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What Role Can Routine Vaccination Play in Pandemic Prevention and Preparedness?

An Economic Evaluation of Mpox Vaccination

TIM LAURENCE · CAROLINE MOORE · JANEEN MADAN KELLER · ROSIE ELDRIDGE

Abstract

Since 2022, mpox has triggered two public health emergencies of international concern, with sustained transmission across Africa and beyond. We conducted a modelling study to assess the cost-effectiveness of routine mpox vaccination in endemic African provinces as a strategy to reduce disease transmission and strengthen pandemic prevention and response.

Although mpox imposes a substantially lower disease burden than malaria, tuberculosis, or diarrheal disease in the Democratic Republic of the Congo (DRC), routine mpox vaccination would still be health-positive for more than half of the DRC population (53.5 million people), including 23.2 million children.

From a local health benefits perspective, routine vaccination of children aged 0–9 years may be cost-effective at $10 per dose compared with no vaccination in the two highest-burden provinces of the DRC. From a global healthcare payer perspective, routine vaccination of 8.5 million children aged 0–9 years in endemic regions of the DRC over a 10-year period—at an estimated cost of $203 million—could reduce the probability and size of mpox pandemics outside Africa—yielding an return on investment exceeding 3:1, even if the vaccine is used considerably past the point of local cost-effectiveness. However, under current budget constraints, additional donor financing would be required to realise these benefits for global pandemic prevention.

We recommend: (1) expanding data on mpox vaccine efficacy and epidemiology; (2) advancing realistic financing strategies that account for trade-offs; (3) assessing routine vaccination for other high-risk pathogens; and (4) convening partners to assess the development of combination vaccines for mpox and other pathogens.

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Key messages

- Since 2022, mpox has caused two public health emergencies of international concern, with human-to-human transmission across Africa. The Democratic Republic of Congo (DRC) remains the epicentre of mpox, with endemic circulation, the highest case burden, and continued exported cases.
- Mpox is a vaccine-preventable disease, emphasising the urgent need for vaccination to prevent disease transmission and reduce global outbreaks.
- We conducted a modelling study to determine the cost-effectiveness of routine mpox vaccination in endemic provinces in Africa, from the perspective of both in-country and global healthcare payers.
- We find that even in its peak year (2024), mpox causes a substantially lower disease burden among children ages 0–9 years compared to malaria, tuberculosis, or diarrhoeal disease in the most affected country in Africa (DRC). These other diseases are likely at least ten times more burdensome.
- Still, routine mpox vaccination would be a health-positive intervention for over half of the population of the DRC (53.5 million people), including 23.2 million children ages 0–9 years. From the in-country perspective, routine vaccination in children ages 0–9 years may be cost-effective when compared to no vaccination in the two highest burden provinces of the DRC, depending on the exact threshold used.
- From a global healthcare payer perspective, routine vaccination of 8.5 million children ages 0–9 years in endemic regions of the DRC over a 10-year period (at an approximate cost of $203 million) could reduce the probability and size of mpox pandemics outside of Africa, with an ROI of more than 3:1 even if the vaccine is used considerably past the point of local cost-effectiveness.
- While safe and effective vaccines exist for mpox, some are not yet approved for use in children outside of emergency situations. A prerequisite for wider administration of mpox vaccines in children is continued support for collection of safety and effectiveness data.
- The benefits of wider use of routine mpox vaccination are greater than the costs from a global healthcare payer perspective, but additional donor funding would be needed due to current budget constraints.

Motivation

Pandemic prevention and response (PPR) is inherently challenging because it requires a rapid and coordinated response based on uncertain data. Nonetheless, it is critical to prioritise investments in PPR given the immense health and economic burden imposed by pandemics like COVID-19 (Keogh-Brown et al. 2008; Cutler et al. 2020; Barro et al. 2020; Beach et al. 2022; Fan et al. 2024; Obeng-Kusi et al. 2024). Routine vaccination has proven to be highly effective at preventing disease spread and reducing mortality from outbreaks, serving as a critical intervention in tackling infectious diseases globally (Shattock et al. 2024; WHO and UNICEF 2025).

With that understanding, we conducted a modelling study (see the full modelling paper here) to explore the role routine vaccination could play in PPR efforts, using mpox as a case study. Our modelling assesses the direct benefits to vaccine recipients in endemic parts of Africa and the resulting benefits of reduced transmission within and outside of Africa.

Our key research questions were as follows:

- For which countries or provinces in Africa do the health benefits of routine mpox vaccination outweigh the modest health losses from adverse side effects?
- What would the health economic impact of routine mpox vaccination be on populations within Africa?
- What impact would routine mpox vaccination in endemic African provinces have on pandemic prevention outside of Africa?
- How does mpox vaccination fit within general orthopoxvirus pandemic prevention efforts?

Background on the epidemiology of orthopoxviruses and recent mpox emergencies

Mpox virus (MPXV) has undergone a marked epidemiological shift since the end of routine vaccination against smallpox (which also provides protection against mpox). As recently as early 2022, mpox was largely considered a zoonotic disease with limited human-to-human spread; it was endemic in parts of Africa and characterised by repeated spillovers from wildlife and occasional short transmission chains (Beer and Rao 2019; Bunge et al. 2022). However, research as early as 2010 noted that both outbreak frequency and size increased as population immunity from routine smallpox vaccination declined (Rimoin et al. 2010).

Since 2022, mpox has caused two public health emergencies of international concern (PHEIC). In 2022, the first PHEIC was driven by the global spread of clade II mpox, disproportionately affecting gay, bisexual, and other men who have sex with men (GBMSM), with most early cases hypothesised

to have spread through sexual contact (Thornhill et al. 2022). At the epicentre of the second PHEIC, declared in 2024, is the DRC, which has historically had the highest reported case counts. During this PHEIC, clade I mpox spread into African countries previously unaffected by the disease, pointing to sustained transmission in new contexts and expanding the known epidemiology of the disease (Emanuel 2025; WHO and UNICEF 2025).

Recent PHEICs indicate a shift away from characterising mpox as a zoonotic disease toward one of sustained human-to-human transmission. In fact, genomic analyses indicate that clade IIb may have been transmitting continuously in humans since at least 2016 (O'Toole et al. 2023), implying hundreds of serial transmission events, while more recent findings suggest human-to-human transmission may have begun even earlier (Parker et al. 2025). Beyond its present risks, MPXV has been mutating in ways that could make it more transmissible in humans (O'Toole et al. 2023; Parker et al. 2025; Maluquer de Motes and Ulaeto 2025). It is theorised that the co-circulation of mpox clades Ia, Ib (in the DRC), IIa (in Cote d'Ivoire), and IIb (in Nigeria and Sierra Leone) may drive further viral adaptation (Maluquer de Motes and Ulaeto 2025).

During the 2022 outbreak in Europe and North America, most reported mpox cases were among GBMSM, which informed risk-based vaccination when vaccine supply was constrained (Thornhill et al. 2022; CDC 2025; UKHSA 2025). Ndembi et al. (2024) concludes that current transmission patterns in parts of the DRC differ from those seen in Europe in 2022, with predominantly heterosexual transmission, including among female sex workers. This is supported by recent data from the outbreak in Sierra Leone reporting nearly equal case numbers in males and females (WHO 2025; Kangbai et al. 2025). These patterns pose a considerable challenge for prevention, as groups at high risk of contracting mpox may be substantially larger and more difficult to define.

Our estimates suggest that the burden of mpox in the DRC is highest among children ages 0–9 years, with Disability-Adjusted Life Years (DALYs) peaking in 2024. However, even in its peak year, mpox causes a substantially lower burden among children ages 0–9 years than malaria, tuberculosis, or diarrhoeal disease, and these other diseases are likely at least ten times more burdensome over a 10-year average (2016–2025, with incomplete data for 2025).

Importantly, mpox is a vaccine-preventable disease, and the vaccine used to immunise against smallpox and MPVX is thought to be effective against other orthopoxviruses (OPXVs) (Gilchuk et al. 2016; Liu et al. 2024). Given the evolving epidemiology and the emergence of multiple OPXVs with pandemic potential, this reinforces the urgency of evaluating the expanded use of mpox vaccination (e.g., through routine vaccination), with additional manufactured vaccines reprioritised in the event of other OPXV outbreaks that pose a greater threat.

The potential value and associated challenges of routine mpox vaccination compared to outbreak response campaigns

Outbreak response immunisation programmes are effective at reducing transmission and the burden of infectious disease outbreaks, cutting deaths by as much as 60 percent (Delport et al. 2025). However, they face some limitations. By definition, outbreak response vaccination happens in response to zoonotic spillovers and does not mitigate the spillover from occurring in the first place (OIE 2022). These strategies also rely on timely surveillance data to detect outbreaks and deploy vaccination before the outbreak becomes too widespread (Grais et al. 2006; Shankar et al. 2024).

Additionally, while vaccine stockpiles can facilitate rapid response, holding appropriately sized stockpiles is challenging due to highly uncertain and variable projected demand (Lerch et al. 2022). In an outbreak year, small stockpiles are rapidly depleted, whereas large stockpiles may go unused, which can undermine public and political support due to perceived waste (HIQA 2023), though the relatively long shelf life of mpox vaccines may reduce these concerns (Hoet 2022).

McQuiston et al. (2025, p.27) conclude that "the availability of vaccines should be expanded not only for outbreak response but also for broader routine use for persons in mpox-endemic countries." More broadly, routine vaccination has proven to be highly effective at preventing disease transmission and reducing mortality, serving as a critical intervention in reducing infectious diseases globally (WHO and UNICEF 2025; Shattock et al. 2024).

Building on this, we consider the role of routine vaccination against mpox in the most affected areas of Africa alongside the outbreak response stockpile that Gavi, the Vaccine Alliance (Gavi) plans to build. We view these approaches as complementary; while a stockpile of 500,000 doses may only have a modest relative impact on a widespread cross-country outbreak, a routine vaccination campaign that prevents transmission in some key geographies could substantially reduce the number of outbreaks requiring catch-up campaigns.

However, there are some considerable challenges associated with using mpox as a routine vaccine, particularly in children:

1. Funding for *official development assistance*, and *development assistance for health* in particular, has declined significantly, increasing pressure on already limited budgets. This makes it challenging to maintain existing immunisation, let alone introduce additional vaccines into routine immunisation schedules (OECD 2025; IHME 2025).
2. In some cases, even where vaccines were made available (The White House 2024), other barriers limited the implementation of vaccination campaigns within Africa.
3. Mpox epidemiology remains highly uncertain. Our analysis suggests that only 6 percent (2 to 13 percent) of infections may be reported as cases in endemic areas; this case reporting

rate likely varies across local areas, making it difficult to determine where disease burden is occurring. Serology data is also challenging to assess due to high false-positive rates and limited sample sizes in previous studies (De Vos et al. 2024).

4. There is a lack of safety and effectiveness data in children for the most commonly used mpox vaccines (Grabenstein and Hacker 2024; Ladhani et al. 2023), though a trial is currently ongoing to collect additional data (CEPI 2024).

Despite these challenges, emerging safety data in children provide a pathway for authorising routine mpox vaccination programmes in endemic parts of Africa. The remaining sections of this brief present evidence on the potential impact of routine mpox vaccination and its implications for global PPR efforts more generally, illustrating the case for external funders to consider supporting expanded use of routine mpox vaccination.

Key findings of assessing routine mpox vaccination

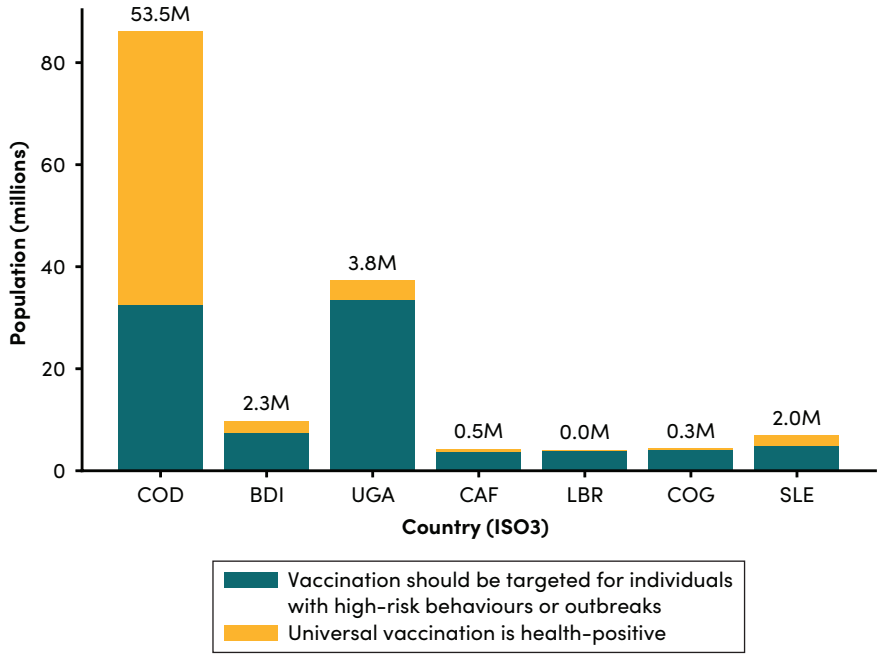
We consider a universal routine vaccination campaign for children ages 0–9 years in the most affected areas across Africa (*routine vaccination*); we also consider adding a catch-up programme for adolescents and adults who are too young to have received the smallpox vaccine (*routine and catch-up vaccination*). If vaccination efforts focused solely on children, transmission among older age groups would persist, limiting the overall effect of any vaccination campaign. However, adult vaccination campaigns are more costly to deliver per dose and tend to have lower uptake (Gerste et al. 2024; ThinkWell 2024).

The modelling study aggregates the best available evidence on adverse events in adults (as a proxy for adverse events in children), estimates of the cost of mpox treatment, and novel estimates of mpox incidence (adjusted for underreporting) and disease burden. We use these inputs to produce initial assessments that identify age groups and provinces in African countries where mpox vaccination is likely to be both health-positive (i.e., the health benefits of mpox vaccination in vaccine recipients outweigh the expected health loss from adverse events, which tend to be minor) and cost-effective (i.e., cost of vaccination per DALY averted is below a locally relevant threshold). Full methodological details can be found in the companion modelling paper.

Over half of the population of the DRC (labelled COD)—a total of 53.5 million people—would benefit from receiving mpox vaccination through a universal programme for their age group, including 23.2 million children ages 0–9 years (see Figure 1). While some provinces in other African countries also show health-positive results for certain age groups, these represent a minority of the overall population.

Our modelling, therefore, identifies the DRC as the clearest target for initial expansion of routine mpox vaccination. Notably, in areas where universal vaccination of entire age groups is not currently found to be health-positive, reported incidence can be as low as 20 cases per 100,000 population over 10 years, suggesting that even relatively modest outbreaks could make routine vaccination health-positive. Though not formally assessed, given the safety profile of the vaccine, the benefit from vaccination in these areas for groups with high-risk behaviours, or in response to outbreaks, is still very likely to outweigh the minor adverse events.

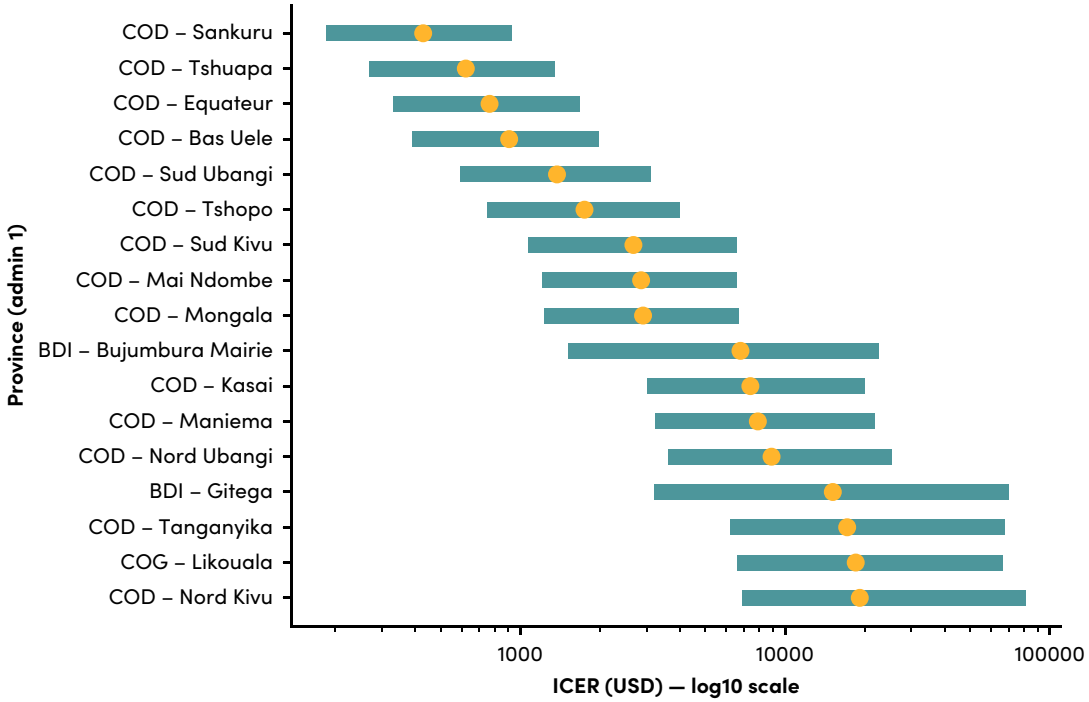
FIGURE 1. Population of areas where universal mpox vaccination is health-positive



Notes: Population figures are based on the average size of each age group from 2016–2025 to effectively match costs and benefits. Therefore, the values shown are likely lower than the most recent official population estimates.

The Incremental Cost-Effectiveness Ratio (ICER) of routine vaccination for children ages 0–9 years is shown in Figure 2. At a price of $10 per dose, the median ICER for one province in the DRC (Sankuru) is below the DRC's GDP per capita (USD $647), while two other provinces (Tshuapa and Equateur) are very near to this value. An intervention may be considered cost-effective if the ICER falls below the country's GDP per capita. Though some estimates suggest that an appropriate cost-effectiveness threshold for the DRC is considerably lower (Ochalek et al. 2018). The cost-effectiveness of this programme varies almost linearly with the vaccine price per dose. Therefore, at costs of $2 to $5 per dose, routine vaccination could be cost-effective in additional provinces of the DRC.

FIGURE 2. Uncertainty around estimated ICERs for routine vaccination (in children ages 0–9 years) by province



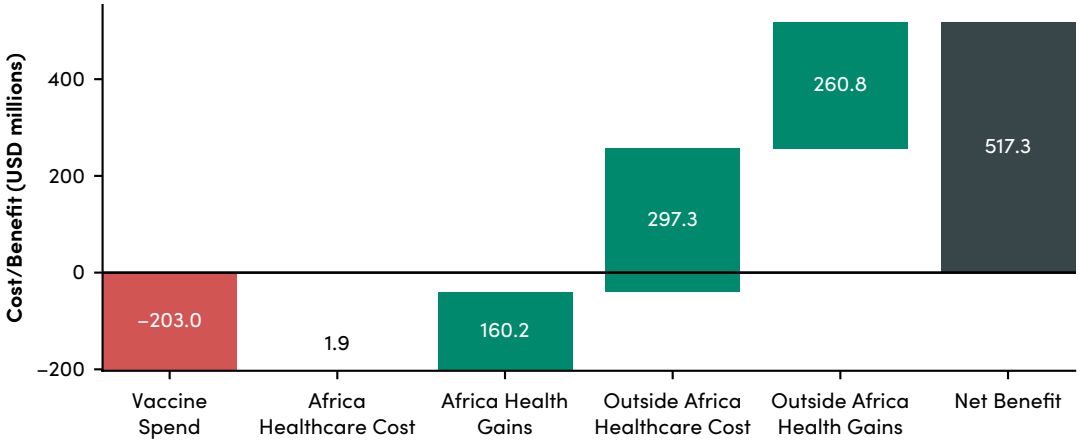
We introduce additional sources of uncertainty into the modelling, such as the impact of mpox vaccination on breaking chains of transmission in Africa and the knock-on effects of averting mpox pandemics outside of Africa. Through this modelling of the possible global impact, we find that vaccinating areas with an ICER of up to $10,000 per DALY averted—over 10 times the cost-effectiveness threshold for the DRC—has a positive ROI.

In our headline scenario, 8.5 million children ages 0–9 years in the highest-risk areas of the DRC are vaccinated over 10 years. This campaign is estimated to reduce mpox infections across Africa by 1.6 million (0.5 million–3.4 million), or 37 percent in the base case. From the perspective of a potential global health funder, this campaign is estimated to have a 3:1 ROI (L: -1-U: 25)[1] at an estimated cost of approximately $203 million over 10 years.

Figure 3 shows how different components contribute to this ROI. This ROI depends on the extent of rollout and other assumptions, with higher ROIs from more targeted campaigns or lower vaccine prices. In addition to the healthcare costs and monetised DALYs averted, this campaign demonstrates a considerable positive externality by reducing pandemic risk outside Africa. This externality is estimated to be five times the benefit within Africa, providing further evidence that pandemic prevention is a global public good.

1 The lower bound of our ROI estimate is negative because, in a small number of simulations, a large pandemic occurs outside of Africa despite vaccination efforts within Africa.

FIGURE 3. Contribution of different components to ROI of more than 3:1 for routine mpox vaccination in Africa



Accounting for the global benefits of averted mpox transmission, routine vaccination delivers positive returns across a much wider range of health-positive areas than would be cost-effective from an in-country perspective alone. A similar pattern holds for routine and catch-up vaccination, which would cost $481 million—reflecting a larger target population and higher delivery costs—and yield an ROI of slightly less than 3:1 (L: 0 - U: 19).

Limitations

There are several limitations, mainly related to the data used in the study, the overall modelling approach, and associated implementation considerations.

Data

- The data and evidence underpinning this modelling study are highly uncertain. Higher-quality epidemiological data and more evidence on the disease burden and transmission of mpox in Africa are needed. Further research into the health economics of mpox, including improved estimates of healthcare costs and patient-reported outcomes of quality of life lost from long-term side effects, would also increase the confidence in the results. Given these uncertainties, the results of our disease burden and cost-effectiveness estimates should be interpreted with **low confidence**.
- To estimate the impact of vaccination subnationally, the main variables that vary across provinces are the rate of infection and the population composition of such areas. Other variables (e.g., cost of mpox treatment) is estimated nationally and assumed to apply to every province.

Modelling

- Given the study's broad scope and data limitations, we employ more basic modelling frameworks than would be used in analyses with stronger data and a more narrow focus on a single geographical area or age group.
- Our approach to estimating case ascertainment does not allow for case ascertainment to change over time. There has been a substantial increase in reported cases since 2022, which may reflect improved surveillance, but we did not have sufficient estimates of ascertainment over time to quantify this effect.
- Our modelling is based on a hypothetical scenario in which vaccination had been rolled out in 2016. However, applying our results to future vaccination campaigns in age groups and regions previously affected by mpox may slightly overstate the impact and the risk of pandemics.
- The results stemming from our pandemic prevention modelling should be interpreted with **very low confidence** due to the inherent uncertainty of pandemics.
- Our pandemic prevention modelling is limited by the exclusion of international travel data. Whereas flight data is available, the extent to which people are travelling from provinces to major airport hubs remains uncertain. Future research should aim to better characterise variations in mpox transmission risk across African geographies and directly model alternative mpox vaccination strategies, such as vaccination campaigns for international travellers.

Implementation considerations

- Implementation challenges in the DRC context could have important real-world implications for the cost-effectiveness analysis we present here. For instance, administering a two-dose vaccine regimen—with specific cold chain requirements and delivered one month apart—in remote areas of the DRC where there is ongoing humanitarian conflict could prove particularly challenging. Our results do not quantitatively capture such implementation constraints due to substantial uncertainty around their implications.
- We have modelled the benefits of vaccination campaigns with 80 percent coverage; assessing whether sufficient demand and vaccine acceptability exist in relevant populations was beyond the scope of this study.
- This routine vaccination campaign would require 1.7 million mpox vaccine doses annually. If a new mpox variant or another OPXV of greater concern emerged, the vaccines could be redirected in the first 100 days of response to this emerging threat.

Policy recommendations

1. **Expand data on mpox vaccine efficacy and epidemiology**
    - Additional safety and efficacy data on vaccination in children would support regulatory approval of mpox vaccination for younger age groups. Such work is ongoing and should continue to be supported (CEPI 2024) as an essential prerequisite to vaccination being administered to younger age groups more widely outside of emergency use.
    - Questions remain about the epidemiology of mpox in Africa. Additional funding for disease surveillance, including rigorous serological surveys of OPXV antibodies, could support effective targeting of mpox vaccination in the highest-burden areas. Donors should support Africa CDC's disease surveillance efforts, and philanthropic global health funders should support additional research studies to address knowledge gaps that hinder our ability to direct limited resources to prevent mpox transmission.
2. **Advance realistic funding strategies for routine mpox vaccination, while acknowledging trade-offs**
    - From the perspective of recipient countries, mpox vaccination is unlikely to be as cost-effective as other vaccine candidates currently competing for limited resources, including external support from global initiatives such as Gavi. Therefore, funding for wider use of mpox vaccination should not necessarily be prioritised within Gavi's existing budget, which already faces significant constraints.
    - However, other funders with a remit focused specifically on pandemic prevention and global health security could make a considerable impact on reducing the pandemic threat of OPXVs for relatively small sums of money (around $20 million per year). A funder like the European Union's Health Emergency Preparedness and Response Authority or philanthropies with similar objectives, such as the Gates Foundation or the Mastercard Foundation, could consider forming a coalition or pooled funding platform to provide additional resources to deliver a routine mpox vaccination programme via Africa CDC in partnership with Gavi, the WHO, and UNICEF.
3. **Explore the role of routine vaccination for other high-risk pathogens**
    - Routine vaccination can play a critical role in reducing the risk posed by MPXV, which is on the WHO's list of high-risk pathogens with pandemic potential. Organisations like the WHO and the Coalition for Epidemic Preparedness Innovations (CEPI) should signal whether additional modelling studies for diseases like Lassa fever could provide further evidence on the role routine vaccination could play in pandemic prevention efforts.

4. **Convene partners to investigate the development of a combination vaccine for mpox and other pathogens**
    - Our analysis demonstrates the considerable benefits of routine vaccination against mpox with a safe and effective vaccine. If scientifically feasible over the long term, creating a next-generation broad combination vaccine against multiple pathogens that includes an OPVX vaccine (similar to how inactivated polio protection is included in hexavalent vaccines) could lower costs and facilitate uptake in endemic areas over time.
    - Key stakeholders such as the WHO and CEPI should convene a technical meeting and subsequently consider funding the development of supporting such technologies.

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Appendix: Key terms

Key Term	Definition
1918 H1N1 influenza	1918–1920 influenza outbreak, commonly referred to as Spanish flu
Administration-one (admin-one) geographies	The highest level of subnational geography at which data is routinely collected (e.g., states in the USA, or provinces in the DRC)
Adverse events (AEs)	Undesired side effects, ranging from mild to serious or fatal, occurring after the administration of a health intervention
Case ascertainment rate	The proportion of human infections with a disease that are diagnosed and reported as cases
Catch-up vaccination	Administering vaccines to individuals who missed (or were not offered) them within the recommended time frame of a national immunisation schedule
Cost-effective	An intervention that achieves intended health outcomes at a reasonable cost, maximising limited resources
Disability-adjusted life year (DALY)	A time-based measure of overall disease burden, calculated as the sum of years of life lost due to premature mortality and years lived with disability; One DALY equals one lost year of healthy life.
Endemic	A disease consistently present in a specific area or population, maintained at a stable baseline level
Health benefit	Positive impact on health outcomes achieved through interventions or policies
Health-positive intervention	The individual expected clinical benefit from an intervention is greater than the health loss from adverse events
Incremental cost effectiveness ratio (ICER)	A metric comparing the additional cost and effectiveness of one intervention relative to another
Immunity	The body's ability to resist infection or disease
Infections	Illnesses caused by pathogens. This differs from cases that are the subset of infections that are diagnosed and reported.
Monetised health loss	Assigning a monetary value to the loss of health to allow comparison of costs and benefits
Mpox	Mpox (formerly known as monkeypox) is an illness caused by the monkeypox virus. It is a viral infection which can spread between people, mainly through close contact. In settings where the monkeypox virus is present among some wild animals, it can also be transmitted from infected animals to people.
Orthopoxviruses (OPXVs)	A genus of zoonotic viruses in the Poxviridae family infecting humans and animals
Outbreaks	Sudden increases in disease cases beyond expected levels in a given area and time
Pandemic	Is formally defined by the WHO as "*a worldwide spread of a **new** disease*." However, we use the following definition: "*An epidemic occurring over a very wide area, crossing international boundaries, and usually affecting a large number of people*" (Porta 2014). We follow this wider definition for consistency with common consideration of pandemic policy including pathogens like MPXV that are not novel.
Pathogens	Microorganisms, such as bacteria, viruses, or parasites, that cause disease
Public health emergency of international concern (PHEIC)	An extraordinary event that is determined to constitute a public health risk to other states through the international spread of disease and to potentially require a coordinated international response.

Key Term	Definition
Province (admin-one unit)	The name of admin-one geographies in the DRC. This is applied to admin ones in any country for convenience.
Return on investment (ROI)	The ratio of the benefits of a program or intervention to its costs (benefits/costs)
Routine vaccination	Systematic administration of vaccines per a national or regional schedule. We use the term here to refer to administration of mpox vaccines to children, as childhood is generally the default time to target a universal vaccination programme (albeit with potential need for catchup in older age groups).
Serology	The study of blood serum, especially antibodies
Subnational geographies	Country subdivisions, such as provinces, states, or regions used in health analysis
Transmission	The process by which infectious agents spread to a new host
Vaccine stockpiles	Reserves of vaccines maintained for use during outbreaks or emergencies
Variant	A version of a virus with genetic differences resulting from mutation
Zoonotic	Describes an infectious disease that can jump from a nonhuman animal to humans. Zoonotic pathogens may be bacterial, viral, or parasitic, or may involve unconventional agents and can spread to humans through direct contact or through food, water, or the environment.