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KEY LESSONS FROM PREPARATORY AND EARLY IMPLEMENTATION PHASE OF A REGIONAL MPOX RESPONSE WITHIN A MULTI-SECTORAL PREPARE PROJECT FRAMEWORK

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ABSTRACT

Background: Outbreaks of viral and zoonotic diseases are increasingly frequent, with Sub-Saharan Africa representing a significant global source of emerging infectious diseases. Health security threats posed by the pandemics and epidemics call for regional, multi-stakeholder, and multi-sectoral approaches.

Objectives: To examine and document events' chronologies and critical lessons during the preparatory and early implementation stages of a three-year Preparedness for Pandemic Response (PREPARE) project in the Intergovernmental Authority on Development (IGAD) region.

Methods: This narrative review synthesizes the evolution of the mpox outbreak, the regional and country level response considerations, and the key lessons learned during the initial implementation phase of the regional PREPARE project from 2024 to 2025.

Discussion: The regional PREPARE project was fast-tracked to respond to the mpox outbreak in IGAD region from November 2024, at a time when Uganda was the only IGAD country that had reported active cases. Lessons from the preparatory and early stages of the initiative arose from: IGAD's vulnerable geo-location in respect to the pandemics epicenters; the sporadic yet important paradigm shift from predominantly single-sector (health) response to a multi-sector approach; the adjustment from the initial 'regional preparedness for

response to pandemics and epidemics' to 'securing regional impact through supporting country-level mpox response'; the unpredictable trajectory of mpox transmission and spread; perplexing observations during the initial phase of the mpox outbreak; administrative challenges arising from the new partnerships; and opportunity presented for policy and strategy reviews, and harmonization across countries.

Conclusions and Recommendations: Regional mpox response presents increased relevance and draw support for expedited implementation when particularly initiated in proximity to the outbreak epicenter. Insights from the initial phase of the PREPARE project provide critical lessons applicable to regional responses to infectious disease outbreaks and other public health emergencies; and may inform refinement of context-specific health security policies and strategic frameworks.

INTRODUCTION

Pandemics and epidemics have hitherto garnered considerable attention in the global health security agenda. Sub-Saharan Africa is a significant global source of viral and zoonotic diseases, and recently there has been a resurgence of the monkeypox virus, currently referred to as the mpox virus. Mpox virus was first identified in cynomolgus monkeys moved from Africa to Copenhagen in 1958 which exhibited presentations similar to, but less severe than, smallpox in humans, resulting in the initial designation 'monkeypox'^{1,2}. Since the first reported case of mpox in humans in the Democratic Republic of the Congo in 1970, additional cases have emerged in various regions worldwide, with origins believed to be in Africa³. Transmission to humans is thought to occur through contact with small forest animals, but the exact modes are still under study⁴.

The mpox outbreak discussed here-in began in May 2022⁵. As at 2024 Democratic Republic of the Congo (DRC) had experienced a significant rise in cases and was identified as the epicenter, with human-to-human transmission contributing to its spread to

Uganda, posing a risk to countries in the Intergovernmental Authority on Development (IGAD) region. Close contact with infected individuals (including sexual contact) was thought to be main mode of human-to-human transmission, where the common symptoms of skin rash or mucosal lesions lasting 2–4 weeks, as well as fever, headache, myalgia, back pain, fatigue, and lymphadenopathy were reported – albeit with lower case fatality than Ebola virus infection⁶. The negative socio-economic impacts of mpox on families and communities, with potential for long- and short-term undesirable effects on national and regional economies were probable.

In 2024, following Africa Centers for Disease Control and Prevention (Africa CDC) declaration of mpox as a Public Health Emergency of Continental Security, countries applied lessons from past pandemics to curb its spread. To complement national efforts, the Preparedness for Pandemic Response (PREPARE) project launched in November 2024 to strengthen multi-sectoral, multi-stakeholder pandemic prevention, preparedness, and response through cross-border One Health collaborations. In its first phase, the project was to support the mpox

response across all IGAD member states: Djibouti, Ethiopia, Kenya, Sudan, Somalia, South Sudan, and Uganda.

Effective regional pandemic prevention, preparedness, and response (PPR) strategies within resource-challenged set-ups require careful consideration of the diverse needs, competing priorities, limited capacities, varying transmission patterns, concurrent outbreaks, complex emergencies, and geopolitical factors that influence public health decision-making and response implementation across countries. This paper reviews regional PPR actions during early and preparatory phases of the mpox response and documents the unprecedented challenges that elicited valuable lessons.

METHODOLOGICAL APPROACH

This narrative review provides a comprehensive account of the events and lessons from November 2024 to March 2025, subsequent to the funding award for the PREPARE project, a regional project covering IGAD countries. The review also covered special cases of certain events occurring prior to the award to complete the discussed mpox outbreak contexts. Project documents and reports provided information on the project design and activities, while relevant websites of key institutions involved, including World Health Organization (WHO) and Africa CDC, were searched for information on the evolution of mpox in the region. This included consideration of and reference to global, continental, and country-level outbreak reports, as well as public health declarations related to mpox and other pandemics. The country-level situation reports (Sitreps) provided the status of the infectious diseases at the reported specific points in time. Searches were also drawn from Google

Scholar and PubMed. Key words used in the searches were: “Pandemic preparedness”, “global mpox outbreak”, “history of mpox”, “mpox outbreak in Uganda” and “mpox response”. First, the appropriateness and relevance of the website pages and papers were determined by examining the titles and abstracts – before exhaustive review of the content.

Numerous joint consultations were convened among the PREPARE project entities (WHO, IGAD, and International Federation of Red Cross and Red Crescent Societies – IFRC) and bilaterally between the entities and between the individual entities and mpox active countries. Reports and minutes derived also contributed to the chronological narrative of events, documenting critical decisions, priorities and consensus on necessary actions for the mpox response – while noting the critical challenges that also informed the documented lessons.

Key themes and constructs were organized as reflected in the sub-titles of the discussion section of this paper: the project and its context; a chronological account of the events, starting with the declaration of mpox as a public health emergency of continental concern to the initiation of the mpox response; and an examination of lessons learned during the project's preparatory and early implementation stages.

DISCUSSION

Preparedness for Pandemic Response (PREPARE) project

The Pandemic Fund supports pandemic PPR capacities in low- and middle-income countries, with the World Bank as trustee. The PREPARE project is supported by the fund to strengthen IGAD's leadership in pandemic preparedness and response within the One

Health framework, and to demonstrate regional impact⁷. IGAD Secretariat applied for funding in the second call of the Pandemic Fund Secretariat to support its member states: Djibouti, Ethiopia, Kenya, Somalia, South Sudan, Sudan, and Uganda. Uganda's geographical proximity to the DRC, Rwanda, and Burundi positions (as shown in Figure 1) is a critical entry point for infectious diseases to the IGAD region and has experienced a

higher frequency of viral and zoonotic disease outbreaks compared to other member states⁸. As of November 2024, when the PREPARE project was fast-tracked, mpox was actively spreading in Uganda, which had reported its first two cases (clade Ib variant) in early July 2024 among those crossing from the DRC⁹. By that time, Kenya had also confirmed its first case (variant clade Ib) in Taita Taveta County, bordering Tanzania¹⁰.

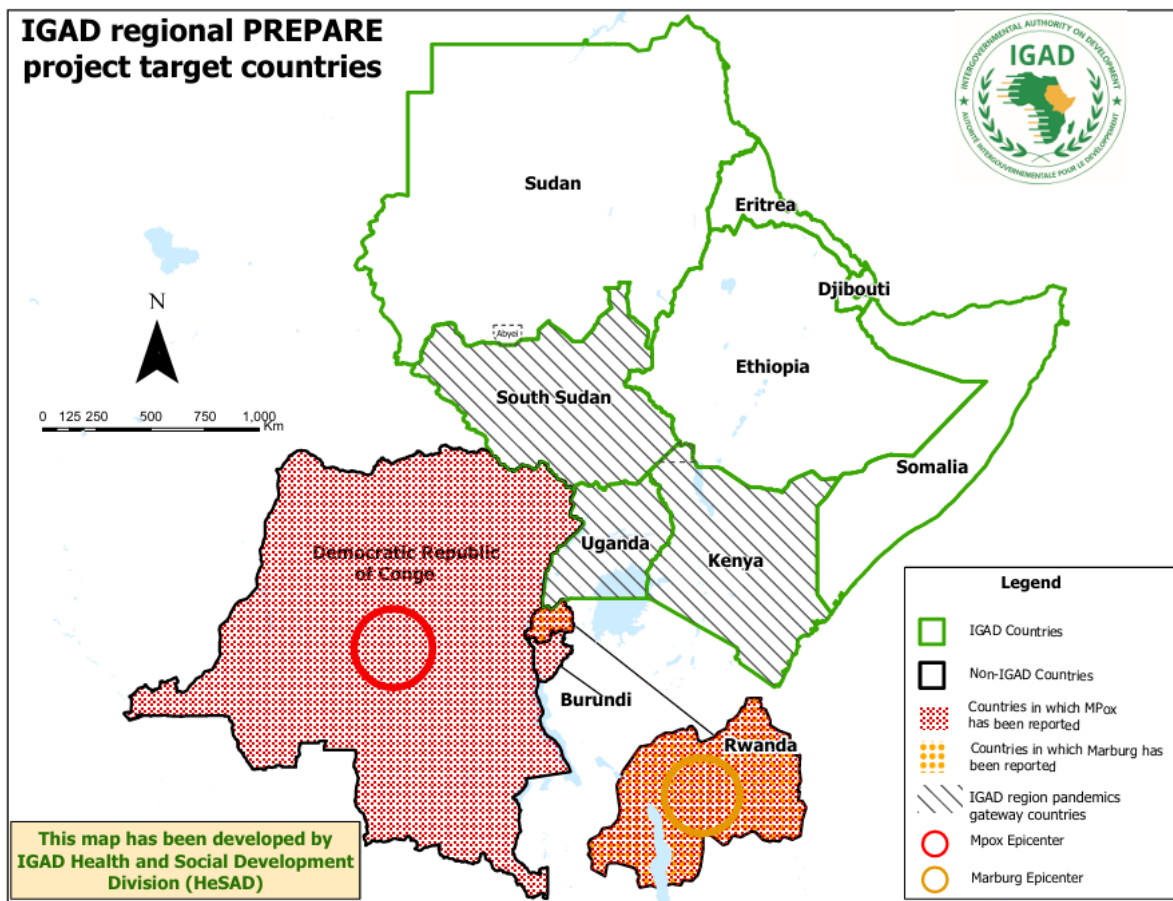


Figure 1: IGAD Member States and epidemic/pandemic epicenters around the region as of November 2024

The PREPARE project has three principal partners: WHO, IGAD Secretariat, and IFRC. WHO provides technical oversight, facilitates funding, and manages project realignments. IGAD Secretariat mobilizes member nations to strengthen cross-border OH systems for PPR. IFRC implements cross-border/Point of Entry

(POE) activities, working with Red Cross and Red Crescent societies to mobilize communities and carry out community-based surveillance and response actions.

The chronology of the preparatory processes of mpox response

Figure 2 illustrates the chronology of events from the declaration of mpox as a public health emergency to project commencement. Mpox was declared a Public Health Emergency of Continental Security (PHECS) by the Africa Centers for Disease Control and Prevention (Africa CDC) on August 13, 2024. Three days later, WHO determined that the escalating number of mpox cases in the DRC and other African countries constituted a Public Health Emergency of International Concern (PHEIC)^{11,12}. In September 2024, the Pandemic Fund allocated US\$128.89 million for expedited projects supporting ten countries¹³. The projects included three single-country projects (DRC, Rwanda, and Burundi) and two regional projects. The first two confirmed mpox cases in the IGAD region

were reported by the Uganda Virus Research Institute (UVRI) on July 24, 2024¹⁴. On September 27, 2024, the first mpox cases were declared in school environment¹⁵. Mpox spread from Uganda's border to Kampala, heightening regional risks due to high mobility and superspreaders along Kenya–Uganda–South Sudan routes. The potential to spread to neighboring countries remained high due to superspreaders. Superspreaders were first identified among truck drivers and their key contacts (including sex workers) along the region's major transport corridors. In cross-border areas, already fragile pandemic surveillance and response systems are further strained by porous borders, which pose a health security risk during outbreaks. Differing health security priorities and policies across countries compound these challenges.

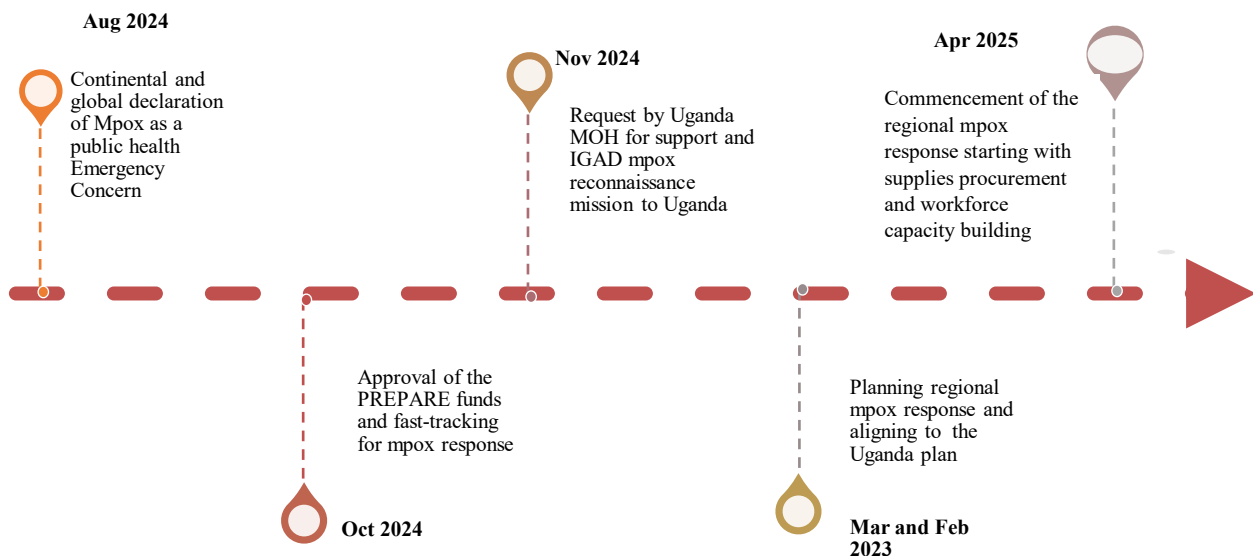


Figure 2: Chronology of events leading to the commencement of a regional mpox response

Uganda alerted IGAD of the worsening mpox outbreak situation, prompting a high-level IGAD reconnaissance mission to assess the situation and identify urgent response needs. Table 1 presents the findings of the IGAD November 2024 mission, along with the corresponding recommendations agreed upon jointly between the IGAD mission and the Uganda MOH. By the second IGAD mission to Uganda, conducted from February 10 to 14, 2025, the mpox situation had escalated, with 2,896 confirmed cases and 19 reported fatalities⁵. Furthermore, the outbreak

of Sudan Virus Disease (SUDV) was declared on January 30, 2025, necessitating an integrated approach to the mpox response¹⁶. A third mission, from March 9 to 15, 2025, reviewed the regional PREPARE project mpox phase plan developed by IGAD and IFRC to ensure alignment with Uganda's proposed response actions. Table 2 delineates the originally planned regional PREPARE project activities and illustrates their alignment with the needs and gaps for Uganda mpox response.

Table 1

Implications of the key findings of the November 2024 IGAD reconnaissance mission to Uganda

Key reconnaissance mission findings (as at November 2024)	Implications
Mpox cases exhibited a consistent upward trend, with the outbreak affecting more than 38 districts out of a total of 146 in the preceding three months.	Decentralize mpox outbreak response to the district level is essential, particularly in light of the unprecedented scale of community transmission.
	Strengthen mpox coordination mechanisms, including the national and district-level outbreak task forces, in order to enhance the overall effectiveness of response efforts.
Community transmission of the Mpox outbreak remained largely unpredictable, with initial critical spreaders identified as a) truck drivers, b) commercial sex workers, and c) the fishing community.	Enhance Risk Communication and Community Engagement (RCCE).
As of November 12, 2024, there were 448 laboratory-confirmed Mpox cases and one fatality. About 345 cases were hospitalized, and 104 recovered and discharged.	Strengthen laboratory capacity for mpox outbreak response including supporting testing kits and supplies for decentralized testing and improving the sample referral system.
	Scale up the decentralized establishment of treatment centers and address the rising challenges in the already existing ones.
There was possible exponential trajectory of the mpox cases in the country, characterized by unpredictable transmission patterns, primarily due to ongoing community transmission and transmission dynamics in the DRC and neighboring countries.	Mpox vaccination. Ensure sufficient vaccine supply and target vulnerable populations and the virus super spreaders
	Enhance vaccine demand through community awareness and educational initiatives.
Some mpox cases were HIV-positive and even antiretroviral therapy shy or non-compliant. Tuberculosis co-infections were also reported.	Contextual risk factors associated with the spread of mpox and the progression of the disease, including

	interactions with HIV, tuberculosis need to well understood.
Pediatric mpox was still perplexing including how they are infected when the mothers/caregivers are not symptomatic and simultaneous with childhood malnutrition.	Better understanding the mpox transmission dynamics, risk factors and interlinkages with other pediatric conditions.

Table 2

Initial alignment of urgent PREPARE project activities as part of support to Uganda mpox response

#	Response component and approach	Alignment to mpox response context
A	Surveillance systems	
1	PHEM training, incorporating 7-1-1 approach - a framework for improving infectious disease outbreak detection and response	Conducting two trainings on PHEM of all IGAD countries incorporating 7-1-7 at regional level, and with special reference to mpox context: 1) Training of PHEOC members 2) Training of Trainers for PHEM cascading to cross-border areas PHEM training targeting One Health workforce in critical cross-border sites in mpox active countries (Uganda, Kenya and South Sudan) by the Training of Trainers
2	Provision of Information, Communication and Technology equipment support to digitize targeted cross-border PHEOCs, prioritizing cross-border areas experiencing active outbreaks such as mpox and Marburg	Procurement of IT equipment mpox response for PHEOCs and IMT at national level and emergency management/response teams at sub-national level. These are computer, landline desk phones, mobile phones and internet routers, among others
B	Laboratory functions	
1	Support regional cross-border laboratory assessment for One Health diagnostic and systems gaps	Needs and gaps analysis of the mpox and Ebola samples analysis laboratory supplies in the mpox active countries including Uganda Procurement of the supplies including but not limited to: Monkey pox assay PCR reagents, Ebola Sudan Strain IgG Elisa Kit, extraction kits DNA (and RNA), swabs and VTM for mpox sample, various types and sizes of pipettes, and Microcentrifuge Safe-Lock™ Tubes Procurement of vehicles and motorcycles to support the quick and effective mobility needed for sample transfer to the national and decentralized laboratories
C	Workforce development	
1	Conduct One Health regional consultations, involving multi-level, public health institutions, academic, institutional and community stakeholders to review, update and validate training curricula and simulation and readiness exercises.	Development and validation of the IGAD One Health Competency Framework by IGAD member states One Health professionals and stakeholders and from the countries and at regional level.

2	Conduct a series of regional cross-border training sessions on One Health epidemic and pandemic preparedness and response for the multisectoral health workforce, including FELTP, with a focus on cross-border personnel engaged in managing active outbreaks such as mpox and Marburg.	Training of the 45 EMTs in selected cross-border and mpox hotspots in mpox active countries
3	Brief and train staff and volunteers on the purpose of the assessment and how to communicate clearly and honestly with stakeholders	Ten Training of Trainers to review and adopt the WHO training curriculum and train 40 ambulance teams to in prehospital mpox and Ebola patient transfer and management Training and incentivization of Community Health Workers on home-based care for mpox
D	Community level- action	
1	Build Cross-border RCRC branches' capacity (training RCRC CBS volunteers and staff, support IT) to advocate for and operationalize CBS systems with a focus on active outbreaks including mpox and Marburg as auxiliary to ministries	Procurement of neonatal and young child type B ambulances for Kampala Metropolitan area and Mbale Area Procurement of admission package for both mpox and Ebola patients Procurement of discharge package for both mpox and Ebola Patients Procurement of patient beds, mattresses, and bedsheets
E	Coordination and learning	
1	Conduct regional peer-to-peer learning events (and attend Scientific conferences) that incorporates one health for PPR and perception surveys to measure cross-learning adoption.	Convene a One Health (multisectoral) learning event to share lessons and best practices in the countries in pandemic response with special focus on active pandemics (mpox and Ebola)
2	Organize high-level strategic policy and advocacy meetings focused on addressing mpox and other pandemics/epidemics.	Support inception meeting between IGAD, IFRC and WHO as well as convene ministerial meeting for technical consultation and launch of the project with IGAD member states, IFRC, WHO and other One Health partners

Key: PHEOCs=Public Health Emergency Operations Centers; IMT=Incidence Management Team; EMT=Emergency Management Team; FELTP=Field Epidemiology and Laboratory Training Program; PHEM=Public Health Emergency Management; PCR=Polymerase Chain Reaction; DNA= deoxyribonucleic acid; RNA=ribonucleic acid; VTM=Viral transport medium

Critical lessons and insights

Lesson 1: A country nearest to the pandemic or epidemic epicenter possesses valuable experiences, technical expertise, and insights that can be leveraged by other countries.

Uganda has been disproportionately affected by pandemics (recently Ebola, Marburg, and

mpox) due to its 950-kilometer land boundary with the DRC, a significant global epicenter of zoonotic and hemorrhagic viral disease outbreaks, as well as a 169-kilometer border with Rwanda, which is also adjacent to the DRC^{17,18}. Due to this reality, the country has developed robust strategies and systems and

has strengthened expertise in pandemic PPR. The country has a national and sub-national trained workforce, demonstrating key competencies in incident/emergency management and providing valuable technical expertise to other countries in the region and beyond. Within the Ministry of Health, it has established an Integrated Epidemiology, Surveillance, and Public Health Emergency Department, which includes a Veterinary Public Health Division led by a veterinarian—an uncommon arrangement in the region that promotes the One Health Approach. The functional One Health secretariat also coordinates multisectoral pandemic PPR efforts, providing a learning hub and a model for other countries to emulate.

Lesson 2: The initial project phase confirmed that this era of complex emergencies require robust advocacy for multisectoral (One Health) approaches to Pandemic PPR.

The PREPARE project adapted its first phase from a regional preparedness model to a centralized, country-specific mpox response, linked with peer-to-peer learning and capacity enhancement based on Uganda's response mechanisms. Planning for a multisectoral mpox response marked a significant shift, as sectors beyond health had previously expressed concerns regarding exclusion, given the zoonotic nature of pandemics and epidemics. The hitherto complexities associated with the One Health approach present challenges. The lack of a harmonized One Health approach and a regional competency framework across IGAD countries are longstanding and will be the subject of the second phase of PREPARE project phase 2. Strengthened advocacy for One Health will ensure effective integration of sectoral efforts to halt animal-to-human and

human-to-human transmission of mpox and other infectious diseases.

Lesson 3: A regional implementation model may limit the ability to fully meet the country's specific national needs, while also creating expectations among other countries for similar levels of support, thereby increasing pressure on regional resources.

Uganda experienced a disproportionate mpox impact, complicated by a looming Ebola outbreak during the reporting period. The regional mpox response model had a fixed budget, requiring alignment with Uganda's needs while sparing resources for other planned actions. Some Ugandan priorities were misaligned with project activities, and even well-aligned ones lacked sufficient resources. Supporting only Uganda caused confusion regarding the PREPARE project's mandate as a regional mechanism, further exacerbated by USAID health fund cuts at that time. The scarcity of financial resources negatively affected health service delivery, leading to the countries' perception that the PREPARE project was a mitigating intervention. To mitigate these concerns, targeted diplomatic engagements were put in place to communicate the criteria and rationale for allocating PREPARE project resources to selected countries, while underscoring the project's regional significance and its intended contribution to strengthening resilience and preparedness across the IGAD region. An official project launch at inception, which was postponed to allow greater focus on the mpox response, may have helped alleviate a number of the concerns raised, particularly by countries located further from the outbreak epicenter. Such a launch could have provided an opportunity to clearly communicate the project's objectives, regional scope, and

expected benefits, thereby fostering a stronger shared understanding among participating countries.

Lesson 4: Originating in the DRC, the spread of mpox in Uganda was highly unpredictable and frequently resulted in the emergence of unexpected transmission hotspots – thus necessitating the continuous redefinition of priority locations, which were not always limited to cross-border areas.

IGAD defines cross-border areas as geographic areas hosting multiple local authorities that are co-located yet belong to different nations and are normally characterized by heightened health vulnerabilities and more fragile health systems¹⁹. Originating from remote DRC areas characterized by poor sanitation, high wildlife-human contact rates, and limited health system capacities for rapid detection, Uganda's first mpox case was confirmed in July 2024 at Bwera Hospital^{18,20}. Cases were soon identified further inland, away from the Uganda-DRC border, fueled by high human mobility. By November 2024, cases had been detected in thirty-eight districts, thirty-three with active community transmission. Lake Kyoga and Kampala, for instance, emerged as major outbreak hotspots, distant from DRC-Uganda border areas. While initial concerns centered on cross-border areas and international airports, crowded public spaces, truck driver stop points, and locations characterized by elevated sexual activity also rapidly emerged as hotspots of high interest.

Lesson 5: The integration of rapid operational research into the mpox response is crucial for enhancing understanding of transmission dynamics and disease progression, thereby providing the evidence

base needed to guide timely and effective response planning and implementation.

Mpox infection presented a range of medical and behavioral phenomena that required clearer understanding to better inform the response actions. It was particularly perplexing that, in some instances, mothers tested negative for mpox while their young children were positive. The possibility of subclinical maternal mpox transmission to infants and young children remained unclear. The risk factors accelerating disease progression, as well as the associations with HIV, tuberculosis (TB), and acute malnutrition also needed to be understood. A significant number of individuals presenting with mpox were HIV-positive and/or had TB. It was not confirmed if malnutrition-induced immune suppression played a significant role in the progression of mpox, or conversely, mpox was a risk factor for childhood acute malnutrition. The unpredictability of mpox spread within the Ugandan socio-cultural and livelihood context highlighted the need for modeling the transmission trajectory and its implications for response.

Lesson 6: Early engagement for clear understanding of the respective mandates, procedures, and operational requirements of participating entities may be instrumental in reducing delays during project commencement and facilitating more efficient implementation.

The financial and operational frameworks of the PREPARE project are aimed at improving implementation and monitoring effectiveness while fostering accountability by the fund's recipients. However, initial administrative requirements in establishing formal partnership arrangements needed to align with the diverse mandates and procedures of the involved entities, and this was

unexpectedly protracted. Before the regional entity could draft a cooperation agreement with the delivery entity, a letter of agreement between the implementing and regional entities had to be finalized. These agreements had to meet the procedural requirements of all organizations, which occasionally diverged, particularly since the collaboration was unprecedented. Finalization of the agreements for organizations partnering for the first time can be prolonged. Additionally, the roles of the entities had to be clarified to dispel possible misunderstanding between the partners involved.

Lesson 7: The outbreak and Uganda's experience presented an unprecedented opportunity to review and harmonize relevant country policies and strategies which should be guided by the relevant regional frameworks.

Although multiple national policies, strategic frameworks, and plans are in place—most notably the One Health Strategies and the National Action Plan for Health Security (NAPHS)—Uganda's experience, together with insights from the regional mpox response, has generated lessons relevant for managing similar outbreaks. These lessons provide a critical evidence base for the review, alignment, and strengthening of existing frameworks. They further highlight the need for greater harmonization to enhance pandemic and epidemic surveillance systems, strengthen laboratory capacity, and support workforce development. In this context, there is a strategic opportunity to develop regional policies, guidelines, tools, and frameworks that can facilitate coordinated harmonization across IGAD Member States.

CONCLUSION

The early stages of the regional mpox response identified related cross-border health security threats and the need for strategic support focusing on selective and context-specific actions near the outbreak's epicenter with potential for regional impact. Strategic sequencing of mpox response activities is essential for building synergies, effectively realigning resources, and prioritizing target locations. A rapid shift to immediate, needs-based pandemic and epidemic response, alongside strengthening existing multi-sectoral preparedness systems, is crucial. Flexibility in redefining pandemic and epidemic hotspots remains pertinent as the outbreak evolves. Integrating early operational research to inform response scale-up is also a potential key success factor. Addressing administrative and partnership challenges early in regional response can avoid actions delays. The documented lessons can inform the review and development of individual country policies and strategies, as well as regional frameworks aimed at promoting harmonization across countries to enhance preparedness and effective responses to pandemics, epidemics, and other public health emergencies.

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developed the map to illustrate the geographical vulnerability of Uganda and it as an entry point of pandemics and epidemics in the IGAD region.

Competing interest

The author(s) declare that they have no competing interests.

Authors' contributions

FA, WG, MM, SO conceptualized the paper and its initial outline. SO, and FA produced the first of the manuscript. MM, AA, HM, AI, HK and HM made further technical inputs after the first draft. Authors reviewed the manuscript before submission to the journal.

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