The Association of Schools of Public Health in the European Region

Could the continuing Mpox epidemic threat in Africa lead to the next pandemic if urgent global action is not sustained?

part of *ASPHER Epidemic Emergencies Lessons Learned Series*

Mohamud Sheek-Hussein, Ariane Bauernfeind, John Middleton, John Reid, Shane Creagh Piper, Vasco Ricoca Friere Duarte Peixoto, Alison McCallum, on behalf of the ASPHER Public Health Emergencies Task Force

ASPHER December 13, 2024

Keywords: Mpox, outbreak, African continent, global threat, one health

Mpox is a growing threat

Mpox is a growing threat, a changing virus, evolving in severity and transmissibility. This zoonotic disease, was first recognised as a global public health threat when the Clade IIb epidemic was declared a public health emergency of international concern (PHEIC) on 23rd July 2022 (1). Global escalation of epidemic countermeasures reduced spread and PHEIC status was discontinued from 11th May 2023. However, mpox is considered endemic in Democratic Republic of Congo (DRC), Liberia, Gabon, Sierra Leone, Cameroon, Nigeria, and the Central African Republic (CAR) with cryptic, sustained human to human infection in parts of Nigeria since 2014 (2) (3).

On August 14, 2024, the World Health Organization (WHO) Director General declared a new PHEIC (4), based on the increase in mpox cases in DRC and rapid spread to neighbouring countries that had not previously reported outbreaks (5). According to recent CDC reporting (6) to date, the global epidemic of clade II mpox has caused more than 100,000 cases in 122 countries, including 115 countries where mpox was not previously reported.

Of particular concern is emergence of a new sub-lineage of the clade I mpox virus (clade Ib) and evidence indicative of ongoing evolution (7). In this new epidemic, two-thirds of cases and 85% of the deaths in DRC, are in children under 15 years old, with infants and young children experiencing an approximately 10% case fatality rate (CFR).

In this statement we revisit our continuing ‘Lessons Learned’ focus on epidemics and pandemics. This builds upon ASPHER’s previous commentary on the first Mpox PHEIC in 2022/23 (8), and on our wider lessons on global preparedness for epidemics from the COVID-19 Pandemic (9). We also view the challenges of this second mpox PHEIC in the context of our recent commentary on the Global Pandemic Agreement (10) where we welcomed progress to date highlighting the need for sustained investment in global early warning systems, prompt public health alerts and co-designed knowledge generation, exchange and application, while noting the depleted public health workforce, requirement for capacity building, and ongoing concern re inequitable access to diagnostics, support, vaccines and countermeasures.

Transmission and transmissibility of disease

Mpox is a (DNA) double-stranded deoxyribonucleic acid virus. It is like smallpox, but generally produces less severe disease, with low mortality rates. The natural reservoir

of mpox remains unknown, but, in West and Central Africa, small rodents, including dormice, Gambian pouched rats, rope and sun squirrels may carry the virus (11).

There are 2 known subtypes (clades) of the mpox virus: clade I and clade II. Clade I is divided into 2 subclades: clade Ia and Ib. Current reports suggest that clade II mpox is less severe than clade Ia. Clade II is divided into 2 subclades: clade IIa and clade IIb. Human-to-human transmission occurs through prolonged direct or close contact with an infected person, or through blood, body fluids, or mucosal lesions. Frontline health workers, household members of an infected patient, sexually active, and reproductive age populations are at higher risk. Mpox can also be transmitted from mother to fetus, via transplacental or intrauterine transmission. Transmission can occur from mothers with mpox to their infants by means of close contact but transmission in breast milk is currently unproven (12). Transmission in Africa, as always, started from animal-to-human transmission but is evolving, with examples of mixed modes of transmission (human-to-human and animal-to-human), causing recurrent outbreaks affecting mainly children and young adults in rural areas (11). From 2022 to 2024 travel-associated cases of mpox marked a significant shift in outbreak and pandemic potential. Cases emerged in non-endemic regions, including Europe, North America, and Asia, linked to international travel and globalization, with confirmed cases in countries such as Australia, Belgium, Canada, France, Germany, Italy, the Netherlands, Portugal, Spain, Sweden, UK, Sweden, India, Thailand, Pakistan, and USA. (13,14). Cases associated with imported rodents and human-animal transmission have also been reported (15).

Control and Prevention

Infectious disease pathogens do not recognise geographical borders. Without appropriate public health intervention, there is a significant risk that mpox could become entrenched globally. Vaccination against mpox is currently limited to adults over 18 years, high risk individuals and people in outbreak areas. People who were vaccinated against smallpox (typically those over 40 years old) may have some immunity against mpox but the vulnerability of children to MPV1b is a significant public health concern.

Our world has a delicate balance between animals, environment, and humans, highlighting the importance for a “one globe, one health approach” to address this risk, such as the ‘Relational One Health’ approach that looks at uncovering and addressing wider and environmental determinants (16). Following the principles of disaster management and leveraging the lessons learned from the COVID-19 we can mitigate the impact of the mpox outbreak. An effective public health response to mpox epidemics relies on the combined impact of public health measures and mpox vaccination. This includes establishing an active surveillance system that rapidly identifies the index case, close contacts, and sources, acts to minimise spread, including in health and care settings, while tackling the underlying determinants of

vulnerability to epidemics. As a priority, people at high-risk should be identified and supported, including health and care workers, household members, and those at increased risk of infection. Active community health outreach, education and awareness campaigns should be implemented to highlight the risk factors for mpox infection, reduce stigma, promote measures to minimize exposure, and limit complications. This includes bundling of preventive measures (for example PREP (pre-exposure prophylaxis against HIV) and mpox immunisation), and practical and financial support to stay at home and isolate.

We welcome the renewed, and easier to access, OpenWHO learning hub focusing on health emergencies and providing expert materials that can be rapidly updated, adapted, applied locally. Mpox materials should be a priority. Interestingly, the legacy of Edward Jenner's work in 1796 is still useful today. Smallpox vaccination protects about 85% of recipient's against mpox infection. (17) In the US, two vaccines, namely JYNNEOS and ACAM2000, have been approved for the prevention of mpox. (18) While JYNNEOS vaccination is not contraindicated in pregnant and breastfeeding women, only ACAM 2000 is available for a restricted group of children, although the safety profile of the JYNNEOS vaccine (Modified Vaccinia Ankara virus MVA-BN) Imvanex is reassuring (19) and at least one study is preparing to recruit (20).

The view of the Association of Schools of Public Heath in the European Region (ASPHER)

ASPHER supports the recent decision by Africa CDC and WHO to declare the mpox outbreak in Africa a Public Health Emergency of International Concern, and the actions announced by the WHO and CDC Africa. (4,21). These declarations amount to a call for action and should lead to the prompt mobilization of money and resources, a co-ordinated international response to the epidemic that shifts the response from charity to solidarity. A review of the first six global PHEICs noted their roles in tackling selected global challenges particularly that such declarations enable streamlining of funding, facilitating urgent research and development of therapeutics, vaccines and/or diagnostics under emergency use authorization. However, not all emergencies can be declared a PHEIC and criticism of previous PHEICs includes conditions being adopted too late or lifted too early. Building on this learning, strong responses to mpox are required on the ground, urgently, enabling deployment of a strengthened health workforce working with underserved communities and settings (22), systems for socio-economic support for the worst affected groups and equitable access to life-saving medical countermeasures including diagnostics, therapeutics, and vaccines. (23)

There are weaknesses still in international responses. The 12th meeting of the Intergovernmental Negotiating Body (INB) for the Pandemic Treaty ended inconclusively in November, with member states requiring more time. (24) In the

worsening mpox epidemic in Africa, immediate cooperation is needed to address mpox's changing epidemiology and transmission dynamics and lessen the impact of outbreaks on vulnerable African populations (25).

We cannot wait for the INB. Across countries and health systems, public health agencies, academic departments, practitioners, and communities must bring their knowledge, networks, and capacity to come together to address the critical unasked and unanswered questions at pace and scale. There are excellent examples of data gathered, analysed, and put to use in partnership at pace (26) but they can be scattered. Hard commitments to sustain funding, infrastructure and relationships on the ground that enables comprehensive case-funding, contact tracing, identification of causes and ongoing improvement in how we implement prevention and response are essential. We cannot tolerate another decade of cryptic spread, avoidable outbreaks, illness, and death for mpox or the next PHEIC in waiting.
Eight PHEICs have been declared since 2009. Zika and the first mpox PHEIC lasted less than a year, but the Polio PHEIC has continued since 2014. The current mpox PHEIC is likely to be more like Polio, requiring sustained leadership and resourcing to avoid a worldwide continuing epidemic or mpox becoming endemic in additional countries. We advocate that more strategic goals are set with urgency, to pursue formal elimination of mpox of non-zoonotic origin in countries and regions where there is sustained human to human transmission.

Table: The first eight Public Health Emergencies of International Concern (PHEICs) - with durations (as at 05/12/2024)

PHEIC	PHEIC Start date	PHEIC Finish date	PHEIC Duration (to 05/12/2024)
Pandemic Influenza H1N1 (Swine Flu)	25/04/2009	10/08/2010	1year, 3 months, 14 days
Polio PHEIC	05/05/2014	Continuing	10 years, 7 months
Ebola (Western Africa)	08/08/2014	29/03/2016	1year, 7 months, 21 days - continuing
Zika PHEIC	01/02/2016	18/11/2016	9 months, 17 days
Ebola (DRC)	17/07/2019	26/06/2020	11 months, 9 days
COVID-19 PHEIC	30/01/2020	05/05/2023	3 years, 3 months, 5 days
Mpox clade IIb	23/07/2022	11/05/2023	10 months, 18 days
Mpox clade Ib	14/08/2024	Continuing	3 months, 20 days

The current PHEIC should not be lifted until elimination objectives have been successful and are sustainable in the WHO African region. While there is a welcome emphasis on growing capacity in Africa, including for diagnostic, surveillance, and vaccine manufacturing (27) (28) and supporting One Health priorities particularly mpox, we advocate the following:

Response
Building systems that support locally led genomic testing across Africa is essential. The World Bank's recent announcement of a second wave of Pandemic Fund investment focussed on laboratory and surveillance capacity (29) and joint CDC Africa/WHO work to strengthen response capacity (30) are welcome steps. We advocate establishing mpox as a case study in the implementation of the updated International Health Regulations (IHR) and Pandemic Agreement.

Vaccination and therapeutics
While Gavi's First Response Fund (31), which aims to secure immediate access to vaccines and to protect routine immunisation programmes during major public health emergencies is a welcome addition, it is a partial, private, charitable response and cannot be a substitute for governments fulfilling their international responsibilities.

Wider impact and future prevention
The human and societal dimensions of mpox are incompletely understood. Resources should be earmarked for WHO African Region to sponsor community studies of the health and wider impacts of Mpox on affected local communities, including on education, economic development, inequalities, and extra strain on healthcare systems. This must include a commitment to implement the findings, improve the response and ensure that these communities and their stories are remembered.

A One Health approach is essential
The growth of mpox highlights the interdependence of human, animal, and environmental health. Public health issues cannot be solved in isolation; a One-Health approach can increase resilience, and implementation will reduce the risk of future worldwide zoonotic diseases outbreaks (32) (33). Multiple factors are triggering mpox and Marburg epidemics on the African continent, including challenges with human capital, extractive and exploitative industrial practices taking advantage of regulatory complexities and competing priorities within and outside the health sector. Despite these difficulties, there is growing momentum to build a sustainable vaccine manufacturing industry in Africa (34,35); nevertheless, there is also limited global vaccine mpox and Marburg production capacity, unequal distribution agreements, and a lack of investment in public health infrastructure in Africa.

Crucially, as reported by Physicians for Human rights, and the Lancet (36) responses focussed solely on control of the mpox virus will fail unless there is also commitment

from the international community to address the issues of ongoing conflict, exploitation in licit and illicit mining, sexual violence, institutionalised racism, and homophobia, worsening poverty, internal and cross border displacement of people in several affected countries in Africa. Any effective response to this complex global crisis must address the interlinked challenges of human rights and public health.

References

1. WHO Director-General declares the ongoing monkeypox outbreak a Public Health Emergency of International Concern [news release]. Geneva: World Health Organization; 23 June 2022. Available from https://www. who.int/europe/news/item/23-07-2022-who-director-general-declares-the-ongoing-monkeypoxoutbreak-a-public-health-event-of-international-concern. Accessed 13 December 2024
2. Wei ZK, Zhao YC, Wang ZD, Sui LY, Zhao YH, Liu Q. Animal models of mpox virus infection and disease. Infect Med (Beijing). 2023;2(3):153-166. Published 2023 Jun 4. Available from doi:10.1016/j.imj.2023.05.004
3. Parker E, Omah IF, Varilly P, et al. Genomic epidemiology uncovers the timing and origin of the emergence of mpox in humans. medRxiv [Preprint]. 2024 Jun 19:2024.06.18.24309104. Available from doi: 10.1101/2024.06.18.24309104
4. World Health Organization. WHO Director-General declares mpox outbreak a public health emergency of international concern**.** Geneva: World Health Organisation; 14 august,. 2024. Available from https://www.who.int/news/item/14-08-2024-who-director-general-declares-mpox-outbreak-a-public-health-emergency-of-international-concern; accessed 26 November 2024.
5. Verma A, Nazli Khatib M, Datt Sharma G, et al. Mpox 2024: new variant, new challenges, and the looming pandemic. Clinic Infect Pract. Published online October 2024:100394. Available from doi:10.1016/j.clinpr.2024.100394.
6. CDC Atlanta. Mpox in the United States and Around the World: Current Situation. November 24th, 2024. Available from https://www.cdc.gov/mpox/situation-summary/index.html; accessed 26 November 2024.
7. Yi XM, Lei YL, Li M, Zhong L, Li S. The monkeypox virus-host interplays. Cell Insight. 2024;3(5):100185. Published 2024 Jul 14. Available from: doi:10.1016/j.cellin.2024.100185
8. Osti T, Beccia F, Peixoto VR, Davidovitch N, Middleton J. Monkeypox: Did we learn the lesson from COVID-19? ASPHER Brussels. June 2022. Available from: https://www.aspher.org/download/1141/monkeypox-did_we_learn_the_lesson_from_covid-19.pdf
9. Lombatti S, Magid A, Davidovitch N, et al. The COVID-19 Pandemic as a Public Health Teacher-the Lessons We Must Learn. Public Health Rev 2024;45:1607232. Available from; https://doi.org/10.3389/phrs.2024.1607232
10. Reid J, Bauernfeind A, Middleton J, et al. The Pandemic Agreement: A Springboard for Urgent Progress or a Safety Net for Basic Commitments? Briefing Document and Statement on the WHA Pandemic Agreement Draft May 2024. ASPHER, Brussels. May 2024. Available from: https://www.aspher.org/download/1530/aspher-briefing-document-and-statement_pandemic-agreement_24_05_24.pdf
11. World Health Organization. Strategic framework for enhancing prevention and control of mpox 2024-2027. Geneva: World Health Organization; 2024. Available from: https://www.who.int/publications/i/item/9789240092907
12. Imani-Musimwa P, Ververs M. Mpox and breastmilk: for once, can we act in time? The Lancet. 2024; 404 (10459): 1191. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(24)01881-6/fulltext

13. Nisar H, Saleem O, Sapna FN, Sham S, Perkash RS, Kiran N, Anjali FN, Mehreen A, Ram B. A Narrative Review on the Monkeypox Virus: An Ongoing Global Outbreak Hitting the Non-Endemic Countries. Cureus. 2023; Aug15(8). Available from: DOI: 10.7759/cureus.43322
14. Xiang Q, Li T, Zou J, Li G, Luo Y, He S, Gu D. Global infectious diseases in August of 2022: Monthly analysis. Zoonoses. 2022 Oct 7;2(1). Available from: DOI: 10.15212/ZOONOSES-2022-1001
15. World Organisation of Animal Health. Woah statement on novel mpox 23 august 2024 https://www.woah.org/en/woah-statement-on-novel-mpox/ Cited 12 December, 2024. Mpox resources available from; https://www.woah.org/en/disease/mpox/#:~:text=The%20virus%20that%20causes%20mpox%20has%20been%20reported%20in%20animals,North%20America%20through%20imported%20rodents. Cited December 13, 2024.
16. Meisner J, McLeland-Wieser H, Traylor EE, Hermesh B, Berg T, Roess A, Van Patter L, Rosenthal A, Davidovitch N, Rabinowitz PM. Relational One Health: A more-than-biomedical framework for more-than-human health, and lessons learned from Brazil, Ethiopia, and Israel. One Health. 2024 Jan 9;18:100676. Available from: doi: 10.1016/j.onehlt.2024.100676.
17. Christodoulidou MM, Mabbott NA. Efficacy of smallpox vaccines against Mpox infections in humans. Immunother Adv. 2023 Oct 7;3(1):ltad020. Available from doi: 10.1093/immadv/ltad020.
18. CDC Atlanta. Interim Clinical Considerations for Use of Vaccine for Mpox Prevention in the United States 25 November 2024.Available from: https://www.cdc.gov/mpox/hcp/vaccine-considerations/vaccination-overview.html
19. EMA Emergency Task Force. ETF statement on the use of Imvanex for the prevention of mpox in children below 12 years of age. Report ref: EMA/528419/2024. Amsterdam: EMA, 12 November, 2024. Available from: https://www.ema.europa.eu/system/files/documents/other/etf-statement-use-imvanex-prevention-mpox-children-below-12-years-age_en.pdf
20. National Library of Medicine. ClinicalTrials.gov Open-label, multicenter, immunogenicity and safety study of MVA-BN from children 2 years to less than 12 years compared to adults for prevention of smallpox, mpox and related orthopox infections. Available from: https://clinicaltrials.gov/study/NCT06549530
21. Africa CDC. The Permanent Representatives Committee Provides Emergency Approval of $10.4 Million to Africa CDC for Mpox Outbreak Response. CDC Africa, July 2024. Available from: https://africacdc.org/wp-content/uploads/2024/08/Emergency-Approval-of-10.4-Million-to-Africa-CDC-for-Mpox-Outbreak-Respons.pdf.
22. Murayama H, Asakura R. T, Dickens L. B, Foo H. J, Jin S, Mukadi K. P, Ejima K, Jung SM, Nishi A, Prem K, Endo A. Roles of community and sexual contacts as drivers of clade I mpox outbreaks. MedRxiv 2024.10.15.24315554; Available from: https://doi.org/10.1101/2024.10.15.24315554
23. Evaborhene NA, Oga JO, Adebayo YA, et al. Caught between violence: Mpox virus and the perils of neglect in Africa. BMJ Glob Health 2024;9:e017090. doi:10.1136/ bmjgh-2024-017090
24. World Health Organization. Twelfth meeting of the Intergovernmental Negotiating Body (INB) for a WHO instrument on pandemic prevention, preparedness and response. https://www.who.int/news-room/events/detail/2024/11/04/default-calendar/twelfth-meeting-of-the-intergovernmental-negotiating-body-(inb)-for-a-who-instrument-on-pandemic-prevention--preparedness-and-response; accessed 29 November 2024
25. Kuppalli K, Dunning J, Damon I, Mukadi-Bamuleka D, Mbala P, Ogoina D. The worsening mpox outbreak in Africa: a call to action. The Lancet Infectious Diseases. 2024 Nov 1;24(11):1190-2. doi:10.1016/S1473-3099(24)00577-2.
26. Science Media Centre. Expert reaction to who declaring mpox a Public Health Emergency of International Concern (PHEIC) 14 August 14 2024..Available from: https://www.sciencemediacentre.org/expert-reaction-to-who-declaring-mpox-a-public-health-emergency-of-international-concern-pheic/

27. Africa CDC. The African Vaccine Manufacturing Accelerator is a boon for the Continent. 28 June 2024. Available from: https://africacdc.org/news-item/the-african-vaccine-manufacturing-accelerator-is-a-boon-for-the-continent/
28. International Vaccine Institute. IVI raises money to open Africa Regional office in Rwanda. 27 February 2024. https://www.ivi.int/ivi-to-open-africa-regional-office-in-rwanda/. Accessed December 13, 2024.
29. World Bank. Pandemic fund allocates second round grants to boost pandemic preparedness in 50 countries., World Bank, October 18th, 2024. Accessed December 2nd, 2024. https://www.worldbank.org/en/news/press-release/2024/10/19/pandemic-fund-allocates-second-round-of-grants-to-boost-pandemic-preparedness-in-50-countries
30. WHO African Region. African CDC and WHO launch joint continental plan to scale up mpox outbreak response**.** 6 September 2024. Available from: https://www.afro.who.int/news/african-cdc-and-who-launch-joint-continental-plan-scale-mpox-outbreak-response; Accessed 29 November 2024.
31. GAVI. GAVI signs agreement with Bavarian Nordic to rapidly secure 500,000 doses of mpox vaccine for Africa. September 28, 2024.Available from: https://www.gavi.org/news/media-room/gavi-signs-agreement-bavarian-nordic-rapidly-secure-500000-doses-mpox-vaccines
32. Veterinarians without borders. The current situation: Mpox outbreak in the DRC. August 26, 2024. Available from: https://www.vwb.org/site/blog/2024/08/26/mpox-health-challenge/. Accessed November 29th, 2024.
33. IDRC- CI Canada. Challenges and opportunities for scaling vaccine manufacturing in Africa, and where research can help. October 17tth 2023. https://idrc-crdi.ca/en/news/challenges-and-opportunities-scaling-vaccine-manufacturing-africa-and-where-research-can-help#:~:text=Africa%20also%20faces%20challenges%20with,vaccine%20manufacturing%20industry%20in%20Africa., accessed 29 November 2024
34. Africa CDC. The change in African vaccine manufacturing landscape 1 November 2024. Available from https://africacdc.org/news-item/the-change-in-african-vaccine-manufacturing-landscape/ Accessed December 13, 2024.
35. Malan H, van der Klashorst G, Chibale K. Health Policy Watch. Empowering Africa's Pharmaceutical Future: The Critical Role of Local API Manufacturing. Available from: https://healthpolicy-watch.news/empowering-africas-pharmaceutical-future-the-critical-role-of-local-api-manufacturing/. Accessed December 13, 2024.
36. Ratevosian J, Heisler M, Carpino T, McHale T, Mushekuru J, Beyrer C. Addressing transnational exploitation and armed conflict in the response to mpox, The Lancet, Volume 404, Issue 10468, 2024, 2137-2140, https://doi.org/10.1016/S0140-6736(24)02418-8.