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mind, authors of observational epidemiological studies should at all times remain careful and modest in their conclusions.

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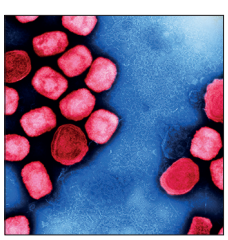
Can a single dose of Modified Vaccinia Ankara-Bavarian Nordic vaccine protect against mpox?



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To address the unprecedented community spread of mpox (formerly known as monkeypox) during the 2022 global outbreak, some affected countries, mostly in Europe and north America, deployed large scale mpox vaccination programmes targeting high-risk groups such as gay, bisexual and men who have sex with men (GBMSM). These vaccination programmes used Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN), a third-generation smallpox vaccine licensed for prevention of mpox based on animal efficacy studies, and human safety and immunogenicity studies.[1,2] Although previous studies from Africa have suggested that first and second-generation smallpox vaccines provide cross-protective immunity against mpox,[3] with an estimated 85% protective effectiveness in one study,[4] there have been no previous studies assessing clinical effectiveness of the third generation MVA-BN before the 2022 outbreak.

In *The Lancet Infectious Diseases*, Marta Bertran[5] and colleagues retrospectively investigated real-world effectiveness of vaccination with a single subcutaneous dose of MVA-BN against symptomatic mpox among GBMSM at higher risk of exposure to mpox in England. The authors assessed vaccine effectiveness using the case-coverage or screening method, which compared vaccine coverage among mpox cases to coverage in the estimated population of 89 240 at-risk GBMSM in England. A total of 1545 laboratory confirmed mpox cases in England diagnosed between July 4 and Oct 9, 2022, were invited to complete an electronic questionnaire on demographics, vaccination history, and symptoms. Of the 1545 cases, 508 (33%) returned the questionnaire and the final analysis included 363 GBMSM mpox cases aged 15–60 years or older who provided the required information.

Of the 363 mpox infections, 322 (89·0%) were unvaccinated, eight (2·2%) occurred at least 14 days after vaccination, and 32 (8·8%) occurred within 0–13 days after vaccination (one case with missing vaccination date was excluded). At the end of the study period, the population vaccine coverage was 50% and the estimated vaccine effectiveness at least 14 days after a single dose of MVA-BN was 78% (95% CI 54 to 89) and within 0–13 days was –4% (–50 to 29). Following a sensitivity analysis, the authors estimated vaccine effectiveness of 85% (95% CI 69 to 93) for high-coverage (63% vaccine coverage) and 71% (40 to 86) for low-coverage (42% vaccine coverage) scenarios. Four of the eight breakthrough infections after 14 days were people living with HIV and only one breakthrough infection occurred in those aged 50 years and older, who were people presumed to have received previous childhood smallpox vaccine. When people older than age 50 years were excluded, the estimated vaccine effectiveness was 74% (95% CI 43 to 88).

The 78% vaccine effectiveness reported by Marta Bertran and colleagues suggests that a single

dose of MVA-BN is considerably protective against symptomatic mpox only after 13 days post-vaccination. Because people living with HIV have been shown to have a higher risk of breakthrough COVID-19 infections post-vaccination,[6] the identification of four of eight breakthrough mpox infections among people living with HIV by Marta Bertran and colleagues is noteworthy. However, the MVA-BN vaccines have previously been shown to be immunogenic among adults with a history of AIDS[7] and larger cohorts of people living with HIV will be required to ascertain if HIV is a risk factor for MVA-BN vaccine failure. The major limitations of their study were the low questionnaire return rate and the inability to systematically adjust for potential confounders of vaccine effectiveness, including age, underlying clinical conditions (such as HIV), previous childhood smallpox vaccination, and behavioral practices related to mpox exposure. Additionally, their study did not estimate the duration of protection. It is likely that the limitations did not significantly affect the estimated vaccine effectiveness since those vaccinated within 0–13 days consistently had a vaccine effectiveness which was close to zero.

Their findings compare with two other similar studies done during the 2022 mpox outbreak. Sagy and colleagues[8] estimated a vaccine effectiveness of 86% (95% CI 59 to 95) at least 21 days after a single subcutaneous dose of MVA-BN vaccination among high-risk male individuals in Israel. In another study of vaccination with a single dose of MVA-BN vaccine among GBMSM in the USA, Payne and colleagues[9] reported a 14·3 times higher incidence of mpox among unvaccinated people compared with those vaccinated 14 days previously or longer. These two studies excluded individuals who were likely to have received previous childhood smallpox vaccination (those aged 50 years and older) and enrolled more study participants (more than 2000). However, the authors did not adjust for relevant confounders of vaccine effectiveness and did not assess duration of protection beyond 147 days.

Overall, these studies suggest that the use of a single dose of MVA-BN as PreP is preferable to post-exposure prophylaxis to guarantee protection against symptomatic mpox. Knowledge gaps related to effectiveness against other clades (more prevalent in Africa); protection against asymptomatic infection; duration of protection following first and second dose; immunological correlates of protection; and the roles of other confounders such as intradermal vaccination, HIV, previous smallpox vaccination, gender, age group, and degree of exposure (including route and type) in the estimation of vaccine effectiveness warrant future studies.

DO is the President of the Nigerian Infectious Diseases Society. NSW declares no competing interests.

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Progress in preventing non-ventilator-associated hospital-acquired pneumonia

Hospital-acquired pneumonia is the most common and fatal health-care-associated infection.[1,2] It affects about 0·5–1% of hospital admissions and is associated with a crude mortality rate of 15–30%.[1–3] About two-thirds of cases occur in non-ventilated patients. Notwithstanding the frequency and morbidity of non-ventilator-associated

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