2022 Monkeypox Outbreak – Canada Research Perspective

Canadian presentation to WHO R&D Blueprint meeting – vaccine effectiveness
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Canadian Epidemiological Situation

Figure 1: Epidemic Curve of confirmed and probable monkeypox cases based on national case report data as of July 20 (n=648):

- **Total publicly reported confirmed cases in Canada as of July 27 (n=745):**
  - There are 745 confirmed cases (346 Quebec, 326 Ontario, 58 British Columbia, 12 Alberta, 2 Saskatchewan 1 Yukon).
    - In Quebec, the majority of cases are in the Montreal area.
    - In Ontario, the majority of confirmed cases are in the Toronto area.
  - First cases were confirmed in Canada on May 19, 2022.
  - Cases are 99% male.
  - Average age: 36 years
    - The majority of cases have occurred in the 20-49 year-old age group.
  - Among confirmed cases, 11 hospitalizations including 2 ICU admission have been reported.
  - No deaths have been reported.

The orange line indicates the 7 day rolling average. Weekend dates are indicated in grey.

Note: there is a delay between symptom onset and reporting to PHAC, currently approximately 14 days.

Symptom onset date was only available for 483 cases.
June 10, 2022, National Advisory Committee on Immunization (NACI) issued recommendations on post-exposure prophylaxis

In summary: NACI recommends that PEP using a single dose of the Imvamune® (Imvanex/Jynneos) vaccine may be offered to individuals with high-risk exposures to a probable or confirmed case of monkeypox, or within a setting where transmission is happening. After 28 days, if an individual is assessed as having a predictable ongoing risk of exposure, a second dose may be offered. Imvamune® may be offered to special populations, including individuals who are immunosuppressed, pregnant, breastfeeding, <18 years of age and/or with atopic dermatitis. Imvamune® should not be given within 4 weeks of a COVID-19 mRNA vaccine, unless in a high-exposure scenario.

Provincial and territorial jurisdictions experiencing monkeypox outbreaks have built on this foundation with criteria for vaccine administration that may be more broad based on feasibility of case identification. National guidance on PEP and PrEP vaccination to be revisited in the context of emerging epidemiology and public health priorities.
NITAG guidance – research priorities

Research priorities identified by NACI:

1. Further study of the protection offered by Imvamune® vaccine against monkeypox infection and disease (in PrEP and PEP scenarios), including:
   - Understanding which immune responses are protective against infection and disease and defining protective thresholds
   - Understanding how the impact of previous orthopox infection or vaccination impacts the protection offered by Imvamune®
   - Real-world evidence on the vaccine effectiveness of Imvamune® against monkeypox and for the use of single dose PrEP and PEP.

2. Further studies to further inform on the safety of Imvamune® vaccine including both clinical trials and post-market safety surveillance.

3. Safety in special populations, including people who are pregnant or breastfeeding, children <18 years of age, and people who are immunocompromised should also be assessed by targeted clinical trials.

4. Further study into the epidemiology of the disease to better understand the modes of transmission, the disease presentation, and to identify the populations at highest risk for severe disease in order to inform and optimize disease prevention strategies.
Research underway

- Working with provinces and territories to better understand case characteristics, including frequency and timing of infection post-vaccination.

- Passive safety surveillance underway through Canadian Adverse Events Following Immunization Surveillance System (CAEFISS). Canadian Immunization Research Network (CIRN) has been mobilised for MPX vaccine studies, an active safety monitoring research study is in final stages of research ethics board approval and should launch soon. Study may also be able to provide some preliminary data on infections, but that is not the focus.

- Researchers in affected provinces are working on protocols for vaccine effectiveness (VE) observational study designs, including at least one proposal for test-negative design (TND).
VE research considerations

- Community engagement will be key for research to be successful, and to meet information needs for both vaccine recipients and policy makers

- Challenge to adjust for sexual behaviours and exposure risk. Not feasible to obtain information on sexual practices from participants, could consider using STI testing and confirmed cases as proxies for sexual behaviours.

- If vaccine is administered in a de-identified way for privacy reasons then immunization registries become less consistently linkable. Those at highest likelihood of being a case may be less inclined to give identifiers with their vaccine record.

- Distinct administrative databases are not linked across the country, precluding national aggregate studies.

- Some are exploring use of sentinel site networks to complement limitations of administrative database approaches.
VE research considerations continued

- Sample size - challenges achieving statistical power with relatively low case numbers and doses administered compared to respiratory diseases (e.g. COVID-19, influenza).
  - Lack of identified clear vaccine failures/breakthrough infection to date, infections shortly post-vaccine are presumed to have been incubating prior to vaccination/immunity.

- When applying TND to datasets assembled for a different clinical or surveillance purpose, can open up to bias and confounding. May result in under-estimates of vaccine protection, which could influence vaccine strategies.

- Variable clinical presentation is a challenge for restricting tested individuals in TND.
  - If need a lesion to get tested, and if vaccine prevents developing lesions but not other symptoms, this may interfere with a proper assessment of VE.

- Implementation science questions are important to consider alongside clinical VE studies – considering effectiveness/success of different models for vaccine deployment given complexities around contact tracing. Pragmatic study designs may be appropriate.
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