Impact of vaccination with third generation modified vaccinia Ankara and sexual behaviour on mpox incidence in men who have sex with men: analysis among participants of the ANRS-174 DOXYVAC trial

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Summary

Background Mpox was first reported in France on May 19 and third-generation live Modified Vaccinia Ankara (MVA-BN) vaccination of multiple-partner men who have sex with men (MSM) was recommended as of July 11, 2022. We assessed the impact of vaccination and of sexual behavior adopted during the epidemic period on mpox incidence in the ANRS-174-DOXYVAC trial enrolling MSM on HIV pre-exposure prophylaxis (PrEP) with history of sexually-transmitted infections (STI) in the previous year.

Methods We compared pre-epidemic socio-behavioral characteristics and change in sexual behaviors after the onset of the epidemic of participants with mpox and mpox-free. Then we compared incidence rates of mpox per 1000 person-months (p-m) between May 9-July 10 (before vaccination of MSM, period-1) and July 11-September 20 2022 (after vaccination launch, period-2) and explored factors explaining the period effect using Poisson regression model.

Findings 472 MSM had data before and after May 9, 2022. Twenty percent had received smallpox vaccine during childhood. Mpox occurred in 77/472 participants (incidence 49.3 per 1000 p-m (95% CI 38.9–61.6)). MVA-BN vaccination roll-out was rapid, with 86% (341/398) of eligible participants having received at least one dose by September 20, 2022. Sexual behavior significantly changed before and after May 9, with a decrease in the proportion of mpox-free participants with >10 partners during last 3 months (45% vs 38%, p = 0.0035). Mpox incidence was 67.4 per 1000 p-m (95% CI 51.6–86.6) in period-1, and 24.4 per 1000 p-m (95% CI 13.9–39.6) in period-2, with an incidence rate ratio of 0.36 (95% CI 0.21–0.63). In multivariable Poisson regression model, only

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MVA-BN vaccination in 2022 remained significantly associated with mpox incidence, with a 99% risk reduction (95% CI 96.6–99.7).

Interpretation **In MSM on PrEP enrolled in the ANRS-174-DOXYVAC trial, rapid roll-out of MVA-BN vaccination was associated with a strong reduction in mpox incidence.**

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Keywords: **Roll-out; Vaccination; Outbreak; Mitigation; Sexual behavior; Incidence; Mpox**

Research in context

Evidence before this study

Since May 2022, mpox has caused outbreaks in more than 100 countries. The first case was reported in France on May 19, 2022, with a fast increase in new infections disproportionally affecting men who have sex with men (MSM). Health measures were implemented to control the outbreak, including isolation of infected individuals, contact tracing and community awareness raising. In addition, vaccination with third-generation live Modified Vaccinia Ankara (MVA-BN) was recommended as of May 27 as post-exposure prophylaxis, and as of July 11, 2022 for multiple-partner MSM regardless of sexual contact. As both mitigations strategies and prophylactic vaccination were recommended, it was difficult to rule out between the impact of each intervention on the incidence of mpox. To assess the respective impact of the vaccination campaign and of the change in sexual behavior following targeted prevention messages, we searched PubMed, bioRxiv and medRxiv for articles published after May 2022 and until February 13, 2024, in English, with the keywords (["mpox" OR "monkeypox" OR "mpx"] AND ["incidence"]). We found several studies assessing the role of change in sexual behavior alone, or the role of vaccination alone. One mathematical modelling study assessed the role of both determinants in the turndown of the outbreak in England. Another study based on phylogenetic and phylographic models showed that mpox transmission in North America began declining before more than 10% of high-risk individuals in the USA had vaccine-induced immunity.

Added value of this study

Here we used data from participants in a clinical trial assessing the efficacy of doxycycline post-exposure prophylaxis and/or meningococcal B MenC4B vaccine against the occurrence of *Chlamydia trachomatis*, syphilis and *Neisseria gonorrhoeae* in MSM on PrEP with a history of STI. Mpox cases were carefully recorded and data on sexual behavior and on vaccination were available. Of note, we urged participating centers to pro-actively reach out to participants and schedule an appointment for a first MVA-BN vaccine as soon as possible. We first showed that incidence of mpox infection was high in MSM on PrEP with a history of STI (49.3 per 1000 participants-month). We also showed that participants were able to rapidly respond to targeted prevention messages and recommendations of risk-reduction, especially those at greater risk with more than 10 sexual partners in the last 3 months. Finally, we showed a significant decrease in mpox incidence between the periods before and after the launch of vaccination campaign (67.4 per 1000 p-m (95% CI 51.6–86.6) in period-1, and 24.4 per 1000 p-m (95% CI 13.9–39.6) in period-2). In multivariate analysis, only MVA-BN vaccination during summer 2022 was associated with mpox incidence, with a 99% risk reduction (95% CI 96.6–99.7).

Implications of all the available evidence

Understanding the determinants that lead to the downturn of an outbreak is key to build effective prevention interventions to face future outbreaks. When several interventions are implemented together, deciphering the role of each one is paramount. With data from MSM on PrEP participating in a clinical trial assessing several prevention strategies against bacterial sexually transmitted infections, we were able to assess the role of mitigation and of the impact of MVA-BN vaccination on mpox incidence in this population. Our results strongly suggest that rapid roll-out of pre-exposure vaccination seemed key to yield a significant impact on mpox incidence. A reduction in sexual risk behavior was evidenced in those most at risk and is likely to have contributed to the reduction in mpox incidence, although to a lesser extent than rapid roll-out of vaccination. Public health authorities should be able to rapidly reach out to key-populations with targeted prevention messages and launch concomitant large vaccination campaigns with a rapid roll-out and uptake of vaccination among at risk individuals in order to control an outbreak such as the 2022 mpox outbreak.

Introduction

Mpox is a zoonotic disease due to an Orthopoxvirus, very similar to smallpox and first identified in 1977 in the Democratic Republic of Congo. Since the discovery of mpox virus, cases have been mainly reported during outbreaks in West and Central Africa and are thought to be related to transmission from animal to humans.[1,2] Human-to-human transmission can occur through exposure to large respiratory droplets during direct contact, through direct skin/mucosa contact with skin/mucosa lesions of an infected person, or indirectly by contact with fomites (surfaces, materials or contaminated objects).[3,4] Since May 6th, 2022, an outbreak has been described in western countries with non-imported cases reported by the Portuguese and British authorities and subsequently in several European countries, the United States and Canada.[5] The first confirmed case of mpox in France occurred on May 19th, 2022.[6] Unlike previous epidemiological descriptions in historically affected countries, gay and bisexual men who have sex with men (MSM) have been disproportionately impacted during the current global outbreak.[4,7] Mpox has been isolated from semen samples and rectal swabs.[8] In addition, clear evidence of asymptomatic rectal carriage as well as case-pair data demonstrating infectivity four days prior to symptom onset suggest that mpox behaves as a sexually transmitted infection (STI).[9,10]

There is no specific vaccine to prevent mpox. With respect to other orthopox viruses, the vaccinia vaccine is >95% effective in preventing smallpox infection. MVA-BN is a third generation live Modified Vaccinia Ankara vaccine (non-replicative in humans), manufactured by Bavarian Nordic, and authorized in 2013 in Europe (EMA) under the commercial name IMVANEX®, to prevent smallpox.[11] Data from challenge trial in macaques and from post-exposure prophylaxis use after mpox exposure during small outbreaks in the United Kingdom in 2018 and 2019 suggested that MVA-BN might confer high-level protection against mpox infection.[12,13] During the current outbreak, small series rapidly reported on the high efficacy of MVA-BN vaccination in preventing mpox acquisition in a setting of post-exposure prophylaxis.[14] Therefore, several countries in Europe and North America have recommended (i) vaccination with the third generation live Modified Vaccinia Ankara (MVA-BN) vaccine for multi-partner MSM and (ii) specific risk-reduction guidelines targeted towards the MSM key population. On May 27, 2022 (Week 22, 2022), French Health Authorities recommended post-exposure vaccination with MVA-BN for individuals with documented exposure to a confirmed mpox-infected partner, and as of July 11, 2022 (Week 28, 2022), pre-exposure vaccination was recommended for multiple-partner MSM regardless of contact. MVA-BN was administered subcutaneously with one dose for those vaccinated against smallpox during childhood and two doses 28 days apart for those with no history of smallpox vaccination. At the same time, prevention campaigns targeted towards the MSM population were launched in gay venues. Mpox cases peaked in France in early July, 2022, then waned. Thus, it was difficult to assess the respective impact of the vaccination campaign and of the change in sexual behavior following targeted prevention messages. ANRS-174-DOXYVAC trial was an ongoing clinical trial assessing the efficacy of doxycycline post-exposure prophylaxis and/or meningococcal B MenC4B vaccine against the occurrence of *C. trachomatis*, syphilis and *N. gonorrhoeae* in MSM on HIV pre-exposure prophylaxis (PrEP) with a history of STI. Given the characteristics of mpox outbreak in 2022, such individuals were at high-risk for mpox infection. Thus, on July 11, 2022, when MVA-BN vaccine was recommended for multi-partner MSM in France, and because of increasing reports of mpox cases among trial participants, we urged participating centers to proactively reach out to participants and schedule an appointment for a first MVA-BN vaccine as soon as possible and no later than August 31, 2022. Here we assess mpox incidence in study participants before and after the launch of MVA-BN vaccination campaign, and explore the respective impact of vaccination and of sexual behavior adopted during the epidemic period on the evolution of incidence overtime.

Methods

ANRS-174-DOXYVAC trial design

The ANRS-174-DOXYVAC trial was a prospective, multicenter, two-by-two factorial, randomized open-label, phase 3 trial comparing the meningococcal group B vaccine to no vaccine and doxycycline post-exposure prophylaxis to no prophylaxis among MSM using PrEP for HIV prevention who have experienced a bacterial STI in the prior 12 months. We enrolled participants at 10 Assistance-Publique Hôpitaux de Paris hospital sites in France, between January 19, 2021 and September 19, 2022. To be eligible for the ANRS-174-DOXYVAC study, participants had to be MSM, at least 18 years of age, HIV negative and already included in the ANRS Prevenir study, a cohort of MSM using PrEP in Paris.[15] Participants also needed to have received HIV PrEP for at least 6 months, and to have a history of bacterial STIs within 12 months before enrollment. Participants attended study visits at enrollment and every 3 months thereafter, and were tested for STI at each visit. Sexual behavior was assessed at enrollment and at each visit thereafter and included the number of condomless sexual acts in the last 4 weeks, the number of sexual partners in the last 3 months, and chemsex for the most recent anal intercourse. Data collected in self-administered questionnaires were education, and venues for meeting casual partners, all other variables were collected in the e-Case Report Forms. All

participants provided written informed consent. The study was approved by the Ile de France XI ethics committee. The study was registered at ClinicalTrials.gov (NCT03256422).

To be included in the present analysis, participants had to have data on their sexual behavior before and after May 9, 2022 (W19, 2022), the start date of the current mpox epidemic in Europe, in order to assess changes in socio-behavioral characteristics among the same individuals. The last available data in each period (before and after W19) were used for the analysis. In the case of mpox virus infection, the last available data after May 9 and prior to diagnosis were used. Data were collected up to September 20, 2022.

From May 19, 2022 to September 20, 2022, centers participating in the ANRS-174-DOXYVAC study were invited to systematically report all confirmed cases of mpox with a positive PCR result as adverse events of special interest. The definition of a confirmed mpox case was: an individual with symptoms suggestive of mpox infection and a PCR-confirmed mpox virus infection in a specimen from any anatomical site. Diagnosis of mpox virus infection by PCR was based on detection of unique sequences of mpox virus DNA, which were published by public health agencies and adopted by clinical laboratories worldwide for the development of local PCR testing platforms. Of note, only individuals with symptoms suggestive of mpox infection were tested.

Statistical analysis

Variables were summarized as proportions for categorical variables, median and interquartile range (IQR) or mean and standard deviation and minimum and maximum (for sexual behaviors) for continuous baseline variables. We first sought to identify pre-epidemic individual socio-behavioral characteristics that might have been significantly associated with mpox acquisition. We compared pre-epidemic (up to May 8, 2022, which was W18) socio-behavioral characteristics of participants with mpox and mpox-free, using the chi-square test or Fisher's exact test for categorical variables, and the non-parametric Man–Whitney test for continuous variables. Variables with univariable p-value < 0.20 were retained for the multivariable logistic regression analysis.

We then assessed whether the mpox epidemic had an impact on the socio-behavioral characteristics of MSM by comparing their sexual behavior between the two periods of the epidemic (May 9–July 10, 2022 and July 11–Sept 20, 2022), using paired Wilcoxon test for continuous variables and Mc Nemar test for categorical variables. These analyses were restricted to participants with evaluations in both period and we assessed whether the participants with evaluation in both periods were different in the pre-epidemic period from those with only one evaluation in the epidemic period (either period-1 or period-2).

Lastly, we aimed to describe mpox incidence among study participants. We calculated incidence rates (IRs) of mpox per 1000 person-months (p-m) over periods as the total number of mpox divided by the p-m of observation in study participants. For the present analysis, follow-up began May 9, 2022 and continued until the onset of mpox infection or the end of the study period or the last follow-up if it occurred prior to the end of the study period. Period-1 ran from May 9 to July 10, 2022, before the general MSM vaccination recommendation, W19–W27, and period-2 from July 11 to September 20, 2022, after the vaccination launch, W28–W38. IRs of mpox were compared between periods using a Poisson regression model with random intercepts to account for within-subject variability. Smallpox vaccination during childhood was based on vaccine records or on self-report with a smallpox vaccination scar. Self-reporting with no smallpox vaccination scar was not taken into account. To assess the impact of childhood smallpox vaccination, of MVA-BN vaccination (at least one dose) and of having >10 partners during the last 3 months on mpox incidence in study participants, we compared incidence of mpox in the two periods, before and after implementation of the vaccination recommendation in the ANRS-174-DOXYVAC study. Therefore, we assessed whether each factor of interest (smallpox vaccination during childhood as a fixed variable, vaccination with MVA-BN vaccine in summer 2022, as a time dependent variable and having more than 10 sexual partners in the last 3 months at the last evaluation as a fixed variable) was significantly associated with incidence of mpox and how each factor modified the period effect (time-dependent variable) in the Poisson regression model after including each factor in a bivariate analysis (period and the variable of interest). Given that not all participants had sexual behavior evaluations in both periods, we used only the last available evaluation before the diagnosis for participants with mpox or the end of follow-up for mpox-free participants. Finally, we performed a multivariable analysis including the period and the three other variables. We also wanted to compare the incidence of mpox in our study population with that of the global MSM population in France at the same time. The number of MSM in France is imprecisely known. We used the estimate from Ousseine et al. and used a size of 104,645 MSM eligible for PrEP to perfom the analysis of mpox incidence (i) from the beginning of the epidemic in France till August 8 and (ii) from August 9 till September 20, 2022.[16] We used the number of PCR-confirmed mpox diagnosis that were reported to French Health authorities during these two periods. We removed the participants included in ANRS-174-DOXYVAC and the number of infections occurring in ANRS-174-DOXYVAC to perform the analysis in the general population of MSM eligible for PrEP in France.

The analyses were conducted using SAS version 9.4, with a type one error set at 0.05.

Role of the funding source
The sponsor of the study (ANRS/MIE) had no role in data collection, data analysis, data interpretation or writing of the report. The authors were not paid to write this article and the corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

Results

Baseline characteristics of study population
At the time of mpox outbreak, 546 MSM had been randomized in the ANRS-174 DOXYVAC trial, including 472 with available data before and after May 9, 2022, which are included in the present analysis. Their characteristics at the last visit prior to the epidemic period are summarized in Table 1. Participants had a median age of 39 years, a median number of 10 sexual partners during the last three months, a median number of five condomless anal intercourses during the last month and 20% had received smallpox vaccine during childhood.

Mpox infection and pre-epidemic characteristics between participants with mpox and mpox-free
Between May 9, 2022 and September 20, 2022 (W40), 77/472 participants were diagnosed with mpox infection, yielding an overall incidence of 49.3 per 1000 p-m (95% CI 38.9 to 61.6). Median delay between pre-epidemic data collection and May 8, 2022 was 41 [19–68] days. As shown in Table 1, at the last visit prior to the epidemic period, participants with mpox were younger (37 vs 40, p = 0.0179), were less frequently vaccinated against smallpox during childhood (4% vs 23%, p < 0.0001), had more sexual partners during the last three months (15 vs 10, p = 0.0022) and had more condomless anal intercourses during the last month (7 vs 5, p = 0.0244) than mpox-free participants. Also, the proportion having more than 10 partners during the last 3 months was much higher in participants with mpox than in mpox-free participants (61.0 vs 39.5%, p = 0.001). There was no difference in educational level, venues for meeting sexual partners or chemsex use between participants with mpox and mpox-free participants. In a multivariable logistic regression analysis, childhood smallpox vaccination was associated with an 85% risk reduction of mpox infection (OR = 0.15, 95% CI 0.04–0.52), the other variables were no longer significant.

Changes in sexual behavior
Median date of data collection on sexual behavior during the epidemic period was August 30, 2022. Overall, 45 of

Variable during pre-epidemic period	Total, N = 472	Participants with mpox (N = 77)	Mpox-free participants (N = 395)	p-value
Age	39 [33–47]	37 [32–44]	40 [33–48]	0.018
History of smallpox childhood vaccination, N (%)				
No	377 (79.9%)	74 (96.1%)	303 (76.7%)	<0.0001
Yes	95 (20.1%)	3 (3.9%)	92 (23.3%)	
Education, N = 330				
College	299 (90.6%)	49 (90.7%)	250 (90.6%)	>0.99
High school	31 (9.4%)	5 (9.3%)	26 (9.4%)	
Missing	142	23	119	
Number of partners during the last 3 months, median (IQR)	10 [5–20]	15 [8–20]	10 [5–20]	0.002
Number of condomless anal intercourse during last month, median (IQR)	5 [2–10]	7 [3–10]	5 [2–10]	0.024
Having > 10 partners in the last 3 months				
No	269 (57.0%)	30 (39.0%)	239 (60.5%)	0.001
Yes	203 (43.0%)	47 (61.0%)	156 (39.5%)	
Chemsex use during last sexual intercourse				
No	382 (80.9%)	61 (79.2%)	321 (81.3%)	0.64
Yes	90 (19.1%)	16 (20.8%)	74 (18.7%)	
Casual partners met at sex-parties/private parties in the past 3 months				
No	95 (68.4%)	13 (68.4%)	82 (68.3%)	>0.99
Yes	44 (31.6%)	6 (31.6%)	38 (31.7%)	
Missing	333	58	275	
Casual partners met at swinger parties				
No	134 (96.4%)	18 (94.7%)	116 (96.7%)	0.53
Yes	5 (3.6%)	1 (5.3%)	4 (3.3%)	
Missing	333	58	275	
Median delay between data collection and May 8, 2022 (days)	41 [19–68]	39 [18–61]	42 [19–70]	

Table 1: **Characteristics of participants included in the present analysis (n = 472) at the last visit prior to the epidemic period, and comparison of pre-epidemic characteristics between participants with mpox (n = 77) and mpox-free participants (n = 395).**

participants with mpox had available evaluation in both periods and 32 did not. For mpox-free participants the corresponding figures were 234 and 161. There were no significant differences in pre-epidemic sexual behavior between those with and without evaluation in both period-1 and period-2 (Supplementary table). Changes in sexual behavior are summarized in Table 2 for participants with available evaluations in both period-1 and period-2. For mpox-free participants, there was a decrease in the mean number of sexual partners during the last three months (p = 0.002), mainly explained by a decrease in the proportion of participants with more than 10 partners (p = 0.003), while no significant change was evidenced for the number of condomless anal intercourses during the last month (p = 0.58). In participants with mpox, the evaluation in period-2 always occurred after the mpox diagnosis, so the changes were linked to being diagnosed not only to the knowledge of the epidemic. There was a decrease in the mean number of sexual partners during the last three months but it did not reach significance (p = 0.12), in the number of condomless anal intercourses during the last month (p = 0.044) and in the proportion of participants with more than 10 partners (p = 0.029).

Mpox incidence before and after July 11, 2022 (W28): impact of smallpox vaccination in childhood, MVA-BN vaccination, and sexual behavior adopted during the epidemic period.

MVA-BN vaccination roll-out was rapid in study participants, with 86% (341/398) of eligible participants having received at least one dose by September 20, 2022 (W38) (Fig. 1). Of these 341 MVA-BN vaccine recipient participants, 156 received one dose and 185 received two doses of MVA-BN vaccine during the study period. All of the 472 participants contributed to period-1, while 384 contributed to period-2 (the 61 participants with mpox diagnosis in period-1 and 27 mpox-free participants were not contributing to period-2). Among mpox free participants the evaluation of having >10 partners in the last 3 months used in the model was available in period-2 for 368 and in period-1 for 27, while in participants with mpox it was available in period-1 for 47 and before the epidemic for 30. Mpox incidences during period-1 and period-2 are shown in Table 3. Sixty-one out of 472 participants were diagnosed with mpox infection in period-1 (May 9–July 10, 2022), yielding an incidence of 67.4 (95% CI 51.6–86.6) p-m. In period-2 (July 11–Sept 20, 2022), 16 participants were diagnosed with mpox infection, with an incidence of 24.4

Median (IQR), mean, std or n (%)	Mpox cases			Mpox-free participants		
	Period-1 May 9–July 10, 2022 N = 45	Period-2 July 11–Sept 20, 2022 N = 45	p-value	Period-1 May 9–July 10, 2022 N = 234	Period-2 July 11–Sept 20, 2022 N = 234	p-value
Number of sexual partners during the last 3 months			0.12			0.002
Median (IQR)	20 [10–30]	10 [5–20]		10 [6–20]	10 [5–17]	
Mean (sd)	22.0 (17.6)	17.7 (21.2)		16.4 (18.0)	13.7 (15.3)	
Range	(0–80)	(0–100)		(0–180)	(0–120)	
Number of condomless anal intercourses during last month			0.044			0.57
Median (IQR)	8 [5–15]	5 [1–10]		5 [3–10]	4 [2–10]	
Mean (sd)	12.2 (16.0)	10.3 (18.2)		7.5 (8.0)	7.4 (8.6)	
Range	(0–100)	(0–100)		(0–60)	(0–50)	
Having > 10 sexual partners in the last 3 months			0.029			0.003
No	16 (35.6%)	25 (55.6%)		124 (53.0%)	148 (63.2%)	
Yes	29 (64.4%)	20 (44.4%)		110 (47.0%)	86 (36.8%)	
Using drugs during last intercourse (Chemsex)			0.79			0.18
No	39 (86.7%)	37 (82.2%)		187 (79.9%)	196 (83.8)	
Yes	6 (13.3%)	8 (17.8%)		47 (20.1)	38 (16.2)	
Casual partners met at sex-parties/private parties in the past 3 months			0.063			<0.0001
No	12 (100%)	7 (58.3%)		68 (97.1%)	48 (68.6%)	
Yes	0 (0.0%)	5 (41.7%)		2 (2.9%)	22 (31.4%)	
Casual partners met at swinger parties un the past 3 months			0.50			0.25
No	12 (100%)	10 (83.3%)		70 (100%)	67 (95.7%)	
Yes	0 (0.0%)	2 (16.7%)		0 (0.0%)	3 (4.3%)	

Table 2: **Sexual behavior and chemsex use at last intercourse in period-1 and period-2 in mpox cases and mpox-free participants.**

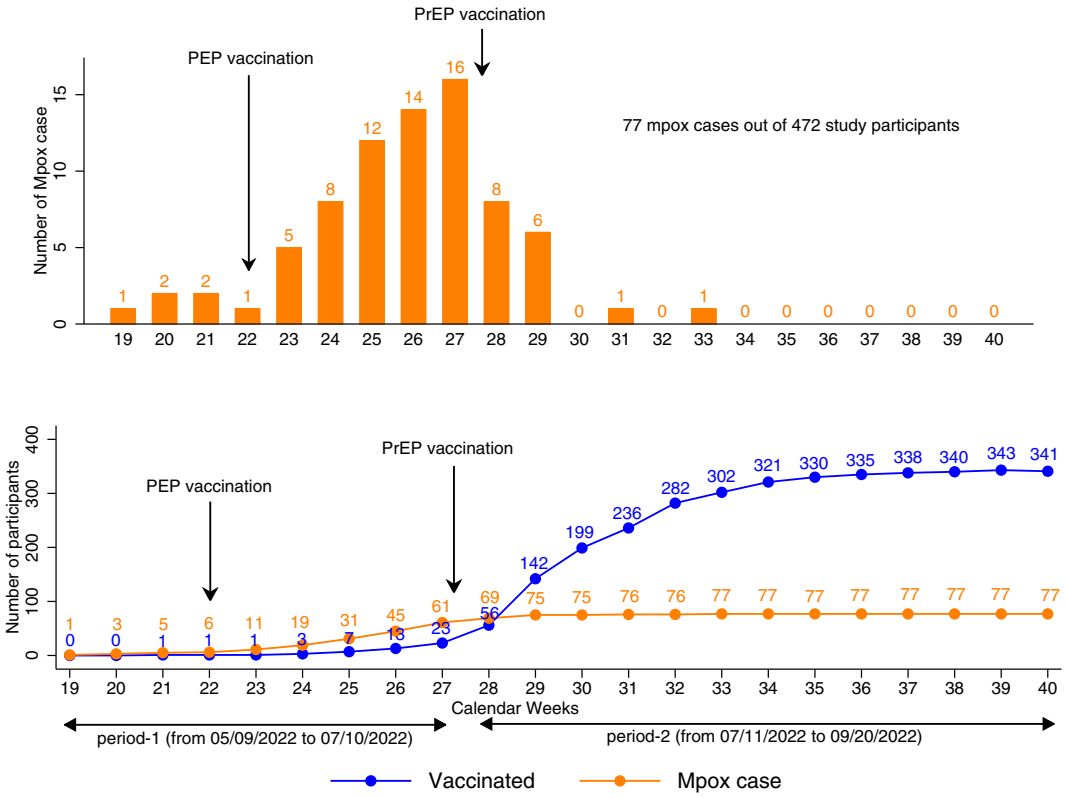

Fig. 1: Cumulative incidence of mpox and MVA-BN vaccination by calendar weeks (PEP: post-exposure prophylactic vaccination; PrEP: pre-exposure prophylactic vaccination).

(95% CI 13.9–39.6) p-m. The last mpox case was reported on Week 33, 2022. Incidence rate ratio between period-2 and period-1 was 0.36 (95% CI 0.21–0.63), showing a significant decrease in mpox incidence between period-1 and period-2.

Bivariate analyses showed that all three variables were significantly associated with the risk of mpox (history of smallpox childhood vaccination, MVA-BN summer 2022 vaccination, and having >10 partners in the last 3 months during the epidemic period) (Table 3, model 2, 3 and 4), but the period effect on mpox incidence remained significant after accounting for smallpox childhood vaccination or for having >10 partners in the last 3 months during the epidemic period (Table 3, model 2 and 4). On the other hand, accounting for MVA-BN vaccination during summer 2022 led to a non-significant period effect (Table 3, model 4).

The multivariable analysis (Table 3, model 5) confirmed that MVA-BN vaccination in 2022 led to a non-significant period effect, and was significantly associated with mpox incidence, with a 99.0% risk reduction (95% CI 96.6–99.7). In this model, the relative risk of having >10 partners in the last 3 months at the last available evaluation, was estimated as 1.57 (p = 0.057), while the relative risk of smallpox childhood vaccination was estimated as 0.81 (p = 0.780).

We also compared mpox incidence in our study population with that in MSM eligible for PrEP in France (Table 4). This "difference in differences" analysis showed that mpox incidence significantly decreased in period-2 in comparison with period-1 in our study population, while there was no significant difference in mpox incidence among MSM in France during the two periods.

Discussion

Here we show that MSM on PrEP with a history of STI were at high risk of mpox acquisition as attested by the high incidence of mpox infection in our study population (77/472, 49.3 per 1000 p-m). Incidence rate of mpox decreased significantly in study participants after MVA-BN vaccination was recommended for multi-partner MSM, with an incidence rate ratio of 0.36 (95% CI 0.21–0.63) between period-1 and period-2, with no new mpox infection after mid-August, 2022. The only factor that remained significantly associated with this reduction in mpox incidence was MVA-BN vaccination with at

	Period	Total N	N cases	Persons-month	Incidence per 1000 p-m (95% CI)	IRR (95% CI)	p value
Model 1							
	Period						0.0003
	Period-1: May 9–July 10, 2022	N = 472	61	904.67	67.4 (51.6–86.6)	1	
	Period-2: July 11–Sept 20, 2022	N = 384	16	656.85	24.4 (13.9–39.6)	0.361 (0.208–0.627)	
Model 2							
	Period						0.001
	Period-1: May 9–July 10, 2022	N = 472	61	904.67	67.4 (51.6–86.6)	1	
	Period-2: July 11–Sept 20, 2022	N = 384	16	656.85	24.4 (13.9–39.6)	0.371 (0.213–0.644)	
	History of vaccination in childhood						0.001
	No	N = 377	74	1217.8	60.8 (47.7–76.3)	1	
	Yes	N = 95	3	343.8	8.7 (1.8–25.5)	0.148 (0.046–0.471)	
Model 3							
	Period						0.250
	Period-1: May 9–July 10, 2022	N = 472	61	904.67	67.4 (51.6–86.6)	1	
	Period-2: July 11–Sept 20, 2022	N = 384	16	656.85	24.4 (13.9–39.6)	0.723 (0.415–1.258)	
	MVA-BN vaccination summer 2022						<0.0001
	No	N = 131	74	298.3	248.1 (194.8–311.4)	1	
	Yes	N = 341	3	1263.3	2.4 [0.5–6.9]	0.010 (0.003–0.033)	
Model 4							
	Period						0.009
	Period-1: May 9–July 10, 2022	N = 472	61	904.67	67.4 (51.6–86.6)	1	
	Period-2: July 11–Sept 20, 2022	N = 384	16	656.85	24.4 (13.9–39.6)	0.426 (0.224–0.809)	
	Having > 10 partners in the last 3 months during the epidemic period						0.003
	No	N = 251	33	946.2	34.9 [24.0–49.0]	1	
	Yes	N = 221	44	615.3	71.5 [52.0–96.0]	2.103 (1.285–3.442)	
Model 5							
	Period						0.355
	Period-1: May 9–July 10, 2022	N = 472	61	904.67	67.4 (51.6–86.6)	1	
	Period-2: July 11–Sept 20, 2022	N = 384	16	656.85	24.4 (13.9–39.6)	0.769 (0.440–1.344)	
	History of vaccination in childhood						0.730
	No	N = 377	74	1217.8	60.8 (47.7–76.3)	1	
	Yes	N = 95	3	343.8	8.7 (1.8–25.5)	0.809 (0.243–2.696)	
	MVA-BN vaccination summer 2022						<0.0001
	No	N = 131	74	298.3	248.1 (194.8–311.4)	1	
	Yes	N = 341	3	1263.3	2.4 [0.5–6.9]	0.011 (0.003–0.035)	
	Having > 10 partners in the last 3 months during the epidemic period						0.057
	No	N = 252	33	946.2	34.9 [24.0–49.0]	1	
	Yes	N = 220	44	615.3	71.5 [52.0–96.0]	1.567 (0.986–2.489)	

IRR: incidence rate ratio.

Table 3: **mpox incidence before and after July 11, 2022 (W28).**

least one dose during summer 2022, with a 99% risk reduction (95% CI 96.6–99.7).

Previous outbreaks of viral infection were stopped by vaccination. Post exposure prophylaxis (PEP) using vaccination has proven its efficacy in several infectious diseases, ranging from 38% for Mumps to 85% for hepatitis B.[17] Sexually transmitted viral hepatitis A outbreak in MSM in Montreal, Canada in 1996 was

	Period 19 May–8 August 2022				Period 9 August–20 September 2022				Difference in incidence rate (95% CI)	p-value
	N at risk	Number of cases	Person-month	Inc rate per 1000 person-month	N at risk	Number of cases	Person-month	Incidence rate per 1000 person-month		
France	104,173	2525	273,864	9.22	101,648	1341	139,337	9.62	0.4 (−0.2; 1.0)	0.2045
Doxyvac	472	76	1224	62.08	308	1	337	2.97	−59.1 (−74.2; −44.0)	<0.0001

Table 4: **Difference in differences: mpox incidence in study participants and the global MSM population in France.**

controlled after the launch of a pre-exposure vaccination campaign for MSM.[18] During the 2002 mpox outbreak, both mitigation strategies and prophylactic vaccination were recommended, making it difficult to assess the respective impact of each intervention in countries where MVA-BN vaccine was made available for MSM.[19] We show here that the MSM community was able to rapidly respond to targeted prevention messages and recommendations of risk-reduction. Indeed, participants diagnosed with mpox did reduce the number of their sexual partners, showing that they did comply with the recommendation of self-isolation. In mpox-free participants, the proportion of those with the highest risk, i.e. those reporting more than 10 sexual partners during the last three months, did significantly decrease between period-1 and period-2. Nevertheless, in our study, the impact of MVA-BN vaccine overweighed the impact of modification in sexual behavior in multivariate analysis in this highly vaccinated population. This may be due to (i) a lack of power to evidence a significant impact of change in sexual behavior, or (ii) the very rapid roll-out of vaccination in our study participants. Indeed, a recent mathematical modelling study based on data from the outbreak in England showed that moderate reduction in sexual risk behavior probably controlled a large outbreak of mpox, and vaccination is expected to have only little impact on the downturn of the outbreak because it was introduced late in the outbreak.[20] Vaccination impact could have been much greater on the number on infections prevented if it was initiated earlier into the outbreak.[20] Another study based on phylogeographic and phylodynamic models showed that mpox transmission in North America began declining before more than 10% of high-risk individuals in the USA had vaccine-induced immunity, suggesting a significant effect of behavioral change among MSM in curbing the epidemic in North America.[21] Here, we urged participating centers to reach out to study participants and have them come in to receive their first dose of MVA-BN vaccine as soon as possible after the launch of the vaccination campaign in France.

Both natural and post vaccination immunity are considered life-long in smallpox. We showed that mpox cases were less frequently vaccinated against smallpox during childhood than mpox-free controls. However, in multivariate analysis, we did not find a significant impact of vaccination against smallpox during childhood. This might be due to the confounding factor being that all mpox-free individuals did receive at least one dose of MVA-BN vaccine during summer 2022.

We showed a significant efficacy of MVA-BN vaccination (at least one dose) on the reduction of mpox incidence. Complete vaccination with two doses of MVA-BN administered subcutaneously or intradermally 28 days apart was found to have an adjusted vaccine effectiveness of 86–89% in multiple observational cohorts.[22–24] However, these findings have been somewhat contradicted by a large case–control study which adjusted for health-seeking behavior and calendar time, demonstrating a significantly lower estimated adjusted vaccine effectiveness rates of 35.8% and 66% after administration of one and two doses of MVA-BN, respectively.[25] There are important differences that may explain the different vaccine effectiveness rate between the latter study by Deputy et al. and ours. First, our study population was very homogenous with exclusively healthy MSM on PrEP, while the study by Deputy et al. enrolled a significant number of immunocompromised and/or HIV positive individuals. Second, 20% of the participants in the ANRS-174-DOXYVAC trial received smallpox vaccine during childhood vs <1% in the study by Deputy et al. Finally, all vaccinated individuals participating in the ANRS-174-DOXYVAC trial received MVA-BN subcutaneously while 24% of the individuals included in the study by Deputy et al. received MVA-BN via this route of injection.[25] Again, in the present analysis, the very rapid roll-out of vaccination might explain the very high efficacy that was observed.

It can be argued that mpox epicurves showed a reduction in incidence even in countries where MVA-BN vaccine was not available. As individuals with highest number of partners are most likely to be infected in the earliest phase, the initial epidemic growth could be accelerated by transmission among these individuals (who also share same meeting venues). But this growth would also be saturated as these individuals become rapidly infected and immune and no longer contribute to the outbreak. This suggests that early infection of individuals with highest-risk may have been sufficient to cause downward trends in mpox epidemic even without effective control measures.[26] Though this might be true, ANRS-174 DOXYVAC participants were all at high-risk for mpox acquisition, as attested by their characteristics at enrollment in the study. Moreover, while only one new mpox case was reported among study participants between August 8 and September 20, 2022, the situation was very different in France with 1342 new mpox cases between August 9 and Sept 20, 2022 (out of a total of 3943 cases in France between May 19 and Sept 20, 2022). This emphasizes the fact that rapid roll-out of vaccination did play a significant role in mpox incidence reduction in our study participants.

Our study has several limitations. First, high mpox incidence and rapid roll-out of vaccination do not reflect the situation in France. Indeed, as mentioned before, we urged participating centers to pro-actively reach out to participants and schedule an appointment for a first MVA-BN vaccine before the end of August 2022, while, at the same time, MSM struggled to get an appointment for a first MVA-BN vaccine dose because sexual health clinics and vaccinations centers needed time to step forward during summer with no additional resources. Second, participants in ANRS-174-DOXYVAC study

might have been more prone to adopt preventive strategies such as vaccination given that they were already on PrEP and participating in a trial assessing prevention of bacterial STIs. This might also explain the high uptake of MVA-BN vaccination herein. Third, we restricted the analysis to 472 study participants with available data before and after May 9, 2022, while there were 502 participants enrolled up to July 11, 2022. However, we do not believe that the thirty individuals who were not included in the analysis would have modified our conclusions. Fourth, we used individual data; we might thus not have been able to evidence a population-level impact of some strategies such as mitigation/change in sexual behavior. In addition, we have re-used data from a randomized clinical trial for another purpose than the original trial objective. Therefore, we might lack power to show a significant impact of the sexual behavior adopted during the epidemic period and we might subsequently have overestimated the impact of MVA-BN vaccine on the reduction of mpox incidence. Moreover, data on sexual behavior were collected every three months, and we might have not captured relevant data according to the delay between study visit and the dates we set for period-1 and period-2. However, median delay between data collection and May 8, 2022 was 41 [19–68] days, and median date of data collection during the epidemic period was August 30, 2022, so we should have been able to capture relevant data close enough to the launch of vaccination campaign and capture relevant data of sexual behavioral change. Finally, we did not use interrupted time series (ITS) because we had individual data available (in particular exposure to vaccination in childhood, number of at-risk partners and precise exposure data to vaccine in the epidemic period), and because the time period was short. Thus, we were unsure to have enough data to model a time trend. In ITS, only linear or exponential trend can be accounted for and the method can be biased in some scenario.[27]

In conclusion, we showed that mpox incidence was high among MSM on PrEP with a history of STI, and that rapid roll-out of MVA-BN vaccine was associated with a significant reduction of mpox incidence. We also showed that the MSM community was willing to modify their sexual behavior in response to targeted prevention messages and risk-reduction recommendations. MVA-BN vaccine should be made available and affordable worldwide. Indeed, even if some countries in Europe and North America can control and eliminate mpox virus, other countries in Africa will remain affected, which will be inequitable in addition to being also a threat of future outbreaks worldwide.[28] With recent accumulating reports on breakthrough infections after complete vaccination or reinfection after mpox infection, data on neutralizing antibodies and their durability in vaccinated and in infected individuals are mandatory.[29,30]

Contributors

JG designed and led the study and wrote the first draft of the report. LA, MO and DC designed the analysis. MAG coordinated the study and oversaw data management with LA and DC. JG, MO, SG, LA, DC and JMM analyzed the data. JG, ER, GP, CK, LS, CD, JP, JPV and JMM did the study at their sites. All authors critically reviewed and approved the manuscript.

Data sharing statement

Data requests may be submitted to the scientific committee of the ANRS DOXYVAC study (by email to jade.ghosn@aphp.fr) and must be approved by the French data protection authority, la Commission Nationale de l'Informatique et des Libertes (CNIL) and ANRS/MIE. French law requires that everyone who wishes to access cohort data or clinical study data on humans must ask the French data protection authority (the CNIL) for permission, by completing a form that can be provided by Lambert Assoumou (lambert.assoumou@iplesp.upmc.fr). For further information, please see https://www.cnil.fr/. The ANRS DOXYVAC scientific committee will evaluate each proposal for compatibility with general objectives, ethical approval, and informed consent forms of the ANRS DOXYVAC project, and for potential overlap with ongoing work. Deidentified participant data, study protocol including informed consent form and statistical analysis plan can be made available upon request, 1 year after publication of this report.

Declaration of interests

Dr Ghosn received consulting fees from Gilead and ViiV Healthcare. Dr Duvivier received consulting fees from Gilead and support for attending meetings and/or travel from Gilead, Merck and ViiV Healthcare. Dr Costagliola received honoraria for lecture from Pfizer. Dr Molina received grants from Gilead and Merck, consulting fees from Gilead, Merck and ViiV Healthcare and payment for participation on a DSMB from Aelix. All other authors have nothing to declare.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanepe.2024.101020.

References

1 Durski KN, McCollum AM, Nakazawa Y, et al. Emergence of monkeypox - West and Central Africa, 1970-2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(10):306–310. https://doi.org/10.15585/mmwr.mm6710a5. Erratum in: MMWR Morb Mortal Wkly Rep. 2018 Apr 27;67(16):479. PMID: 29543790; PMCID: PMC5857192.

2 Bunge EM, Hoet B, Chen L, et al. The changing epidemiology of human monkeypox-A potential threat? A systematic review. *PLoS Negl Trop Dis*. 2022;16(2):e0010141. https://doi.org/10.1371/journal.pntd.0010141. PMID: 35148313; PMCID: PMC8870502.

3 Reynolds MG, Yorita KL, Kuehnert MJ, et al. Clinical manifestations of human monkeypox influenced by route of infection. *J Infect Dis*. 2006;194(6):773–780. https://doi.org/10.1086/505880. Epub 2006 Aug 8. PMID: 16941343.

4 Gessain A, Nakoune E, Yazdanpanah Y. Monkeypox. *N Engl J Med*. 2022;387(19):1783–1793. https://doi.org/10.1056/NEJMra2208860. Epub 2022 Oct 26. PMID: 36286263.

5 Girometti N, Byrne R, Bracchi M, et al. Demographic and clinical characteristics of confirmed human monkeypox virus cases in individuals attending a sexual health centre in London, UK: an observational analysis. *Lancet Infect Dis*. 2022;22(9):1321–1328. https://doi.org/10.1016/S1473-3099(22)00411-X. Epub 2022 Jul 1. PMID: 35785793; PMCID: PMC9534773.

6 Cas de variole du singe : point de situation au 5 juillet 2022. Available from: https://www.santepubliquefrance.fr/les-actualites/2022/cas-de-variole-du-singe-point-de-situation-au-5-juillet-2022.

7 Thornhill JP, Barkati S, Walmsley S, et al. Monkeypox virus infection in humans across 16 countries - April-June 2022. *N Engl J Med*. 2022;387(8):679–691. https://doi.org/10.1056/NEJMoa2207323. Epub 2022 Jul 21. PMID: 35866746.

8 Palich R, Burrel S, Monsel G, et al. Viral loads in clinical samples of men with monkeypox virus infection: a French case series. *Lancet Infect Dis*. 2023;23(1):74–80. https://doi.org/10.1016/S1473-3099(22)00586-2. Epub 2022 Sep 29. PMID: 36183707; PMCID: PMC9534074.

9 Ferré VM, Bachelard A, Zaidi M, et al. Detection of monkeypox virus in anorectal swabs from asymptomatic men who have sex with men in a sexually transmitted infection screening program in Paris, France. *Ann Intern Med*. 2022;175(10):1491–1492. https://doi.org/10.7326/M22-2183. Epub 2022 Aug 16. PMID: 35969863.

10 Ward T, Christie R, Paton RS, Cumming F, Overton CE. Transmission dynamics of monkeypox in the United Kingdom: contact tracing study. *BMJ*. 2022;379:e073153. https://doi.org/10.1136/bmj-2022-073153. PMID: 36323407; PMCID: PMC9627597.

11 EMA. *Imvanex*. European Medicines Agency; 2018. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/imvanex.

12 Pittman PR, Hahn M, Lee HS, et al. Phase 3 efficacy trial of modified vaccinia Ankara as a vaccine against smallpox. *N Engl J Med*. 2019;381(20):1897–1908. https://doi.org/10.1056/NEJMoa1817307. PMID: 31722150.

13 Monkeypox outbreak: vaccination strategy. GOV.UK. Available from: https://www.gov.uk/guidance/monkeypox-outbreak-vaccination-strategy.

14 Thy M, Peiffer-Smadja N, Mailhe M, et al. Breakthrough infections after postexposure vaccination against mpox. *N Engl J Med*. 2022;387(26):2477–2479. https://doi.org/10.1056/NEJMc2211944. Epub 2022 Dec 7. PMID: 36477495.

15 Molina JM, Ghosn J, Assoumou L, et al. Daily and on-demand HIV pre-exposure prophylaxis with emtricitabine and tenofovir disoproxil (ANRS PREVENIR): a prospective observational cohort study. *Lancet HIV*. 2022;9(8):e554–e562. https://doi.org/10.1016/S2352-3018(22)00133-3. Epub 2022 Jun 27. PMID: 35772417.

16 Ousseine YM, Lydié N, Velter A. Pre-exposure prophylaxis in France : how many MSM are eligible and how much will it cost. *PLoS One*. 2022;17(12):e0278016. https://doi.org/10.1371/journal.pone.0278016. eCollection 2022.

17 Gallagher T, Lipsitch M. Postexposure effects of vaccines on infectious diseases. *Epidemiol Rev*. 2019;41(1):13–27. https://doi.org/10.1093/epirev/mxz014. PMID: 31680134; PMCID: PMC7159179.

18 Allard R, Beauchemin J, Bédard L, Dion R, Tremblay M, Carsley J. Hepatitis A vaccination during an outbreak among gay men in Montréal, Canada, 1995-1997. *J Epidemiol Community Health*. 2001;55(4):251–256. https://doi.org/10.1136/jech.55.4.251. PMID: 11238580; PMCID: PMC1731875.

19 Hubach RD, Owens C. Findings on the monkeypox exposure mitigation strategies employed by men who have sex with men and transgender women in the United States. *Arch Sex Behav*. 2022;51(8):3653–3658. https://doi.org/10.1007/s10508-022-02423-3. Epub 2022 Sep 14. PMID: 36103027; PMCID: PMC9472716.

20 Zhang XS, Mandal S, Mohammed H, et al. Transmission dynamics and effect of control measures on the 2022 outbreak of mpox among gay, bisexual, and other men who have sex with men in England: a mathematical modelling study. *Lancet Infect Dis*. 2024;24(1):65–74. https://doi.org/10.1016/S1473-3099(23)00451-6. Epub 2023 Sep 11. PMID: 37708908.

21 Paredes MI, Ahmed N, Figgins M, et al. Underdetected dispersal and extensive local transmission drove the 2022 mpox epidemic. *Cell*. 2024;187(6):1374–1386.e13. https://doi.org/10.1016/j.cell.2024.02.003. Epub 2024 Feb 29. PMID: 38428425.

22 Wolff Sagy Y, Zucker R, Hammerman A, et al. Real-world effectiveness of a single dose of mpox vaccine in males. *Nat Med*. 2023;29(3):748–752. https://doi.org/10.1038/s41591-023-02229-3. Epub 2023 Jan 31. PMID: 36720271; PMCID: PMC9930701.

23 Hazra A, Rusie L, Hedberg T, Schneider JA. Human monkeypox virus infection in the immediate period after receiving modified vaccinia Ankara vaccine. *JAMA*. 2022;328(20):2064–2067. https://doi.org/10.1001/jama.2022.18320. PMID: 36178700; PMCID: PMC9526114.

24 Payne AB, Ray LC, Cole MM, et al. Reduced risk for mpox after receipt of 1 or 2 doses of JYNNEOS vaccine compared with risk among unvaccinated persons - 43 U.S. Jurisdictions, July 31-October 1, 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71(49):1560–1564. https://doi.org/10.15585/mmwr.mm7149a5. PMID: 36480479; PMCID: PMC9762900.

25 Deputy NP, Deckert J, Chard AN, et al. Vaccine effectiveness of JYNNEOS against mpox disease in the United States. *N Engl J Med*. 2023;388(26):2434–2443. https://doi.org/10.1056/NEJMoa2215201. Epub 2023 May 18. PMID: 37199451.

26 Murayama H, Pearson CAB, Abbott S, et al. Accumulation of immunity in heavy-tailed sexual contact networks shapes mpox outbreak sizes. *J Infect Dis*. 2024;229(1):59–63. https://doi.org/10.1093/infdis/jiad254. PMID: 37402631; PMCID: PMC10786257.

27 Wong A, Kramer SC, Piccininni M, et al. Using Lasso Regression to estimate the population-level impact of pneumococcal conjugate vaccines. *Am J Epidemiol*. 2023;92(7):1166–1180.

28 Mitjà O, Ogoina D, Titanji BK, et al. Monkeypox. *Lancet*. 2023;401(10370):60–74. https://doi.org/10.1016/S0140-6736(22)02075-X. Epub 2022 Nov 17. Erratum in: Lancet. 2022 Dec 3;400(10367):1926. PMID: 36403582; PMCID: PMC9671644.

29 Zeggagh J, Ferraris O, Salmona M, Tarantola A, Molina JM, Delaugerre C. Second clinical episode of hMPX virus in a man having sex with men. *Lancet*. 2023;401(10388):1610. https://doi.org/10.1016/S0140-6736(23)00509-3. Epub 2023 Mar 24. PMID: 36972717.

30 Hazra A, Zucker J, Bell E, et al. Mpox in people with past infection or a complete vaccination course: a global case series. *Lancet Infect Dis*. 2024;24(1):57–64. https://doi.org/10.1016/S1473-3099(23)00492-9. Epub 2023 Sep 4. PMID: 37678309.