WHO SAGE Working Group on Smallpox & Monkeypox Vaccines

Dr. Anne Rimoin, member

Priority knowledge gaps for monkeypox vaccines?

- Clinical efficacy/effectiveness
- Schedule
- Other populations
- Behavioural insights
- Deployment strategies
Clinical Efficacy & Effectiveness – Knowledge Gaps

- What is the predicted/anticipated clinical efficacy of different vaccines?
- Efficacy for preventive/PrEP vaccination of different at-risk groups?
- Clinical efficacy of 1-dose schedule of MVA–BN in humans? As a preventive/PrEP vaccination? As PEP? Compared to 2 doses of MVA–BN.
- Effectiveness for prevention/PrEP in groups at high risk of exposure, including household contacts of non-infected persons at high risk?
- For post-exposure prophylaxis/PEP of contacts (different groups, e.g. family, sexual)?
- Effectiveness of vaccines in preventing monkeypox for different modes of exposure:
  - skin-to-skin contact
  - respiratory exposure (e.g. face-to-face (droplet), aerosolized)
  - exposure through sexual activities
  - different forms of mucosal exposure including mouth-to-mouth (e.g. kissing), exposure of eyes, anal/rectal mucosal exposure
  - Exposure through contact with fomites, e.g. bedding, objects, frequently touched surfaces
  - Household exposure where mode of exposure is not known.
- Modelling: How various scenarios for efficacy will affect vaccine effectiveness and impact? Is herd immunity possible? At what levels of coverage?
Schedule – Knowledge Gaps

- How many weeks after completing a vaccination series (1 or 2 doses) until considered protected?

- How long does protection last?

- For breakthrough cases, does vaccination reduce severity of disease?

- What is the evidence for PEP to be limited to 4–14 days post exposure? With delays in detection/confirmation of cases is this a practical strategy?

- Dose sparing studies: Can ACAM2000 or LC16 be used as 2nd dose for MVA-BN vaccinated (i.e. to free up MVA-BN doses for those who ACAM2000 & LC1 are contraindicated)? Could this enhance safety & effectiveness of ACAM2000?

- Fractional doses?

- If previously SPX vaccinated, is 1 dose of MVA-BN sufficient as a booster? Does this apply to persons vaccinated before eradication? When would booster doses of LC16 or ACAM2000 be required?

- If vaccine supply is limited, what is the public health impact of MVA-BN 2 doses vs MVA-BN 1 dose with delayed 2nd dose/extended schedule? How much later can the 2nd dose be offered?
Knowledge Gaps

Other Populations

- Safety of MVA in broader range of immune compromised groups, including poorly/inadequately treated HIV infection?
- At scale safety of vaccination in HIV+ individuals who are well controlled?
- Safety during pregnancy, safety in children?

Behavioral Insights

- KAPB surveys: Beliefs about vaccine effectiveness, safety, relevance?
- Willingness to limit high risk activity while waiting for immune response time and/or second dose?
- Willingness of individuals to delay their second dose so that others may have a first dose?
Deployment Strategies – Knowledge Gaps

- What is the overall goal of the vaccination programmes in various countries and globally?
- Can vaccines interrupt/reduce transmission?
- If vaccine supply is limited, should PEP be prioritized over preventive vaccination? Or should supply first be offered 'preventively' to those at highest risk of exposure? e.g. sexual health clinic attendees with STIs. Which strategy will contribute more to stop outbreak?
- Value of behavioural interventions: behavioural interventions and condom use + vaccine vs vaccine alone (minimal behavioural intervention)?
- In which context can ring vaccination of contacts be an effective strategy?
- If person who is recovered from MPX is identified as a contact, should they be vaccinated (PEP)?
- Vaccination delivery to high risk populations without generating stigma?
- Outbreak response & preventive strategies in rural areas where zoonotic transmission occurs? Effectiveness of community vaccination? Eligibility criteria depending on vaccine(s) used? Age groups? Occupational risk or activity based (e.g. HWs, hunting)?