At the Intersection of Mpox and HIV Infection: There Is Hope

More severe cases mpox has been reported in people whose HIV is not well controlled or during immunosuppression due to low CD4 counts.

June 26, 2025 By H. Lewis and Fred Hutch Cancer Center

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As we have learned multiple times in the past few centuries, pathogens have no respect for borders. Any local germ circulating in small outbreaks has the potential to suddenly make a global jump, causing pandemics and entrenching itself in new communities.

Such was the case with mpox (formerly known as monkeypox), which until recently was a neglected virus endemic to west and central Africa. In May 2022, a dramatic uptick of worldwide cases spread via sexual transmission lead the World Health Organization to declare a global mpox outbreak—which, although the pace of new infections is slowing, is not over yet. (And there's a risk of it happening again: the same strain that caused the 2022 outbreak is currently surging in Sierra Leone).

This ongoing global mpox outbreak disproportionately impacts people infected with human immunodeficiency virus (HIV), who are at higher risk of many diseases including some cancers. More severe cases of mpox have been reported in this population when HIV is not well controlled or during immunosuppression caused by low CD4 T cell counts. However, people living with HIV (PWH) face many health disparities such as exclusion from clinical trials, and the full impact of HIV and mpox coinfection has not been studied.

"Prior to 2022, little was known about mpox clinical outcomes and vaccine effectiveness among people with HIV," says Dr. Ina Montaño, a Research Associate in the HIV Outcomes, Prevention, and Epidemiology (HOPE) Group. "Prior studies of mpox usually had limited numbers of PWH, or were case series of people with mpox, comparing clinical outcomes among PWH to people without HIV," leaving a critical gap in understanding the risk and impact in this vulnerable population.

Dr. Montaño is the first author of a recent study in *Clinical Infectious Diseases* which addresses this gap for PWH in the United States. Together with co-author Dr. Adrienne Shapiro and senior author

Dr. Rachel Bender Ignacio, she collaborated with the Center for AIDS Research (CFAR) Network of Integrated Clinics Systems (CNICS) to identify the correlates of mpox risk and protection by surveying clinical and demographic data from a large, geographically diverse cohort of PWH. Information collected during primary care visits in this system, which take place at 10 medical centers across the geographical US, are integrated with electronic medical records, vaccination registry data, and are open-access to investigators researching the burden of the US HIV epidemic.

Out of 19,177 CNICS participants, the authors identified 413 mpox cases for an average incidence rate of 2.2 out of 100 people per year. Subgroups more at risk of mpox diagnosis were people under the age of 40, participants identifying as Hispanic/Latine, those who were diagnosed with a bacterial STI within the past 12 months, or people whose HIV was not fully suppressed.

Two vaccines are available for mpox; both are replication-incompetent and were originally developed to protect against smallpox. By comparing the number of mpox cases in unvaccinated and vaccinated participants with HIV, the authors calculated the overall vaccine effectiveness at 84%. “This means that the mpox vaccine prevented 84% of mpox cases that would have occurred in the absence of the vaccine,” Dr. Montaño explains (emphasis added). “Encouragingly, this is similar to estimates of mpox vaccine effectiveness in populations without HIV.”

What’s more, there are signs that vaccination prevents severe mpox outcomes in this population: vaccines given during the incubation period—3 to 17 days after exposure—helped prevent symptomatic disease. Of the 34 hospitalized patients in this cohort, only 2 were vaccinated, and neither had received their vaccine more than 7 days before diagnosis.

The strongest predictors of hospitalization were lack of viral suppression, being off antiretroviral therapy (ART), or CD4 T cell counts lower than 350 cells/mm^3.

The authors hypothesize that mpox diagnoses among these people may be due to dysregulated immune function, or that “the same constellation of social and medical vulnerabilities that lead to detectable viremia and ART interruption could also increase likelihood of exposure.”

There were disparities in who received mpox vaccination or treatment. For example, PWH with extremely low CD4 T cell count (<200 cells/mm^3) were only about half as likely to be vaccinated as other populations, but more likely to receive antiviral therapy. This suggests that PWH or their providers may have concerns about vaccine safety, even though the viral strains in the vaccines cannot replicate in the human body and are safe to administer even with advanced immunosuppression.

Dr. Bender Ignacio, the senior author, cautions that two large randomized trials of tecovirimat, an anti-smallpox drug often prescribed to treat severe cases of mpox, showed no clinical impact on either of the common mpox strains. “Focus on vaccination is even more important, since we still lack effective treatment tools,” she emphasizes.

There were also racial differences in this cohort; there were higher mpox incidence rates in people

identifying as Hispanic/Latine—possibly due to sexual network homogeneity, disparities in healthcare access, or lack of Spanish language communication in mpox public health outreach. However, encouragingly, this population had high vaccine uptake. In contrast, non-Hispanic Black participants were only a third as likely to be vaccinated as other racial or ethnic groups despite being over-represented in mpox diagnoses. This finding mirrors other studies that show persistent vaccination disparities despite the disproportionate burden of HIV in Black communities in the United States.

Looking to the future, Dr. Montaño and the HOPE team have many questions they'd like to answer, but they are worried that funding for this work may be at risk. This study focused on US populations, but the high overlap of HIV and mpox in Africa warrants similar work, as the team argues in a recent article in *Lancet*.

"Our findings show that the mpox vaccine is highly effective among PWH," Dr. Montaño says, "and moderately to highly effective even among those with poorly controlled HIV. In the current context of limited mpox vaccine supply and scarcity of global health funding/aid, how can we best prioritize vaccine access and outreach to populations most impacted by HIV and most at risk of mpox acquisition and severe outcomes?"

"This virus will continue to re-emerge globally," she adds.

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The spotlighted research was funded by the National Institute of Allergy and Infectious Diseases and a developmental grant from the University of Washington and Fred Hutchinson Center for AIDS Research supported by the following NIH Institutes and Centers: NIAID, NCI, NIMH, NIDA, NICHD, NHLBI, NIA, NIGMS, NIDDK.

Montaño M et al. Mpox in People With Human Immunodeficiency Virus: Predictors of Diagnosis, Outcomes, and Vaccine Effectiveness in a Multisite Cohort. Clin Infect Dis. 2024.

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