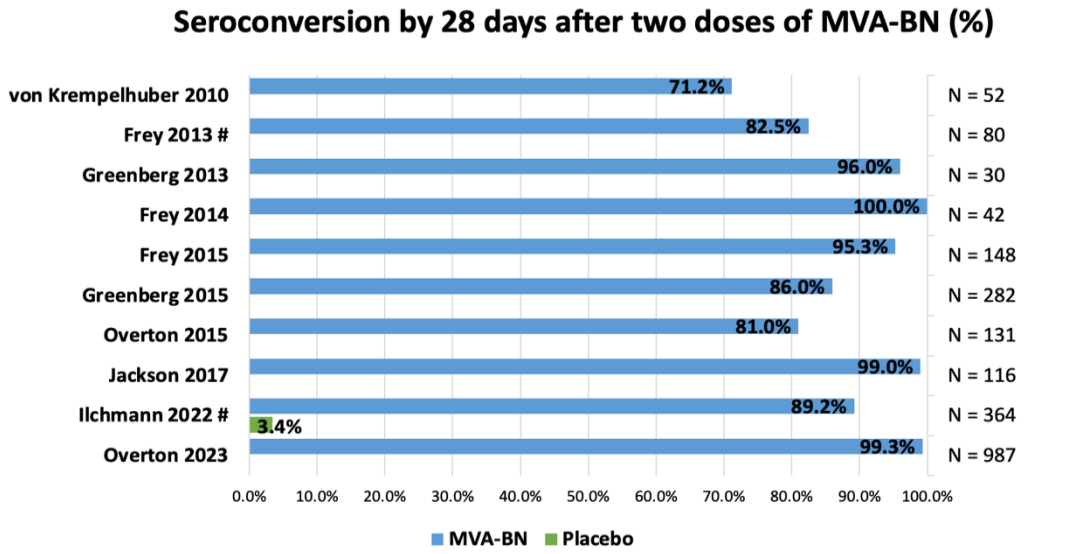
GRADE tables: Comparison of MVA-BN (JYNNEOS) with placebo or no vaccine in healthy adults

NCIRS is conducting GRADE assessments in support of the Australian Technical Advisory Group on Immunisation (ATAGI) and making results available on the Centre's website. Please read this material as a supplement to the Australian Immunisation Handbook Mpox (previously known as monkeypox) chapter.

MVA-BN compared with placebo or no vaccine for healthy adults

Patient or population: Healthy adults
Intervention: MVA-BN
Comparison: Placebo or no vaccine

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Seroconversion Assessed with: PRNT assay (MVA/Western Reserve vaccinia) Follow-up: range 8 days to 28 days	 # Two studies have a placebo arm, but only Ilchmann 2022 has available outcome data (displayed in green).	2232 (10 trials)[1-10,a,b,c]	⨁⨁◯◯ Low[d,e,f]	The evidence suggests that MVA-BN results in a large increase in seroconversion.

MVA-BN compared with placebo or no vaccine for healthy adults

Patient or population: Healthy adults
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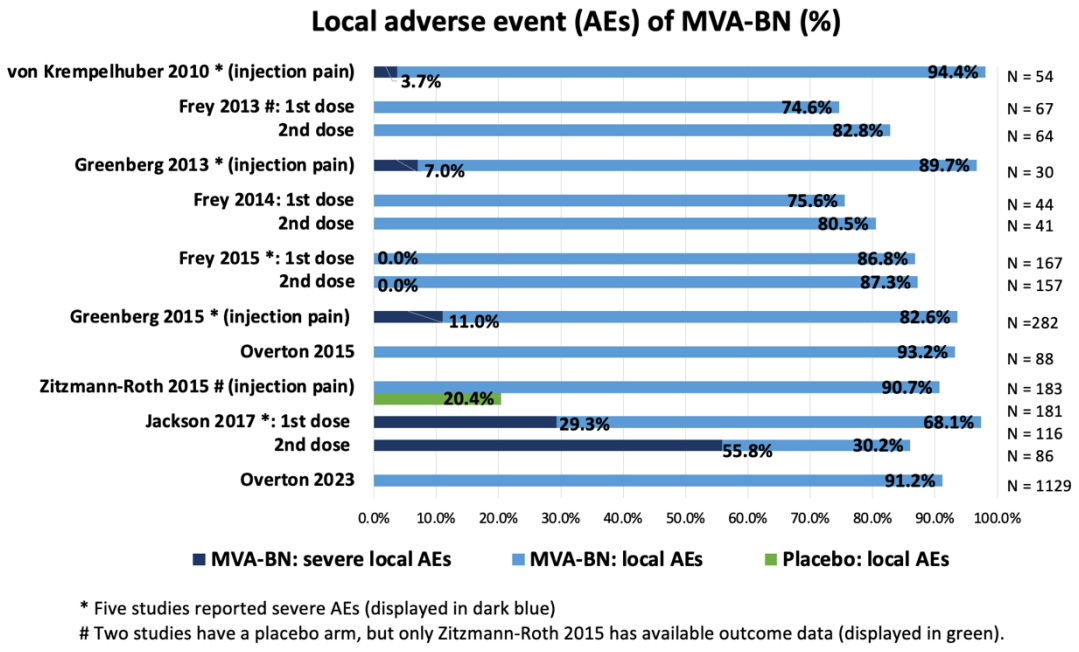
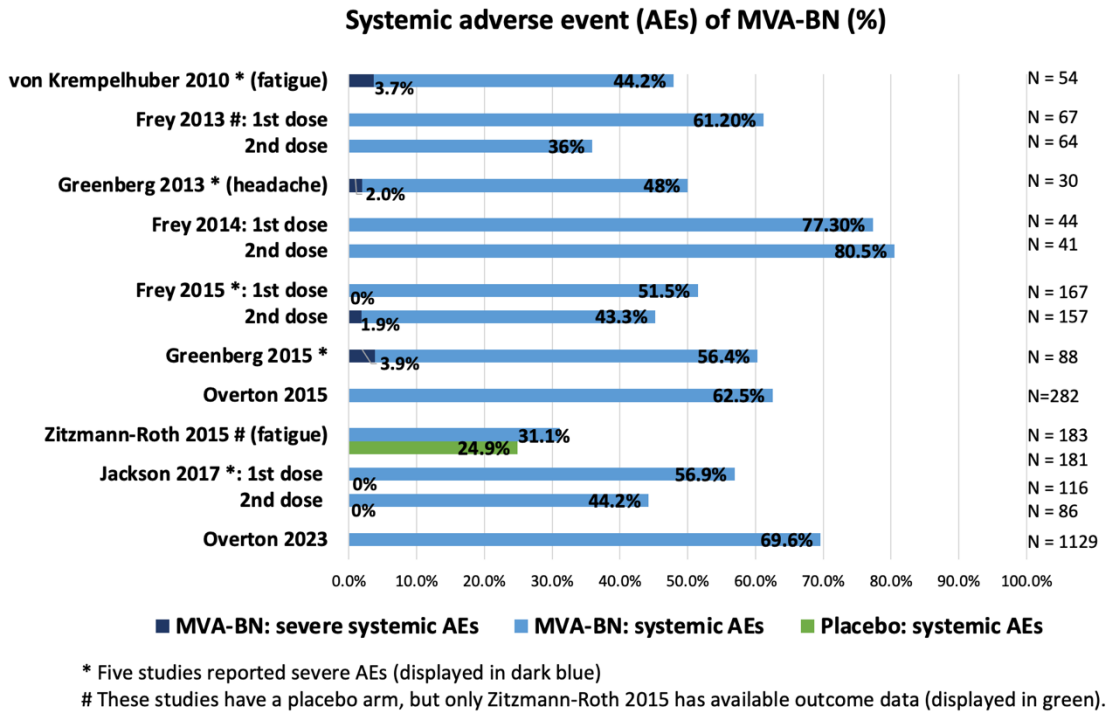
Comparison: Placebo or no vaccine

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Local adverse events (AEs) Assessed with: self-reported and/or clinically-confirmed event rate Follow-up: range 14 days to 8 weeks	 * Five studies reported severe AEs (displayed in dark blue) # Two studies have a placebo arm, but only Zitzmann-Roth 2015 has available outcome data (displayed in green).	2358 (10 trials)[1-6,8-11,a,b,g]	⊕⊕⊕◯ Moderate[d,e]	MVA-BN probably increases local AEs.

MVA-BN compared with placebo or no vaccine for healthy adults

Patient or population: Healthy adults
Intervention: MVA-BN
Comparison: Placebo or no vaccine

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Systemic AEs Assessed with: self-reported and/or clinically confirmed event rate Follow-up: range 14 days to 8 weeks	 * Five studies reported severe AEs (displayed in dark blue) # These studies have a placebo arm, but only Zitzmann-Roth 2015 has available outcome data (displayed in green).	2358 (10 trials)[1-6,8-11,a,b,g]	⊕⊕⊕◯ Moderate[d,e]	MVA-BN probably increases systemic AEs.

MVA-BN compared with placebo or no vaccine for healthy adults				
Patient or population: Healthy adults **Intervention:** MVA-BN **Comparison:** Placebo or no vaccine				
Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Serious adverse events (SAEs) Assessed with: self-reported and/or clinically confirmed event number Follow-up: range 4 weeks to 12 months	Four possible vaccine-related SAEs were reported in 3 studies: • one confirmed case of sarcoidosis 10 weeks after the second dose of MVA-BN, for which causality could not be ruled out • one case of a non-ST elevation myocardial infarction without epicardial coronary artery disease occurring 117 days after the first vaccination • hypersensitivity reaction one case of extraocular muscle paresis occurring 8 days after the second vaccination.[b]	2558 (10 trials)[1-6,8-11,a,b,g]	⨁⨁⨁◯ Moderate[d,e]	MVA-BN probably results in little to no difference in SAEs.
Myo/pericarditis Assessed with: clinically confirmed event number Follow-up: range 4 weeks to 12 months	No confirmed cases of myocarditis or pericarditis were reported from the included studies.[b]	2558 (10 trials)[1-6,8-11,a,b,g]	⨁⨁⨁◯ Moderate[d,e]	MVA-BN probably does not increase myo/pericarditis.

MVA-BN compared with placebo or no vaccine for healthy adults

Patient or population: Healthy adults
Intervention: MVA-BN
Comparison: Placebo or no vaccine

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation

Explanations

a. There were 2 non-randomised trials (Greenberg 2013, Overton 2015)
b. Despite most studies having multiple arms, only participants who received standard formulation, dose and route of MVA-BN were included, according to current practice (i.e. a liquid formulation for subcutaneous administration at a dose of 1×10^8 infectious units of MVA-BN virus in a volume of 0.5 mL, given by a 2-dose schedule with 1 week apart)
c. 1 placebo-controlled study reported seroconversion outcome (Ilchmann 2022)
d. Downgrade on risk of bias due to 7 out of 9 studies being single-arm trials (without unvaccinated controls)
e. Downgrade on risk of bias due to missing placebo data in one study
f. Downgrade on indirectness due to indirect antigen (vaccinia virus) used in laboratory tests
g. 1 placebo-controlled study reported safety outcomes (Zitzmann-Roth 2015)

Abbreviations: AE=adverse event; CI=confidence interval; MVA-BN=modified vaccinia Ankara–Bavarian Nordic; SAE=serious adverse event

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect.

GRADE evidence profile

MVA-BN vs placebo or no vaccine in healthy adults

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	MVA-BN	placebo or no vaccine	Relative (95% CI)	Absolute (95% CI)		
Seroconversion (follow-up: range 8 days to 28 days; assessed with: PRNT assay [MVA/Western Reserve vaccinia])												
10	Clinical trials[a,b,c]	Serious[d,e]	Not serious	Serious[f]	Not serious	None	The majority (71.2% to 100%) of participants who received MVA-BN seroconverted by 28 days after the 2nd dose. Data from one randomised controlled trial (RCT) showed a seroconversion rate of 89.2% in the MVA-BN group and 3.4% in the placebo group.				⨁⨁◯◯ Low	IMPORTANT
Local adverse events (AEs) (follow-up: range 14 days to 8 weeks; assessed with: self-reported and/or clinically confirmed event rate)												
10	Clinical trials[a,b,g]	Serious[d,e]	Not serious	Not serious	Not serious	None	The most common symptoms were local injection site pain, erythema, swelling and induration. 74.6% to 98.1% of participants who received MVA-BN reported at least one local AE. Data from one RCT showed 20.4% of participants (N=181) in the placebo group reported injection site pain, compared with 90.7% in the MVA-BN group. Proportions of local AEs after dose 1 and dose 2 were similar. 3.7% to 55.8% of participants reported severe local AEs from 4 studies and 0 cases were observed in 1 study (Frey 2015).[b]				⨁⨁⨁◯ Moderate	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	MVA-BN	placebo or no vaccine	Relative (95% CI)	Absolute (95% CI)		
Systemic AEs (follow-up: range 14 days to 8 weeks; assessed with: self-reported and/or clinically confirmed event rate)												
10	Clinical trials[a,b,g]	Serious[d,e]	Not serious	Not serious	Not serious	None	Proportions of participants in the MVA-BN group who reported at least one systemic AE varied from 35.9% to 80.5%. Data from one RCT showed 24.9% of participants (N=181) in the placebo group reported fatigue, compared with 31.1% in the MVA-BN group in the same study. 1.9% to 3.7% of severe systemic AEs were reported from 4 studies and 0% in 1 study (Jackson 2017).[b]				⊕⊕⊕◯ Moderate	IMPORTANT
Serious adverse events (follow-up: range 4 weeks to 12 months; assessed with: Self-reported and/or clinically confirmed event number)												
10	Clinical trials[a,b,g]	Serious[d,e]	Not serious	Not serious	Not serious	None	Four possible vaccine-related SAEs were reported in 3 studies: • one confirmed case of sarcoidosis 10 weeks after the second dose of MVA-BN, for which causality could not be ruled out • one case is a non-ST elevation myocardial infarction without epicardial coronary artery disease occurring 117 days after the first vaccination • hypersensitivity reaction • 4) one case of extraocular muscle paresis occurring 8 days after the second vaccination.[b]				⊕⊕⊕◯ Moderate	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	MVA-BN	placebo or no vaccine	Relative (95% CI)	Absolute (95% CI)		
Myo-/peri-carditis (follow-up: range 4 weeks to 12 months; assessed with: Clinically confirmed event number)												
10	Clinical trials[a,b,g]	Serious[d,e]	Not serious	Not serious	Not serious	None	No confirmed cases of myocarditis or pericarditis were reported from the included studies.[b]				⨁⨁⨁◯ Moderate	IMPORTANT

Explanations

a. There was 2 non-randomised trials (Greenberg 2013, Overton 2015)
b. Despite most studies having multiple arms, only participants who received standard formulation, dose and route of MVA-BN were included, according to current practice (i.e. a liquid formulation for subcutaneous administration at a dose of 1×10^8 infectious units of MVA-BN virus in a volume of 0.5 mL, given by a 2-dose schedule with 1 week apart)
c. 1 placebo-controlled study reported seroconversion outcome (Ilchmann 2022)
d. Downgrade on risk of bias due to 7 out of 9 studies being single-arm trials (without unvaccinated controls)
e. Downgrade on risk of bias due to missing placebo data in one study
f. Downgrade on indirectness due to indirect antigen (vaccinia virus) used in laboratory tests
g. 1 placebo-controlled study reported safety outcomes (Zitzmann-Roth 2015)

Abbreviations: AE=adverse event; CI = confidence interval; RCT=randomised controlled trial

Evidence to Decision framework: MVA-BN (JYNNEOS) compared with placebo or no vaccine in healthy adults

Should MVA-BN (JYNNEOS) be used in healthy adults for the prevention of mpox disease?	
Population	Healthy adults
Intervention	MVA-BN (two standard subcutaneous doses, 28 days apart)
Comparison	Placebo, no vaccine
Main outcomes	*Critical* • Serious adverse events • Important • Percentage of participants with seroconversion (Monkeypox virus neutralising antibody seroconversion rate) 28 days post vaccination • Effectiveness • Efficacy • Local adverse events • Systemic adverse events • Myo-/peri-carditis (clinically confirmed) Note: Some outcomes may be missing in GRADE projects due to absence of data from available studies. Additional outcomes specifically reported in studies were included due to relevance.
Setting	Global high-income countries
Perspective	Individual

ASSESSMENT

Problem
Is the problem a priority?

Don't know	Varies	No	Probably No	Probably Yes	Yes

- In May 2022, the World Health Organization (WHO) alerted member states to a multi-country outbreak of mpox outside the endemic countries, originating from clade II of the virus.[12] Mpox was declared a Communicable Disease Incident of National Significance by the Australian Government in July 2022,[13] following WHO declaring the global situation regarding mpox to be a public health emergency of international concern (PHEIC). Although the incidence of mpox stabilised across Australia in late September 2022,[14] there is potential for future outbreaks.
- Mpox disease is often self-limiting and most people recover within a few weeks.[15] However, risk of severe disease and complications such as secondary infection, sepsis, pneumonia and encephalitis is likely to be increased in people with immunocompromise,[16] young children and pregnant women, but can occur in anyone with mpox. Symptoms such as severe oropharyngeal or anorectal pain may also lead to hospitalisation.[17]

- Anyone can contract mpox through contact with infected lesions. Global data in 2022 identified higher case numbers within the sexual networks of mainly, but not exclusively, gay, bisexual and other men who have sex with men (GBMSM).[18] Mpox vaccination is recommended for high-risk groups at increased risk of mpox infection, including GBMSM with multiple sex partners, sex workers, or people who have high contact risk. While the risk is not limited to these groups, the outbreak has become an additional focus for stigma and discrimination directed against GBMSM, people with HIV and communities from previously affected regions. Stigmatisation can trigger mpox-infected individuals, especially marginalised individuals, to abandon formal health care services, limiting the use of mpox counselling and testing services, which may lead to further spread of the disease.[19] Therefore, WHO and the Centers for Disease Control and Prevention have appealed to reduce the stigma toward mpox through proper public communication and community engagement.[20,21]
- People who had occupational exposure to monkeypox, smallpox or vaccinia viruses, such as laboratory personnel or healthcare workers, are also recommended to receive mpox vaccine.

Desirable effects
How substantial are the desirable anticipated effects?

Don't know	Varies	Large	Moderate	Small	Trivial

Immunogenicity

- Data predominantly from clinical trials without unvaccinated controls showed proportions of participants demonstrating seroconversion (measured as PRNT against vaccinia virus) to be 71.2% to 100% at 2 weeks following the second subcutaneous dose of MVA-BN.[1-4,6-10,22]
- Percentages of participants demonstrating seroconversion were comparable after receiving 2 standard subcutaneous doses (95.3%) and 2 fractional intradermal doses (94.5%) of MVA-BN; and the immunogenicity results of the intradermal group were considered non-inferior to those of the subcutaneous group).[2]

VE in primary preventive vaccination (PPV)

- To date, no randomised controlled trials (RCTs) have evaluated the clinical efficacy or effectiveness of MVA-BN versus no vaccination in preventing mpox.
- A few post-licensure retrospective observational studies (including preprints) have been conducted in people considered at high risk of mpox infection (e.g. GBMSM, men diagnosed with HIV or receiving HIV pre-exposure prophylaxis). The estimated vaccine effectiveness (VE) ranged from 35.8% to 86% (follow up from 14 to 147 days post-vaccination) after a single dose of MVA-BN,[23-26] and 66% (95% CI = 47.4% to 78.1%)[27] to 85.9% (95% CI = 73.8% to 92.4%)[24] after a complete 2-dose course.
- According to the a US case-control study, the adjusted VE for a single dose of MVA-BN is 80.6% via intradermal administration and 77.0% via subcutaneous route; for 2 doses, adjusted VE is 80.3% via the intradermal route, and 88.9% via the subcutaneous route.[24]

VE in post-exposure preventive vaccination (PEPV)

- No clinical trial data available for PEPV against mpox. Evidence of PEPV for mpox was based on extrapolation from low-quality historical data of protection against smallpox, and more recent use in isolated outbreaks of mpox in non-endemic countries.
- A 2019 review of human smallpox outbreak data from 1882 to 1973 calculated an overall effectiveness of PEPV against smallpox with any smallpox vaccine of 45% (interquartile 25.5% to 64.5%), noting wide variation in the timing of vaccination after exposure.[28] A study obtaining consensus opinions from experts using the Delphi technique estimated a 80% effectiveness of post-exposure smallpox vaccination in preventing disease at 1–3 days after exposure.[29]
- Two French single-centre and uncontrolled studies investigated PEPV in adults who received MVA-BN after exposure to mpox. One study reported 4% (12/276) of vaccinated individuals developed breakthrough infection after one dose, this includes 10 cases occurred within 5 days of vaccination.[30] The second study reported breakthrough infections in 10% (11/108) individuals after a single dose of MVA-BN PEPV, with a median time between vaccination and symptom onset of 5 days (interquartile range: 1-6).[31] Both studies

showed the clinical course of breakthrough cases was mild and no patient required hospitalisation. The incubation time of the mpox virus was shown to be 7–9 days.[32] Breakthrough cases presenting within 5–7 days after vaccination is not considered fully immunised.

Special risk groups

- Data from US showed adjusted VE for 2-dose vaccination among immunocompromised participants was 70.2% (95% CI = −37.9% to 93.6%) and among immunocompetent participants was 87.8% (95% CI = 57.5% to 96.5%).[24]
- Safety and effectiveness data in people living with HIV infection are limited.
  - One study reported similar antibody response between HIV-infected ($CD4^+$ cell count ≥350 cells/mm^3) and uninfected participants, with a seroconversion rate of 89% and 96% following the second dose, respectively.[6]
  - Another study found significantly lower seropositivity rates in HIV-infected participants (CD4 cell count of 200–750 cells/mm^3) (61%) compared with controls (81%) after dose 2.[22] In this study, when response in HIV-infected participants was stratified by CD4 cell count, there was a trend of lower geometric mean titre with decreasing CD4 count, although the differences were not statistically significant, and the clinical significance is uncertain.
  - A study of people living with HIV showed the standard regimen of MVA-BN induced adequate immune response in all participants including a subset (20%) of people with CD4 cell count <200 cells/mm^3 at baseline.[33]
- So far there are no published data evaluating VE or immunogenicity in children. Serum samples from 87 children who had received a single dose of MVA-BN for PEPV observed robust antibody and cellular immune responses up to 15 weeks after vaccination compared with unvaccinated paediatric controls who had never been exposed to mpox.[34]

Populations with a history of smallpox vaccine (prior to the declaration of worldwide smallpox eradication in 1980)

- A systematic review suggests some protection against smallpox virus may persist for greater than 20 years after smallpox vaccination.[35] However, it is unclear how these data can be extrapolated to infer the duration of protection against mpox.
- Studies have found neutralising antibody levels were comparable in vaccinia-experienced participants who received one single dose of MVA-BN and vaccinia-naïve participants who received 2 primary doses.[7,22]
- In previous clinical trials, the frequency of adverse events, particularly local site reactions, trended higher in those who had received previous smallpox vaccines.[36]

Undesirable effects
How substantial are the undesirable anticipated effects?

Don't know	Varies	Large	Moderate	Small	Trivial

Adverse events (AEs)

- Common AEs reported from both clinical trials and post-marketing reports were largely consistent, describing local redness, itching, pain, swelling, tiredness, myalgia, headache and fatigue following both subcutaneous and intradermal administration of MVA-BN.
- Data from clinical trials without unvaccinated controls showed 74.6% to 98.1% of participants reported at least one local AE after receiving MVA-BN vaccine.[1-4,6,8-10,22] Data from one placebo-controlled RCT showed 20.4% of participants (N=181) in the placebo group reported injection site pain, compared with 90.7% in the MVA-BN group in the same study.[11]

- Data from non-controlled trials showed 35.9% to 80.5% of participants reported at least one systemic AE after receiving MVA-BN vaccine.[1-4,6,8-10,22] Data from one placebo-controlled RCT showed 24.9% of participants (N=181) in the placebo group reported fatigue, compared with 31.1% in the MVA-BN group in the same study.[11] Severe systemic AEs were rarely reported (up to 3.9% from 5 studies).
- Post-marketing active surveillance safety data through AusVaxSafety showed local AEs being self-reported by 31% (subcutaneous dose 2) to 53% (intradermal dose 1) of 21,601 individuals who received MVA-BN between August 2022 to March 2023.[37]
- The frequency of vaccine-related SAEs following MVA-BN is very low in prior clinical trials and subsequent deployment in the 2022 international mpox outbreak.
- Over one million doses of MVA-BN were administered during the 2022 international mpox outbreak, with no safety concerns identified. However, interpretation of these safety data should take into account that most of the doses were given to younger adult males (>90% vaccinated populations were aged 18-49 years).[38]
- No confirmed cases of myocarditis or other vaccine-related cardiovascular events were observed in people receiving MVA-BN from the current available evidence, including clinical trials and post-marketing data. Minor cardiac manifestations such as tachycardia, palpitations, abnormal ECG findings (T wave inversion or ST elevation)[39] were observed in clinical trials.

Concerns in special risk groups

- So far, no safety concerns have been reported in immunocompromised populations, including people living with HIV infection. MVA-BN appeared to be well tolerated in HIV-infected participants, with no adverse impact on viral load or CD4 cell count.[6,22,33]
- A dose-escalation study reported no vaccine-related SAEs after 2 doses of MVA-BN in 24 hematopoietic stem cell transplant recipients.[40]
- Very limited information exists on the use of MVA-BN in children. In a study of 87 children who received a single dose of MVA-BN for PEPV during the public health response to mpox in the UK, none of the children developed any SAEs or mpox disease after vaccination. Among 45 children who completed the follow-up questionnaire, 18 (40%) reported local reactions only and 11 (24%) reported systemic symptoms with or without local reactions.[34]
- The literature offers very limited data on pregnancy. Prior to the 2022 outbreak, MVA-BN had been administered to approximately 300 pregnant women with no adverse effects of concern reported.[36]
- The safety and immunogenicity profiles of MVA-BN were similar in healthy subjects and those with atopic dermatitis or allergic rhinitis reported in previous clinical trials.[41,42] However, Australian safety surveillance data showed a higher rate of AEs in people with atopic dermatitis when MVA-BN was administered either intradermally (dose 1: 81%; dose 2: 55%) or subcutaneously (dose 1: 62%; dose 2: 47%) compared with the average AE rates for intradermal (dose 1: 53%; dose 2: 35%) or subcutaneous routes (dose 1: 47%; dose 2: 31%).[37]

Certainty of evidence
What is the overall certainty of the evidence of effects?

No Included Studies	Very Low	Low	Moderate	High

- Certainty of evidence for seroconversion was downgraded due to a serious risk of bias, including lack of a control arm and selective outcome reporting. All existing trials used vaccinia virus rather than monkeypox virus for testing neutralising antibody titre, which was considered indirect evidence that further downgrade the evidence to "low".
- The overall certainty of evidence for all the safety outcomes was downgraded to "moderate" because of a serious risk of bias, including lack of a control arm and selective outcome reporting.

- Early VE estimates were exclusively from preprint and observational studies using registry data or medical records. Common quality concerns included retrospective design, selection bias (e.g. participants were mostly GBMSM or with a history of HIV, limited recruitment sites via sexual clinics), self-reported data collection and recall bias (e.g. vaccination status, medical history etc.), no controls and underpowered sample size. Since there is no screening or pre-vaccination tests for mpox in many countries, the actual number of mpox cases in post-marketing data might be under-estimates.
- There was very limited evidence on the effects for MVA-BN used for PPV in immunocompromised people, children and pregnant/breastfeeding women, as well as on the effects of PEPV across all populations.

Values
Is there important uncertainty about or variability in how much people value the main outcomes?

Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability

- No Australian research identified in the literature search addressed this specifically. Clinical experts have observed important variability in values and engagement with vaccination programs between high-risk groups and the general public. Demographics affected by future outbreaks are unclear; thus, it is unknown if values expressed by population most affected by the 2022 mpox outbreak can be extrapolated to all other populations.
- Evidence from surveys conducted in many countries showed healthcare professionals had insufficient knowledge of mpox, which may encounter some struggle in recognising and treating the disease.
  - In a 2020 Indonesian study, 10.0% and 36.5% of general practitioners had good knowledge using 80% and 70% cutoff points for the knowledge domain, respectively.[43] Younger doctors had better knowledge, but the overall knowledge of mpox was low in all groups.[43]
  - A US online survey of 197 clinicians showed they had relatively poor levels of knowledge and mixed attitudes about the eventual control of mpox and the threat posed by the disease. About 1 in 4 participants reported previous knowledge of mpox. Clinicians reported insufficient levels of intention to adopt preventive practices.[44]
  - A study of 163 general practitioners and public health/occupational physicians conducted in Italy in May 2022 demonstrated that the knowledge status for mpox infections was poor. Substantial knowledge gaps existed in all aspects of the disease, particularly when compared with SARS-CoV-2, TB, HIV and HBV.[45] The attitude toward vaccination was positive.[45]
  - An online study of healthcare professionals in Arabic countries showed 0.6% (36/5874) of respondents had a good knowledge of mpox and most were unfamiliar with the natural host, incubation period and transmission route of mpox disease.[46]
- Population-based online surveys from the Philippines,[47] Lebanon[48] and the US[49] found most general public had insufficient knowledge of mpox disease or monkeypox virus and around 40% of survey respondents were concerned about the outbreak or getting infected.[48,49] Education level and older age were consistently associated with better mpox knowledge and attitudes in disease prevention.[47,48]

Balance of effects
Does the balance between desirable and undesirable effects favour the intervention or the comparison?

Don't Know	Varies	Favours comparison	Probably favours comparison	Does not favour either comparison or intervention	Probably favours intervention	Favours intervention

- Overall, the protection provided by MVA-BN is likely to outweigh the risk of non-serious AEs, although based on limited placebo-controlled data.
- Evidence of MVA-BN used in immunocompromised populations, children, pregnant or breastfeeding women is limited but with no safety concerns identified to date. Any decision on the use of vaccine should consider the likelihood and clinical consequences of mpox infection in those special groups, including both maternal and fetal outcomes in pregnant women.

Acceptability
Is the intervention acceptable to key stakeholders?

Don't know	Varies	No	Probably No	Probably Yes	Yes

- No Australian research identified in the literature search addressed this specifically.
- During the 2022 mpox outbreak, willingness to vaccinate was dynamic and dependent on the perceived risk posed by the disease.
- Evidence from global experience suggests vaccination against mpox is largely acceptable among high-risk groups.
  - A survey of vaccinated laboratory workers showed either subcutaneous or intradermal use of MVA-BN was largely acceptable among research and clinical laboratory personnel who identified as having an occupational exposure risk.[50]
  - In Indonesia, before the COVID-19 pandemic, over 90% of doctors participating in a cross-sectional study about the attitude toward mpox vaccination were willing to be vaccinated.[51]
  - A pre-print study in France and Belgium reported that 55.4% of health workers would probably get the vaccine if it was recommended.[52]
  - A Chinese study of MSM showed only 13.85% (151/1090) of respondents expressed high mpox vaccination hesitancy. The predominant reason for rejecting vaccination was concern about the side effects (81.19%). Compared with HIV-uninfected MSM, HIV-infected MSM were more supportive of vaccination promotion.[53]
  - A single-centre study showed 65.5% mpox vaccine uptake among eligible GBMSM who attended a sexual health clinic operated by British Columbia government in Vancouver, Canada. Eligible unvaccinated participants had lower perceived susceptibility, increased constraints to vaccine access and greater privacy concerns.[54]
  - A US study showed rural MSM had a lower intention to get vaccinated for mpox and were less likely to report modifying their behaviours to decrease mpox exposure.[55]
  - An Israeli study showed HIV pre-exposure prophylaxis utilisation was associated with 70% higher vaccine uptake.[23]
- Stakeholder perceptions
  - The Australian health departments and state jurisdictions have been promoting the mpox vaccine and organising vaccination campaigns in partnership with peak and state-based organisations.[56]

Feasibility
Is the intervention feasible to implement?

Don't know	Varies	No	Probably No	Probably Yes	Yes

- No direct evidence identified for this issue; however, vaccination programs have been implemented in multiple states in Australia and over 20,000 people have been vaccinated.
- Mpox vaccine is not routinely given and only recommended for people at high risk of exposure in the current outbreak.

- Additional resources required to implement its use in current practice include, but are not restricted to, human resources, facilities (e.g. temporary mpox vaccination hubs), health systems (patient consent obtained via telehealth, booking system and safety reporting), vaccine costs, storage, logistics, planning and coordination, staff training, communications and immunisation safety surveillance.
- Existing resources could be leveraged to implement mpox vaccination (e.g. sexual health facilities).

- Vaccine availability is limited in some states, which posed an accessibility issue and delay of vaccination delivery.
- Global MVA-BN vaccine shortage has been a barrier to securing sufficient doses.
  - Some strategies have been implemented to offset supply constraints, including prioritising first doses to high-risk groups and fractional dosing with intradermal delivery.
  - A few potential challenges exist when implementing intradermal administration of MVA-BN.[2,57] Immunisation providers need to be trained to administer MVA-BN intradermally and there is a higher potential for administration error.[57]
- Reaching groups with high-risk exposure to mpox for administration of the vaccine may pose a challenge, especially in GBMSM, rural, Indigenous communities or culturally and linguistically diverse groups.
  - Feedback of mpox vaccination from GBMSM recommended better accessible communication, information dissemination with regularity and stigma-free, facts on mpox disease, vaccination and procedures, as well as availability of other preventive options.[55,58]

References

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