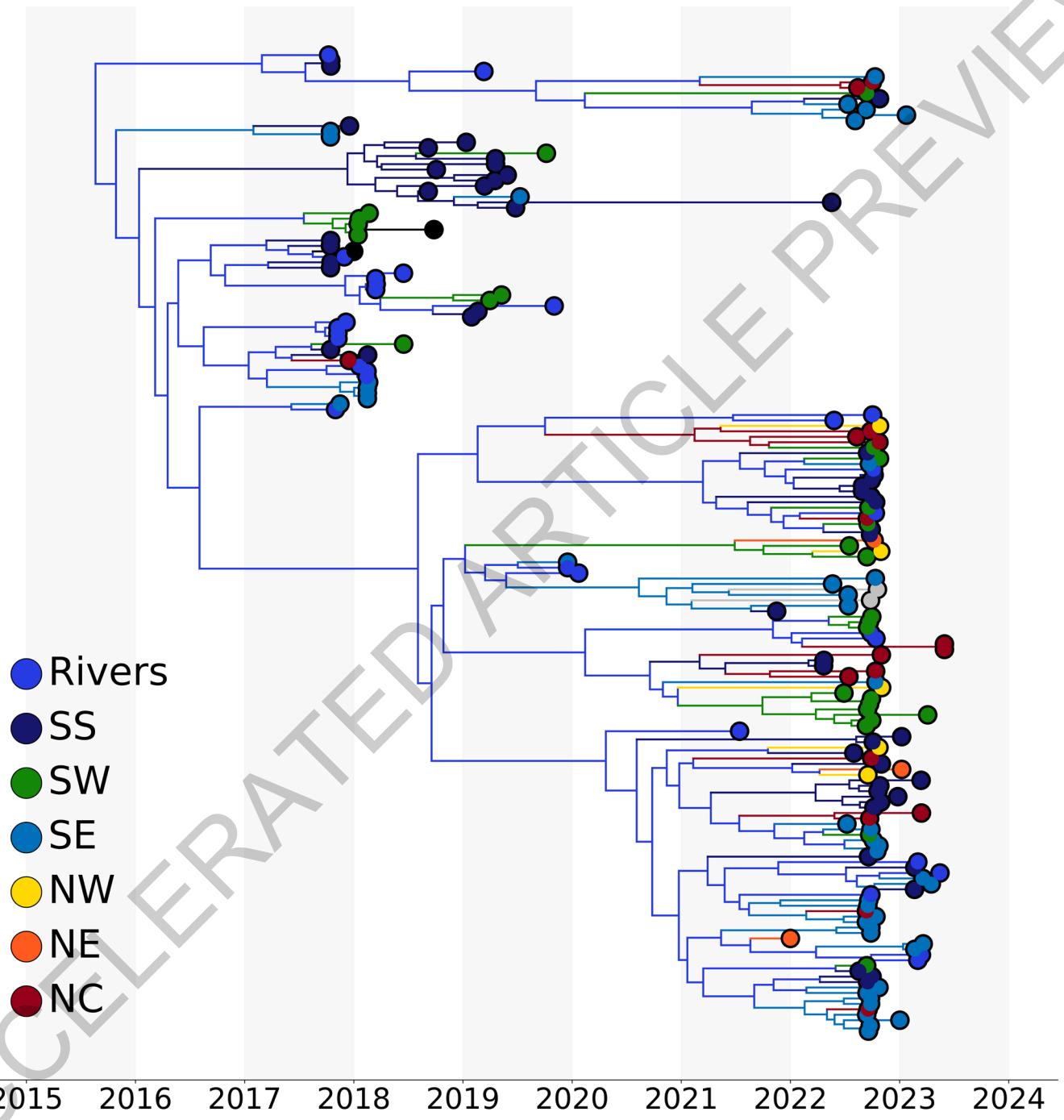
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- SS
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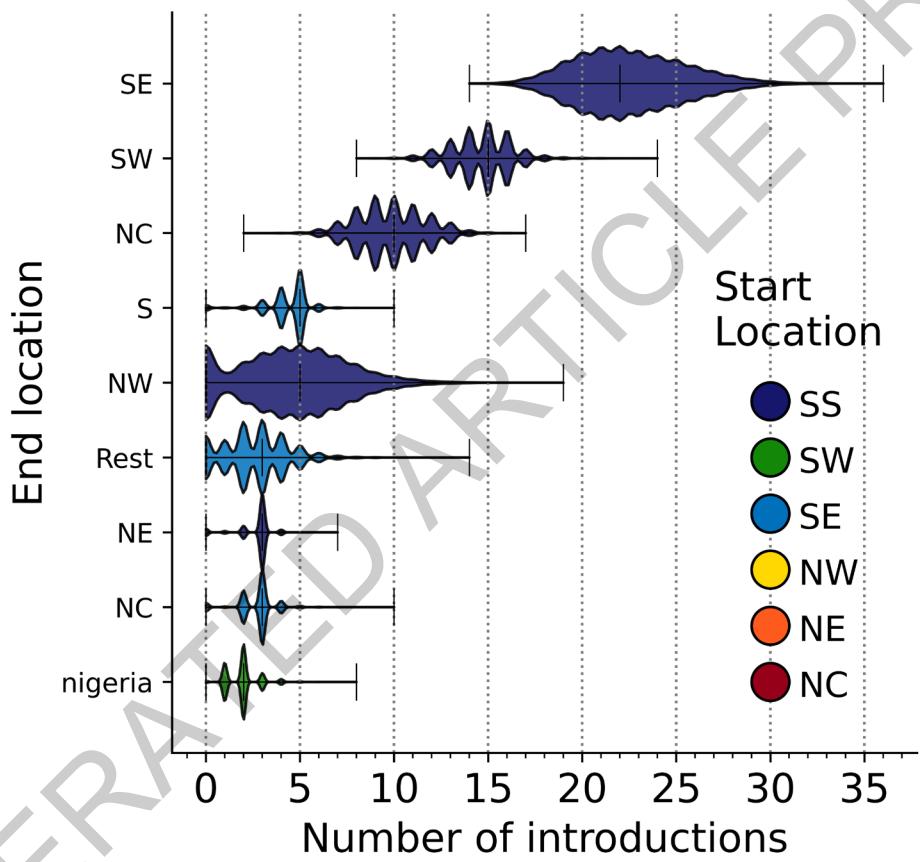
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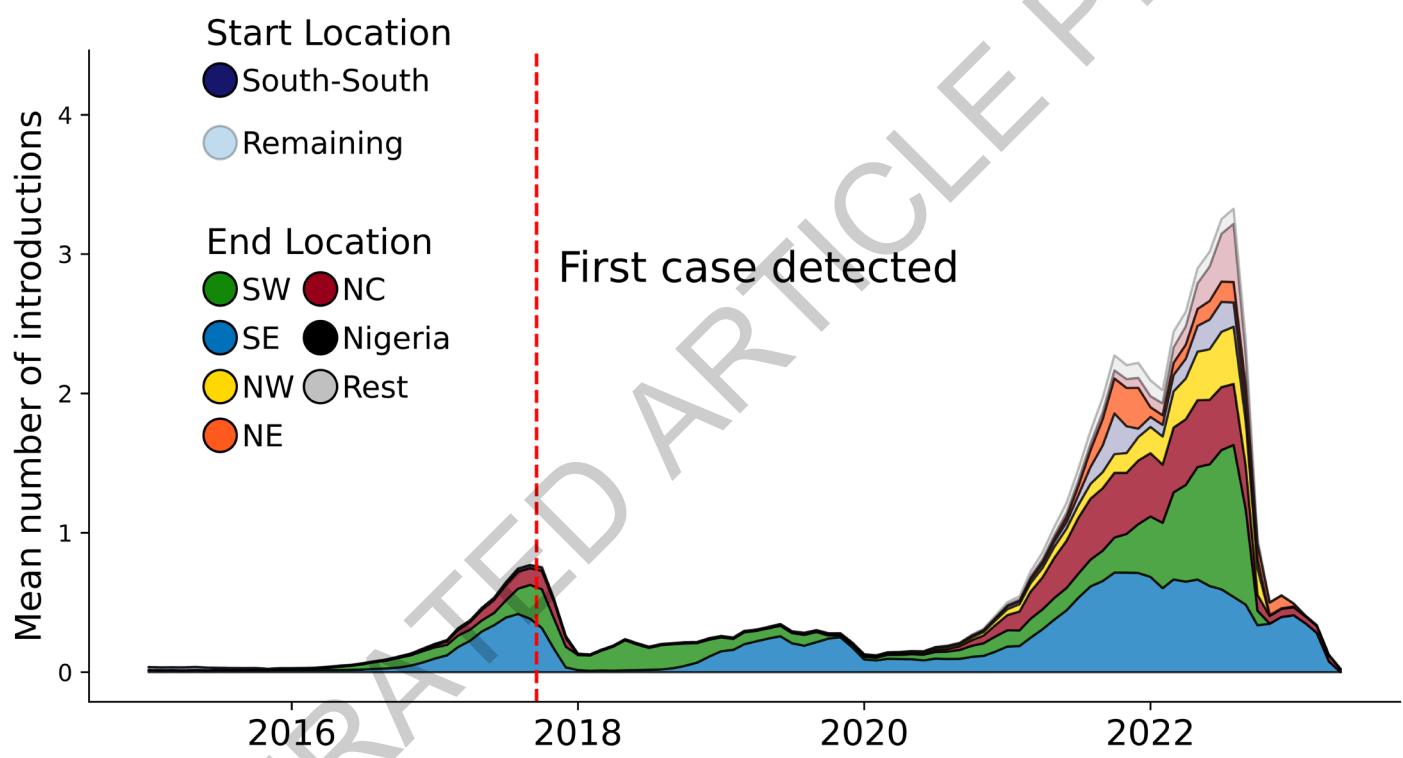
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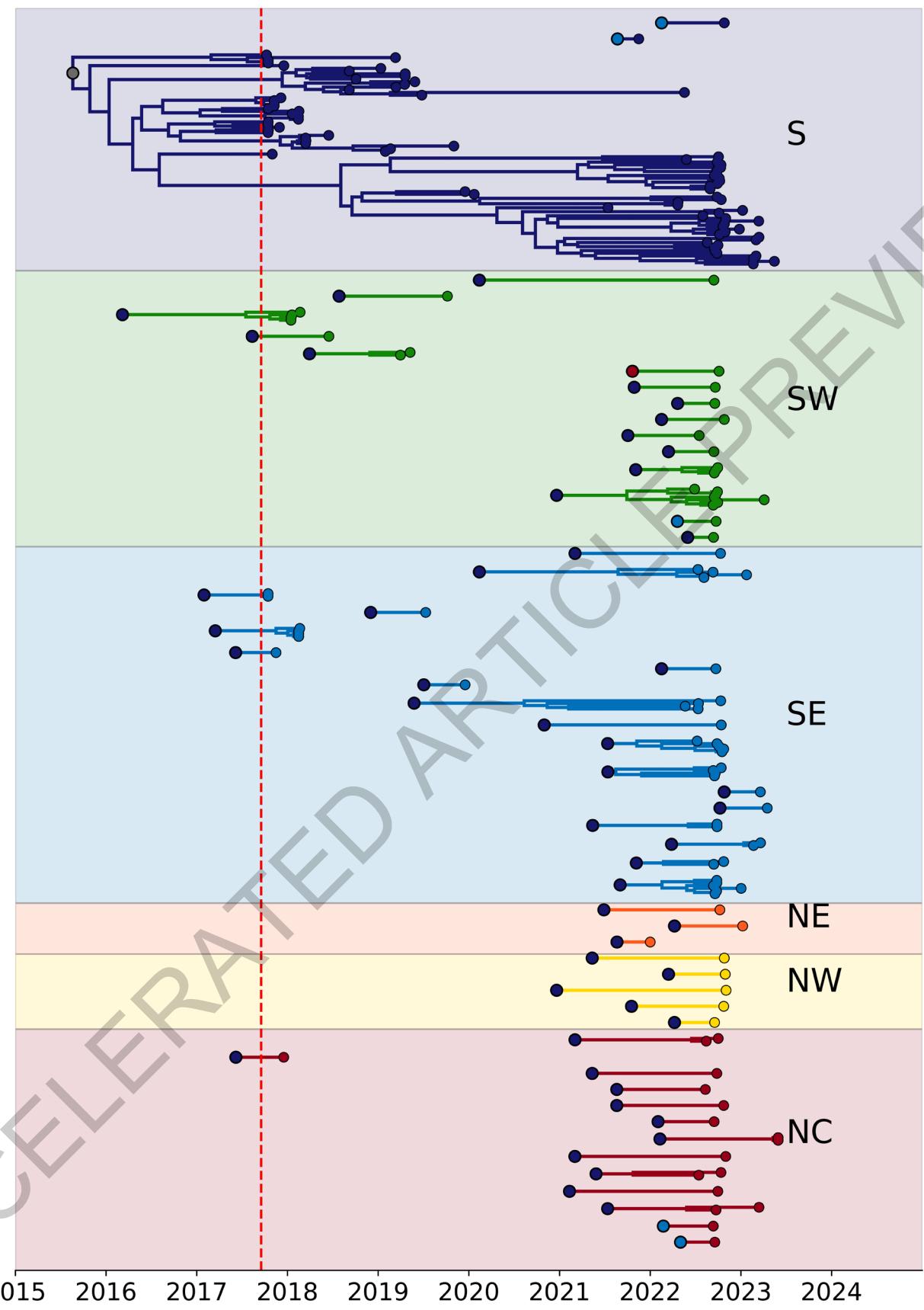


Extended Data Fig. 1

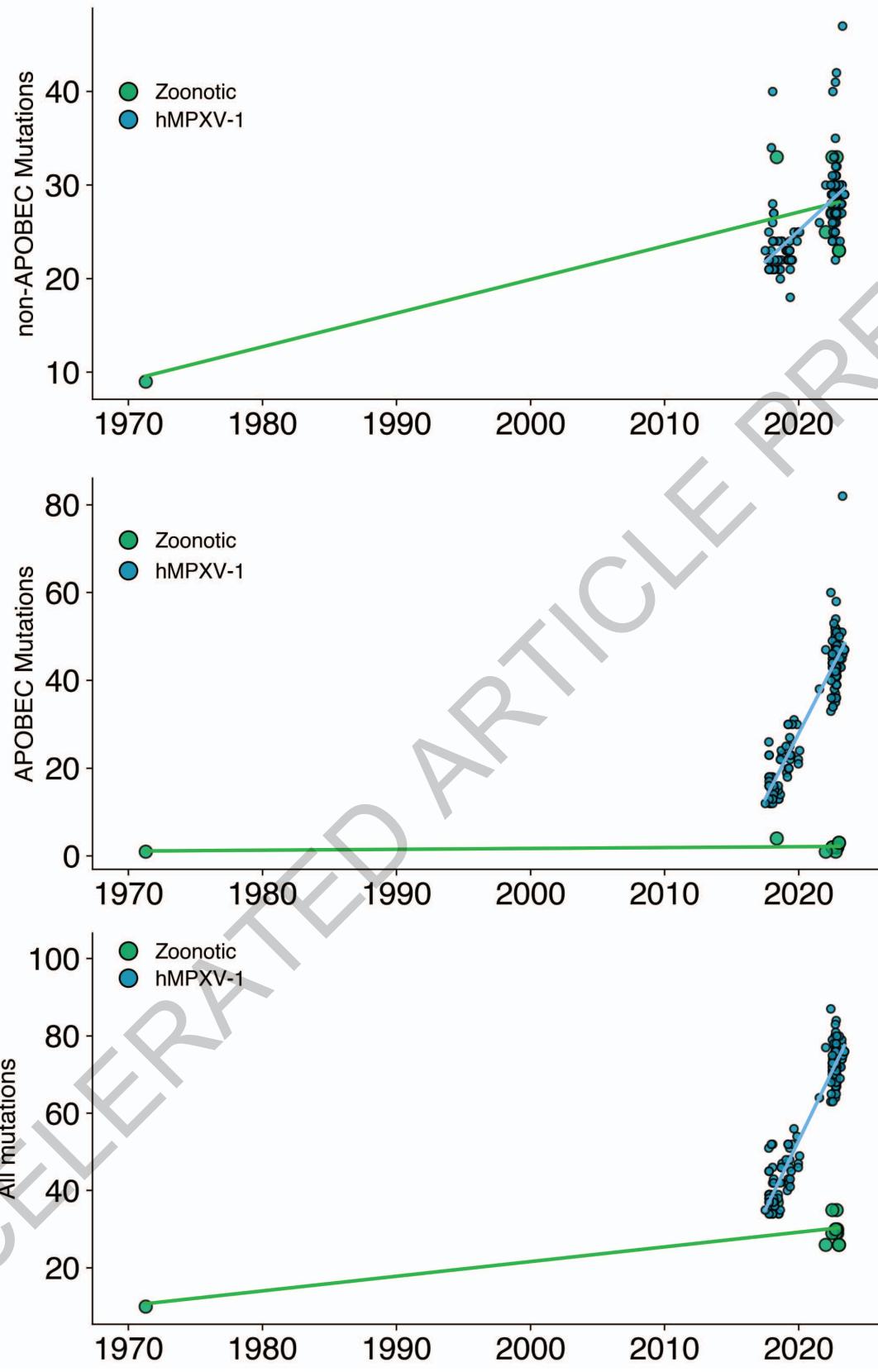


Extended Data Fig. 2

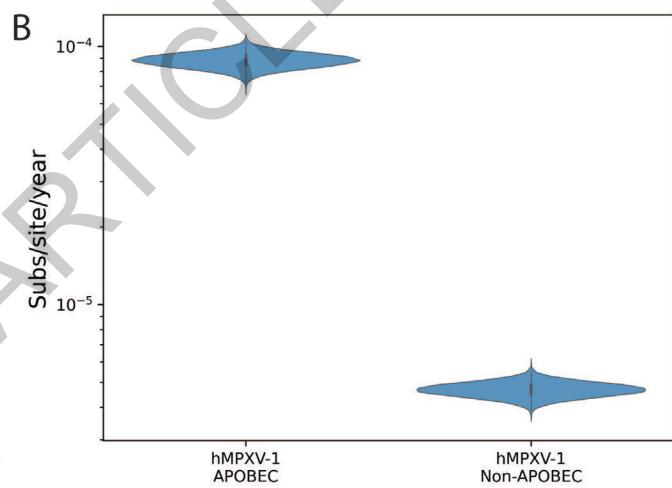
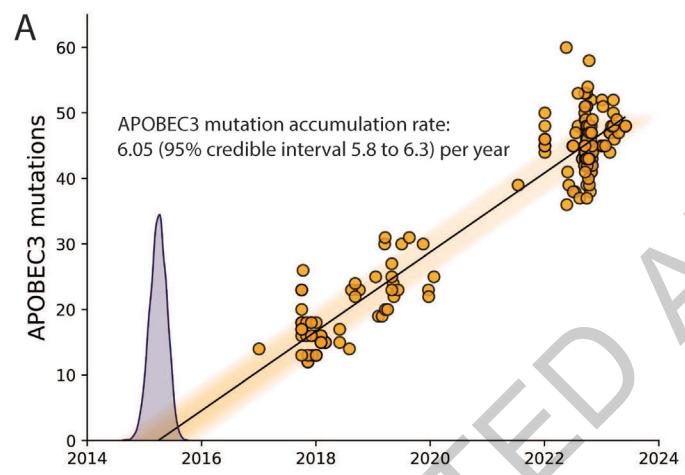




Extended Data Fig. 4



Extended Data Fig. 5



Extended Data Fig. 6

Covariates Type	Abbreviation	Covariates description
Administrative	Lagos(O)	Lagos as origin of infection
Administrative	Lagos(D)	Lagos as Destination of infection
Administrative	Rivers(O)	Rivers as origin of infection
Administrative	Rivers(D)	Rivers as Destination of infection
Demographic	Pop Size(O)	Origin population size, log-transformed, standardised
Demographic	Pop Size(D)	Destination population size, log-transformed, standardised
Demographic	Pop Dens(O)	Origin population density, log-transformed, standardised
Demographic	Pop Dens(D)	Destination population density, log-transformed, standardised
Demographic	Time100k (O)	Average log-transformed travel time in minutes to the closest city with a population of over 100,000 from the origin location, standardised.
Demographic	Time 100k (D)	Average log-transformed travel time in minutes to the closest city with a population of over 100,000 from the destination location, standardised.
Economics	GDP	Economic output, log-transformed, standardised
Epidemiology	Residuals(O)	Sampled genomes relative to the incidence case in Origin log-transformed, standardise
Epidemiology	Residuals(D)	Sampled genomes relative to the incidence case in Destination log-transformed, standardise
Epidemiology	HIV(O)	HIV cases at Origin log-transformed, standardise
Epidemiology	HIV(D)	HIV cases at Destination log-transformed, standardise
Epidemiology	Drug use(O)	Drug use at the origin log-transformed, standardise
Epidemiology	Drug use(D)	Destination Drug use, log-transformed, standardise
Geography	GCDistances	Great circle distances between the locations' population centroids, standardise log-transformed,
Geography	RDistances	Road distance by driving, log-transformed, standardise

Extended Data Table 1

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Last updated by author(s): 4.03.2025

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Give P values as exact values whenever suitable.
- For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
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Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

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Data collection	No software used for data collection
Data analysis	All analyses code and files made available via: https://github.com/andersen-lab/Mpox_West_Africa . De novo assembly with viral/ngs pipeline v2.1.33.17. Reference based pipeline consisted of: fastqc v 0.11.8, trimmomatic v0.39, bwa v0.7.17, samtools v1.17, ivar v1.4.2. Phylogenetic analyses include squirrel 1.0.10, iqtree v2.2.5, BEAST 1.10.5, TreeAnnotator 1.10, Tracer 1.7.2. All code to run the analyses is available in https://github.com/andersen-lab/Mpox_West_Africa , excluding shape files which are available at https://www.fao.org/land-water/databases-and-software/geonetwork/en/

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Publicly available genomic data was obtained from Genbank as of August 2023. All sequences from this study are available on Genbank under Accession numbers PP852943 - PP853055. Covariates included in the GLM were collected from the following sources: Epidemiological data was obtained from the Nigerian CDC; Economic covariates were sourced from Okeowo et al.; Population covariates were sourced from the Bulletin of the National Bureau of Statistics; HIV prevalence was obtained from the PEPFAR program; Drug use statistics were obtained from the National Bureau of Statistics. The distance by road travel between each states was calculated from Google Maps. Administrative level 2 (admin2) metadata for the sampling location of sequences in the dataset were mapped to official admin2 as found in the Global Administrative Database (GADM, <https://gadm.org>). All shapes files were obtained from the FAO geoNetwork (<https://www.fao.org/land-water/databases-and-software/geonetwork/en/>). All other data are available at https://github.com/andersen-lab/Mpox_West_Africa, excluding shape files which are available at <https://www.fao.org/land-water/databases-and-software/geonetwork/en/>

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Ethical approval obtained included in the manuscript.

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

Sample size

112 novel sequences, 202 with public data included. All clinical samples of sufficient quality available to the Nigerian CDC and the Institute Pasteur Cameroon were included in the current study. The samples were obtained from their national surveillance programs. This sample size is sufficient, as it's the largest sample size from both countries up to the date of the study and contributes novel insights as per paper. Also, there were no additional samples at the time.

Data exclusions

No data was excluded, excepting 10 failed genome assemblies.

Replication	Three chains of each Bayesian phylogenetic reconstruction was performed to assess whether they converge on the same posterior. They did. Uncertainty is quantified across the three combined independent chains, and across 10 000 phylogenetic trees in the posterior.
Randomization	Irrelevant as there are no experimental groups.
Blinding	Irrelevant as metadata is vital to analyses.

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