HEALTH EQUITY MATTERS
HIV. LGBTIQA+. COMMUNITIES.

BRIEFING PAPER: CLINICAL RESEARCH PRIORITIES FOR MPOX

29 July 2025

Mpox continues to impact communities across many parts of the world, including through new outbreaks caused by more severe strains of the virus. While Australia currently has low case numbers, global trends highlight the importance of remaining prepared. A key way to do this is through ongoing clinical research, especially in testing the effectiveness of current vaccines and treatments, as well as developing new, longer-lasting vaccines and identifying new therapies for those who become severely ill with mpox.

What we know about the mpox vaccine

The primary vaccine used in Australia to protect against mpox is JYNNEOS (also known as MVA-BN). It is administered in a two-dose schedule, 28 days apart. The vaccine is free and available through state and territory health departments.

Real-world studies show that two doses of JYNNEOS provide moderate to high protection, with the Australian Technical Advisory Group on Immunisation (ATAGI) clinical guidance indicating that research has found effectiveness estimates ranging from 66% to 89.5%.[i] The guideline also notes that one dose offers some protection (estimated between 35.8% and 86.4%), but completing the full two-dose schedule is necessary to maximise benefit. Vaccination also appears to reduce the severity of symptoms and shorten the duration of illness in people who contract mpox after vaccination.

However, questions remain about how long vaccine-induced protection lasts. Some studies show a decline in antibody levels beginning around three to six months after vaccination, potentially returning close to baseline within 10 to 24 months. However, ATAGI reports that this is based on a limited number of studies. While the clinical impact of waning immunity is not yet clear, breakthrough infections have occurred, and further monitoring is needed. The vaccine is less effective in immunocompromised individuals, including people with HIV, where protection is somewhat lower compared to those with healthy immune systems.

Currently, booster doses are not recommended in Australia, however, ATAGI continues to review emerging evidence. No clinical data yet exist on the effectiveness of a third (booster) dose. These

uncertainties highlight clear priorities for clinical research. Further studies are needed to evaluate the long-term effectiveness of JYNNEOS, especially against newly circulating strains such as Clade Ib. Research is also needed to understand vaccine performance in immunocompromised people, the potential role of booster doses, and whether alternative dosing strategies could improve access and protection.

What's next for mpox vaccines

Current mpox vaccines are based on modified smallpox vaccines, which were quickly repurposed during recent outbreaks. While these vaccines, including JYNNEOS, have provided a useful first line of defence, global health agencies recognise the need for next-generation vaccines that are better suited to the evolving nature of mpox outbreaks.

The World Health Organization is closely monitoring new vaccine candidates through its Mpox Vaccine Tracker. These include both repurposed smallpox-based vaccines and entirely new options, such as mRNA vaccines. Several companies, including Moderna and BioNTech, are developing mpox-specific mRNA vaccine candidates that are currently in early-phase trials. These are designed to enable quicker production and potentially offer broader protection.

Other vaccines include LC16m8, a Japanese smallpox vaccine that became the second mpox vaccine to receive WHO emergency use listing in 2024, and SCV-SMPOX, an mpox vaccine being developed by the Australian company Sementis, designed for rapid and large-scale manufacture.

The clinical research priorities include developing vaccines that offer longer-lasting immunity and higher protection, especially against newer strains like Clade Ib. There is also a strong need to assess vaccine safety and effectiveness across all population groups, including immunocompromised individuals, children, and pregnant women. Ensuring global access remains crucial, particularly for low- and middle-income countries where mpox is often endemic.

What we know about mpox treatment

Most mpox cases are mild and can be managed with supportive care, such as pain relief, fluids, and treatment for secondary infections. However, individuals with severe illness or at higher risk of complications may need antiviral treatment. In Australia, the antiviral Tecovirimat (marketed as Tpoxx) is currently the preferred option for these cases. It is available through the National Medical Stockpile and can be prescribed after consultation with infectious diseases or sexual health specialists.

Tpoxx is recommended for people with severe symptoms or those at higher risk of serious outcomes, including individuals with weakened immune systems (such as those with untreated HIV), children under eight, pregnant or breastfeeding women, and people infected with Clade I mpox. While Tpoxx is actively used in Australia and abroad, recent studies have raised questions about its effectiveness in improving outcomes.

Clinical trials have shown mixed results. The PALM007 trial, which assessed Tpoxx for hospitalised patients with Clade I mpox in the Democratic Republic of Congo (DRC), found no significant difference in the time it took for lesions to heal compared to a placebo.[ii] However, the trial reported a lower mortality rate among those who received Tpoxx (1.7%) compared to the case fatality rate reported in the DRC in 2023 (4.6%), suggesting a potential benefit when used alongside high-quality clinical care. A second trial, STOMP, found Tpoxx did not reduce the time to lesion resolution or have an effect on pain among adults with mild to moderate Clade II mpox.[iii] Other studies, such as MOSAIC, EPOXI, and MOSA, are continuing to explore its safety and effectiveness in various settings.[iv]

These findings highlight clear priorities for clinical research. Further studies are necessary to clarify the role of Tpoxx in treating mpox, particularly in outpatient settings and among individuals with mild to moderate illness. Research should also investigate whether antiviral treatment can help prevent complications or reduce transmission and whether different treatments are required for different virus clades. Understanding who benefits most from treatment and under what conditions is vital for developing effective treatment guidelines and making the best use of limited antiviral supplies.

Where further research is required on treatments for severe mpox

Although most mpox cases are mild, some individuals develop severe illness and may need more than just supportive care. Antiviral treatment with Tpoxx is currently the main option for those at higher risk of serious complications, including those who are immunocompromised, children, and pregnant women. However, as noted above, findings from the STOMP trial suggest that Tpoxx may not significantly accelerate recovery or alleviate pain in adults with mild to moderate Clade II mpox. While no safety issues were identified, the results underscore the importance of gaining a deeper understanding of how, when, and for whom this antiviral is most effective.

International research priorities reflect a shared view that better treatment options are needed. The World Health Organization and the US National Institutes of Health have both called for the development of new therapies, including monoclonal antibodies and next-generation antivirals. There is also interest in combination treatments and in assessing whether post-exposure treatment can help prevent illness after contact. Future research should focus on people with severe disease or those at

higher risk of complications. It is also crucial to evaluate how treatments function in outpatient settings and in low-resource environments.

Policy and practice implications

As clinical research on mpox vaccines and treatments continues to evolve, it is important that Australia remains informed about emerging evidence. The Australian Centre for Disease Control and ATAGI have responsibility for reviewing and updating national clinical and vaccination guidelines as new data become available.

Health Equity Matters will continue to monitor international trials and developments in collaboration with Australian infectious diseases researchers. This will support timely and informed community engagement and help ensure responses remain aligned with the latest global evidence, particularly if new outbreaks emerge.

---

[i] Australian Technical Advisory Group on Immunisation. Clinical guidance on the use of vaccines for prevention of mpox in 2024 (Version 3.0, 19 December 2024). Australian Government Department of Health and Aged Carehttps://www.health.gov.au/sites/default/files/2025-01/atagi-clinical-guidance-on-the-use-of-vaccines-for-the-prevention-of-mpox.pdf

[ii] Ali R, Alonga J, Biampata JL, et al. Tecovirimat for Clade I MPXV Infection in the Democratic Republic of Congo. N Engl J Med. 2025;392(15):1484-96.

[iii] National Institutes of Health. NIH study finds tecovirimat was safe but did not improve mpox resolution or pain. https://www.nih.gov/news-events/news-releases/nih-study-finds-tecovirimat-was-safe-did-not-improve-mpox-resolution-or-pain. Accessed 27 June 2025.

[iv] MPX-Response. https://mpx-response.eu/studies/. Accessed 27 June 2025.