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Effectiveness of Smallpox Vaccination to Prevent Mpox in Military Personnel

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TO THE EDITOR:

During the ongoing global outbreak of mpox (formerly called monkeypox), smallpox vaccines have been used to prevent infection and reduce the severity of disease in those at increased risk for infection.¹ However, the effectiveness of smallpox vaccines against mpox is unknown.

We conducted a retrospective, test-negative case–control study among current and former U.S. military personnel to determine the effectiveness of smallpox vaccines against mpox. From 2002 through 2017, more than 2.6 million U.S. military personnel had received smallpox vaccinations (Dryvax, ACAM2000, or JYNNEOS vaccines) as part of their military deployment or occupational requirements. We aggregated two data sources — the Department of Defense electronic laboratory data and the Veterans Affairs (VA) Corporate Data Warehouse — to identify eligible participants. The study was approved by the institutional review board of Emory University and was granted an exemption for consent.

Logistic regression was used to calculate odds ratios with 95% confidence intervals for the association between a positive test result for orthopoxvirus species (which include smallpox, cowpox, and mpox, among other viruses) and previous receipt of a smallpox vaccine. We included age, race, sex, and HIV status as potential confounders in the final model. Among the participants tested in the VA, the severity of disease was defined as admission to a hospital for mpox; this information was not available for participants outside a VA facility. Analyses were conducted with the use of R software, version 4.0.3. Further details regarding the study design and results are provided in the Supplementary Appendix, available with the full text of this letter at [NEJM.org](https://www.nejm.org).

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From July 1 to October 31, 2022, a total of 1014 current military personnel and veterans who had presented with a clinical syndrome concerning for mpox and who had undergone testing for orthopoxvirus were included in the analyses. Of these participants, 184 (18%) had a documented history of previous smallpox vaccination. Among the 293 participants (29%) who tested positive for orthopoxvirus, 10 (3%) had been vaccinated with Dryvax (a first-generation smallpox vaccine) and 20 (7%) had been vaccinated with ACAM2000 (a second-generation smallpox vaccine). The median time from receipt of the smallpox vaccination to the diagnosis of mpox was 13 years (interquartile range, 6 to 20).

Participants who had received smallpox vaccination were less likely to test positive for mpox than those with no record of vaccination (odds ratio, 0.28; 95% confidence interval [CI], 0.13 to 0.58 with Dryvax; odds ratio, 0.25; 95% CI, 0.15 to 0.42 with ACAM2000) (Table 1). The estimated vaccine efficacy was 72% for Dryvax and 75% for ACAM2000. Among the participants who tested positive for orthopoxvirus, 121 (41%) had been diagnosed with HIV infection (odds ratio, 2.34; 95% CI, 1.65 to 3.35). Within the VA portion of the study, 19 of 186 participants (10%) required hospitalization; there were no deaths from mpox, and all the participants had an uneventful recovery.

Previous vaccination at a median of 13 years earlier with either a first- or second-generation smallpox vaccine reduced the likelihood of testing positive for orthopoxvirus among current or former military personnel for whom vaccination data were available.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

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Table 1.

Risk of Human Mpox Diagnosis, According to Subgroup.

Variable	Odds Ratio (95% CI)	
	Unadjusted	Adjusted*
Vaccine type		
ACAM2000	0.44 (0.26–0.70)	0.25 (0.15–0.42)
Dryvax	0.39 (0.19–0.75)	0.28 (0.13–0.58)
Age group		
35–44 yr	0.96 (0.67–1.37)	0.84 (0.55–1.28)
45–64 yr	0.50 (0.36–0.70)	0.34 (0.23–0.49)
65 yr	0.05 (0.02–0.11)	0.04 (0.01–0.08)
Race or ethnic group [†]		
Black	1.73 (1.26–2.40)	1.29 (0.90–1.87)
Hispanic	1.24 (0.83–1.85)	1.00 (0.64–1.55)
Other or unknown	1.34 (0.74–2.36)	0.90 (0.46–1.66)
Male sex	7.39 (3.28–21.18)	6.83 (2.95–19.89)
HIV diagnosis	2.89 (2.15–3.89)	2.34 (1.65–3.35)

* The logistic regression model was adjusted for age, race, sex, and HIV status.

[†] Race or ethnic group was reported by the participants. White race was used as the reference group in this analysis.