

Supplementary Appendix

Supplement to: Deputy NP, Deckert J, Chard AN, et al. Vaccine effectiveness of JYNNEOS against mpox disease in the United States. N Engl J Med 2023;388:2434-43. DOI: 10.1056/NEJMoa2215201

This appendix has been provided by the authors to give readers additional information about the work.

Supplementary Appendix

Contents

Supplementary Appendix	1
Supplementary Methods:	2
Table S1: Definitions for Eligible Case and Control Patients and Associated International Classification of Diseases, Tenth Revision (ICD-10) Codes and Logical Observation Identifiers Names and Codes (LOINC).....	3
Table S2. List of Immunocompromising Conditions and Associated International Classification of Diseases, Tenth Revision (ICD-10) Codes and Immunosuppressive Medications.....	6
Table S3: Associations Between Selected Patient Characteristics and Case or Control Patient Status – United States, August 15 – November 19, 2022	8
Table S4: Characteristics of Case Patients and Control Patients by Vaccination Status – United States, August 15 – November 19, 2022.....	9
Table S5: Characteristics of Case Patients with Mpox and Control Patients with an HIV Diagnosis or HIV Pre-Exposure Prophylaxis (PrEP) Prescription, among Individuals Seeking Health Care – United States, August 15 – November 19, 2022*	12
Table S6: E-Values for Point Estimates and Upper 95% Confidence Intervals for Association Between Vaccination Status and Case or Control Patient Status, Overall and By Subpopulations of Interest .	16
Table S7. List of Underlying Conditions and Associated International Classification of Diseases, Tenth Revision (ICD-10) Codes.....	17
Table S8. List of Pain Medication Prescribed Within 14 Days Prior to Diagnosis or Any Time After Diagnosis During the Study Period	20

Supplementary Methods:

Epic's Cosmos platform, an integrated electronic health care record (EHR) database, comprises data from health care organizations, including hospitals, clinics, academic medical centers, federally qualified health centers, and rural and critical access centers. These organizations voluntarily submit information to Cosmos through their Epic EHR. A Health Insurance Portability and Accountability Act (HIPAA)-defined limited data set is then created that includes demographic information, International Classification of Diseases, Tenth Revision codes (ICD-10), medications, and laboratory codes and values.

Table S1: Definitions for Eligible Case and Control Patients and Associated International Classification of Diseases, Tenth Revision (ICD-10) Codes and Logical Observation Identifiers Names and Codes (LOINC)

Monkeypox	
<i>One or more of the following codes or positive results present between August 15, 2022 and November 19, 2022</i>	
ICD-10 Code	Description
B04	Monkeypox
LOINC Code	Long Common Name
41853-3	Orthopoxvirus Deoxyribonucleic acid, or DNA [Presence] in Specimen by Nucleic Acid Amplification, or NAA with probe detection
100434-0	Orthopoxvirus non-variola DNA [Presence] in Specimen by NAA with probe detection
100383-9	Monkeypox virus DNA [Presence] in Specimen by NAA with probe detection
100888-7	West African monkeypox virus DNA [Presence] in Specimen by NAA with probe detection
100889-5	Congo Basin monkeypox virus DNA [Presence] in Specimen by NAA with probe detection
100892-9	Orthopoxvirus IgM Ab [Presence] in Serum or Plasma by Immunoassay
Unmapped Laboratory test	Laboratory test name
	BH AMB LAB ORTHOPOXVIRUS DNA, QL PCR
	CDC Monkeypox PCR
	EXT Monkeypox PCR
	External ORTHOPOXVIRUS DNA, PCR
	MONKEYPOX
	Monkeypox (Non-variola Orthopoxvirus) screen, PCR
	MONKEYPOX (ORTHOPOXVIRUS) BY PCR
	Monkeypox (Orthopoxvirus) DNA PCR
	Monkeypox (Orthopoxvirus) PCR
	Monkeypox (Orthopoxvirus), PCR
	Monkeypox CDC
	MonkeyPox DNA
	Monkeypox DNA PCR
	Monkeypox generic
	Monkeypox ISDH
	Monkeypox PCR
	Monkeypox Result
	Monkeypox Virus
	Monkeypox virus (Orthopoxvirus) PCR
	Monkeypox Virus by PCR
	Monkeypox virus Clade I
	Monkeypox virus Clade II

JYNNEOS Vaccine Effectiveness Against Monkeypox Disease in the U.S

	Monkeypox virus DNA
	Monkeypox Virus DNA PCR
	Monkeypox virus DNA QL PCR
	Monkeypox Virus DNA Qual
	Monkeypox Virus DNA, QL
	MONKEYPOX VIRUS DNA, QL PCR
	Monkeypox Virus DNA, QL-PCR
	Monkeypox Virus DNA, Qual PCR
	Monkeypox Virus DNA, Qualitative PCR
	Monkeypox Virus DNA, Qualitative, Real-time PCR
	Monkeypox Virus DNA,QL PCR
	Monkeypox Virus DNA,QL PCR Grady
	MONKEYPOX VIRUS NAAT EXTERNAL
	Monkeypox Virus PCR
	Monkeypox Virus, DNA PCR
	Monkeypox Virus, DNA, PCR
	Monkeypox Virus, PCR
	Monkeypox WA specific
	MONKEYPOX, PCR
	Monkeypox/Orthopox
	Monkeypoxvirus DNA
	Monkeypoxvirus DNA, qualitative PCR
	MPXDX, ORTHOPOXVIRUS DNA, PCR
	Non-Variola Orthopox
	Non-Variola Orthopox DNA
	NON-VARIOLA ORTHOPOX EXTERNAL
	Non-Variola Orthopox PCR (DOH)
	Non-Variola Orthopox Virus
	Non-Variola Orthopox Virus by RT-PCR
	NON-VARIOLA ORTHOPOXVIRUS DNA
	Non-variola Orthopoxvirus DNA by PCR
	Non-variola Orthopoxvirus DNA PCR
	Non-variola orthopoxvirus Real-Time PCR
	Non-Variola Orthopoxvirus, Qualitative
	Note, Monkeypox
	ORTHOPOX
	Orthopox DNA, Qualitative PCR
	Orthopox PCR
	Orthopox Virus
	Orthopox Virus DNA
	Orthopox virus DNA QL PCR

JYNNEOS Vaccine Effectiveness Against Monkeypox Disease in the U.S

	Orthopox Virus DNA, QL PCR
	Orthopox Virus Nonvariola DNA, QL-PCR
	Orthopox Virus Sample Conclusion
	Orthopox, PCR Assay
	Orthopoxvirus DNA
	Orthopoxvirus
	Orthopoxvirus (Including Monkeypox) by PCR
	Orthopoxvirus (Monkeypox Virus by PCR)
	Orthopoxvirus DNA
	Orthopoxvirus Dna (Labcorp)
	ORTHOPOXVIRUS DNA LC
	Orthopoxvirus DNA PCR
	Orthopoxvirus DNA QL PCR
	Orthopoxvirus DNA Qual
	Orthopoxvirus DNA, PCR
	ORTHOPOXVIRUS DNA, QL PCR
	Orthopoxvirus DNA, QL PCR Grady
	Orthopoxvirus DNA, QL, PCR
	Orthopoxvirus DNA, Qual PCR
	Orthopoxvirus DNA, qualitative PCR
	Orthopoxvirus DNA,QL PCR
	Orthopoxvirus Non-Variola DNA
	Orthopoxvirus PCR
	Orthopoxvirus, DNA
	Orthopoxvirus, DNA QL
	Orthopoxvirus, DNA, PCR
	Orthopoxvirus.non-variola DNA
	PCR FOR NON-VARIOLA ORTHOPOX GROUP VIRUSES
	Quest Orthopoxvirus DNA QL PCR (External)
	WEST AFRICAN MONKEYPOX
	West African monkeypox virus DNA
HIV	
<i>One or more of the following codes present between August 15, 2022 and October 29, 2022 and no indication of these codes prior to November 19, 2022</i>	
ICD-10 Code	Description
B20	Human immunodeficiency virus [HIV] disease
LOINC Code	Test
7917-8	HIV 1 Ab [Presence] in Serum
7919-4	HIV 2 Ab [Presence] in Serum
56888-1	HIV 1+2 Ab+HIV1 p24 Ag [Presence] in Serum or Plasma by Immunoassay
PrEP	
<i>Medication order for Truvada® or Descovy® between August 15, 2022 and November 19, 2022 and no HIV ICD-10 or LOINC code</i>	

Table S2. List of Immunocompromising Conditions and Associated International Classification of Diseases, Tenth Revision (ICD-10) Codes and Immunosuppressive Medications

Immunocompromising codes*	Organ Transplant	T86.1, T86.2, T86.3, T86.4, T86.81, T86.85, Z48.2, Z94.0, Z94.1, Z94.2, Z94.3, Z94.4, Z94.82, Z94.83
	Stem Cell Transplant	Z94.84, T86.0, T86.5
	Underlying Immunodeficiency	D80, D81.0, D81.1, D81.2, D81.9, D82, D83, D84, D89.8, D89.9
	Chemotherapy or Radiation Therapy	Z51.0, Z51.1
	Hematologic Conditions	C95.00, C95.10, D61.0, D61.2, D61.9, D70 (except D70.9), D71, D72 (except D72.829 or D72.819), D73.0, C81, C82, C83, C84, C85, C86, C88, C90, C91, C92, C93, C94, C96, D46
	Chronic Use of Steroids	Z79.5
	HIV	B20, B97.35, O98.7, Z21
Pharmaceutical Class	Medications	
5-Aminosalicylic Acid Derivative	Mesalamine, sulfasalazine	
Antihelminthic	Levamisole	
Antineoplastic Agent	Adriamycin, aldesleukin, altretamine, amsacrine, arsenic trioxide, asparaginase, axicabtagene ciloleucel, azacitidine, bendamustine hydrochloride, bexarotene, bleomycin sulfate, bortezomib, brexucabtagene autoleucel, busulfan, cabazitaxel, capecitabine, carboplatin, carfilzomib, carmustine, chlorambucil, ciltacabtagene autoleucel, cisplatin, cladribine, clofarabine, cyclophosphamide, cytarabine, cytarabine liposome, dacarbazine, dactinomycin, dasatinib, daunorubicin, daunorubicin citrate liposome, decitabine, denileukin diftitox, docetaxel, doxorubicin, doxorubicin hydrochloride, doxorubicin hydrochloride liposome, epirubicin, eribulin mesylate, erlotinib, estramustine phosphate sodium, etoposide, everolimus, floxuridine, fludarabine, fluorouracil, gefitinib, gemcitabine, idarubicin, idecabtagene vicleucel, ifosfamide, ifosfamide / mesna, imatinib, irinotecan, ixabepilone, ixazomib, lapatinib, lenalidomide, lisocabtagene maraleucel, lomustine, mechlorethamine, melphalan, mercaptopurine, methotrexate, mitomycin, mitotane, mitoxantrone, nelarabine, nilotinib, osimertinib, oxaliplatin, paclitaxel, pazopanib, pegaspargase, pemetrexed, pentostatin, plicamycin, porfimer sodium, pralatrexate, procarbazine, romidepsin, selinexor, sirolimus, sorafenib, streptozocin, sunitinib, temozolomide, temsirolimus, teniposide, thalidomide, thioguanine, thiotepa, topotecan, tretinoin, uracil mustard, venetoclax, vinblastine, vincristine, vinorelbine, or vorinostat	
Antirheumatic	Abatacept, auranofin, aurothioglucose, belatacept, gold sodium thiomalate, hydroxychloroquine, leflunomide, or tocilizumab	
Biological	Glatiramer acetate	

JYNNEOS Vaccine Effectiveness Against Monkeypox Disease in the U.S

Chemoprotective Agent	Amifostine, dexrazoxane, mesna, or palifermin
Corticosteroid, Systemic	Betamethasone, budesonide, dexamethasone, methylprednisolone, methylprednisolone sodium succinate, prednisolone, prednisone, or triamcinolone
Enzyme	Pegademase bovine
Hematopoietic Agent	Filgrastim, lenograstim, or lipegfilgrastim
Immunosuppressant Agent	Alefacept, azathioprine, basiliximab, cyclosporine, mycophenolate, pimecrolimus, or tacrolimus
Immunotherapy	Sipuleucel-T or tisagenlecleucel
Biological Response Modulator	Interferon alfa-2a, interferon alfa-2b, interferon alfacon-1, interferon alfa-n3, interferon beta-1a, interferon beta-1b, interferon gamma-1b, peginterferon alfa-2a, or peginterferon alfa-2b
Monoclonal Antibody	Adalimumab, alemtuzumab, anakinra, belimumab, benralizumab, bevacizumab, blinatumomab, brentuximab vedotin, canakinumab, certolizumab pegol, cetuximab, daclizumab, denosumab, eculizumab, efalizumab, emapalumab-lzsg, etanercept, gemtuzumab ozogamicin, golimumab, guselkumab, ibritumomab tiuxetan, infliximab, inotuzumab ozogamicin, ipilimumab, mepolizumab, muromonab-CD3, natalizumab, obinutuzumab, ocrelizumab, ofatumumab, palivizumab, panitumumab, pertuzumab, riloncept, rituximab, trastuzumab, ustekinumab, or vedolizumab
Radiopharmaceutical	Iodine-131-tositumomab
Sphingosine 1-Phosphate (S1P) Receptor Modulator	Fingolimod
Thrombolytic Agent	Defibrotide

*For parent codes that are listed, all sub-codes are included unless specified.

Table S3: Associations Between Selected Patient Characteristics and Case or Control Patient Status – United States, August 15 – November 19, 2022

	No. of case patients	No. of control patients	Unadjusted Odds Ratio (95% CI)	Adjusted* Odds Ratio (95% CI)
Age				
18-35 (ref)	1216	4054		
36-49	679	2347	1.0 (0.9 - 1.1)	1.0 (0.8 - 1.1)
50+	298	1918	0.5 (0.5 - 0.6)	0.5 (0.4 - 0.5)
Race/ethnicity				
White, Non-Hispanic (ref)	764	4605		
Black, Non-Hispanic	797	1516	3.3 (3.0 - 3.8)	2.1 (1.9 - 2.4)
Hispanic/Latino	480	1450	2.0 (1.7 - 2.2)	1.5 (1.3 - 1.8)
Other, Non-Hispanic (including AN/AI, Asian)	152	748	1.2 (1.0 - 1.5)	1.1 (0.9 - 1.4)
Social Vulnerability Index				
Q1 [0,.24] (ref)	254	1353		
Q2 [.25,.49]	362	1947	1.0 (0.9 - 1.2)	0.9 (0.8 - 1.1)
Q3 [.50,.74]	489	2139	1.3 (1.1 - 1.5)	1.1 (0.9 - 1.3)
Q4 [.75,1]	1071	2847	2.1 (1.8 - 2.4)	1.4 (1.2 - 1.6)
Immunocompromising condition				
No (ref)	1267	6612		
Yes	926	1707	2.9 (2.6 - 3.2)	2.5 (2.3 - 2.9)

*Adjusted for vaccination status, age group, race/ethnicity, Social Vulnerability Index, and presence or absence of immunocompromising conditions defined in Table S2.

Table S4: Characteristics of Case Patients and Control Patients by Vaccination Status – United States, August 15 – November 19, 2022

	Unvaccinated*		Partially vaccinated†		Fully vaccinated‡	
	n	column %	n	column %	n	column %
Total	9006	100	1146	100	360	100
Age in years						
18-35	4548	50.5	576	50.3	146	40.6
36-49	2547	28.3	353	30.8	126	35.0
50-64	1553	17.2	186	16.2	78	21.7
65+	358	4.0	31	2.7	10	2.8
Sex (legal)						
Male	7988	88.7	1134	99.0	358	99.4
Female	1003	11.1	11	1.0	2	0.6
Other	5	0.1	1	0.1	0	0
Unknown	10	0.1	0	0	0	0
Gender Identity						
Male	7867	87.4	1119	97.6	360	100
Female	981	10.9	5	0.4	0	0
Transgender Male	5	0.1	1	0.1	0	0
Transgender Female	87	1.0	10	0.9	0	0
Other	65	0.7	11	1	0	0
Chose not to disclose	1	0.01	0	0	0	0
Race/Ethnicity						
White Non-Hispanic	4422	49.1	697	60.8	250	69.4
Black Non-Hispanic	2180	24.2	110	9.6	23	6.4
Hispanic/Latino	1657	18.4	211	18.4	62	17.2
Asian Non-Hispanic	353	3.9	87	7.6	12	3.3
Alaska Native/American Indian, Non-Hispanic	31	0.3	1	0.1	0	0
Other, Non-Hispanic	363	4.0	40	3.5	13	3.6
Social Vulnerability Index Quartile†						
[0, 0.24]	1242	13.8	258	22.5	107	29.7
[0.25, 0.49]	1946	21.6	289	25.2	74	20.6
[0.50, 0.74]	2213	24.6	319	27.8	96	26.7
[0.75, 1]	3558	39.5	278	24.3	82	22.8
Unknown	47	0.5	2	0.2	1	0.3
U.S. Census Region						
South	3697	41.1	215	18.8	99	27.5
Northeast	1292	14.4	228	19.9	32	8.9
West	2535	28.2	537	46.9	148	41.1
Midwest	1482	16.5	166	14.5	81	22.5
U.S. Department of Health and Human Services Census Region						
Region 1 (CT, ME, MA, NH, RI, VT)	218	2.4	51	4.5	14	3.9

JYNNEOS Vaccine Effectiveness Against Monkeypox Disease in the U.S

Region 2 (NJ, NY)	442	4.9	26	2.3	7	1.9
Region 3 (DE, DC, MD, PA, VA, WV)	1404	15.6	177	15.5	22	6.1
Region 4 (AL, FL, GA, KY, MS, NC, SC, TN)	1808	20.1	126	11.0	52	14.4
Region 5 (IL, IN, MI, MN, OH, WI)	1376	15.3	159	13.9	74	20.6
Region 6 (AR, LA, NM, OK, TX)	1130	12.6	64	5.6	37	10.3
Region 7 (IA, KS, MO, NE)	87	1.0	6	0.5	6	1.7
Region 8 (CO, MT, ND, SD, UT, WY)	479	5.3	130	11.3	78	21.7
Region 9 (AZ, CA, HI, NV)	1422	15.8	339	29.6	67	18.6
Region 10 (AK, ID, OR, WA)	640	7.1	68	5.9	3	0.8
Index Encounter Type (assoc. w/dx or lab)						
In-person outpatient	7026	78.0	1105	96.4	352	97.8
Emergency department	1458	16.2	25	2.2	5	1.4
Urgent care	19	0.2	0	0	0	0
Hospital admission	424	4.7	15	1.3	2	0.6
ICU admission	79	0.9	1	0.1	1	0.3
Source of index encounter event						
Diagnosis code	1610	17.9	111	9.7	17	4.7
Laboratory confirmed result	1030	11.4	53	4.6	10	2.8
Diagnosis code + laboratory confirmed	726	8.1	24	2.1	10	2.8
Prescription medication	5640	62.6	958	83.6	323	89.7
Number of underlying medical conditions 						
0	2625	29.2	437	38.1	126	35.0
1	2744	30.5	347	30.3	105	29.2
2	1805	20.0	196	17.1	70	19.4
3	986	11.0	101	8.8	34	9.4
4	455	5.1	43	3.8	16	4.4
5+	391	4.3	22	1.9	9	2.5
Number of face-to-face encounters in past year						
0	565	6.3	46	4.0	6	1.7
1	1653	18.4	161	14.1	34	9.4
2	1287	14.3	141	12.3	44	12.2
3	1062	11.8	137	12.0	38	10.6
4	893	9.9	124	10.8	48	13.3
5+	3546	39.4	537	46.9	190	52.8
Immunocompromising condition ¶						
No	6519	72.4	1034	90.2	326	90.6
Yes	2487	27.6	112	9.8	34	9.4
Living with HIV						
No	6889	76.5	1063	92.8	338	93.9
Yes	2117	23.5	83	7.2	22	6.1
Newly diagnosed with HIV **						
No	6889	82.6	1063	95.9	338	96.3
Yes	1456	17.5	46	4.2	13	3.7
Has active PrEP prescription (among persons not living with HIV)						

JYNNEOS Vaccine Effectiveness Against Monkeypox Disease in the U.S

No	1116	16.2	64	6.0	7	2.1
Yes	5773	83.8	999	94.0	331	97.9
Vaccinated with ACAM2000 prior to index date	81	0.9	11	1.0	2	0.6

*Patients were considered unvaccinated if there were no documented doses before the index event.

†Patients were considered partially vaccinated if they received one dose ≥ 14 days before the index event, or the second dose was <14 days before the index event; patients who received one dose <14 days before the index event were excluded as vaccination might represent post-exposure prophylaxis (n=73 for case patients and n=323 for control patients).

‡Patients were considered fully vaccinated if they received two doses of JYNNEOS vaccine ≥ 24 days apart and the second dose was ≥ 14 days before the index event. Patients were excluded if they received two doses < 24 days apart (n=0 for case patients and n=7 for control patients).

§Social Vulnerability Index is an indicator of community-level vulnerability that ranges from 0 to 1.0, with higher scores indicating greater vulnerability.

||Medical conditions are defined in Table S7.

¶Includes selected conditions defined by presence of selected conditions identified by ICD-10 codes or immunosuppressive medication prescribed in the past 6 months defined in Table S2.

**Denominator excludes patients who are not at risk for a new HIV diagnosis (due to an existing HIV diagnosis).

Table S5: Characteristics of Case Patients with Mpox and Control Patients with an HIV Diagnosis or HIV Pre-Exposure Prophylaxis (PrEP) Prescription, among Individuals Seeking Health Care – United States, August 15 – November 19, 2022*

Characteristics	Mpox Case patients		Control patients (PrEP or HIV)	
	N	Col %	N	Col %
Total	2,266	100.0	8,649	100.0
Age in years				
18-35	1,252	55.3	4,221	48.8
36-49	707	31.2	2,434	28.1
50-64	273	12.1	1,619	18.7
65+	34	1.5	375	4.3
Sex (legal)				
Male	2,059	90.9	7,821	90.4
Female	204	9.0	815	9.4
Other	1	0.0	5	0.1
Unknown	2	0.1	8	0.1
Gender Identity				
Male	2,022	89.2	7,717	89.2
Female	199	8.8	790	9.1
Transgender Male	2	0.1	4	0.1
Transgender Female	23	1.0	75	0.9
Other	19	0.8	62	0.7
Chose not to disclose	1	0.0	1	0.0
Race/Ethnicity				
White, Non-Hispanic	792	35.0	4,800	55.5
Black, Non-Hispanic	816	36.0	1,545	17.9
Hispanic/Latino	500	22.1	1,519	17.6
Asian Non-Hispanic	71	3.1	413	4.8
Alaska Native/American Indian, Non-Hispanic	8	0.4	24	0.3
Other, Non-Hispanic	79	3.5	348	4.0
Social Vulnerability Index Quartile†				
[0, 0.24]	268	11.8	1,423	16.5
[0.25, 0.49]	374	16.5	2,030	23.5
[0.50, 0.74]	501	22.1	2,209	25.5
[0.75, 1]	1,106	48.8	2,954	34.2
Unknown	17	0.8	33	0.4
U.S. Census Region				
South	879	38.8	3,235	37.4
Northeast	322	14.2	1,273	14.7
West	708	31.2	2,693	31.1
Midwest	357	15.8	1,448	16.7
U.S. Department of Health and Human Services Census Region				

JYNNEOS Vaccine Effectiveness Against Monkeypox Disease in the U.S

Region 1 (CT, ME, MA, NH, RI, VT)	60	2.7	237	2.7
Region 2 (NJ, NY)	97	4.3	383	4.4
Region 3 (DE, DC, MD, PA, VA, WV)	329	14.5	1,307	15.1
Region 4 (AL, FL, GA, KY, MS, NC, SC, TN)	462	20.4	1,594	18.4
Region 5 (IL, IN, MI, MN, OH, WI)	336	14.8	1,343	15.5
Region 6 (AR, LA, NM, OK, TX)	253	11.2	1,002	11.6
Region 7 (IA, KS, MO, NE)	21	0.9	83	1.0
Region 8 (CO, MT, ND, SD, UT, WY)	146	6.4	584	6.8
Region 9 (AZ, CA, HI, NV)	413	18.2	1,525	17.6
Region 10 (AK, ID, OR, WA)	149	6.6	591	6.8
Index Event Type				
In-person outpatient	1,308	57.7	7,555	87.4
Emergency department	787	34.7	717	8.3
Urgent care	12	0.5	10	0.1
Hospital admission	142	6.3	302	3.5
ICU admission	17	0.8	65	0.8
Source of index event				
Diagnosis code	729	32.2	1028	11.9
Laboratory confirmed result	874	38.6	252	2.9
Diagnosis code + laboratory confirmed	663	29.3	128	1.5
Prescription medication	0	0.0	7,241	83.7
Hospital admission duration (median days, IQR)‡	5.0, 5.5		5.0, 5.0	
Number of underlying medical conditions §				
0	740	32.7	2,597	30.0
1	727	32.1	2,583	29.9
2	436	19.2	1,704	19.7
3	221	9.8	941	10.9
4	84	3.7	448	5.2
5+	58	2.6	376	4.4
Number of face-to-face encounters in past year				
0	118	5.2	508	5.9
1	517	22.8	1,389	16.1
2	342	15.1	1,191	13.8
3	253	11.2	1,026	11.9
4	167	7.4	945	10.9
5+	869	38.4	3,590	41.5
Immunocompromising condition 				
No	1,304	57.6	6,924	80.1
Yes	962	42.5	1,725	19.9
Persons with HIV				
No	1,407	62.1	7,241	83.7
Yes	859	37.9	1,408	16.3
Persons with HIV and CD4 count <200 in last 6 months				
No	2,052	90.6	8,394	97.1

JYNNEOS Vaccine Effectiveness Against Monkeypox Disease in the U.S

Yes	214	9.4	255	3.0
Newly diagnosed with HIV¶				
No	1,407	92.2	7,241	83.7
Yes	119	7.8	1,408	16.3
Has active HIV PrEP prescription (among persons without HIV)				
No	1,217	86.5	0	0.0
Yes	190	13.5	7,241	100.0
Tecovirimat (TPOXX) prescription**				
No	1,816	80.1	8,649	100.0
Yes	450	19.9	0	0.0
Pain medication††				
None	1,811	79.9	7,942	91.8
Prescription medication (oral or topical)	302	13.3	408	4.7
Intravenous medication	153	6.8	299	3.5
Vaccinated with ACAM2000 prior to 2022				
No	2,258	99.7	8,562	99.0
Yes	8	0.4	87	1.0
Calendar week of diagnosis				
8/14	367	16.2	1,275	14.7
8/21	375	16.6	1,406	16.3
8/28	339	15.0	1,285	14.9
9/4	257	11.3	988	11.4
9/11	223	9.8	885	10.2
9/18	167	7.4	662	7.7
9/25	112	4.9	447	5.2
10/2	102	4.5	406	4.7
10/9	82	3.6	328	3.8
10/16	61	2.7	243	2.8
10/23	63	2.8	252	2.9
10/30	46	2.0	184	2.1
11/06	51	2.3	204	2.4
11/13	21	0.9	84	1.0
Vaccination Status				
Fully Vaccinated‡‡				
Overall	25	1.1	335	4.0
Administration Timing Relative to Index Event (IE)				
Dose 2 24-28 day interval and ≥ 14 days before IE	11	44.0	133	39.7
Dose 2 29-45 day interval and ≥ 14 days before IE	11	44.0	164	49.0
Dose 2 ≥46 day interval and ≥ 14 days before IE	3	12.0	38	11.3
Administration Route				
Both administrations subcutaneous	6	24.0	63	18.8
Both administrations intradermal	5	20.0	42	12.5
Heterologous administration	8	32.0	150	44.8
Other/Missing	6	24.0	80	23.9

<i>Partially Vaccinated§§</i>				
Overall	146	6.7	1,000	12.0
<i>Administration Timing Relative to IE</i>				
Dose 1 ≥ 14 days before IE	80	54.8	366	36.6
Dose 2 ≥ 24-day interval and < 14 days before IE	53	36.3	269	26.9
Dose 2 after IE	13	8.9	365	36.5
<i>Administration Route</i>				
Subcutaneous administration	106	72.6	704	70.4
Intradermal administration	27	18.5	186	18.6
Other/Missing	13	8.9	110	11.0
<i>Unvaccinated¶¶</i>				
Overall	2,022	92.2	6,984	84.0
<i>Administration Timing Relative to IE</i>				
No documented doses	1,922	95.1	6,406	91.7
Dose 1 on same day as IE	70	3.5	171	2.4
Dose 1 after IE	30	1.5	407	5.8

*Percentages may not sum to 100% due to rounding.

†Social Vulnerability Index is an indicator of community-level vulnerability that ranges from 0 to 1.0, with higher scores indicating greater vulnerability.

‡Hospital admission duration was defined as the first hospital admission within 28 days of the index event and may not have been specifically linked to the index event.

§Medical conditions are listed in Table S7.

||Includes selected conditions defined by presence of selected conditions identified by ICD-10 codes or immunosuppressive medication prescribed in the past 6 months defined in Table S2.

¶Denominator excludes patients who are not at risk for a new HIV diagnosis (due to an existing HIV diagnosis).

**Prescribed within 14 days prior to diagnosis or any time after diagnosis during the study period.

††Pain medications are listed in Table S8.

‡‡Patients were considered fully vaccinated if they received two doses of JYNNEOS vaccine ≥ 24 days apart and the second dose was ≥ 14 days before the index event. Patients were excluded if they received two doses < 24 days apart (n=0 for case patients and n=7 for control patients).

§§Patients were considered partially vaccinated if they received one dose ≥ 14 days before the index event, or if the second dose was <14 days before the index event; patients who received one dose <14 days before the index event were excluded as vaccination might represent post-exposure prophylaxis (n=73 for case patients and n=323 for control patients).

Table S6: E-Values for Point Estimates and Upper 95% Confidence Intervals for Association Between Vaccination Status and Case or Control Patient Status, Overall and By Subpopulations of Interest

Model (Table Where Presented)	Vaccination Status	aOR (95% CI)*	Adjusted Vaccine Effectiveness (95% CI)†	E-Value for Point Estimate	E-value for Upper 95% CI
Overall (Table 2)	Partially Vaccinated	0.642 (0.529 – 0.779)	35.8 (22.1 - 47.1)	2.49	1.89
	Fully Vaccinated	0.340 (0.219 – 0.526)	66.0 (47.4 - 78.1)	5.33	3.21
Males Only (Table 3)	Partially Vaccinated	0.641 (0.524 - 0.784)	35.9 (21.6 - 47.6)	2.49	1.87
	Fully Vaccinated	0.352 (0.227 - 0.548)	64.8 (45.2 - 77.3)	5.13	3.05
Males only, 18-49 years and without ACAM2000 vaccination (Table 3)	Partially Vaccinated	0.645 (0.514 - 0.809)	35.5 (19.1 - 48.6)	2.47	1.78
	Fully Vaccinated	0.413 (0.257 - 0.661)	58.7 (33.9 - 74.3)	4.28	2.39
Immunocompetent (Table 3)	Partially Vaccinated	0.592 (0.466 - 0.752)	40.8 (24.8 - 53.4)	2.77	1.99
	Fully Vaccinated	0.237 (0.132 - 0.423)	76.3 (57.7 - 86.8)	7.91	4.16

*Adjusted odds ratio and 95% CI from conditional logistic regression models used to evaluate associations between vaccination status and case or control patient status.

†Adjusted vaccine effectiveness was calculated as $(1 - \text{aOR}) \times 100$.

‡ The E-value is the minimum strength of association that an unmeasured confounder would need to have with both the exposure (vaccination status) and the outcome (case or control patient status), beyond the covariates included in the model, to explain the observed association (i.e., to move the point estimate, or the upper bound of the 95% CI, to the null).

Table S7. List of Underlying Conditions and Associated International Classification of Diseases, Tenth Revision (ICD-10) Codes

Underlying condition*	ICD-10 Code
Asthma	J45 or J82.83
Bronchiectasis	J47.0, J47.1, or J47.9
Cancer	C00-26, C30-34, C37-41, C43, C45-58, C60-79, C7A, C7B, C80, C81, D09.0, Z85.038, Z85.040, Z85.048, Z85.110, Z85.118, Z85.3, Z85.42, Z85.46, or Z85.79
Cerebrovascular Disease	G45.0, G45.1, G45.2, G45.8, G45.9, G46.0-8, G97.31, G97.32, I60-63, I65-66, I67.2, I67.81-5, I69, I97.810, I97.811, I97.820, I97.821, or Z86.73
Chronic Kidney Disease	D59.3, E08.2, E09.2, E10.2, E11.2, E13.2, I12, I13.0, I13.1, I13.2, I70.1, I72.2, K76.7, M10.3, M32.14, M32.15, M35.04, N02-08, N11, N12, N13.1, N13.2, N13.30, N13.39, N14-16, N18-19, N25, N26.1, N26.9, O26.83, P96.0, Q61.1-4, Q62.0, Q62.10-12, Q62.2, Q62.31, Q62.32, Q62.39, R94.4, or Z99.2
Chronic Liver Disease	K70, K74, K75.4, K75.81, or K76.0
COPD	J40, J41.0, J41.1, J41.8, J42, J43.0, J43.1, J43.2, J43.8, J43.9, or J44
Cystic Fibrosis	E84
Diabetes	E10, E11.0-6, E11.8, E11.9, E13.01, E13.10, E13.21, E13.22, E13.29, E13.311, E13.319, E13.321, E13.329, E13.331, E13.339, E13.341, E13.3491-3, E13.3499, E13.351, E13.3521, E13.3522, E13.3523, E13.3529, E13.3531, E13.3532, E13.3539, E13.3541, E13.3542, E13.3542, E13.3543, E13.3549, E13.3551, E13.3552, E13.3559, E13.359, E13.36, E13.40-44, E13.49, E13.51, E13.52, E13.59, E13.618, E13.620, E13.621, E13.622, E13.628, E13.630, E13.638, E13.641, E13.65, E13.69, E13.8, E13.9, Z79.4, or Z79.84
Disabilities	E13.69, E13.8, E75.22, E78.71, E78.72, E88.41, E88.42, E88.49, F07.0, F07.81, F07.89, F48.2, F70-F73, F78, F79, F80.0, F80.1, F80.2, F80.4, F80.81, F80.82, F80.89, F80.9, F81.0, F81.2, F81.81, F81.89, F81.9, F82, F84, F88, F89, F90.0, F90.1, F90.2, F90.8, F90.9, F95.2, G04.1, G10, G11.4, G12, G13, G20, G21, G23.1, G23.8, G31.82, G36.0, G70, G71.11, G71.3, G73, G80.0-4, G80.8, G80.9, G81-83, H47.22, H54.0X33-35, H54.0X43-45, H54.0X53-55, H54.10-12, H54.2, H54.3, H54.8, H90.3, H90.41, H90.42, H90.5, H90.6, H90.71, H90.72, H90.8, H90.A21, H90.A22, H90.A31, H90.A32, H91.01-03, H91.09, H91.8X1-3, H91.8X9, H91.90-93, H93.25, I69.031, I69.032, I69.034, I69.039, I69.041-4, I69.049, I69.051-4, I69.059, I69.061-5, I69.069, I69.131-4, I69.139, I69.141-4, I60.149, I69.151-4, I69.159, I69.161-5, I69.169, I69.231-4, I69.239, I69.241-4, I69.249, I69.251-4, I69.259, I69.261-5, I69.269, I69.331-4, I69.339, I69.341-4, I69.349, I69.351-4, I69.359, I69.361-5, I69.369, I69.831-4, I69.839, I69.841-4, I69.849, I69.851-4, I69.859, I69.861-5, I69.869, I69.931-4, I69.939, I69.941-4, I69.949, I69.951-4, I69.959, I69.961-5, I69.969, M14.67, P04.3, Q00.0-2, Q01.0-2, Q01.8, Q01.9, Q02, Q03.0, Q03.1, Q03.8, Q03.9, Q04.1-6, Q04.8, Q04.9, Q05.0-9, Q06.1-4, Q06.8, Q06.9, Q07, Q10-Q45, Q50-Q56, Q60-Q85, Q86.0, Q86.1, Q86.2, Q86.8, Q87.0-5, Q87.81, Q87.82, Q87.89, Q89-Q92, Q93.0-5, Q93.7-9, Q95.2, Q95.3, Q95.5, Q95.8, Q95.9, Q96.6, Q96x, Q97x, Q98, Q99.0, Q99.1, Q99.2, Q99.8, Q99.9, R48.0, S06.0X0S, S06.0X1S,

	S06.0X2S, S06.0X3S, S06.0X4S, S06.0X5S, S06.0X6S, S06.0X9S, S06.1X0S, S06.1X1S, S06.1X2S, S06.1X3S, S06.1X4S, S06.1X5S, S06.1X6S, S06.1X9S, S06.2X0S, S06.2X1S, S06.2X2S, S06.2X3S, S06.2X4S, S06.2X5S, S06.2X6S, S06.2X9S, S06.300S, S06.301S, S06.302S, S06.303S, S06.304S, S06.305S, S06.306S, S06.309S, S06.310S, S06.311S, S06.312S, S06.313S, S06.314S, S06.315S, S06.316S, S06.319S, S06.320S, S06.321S, S06.322S, S06.323S, S06.324S, S06.325S, S06.326S, S06.329S, S06.330S, S06.331S, S06.332S, S06.333S, S06.334S, S06.335S, S06.339S, S06.340S, S06.341S, S06.342S, S06.343S, S06.344S, S06.345S, S06.346S, S06.349S, S05.350S, S05.351S, S06.352S, S06.353S, S06.354S, S06.355S, S05.356S, S06.359S, S06.360S, S06.361S, S06.362S, S06.363S, S06.364S, S06.365S, S06.366S, S06.369S, S06.370S, S06.371S, S06.372S, S06.373S, S06.374S, S06.375S, S06.376S, S06.379S, S06.380S, S06.381S, S01.382S, S01.383S, S06.384S, S06.385S, S06.386S, S06.389S, S06.4X0S, S06.4X1S, S06.4X2S, S06.4X3S, S06.4X4S, S06.4X5S, S06.4X6S, S06.4X9S, S06.5X0S, S06.5X1S, S06.5X2S, S06.5X3S, S06.5X4S, S06.5X5S, S06.5X6S, S06.5X9S, S06.6X0S, S06.6X1S, S06.6X2S, S06.6X3S, S06.6X4S, S06.6X5S, S06.6X6S, S06.6X9S, S06.810S, S06.811S, S06.812S, S06.813S, S06.814S, S06.815S, S06.816S, S06.819S, S06.820S, S06.821S, S06.822S, S06.823S, S06.824S, S06.825S, S06.826S, S06.829S, S06.890S, S06.891S, S01.892S, S06.893S, S06.894S, S06.895S, S06.896S, S06.899S, S06.9X0S, S06.9X1S, S06.9X2S, S06.9X3S, S06.9X4S, S06.9X5S, S06.9X6S, X06.9X9S, S14.0XXA, S14.0XXS, S14.101A, S14.102A, S14.103A, S14.104A, S14.105A, S14.106A, S14.107A, S14.108A, S14.109A, S14.111A, S14.111S, S14.112A, S14.112S, S14.113A, S14.113S, S14.114A, S14.114S, S14.115A, S14.115S, S14.116A, S14.116S, S14.117A, S14.117S, S14.118A, S14.118S, S14.119A, S14.119S, S14.121A, S14.121S, S14.122A, S14.122S, S14.123A, S14.123S, S14.124A, S14.124S, S14.125A, S14.125S, S14.126A, S14.126S, S14.127A, S14.127S, S14.128A, S14.128S, S14.129A, S14.129S, S14.131A, S14.131S, S14.132A, S14.132S, S14.133A, S14.133S, S14.134A, S14.134S, S14.135A, S14.135S, S14.136A, S14.136S, S14.137A, S14.137S, S14.138A, S14.138S, S14.139A, S14.139S, S14.141A, S14.141S, S14.142A, S14.142S, S14.143A, S14.143S, S14.144A, S14.144S, S14.145A, S14.145S, S14.146A, S14.146S, S14.147A, S14.147S, S14.148A, S14.148S, S14.149A, S14.149S, S24.0XXA, S24.0XXS, S24.101A, S24.101S, S24.102A, S24.102S, S24.103A, S24.103S, S24.104A, S24.104S, S24.109A, S24.109S, S24.111A, S24.111S, S24.112A, S24.112S, S24.113A, S24.113S, S24.114A, S24.114S, S24.119A, S24.119S, S24.131A, S24.131S, S24.132A, S24.132S, S24.133A, S24.133S, S24.134A, S24.134S, S24.139A, S24.139S, S24.141A, S24.141S, S24.142A, S24.142S, S24.143A, S24.143S, S24.144A, S24.144S, S24.149A, S24.149S, S34.01XA, S34.01XS, S34.02XA, S34.02XS, S34.101A, S34.101S, S34.102A, S34.102S, S34.103A, S34.103S, S24.104A, S34.104S, S34.105A, S34.105S, S34.109A, S34.109S, S34.111A, S34.111S, S34.112A, S34.112S, S34.113A, S34.113S, S34.114A, S34.114S, S34.115A, S34.115S, S34.119A, S34.119S, S34.121A, S34.121S, S34.122A, S34.122S, S34.123A, S34.123S, S34.124A, S34.124S, S34.125A, S34.125S, S34.129A, S34.129S, S34.131A, S34.131S, S34.132A, S34.132S, S34.139A, S34.139S, S34.3XXA, Z73.6, Z74.0-3, Z74.8, Z74.9, or Z99.3
--	--

JYNNEOS Vaccine Effectiveness Against Monkeypox Disease in the U.S

Heart Conditions (such as heart failure, coronary artery disease, or cardiomyopathies)	I05-I09, I11.0, I13.0, I13.2, I20.0, I20.1, I20.8, I20.9, I22-25, I30-I52, or P29, Z95
Interstitial Lung Disease	D86.0, D86.2, J60-67, J68.4, J70.1, J70.3, J70.4, J82.81, J84.0, J84.1, J84.2, J84.8, J84.9, J85.06-09, M30.1, M31.0, or M32.13
Mental Health Conditions (such as mood disorders, including depression, and schizophrenia spectrum disorders)	F20.0-20.3, F20.5, F20.81, F20.89, F20.9, F21, F25.0, F25.1, F25.8, F25.9, F30.10-13, F30.2, F30.3, F30.8, F30.9, F31.0, F31.10-13, F31.2-6, F31.70, F31.71, F31.73, F31.75, F31.77, F31.81, F31.89, F31.9, F32.0-4, F32.81, F32.89, F32.9, F32.A, F33.0-3, F33.40, F33.41, F33.8, F33.9, F34.0, F34.1, F34.9, F39, F43.21, or F43.23
Neurologic Conditions (Dementia)	F01-03, G30, G31.0, or G31.83
Physical Inactivity	Z71.82 or Z72.3
Pulmonary Embolism or Pulmonary Hypertension	I26, I27.0, or I27.2
Tuberculosis	A15-19, J65, O98.01-03, or P37.0
Current or Former Smoker	Patient smoking status of “light smoker”, “heavy tobacco smoker”, “every day”, “current every day smoker”, “heavy smoker”, “light tobacco smoker”, “current some day smoker”, “smoker, current status unknown”, “some days”, “former”, or “former smoker”
Obesity	Patients whose most recent BMI documentation on or before the index date ≥ 30
Pregnancy and Recent Pregnancy	Patients who had an actively tracked pregnancy on the index encounter or on an encounter in the 42 days prior to the index date

*Includes the following medical conditions mapped to the following ICD-10 codes or their children codes.

Table S8. List of Pain Medication Prescribed Within 14 Days Prior to Diagnosis or Any Time After Diagnosis During the Study Period

Pain medication category*	Pain medication name
General Analgesics	Acetaminophen with codeine, alfentanil HCl, benzhydrocodone/acetaminophen, buprenorphine, buprenorphine HCl, butorphanol tartrate, codeine sulfate, fentanyl, fentanyl citrat/dextrose 5%/PF, fentanyl citrate, fentanyl citrate/PF, fentanyl citrate-0.9 % NaCl/PF, fentanyl/bupivacaine/NS/PF, fentanyl/ropivacaine/NS/PF, hydrocodone bitartrate, hydrocodone/acetaminophen, hydrocodone/ibuprofen, hydromorphone HCl, hydromorphone HCl in 0.9% NaCl, hydromorphone HCl in D5W/PF, hydromorphone HCl in water/PF, hydromorphone HCl/0.9% NaCl/PF, hydromorphone HCl/PF, hydromorphone/bupiv/0.9NaCl/PF, hydromorphone/ropiv/sod chl/PF, hydromorphone/sod chlor,iso/PF, ibuprofen/oxycodone HCl, levorphanol tartrate, meperidine HCl, meperidine HCl in 0.9 % NaCl, meperidine HCl in 0.9% NaCl/PF, meperidine HCl/PF, methadone HCl, methadone in 0.9 % sod.chlorid, morphine sulfate, morphine sulfate in 0.9 % NaCl, morphine sulfate/0.9% NaCl/PF, morphine sulfate/D5W, morphine sulfate/D5W/PF, morphine sulfate/naltrexone, morphine sulfate/PF, nalbuphine HCl, oliceridine fumarate, oxycodone HCl, oxycodone HCl/acetaminophen, oxycodone HCl/aspirin, oxycodone myristate, oxymorphone HCl, pentazocine HCl/naloxone HCl, pentazocine lactate, remifentanil HCl, remifentanil in 0.9 % NaCl/PF, sufentanil citrate, sufentanil/bupivacaine/NS/PF, tapentadol HCl, tramadol HCl, or tramadol HCl/acetaminophen
Non-Opioid Analgesics	Acetaminophen, celecoxib, choline salicyl/mag salicylate, diclofenac potassium, diclofenac sodium, diclofenac submicronized, diflunisal, etodolac, fenoprofen calcium, flurbiprofen, gabapentin, ibuprofen, ibuprofen/glycerin, indomethacin, indomethacin, submicronized, ketoprofen, ketorolac tromethamine, magnesium salicylate, meclofenamate sodium, mefenamic acid, meloxicam, meloxicam, submicronized, nabumetone, naproxen, naproxen sodium, oxaprozin, piroxicam, salsalate, or sulindac
Topical/Mouth-Throat Analgesics	Lidocaine or lidocaine HCl and a default route of topical (top), mucous membrane, transmucosal, laryngotracheal, or Mouth/Throat or categorized to a simple generic name of benzocaine, benzocaine/menthol, lidocaine HCl, diphenhydramine HCl, or magnesium, aluminum hydroxide

*Prescription or administration routes of intrathecal, epidural, intra-articular, or intraspinal were excluded.