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Potential determinants of the decline in mpox cases in Belgium: A behavioral, epidemiological and seroprevalence study

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ABSTRACT

Objectives: The 2022 mpox epidemic reached a peak in Belgium and the rest of Europe in July 2022, after which it unexpectedly subsided. This study investigates epidemiological, behavioral, and immunological factors behind the waning of the epidemic in Belgium.

Methods: We investigated temporal evolutions in the characteristics and behavior of mpox patients using national surveillance data and data from a prospective registry of mpox patients in the Institute of Tropical Medicine (Antwerp). We studied behavioral changes in the population at risk using a survey among HIV-preexposure prophylaxis (PrEP) users. We determined the seroprevalence of anti-orthopoxvirus antibodies among HIV-PrEP users across four-time points in 2022.

Results: Mpox patients diagnosed at the end of the epidemic had less sexual risk behavior compared to those diagnosed earlier: they engaged less in sex at mass events, had fewer sexual partners, and were less likely to belong to the sexual network's central group. Among HIV-PrEP users there were no notable changes in sexual behavior. Anti-orthopoxvirus seroprevalence did not notably increase before the start of national vaccination campaigns.

Conclusion: The observed changes in group immunity and behavior in the population at greater risk of exposure to mpox seem unable to explain the waning of the mpox epidemic. A change in the profile of mpox patients might have contributed to the decline in cases.

Introduction

In 2022, a global epidemic of mpox (formerly monkeypox) took the world by surprise [1,2]. Unlike most previously reported outbreaks in sub-Saharan Africa, this clade IIb epidemic was characterized by extensive and sustained human-to-human

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transmission, primarily through sexual contact [1,2]. By November 2023, more than 91.000 cases had been reported in 115 countries [3]. More than 80% of cases identified as men who have sex with men (MSM), the large majority of whom were either people living with HIV or using HIV preexposure prophylaxis (PrEP) [1,2,4].

After the detection of the first mpox cases in the United Kingdom in May 2022, the daily incidence rose rapidly in Europe and the Americas, reaching a peak in July-August 2022, followed by a rapid decline [3]. The rapid rise in cases was likely facilitated by efficient transmission across a closely interconnected and geographically extended sexual network [1]. Insufficient awareness of mpox, as well as asymptomatic and presymptomatic transmission, further contributed to efficient spread [5-7].

In contrast, the drivers behind the waning of the epidemic remain elusive. Like in many other European countries, the Belgium authorities implemented a vaccination campaign with third-generation smallpox vaccines. However, preexposure vaccination only became available on August 8, 2022, when the epidemic was already declining. Alternative explanations for the decline in cases include improved awareness among individuals at higher risk of exposure to mpox, improved diagnosis, changes in sexual behavior, population immunity, and changes in virus characteristics [8]. However, the relative contribution of these factors remains to be determined. Understanding the mechanisms underlying the sudden decline in mpox circulation is crucial to estimate the risk of resurgences and to prevent new epidemic waves. In this study, we explored a selection of factors that could have contributed to the decline of the 2022 mpox epidemic in Belgium.

Materials and methods

Study populations

We analyzed samples and data from three main sources. To study temporal evolutions in epidemiological characteristics and behavior among mpox patients we used data from the Belgian national mpox surveillance program and from a prospective clinical mpox registry conducted at the Institute of Tropical Medicine (ITM) in Antwerp, Belgium. To study changes within the population at greater risk for exposure to monkeypox virus (MPXV) infection, hereafter referred to as "the population at risk," we used samples and data from a prospective cohort of HIV-PrEP users at ITM [1,9,10]. Details on the different data sources are provided below and in Supplementary Materials (Supplementary Figure 1).

Within the different populations (mpox patients and HIV-PrEP users), we defined a subpopulation of individuals who we considered most centrally located in the sexual network (i.e., with the highest sexual partner turnover, and therefore at the highest risk of sexually transmitted infections [STIs]) [11]. For this, we used the results of the participants' *Treponema pallidum* antibody (TPA) tests as a surrogate marker for sexual risk, since a history of syphilis infection is a known predictor for infection with HIV or hepatitis C [12-16]. Individuals with high TPA titers (TPA $>$ 50) were categorized as individuals with positive TPA, and individuals with lower TPA values as individuals with negative TPA.

Temporal evolutions in epidemiological characteristics and behavior of mpox patients

To study temporal trends among mpox patients, we analyzed national surveillance data, collected by the Belgian National Public Health Institute, Sciensano, from May to December 2022, on all registered mpox cases that conformed to the national case definition (i.e., individuals with a positive MPXV-specific or orthopoxvirus-specific PCR assay, and symptom onset after March 1, 2023). After being notified by the diagnosing physician, regional public health authorities contacted mpox patients to collect data on age, sexual orientation, HIV status, HIV-PrEP use, time-to-diagnosis, likely mode of transmission, and (sexual) behavior and exposure setting. These data were plotted over time. Time-to-diagnosis was calculated as the interval in days between the first day of onset of symptoms and the date of MPXV-PCR positive sample date testing among patients for whom both dates were known.

In addition, we analyzed more in-depth data from 162 consenting mpox patients included in a monocentric prospective clinical registry between May and November 2022 (for details on signs and symptoms eligible for diagnostic testing, as well as recruitment, see Hens [17]). For these participants, we used Poisson regression to model the number of sexual partners in function of time of diagnosis. Number of sexual partners was defined as a count in the 3 weeks before diagnosis; as this corresponds to the maximal incubation time. Time of diagnosis was defined as weeks since start of the epidemic. This analysis aimed to assess whether patients diagnosed early in the epidemic were more likely to report a higher number of sexual partners compared to those diagnosed later in the epidemic. Furthermore, we tested whether individuals with positive TPA were infected earlier in the epidemic than individuals with negative TPA using a nonparametric Wilcoxon rank sum test on the distribution of both groups' time to diagnosis since the onset of the epidemic.

Temporal evolutions in behavior of the population at risk for mpox (HIV PrEP-users)

To study the behavioral characteristics of the population at risk, we used data from 2022 of an ongoing prospective behavioral survey conducted among HIV-PrEP users attending ITM's sexual health clinic (described by Vuylsteke [18]). HIV-PrEP users visit the clinic every three to 6 months for drug prescriptions, STI testing, and sexual health counseling. A questionnaire is completed during each visit, containing questions on HIV-PrEP use and sexual behavior such as number of partners, participation in group sex, chemsex, condom use, and perceived STI risk [18] (Online Supplementary p.3).

From February 16, 2023, until May 2023 we incorporated retrospective questions into these PrEP questionnaires asking about the impact of the 2022 mpox outbreak on participants' sexual behavior. A total of 1033 HIV-PrEP users answered these retrospective questions on their sexual behavior during the mpox outbreak.

As an additional way of assessing potential changes in sexual risk behavior, we analyzed the occurrence of other STIs among HIV-PrEP users. We hypothesized that any changes in sexual risk behavior would be reflected in changes in the rates of these other STIs [19]. To this end, we collected the results of routine STI testing (chlamydia and gonorrhea) among HIV-PrEP users followed up during 2022 (February 1-December 21).

To determine presence of within-person behavioral change over time in PrEP users, we made full use of the repeated measurement data by modeling the number of partners over time among HIV-PrEP users using a Poisson mixed-effects model (MEM) [20]. To determine whether on average, individuals' number of partners changed over time, we chose a MEM with random intercept, allowing inter-individual variability in baseline number of partners. Predictors included in the model where time in months and TPA serostatus. We explored interactions with time and TPA serostatus and determined final model based on model fit parameters (AIC/BIC/deviance). To analyze participation in group sex and chemsex, we built a random-intercept logistic MEM with the same predictors.

We plotted the following variables over time: (i) number of sexual partners, (ii) participation in group sex, (iii) participation in

chemsex, (iv) condom use during anal sex within a steady relationship, (v) condom use during anal sex with people other than a steady partner, (vi) self-perceived HIV risk, (vii) self-perceived STI risk and (viii) proportion of chlamydia/gonorrhea test positivity.

Temporal evolutions in immunity against MPXV in the population at risk for mpox (HIV-PrEP users)

To estimate the proportion of vaccination- and infection-induced immunity among HIV-PrEP users at ITM, we determined the number of mpox-diagnosed and vaccinated individuals over time among all HIV-PrEP users followed up at ITM in 2022. In addition, we estimated the seroprevalence of orthopoxvirus-specific antibodies in stored blood samples collected from HIV-PrEP users. Samples from four-time points from the epidemic curve were selected: preepidemic (the 110 earliest samples available, from February 14-February 26, 2022); at the onset of the epidemic (the 270 most recent samples collected by May 8, 2022, which corresponds to the date of the first mpox diagnosis in Belgium); at the peak of the epidemic (the 270 most recent samples collected by August 2, 2022); and postepidemic (the 270 most recent samples collected by November 9, 2022). For the primary analysis, we considered only individuals born after 1976, the year in which smallpox vaccination in Belgium stopped. For a secondary analysis, all available samples from HIV-PrEP users of any age were included.

Since no accurate MPXV-specific serological assay was available, we estimated the presence of orthopoxvirus-specific antibodies using an in-house vaccina-virus (VACV)-based serological ELISA. This ELISA uses the lysate of VACV Elstree-infected HeLa cells as antigen, as previously described [21]. Two separate assays were performed: (i) a screening assay in which sera were assessed for the presence of VACV-reactive antibodies at two serum dilutions (1:10 and 1:50), and (ii) a quantification assay in which sera regarded as at least borderline positive (OD VACV-HeLa minus OD mock-Hela $\geq$ 0.2) in the screening assay were assessed for IgG titer in a full dilution series. To this end, a minimum-to-maximum S-curve was generated by adding a serially diluted positive control serum to each ELISA plate. Five-fold dilution series of samples was transformed to this control S-curve, and IgG was quantified as 30% endpoint titer [21]. Estimates of the prevalence of orthopoxvirus-specific antibodies among HIV-PrEP users for each of the four-time periods were stratified according to year of birth (born $\leq$1976 or $>$1976, i.e., before or after the cessation of smallpox vaccination in Belgium). A subgroup analysis was performed for individuals with positive versus negative TPA, aimed at distinguishing those who are more centrally located in the sexual network.

Results

Temporal evolutions in epidemiological characteristics and behavior of mpox patients

From May to December 2022, 790 mpox cases were reported to Sciensano. The majority of cases were reported in the Brussels capital region and in the province of Antwerp (Figure 1a). The first case was identified on May 19, 2022, followed by a rapid increase in cases, reaching a peak in the last week of July 2022 (Figure 1b). The epidemic rapidly subsided in the first week of August 2022. At ITM, located in the province of Antwerp, we diagnosed approximately one-third (n = 230) of Belgian mpox cases. Of those, 162 were included in a prospective clinical registry. The incidence in ITM cases mirrored the incidence of mpox in Belgium (Figure 1b).

Eighty-six percent (86%) of mpox patients reported to the national surveillance program identified as MSM (Figure 1c). Thirty-two percent of patients were people living with HIV, and among those not living with HIV, 34% used HIV-PrEP (Figure 1d). The median age of patients (37 years, IQR 30-44) was stable throughout the epidemic (Figure 1e). Furthermore, time-to-diagnosis remained similar over time (Figure 1f). Figure 2 shows the temporal evolution in the type of exposure and risk factors among mpox patients reported to Sciensano (n = 770). In the majority of cases, the reported mode of transmission was through sexual contact, as opposed to fomites or person-to-person transmission (Figure 2a). More importantly, a shift in the setting of sexual exposure was observed; in the first few weeks of the outbreak, the majority of mpox patients reported sexual contact during large events, and this proportion decreased over time (Figure 2b). In contrast, the proportion of mpox patients reporting sexual contact in a private setting was close to zero in the first few weeks and increased later to approximately 50% (Figure 2c). From end of July, we observe a decrease in the proportion of patients who attended a private party (without sexual contact) but no noteworthy trends in patients travel in the 3 weeks prior to infection (Figure 2d,e).

Figure 2f,g shows data obtained from patients included in ITM's clinical registry. When stratifying mpox patients according to TPA-positive serostatus, which is indicative of a more central position in the sexual network. We noticed that mpox cases diagnosed early in the epidemic were more likely to be more centrally positioned within the sexual network compared to those diagnosed later (Figure 2f). This was confirmed by comparing the time of diagnosis-counted from the start of the epidemic, that is, May 23, 2022. Patients with a more central position in the sexual network, as indicated by TPA-positive serostatus, showed a median diagnosis time of 32 days (IQR 4-54) postepidemic onset, while those with a less central position (TPA-negative patients) had a median of 43 days (IQR 0-62), (P = 0.04, W = 2374). In addition, the number of sexual partners in the 3 weeks before infection reported by patients decreased significantly by 13% per week (IRR 0.87, 95% CI 0.86-0.89, Figure 2g).

Temporal evolutions in behavior of the population at risk for mpox (HIV PrEP-users)

To investigate whether individuals at risk for mpox changed their behavior during the mpox outbreak, we analyzed 3409 questionnaires filled in by 1 332 HIV-PrEP users (median of 2 visits/participant, IQR 1-3) between February 1 and December 31, 2022. The median age of HIV PrEP users was 40 (IQR 32-48), and 97% were of the male sex. The mean number of sexual partners in the preepidemic period was 7.7 (standard deviation [sd], 9.26), for the onset, peak, and post epidemic-periods the means (sd) respectively were 8.09 (9.84), 8.83 (9.91) and 9.32 (11.36). The average number of reported sexual partners increased by 3% per month in 2022 (IRR 1.03, 95% CI 1.03-1.04, Figure 3a), with no significant effect of summer period on the reported number of partners. Over the course of 2022, no significant changes were observed in engagement in group sex (OR 1.01, 95% CI 0.97-1.05, Figure 3b), engagement in chemsex (OR 1.06, 95% CI 0.96-1.18, Figure 3c), or self-reported condom use during anal sex, either with steady partners (OR 1.02, 95% CI 0.97-1.07, Figure 3d) or with casual partners (OR 1.00, 95% CI 0.98-1.03, Figure 3e). Self-perceived risk scores of STIs and HIV showed negligible increases over 2022 (OR 1.03, 95% CI 1.00-1.05, and OR 1.04 95% CI 1.01-1.06, respectively, Figure 3f,g).

Individuals with positive TPA (n = 309, 23.2% of all HIV-PrEP users in 2022) reported a consistently higher number of sexual partners than individuals with negative TPA (n = 1023, 76.8% of HIV-PrEP users; +1.19 partners, 95% CI 1.04-1.63, Figure 3a); but no significant difference in trend over time. Additionally, they showed more participation in group sex (OR 1.96, 95% CI 1.15-2.91) and chemsex (OR 3.03, 95% CI 1.09-8.45) throughout 2022. However, no noticeable changes in the number of partners, participation in

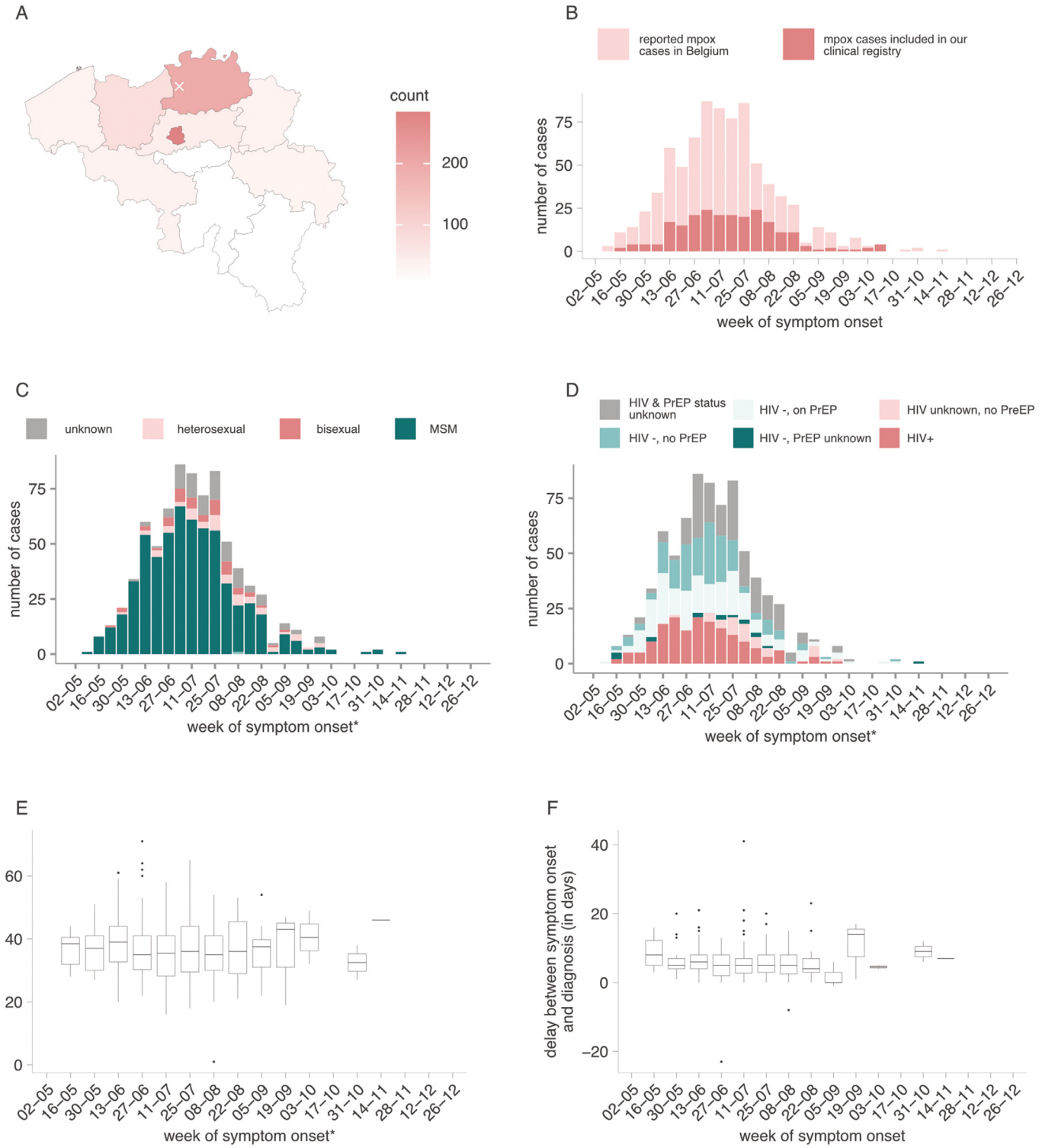

Figure 1. Mpox cases reported to the Belgian National Institute of Public Health Sciensano, 2022: (a) geographic origin (X marks the Institute of Tropical Medicine, Antwerp); (b) epidemic curve; (c) sexual orientation (*MSM*, men who have sex with men); (d) HIV status and HIV-PrEP use; (e) age; (f) time-to-diagnosis.

group sex, or participation in chemsex were detected over time in individuals with positive TPA (Supplementary Figure 2).

To corroborate the findings on sexual risk behavior, we analyzed the occurrence of STI infections among HIV-PrEP users over the course of 2022. In line with data from the behavioral questionnaire, we did not detect a meaningful trend in the overall proportion of positive chlamydia/gonorrhea tests conducted during HIV-PrEP consultations (Figure 3h).

Between February 2023 and May 2023, 1033 HIV-PrEP users answered questions on their sexual behavior during the mpox outbreak. About half of them (n = 586, 56.7%) were also included in the 2022 survey. Among HIV-PEP users who provided information on their sexual behavior, 46.8% (n = 483) reported a decrease in the number of sexual partners compared to before the outbreak, and respectively 38.3% (n = 396), 12.8% (n = 132), and 12.8% (n = 132) of respondents reported that they had less one-time

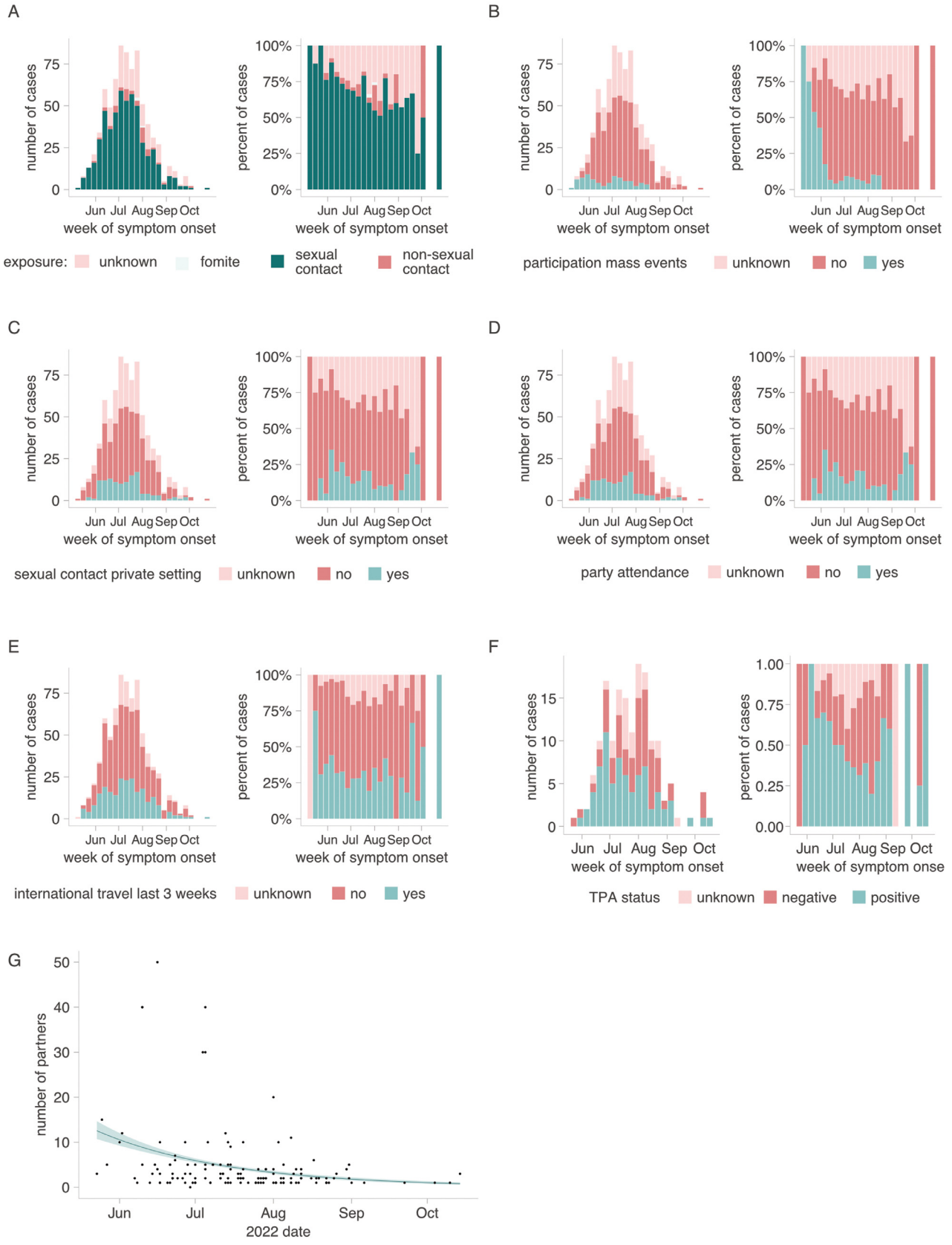

Figure 2. Mpox cases reported to the Belgian National Institute of Public Health Sciensano, 2022 (a-e) and mpox cases enrolled in a clinical registry at the Institute of Tropical Medicine Antwerp, Belgium 2022 (f and g): (a) reported mode of transmission; (b) sexual contact during large domestic or international event; (c) sexual contact in private setting; (d) participation in a nonsexual group event (party or similar); (e) travel in the previous 3 weeks; (f) categorization into individuals with positive *Treponema pallidum* antibodies (TPA) or individuals with negative or low TPA (TPA $>$ 50 or TPA $\leq$ 50); (g) observed (dots) and predicted (line) number of partners in the 3 weeks prior to diagnosis according to Poisson regression model, with 95% confidence interval (shaded area). Light pink areas marked as "unknown" represent missing data in the outcome variable.

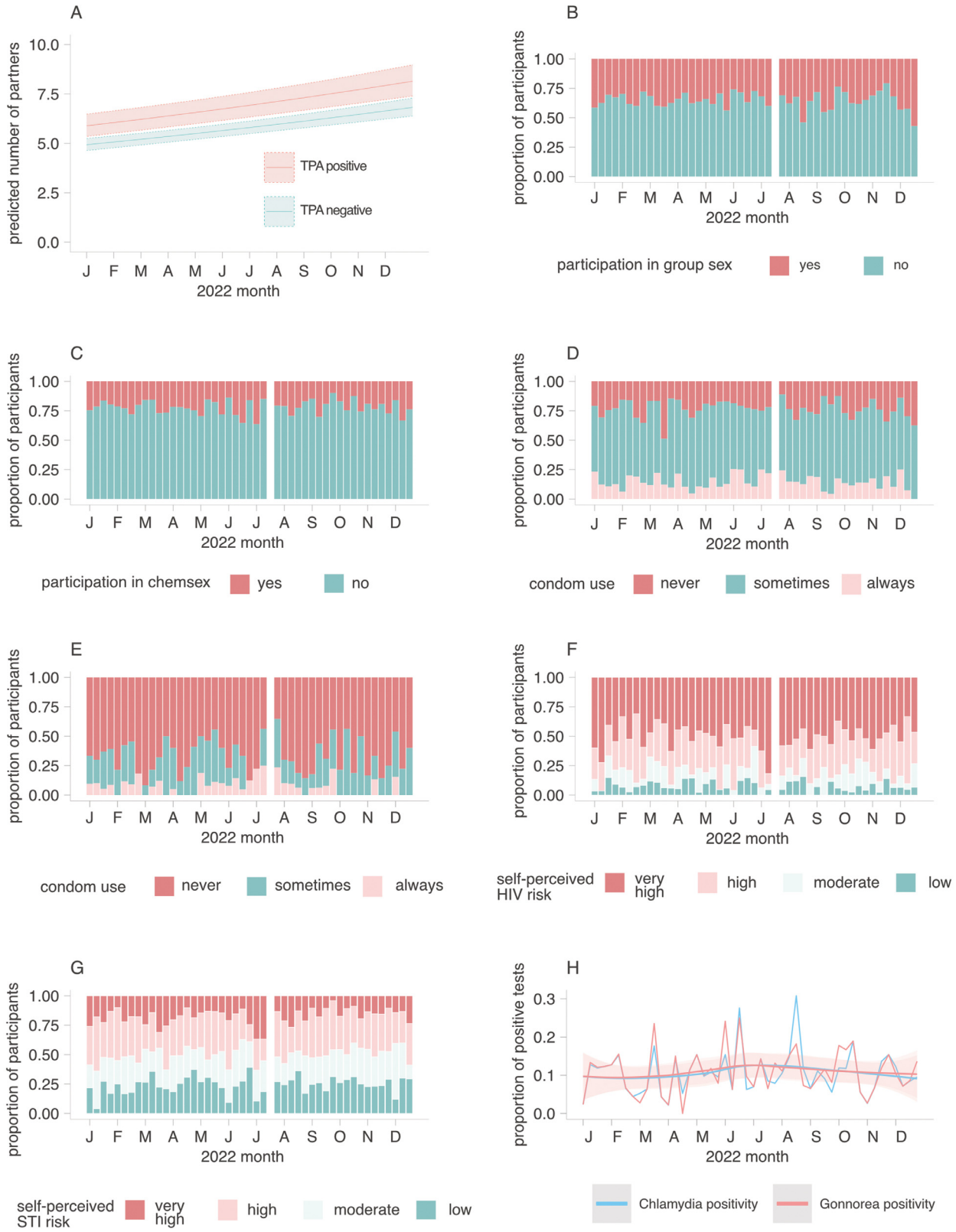

Figure 3. Sexual behavior, sexual risk perception and gonorrhea/chlamydia test positivity among HIV-preexposure prophylaxis users at the Institute of Tropical Medicine Antwerp, 2022: (a) predicted (line) number of partners in the 3 months prior to diagnosis according to linear regression model, with 95% confidence intervals (shaded areas); (b) engagement in group sex in the 3 months prior to diagnosis; (c) engagement in chemsex in the 3 months prior to diagnosis; (d) condom use during anal intercourse with partners outside of the steady relationship in the 3 months prior to diagnosis; (e) condom use during anal intercourse with steady partners in the 3 months prior to diagnosis; (f) self-perceived risk for HIV in the 3 months prior to diagnosis; (g) self-perceived risk for bacterial sexually transmitted infections in the 3 months prior to diagnosis; (h) proportion of positive test results among tests done for chlamydia and gonorrhea.

sexual encounters, group sex, or chemsex than before the outbreak.

Temporal evolutions in immunity against MPXV in the population at risk for mpox (HIV-PrEP users)

We explored the role of immunity acquired through infection or vaccination in the population at risk for mpox, represented by HIV-PrEP users visiting ITM ($n = 1332$). By July 31, 2022, the peak of the epidemic, 2.7% ($n = 45$) of HIV-PrEP users visiting ITM had been diagnosed with mpox. This proportion was 3.4% ($n = 57$) on October 11, when the last mpox case in this cohort was diagnosed (Figure 4b). Figure 4a shows the number of doses administered in Belgium in relation to the epidemic, illustrating that the vaccination campaign started when the epidemic was already declining. The vaccination coverage of HIV-PrEP users is illustrated in Figure 4b. At the peak of the outbreak (July 31), less than 1% ($n = 7$) of HIV-PrEP users had received a first vaccine dose, and none had received a second dose. Vaccination coverage (at least one dose) was 36.3% ($n = 610$) by the end of October 2022 and 46.0% ($n = 773$) by the end of December 2022.

In the seroprevalence study among HIV-PrEP users born after 1976 (Figure 4c), the seroprevalence of anti-orthopoxvirus antibodies in preepidemic samples was 5.5% (95% CI 2.3-12.1%, $n = 6/109$), a proportion which may correspond to the false positivity ratio of the test in a population without prior orthopoxvirus exposure (for more details on the assay we refer the reader to Zaeck et al. [21]). The seroprevalence was similar at the start and the peak of the epidemic with estimated seroprevalences of 7.4% (95% CI 4.7-11.3%, $n = 19/265$) and 6.3% (95% CI 3.4-10.1%, $n = 16/262$), respectively. In the postepidemic period, the seroprevalence increased to 45.3% (95% CI 39.3-51.2%, $n = 121/270$), mirroring the vaccine coverage within this group.

Among HIV-PrEP users born before or in 1976, the baseline seroprevalence in preepidemic samples was markedly higher (90%, 95% CI 77.4-96.2%, $n = 45/50$) than in those born after 1976, most of whom likely having orthopoxvirus-reactive antibodies induced by childhood smallpox vaccination. The seroprevalence in this older population remained stable throughout the subsequent study periods (80.3%, 95% CI 71.9-86.8%, $n = 99/128$ at the start of the epidemic; 91.1%, 95% CI 84.3-95.3, $n = 114/131$ at the peak of the epidemic; and 91.7%, 95% CI 84.4-95.9, $n = 102/112$ postepidemically; Figure 4c). Overall, seroprevalence was similar between individuals with positive TPA and individuals without positive TPA across the four-time periods (Figure 4d).

Discussion

We used multiple data sources to investigate potential causes of the decline of the Belgian mpox outbreak in 2022. Our analyses could not identify a singular cause for the decline in cases but revealed several interesting findings.

First, immunity within the at-risk population (here represented by HIV-PrEP users) seems unlikely to have caused the decline in mpox cases. The vaccination campaign started after the decline in cases had begun, and at the peak of the epidemic, only an estimated 2.7% of our HIV-PrEP users had been diagnosed with mpox. This is confirmed by our seroprevalence study, in which no discernable differences in seroprevalence between preepidemic samples and samples taken at the peak of the epidemic were found. These observations suggest that infection- and vaccination-induced group immunity played no major role in ending the epidemic.

A second important determinant of mpox transmission besides immunity, is sexual behavior. By August 2023, the mpox epidemic was widely known among MSM, allowing at-risk individuals to reduce their number of contacts. Surveys among MSM in the US in August 2022 found that about half of the respondents reported outbreak-related modifications in their sexual behavior, in particular a reduction in number of partners and one-time sexual encounters [22-24]. Likewise, when HIV-PrEP users in our study were asked to retrospectively report in 2023 if their sexual activity in 2022 had been influenced by the mpox epidemic, almost 50% reported having had fewer sexual partners than before. Surprisingly, in ITM's prospective survey among HIV-PrEP users throughout 2022, we did not observe a decrease in number of partners nor in engagement in group sex or chemsex. These apparent contrasts between surveys may be caused by the biases inherent to both types of surveys: retrospective surveys may overestimate behavioral change due to recall bias and social desirability bias; prospective surveys may underestimate behavioral change due to a selection bias (individuals with reduced sexual activity are less likely to attend the clinic). Yet, the absence of behavioral change in ITM's HIV-PrEP cohort was corroborated by a lack of change in gonorrhea and chlamydia test positivity throughout 2022. Together, these findings suggest that behavioral change of the at-risk population as a whole did not play a major role in the fading of the Belgian outbreak in 2022.

Last, we investigated trends among patients infected with MPXV. Modeling studies have estimated that patients recognized their symptoms sooner toward the end of the epidemic [25] and that earlier diagnosis may substantially slow down the epidemic [26]. However, we did not find a reduction in time-to-diagnosis as a sign of more rapid recognition of symptoms in mpox patients. Interestingly, however, we observed a subtle shift in the population affected by mpox over time: at the start of the epidemic, mpox patients more often had sex at mass events and less in private settings, had more sexual partners, and were more likely to be seropositive for syphilis compared to individuals diagnosed at the end of the epidemic. The exact reasons for this shift in profile remain elusive. We propose that one explanation for this phenomenon is that individuals at the center of the sexual network (here defined as those with positive TPA), may have been among the first to be infected during the epidemic. They could have subsequently transmitted the infection to other individuals within the network, and then developed immunity themselves, acting as network nodes resistant to further infection, unlinking transmission chains between other individuals in the network. This hypothesis, which we call network immunity, is supported by various mathematical models suggesting that the immunity acquired by those with high partner turnover can effectively interrupt the transmission of mpox within a population [25,27,28]. However, despite our study revealing that the 23.2% HIV-PrEP users classified as "central network nodes" due to their TPA-positivity reported a higher number of sexual partners, they were not found to be more likely to have orthopoxvirus-specific antibodies compared to TPA-negative HIV-PrEP users. Consequently, we were unable to find serologic evidence supporting the theory of network immunity. This could be attributed to several factors, such as the subgroup definition based on TPA positivity potentially not accurately capturing individuals at the center of the sexual network, limitations in the accuracy of the serological test used, or selection bias due to individuals withdrawing from HIV-PrEP following recent mpox infection.

At the time of writing (March 2024), the 2022 clade IIb MPXV outbreak has subsided in most countries [3]. Our observations indicate that the epidemic subsided after a shift in sexual activity profile of individuals infected with mpox over time. Although we have not been able to identify the cause of this shift, the change in affected population *per se* might have played a causal role in the end of the 2022 clade mpox outbreak in most countries. Future studies may be able to characterize the anatomy of the outbreak in more detail.

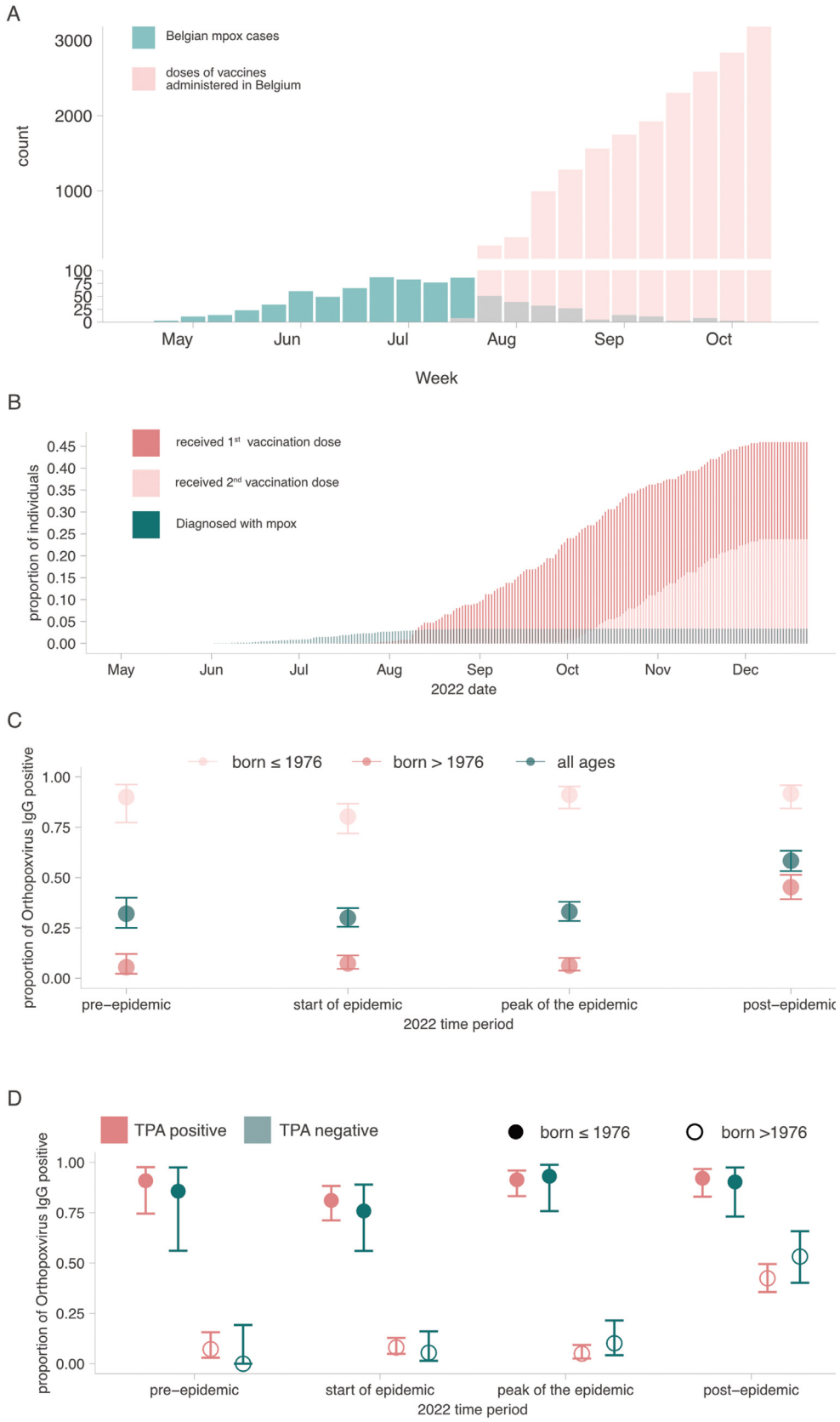

Figure 4. Mpox cases and vaccination doses administered in Belgium (a); mpox cases among HIV-preexposure prophylaxis users and vaccination doses administered to HIV-preexposure prophylaxis users at the Institute of Tropical Medicine Antwerp (b); presence of orthopoxvirus-specific antibodies among HIV-preexposure prophylaxis users at the Institute of Tropical Medicine Antwerp (c), presence of orthopoxvirus-specific antibodies among HIV-preexposure prophylaxis users stratified by TPA seropositivity and age at the Institute of Tropical Medicine Antwerp (d).

So far, sporadic flare-ups have caused no major new outbreaks in Europe and the United States, where the epidemic was first detected. This indicates that previously affected sexual networks appear to have become relatively resilient to new mpox outbreaks. How long this resilience will last remains unknown and probably depends on the longevity of the immune response after MPXV infection or vaccination and on the connectivity of sexual networks over time. Considering these unknown parameters, we must remain vigilant for new outbreaks caused by a reintroduction of clade IIb MPXV, or the introduction of sexually transmitted clade I MPXV which was recently reported in the Democratic Republic of the Congo [29,30]. Persistent clinical awareness, adequate surveillance in combination with immunological, behavioral, and modeling studies remain crucial to prevent and counter mpox resurgence.

Declarations of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

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Ethical approval

This study was approved by ITM's Institutional Review Board (1641/22, d.d. 31/10/2022; and 1630/23, d.d. 22/11/2023) and by the University of Antwerp Ethics Committee (4981, d.d. 31/10/2022; and 3904, d.d. 28/11/2023).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2024.107132.

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