REVIEW ARTICLE

Preventive Measures Against Monkeypox: A Scoping Review

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ABSTRACT

Objectives: Monkeypox (MPX), a viral zoonotic disease, is causing current outbreaks with a rise in cases. This study aims to describe available monkeypox preventive measures and summarize their results.

Methods: We conducted a scoping review on monkeypox prevention methods. A search strategy including keywords of (1) monkeypox and (2) prevention was performed on PubMed, Scopus, and Embase.

Results: Out of 2198 retrieved articles, 1046 duplicates were removed. After title, abstract, and full-text examination, 8 eligible studies on specific preventive measures were included. The most common monkeypox prevention methods were vaccination and health communication. Smallpox vaccines are effective, but immunity may decline over time. Film-based educational activities were successful in enhancing understanding and promoting healthy behaviors, while media campaigns had little impact.

Conclusions: Monkeypox has limited data on prevention methods for humans. Future research on the effectiveness of these vaccines in humans, the relationship between vaccine efficacy and time since immunization, and the requirement to more thoroughly evaluate the impact of media campaigns are essential.

Keywords: *Monkeypox, Prevention, Vaccination, Health communication.*

INTRODUCTION

Monkeypox is caused by the Monkeypox virus, of the Orthopoxvirus genus and the Poxviridae family (1). This virus has a natural reservoir in rodents and can be transmitted by monkeys and humans (2). It spreads through direct contact with infected animals, respiratory secretions, skin lesions, or contaminated materials. Symptoms of monkeypox are similar to those of previous patients with smallpox but are less severe.

Monkeypox was discovered in 1958, first human cases were recorded in 1970 (3). Since early May 2022, new cases have been reported in multiple countries, causing a new outbreak with simultaneous occurrences in non-endemic and endemic regions (4).

According to the Center for Disease Control and Prevention (CDC), there are no available treatments specifically for monkeypox virus infection (5). Although outbreaks can be prevented with smallpox vaccines, antivirals, and vaccinia immune globulin (VIG) available through CDC consultation (5,6), numerous studies highlighting the urgency of monkeypox and the importance of monkeypox prevention have been performed. Several monkeypox studies have demonstrated non-human efficacy of monkeypox prevention (7–9); however, evidence on the effectiveness of monkeypox prevention on humans remains scarce. Therefore, our study was conducted with two objectives: (i) Describe available monkeypox preventive measures on human and (ii) Summarize results of available monkeypox preventive measures for human.

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METHOD

Study design: This scoping review was conducted from December 2022 to July 2023 and carried out following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Review (PRISMA-ScR) guidelines (10).

Search strategy: Search terms in Table 1 were combined using Boolean operators (AND, OR, NOT) for a complete search strategy, which was performed on Pubmed, Scopus, and Embase.

Table 1. Search terms

Component	Search terms
Monkeypox	monkeypox
Prevention method	prevent*, protect*, vaccin*, hygiene, prophylaxis, contact* AND avoid*, JYNNEOS, ACAM2000, MVA*, Imvanex, Imvamune

Data analysis: Data were retrieved from the databases and duplicates were removed by Zotero. Two investigators independently screened the studies. The first screening was for titles and abstracts, based on exclusion criteria: (1) unrelated to monkeypox, (2) no prevention, (3) non-English, (4) non-human studies. Studies were also excluded if they (1) did not include at least 1 prevention applied in humans, (2) did not describe the results of prevention clearly, (3) High risk of bias.

Ethical approval: This review used data from research articles that were internationally published and available for secondary analysis, therefore, ethical approval is not applicable.

RESULTS

Study Selection

The number of results was recorded in the PRISMA flowchart (Figure 1). Out of 2198 results, 234 studies were screened for eligibility, and eight articles were eligible for inclusion.

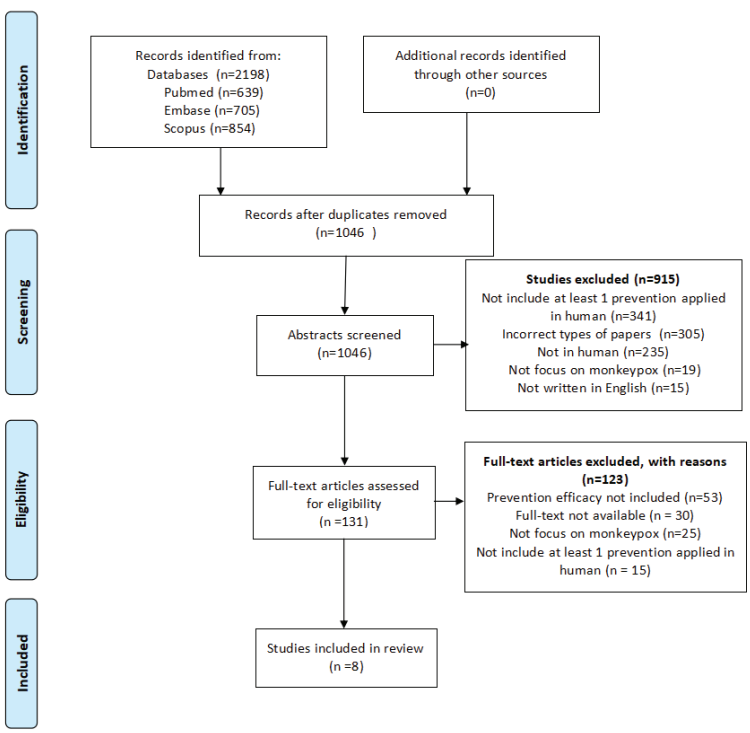

Figure 1. PRISMA flow chart

Study Characteristics

Table 2 summarizes the characteristics of the included studies. 6/8 included studies were cohort study, and two were cross-sectional. The studies were published between 1986 and 2020. Three studies were carried out in Zaire (3), the United States (2), the Democratic Republic of the Congo (2), and Southern Nigeria (1).

Table 2. Characteristics of the included studies

Ref.	Year of publication	Title	Country	Study design	Sample size
(11)	2007	Monkeypox-Induced Immunity and Failure of Childhood Smallpox Vaccination to Provide Complete Protection.	US	Cohort	72
(12)	2020	Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo.	Democratic Republic of the Congo	Cohort	676839
(13)	1986	Human monkeypox: a study of 2,510 contacts of 214 patients.	Zaire	Cohort	2510
(14)	2005	Multiple diagnostic techniques identify previously vaccinated individuals with protective immunity against monkeypox.	US	Cohort	
(15)	1988	The Transmission Potential of Monkeypox Virus in Human Populations.	Zaire	Cohort	209
(16)	1988	Human monkeypox: secondary attack rates.	Zaire	Cohort	338
(17)	2019	Assessment of media reportage of monkeypox in southern Nigeria.	Southern Nigeria	Cross-sectional	600
(18)	2011	Assessing the effectiveness of a community intervention for monkeypox prevention in the Congo basin.	Democratic Republic of Congo	Cross-sectional	271

Monkeypox prevention description and outcomes

Out of 8 studies analyzed, two main measures for monkeypox prevention were identified: 1) Vaccination using subjects' vaccination status, showing effectiveness against monkeypox but declining immunity over time, and 2) Health communication, with film-based community outreach program being effective in perception change, while media campaigns showed limited impact on behavior (Table 3).

Table 3. Monkeypox prevention description and results

Ref.	Preventive measures	Prevention Description	Results
(11)	**Smallpox vaccination**	**Participants:** 72 individuals (include 4 groups: 6 previous smallpox vaccination, 21 no previous smallpox vaccination, 27 contacts with previous smallpox vaccination, 18 contacts without previous smallpox vaccination) - analysis of immune responses - convalescent & 1-year time points. **Disease severity:** Humoral immunity. Serum samples - ELISA ⇒ detect specific antibodies.	**Disease severity:** Smallpox vaccination (9,09% severe, 27,78% mild), No smallpox vaccination (90,91% severe, 72,22% mild). **Humoral immune** - Anti-OPX IgM responses + Unvaccinated: highest median IgM response in convalescent period. + Both vaccinated and unvaccinated cases: IgM responses maintained at reduced levels 1-year post-rash onset. + Vaccinated cases with IgM responses: 1/3 in range of unvaccinated, 2/3 with low but detectable IgM. + No unvaccinated contacts had detectable IgM responses > equivocal range. - Anti-OPX IgG levels (convalescent - 1-year time points) + Vaccinated cases: ~ 20% loss. + Unvaccinated cases: ~ 40% loss. + Previously vaccinated contacts - substantial residual levels. + Unvaccinated contacts - no measurable anti-OPX IgG (exception: three individuals). ⇒ Remote vaccinia vaccination does not provide complete protection against systemic OPX infection.
(12)	**Vaccination**	**Location and Population:** 9 contiguous health zones - Sankuru district (676,839 in 2006 - 14.28/km2). **Case investigation:** - Each suspected case: physical examination; clinical, epidemiologic data. - Standardized questionnaire. **Laboratory methods:** PCR-based molecular assays - diagnosis of monkeypox and/or orthopoxvirus infection. **Statistical methods:** Univariate analysis - $\chi 2$ or Fisher's exact test. **Data sources:** Difference between cumulative incidence in the unimmunized versus the immunized populations, divided by cumulative incidence in the unimmunized.	- 760 cases of laboratory confirmed monkeypox (annual crude incidence: 5.53 / 10,000). - Average age of cases: 11.9. - 92.1% cases - born after mass smallpox vaccination campaigns ended. - 3.8% (29/760) cases had evidence of previous smallpox vaccination - 26.4% of the overall population. - Risk of human monkeypox - inverse with smallpox vaccination. - Individuals born before cessation of official vaccination campaigns: Vaccinated persons (5.21-fold lower risk of monkeypox - vs. unvaccinated persons (0.78 vs. 4.05 / 10,000). ⇒ Vaccine efficacy ~ 80.7%

Ref.	Preventive measures	Prevention Description	Results
(13)	**Vaccination**	**Field investigations** - Persons with lesions: Examined + clinical + epidemiological diagnosis. - Household / other contacts (index case): Identified, registered, interviewed, physically examined. **Specimen collection and laboratory diagnosis.** **Sampling and testing of specimens.** **Statistical evaluation:** The $\chi 2$ test - Yates's correction for continuity. Calculating attack rates for contacts with and without vaccination scar, attack rate by age.	- Contacts: 1,187 household members, 1,323 other persons. 74% had vaccination scar, 26% unvaccinated. - Overall attack rate for contacts without vaccination scar (7.2%) significantly differed from vaccinated contacts (0.9%). Unvaccinated contacts - most of the positive results. - Attack rate higher for household contacts compared to other contacts - 4 times higher for unvaccinated and 7 times higher for vaccinated household contacts.
(14)	**Vaccination**	- Adult volunteers (n = 44) with close contact with monkeypox-infected cases were categorized into suspect, probable or confirmed cases. - Other control subjects: Oregon residents (n = 21) (vaccinated against smallpox / provided multiple serum samples at 33–37 years after vaccination)	**Analysis of orthopoxvirus–specific antibodies** - Monkeypox infection of vaccinated - heterogeneity. High antibody titers against vaccinia + strong antibody titers to monkeypox, - 3 vaccinated subjects: high serological responses (recent orthopoxvirus infection) ⇒ distinguished from uninfected vaccinia-immune contacts ⇒ Identified subjects with fully protective immunity against monkeypox
(15)	**Vaccination**	**Materials:** Data on monkeypox in Zaire over the five years 1980-1984. **Analysis:** - Monkeypox surveillance in Zaire strengthened in 1980 (after cessation of smallpox vaccination). - 1980-1984, the 209 cases analyzed here arose in 125 separate episodes.	**Field investigations** - 125 episodes: 1573 contacts of 147 primary (125) and coprimary (22) cases. **Smallpox vaccine efficacy against monkeypox** - Same residence, other residence and all contacts of primary/coprimary cases: approximately 85%, 89% and 85%. - In same residence, attack rates are higher (0.110 > 0.038 and 0.017 > 0.004).
(16)	**Vaccination**	**Field investigation** - Local inhabitants: vesiculo-pustular disease, the presence of vaccination scars. - Persons with skin lesions. - Household members, other close contacts of the identified patients. **Evaluation:** using the x2 test with Yates' correction for continuity.	**Secondary attack rates** - Vaccination scars: 1555 contacts. - Attack rate among unvaccinated persons (7.47%) - vaccinated persons (0.96%). - Highest attack rate: 9.3% in unvaccinated contacts - 1.3% in vaccinated household members. - Unvaccinated household contacts: highest in the 0-4-year age group (11.7%) and decreasing with age.

Ref.	Preventive measures	Prevention Description	Results
(17)	**Media campaigns**	**Sample size**: 600 respondents. **Evaluation method:** 10-item "Monkeypox Awareness through Media Campaign Questionnaire" with 5-point scale. Sections: socio-demographics and media coverage in Southern Nigeria. Administered in 3 weeks, re-tested after 2 weeks for reliability.	- Learnt about monkeypox through mass media/new media: 2.02. - The media created effective awareness campaigns about the virus that mobilized an army of the masses against monkeypox: 1.86. ⇒ The mass media campaigns: little or no effect on people's health behavior.
(18)	**Film-based community outreach program**	**Films and content:** 2 films. - "Monkeypox Testimonies" - monkeypox recognition, modes of acquisition, and consequences - "Understanding Monkeypox" - virus transmission, disease prevention and seeking medical care. **Dissemination Method:** Outreach activities, small-group sessions involving 10–100 persons per group. Conduct individually - two days and 5 groups.	**Knowledge Gained:** 271 answers (mean age: 33). - Recognizing at least one symptom: 49% → 95% - Willingness to take a family member with monkeypox to the hospital 45% → 87%. **Retention of Prior Knowledge:** 79 'experienced' people, the remaining 'naıve'.

Regarding their strengths and limitations, vaccination is generally effective but may not provide complete protection. Health communication methods (film-based outreach and media campaigns) have varying strengths and limitations. Each study has its own strengths and limitations. Therefore, further studies are needed for accurate and comprehensive monkeypox prevention assessment (Table 4)

Table 4. Strengths/Limitations of preventives measures

Preventive measures	Strength	Limitation
Vaccination (depending on the type of vaccines)	- Vaccination enhances protection against monkeypox. - Vaccine immunity presents, high IgG levels indicate partial protection. - Disease severity mitigated. - Some levels of long-term protective immunity against monkeypox. - All unvaccinated subjects contracted monkeypox. - Reduced attack rate by vaccination.	- Rare or absent anti-OPX IgM and T-cell responses. - Childhood vaccination does not provide adults with complete protection. - Vaccine quality and administration were questionable. - It is evident that the immunity of vaccinated individuals is diminishing over time.

Preventive measures	Strength	Limitation
Media campaigns	- Media has had little or no effect on people's health behavior and seems to have failed to produce any form of danger consciousness associated with the virus: significant changes in the Nigerian culture of hugging, handshaking, eating bushmeats, and social gathering and ceremonies which are modes of transmission of virus.	- Inappropriate and insufficient media programs and lack of funds.
Film-based community outreach program	- Improve disease-specific knowledge in both juvenile and adult communities. - Encourage seeking healthcare advice when infection is suspected.	- There are multiple subject areas for which the messages about disease transmission or risk mitigation strategies resonated less successfully: identification avoidance of potentially contaminated items as a means to reduce the risk of contracting monkeypox; continuing to eat the carcasses of dead primates found in the forest.

DISCUSSION

Smallpox vaccines showed protection in most studies, but one study indicates incomplete protection against systemic OPX infection. Film-based outreach improved knowledge, while media campaigns had little impact on behavior. Further research is needed for both prevention methods.

Our data suggest two significant monkeypox prevention measures: Vaccination and Health Communication. Previous studies included in this review indicate protection against monkeypox can be conferred in people vaccinated with smallpox vaccines (12, 13, 15, 16). However, one study, including biochemistry tests on 72 people, suggests that remote vaccinia vaccination does not provide complete protection against systemic OPX infection (11). The film-based community outreach program raised knowledge about monkeypox prevention, while media campaigns had limited impact on monkeypox-related health behavior (17, 18) Below, we discuss preventive measures' efficacy against monkeypox and potential for future research.

Two Congo studies estimated vaccination efficacy at 80.7-85% (12, 15). Highest attack rates (9.3-12.3%) in unvaccinated contacts living with monkeypox patients in the same household. Vaccinated household contacts have lower attack rates (1.31-1.7%) compared to unvaccinated ones (7.2-7.47%), with the latter being higher than vaccinated individuals (0.9-1.1%) (13, 15, 16). These data suggest prior immunization with the smallpox vaccine can decrease the attack rates of the monkeypox virus in humans and confer significant protection for humans against the monkeypox virus. Currently, in the United States, JYNNEOS and ACAM2000 are used to prevent monkeypox, with JYNNEOS being the primary vaccine during the 2022 outbreak (5). The attack rates in contacts living in the same household as a monkeypox patient are higher than those in the other household (13, 15, 16). This suggests that physical distancing from monkeypox cases may prevent monkeypox transmission (19). Pre-1980 vaccinated individuals had 5.21 times lower monkeypox risk than unvaccinated (0.78 vs. 4.05 per 10,000) (12). Among the unvaccinated household

contacts, the highest attack rate is observed in the 0-4-year age group (11.7-13.9%) (13, 16). More preventive methods should be implemented to protect this vulnerable group from monkeypox virus.

However, in smaller studies, vaccination showed less significant preexisting immunity. One study (19) shows that remote vaccination may prevent systemic disease, but infectious inoculum and exposure route also influence outcome. In this study, unvaccinated cases had 43.5% moderate to severe illness vs. 16.6% in vaccinated cases. This result was considered insignificant by its authors, who speculated that the long interval from vaccination might have caused the absence of vaccine-induced immunity. Another study (14) shows that 3/8 vaccinated patients had no apparent symptoms despite being infected in Wisconsin during the monkeypox outbreak in 2003. The remaining five patients presented with rash and swollen lymph nodes, the two most frequent manifestations of monkeypox. We noticed that clinically inappropriate infections were more common in recently vaccinated individuals.

Raising awareness of risk factors and educating people about the measures they can take to reduce exposure to the virus is the primary prevention strategy for monkeypox (3). After viewing two films addressing monkeypox, film-based outreach program increased symptom recognition (49% to 95%), willingness to seek hospital care (45% to 87%), and awareness of avoiding contact (26% to 59%) (18). But the data collected can be affected because of some limitations in this study, including volunteer and attention bias, inexperience with questionnaires. However, media campaigns had limited impact according to participants' responses (participants disagreed with the media's effectiveness in raising awareness about monkeypox (2.02 points) and mobilizing the masses against it (1.86 points) (17). Further studies needed to comprehensively assess media campaign impact due to inadequate programs and funding. These results indicate that film-based education improved knowledge and behavior. In contrast, mass media campaigns had limited effect on health behavior during the monkeypox outbreak (17, 18). Nevertheless, condom use for pregnancy prevention increased significantly from 5.3% to 18.8% among young African women from 1993 to 2001, attributed to HIV-related condom promotion campaigns (20). Besides, effective health communication, including stigmatization of monkeypox, should be developed and implemented. Stigma may lead to social isolation and lack of support for infected individuals (21).

Although the monkeypox vaccine was widely accepted and our research has shown the smallpox vaccine to be effective in preventing monkeypox, some Vietnamese people still express hesitation in getting vaccinated. One study showed that only a mere 20% of Vietnamese participants expressed readiness to incur expenses for the vaccine, even when possessing an understanding of the disease and its associated risks (22). The foremost factor influencing this hesitancy was consistently identified as apprehensions regarding the formulation of the monkeypox vaccine, whereas cost held minimal sway in vaccine-related decision-making. The communication strategy also did not show effectiveness. In contrast to the widespread communication about COVID-19, information dissemination regarding monkeypox was notably less successful in reaching the general public. Therefore, this study (22) proposes the need for timely and efficient distribution of information, as well as prioritizing the high-risk population for vaccine allocation. A study conducted on outpatients at Le Van Thinh Hospital (23) also revealed that there is a lack

of knowledge among the subjects regarding the symptoms and preventive measures of monkeypox. The study recommends creating a media message based on its findings to spread awareness about the disease.

Our scoping review has a few limitations to be acknowledged: only 8 English studies were included, only included publications written in English lead to potentially missing local settings' research. Insufficient data for comprehensive guidelines or suggestions on other preventive measures. Nonetheless, this study offers an overview, identifies research gaps, and lays the foundation for future monkeypox prevention research.

CONCLUSION

Due to the genetic relation between smallpox and monkeypox, smallpox vaccines can be used to protect against monkeypox. Besides vaccination, media and education programs are also evaluated for reducing virus exposure. Future research is crucial for human vaccination efficacy, physical distancing effectiveness, and monkeypox vaccination in the 0-4-year age group. Further studies on vaccine efficacy intervals and asymptomatic cases are needed. Film-based outreach program evaluation requires addressing biases and population inexperience.

By employing our research as a fundamental basis, a greater emphasis should be placed on researchers directing their attention towards the effectiveness of vaccines. Additionally, studies involving different diseases apart from monkeypox can utilize our models as a foundation to formulate impactful health communication tactics. Furthermore, the adjustment of monkeypox prevention initiatives for Vietnam should be explicitly informed by the discernments gleaned from our study, thereby rendering them more fitting for implementation in the Vietnamese context.

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