SUPPLEMENTARY MATERIAL

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Additional methods

Methods and results of the sensitivity analysis using Poisson regression

To test the impact of the analytical approach, we alternatively addressed the study question using incidence rates and Poisson regression to estimate incidence rate ratios (IRR) and derive vaccine effectiveness (VE = (1-IRR)*100).

The exposure was defined as receiving at least one dose of MVA-BN vaccine, and vaccination status was assigned dynamically. All individuals started their follow-up into the study on 12 July 2022 as unvaccinated, and continued at risk in that status up to the earliest of: date of MPXV infection, date of death, date of administration of a first MVA-BN vaccine dose (regardless of indication as pre or post-exposure prophylaxis) or 12 December 2022. If a first MVA-BN vaccine dose was administered as pre-exposure prophylaxis before MPXV infection, death or 12 December 2022, the individual was classified as vaccinated and started contributing time at risk in that group up to the earliest of: date of MPXV infection, date of death, or 12 December 2022. Follow-up ended with an event when the censoring reason was MPXV infection. To assess vaccine effectiveness (VE) by number of days since dose administration, time since vaccination was further split into days 0 to 6 or ≥7 post-vaccination or, alternatively, into days 0 to 13 or ≥14 post-vaccination.

We aggregated the number of person-days of follow-up and the number of events in each vaccination status category by region (n=15), epidemiological week and age-group (18-29 / 30-39 / 40-49 / ≥50)

We used Poisson regression models to estimate the incidence rate ratio (IRR) with 95% confidence interval (95%CI), using the number of events as dependent variable, vaccination status as independent variable, and the logarithm of the number of person-days as offset. We estimated the crude IRR and the adjusted IRR by epidemiological week (using restricted cubic splines with three knots), age-group and region (as categorical variables).

Supplementary tables

Table S1. Baseline characteristics of the initial, the eligible and the matched sample

	Initial sample (N=10,771)		Eligible sample (N=10,449)		Matched sample (N=11,320)	
	n	%	n	%	n	%
Age, years						
18-29	2,077	19.3	2,013	19.3	1,967	17.4
30-39	4,605	42.8	4,467	42.7	5,229	46.2
40-49	2,848	26.4	2,756	26.4	3,091	27.3
≥ 50	1,241	11.5	1,213	11.6	1,033	9.1
Childhood smallpox vaccination						
Yes	163	1.5	135	1.3	2	0.0
No	33	0.3	27	0.3	92	0.8
Unknown	10,574	98.2	10,287	98.4	11,226	99.2
Autonomous Region						
Andalusia	1,923	17.8	1,862	17.8	1,852	16.4
Asturias	53	0.5	52	0.5	74	0.6
Balearic Islands	768	7.1	686	6.6	722	6.4
Canary Islands	333	3.1	325	3.1	424	3.7
Castile and León	103	1.0	101	1.0	32	0.3
Castilla-La Mancha	76	0.7	76	0.7	118	1.0
Catalonia	2,925	27.3	2,813	26.9	4,242	37.5
Valencian Community	821	7.6	812	7.8	702	6.2
Extremadura	87	0.8	86	0.8	54	0.5
Galicia	412	3.8	407	3.9	504	4.4
Community of Madrid	2,493	23.1	2,473	23.7	1,660	14.7

Region of Murcia	194	1.8	193	1.8	258	2.3
Navarre	57	0.5	56	0.5	88	0.8
Basque Country	516	4.8	498	4.8	586	5.2
La Rioja	10	0.1	9	0.1	4	0.0
MVA-BN vaccination						
Yes	5,862	55.4	5,831	55.8	5,660	50.0
No	4,909	45.6	4,618	44.2	5,660	50.0
MVA-BN vaccine product						
IMVANEX	449	7.8	448	7.7	340	6.0
JYNNEOS	3,708	63.2	3,700	63.4	3,554	62.8
Unkown	1,705	29.0	1,683	28.9	1,766	31.2
MVA-BN route of administration						
Intradermal (0.1 ml)	3,756	64.1	3,745	65.2	3502	61.9
Subcutaneous (0.5 ml)	1,727	29.5	1,720	29.5	1,707	30.2
Unknown	379	6.4	366	6.3	451	7.9
MPXV infection						
Yes	738	6.8	431	4.1	43	0.4
No	10,033	93.2	10,018	95.9	11,277	99.6
Mpox symptoms*						
Yes	723	98.0	425	98.6	43	100.0
No	15	2.0	6	1.4	0	0.0
Hospitalization*						
Yes	19	2.6	11	2.5	0	0.0
No	719	97.4	420	97.5	43	100.0
Admitted to ICU*						
Yes	0	0.0	0	0.0	0	0.0

	No	738	100.0	431	100.0	43	100.0
Death*							
	Yes	0	0.0	0	0.0	0	0.0
	No	738	100.0	431	100.0	43	100.0

*Proportion is over the total number of MPXV infections

Table S2. Number of events, person-days of follow-up, estimated risk, adjusted incidence rate ratio (IRR), vaccine effectiveness (VE) and 95% confidence intervals (95%CI), of one dose of MVA-BN vaccine using adjusted Poisson regression models

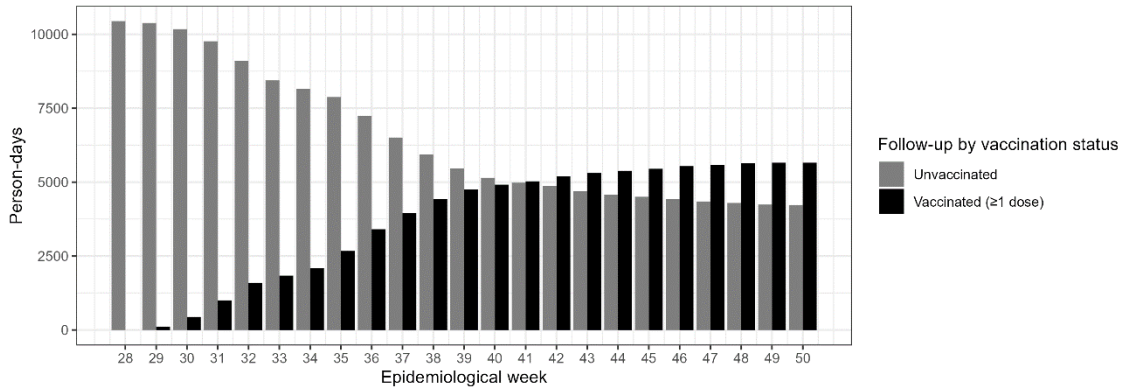
Vaccination status		Events	Person-days	Cumulative incidence (per 10,000)	Adjusted* IRR (IC95%)	VE (95%CI)
Unvaccinated		411	978,730	4.20	Ref.	Ref.
Vaccinated (time since vaccination)	Overall	20	552,399	0.36	0.57 (0.35 ; 0.93)	43% (7 ; 65)
	0-6 days	11	34,013	3.23	1.30 (0.71 ; 2.38)	-30% (-138 ; 29)
	0-13 days	15	73,464	2.04	0.94 (0.55 ; 1.59)	6% (-59 ; 45)
	≥ 7 days	9	514,117	0.18	0.32 (0.16 ; 0.65)	68% (35 ; 84)
	≥ 14 days	5	474,666	0.11	0.24 (0.10 ; 0.61)	76% (39 ; 90)

*Adjusted by calendar week, age and region within Spain.

Supplementary figure

Figure S1. Time of follow-up (a), and number of events and incidence rate (b) by vaccination status and epidemiological week in the eligible population (N=10,449)

(a)



(b)