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What Role Can Routine Vaccination Play in Pandemic Prevention and Response? An Economic Evaluation of Mpox Vaccination

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Abstract

The study assesses the cost-effectiveness of routine vaccination for preventing future pandemics. Using mpox as a case study, we evaluate the cost-effectiveness of routine and catch-up mpox vaccination in affected areas of African countries and assess the potential role of routine vaccination in pandemic prevention and response to the mpox virus and other orthopoxviruses. Our economic evaluation combines data on mpox epidemiology, disease burden, and vaccination and treatment costs, alongside two novel systematic reviews on serology and case ascertainment, in a modelling framework.

We find considerable under-ascertainment of mpox cases in Africa. Even after adjusting for under-ascertainment, mpox remains a relatively low-burden disease in the Democratic Republic of the Congo (DRC) compared with other leading causes of ill health. An mpox vaccination campaign targeting high-burden provinces would be *health-positive* (expected health benefits outweigh minor adverse events) for more than half of the DRC population. At a price of US$10 per dose, vaccination is cost-effective only for children ages 0–9 years in two provinces from a national healthcare payer perspective. Though this finding is sensitive to the exact cost-effectiveness threshold for the DRC.

Under alternative model specifications that incorporate additional (and more uncertain) parameters, a 10-year routine vaccination campaign costing approximately US$203 million would directly protect 8.5 million children ages 0–9 years. From a global healthcare payer perspective, this campaign yields an expected return on investment (ROI) exceeding 3:1 (lower bound: -1; upper bound: 25). A combined routine and catch-up programme would cost US$481 million, reflecting a larger target population and higher delivery costs, but would still yield an ROI just below 3:1 (lower bound: 0; upper bound: 19).

The study provides province-level estimates of mpox infections and disability-adjusted life years; presents the first province-level cost-effectiveness assessment of mpox vaccination across multiple African countries; and offers initial evidence on how vaccination in Africa may influence global mpox transmission and the ROI of mpox vaccination in endemic settings. The findings also highlight both the challenges of pandemic prevention and the potential role of vaccination campaigns as an effective policy tool for reducing pandemic risk.

BACKGROUND PAPER

Contents

Figures

Tables

Key terms

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 are routinely collected (e.g., states in the USA)
Adverse events (AEs)	Undesired side effects, ranging from mild to serious or fatal, occurring after the administration of a health intervention
Antibodies	Proteins produced by the immune system to identify and neutralize harmful antigens
Antigen	Any molecule recognized by the immune system as foreign, triggering a defensive response
Binomial distribution	A probability distribution of the number of successes in a fixed number of independent yes or no trials, each with the same probability of success
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, maximizing 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
Direct transmission	The transfer of an infectious pathogen from one individual or reservoir to a susceptible host through direct contact or droplets
Disability weight	A numerical factor (from 0 to 1) that represents the severity of health loss due to a specific condition; 0 = perfect health, 1 = equivalent to death
Disutility	The negative impact of a health state or treatment on an individual's quality of life
Endemic	A disease consistently present in a specific area or population, maintained at a stable baseline level
GBMSM	Gay, bisexual, or other men who have sex with men
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
Infection fatality rate (IFR)	The proportion of individuals who die after contracting an infection
IgG	The most common type of antibody in human blood
IgM	The first antibody produced by the immune system in response to a new antigen
Immunity	The body's ability to resist infection or disease
Indirect transmission	Spread of infection via intermediary objects or substances rather than direct contact
Infection burden	The overall impact of an infectious disease on a population

Term	Definition
Infection hospitalisation rate (IHR)	The rate at which people infected with a pathogen get admitted to hospital
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 virus (MPXV)	The virus that causes mpox
MVA-BN	Bavarian Nordic's vaccine that is effective against mpox and smallpox, and likely other OPXVs. Also known as Jynneos in the United States, Imvanex in the UK and Europe, and Imvamune in Canada and other regions
Negative binomial distribution	The distribution of the number of failures observed before the *r*-th success in independent Bernoulli(p) trials. It is a count model for overdispersed data where the variance exceeds the mean
One Health	One Health is an integrated, unifying approach that aims to sustainably balance and optimise the health of people, animals, and ecosystems. (WHO, 2025i)
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
Overdispersion	A property of a count distribution that has a variance higher than its mean would predict (higher variance than a Poisson distribution)
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
Polymerase chain reaction test (PRC)	A lab technique to detect genetic material (DNA or RNA) of a pathogen from a sample
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
Province (admin-one unit)	The name of admin-one geographies in the DRC. This is applied to admin-ones in any country for convenience
Regression model	A statistical model estimating the relationship between a dependent variable and one or more independent variables
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 catch-up in older age groups)

Term	Definition
Sequelae	Long-term consequences following the resolution of an initial disease or injury
Sero-naïve	Individuals or populations not previously exposed to a pathogen and lacking antibodies against it
Serology	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
Utilities	Preference-based values assigned to different health states, often used in health economics
Vaccine stockpiles	Reserves of vaccines maintained for use during outbreaks or emergencies
Variant	A version of a virus with genetic differences resulting from mutation
Years of life lost (YLL)	Years lost due to premature death
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

Introduction and background

Pandemic prevention and response (PPR) policy is inherently challenging because it requires a rapid, 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 and Smith, 2008; Cutler and Summers, 2020; Barro et al., 2020; Beach et al., 2022; Fan et al., 2024; Obeng-Kusi et al., 2024). Routine vaccination has proven 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).

Against this backdrop, we conducted a modelling study to explore the role routine vaccination could play in PPR efforts, using mpox as a case study.[1] Our modelling assesses the direct benefits to vaccine recipients in endemic parts of Africa, as well as the resulting benefits of reduced transmission within and outside of Africa.

The rest of this section sets out the broader context that underpins the study, including the epidemiology of mpox virus (MPXV) and other orthopoxviruses; the challenges and benefits of PPR policy; the potential benefits of routine vaccination against mpox; related modelling; and our research objectives. The remainder of the paper is devoted to describing the modelling study, its results and limitations, and key findings and recommendations. The appendices provide additional technical detail to lend greater transparency to the modelling undertaken.

Background on the epidemiology of orthopoxviruses and recent mpox emergencies

MPXV has undergone a marked shift in epidemiology since the end of routine smallpox vaccination (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 started with clade II of mpox spreading globally, 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 has spread to African countries that were previously unaffected by the disease

1 Due to its stigmatising connotations, the WHO renamed monkeypox to mpox. The monkeypox virus (which causes mpox) has never been renamed, so we herein refer to it as MPXV.

and that lack known animal reservoirs. The Africa Centres for Disease Control and Prevention (Africa CDC) estimated more than 174,000 suspected mpox cases across Africa in the year leading up to August 2025 (WHO, 2025f), but that is likely a considerable underestimate of true infections given the stigma associated with mpox transmission through sexual contact, as well as variable surveillance and diagnostic testing capacity across areas.

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). These genomic studies also suggest the possibility of considerable underreporting of mpox cases in affected African countries.

During the 2022 pandemic in Europe and North America, most reported mpox cases were among GBMSM, which informed risk-based vaccination when supply has been constrained (Thornhill et al., 2022; CDC, 2025a; UKHSA, 2025a). Ndembi et al. (2024) conclude 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, which report nearly equal case numbers in males and females (WHO, 2025c, 54; Kangbai et al., 2025). This presents a considerable challenge, as groups at high risk of contracting mpox may be substantially larger and more difficult to define. These data also demonstrate sustained transmission in new contexts, expanding the known epidemiology of the disease.

Beyond its present risks, MPXV has been mutating, which could in time change the properties of the virus to 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 Côte d'Ivoire), and IIb (in Nigeria and Sierra Leone) in the DRC and now Côte d'Ivoire could create competition between viruses for human hosts and drive further viral adaptation (Maluquer de Motes and Ulaeto, 2025).

While MPXV is currently the orthopoxvirus (OPXV) that causes the highest disease burden in humans, orthopoxvirus variola (which causes smallpox) is the OPXV that has historically caused the greatest burden in humans. An estimated 300 million people died from smallpox in the 20th century alone (Henderson, 2011). In sero-naïve populations of indigenous people in the Americas, it is estimated to have killed half the population (Patterson and Runge, 2002). Despite its eradication, variola remains a health security concern, and the World Health Organization (WHO) lists it among high-risk pathogens with pandemic potential, along with mpox and vaccinia viruses (Henderson et al., 1999; Patterson and Runge, 2002; WHO, 2024d). Vaccinia and other orthopoxes also affect humans, though with less recorded burden than mpox (Diaz, 2021; e Silva et al., 2024; Maluquer de Motes and Ulaeto, 2025).

Importantly, mpox is a vaccine-preventable disease. The vaccine used to immunise against smallpox and MPXV is thought to be effective against other OPXVs (Gilchuk et al., 2016; Liu et al., 2024).

The evolving epidemiology of multiple OPXVs with pandemic potential reinforces the urgency of evaluating the expanded use of mpox vaccination, because additionally manufactured vaccines could be reprioritised in the event necessary to mitigate other OPXV outbreaks that represent a greater threat.

Challenges and benefits of effective pandemic prevention and response policy

The WHO list of pathogens with pandemic potential contains as much diversity as consistency. While some diseases are endemic in all WHO regions (for instance, coronaviruses and influenza viruses), others are endemic only in certain geographies (orthopoxvirus mpox and Mammarenavirus lassaense [Lassa fever]) and some are not currently circulating in humans (Disease X) (WHO, 2024d).

Delivering effective PPR is challenging for several reasons:

1. Pandemic preparedness is a global public good, so individual countries are disincentivised to invest (Fan et al., 2024).
2. Outbreaks move rapidly, and global, regional, and national entities and systems struggle to mount effective responses quickly enough (Currie et al., 2016; Keller and Guzman, 2024).
3. Cases can grow exponentially, but deployment of countermeasures often scales linearly (Lal et al., 2022).
4. Responding to pandemics often requires significant sums of financing, with evidence suggesting the critical importance of resource availability on day zero, further complicating response (Fan et al., 2024; Keller and Guzman, 2024).
5. Many of the places most affected by pathogens of pandemic potential have weak health systems, which means the challenges are felt particularly keenly.

While PPR represents an immense global challenge, the rewards of effective pandemic policy are enormous given the costs pandemics impose on health and the economy. The 1918 H1N1 influenza pandemic is estimated to have reduced real gross domestic product (GDP) by an average of 6 percent across affected countries (Barro et al., 2020; Beach et al., 2022). SARS is estimated to have cost US$7–10 billion (Keogh-Brown and Smith, 2008), the 2014 Ebola outbreak cost US$30–50 billion in Africa alone (Obeng-Kusi et al., 2024), and the COVID-19 pandemic-imposed losses in the United States alone exceeding US$16 trillion (Cutler and Summers, 2020). These costs demonstrate that different disease outbreaks, which we define as pandemics, vary in their economic impacts by many orders of magnitude.

Routine vaccination is an evidence-based policy intervention

Compared with the challenges of PPR, global routine vaccination is among the most effective public health interventions. Routine vaccination has proven 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). However, challenges remain in delivering vaccines in some countries affected by mpox and other diseases of pandemic potential (WHO, 2024d).

Outbreak response immunisation programmes are effective at reducing transmission and the burden of infectious disease outbreaks, cutting deaths by up to 60 percent (Delport et al., 2025). However, they face some limitations. By definition, outbreak response vaccination occurs in response to zoonotic spillovers and does not prevent spillovers from occurring in the first place (OIE, 2022). Hayman et al. (2025) consider mpox from a One Health perspective and highlight the potential benefits of targeting human vaccination to mitigate zoonotic transmission and prevent seeding future outbreaks. Outbreak response vaccination also relies on timely and effective data to identify outbreaks and deploy vaccination before the outbreak becomes too widespread (Grais et al., 2006; Shankar et al., 2024).

Additionally, while stockpiles can be useful for rapid response, holding appropriately sized stockpiles is challenging because projected demand is highly variable (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"; however, they do not conduct a detailed assessment of the impact of this wider distribution. Therefore, our research aims to assess the net health benefit and cost-effectiveness of routine mpox vaccination from the perspective of national healthcare payers in Africa, and globally. This is because routine vaccination would likely have a greater epidemiological impact than outbreak response vaccination.

We define routine vaccination as the universal vaccination of children in a given geographic area around the age when they receive other routine childhood vaccines. We also consider routine and catch-up vaccination, in which vaccines would be administered to adolescents and adults who are too young to have previously received smallpox vaccination (i.e., younger than approximately 50 years).

Related mpox modelling

Since the launch of our study, other modelling studies on mpox vaccination in Africa have been published. First, Savinkina et al. (2024) use a dynamic transmission model to simulate the impact of age-stratified vaccination in the DRC. They find that vaccination of 80 percent of children under 5 in endemic regions would reduce infections by 27 percent and deaths by 43 percent, requiring 10.5 million vaccine doses. They do estimate change in cases by subnational areas, but they do not consider vaccination outside the DRC, do not include cost-effectiveness results, and do not capture the potential benefits of vaccination outside the DRC. Second, Jin et al. (2025) adapted a next-generation matrix model to simulate the disease transmission potential for 47 sub-Saharan countries. They estimate the effective reproduction number at present and through 2050 under four transmission scenarios with varying contributions from community versus sexual contacts. They find that, depending on their assumptions about contact patterns, the minimum required coverage to end the epidemic ranges from 0 to 19.5 percent, and this threshold is expected to increase over time.

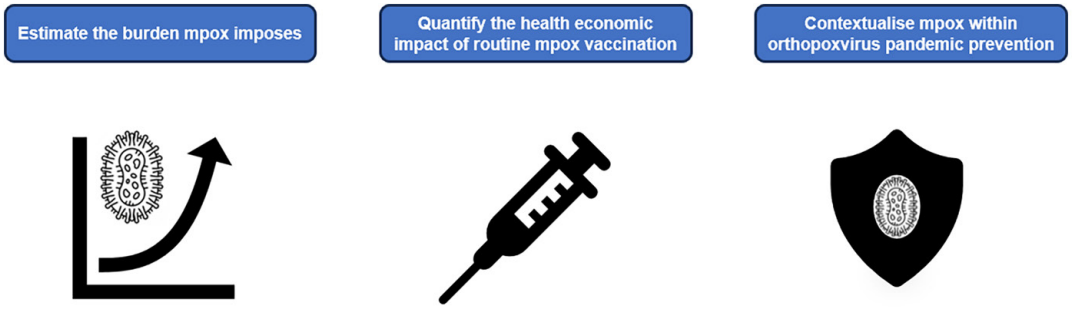
The authors discuss the challenges of appropriately modelling the epidemic using dynamic methods, due to limitations and uncertainties in the evidence on contact patterns, which are further discussed in Appendix 12. The authors do not provide subnational estimates, cost-effectiveness estimates, or estimates of the impact of reducing transmission in Africa on the global spread of MPXV.

Research objectives

Given the growing threat mpox poses and the demonstrated value of vaccination, this research investigates the potential role of routine mpox vaccination in preventing future pandemics. Specifically, we address the following research questions:

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

FIGURE 1. Summary of modelling study



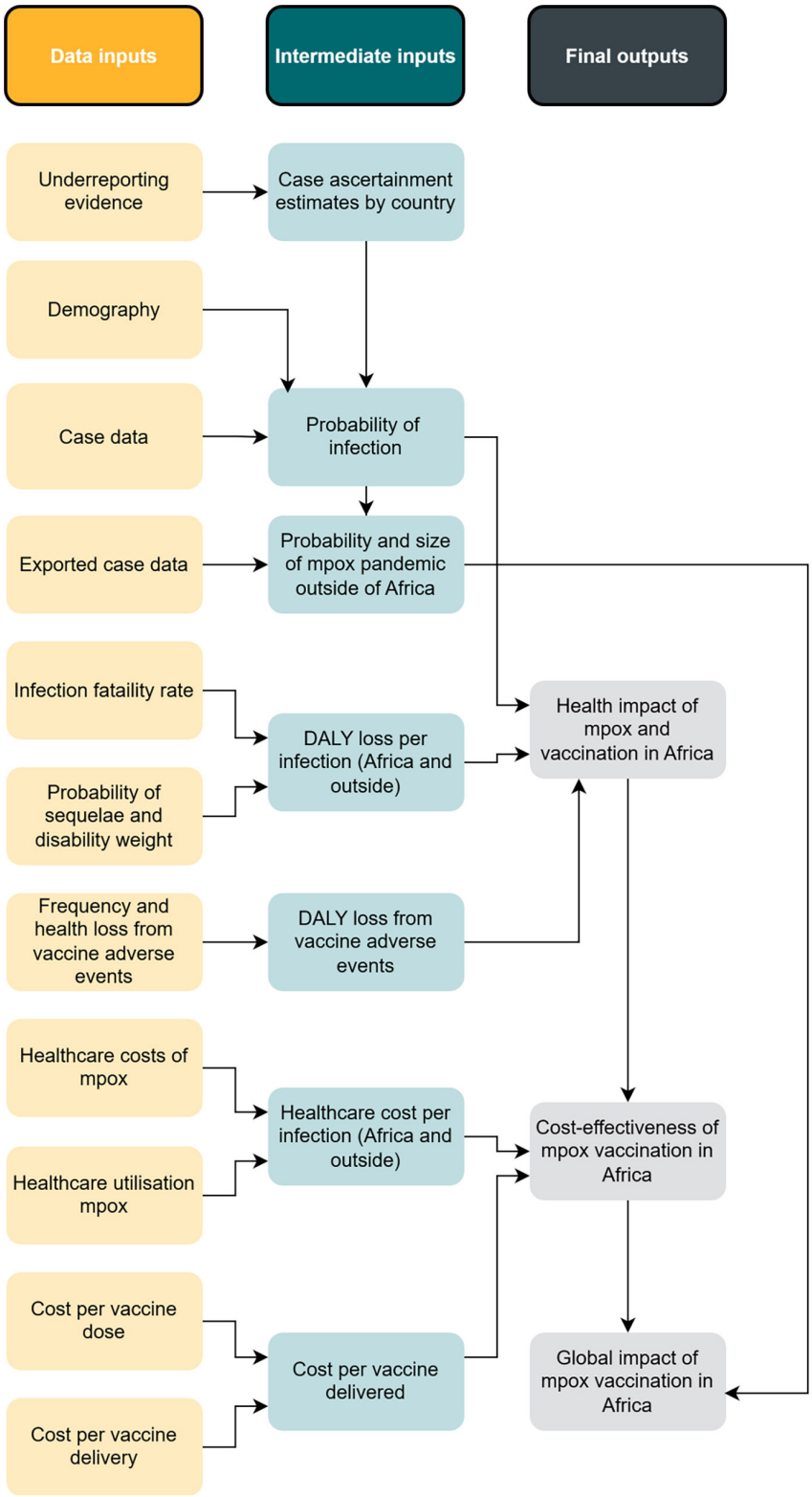
Methods

Figure 2 shows the study's overall methodological structure. We combine data and evidence on mpox epidemiology, disease burden, and costs of mpox vaccination and treatment into an integrated modelling framework.

Given that mpox disproportionately affects certain age groups and subnational geographies, we map all data to these granular categories. The approach has two key limitations:

1. Data on mpox in Africa are already very imprecise, even compared with other epidemiological data. This imprecision (and resulting uncertainty) increases as the level of disaggregation increases.

FIGURE 2. Modelling structure to assess the potential cost-effectiveness of mpox routine vaccination in endemic regions and its impact on pandemics



2. We have mapped subnational geographic data to administration level 1 (admin-one) geographies. Admin-one geographies are called provinces in the DRC; henceforth referred to as provinces for all countries. Some countries have far greater populations in admin-one geographies than others. Therefore, we disaggregate data for some countries more than others. The more we disaggregate data, the more likely it is to identify a subgroup within a country that may benefit from a universal routine vaccination programme for everyone in an age group in that area.

We include countries in the model that reported more than 100 cases or had positive serology data when we started the study in January 2025 (see Table 1).[2]

TABLE 1. Countries included in the model

ISO3	Country (official short name)
COD	Democratic Republic of the Congo
BDI	Burundi
UGA	Uganda
NGA	Nigeria
CAF	Central African Republic
GHA	Ghana
CIV	Côte d'Ivoire
RWA	Rwanda
LBR	Liberia
CMR	Cameroon
COG	Republic of the Congo
KEN	Kenya
SDN	Sudan
SSD	South Sudan
SLE	Sierra Leone

We also disaggregate cases and parameters by sub-clade of MPXV where possible. The sub-clades we capture are Ia, Ib, IIa, and IIb. The exact parameters are included in relevant sections. At a high level, we assume clade Ia is less transmissible than other clades. We assume case fatality risk is highest for Ia, followed by IIa and IIb, and lowest for Ib. The exact characteristics of clade IIa are the least important for the model results, because that clade is estimated to cause the fewest infections post-2016. We assume nonfatal symptom frequencies are constant. Our assessment of transmissibility and fatality risk is highly uncertain because these clades have not been studied in comparable populations with robust data (Hoffmann, 2024; UKHSA, 2025d). We assume the vaccine is similarly effective against all strains.

2 We did not include Guinea in the modelling because it did not meet the inclusion criteria at the time the study was initiated.

Data

Population data

Unfortunately, disaggregated data by age and province over time were not available for all countries in our model. We use data from the Humanitarian Data Exchange and the US Census Bureau International Database to produce estimates (at province level) of population by age back to 1970 (US Census Bureau, 2024; OCHA, 2025). The methodology and data sets used for this are presented in Appendix 1.

Case data

Sources for national case data used are set out in Appendix 2. At a high level, cases are aggregated by Bunge et al. (2022) for 1970–2019; by McCollum et al. (2023), a US Centers for Disease Control and Prevention (CDC) report, for 1971–2021; and by the WHO mpox dashboard for 2022–2025 (WHO, 2025a). Suspected case data were preferred over confirmed cases if available for countries in Africa; this choice was made because mpox is a relatively specific condition to diagnose without laboratory confirmation, leading to a relatively high rate of confirmation (WHO, 2025a).

Furthermore, laboratory confirmation is disproportionately unavailable in some areas with a high mpox burden. This means the confirmed case data can be hard to interpret. The suspected case data also have considerable limitations, which are further explored in Appendix 2. All case data are up to date as of the end of July 2025. As a result, the 2025 data reflect only a partial year, but including that partial year is key for some countries affected by ongoing outbreaks.

We estimate the proportion of cases in a given subnational geography attributable to a given clade using data from the WHO (WHO, 2025a). In general, it is better understood whether clade I or clade II is causing cases in a local area, rather than which specific sub-clade.

Case ascertainment estimates

Our systematic literature review identified 15 eligible papers based on the criteria in Appendix 3. Among those papers, we identify 39 different case ascertainment estimates, only three of which are for countries in Africa. The estimates are 11 percent (7 percent–20 percent) for the DRC (Hoff, 2014), 0.8 percent (0.3 percent–3.7 percent) for Nigeria (Marwah et al., 2022), and 3 percent (1 percent–8 percent) for South Africa (McCabe et al., 2025). The estimate for the DRC involves modelling but does not adjust for people experiencing mild symptoms or not realising they have mpox. The 2022 mpox pandemic made it clear that many patients with mpox may have no symptoms, mild symptoms, or symptoms on parts of the body that carry stigma, and therefore are unlikely to seek treatment in the DRC (Matusali et al., 2023; Prasad et al., 2023; Rossotti et al., 2023). We adjust the DRC value, reducing the case ascertainment estimates by 50 percent to account for this. That estimate is still considerably

higher than the other two for countries in Africa that spend more on health and achieve better health outcomes than the DRC.

Serology data

Our systematic review identified 10 papers that were screened as eligible for inclusion. The criteria are set out in Appendix 4. Those 10 papers yield 19 estimates of IgG antibodies against OPXVs from 1982 to 2017 and three estimates of IgM antibodies for the same period.

For IgG, the estimates are 6.3 percent for Centre (Cameroon), 19 percent (14 percent–26 percent) for Cavally (*Cote d'Ivoire sample from 2007*), 25 percent (16 percent–37 percent) for Cavally (*Cote d'Ivoire sample from 2012*), 26 percent (18 percent–35 percent) for Nord Kivu (DRC), 26 percent (18 percent–35 percent) for Mai Ndombe (DRC), 46 percent for Eastern (Ghana), 49 percent for Likouala (Republic of Congo), 0.3 percent–2.4 percent for Sankuru (DRC) depending on ages 0–19, 4.8 percent for Nairobi (Kenya), 19 percent for Pool (Republic of Congo), 11 percent for Sangha (Republic of Congo), and 1.3 percent for Eastern (Sierra Leone).

For the final four IgG estimates, the exact geographic sampling strategies were not described—therefore, we assume them to be national estimates focusing sampling in endemic areas. Those estimates are 17 percent for Côte d'Ivoire, 16 percent for Sierra Leone, 15 percent for the DRC, and 3.6 percent for the DRC.

For IgM, the estimates are 1.6 percent Centre (Cameroon), 1.1 percent Likouala (Republic of Congo), and 0.5 percent Eastern (Sierra Leone).

We encounter several challenges in interpreting the serology data. First, serology suggests that unvaccinated individuals may have OPXV antibodies in regions where they have likely never been exposed to MPXV or other OPXV (Ogola et al., 2021; De Vos et al., 2024). Second, the serology data imply that a substantial proportion of people are contracting OPXVs in places where MPXV transmission is possible but where few or no cases of mpox (or other OPXV) have been reported. Finally, none of these serology studies are representative of a national (or even province) population; they are generally opportunistic, in high-risk groups, or in response to an outbreak, and so they likely quantify antibody levels in unrepresentative populations.

Modelling

Overall

We assess the cost-effectiveness of mpox vaccination by modelling a hypothetical campaign that would have been rolled out in 2016. This is because we do not make detailed predictions about future mpox transmission, so instead we consider the value vaccination could have had in a "what-if"

scenario. To make our modelling more tractable, we assume the vaccine provides protection to the affected age groups from the start of 2016 and do not consider people aging out of the protected age group. Although this means that, in practice, babies born after 2016 receive protection, it effectively matches the 10-year costs and benefits of a campaign.

Case ascertainment regression

Our case ascertainment review yielded estimates for just three African countries, two of which are in our model. Therefore, we need to estimate realistic case ascertainment rates for the other countries in our model (see Table 1). We can also use the results of the case ascertainment regression in our outside-of-Africa pandemic model to estimate the true number of infections globally.

We use a Bayesian beta regression model to estimate the relationship between covariates (per capita health spending and the Institute for Health Metrics and Evaluation's [IHME's] Health Access and Quality Index) and case ascertainment estimates identified in our review. For the full methodology for this regression model see Appendix 10.

Infection modelling

We adjust case estimates to account for infections using a simple methodology that adjusts for nationally estimated underreporting of cases (see Appendix 6 for more details). We also attempted to develop a more comprehensive Bayesian model of infection risk for individuals in the African countries included in the model. This modelling aimed to account for case ascertainment estimates, cases reported, and serology. Unfortunately, the serology data were deemed of insufficient quality and often inconsistent with case data, so fitting a more complex model was not possible (see Appendix 7 for more details).

Direct within-Africa cost-effectiveness

In our modelling, we account for the benefits of mpox vaccination both in Africa and globally. However, this section focuses solely on the mpox vaccine's impact from the perspective of people in affected areas in Africa, in line with the principle of non-maleficence. While global benefits—such as preventing exported infections and reducing the risk of broader pandemics—are important, our ethical starting point is whether individuals would receive greater benefits than harms from vaccination.

Therefore, we start by assessing the impact of vaccines on the probability an individual is infected with mpox without vaccination using equation 1.

$$cumul\_I_{j,a,y} = \sum_{y_p=y_v}^{y_p=y} I_{j,a_p,y_p}, \quad (1)$$

where $cumul\_I_{j,a,y}$ is the cumulative infection risk for someone in province j, at the upper limit of age group a in year y; I_{j,a_p,y_p} is the infection risk for an individual in province j, in age group a_p, which is the age group someone in age group a would have been in in year p; and y_p is the year p. This infection risk is summed between y_v and year y.

Adding vaccination to equation 1 leads to equation 2.

$$cumul\_I_{j,a,y} = \sum_{y_p=y_v}^{y_p=y} I_{j,a_p,y_p} \times V \times C_{j,a_p,y_p}, \quad (2)$$

where V is vaccine effectiveness (for two doses) and C_{j,a_p,y_p} is the coverage rate of the vaccination in province j, in the age group a_p and year y_p.

The expected health loss from mpox infections and adverse events (AEs) is captured in equation 3.

$$DALY_{j,a,y} = DALY_{mpox} \times cumul\_I_{j,a,y} + DALY_{vacc} \times C_{j,a,y_v} \times Pop_{j,a,y_v}, \quad (3)$$

where $DALY_{j,a,y}$ is the disability-adjusted life year (DALY) loss for people in province j, in the age group a_p and year y; $DALY_{mpox}$ is the average DALY loss from an mpox infection; $DALY_{vacc}$ is the average (minor) DALY loss from vaccine AEs; and Pop_{j,a,y_v} is the population size province j, in the age group a and year y_v when they received their vaccines.

The expected expenditure on healthcare is estimated with equation 4, where both the cost of vaccines and the cost of mpox treatment are included.

$$E_{j,a,y} = (r_O \times P_O + r_I \times P_I) \times cumul\_I_{j,a,y} + P_{v,a} \times C_{j,a,y_v} \times Pop_{j,a,y_v}, \quad (4)$$

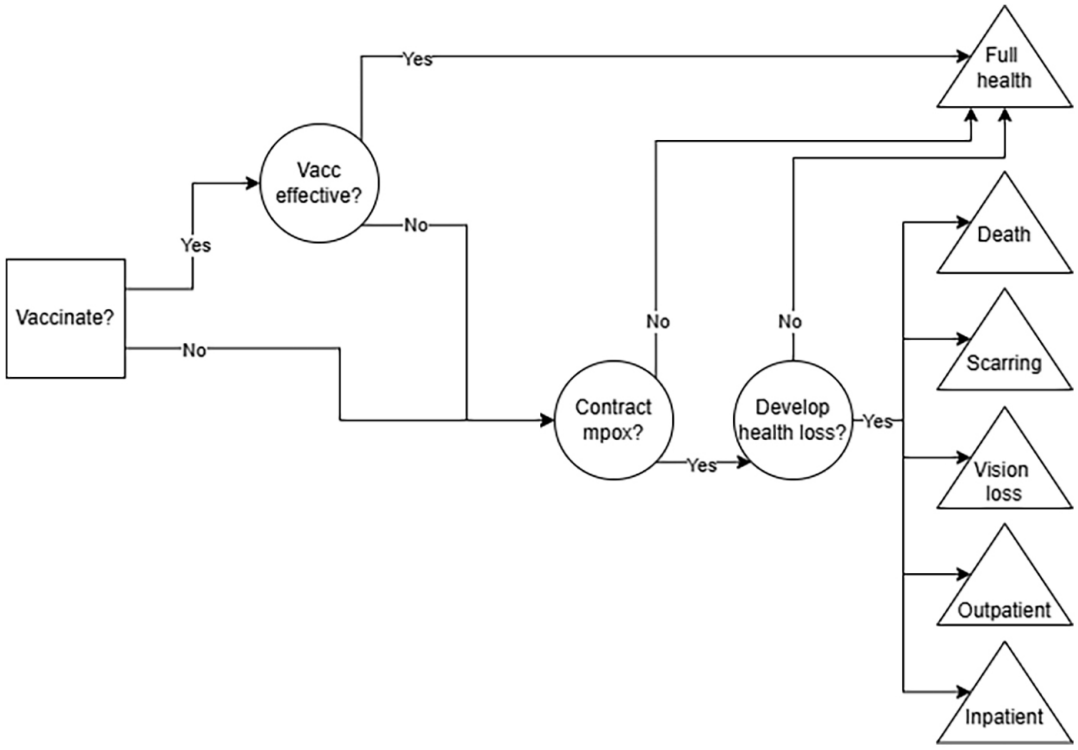
where $E_{j,a,y}$ is the expenditure on health care in province j, in the age group a and year y; r_o and r_I are the outpatient treatment rate and inpatient treatment rate, respectively; P_O and P_I are the cost of outpatient treatment and inpatient treatment, respectively; and $P_{v,a}$ is the cost of vaccinating an individual in age group a against mpox with two doses (it accounts for the cost of vaccines and the cost of delivery).

The ICER (incremental cost-effectiveness ratio) is shown in equation 5.

$$ICER_{j,a,y} = \frac{E_{vacc} - E_{no}}{DALY_{vacc} - DALY_{no}}. \quad (5)$$

We depict the logic of the model diagrammatically in Figure 3.

FIGURE 3. Vaccination model structure for the cost-effectiveness of mpox vaccination from the perspective of a national healthcare payer in Africa



Indirect pandemic prevention return on investment

Equation 2 in the "Direct within-Africa cost-effectiveness" section outlines how we model the vaccine's impact on the direct transmission of mpox. Vaccinating people indirectly affects transmission because vaccinated individuals who do not acquire the disease do not spread it to others. A full model of disease transmission dynamics (in a compartmental or individual network model) was deemed not in scope for several reasons set out in Appendix 9. Instead, we include an illustrative fixed parameter for the impact of infections directly avoided through vaccination on indirectly avoided infections. We assume 0.5 indirectly averted infections per directly averted infection (Appendix 9). After this adjustment, we have our estimated number of infections in Africa with and without vaccination. We run this model separately for each of the four sub-clades in our analysis.

We then consider the rate of exported infections from Africa to countries outside of Africa and compare that with our estimated burden of infections in Africa. This suggests that almost all infections do not leave the continent, because of the relatively low rate of international travel in regions disproportionately affected by mpox and the short infectious period. For context, there

were 64 confirmed cases outside Africa before the 2022 clade II pandemic (only 17 of which were directly exported, with 47 linked to the 2003 outbreak in the United States from infected imported prairie dogs). We calibrate the model so that ~64 exported cases corresponds to a 50 percent probability of a large outbreak outside Africa, and assume this probability can be converted into a binomial as specified in equation 6.

$$n_{pandemic} = Binomial(n, p). \quad (6)$$

The chance of an individual confirmed export starting a pandemic is p for each export.

In practice, ascertainment of exported cases is likely considerably below 1, so this is a partially hidden process; however, higher ascertainment would lead our estimate of n to be proportionately higher and so p proportionately lower.

We use historical data, without adjusting for whether a pandemic is now more or less likely than previous data imply. This assumption is discussed in detail in Appendix 12.

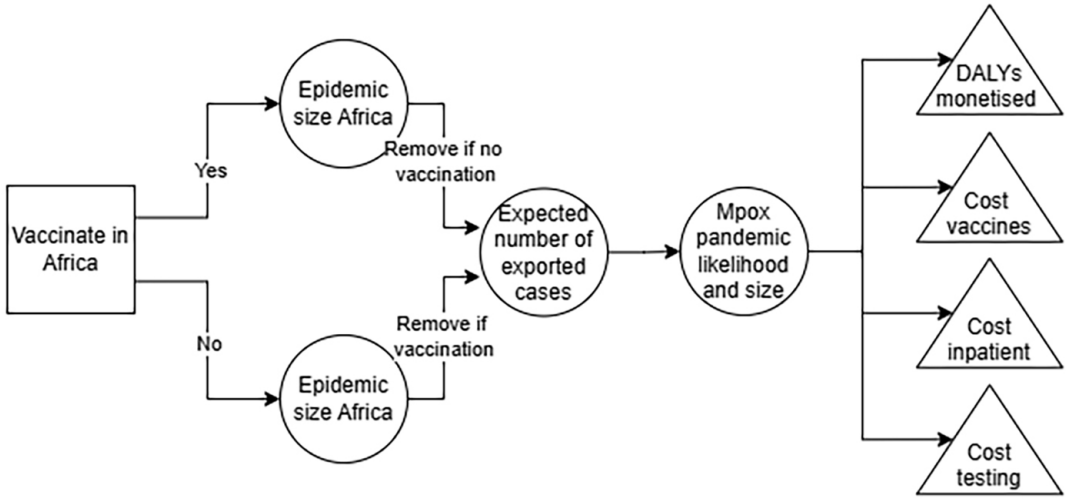
Each pandemic can vary in size as shown in equation 7.

$$(I_1, \ldots, I_n) \sim NegBin(r = k, p = k + \mu k). \quad (7)$$

NegBin is a negative binomial distribution, commonly used for outbreak size estimation (Lloyd-Smith, 2007; Blumberg and Lloyd-Smith, 2013; Love et al., 2023; Charniga et al., 2024). In the central case, we run the model 100,000 times to simulate different distributions of possible pandemics and compute the average. In our probabilistic sensitivity analysis, we simulate one draw only for the number of pandemics and the size of each over the 10-year modelling period. This means that, in some model runs, vaccination may appear to have no effect when a pandemic occurs in neither the vaccinated nor the unvaccinated case. None of these pandemics allows for a mutation in MPXV to be more transmissible in humans, as these simulations are only modelling different potential distributions of the current pathogen(s).

We use the size of the ongoing 2022 pandemic of clade IIb outside of Africa (assuming it has reached its limit) as μ (the mean size of a pandemic), and we use the level of overdispersion estimated by Paredes et al. (2024) as k. We adjust the mean size downward for clade Ia, because that sub-clade may be less transmissible, although the different epidemiological and clinical characteristics of the clades are highly uncertain (Hoffmann, 2024; UKHSA, 2025d). Figure 4 shows the overall logical flow of the model.

FIGURE 4. Overall logical flow of the global pandemic modelling



Health and economic parameters

Parameter values in the model are set out in Tables A9.1, A9.2, and A9.3 in Appendix 9, along with a detailed explanation of the rationale for certain parameters and adjustments performed on them.

Parameters used across the modelling

This section focuses on the most influential parameters used. We assume the threshold for cost-effectiveness and the monetised value of a DALY is a country's GDP per capita, the lower end of the WHO's recommended cost-effectiveness threshold (Kazibwe et al., 2022). This is higher than supply-side estimates of the opportunity cost of healthcare spending for relevant countries (Ochalek et al., 2018), but likely lower than relevant demand-side willingness-to-pay estimates (Vallejo-Torres et al., 2016; Thokala et al., 2018), which have been found to be multiples of GDP per capita. Supply-side estimates of the opportunity cost of healthcare spending are not available for all countries in our global model; therefore, this approach is not feasible for our study, even though it is increasingly considered best practice (Drake et al., 2023). However, where supply-side estimates are available for specific countries (like the DRC), we compare incremental cost-effectiveness ratios (ICERs) to both these empirical estimates and the simpler 1x GDP per capita threshold. We use a discount rate of 3 percent for both costs and benefits.

Parameters used for Africa only

Vaccine costs are assumed to be US$10 per dose, with various sensitivities run (US$2–100). Healthcare costs are quantified using WHO-Choice and length-of-stay evidence for mpox inpatients (WHO-Choice, 2021). We assume vaccination coverage of 80 percent for either routine vaccination (in young children) or for catch-up vaccination (in people 10 years old and above); this is the coverage

observed in key geographies for some forms of routine vaccination, but it may be too high in practice for mpox vaccination uptake, particularly catch-up vaccine programmes. Modelling vaccine demand was considered outside the scope of this project. DALY loss from mpox and vaccine AEs is estimated for Africa.

Some subnational areas included in the model are classified as "fragile and conflict-affected." Insecurity can raise delivery costs and reduce achievable vaccination coverage. Unfortunately, we do not currently have a robust, generalisable basis for parameterising subnational cost and coverage across countries, either to account for this effect or others. We cover the implications of this lack of data and evidence in the "Discussion" section.

The mpox outcomes selected for their materiality in contribution to total DALY burden are as follows: mortality, lifetime scarring, and minor lifetime vision impairment. To capture mortality, the base infection fatality rate (IFR) for ascertained cases in Africa is 0.25 to 2.5 percent, depending on the clade, and life expectancy is sourced from the World Bank. Vaccine AEs are not available for infants in Africa, but a trial is ongoing; therefore, we approximated the expected DALY loss from AEs based on data from adults in high-income countries (HICs), where the vaccine has been demonstrated to be safe, with only minor AEs reported. Further details of this methodology are provided in Appendix 8.

Parameters used for the rest-of-the-world pandemic modelling only

In this part of the modelling, we assess the global return on investment (ROI) of vaccinating in Africa past the point of cost-effectiveness (only considering the perspective of African populations). To do this, we assume vaccination is rolled out up to the point of US$10,000 per ICER. This exact parameter is arbitrary. Setting it lower would lead to a narrower, more targeted campaign, with a smaller impact on infections but at a higher global ROI (see Figure 22 in the results).

We take a similar approach to estimating DALYs from mpox in the rest of the world, albeit with lower risk of mortality and sequelae due to better access to healthcare (see Table A9.3). We also approximately value testing, responsive vaccination, and direct treatment costs in the rest of the world. Where rest-of-the-world estimates are based on the 2022 pandemic caused by clade II, we adjust those values to account for clade Ia potentially being more severe and clade Ib potentially being less severe, when a simulated pandemic is caused by a different clade.

Sensitivity analysis

For each analysis, we vary most parameters in a probabilistic uncertainty analysis, with the parameter bounds and distributions listed in Table A9.4. In our probabilistic sensitivity analysis,

all parameters are varied independently. These simulated parameters are then shared in the vaccination and no-vaccination arms of each scenario to aid interpretability. When we report ranges around results in brackets—that is, (L: xx–U: xx), where L stands for lower bound and U for upper bound—those ranges represent the 5th and 95th percentiles of the credible intervals resulting from the simulations. We also conduct deterministic sensitivity analyses for each parameter and assess its contribution to the headline results. Finally, we vary specific key parameters (vaccine cost per dose and the extent of vaccine administration in the pandemic modelling) across a range of plausible values.

Results

Summary of confidence in the following results

Table 2 sets out the confidence ratings for the different results presented in this paper. The drivers of the confidence ratings are explored in the "Discussion" section but are highlighted here to help readers frame the results.

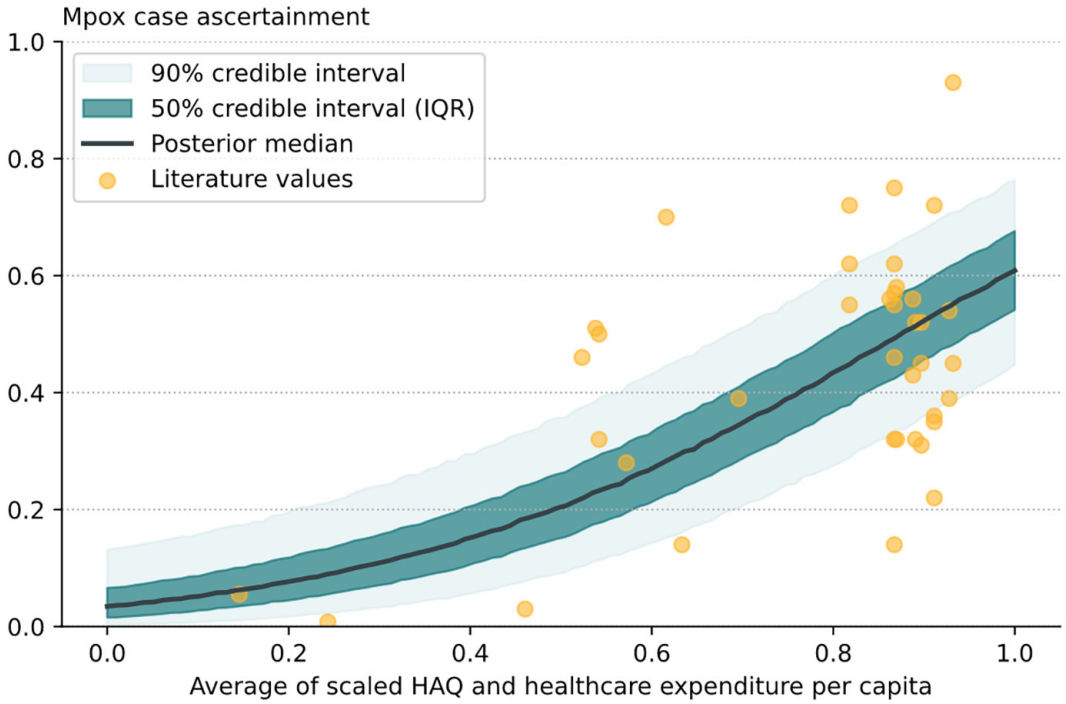
TABLE 2. Confidence ratings for the analytical methods and emerging results

Results Section	Confidence Rating
Case ascertainment regression modelling	Low confidence
Simple infection modelling	Low confidence
Within-Africa cost-effectiveness	Low confidence
Global pandemic modelling	Very low confidence

Case ascertainment regression modelling

Diagnostics suggest good convergence and stable posterior estimates across the model. For exact values of the parameters of the regression, see Appendix 5. The relationship estimated between case ascertainment and the covariates (IHME's Health Access and Quality Index and log-transformed healthcare expenditure per capita) is shown in Figure 5. It shows that as the covariates increase from their minimum value to their maximum value, median case ascertainment is expected to increase from 3 percent (1 in 33 infections reported as cases) to 61 percent (3 in 5 infections reported). There is considerable uncertainty in these estimates, and some observed values from the literature used to estimate the model fall outside this wide uncertainty. Even in HICs (which have covariates roughly above 0.8), case ascertainment can plausibly be between 30 and 75 percent.

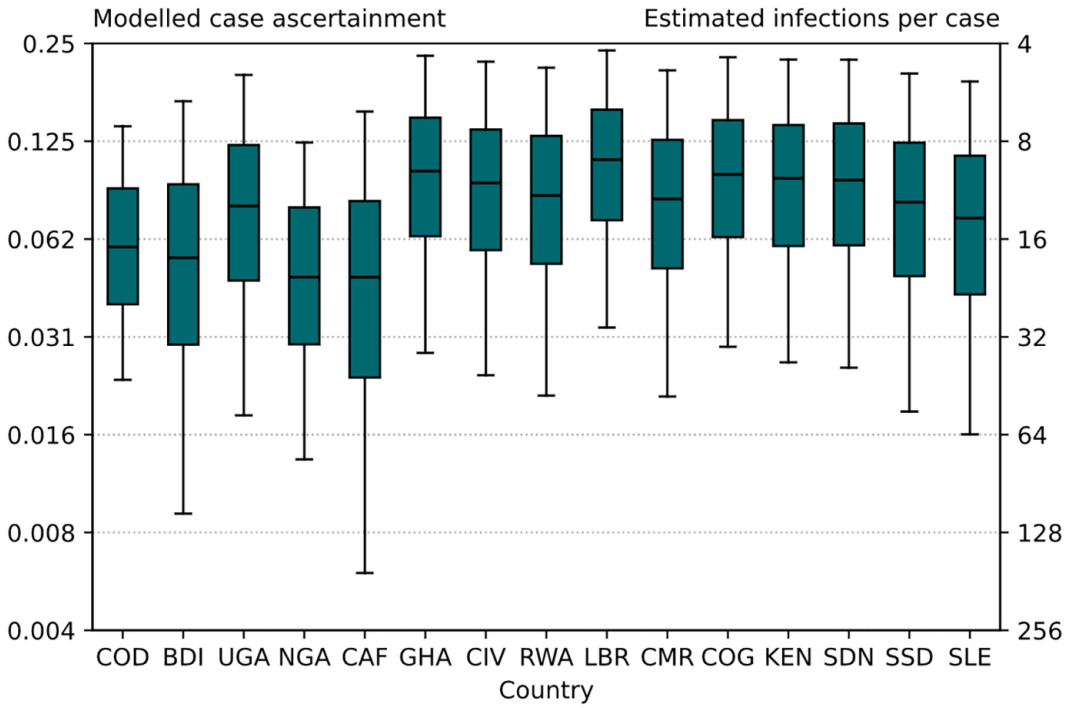
FIGURE 5. Modelled mpox case ascertainment compared to estimated case ascertainment from the literature



Notes: IQR = interquartile range; HAQ = Health Access and Quality Index.

Figure 6 shows the case-ascertainment estimates for each model country. The DRC and Nigeria have tighter estimates because the displayed values are the combination of the model and the estimate from Hoff (2014) for DRC and Marwah et al. (2022) for Nigeria. For the DRC (COD), the median case ascertainment is 6 percent, with an interquartile range of 4–10 percent. The 90 percent credible interval is approximately 2 percent–13 percent. The lower value (2 percent) is potentially infeasible because there were approximately 80,000 cases in the DRC in 2024, implying 4 million infections out of approximately 100 million people, or 4 percent of the population infected. However, this statistical model has no mechanism to constrain these potentially infeasible values. Countries like Burundi (BDI) and Central African Republic (CAF) have lower expected values because their values of the covariates are lower, while countries like Ghana (GHA) have higher expected values.

FIGURE 6. Boxplot showing uncertainty of modelled mpox case ascertainment by country



Notes: The horizontal dashes at the end of the *whiskers* are the 90 percent credible intervals. The external horizontal lines of the boxes are the l interquartile ranges. And the median values are the horizontal lines internal to the boxes.

Simple infection modelling

Table 3 shows the 20 province/age group pairs with the highest cumulative lifetime infection risk from mpox; it shows the risk of being infected by the upper limit of the band (e.g., 0–9 is the risk of infection before the child's 10th birthday). All of these populations are in the DRC, with the highest expected cumulative lifetime infection risk estimated at 38 percent for 10-to-19-year-olds in Sankuru. The higher upper estimate of infection risk in this case, at approximately 97 percent, is likely infeasibly high because there is no constraint on the model estimating infections above 100 percent (which we do not observe in practice). These provinces may have higher case ascertainment than others, which would overestimate infections in the base case; however, our wide range of case ascertainment should encompass the true value. Some of the provinces shown may also have underestimated populations, given that population estimates for hard-to-reach areas are relatively uncertain (Boo et al., 2022).

TABLE 3. Results of the infection modelling for the 20 most affected age group/province combinations

ISO3	Province	Age Range 2025	Mpox Cases per Capita	Infections Estimate Median	Infections Estimate Lower	Infections Estimate Lower IQR	Infections Estimate Upper IQR	Infections Estimate Upper
COD	SANKURU	10–19	2.24%	37.93%	16.15%	25.06%	56.93%	97.33%
COD	SANKURU	00–09	2.23%	37.64%	16.02%	24.87%	56.49%	96.58%
COD	TSHUAPA	10–19	1.62%	27.35%	11.64%	18.07%	41.05%	70.18%
COD	SANKURU	20–29	1.58%	26.77%	11.39%	17.69%	40.18%	68.69%
COD	TSHUAPA	00–09	1.55%	26.18%	11.14%	17.30%	39.29%	67.17%
COD	EQUATEUR	00–09	1.27%	21.39%	9.11%	14.13%	32.11%	54.89%
COD	TSHUAPA	20–29	1.11%	18.79%	8.00%	12.42%	28.21%	48.22%
COD	SANKURU	30–39	1.09%	18.40%	7.83%	12.16%	27.62%	47.22%
COD	BAS UELE	00–09	1.07%	18.13%	7.72%	11.98%	27.21%	46.51%
COD	EQUATEUR	10–19	0.98%	16.58%	7.06%	10.96%	24.89%	42.55%
COD	BAS UELE	10–19	0.90%	15.28%	6.50%	10.10%	22.93%	39.21%
COD	SANKURU	40–49	0.87%	14.73%	6.27%	9.73%	22.11%	37.80%
COD	TSHUAPA	30–39	0.74%	12.57%	5.35%	8.31%	18.87%	32.27%
COD	SUD UBANGI	00–09	0.72%	12.09%	5.15%	7.99%	18.15%	31.03%
COD	SUD KIVU	00–09	0.67%	11.32%	4.82%	7.48%	16.98%	29.03%
COD	SUD UBANGI	10–19	0.61%	10.24%	4.36%	6.77%	15.37%	26.27%
COD	TSHUAPA	40–49	0.59%	10.03%	4.27%	6.63%	15.05%	25.74%
COD	SUD KIVU	10–19	0.57%	9.70%	4.13%	6.41%	14.56%	24.89%
COD	TSHOPO	00–09	0.57%	9.61%	4.09%	6.35%	14.42%	24.65%
COD	BAS UELE	20–29	0.57%	9.56%	4.07%	6.32%	14.35%	24.53%

Note: IQR = interquartile range.

Figure 7 shows a map of infections, coloured on a logarithmic scale, indicating the proportion of children turning 10 who are estimated to have been infected in 2025. It shows that mpox transmission is highly concentrated in the DRC, with other surrounding countries also somewhat affected. Other countries in West Africa that have historically had endemic clade II are estimated to have been less affected over the last 10 years. Figure A11.2 shows the same map but for cumulative risk by age 30, as some areas have experienced larger outbreaks among young adults, with children ages 0–9 years less affected. Figure 8 shows that we estimate infections to have increased over time, consistent with the rise in reported cases; this is a direct result of our model structure, which does not allow case ascertainment to vary over time.

FIGURE 7. Cumulative probability of having been infected with mpox for a child turning 10 years old in 2025 (colour log scaled)

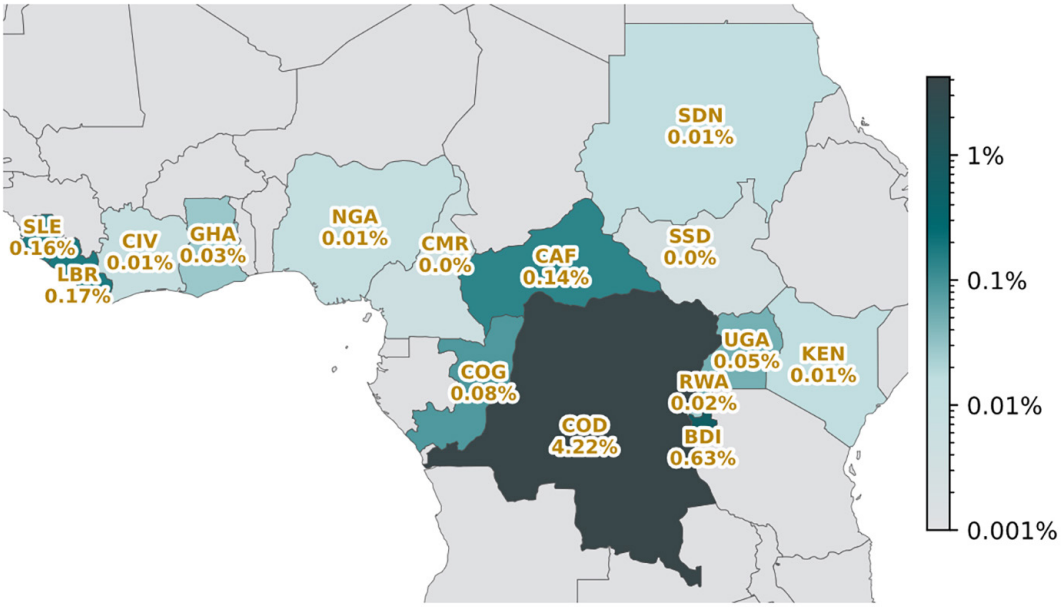
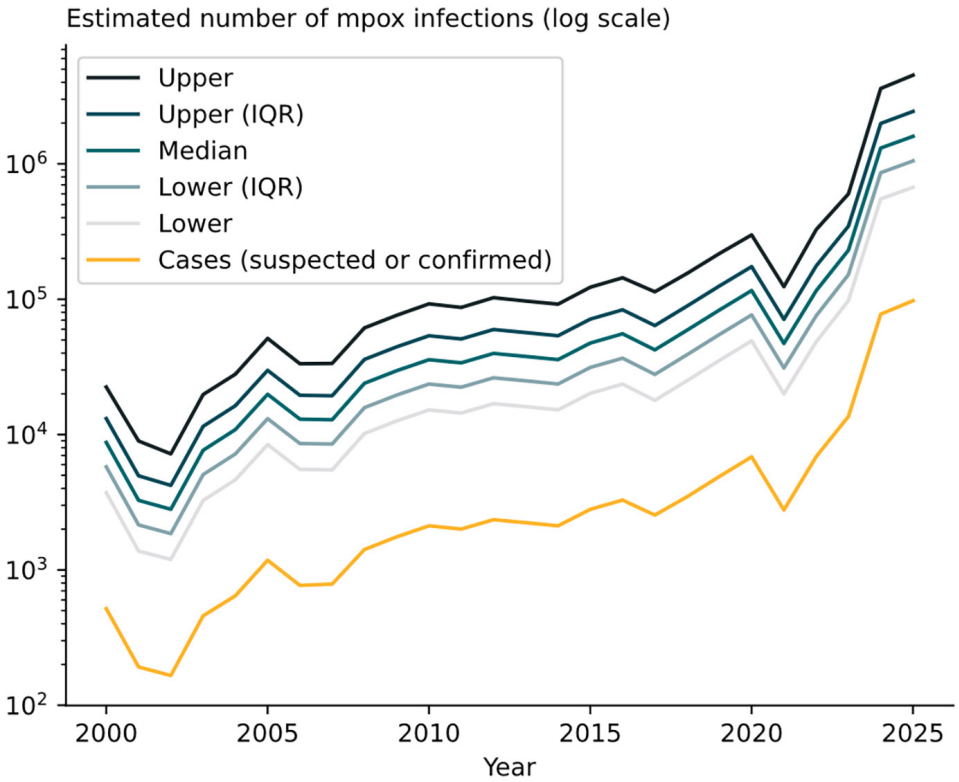


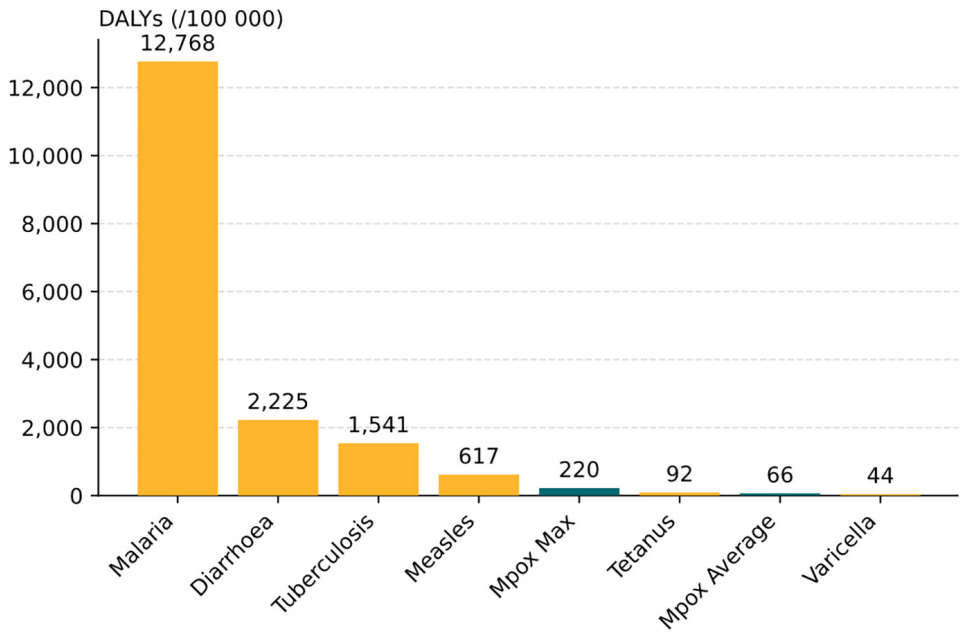
FIGURE 8. Estimated number of mpox infections increases over time linearly with reported cases



Note: IQR = interquartile range.

Figure 9 shows DALY rates per 100,000 for mpox, compared with those for other diseases in the DRC. While the illustration masks some subnational heterogeneity—since mpox is concentrated in specific regions—other diseases likely show considerable geographical variability as well. Even in its peak year (2024, "mpox max"), mpox causes substantially less burden among children ages 0–9 years than malaria, tuberculosis, or diarrhoeal disease, and far less in the 10-year average ("mpox average"), where those other diseases are likely to cause at least an order of magnitude higher burden.

FIGURE 9. DALYs per 100,000 population for Mpox and other diseases in the DRC for children



Notes: Our mpox DALYs are estimated for children ages 0–9 years, but non-mpox estimates are from the Global Burden of Disease Study 2021 for 0–14 year olds, which is a slightly broader age group (GBD 2021 Causes of Death Collaborators, 2024).

Within-Africa cost-effectiveness

Figure 10 shows that vaccination is health-positive among 23.2 million children ages 0–9 years in the DRC, where the mpox burden is high enough that benefits outweigh minor adverse events from vaccination. In areas that report more than 20 mpox cases per 100,000 population cumulatively over a 10-year period, routine vaccination is generally health-positive, suggesting that even modest outbreaks make routine vaccination health-improving. In low-burden provinces (shown in teal), even minor side effects may outweigh the benefits of a universal routine vaccine programme for a given age group. In such provinces, targeted vaccination (i.e., vaccination targeted in response to outbreaks or for individuals with behaviours that put them at higher risk of catching MPXV) is still likely to be health-positive.

FIGURE 10. 0–9 year old population of areas where universal vaccination is health-positive

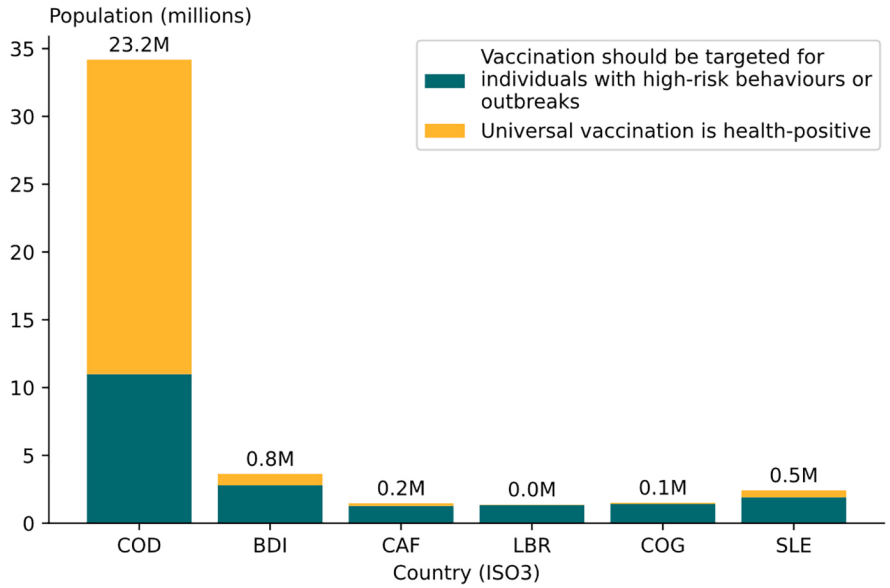


Figure 11 shows the same chart but allows for routine and catch-up vaccination in older ages as well. Vaccination would be health-positive for an additional 53.5 million people in the DRC. Uganda has one age group in one province (20–29 year olds) for whom universal vaccination is health-positive, despite having none where universal vaccination is health-positive for children ages 0–9 years. This is because mpox has been more prevalent among older age groups in Uganda. Again, many individuals in the teal areas would still benefit from more targeted vaccination campaigns.

FIGURE 11. Population of areas (routine and catch-up) where universal vaccination is health-positive

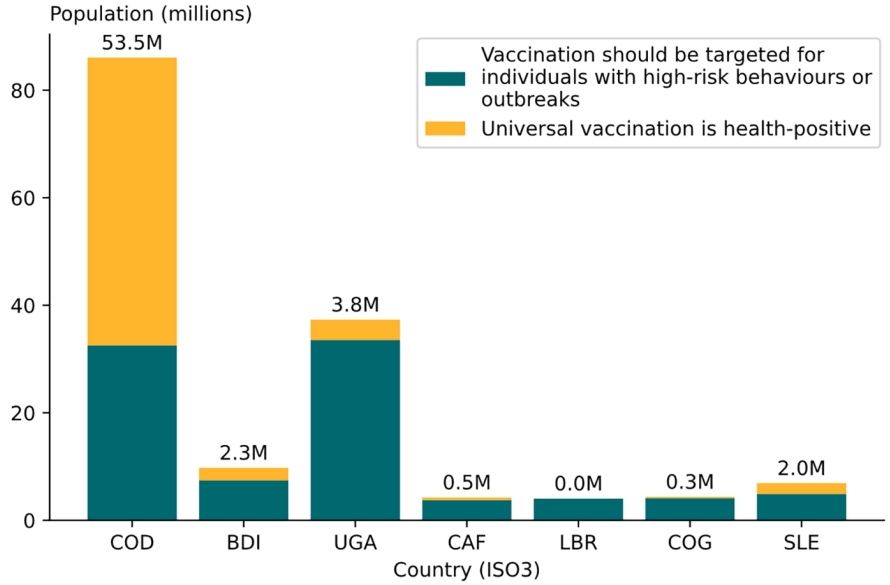


Table 4 presents the results of cost-effectiveness modelling of vaccination compared to no vaccination, considering only direct protection at US$10 per dose, from a national healthcare payer perspective. Only vaccination in children ages 0–9 years in Sankuru and Tshuapa has an ICER per DALY averted below GDP per capita (US$647), although some other areas (Equateur and Bas Uele) approach that threshold. Using the Ochalek et al. (2018) threshold of US$54 (2015 US dollars), routine mpox vaccination would not be cost-effective for any group.

Vaccination is cost-effective for places where more than 25 percent of the population is estimated to have been infected over a 10-year modelling period. Given resource constraints in such settings and an assumed cost per dose of US$10, high mpox attack rates would be necessary for vaccination to be considered cost-effective. This deliberately underestimates cost-effectiveness by excluding the benefits of averting onward transmission (within and outside Africa) to focus on the direct benefits to vaccine recipients.

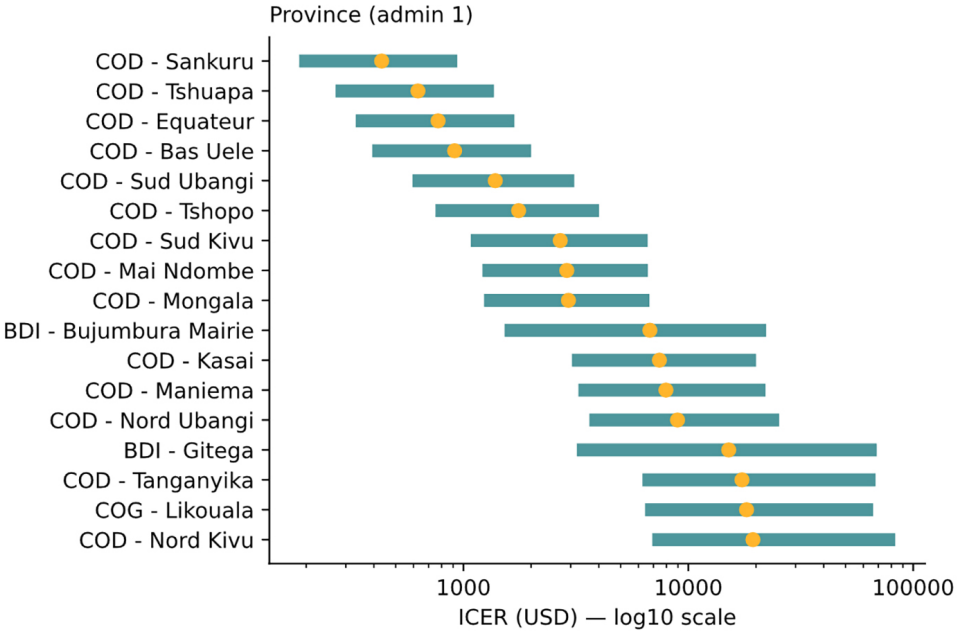
TABLE 4. Results of the cost-effectiveness modelling for the age group and geography combinations where vaccination is most cost-effective

ISO3	Admin-One Name	Age Range	Cases (/100k)	Infections (/100k)	Mpox DALYs Averted	Vaccine AE DALYs	Deaths Averted	ICER
COD	SANKURU	00–09	2,226	37,639	30,676	226	144	418
COD	TSHUAPA	00–09	1,548	26,179	19,988	211	100	606
COD	EQUATEUR	00–09	1,265	21,392	18,871	244	82	745
COD	SANKURU	10–19	1,684	28,476	14,630	154	109	762
COD	BAS UELE	00–09	1,072	18,128	7,220	110	69	883
COD	TSHUAPA	10–19	1,111	18,781	9,794	156	72	1,166
COD	SUD UBANGI	00–09	715	12,094	12,508	286	46	1,338
COD	SANKURU	20–29	945	15,973	5,020	106	61	1,550
COD	TSHOPO	00–09	568	9,606	9,540	275	37	1,698
COD	EQUATEUR	10–19	743	12,569	7,572	180	48	1,761
COD	BAS UELE	10–19	715	12,083	3,612	90	46	1,833
COD	TSHUAPA	20–29	729	12,323	4,149	113	47	2,026
COD	SANKURU	30–39	861	14,557	2,647	73	56	2,056
COD	SUD UBANGI	10–19	536	9,071	6,413	212	35	2,466
COD	SUD KIVU	00–09	669	11,316	17,620	753	13	2,553
COD	TSHUAPA	30–39	654	11,058	2,185	80	42	2,736
COD	MAI NDOMBE	00–09	355	5,996	4,498	208	23	2,774
COD	MONGALA	00–09	349	5,901	5,363	252	23	2,821
COD	BAS UELE	20–29	451	7,627	1,570	69	29	3,337
COD	TSHOPO	10–19	378	6,386	4,785	224	24	3,558
COD	SUD UBANGI	20–29	405	6,849	3,118	153	26	3,737
COD	EQUATEUR	20–29	402	6,802	2,629	130	26	3,764
COD	SUD KIVU	10–19	574	9,698	9,284	501	11	4,120
COD	BAS UELE	30–39	405	6,854	829	49	26	4,526
COD	MAI NDOMBE	10–19	278	4,702	2,191	140	18	4,922
COD	SUD UBANGI	30–39	362	6,121	1,640	108	23	5,108

Notes: DALYs = disability-adjusted life years; AE = adverse event; ICER = incremental cost-effectiveness ratio.

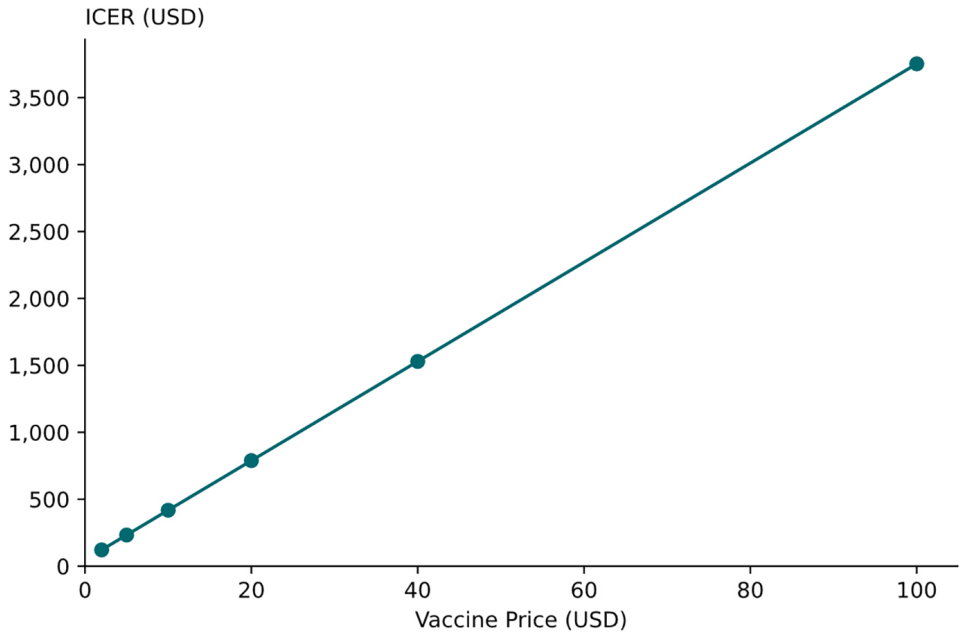
Figure 12 presents uncertainty estimates from a probabilistic sensitivity analysis. While the base case ICER for routine mpox vaccination often exceeds GDP per capita, there is some probability it could fall below that threshold for some areas. See Table A11.1 for the exact values of ICER uncertainty for all geographies where vaccine rollout is modelled for the global pandemic modelling scenarios. Figure 13 shows that ICERs vary approximately linearly with vaccine cost. Therefore, vaccine prices of US$2–5 per dose could make vaccination cost-effective in more provinces and age groups. Figure 14 shows the trade-off between infections averted and cost of a vaccination campaign. It shows that a campaign in children ages 0–9 years could cost up to US$400 million over 10 years, directly averting more than 25 percent of total infections; however, there are diminishing returns to such a campaign. This figure is reproduced for routine and catch-up vaccination (Figure A11.1 in Appendix 11). Finally, the sensitivity analysis shown in Figure 15 highlights that uncertainty in mpox epidemiology is the largest driver of ICER variation, followed by assumptions about complication risks (death, vision loss, and scarring).

FIGURE 12. Uncertainty around estimated ICERs for routine vaccination (children ages 0–9 years) by province



Note: ICER = incremental cost-effectiveness ratio.

FIGURE 13. The ICER estimated for Sankuru (DRC) increases roughly linearly with vaccine price for the routine scenario



Notes: Only the incremental cost-effectiveness ratio (ICER) for Sankuru is shown as an example. It is the province for which routine vaccination of children ages 0–9 years is the most cost-effective.

FIGURE 14. Additional spend on routine vaccination has a diminishing impact on directly averted infections

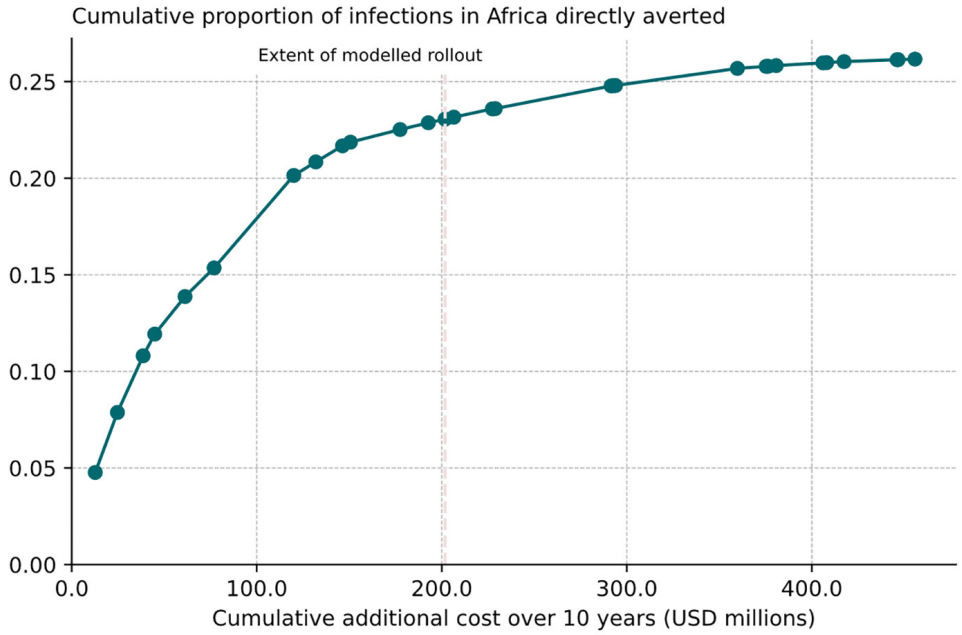
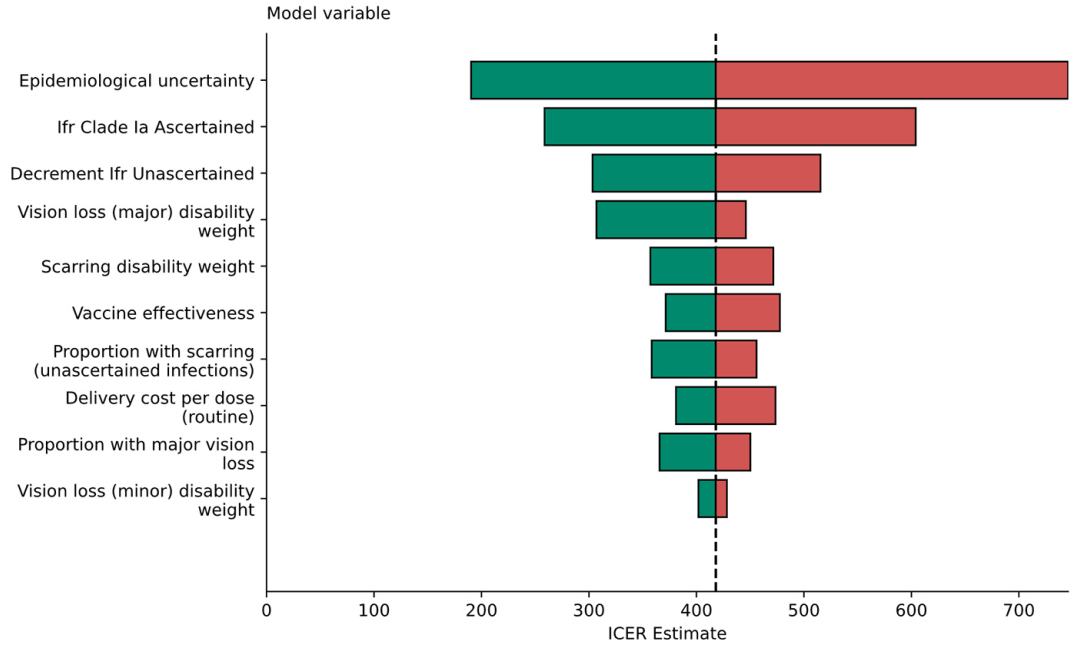


FIGURE 15. Key parameters driving uncertainly of the ICER estimate in Sankuru (DRC)



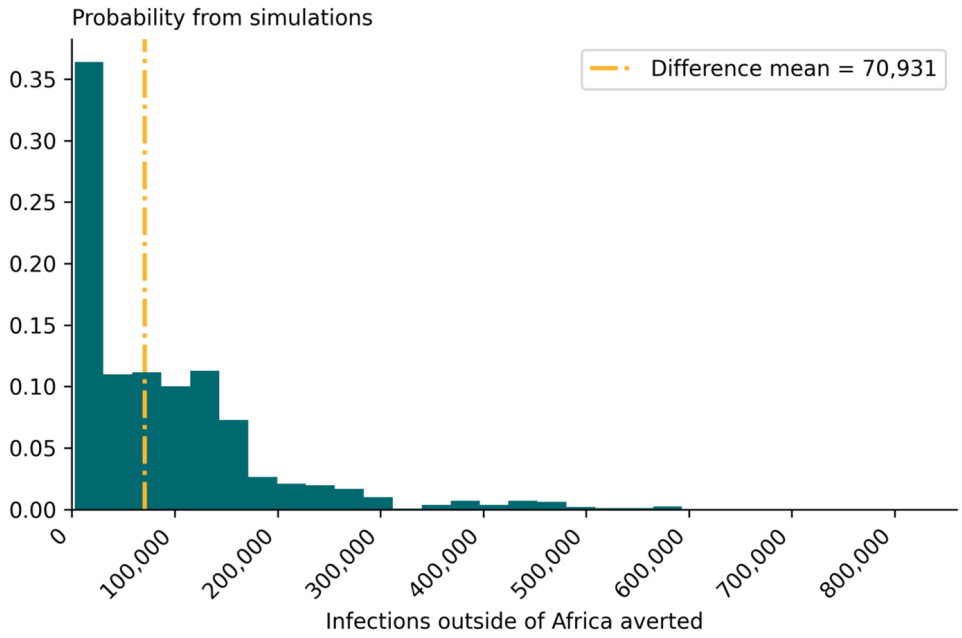
Note: ICER = incremental cost-effectiveness ratio.

Global pandemic modelling

Based on cases reported in the WHO dashboard and our estimates of case ascertainment by country, we estimate that the 2022–2025 clade IIb mpox pandemic has caused 268,000 infections outside of Africa (L: 183,000–U: 460,000). Incorporating our estimates of cost and health loss parameters, we estimate the monetised health and healthcare costs of those infections to be US$1.1 billion (L: $0.6 billion–U: $2.2 billion).

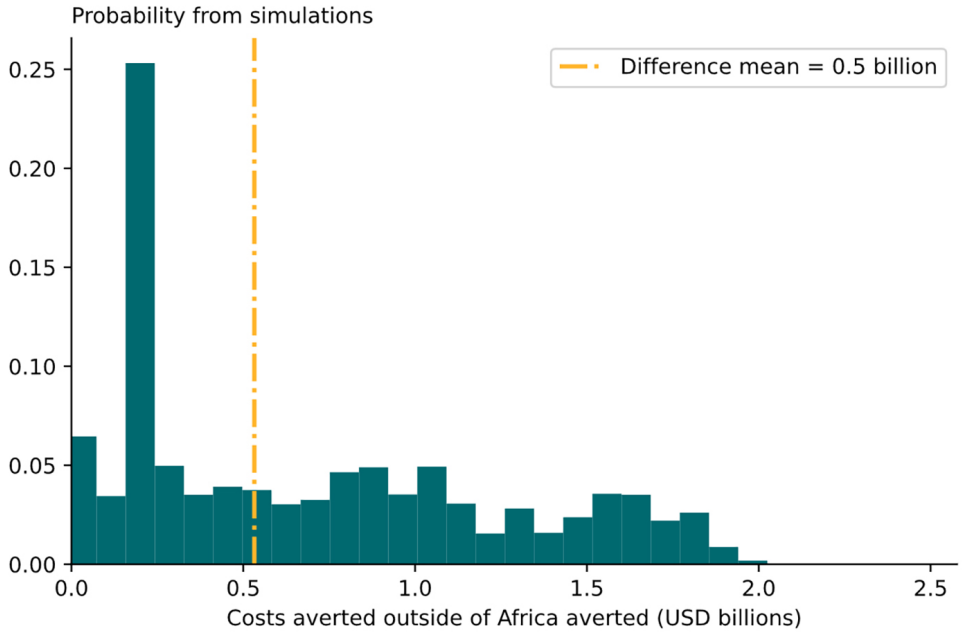
Figure 16 shows the impact of routine vaccination (children ages 0–9 years) being rolled out until the ICER reaches US$10,000 per DALY averted, where the ICER is estimated based solely on the direct benefits to the people in that province. It shows that in many simulations, vaccination averts zero infections outside Africa because no pandemic occurs in either scenario. In the mean case, about 71,000 infections outside of Africa are expected to be averted through vaccination in Africa, but this is subject to considerable uncertainty, with occasional larger pandemics averted or reduced. Figure 17 shows the impact on cost, where US$0.5 billion of monetised health losses and healthcare costs outside of Africa may be averted through vaccination in Africa.

FIGURE 16. Potential number of infections averted outside of Africa from vaccination in different simulations (routine)



Note: The seemingly large white space at the right-hand side of the graph reflects low-probability large pandemics being averted, but their 1/1,000 probability is too low to be visible.

FIGURE 17. Economic gains (outside-of-Africa) from vaccination in different simulations (routine)

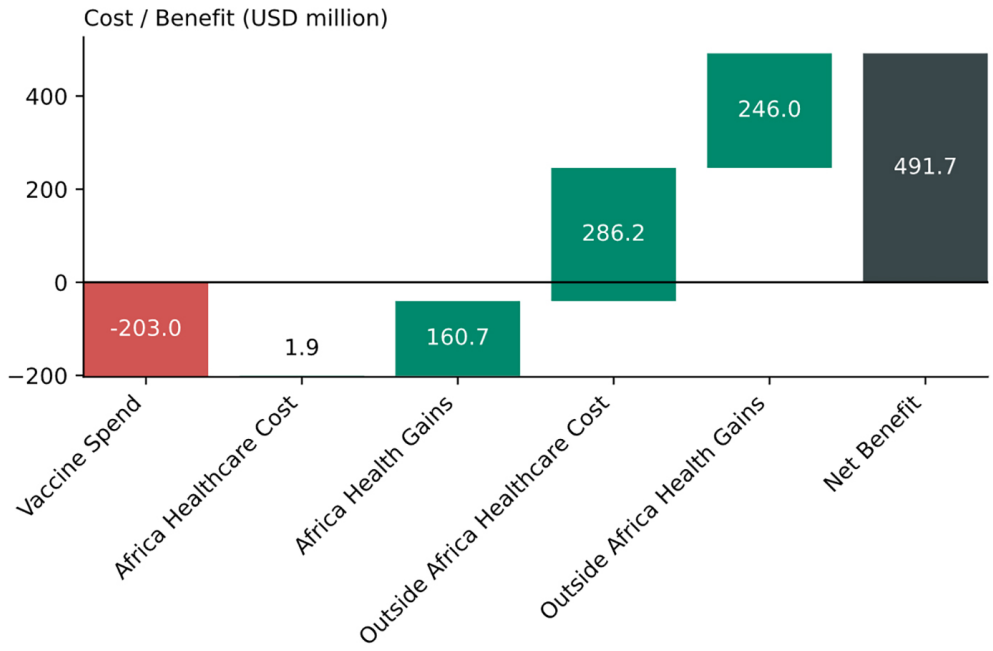


Note: The seemingly large white space at the right-hand side of the graph reflects low-probability costly pandemics being averted, but their 1/1,000 probability is too low to be visible.

Figure 18 shows that investing US$203 million to vaccinate children in high-burden areas of Africa yields a global ROI of more than 3:1 (L: -1–U: 25). This remains true even though the intervention exceeds cost-effectiveness thresholds locally, due to greater healthcare savings and monetised health gains outside Africa. A similar pattern holds for routine plus catch-up vaccination (see Figure 19), which would cost US$481 million—reflecting a larger target population and higher delivery costs—and yield a slightly lower ROI of slightly less than 3:1 (L: 0–U: 19).

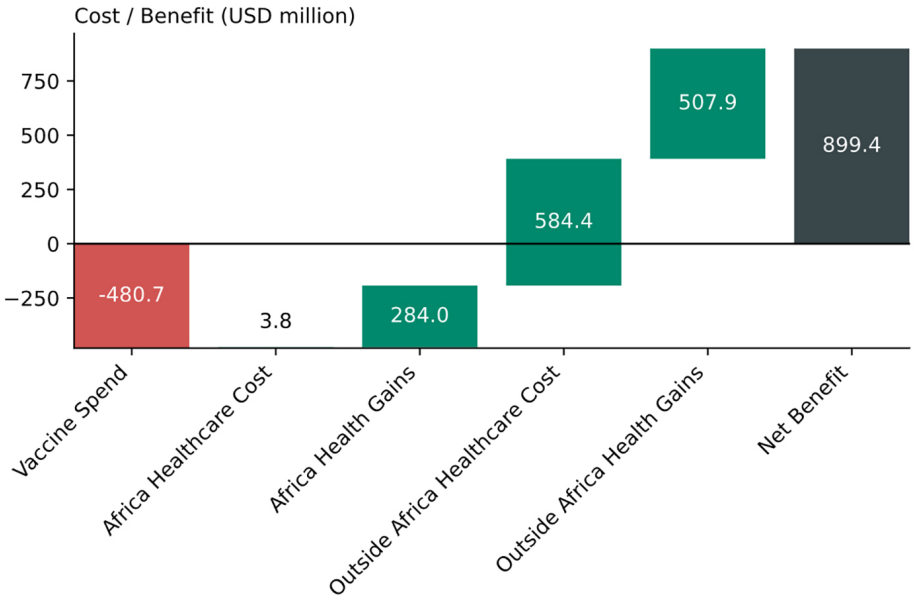
Figures 20 and 21 show that while this central case is useful for illustrative purposes, it masks the fact that the ROI varies markedly depending on the model run. In a 10-year modelling period, the expected ROI is disproportionately driven by the runs where a pandemic larger than the 2022–2025 pandemic outside Africa is averted or reduced by vaccination in Africa. They also show that even if vaccination *should* help avert pandemics, in a given model run *by chance* there can be greater transmission outside of Africa in spite of a campaign within Africa—which leads the ROI for that model run to be negative. This is considerably less likely in Figure 21 because greater disease control in Africa reduces the risk of pandemics spreading outside Africa.

FIGURE 18. Contribution of different components to the overall benefit and ROI over 10 years (routine)



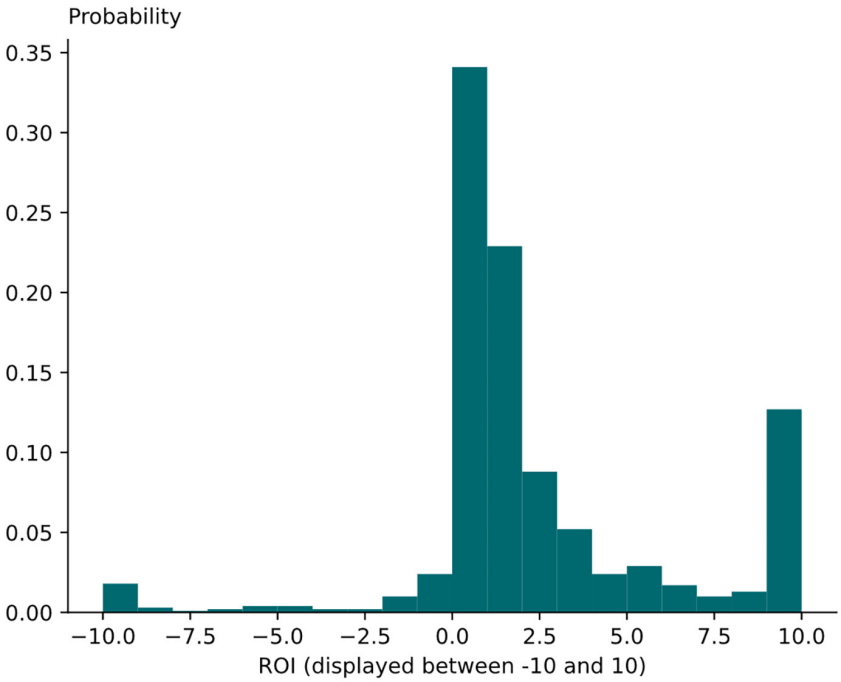
Notes: Africa healthcare cost here refers to nonvaccine healthcare costs averted, but *outside-Africa healthcare cost* includes reduced use of reactive vaccine campaigns outside of Africa. *Health gains* are the monetised value of DALYs averted.

FIGURE 19. Contribution of different components to the overall benefit and ROI over 10 years (routine and catch-up)



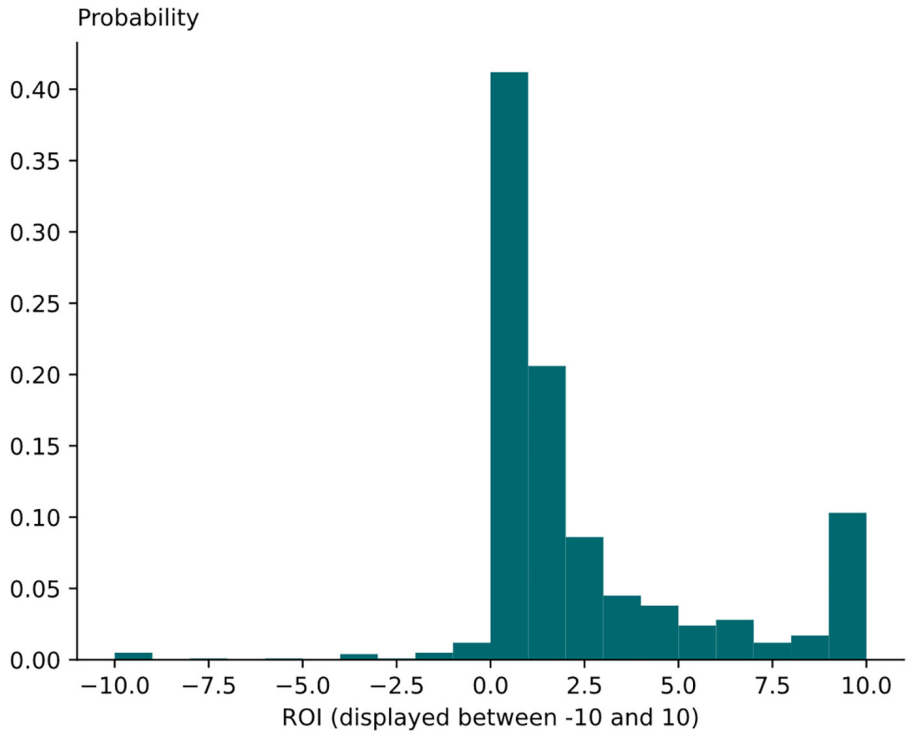
Notes: Africa healthcare cost here refers to nonvaccine healthcare costs averted, but *outside-Africa healthcare cost* includes reduced use of reactive vaccine campaigns outside of Africa. *Health gains* are the monetised value of DALYs averted.

FIGURE 20. There is considerable uncertainty on the ROI in the routine vaccination scenario



Notes: The ROI in this chart is capped at –10 for readability. The first bar should be read as the probability of an ROI of less than –9.5. In negative scenarios, by chance, a larger outbreak occurs in the vaccination arm than in the nonvaccination arm. It is also capped at 10.

FIGURE 21. There is considerable uncertainty on the ROI in the routine and catch-up vaccination scenario



Notes: The ROI in this chart is capped at –10 for readability. The first bar should be read as the probability of an ROI of less than –9.5. In negative scenarios, by chance, a larger outbreak occurs in the vaccination arm than in the no vaccination arm. It is also capped at 10.

The key parameter driving these results is the vaccine price per dose. Figure 22 shows that if the mpox vaccine were available for countries in Africa at US$2 a dose (a cost for which many other vaccines are available to Gavi-eligible countries), the central ROI would be greater than 7:1, whereas at US$100 a dose (HIC prices), the ROI would be close to 1. The other key assumption we have made is the extent of rollout. If the vaccine were limited to use only in the most cost-effective geographies, the global ROI would be greater than 8:1 (see Figure 23).

The maximum ICER threshold for which to rollout vaccines affects the ROI and also the scale of the vaccine campaign and resulting cost. Our headline results, shown in Figure 24, assume a US$10,000 per DALY averted threshold, leading to a US$203 million programme over 10 years. This is equivalent to administering about 1.7 million doses per year.

Figure 25 shows the contribution of different parameters to the overall global ROI. It shows that the most material parameters concern the assumed rate of exports of mpox cases from Africa and how these exports affect the likelihood of pandemics. Additionally, responsive vaccination programmes in HICs impose high costs on healthcare payers, so parameters related to the scale and cost of such programmes are also major drivers of modelled expected healthcare costs.

FIGURE 22. The estimated global ROI increases as vaccine price decreases for the routine scenario

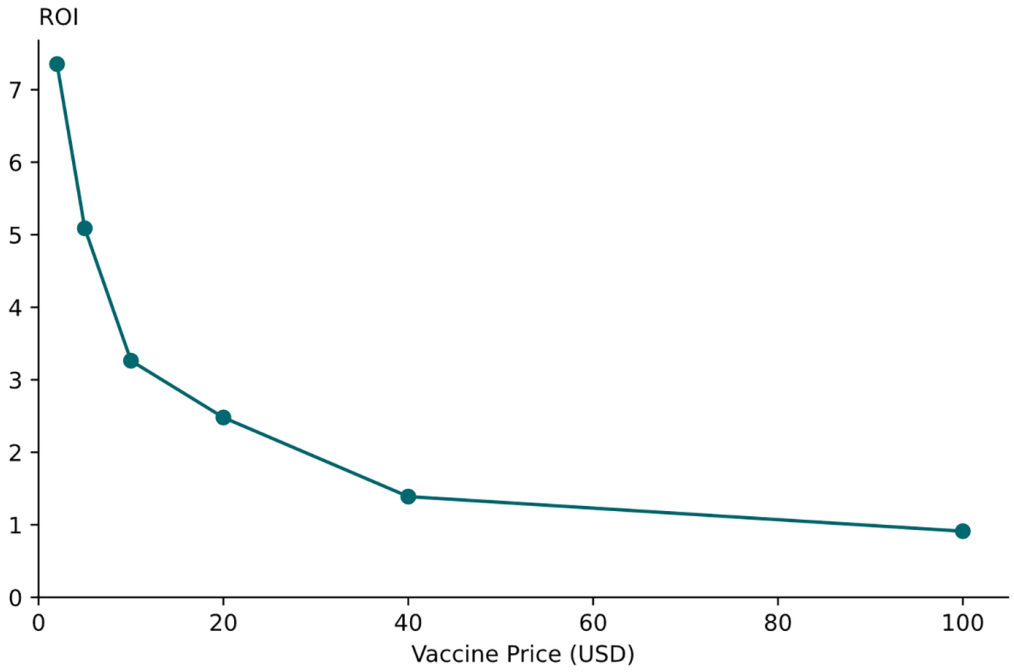
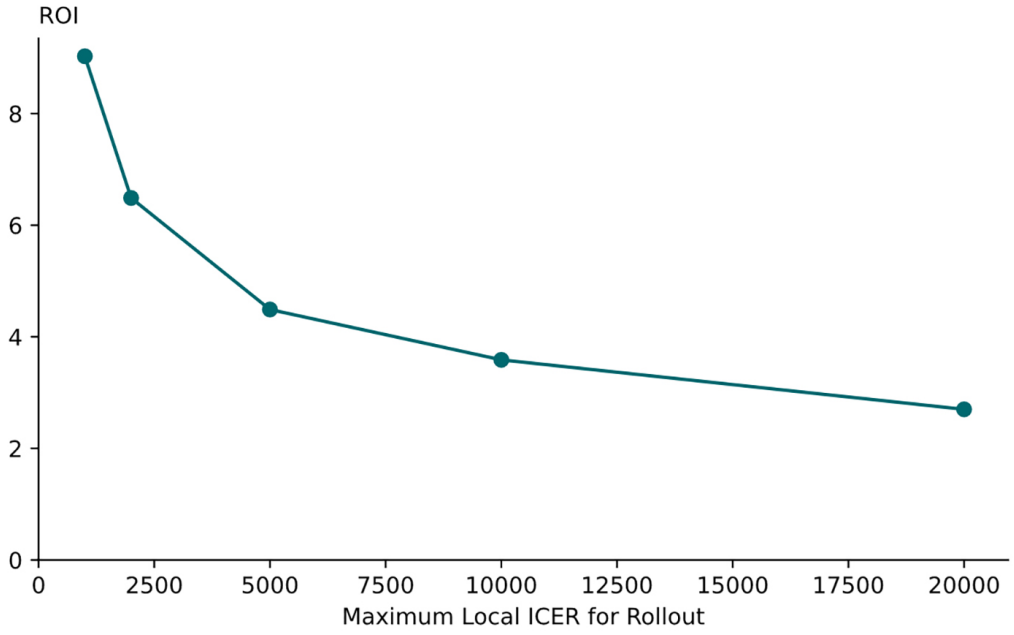
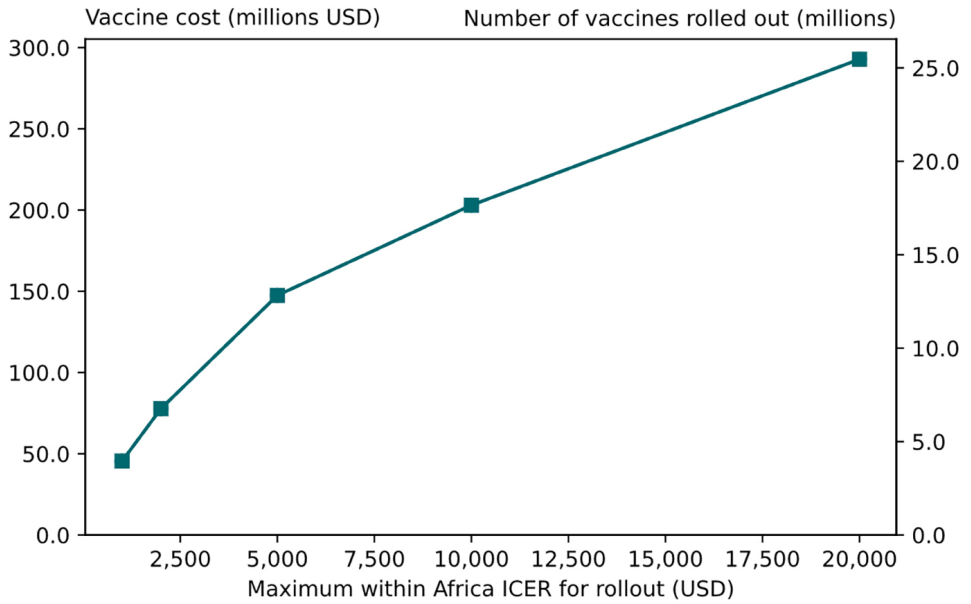


FIGURE 23. The estimated global ROI decreases for higher values of the cost-effectiveness threshold dictating rollout because the modelled campaign is less targeted for the routine scenario



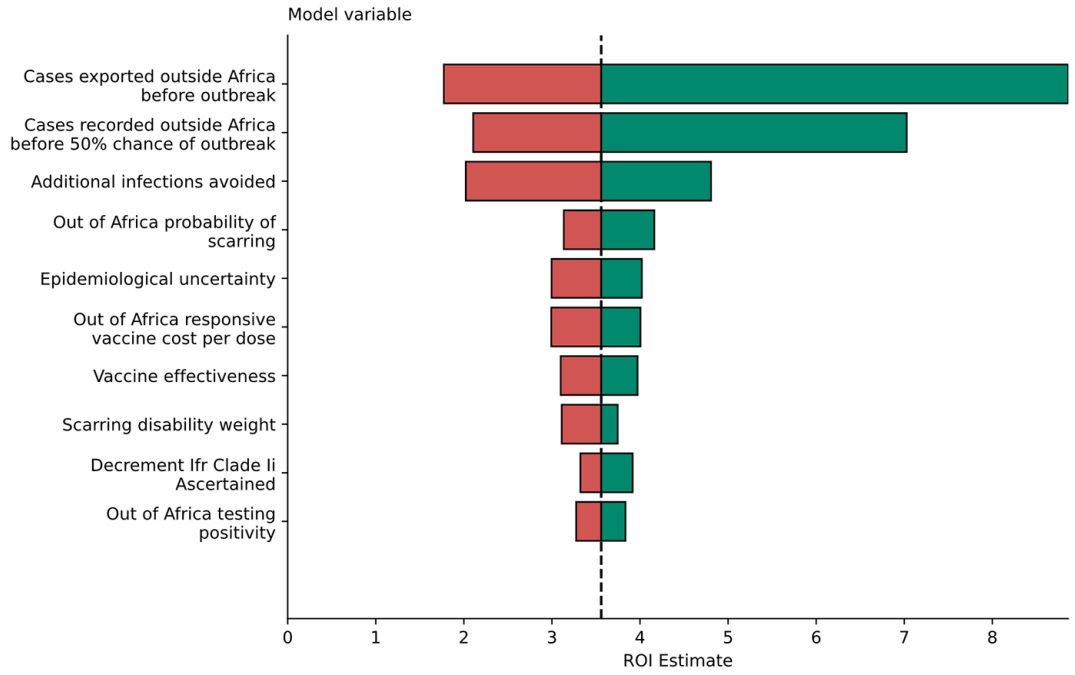
Note: ICER = incremental cost-effectiveness ratio.

FIGURE 24. Lowering the cost-effectiveness threshold increases the number and cost of vaccines rolled out over 10 years (routine)



Note: ICER = incremental cost-effectiveness ratio.

FIGURE 25. Key parameters driving uncertainty of the global ROI estimate (routine)



Discussion

Contributions

- To our knowledge, this is the first study to produce comparable estimates of the burden of mpox across different provinces in Africa in terms of DALYs, the cost-effectiveness of routine vaccination against mpox, and the impact that routine vaccination might have on global mpox pandemics. However, confidence is low for several results due to limitations in the underlying data.
- We use highly transparent methods and detail all data and evidence carefully so others can build on this work or challenge our approach to dealing with uncertain evidence. Our results are broadly consistent with those from other modelling studies on mpox, which also suggest that vaccination of children and young adults, even at relatively low levels of national coverage, can have a big impact on reducing the mpox burden (Savinkina et al., 2024; Jin et al., 2025).
- We make a series of adjustments (e.g., adjusting for case ascertainment) to attempt to increase the comparability of data across geographies.
- We have erred on the side of conservatism wherever possible, so the study may produce lower estimates of burden and cost-effectiveness than other studies advocating for mpox vaccination.

Appendix 12 provides detailed discussions of the strengths and limitations of each type of analysis used in the modelling study.

Limitations

Data

- The data and evidence underpinning this modelling study are highly uncertain. Data on mpox in Africa are limited and imprecise, even relative to other epidemiological data; this imprecision increases at more disaggregated levels. 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 quality-of-life losses from long-term side effects, would also increase 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 we can change between provinces are the rate of infection and the population composition of such areas. Other evidence (e.g., the cost of mpox treatment) is estimated nationally and assumed to apply across all provinces. This could particularly bias the results for certain provinces

where insecurity is high and vaccination is estimated to have an ICER that would be prohibitively expensive or infeasible in practice.

- Our comparator group is *no vaccination* because very few mpox vaccinations had been administered in Africa when we started this study in December 2024. Further work should contrast the cost-effectiveness of routine vaccination with reactive vaccination, and with vaccination targeting high-risk groups.

Modelling

- The broad scope of our study and the lack of available data and evidence mean we have often used more basic modelling frameworks than researchers may use if they have strong data and a 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 because we did not observe enough data to model this. There has been a substantial increase in reported cases since 2022, which may reflect improved surveillance, but we lacked sufficient evidence (e.g., estimates of ascertainment over time) to quantify this.
- Our modelling is based on a hypothetical scenario in which vaccination had been rolled out in 2016, which removes the need for detailed projections of potential mpox burden. However, applying our results to future vaccination campaigns in age groups and regions previously affected by mpox may slightly overstate the impact, as some individuals are likely to have acquired natural immunity to the virus. It may also overstate the risk of pandemics if countries outside Africa are better equipped to mitigate mpox transmission than they were before 2022.
- The results stemming from our pandemic prevention modelling should be interpreted with very low confidence due to the inherent uncertainty of pandemics. We used a simplified modelling framework to improve the transparency of our assumptions and methodology.
- Our pandemic prevention modelling is limited by the exclusion of international travel data, which could be used to track the movement of people and so the spread of MPXV. Whereas flight data are 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.
- Our pandemic modelling work does not explicitly include new variants of mpox with higher transmissibility or worse severity; this may mean our pandemic modelling results are biased to be more conservative than a base case that incorporated more burdensome variants with a non-zero probability.

Wider applicability to other pathogens with pandemic potential

Even if pandemics such as the 1918 H1N1 influenza and COVID-19 are 1-in-100-year events, their wide-ranging impacts will take a substantial toll on the global economy. Identifying health-improving, cost-effective, evidence-based policies to reduce the frequency and scale of pandemics is a health policy goal with a large potential payoff.

Some pathogens infect humans relatively frequently and are concentrated in relatively well-defined populations. Astbury et al. (2023) identify targeted vaccination in humans as a policy option to avoid these zoonotic spillovers. We chose mpox as a case study because a routine vaccination campaign to prevent future pandemics would yield the greatest short-term benefits by mitigating current MPXV transmission across a range of African countries.

Outside of influenza and COVID-19, another pathogen with pandemic potential that imposes a disease burden in humans is Lassa fever, for which numerous studies have reported substantial seroprevalence in several key areas of West Africa (Kenmoe et al., 2020). The epidemiology of Lassa fever makes it a promising next modelling case study to evaluate the benefits of a routine vaccination campaign in affected communities. There are other pathogens that are less analogous to MPXV, but similar studies could also yield interesting results. For instance, human cases of avian influenza have been disproportionately recorded among agricultural workers and are likely to occur in areas where avian influenza has been identified in farmed animals (Chen et al., 2020; Mellis et al., 2024; CDC, 2025c). Modelling the costs and benefits of precautionary vaccination in these communities (assuming a safe vaccine and a sufficiently high estimated risk of infection) would also be an interesting future study.

This work presents a case study of mpox alone, rather than a prioritised list of pathogens, based on the estimated benefits of routine vaccination. As the epidemiology of other pathogens continues to evolve and new, safer, and more effective vaccines are developed, such modelling could be extended to assess the health benefits and cost-effectiveness of similar vaccination campaigns against other pathogens. The goal of these modelled campaigns would be to stop zoonotic transmission where it occurs, or at least reduce the likelihood that the pathogen spreads beyond well-defined populations, thereby reducing the frequency and scale of potential pandemics.

Vaccine technologies continue to evolve, with single vaccines offering protection against multiple pathogens. The development of safe and effective combination vaccines that protect against pathogens with pandemic potential could enhance the cost-effectiveness and feasibility of this strategy.

Key findings

Burden of disease

1. Mpox is a smaller cause of disease burden in the DRC than the highest-burden infectious diseases, including tuberculosis, malaria, and diarrhoeal disease. Still, in some endemic provinces of Africa, the mpox burden is sufficiently high to justify routine vaccination from a public health perspective (despite common but mild adverse events associated with vaccination). We estimate that almost half of the population in the DRC—53.5 million people, 23.2 million of which are children ages 0–9 years—would benefit from routine vaccination.

Health impacts of vaccination

2. In areas where vaccination is health-positive, reported incidence can be as low as 20 cases per 100,000 population cumulatively over 10 years, suggesting that even relatively modest outbreaks could shift the balance in favour of routine vaccination to improve population health. In these areas where universal vaccination is not health-positive, vaccination of high-risk individuals, or in response to outbreaks, is still likely to be health-positive.
3. Our modelling suggests that rolling out vaccination to a relatively small number of high-priority geographies in a targeted campaign could have averted 1.6 million (L: 0.5 million–U: 3.6 million) infections across Africa, reducing the estimated number of mpox infections by 38 percent in a base case. Including catch-up vaccination for adolescents and adults would avert 3.0 million (L: 0.9 million–6.9 million), reducing baseline infections by 71 percent. Mitigating these infections would improve population health and reduce the risk of a new variant emerging.

Cost-effectiveness and ROI

4. At a price of US$10 per dose, routine vaccination is nearly cost-effective in two provinces of the DRC, depending on the specific cost-effectiveness threshold applied. Vaccinating past the point of local cost-effectiveness may still be justified given its potential to reduce disease burden in other parts of Africa and globally. However, given resource constraints, wider use of mpox vaccination should be weighed against other uses of funding.
5. The cost-effectiveness of this programme varies almost linearly with the vaccine price per dose. Therefore, at costs of US$2 or US$5 per dose, routine vaccination could be cost-effective in additional provinces of the DRC.
6. In our headline specification, vaccinating 8.5 million children ages 0–9 years in the highest-risk areas of the DRC over 10 years (at a cost of US$203 million) would yield an estimated global ROI of more than 3:1 (L: -1–U: 25). This ROI is subject to considerable uncertainty and is dependent on the extent of rollout, with higher ROIs from more targeted campaigns or lower vaccine prices.

7. A similar pattern holds for routine and catch-up vaccination, which would cost US$481 million—reflecting a larger target population and higher delivery costs—and yield an ROI slightly lower than 3:1 (L: 0–U: 19).

Global benefits of averted transmission

8. A large positive externality from vaccinating populations in Africa accrues to populations outside of Africa. That externality is five times the size of the benefits within Africa, providing a strong rationale for funding routine mpox vaccination through external sources.
9. If we account 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 a local perspective alone.

Implementation considerations

10. Administering two doses of a vaccine (with specific cold chain requirements), one month apart, in remote areas of the DRC where there is ongoing humanitarian conflict could prove particularly challenging. Such challenges are not captured quantitatively in this modelling.
11. 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.
12. 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, these vaccines could be redirected within the first 100 days of the response to this 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 for the administration of vaccination to younger age groups more widely, beyond 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 research funders should support additional studies to address knowledge gaps that hinder our ability to direct limited resources toward preventing MPXV 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 support from global partners such as Gavi, the Vaccine Alliance (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 health security could make a considerable impact on reducing the pandemic threat of OPXVs for relatively small sums of money (around US$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 and 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 such as the WHO and the Coalition for Epidemic Preparedness Innovations (CEPI) should indicate whether additional modelling studies of diseases such as Lassa fever could provide further evidence on the role of routine vaccination in pandemic prevention.

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 technologies.

Appendix 1: Population data

Different ages and areas in Africa have different transmission patterns of MPXV. Therefore, it was necessary to understand the population totals by age and by admin-one geographies, to inform admin-one level assessments. We use relatively simple measures to construct these estimates, because the focus of our study is epidemiological rather than demographic, and we know that historic inaccuracies in our population estimates will likely be immaterial for the results of the modelling.

We used data aggregated by the Humanitarian Data Exchange (HDX) to get the latest province estimates of population for each of the countries in the model. This data are aggregated based on countries' most recent census (OCHA, 2025).

We used data from the U.S. Census Bureau's International Database to assess changes in population over time (US Census Bureau, 2024). Where available, we obtained estimates disaggregated by age and province geography (admin-one). If admin-one time series data were unavailable, we used age-disaggregated national data over time. As a last resort, we relied on national-level population estimates. Growth rates by age group were then applied to estimate population sizes over time, using the most detailed data available. This approach ensures that recent estimates align with the latest official figures from HDX and, where possible, reflect admin-one demographic transitions. At a minimum, the sum of admin-one data matches national totals provided by the U.S. Census Bureau, capturing broader demographic trends.

Sometimes heterogeneity in available data meant we had to make assumptions to standardise age groups; for instance, if a country only reported population data for 60+ we would split this into narrower age categories using the distribution of age 60+ reported in other countries. The final data used in the model was aggregated for all 50+ because that age group is expected to have received smallpox vaccination.

TABLE A1.1. Summary of population data availability

Country (ISO3)	Admin-One Data Available HDX	Data Available US Census International Database
COD	Yes	Admin-one data by age over time available
BDI	Yes	Admin-one data by age over time available
UGA	Yes	Admin-one data by age over time available
NGA	Yes	Admin-one data by age over time available
CAF	Yes	Only national estimates by age over time
GHA	Yes	Admin-one data by age over time available
CIV	Yes	Only national estimates by age over time
RWA	Yes	Only national estimates by age over time
LBR	Yes	Admin-one data by age over time available
CMR	Yes	Only national estimates by age over time
COG	Yes	Only national estimates by age over time
KEN	Yes	Admin-one data by age over time available
SDN	Yes	Only national estimates by age over time
SSD	Yes	Only national estimates by age over time
SLE	Yes	Admin-one data by age over time available

Appendix 2: Case data

The case data for the model comes from three main sources of aggregated case data: Bunge et al. (2022), between 1970 and 2019; McCollum et al. (2023) CDC report, between 1971 and 2021; and the WHO mpox dashboard (WHO, 2025a), between 2022 and 2025. These estimates define overall case numbers at a national level, with sporadic information on subnational distribution. For the DRC, there are two studies which report more disaggregated case data from the DRC's Integrated Disease Surveillance and Response system. They are: Mandja et al. (2022); Bangwen et al. (2025). We use the admin-one and age disaggregated data from these papers to break down the national estimates by age and geography. To obtain age and admin-one disaggregated data we have to go directly to outbreak reports of affected countries, because these are not covered by any of the main aggregated datasets. Where definitive data for the whole time period of interest is often not available for admin-one geographies, we use partially or imprecisely available data (e.g., data for part of the outbreak only) to inform approximate allocations of national case data to ages and admin-one geographies.

National estimates were supplemented by additional sources which had indications into admin-one cases in Table A2.1.

The case data are made further uncertain by the challenges of suspected cases. In a cross-sectional study of suspected cases in Cameroon, Djuicy et al. (2024) found that 22 percent of suspected cases tested positive with a polymerase chain reaction (PCR) test. In places with limited resources, PCR tests are not reliably available, leaving room for ambiguity in suspected case diagnoses. Furthermore, the symptoms for mpox and Varicella Zoster Virus (VZV) can present similarly, increasing the complication in making a precise diagnosis (Jezek et al., 1988; Pattnaik et al., 2023; Vierbaum et al., 2023). However, in many parts of the DRC, testing positivity is over 50 percent (WHO, 2025a).

One challenge with interpreting the data is the inconsistent decrementing of confirmed (positive or negative) cases from suspected cases (WHO, 2025b). From the data it is clear that this is happening in some areas because it is referenced in the WHO's dashboard as occurring in Nord-Kivu, and we can also infer that it is happening in Kinshasa because tested cases are greater than suspected cases suggesting that cases could be confirmed but not suspected, or are being removed from suspected once tested (WHO, 2025a). Therefore we take a simple pragmatic approach of adding suspected and confirmed cases, though this risks double counting, this is likely to be immaterial because the rate of case confirmation is low and this decrementing appears to be happening in two geographies representing roughly a third of total confirmed cases in the DRC.

Finally, there is a major inconsistency between the suspected cases reported by the WHO and Rwanda's Biomedical Centre (RBC), with WHO reporting low hundreds of suspected cases and the Rwandan government reporting over 7,000 (RBC, 2024). We have not been able to validate this discrepancy, so are aligning our estimates with WHO reporting as that is more consistent with our

approach in other countries. Increasing case counts by a factor of 20 would clearly have material implications for our results for Rwanda.

TABLE A2.1. Sources of case data

Country	Source of National Case Data	Source of Admin-One Case Data Breakdown
COD	(Bunge et al., 2022; McCollum et al., 2023; WHO, 2025a)	(Mandja et al., 2022; Bangwen et al., 2025; WHO, 2025a, 2025e)
BDI	(WHO, 2025a)	(Nzoyikorera et al., 2024; WHO, 2024c, 2025e, 2025a; UNICEF, 2025)
UGA	(WHO, 2025a)	(Uganda Ministry of Health, 2025; WHO, 2025a; WHO Africa, 2025)
NGA	(Bunge et al., 2022; McCollum et al., 2023; WHO, 2025a)	(NCDC, 2024a, 2024b, 2025; WHO, 2025a)
CAF	(WHO, 2025a)	(Besombes et al., 2022; Garba-Ouangole et al., 2023; Africa CDC, 2024; Cheuyem et al., 2025; WHO, 2025a, 2025g)
GHA	(WHO, 2025a)	(Aminu, 2022; Baisie, 2025; IFRC, 2025; WHO, 2025a, 2025h)
CIV	(Bunge et al., 2022; McCollum et al., 2023; WHO, 2025a)	(Alain, 2024; Assin, 2024; Ehui, 2024; Koffi, 2024; Taukla, 2024; Sikensi, 2025; WHO, 2025a)
RWA	(WHO, 2025a)	(RBC, 2024; UNICEF, 2024b; WHO, 2024c, 2024b, 2025a; Mbabazi, 2025; RBC and Republic of Rwanda Ministry of Health, 2025)
LBR	(Bunge et al., 2022; McCollum et al., 2023; WHO, 2025a)	(WHO Liberia, 2022; Genoway Jr., 2024; NPHIL, 2025; WHO, 2025a)
CMR	(Bunge et al., 2022; McCollum et al., 2023; WHO, 2025a)	(Djuicy et al., 2024; WHO, 2025a)
COG	(Bunge et al., 2022; McCollum et al., 2023; WHO, 2025a)	(Yinda et al., 2024; WHO, 2025a)
KEN	(WHO, 2025a)	(UNICEF, 2024a; Ledama, 2025; WHO, 2025a, 2025h, 2025d)
SDN	(Bunge et al., 2022; McCollum et al., 2023; WHO, 2025a)	(Izzoddeen et al., 2025; WHO, 2025a)
SSD	(McCollum et al., 2023)	(McCollum et al., 2023; Republic of South Sudan Ministry of Health, 2025; WHO, 2025a)
SLE	(Bunge et al., 2022; McCollum et al., 2023; WHO, 2025a)	(Kangbai et al., 2025; Mathiang et al., 2025; Mitjà et al., 2025; WHO, 2025a, 2025g)

Appendix 3: Case ascertainment literature review

Data sources and search strategy

We performed a literature search using PubMed, focusing on quantitative estimates of mpox case ascertainment reported in a population. Emphasis was placed on studies that estimate the difference between infections and confirmed cases or suspect cases of mpox infection. The search strategy is outlined in Table A3.1. Search terms included a combination of title and abstract terms. We filtered

PubMed results by specifying species as human and adjusting results by year to publications after the first scientific characterisation of mpox in 1970.

TABLE A3.1. Search terms for the case ascertainment literature review

PubMed
("mpox"[Title/Abstract] OR "monkeypox"[Title/Abstract] OR "monkey pox"[Title/Abstract] OR "MPXV"[Title/Abstract] OR "orthopox*"[Title/Abstract] OR "Poxvirus"[Title/Abstract])
AND
("underreport*"[Title/Abstract] OR "under-report*"[Title/Abstract] OR "reporting"[Title/Abstract] OR "reported"[Title/Abstract] OR "misdiagnos*"[Title/Abstract] OR "undiagnos*"[Title/Abstract] OR "ascertain*"[Title/Abstract] OR "underascertain*"[Title/Abstract] OR "under-ascertain*"[Title/Abstract] OR "underestimate*"[Title/Abstract] OR "under-estimate*"[Title/Abstract] OR "detection"[Title/Abstract] OR "missed"[Title/Abstract] OR "subclinical"[Title/Abstract] OR "asymptomatic"[Title/Abstract] OR "surveillance"[Title/Abstract] OR "estimated incidence"[Title/Abstract] OR "epidemic size"[Title/Abstract])

Study selection and eligibility criteria

Search results were imported into citation software to ensure no duplicates were being screened. The remaining records were screened by two reviewers for potential relevance and then full texts of potentially relevant publications were retrieved and assessed.

Publications were selected based on the following inclusion criteria:

1. Quantitative (or quantifiable) estimates of underreporting of mpox infection
2. Estimates of true epidemic size that can be compared to recorded cases
3. Studies conducted between 1970–2025
4. The study must be in French or English

Certain types of studies were deemed ineligible explicitly:

5. Wastewater sampling which confirmed the presence of unascertained infections but did not quantify a number of infections

No criteria restrictions were applied to gender of study participants, or geographic location.

Data extraction and synthesis

Screened papers assessed as eligible for inclusion were extracted. The list of variables extracted is outlined and explained below in Table A3.2. Another reason for the exclusion of many of the publications was they lacked quantitative estimates for true epidemic size, or we were not able to quantify true epidemic size based on their methods description. Our main focus and inclusion for the final model was publications which reported asymptomatic testing and/or serology, modelled case ascertainment, and quantified health seeking behaviour in regions.

TABLE A3.2. Extraction template for the case ascertainment literature review with the attributes extracted from papers and supplementary materials when needed

Field Extracted	Explanation
PubMed ID	No explanation required
DOI	No explanation required
Paper Title	No explanation required
Publication Year	Year the paper was published
Paper Abstract	No explanation required
Added	Original/Added depending on whether the publication was found from the initial PubMed search or added later as a single article
Pass Abstract Screen (Yes/No)	Yes/No depending on relevancy
Abstract Screen Comment	Any comments for excluding an abstract
Pass Full Text Screen (Yes/No)	Yes/No depending on relevancy and inclusion of sufficient information
Full Text Comment	Any comments for excluding full text
Study Year	Time period when the study was conducted
Admin-One Geography	Subnational geographic area
Country	Country where the study took place
Study Type	Study design – e.g., systematic review, cohort study, cross-sectional with prior data
Sample Size	Sample size for the study
Age Group	Row for each age group included in the study; important factor in determining potential prior vaccination status
Patient Population	Potential study specification (MSM, rural residents, nationally representative)
Pathogen	Specification of an orthopoxvirus (presumed mpox virus) or confirmed mpox virus
Pathogen Comment	Any details or clarification on the pathogen classification
Cases Confirmed	Number of PCR confirmed cases of mpox in a population
Cases Suspected	Number of suspected cases, based on symptoms, but not confirmed by PCR test
True Infections Estimated	Number of estimated infections
Parameter of Interest	Rate of mpox case ascertainment within a population
Numerator	Explanation of the numerator value to calculate the parameter of interest
Denominator	Explanation of the denominator value to calculate the parameter of interest
Value	Value reported in the paper for the parameter of interest
Upper Value	Upper value reported in the paper for the parameter of interest
Lower Value	Lower value reported in the paper for the parameter of interest
Variable Comment	Any additional clarification about value reported

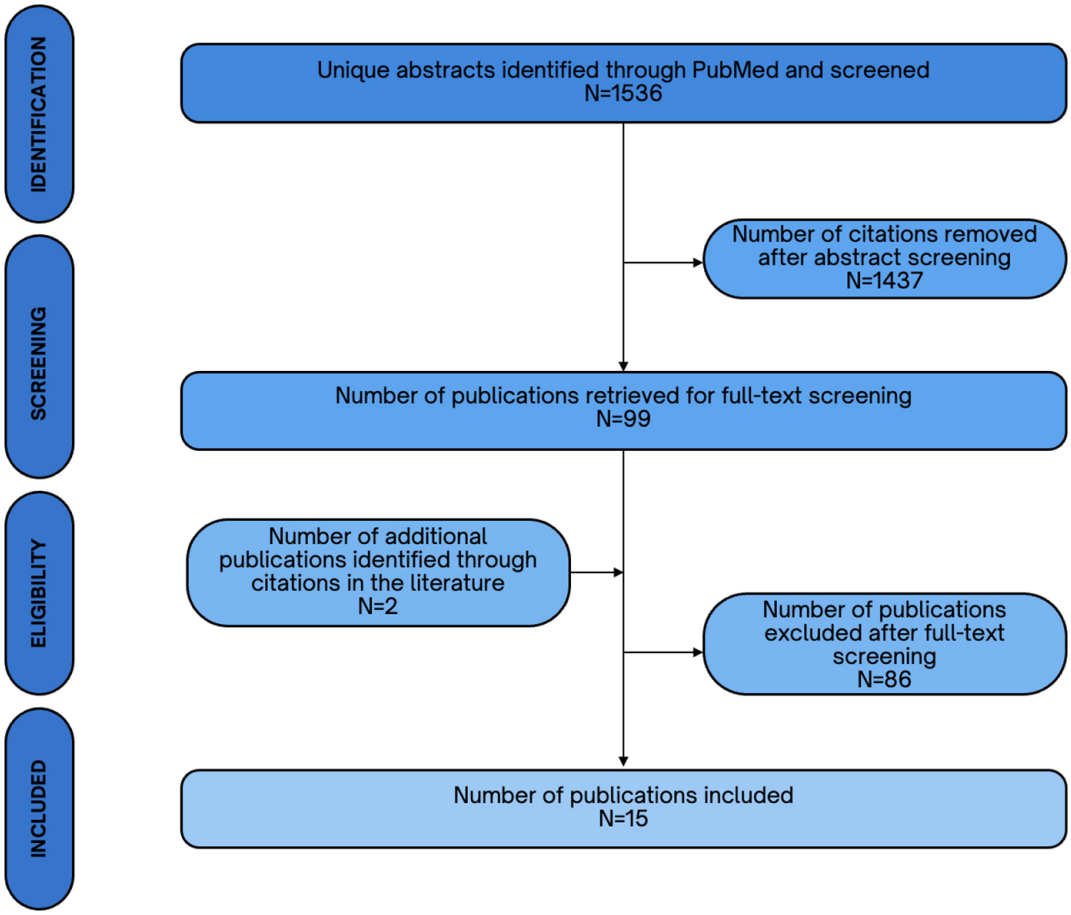
Note: MSM = men who have sex with men.

Search results

The study selection process is shown in the flowchart below (Figure A3.1). In total, 1536 papers were identified in PubMed. After deduplication and abstract screening, 99 publications were identified

as potentially relevant for further screening. Full-text screening of those selected publications identified 13 relevant publications. Two additional publications were identified through citations in the literature and screened as relevant; one of these publications is a PhD thesis and another was published after our literature search period, but the pre-print version was cited by documents in our review. Finally, 15 publications were included.

FIGURE A3.1. Flowchart for case ascertainment article selection



Appendix 4: Serology literature review

Data sources and search strategy

We performed a literature search using PubMed, focusing on quantitative estimates of mpox antibodies present in human population serology data. The search strategy is outlined in Table A4.1. Search terms included a combination of title and abstract terms. The first part of the search string focuses on different terms for mpox, and the second part captures terms related to antibody measurements. We further filtered PubMed results by specifying species as human, as we cannot build animal serology data into this modelling effectively. We limited the search to publications

after 1970, to avoid capturing smallpox (variola) serology studies, and instead focus on mpox (which was first recorded in humans in 1970 (CDC, 2025a)).

TABLE A4.1. Search terms for the serology antibody literature review

PubMed
Search: ("Mpox"[Title/Abstract] OR "monkeypox*"[Title/Abstract] OR "monkey pox"[Title/Abstract] OR "MPXV"[Title/Abstract] OR "orthopox*"[Title/Abstract] OR "Poxvirus"[Title/Abstract])
AND
("Serology"[Title/Abstract] OR "antibodies"[Title/Abstract] OR "IgG"[Title/Abstract] OR "IgM"[Title/Abstract] OR "antibody"[Title/Abstract] OR "anti-MPXV"[Title/Abstract] OR "anti-orthopox"[Title/Abstract] OR "seroprevalence"[Title/Abstract] OR "sero-prevalence"[Title/Abstract] OR "Seropositive"[Title/Abstract] OR "ELISA"[Title/Abstract] OR "immunoassay"[Title/Abstract] OR "immune response"[Title/Abstract])

Study selection and eligibility criteria

Search results were imported into citation software to ensure no duplicates were being screened. Abstracts of remaining records were screened by two reviewers for potential relevance and then full texts of potentially relevant publications were retrieved and assessed.

Publications were selected based on the following inclusion criteria:

1. Study contains quantifiable serological evidence of OPXV antibody response. OPXV antibodies in post-1979 cohorts in Africa are treated as proxy evidence for MPXV exposure.
2. Antibody response is defined as either IgG or IgM antibody response
3. Study population (e.g., age, geography, targeting) is well defined
4. Studies conducted between 1970–2025
5. Study was conducted in the continent of Africa
6. The study must be in French or English

No criteria restrictions were applied to gender of study participants, and geographic location.

Data extraction and synthesis

Screened papers assessed as eligible for inclusion were extracted. The list of variables extracted is outlined and explained below in Table A4.2. In order to refine estimates for the final model during data extraction of full texts, areas of study were classified under determined health region names and codes within countries, as well as standardised country names and ISO3 codes.

TABLE A4.2. Serology antibody extraction template with the attributes extracted from papers and supplementary materials when needed

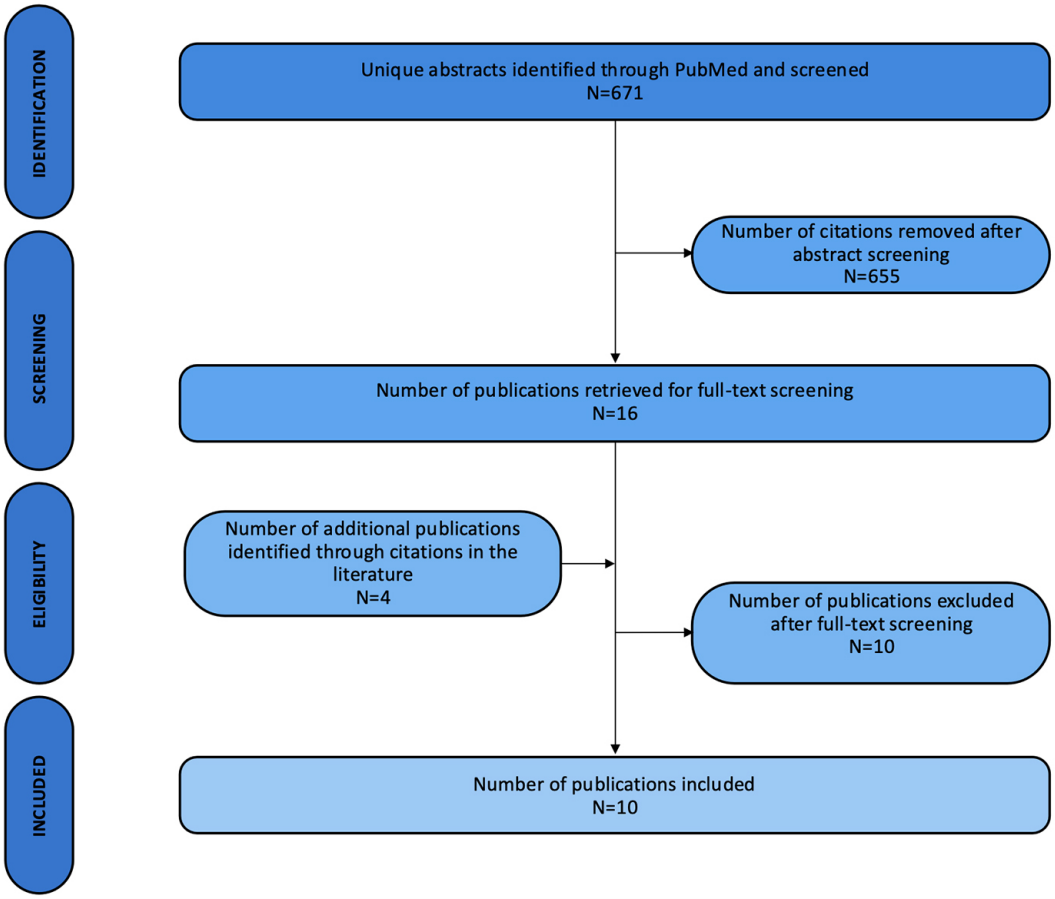
Field Extracted	Explanation
PubMed ID	No explanation required
DOI	No explanation required
Paper Title	No explanation required
Publication Year	Year the paper was published
Paper Abstract	No explanation required
Added	Original/Added depending on whether the publication was found from the initial PubMed search or added later as a single article
Pass Abstract Screen (Yes/No)	Yes/No depending on relevancy
Abstract Screen Comment	Any comments for excluding an abstract
Pass Full Text Screen (Yes/No)	Yes/No depending on relevancy and inclusion of sufficient information
Full Text Comment	Any comments for excluding full text
Study Year	Time period when the study was conducted
Admin-One Geography	Subnational geographic area
Country	Country where the study took place
Study Type	Study design – e.g., systematic review, cohort study, cross-sectional survey
Sample Size	Sample size for the study
Age Group	Row for each age group included in the study; important factor in determining potential prior vaccination status
Patient Population	Potential study specification (agriculture workers, medical clinician volunteers, random volunteers from another haematology study)
Pathogen	Specification of an orthopoxvirus (presumed mpox virus) or confirmed mpox virus
Pathogen Comment	Any details or clarification on the pathogen classification
Antibody Measures	Antibodies present in serology data, i.e., IgG, IgM
Antibody Measures Comment	Additional clarification in determining antibody response within serology data
Parameter of Interest	Positivity rate for orthopox antibodies in previously unvaccinated individuals uninfected by smallpox
Numerator	Explanation of the numerator value to calculate the parameter of interest
Denominator	Explanation of the denominator value to calculate the parameter of interest
Value	Value reported in the paper for the parameter of interest
Upper Value	Upper value reported in the paper for the parameter of interest
Lower Value	Lower value reported in the paper for the parameter of interest
Variable Comment	Any additional clarification about value reported

Search results

The study selection process is shown in the flowchart below (Figure A4.1). A total of 671 papers were identified in PubMed. After deduplication and abstract screening, 16 publications were identified

as potentially relevant for further screening. Full-text screening of those selected publications identified six relevant publications. Four additional publications were identified through citations in the literature and screened as relevant. Our initial search had missed three of these studies because they were publications without clear abstracts outlining the presence of serology data, and one had erroneously not received the MeSH term *Human*. Finally, 10 publications were included.

FIGURE A4.1. Flowchart for serology article selection



Appendix 5: Case ascertainment regression

We use a Bayesian approach to estimate our case ascertainment regression. The equations summarising this approach are set out in A5.1 to A5.6, and then our priors are motivated at the end of this section.

$$\eta_i = \alpha + \beta_1 HAQ_i + \beta_2 E_i \quad \text{(A5.1)}$$

η_i is the raw predicted value of case ascertainment before it is inverse logit transformed.

α is the intercept

β_1 is the coefficient on HAQ_i which is the Healthcare Access Quality Index for country i.

β_2 is the coefficient on E_i which is the log-transformed per capita healthcare expenditure for country i.

Both covariates have been scaled to be between 0 and 1, so the country with the lowest value is 0 and the country with the highest value is 1.

$$\theta_i = logit^{-1}(\eta_i) = \frac{1}{1+exp(-\eta_i)} \quad \text{(A5.2)}$$

θ_i is the transformed predicted value of case ascertainment such that it is bounded between 0 and 1.

$$CA_i \sim Beta(\kappa\theta_i, \kappa(1-\theta_i)) \quad \text{(A5.3)}$$

CA_i is an observation of case ascertainment for country *i*.

κ is a parameter that controls the level of overdispersion in the likelihood. Higher values of κ would imply higher values of overdispersion (more weight near 0 and 1 and less weight around the mean).

Where the priors are:

$$\alpha \sim \mathcal{N}(-4, 0.5^2) \quad \text{(A5.4)}$$

$$\beta_j \sim \mathcal{N}(1.5, 0.5^2) \quad \text{(A5.5)}$$

$$\kappa \sim Gamma(50, 1.25) \quad \text{(A5.6)}$$

α is chosen such that a hypothetical country with the lowest spend and worst healthcare outcomes (a combination of Somalia and South Sudan) would most likely have case ascertainment between 0.7 percent and 7.1 percent. These are weakly informative priors. The lower the value of case ascertainment, the higher the burden would be (thereby increasing cost-effectiveness of vaccination), so though 7.0 percent case ascertainment may not be feasible for a country with so many health system challenges, it is better to avoid priors driving cost-effectiveness findings.

β_j the prior for either covariate is set such that case ascertainment would be 4 percent, 21 percent and 60 percent for the lowest covariate, middle covariate and highest covariate country respectively if $\beta_j = 1.5$ for all *j* (at the central value of α). The uncertainty on these priors also allows for sufficient probability mass such that:

- case ascertainment would instead be 4 percent, 12 percent, and 28 percent for the same countries (at the central value of α) if $\beta_j = 0.5$.
- or case ascertainment would instead be 4 percent, 35 percent, and 86 percent for the same countries (at the central value of α) if $\beta_j = 2.5$.

κ is set to avoid having too much overdispersion but allowing there to be plenty of variance in the resulting estimates (as this uncertainty can then propagate through the infection modelling).

The regression is fitted with PyMC using Hamiltonian Monte Carlo.

Appendix 6: Simple infection methodology

We estimate infections rather than using reported cases unadjusted in our assessment of the cost-effectiveness of mpox vaccination because:

1. There is likely to be considerable underreporting of cases for mpox in Africa.
2. Even if a case is not reported as mpox it could still cause burden to the affected individuals, and trigger healthcare costs.
3. Given the geographies affected by mpox, there is a risk of underreporting of more serious disease burden (for instance deaths) caused by mpox.

Therefore, we estimate mpox infections based on reported cases with equation A6.1.

$$I_{j,a,y} = C_{j,a,y} / CA_i \quad \text{(A6.1)}$$

$I_{j,a,y}$ is the estimated proportion of people infected for province j, for age group a in year y.

$C_{j,a,y}$ is the proportion of people who are reported mpox cases for province j, for age group a in year y. Here cases are either suspected or confirmed, depending on whether countries report suspected cases. Suspected cases are preferred to confirmed cases.

CA_i is case ascertainment estimated for country i using the regression set out in Appendix 5.

We then aggregate the probability of infection over an individual's life-course using equation A6.2. Equation A6.2 simply constructs someone's age-group for previous years and assigns them an infection probability for that year accordingly before summing their infection probability between birth and the current year y. It is also possible to start after a person's birth, for instance to get their infection risk over the last 10 years.

$$cumul\_I_{j,a,y} = \sum_{p=birth}^{p=y} I_{j,a_p,p} \quad \text{(A6.2)}$$

$cumul\_I_{j,a,y}$ is the cumulative probability an individual has been infected for province j, for the final age of age-group a in year y.

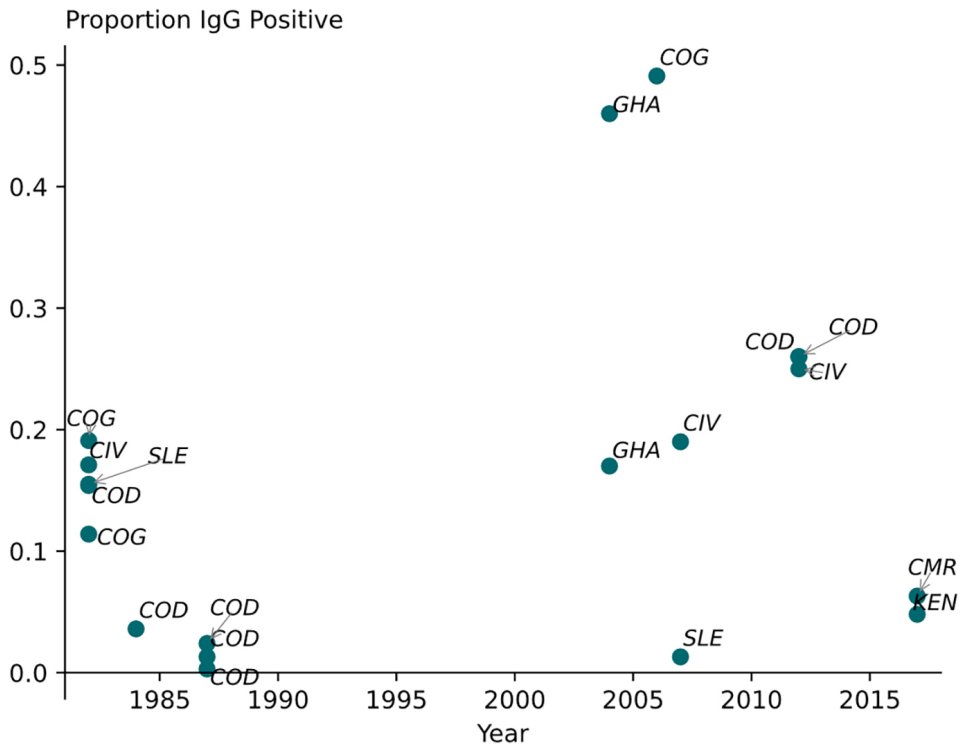
$I_{j,a_p,p}$ is the probability of being infected for province j, in a_p which is the age-group a in which someone would have been in year p.

Appendix 7: Challenges in complex infection modelling

Figure A7.1 shows the serology estimates for different countries in Africa over time. It shows that in several studies, studies report a high proportion of the population having OPXV antibodies, which could reflect exposure to MPXV or less likely another OPXV or broader cross-reactivity. For instance, the two observations for Ghana in 2004 imply lifetime infection risk of 17.1 percent and 45.7 percent respectively (Reynolds et al., 2010), implying that a substantial proportion of the population is being infected with mpox despite no cases being reported in that area. Even countries

like Kenya, which is geographically far from mpox endemic areas, one study reported 4.8 percent OPXV antibody positivity, despite no cases of mpox being reported in Kenya over this time period (Ogola et al., 2021).

FIGURE A7.1. Measured seroprevalence of mpox IgG antibodies over time by country



Normally, Bayesian models support synthesis of diverse sources of information to improve the overall quality of evidence. However, modelling decisions in this project would fundamentally decide the infection estimates, because if serology suggests many people are infected and case data suggests no one is infected, then any middle calibration fits to neither pieces of evidence, and so weighting to one data series means the model will then fit exclusively to that evidence.

Therefore, we exclude the serology data rather than the case data because:

1. The serology data are often collected opportunistically rather than systematically like case data, meaning it is not representative of national or province level populations.
2. The serology data are sometimes collected in response to mpox outbreaks, or in specific settings (like primate sanctuaries or informal settlements), and likely represent the antibodies of people at higher risk of disease acquisition.
3. The serology data are only available in some geographies in snapshots at arbitrary time periods.

4. Authors have noted that there may be a substantial false positive rate in orthopox antibody testing. If the true positive rate of cumulative mpox is 1 percent, but the false positive rate is 5 percent +-2 percent then it is hard to meaningfully fit a model, especially if this false positivity is affected by specific study design factors.

Having reliable serology data over geography and time in endemic areas would represent a considerable increase in our understanding in the epidemiology of mpox and support assessing policy interventions.

Appendix 8: Adverse events assessment

Mpox vaccination development has gone through generations. This assessment focuses on the third-generation mpox vaccine, MVA-BN (known as Jynneos in the US), which is currently the most widely used mpox vaccination in Africa (Africa CDC, 2025). Compared to the previous generations, MVA-BN has an improved efficacy and safety profile, offering greater protection against infection while resulting in fewer serious adverse health events, and those remaining have been extensively reviewed (Grabenstein and Hacker, 2024). Grabenstein and Hacker recognise that while available paediatric data are limited, multiple responsible government agencies have recommended MVA-BN for children at risk of mpox infection during outbreaks. Paediatric safety and efficacy evidence is currently being collected by the manufacturer (Bavarian Nordic, 2024; CEPI, 2024). Additionally, studies have examined the frequency and severity of AEs, including serious adverse reactions (Duffy et al., 2022).

Several authors have attempted to analyse and quantify serious AEs linked to mpox vaccination (Duffy et al., 2022; 2024; Sharff et al., 2023). Where these papers focus on adults, the analysis below makes the assumption that AEs in adults are likely to be similar to children. An assumption that needs to be supported by direct measurement of AE rates in a paediatric patient cohort and marketing approval by relevant Medicines Regulators.

Adverse events in vaccination cost-effectiveness studies

There is generally a paucity of patient reported outcome data available to help quantify the health loss experienced due to vaccine AEs. A recent systematic review finds that only 25 percent of economic evaluation studies on vaccine safety account for AEs (Doggen et al., 2023). Additionally, adverse effects were reported more frequently and deemed more relevant in cost-effectiveness studies conducted in HICs, likely due to the associated costs generated by AEs in patients (Doggen et al., 2023).

Even in high quality economic evaluations of mpox vaccination specifically, AEs are not included (Zhang et al., 2024). The lack of emphasis of incorporating AEs into these modelling studies is likely

due to the MVA-BN vaccine's strong safety profile and the lack of widespread patient-reported serious AEs (Sah et al., 2023). However, where this model considers provision of mpox vaccination outside of an outbreak setting, it is important to consider more minor AEs, which may be more material if the vaccine recipient is highly unlikely to contract mpox in the short-term.

Triangulating data for patient-reported outcomes and disability weights

In the absence of specific patient-reported utilities for infants, we triangulate data from various sources reporting on AEs due to vaccination to mitigate uncertainty (Liu et al., 2024). We compare common local and systemic AEs reported for mpox vaccination to the nearest health state, which informs our mean, lower, and upper disability weight (DW) for each AE (WHO, 2020). The estimated duration of these AEs in recipients is then used alongside the DWs to calculate the DALYs for mpox vaccination; see Table A8.1 (Deng et al., 2023; Frey et al., 2023; Montalti et al., 2023).

TABLE A8.1. Detail on estimation of common mild adverse events

Side Effect	Probability of Occurrence*	Duration in Days^ Mean (Lower–Upper)	Health Loss (DW)~ Mean (Lower–Upper)
Erythema	0.39	2 (1–3)	0.027 (0.015–0.042)
Swelling	0.29	3.5 (2–5)	0.027 (0.015–0.042)
Itching	0.28	3.5 (2–5)	0.027 (0.015–0.042)
Induration	0.3	2 (1–3)	0.006 (0.002–0.012)
Pain	0.18	3.5 (2–5)	0.027 (0.015–0.042)
Rash	0.11	3.5 (2–5)	0.027 (0.015–0.042)
Fever	0.03	3.5 (2–5)	0.006 (0.002–0.012)
Headache	0.08	3.5 (2–5)	0.037 (0.022–0.057)
Myalgia	0.09	3.5 (2–5)	0.051 (0.032–0.074)
Shivering	0.03	3.5 (2–5)	0.051 (0.032–0.074)
Vomiting	0.02	3.5 (2–5)	0.011 (0.005–0.021)
Fatigue	0.12	3.5 (2–5)	0.052 (0.034–0.076)

Notes: *Source for probability: Liu et al., 2024. ^Sources for duration: Deng et al., 2023; Frey et al., 2023; Montalti et al., 2023. ~Source for health loss: WHO, 2020.

TABLE A8.2. Calculated mpox DALY from mild adverse events

Mpox Vaccination DALY	Per Vaccine Recipient	Per Million Vaccine Recipients
Mean	0.0004	441.0
Lower	0.0001	142.3
Upper	0.0010	978.7

Alternative DALY calculations using disutility values

Where we use DWs from health states not related to vaccine AEs directly, we seek to validate our DALY figure compared to other related estimates in the literature. Therefore, we also calculated DALYs using disutility values instead of DWs; in an assessment of disutility due to HPV vaccination, authors assumed mild AEs as having a 0.034 disutility lasting for a mean of two days (HIQA, 2018). If we applied these assumptions to our AEs we get a DALY figure of 0.0004; the same as the mean DALY loss. Other studies elicited the willingness of caregivers to sacrifice time or money to avoid AEs in their children following vaccination (Kuppermann et al., 2000; Lee et al., 2005) or for adults to avoid certain AEs from treatments (Gress et al., 2020). Using the disutility estimates from these studies, and our estimates of duration of symptoms, yields a higher mean DALY loss of 0.0008, which is higher than our central estimate but in the overall range estimated in Table A8.2. While direct recording of patient reported outcomes for mpox vaccination would represent the gold standard of evidence in our study, the complementarity of three methods suggests our estimation of AEs is likely to be approximately accurate.

Serious adverse events

While few serious AEs have been reported for the MVA-BN vaccine (Grabenstein and Hacker, 2024), we reviewed available evidence on risk of these AEs. Deng et al. (2023) find that the rate of attendance at a hospital emergency department following vaccination is less than one in 1,000, and none of the reasons for attendance were likely to lead to long-term disability. Duffy et al. (2024) find no evidence of statistically significant increases in any of the ten AEs they consider following mpox vaccination. As such, we do not model any long-term disability from mpox vaccination AEs.

Duffy et al. (2022) review the safety monitoring report of the MVA-BN vaccine; they find that of around a million vaccines administered, two men died within two days of receiving the vaccine – one from drowning and one under review at the time of publication. This remaining death is likely not caused by the vaccine, as one death per million is in line with expected mortality rates in the population (Duffy et al., 2022), so we include no fatal AEs in our base case. However, for conservatism, we include an assumed rate of fatal AEs as one in a million vaccinees in our upper estimate of DALYs from AEs.

TABLE A8.3. Calculated mpox vaccination DALY from all AEs

Mpox Vaccination DALY	Per Vaccine Recipient	Per Million Vaccine Recipients
Mean	0.0004	441.0
Lower	0.0001	142.3
Upper	0.0010	1,018.7

Appendix 9: Additional modelling parameters and CHEERS checklist

Topic	No.	Item	Location Where Item is Reported
Title			
	1	Identify the study as an economic evaluation and specify the interventions being compared.	Title
Abstract			
	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	Abstract
Introduction			
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.	First sections before the methods
Methods			
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	No plan was published, but a concept note was developed that became the methodology with minimal changes
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	Methods, Appendix 1, and Appendix 2
Setting and location	6	Provide relevant contextual information that may influence findings.	Methods, Appendix 1, and Appendix 2
Comparators	7	Describe the interventions or strategies being compared and why chosen.	Methods
Perspective	8	State the perspective(s) adopted by the study and why chosen.	Two perspectives are used, both healthcare payers, one local and one global; this is set out in the methods
Time horizon	9	State the time horizon for the study and why appropriate.	Set out in the methods
Discount rate	10	Report the discount rate(s) and reason chosen.	Set out in the methods
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	Set out in the methods and Appendices 8 and 9
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	Set out in the methods and Appendices 8 and 9
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	Set out in the methods and Appendices 8 and 9
Measurement and valuation of resources and costs	14	Describe how costs were valued.	Set out in Appendix 9
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	Set out in Appendix 9
Rationale and description of model	16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	Set out in the methods, Appendices 5, 6, 7, 9, and 12
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	Set out in the methods, results, discussion, and Appendix 12

Topic	No.	Item	Location Where Item is Reported
Characterising heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.	Discussion of different geographies and ages in the methods and results
Characterising distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	Discussion of different geographies and ages in the methods and results
Characterising uncertainty	20	Describe methods to characterise any sources of uncertainty in the analysis.	All headline results have uncertainty as standard, the approach to this is explained in the methods, Appendices 5, 6, and 9
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study.	The methods and draft manuscript have been shared with experts from many different disciplines, and the paper has been through peer review
Results			
Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	Appendix 9
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.	Results section
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	Considerable discussion of uncertainty about analytical judgements and inputs and resulting confidence
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study	Not reported
Discussion			
Study findings, limitations, generalisability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	Results and discussion sections
Other relevant information			
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	Reported at the start of the paper
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	No conflicts to declare; the lead author Tim Laurence has performed paid work for the UK Health Security Agency, the National Institutes of Health and Care Research, Cancer Research UK, Zipline Ltd, and the Alliance for Reducing Microbial Resistance in the last five years

Note: (Husereau et al., 2022).

All costs reported here are chosen to be consistent with 2022 USD.

Probability of long-term scarring

Scarring from prior lesions is a common sequela in both mpox clade I and clade II (Chromy et al., 2024). The probability of long-term scarring was therefore selected as a key additional parameter for modelling. Estimates from DRC studies suggest a median scarring prevalence of 63 percent observed up to four years following infection (Jezek et al., 1987; Brosius et al., 2025). A literature review of HICs found scarring probability to be between 5–40 percent, noting that scarring more commonly affects individuals living with advanced HIV (Titanji et al., 2024). Secondary bacterial infections are also linked to increased scarring (Chromy et al., 2024). Inflated reports of scarring are likely due to the decrease in individuals who return for follow-up consultations after infection and the fact that scars can take several months to years to develop, meaning that shorter follow-up periods may lead to healing lesions identified as scars (Iroezindu et al., 2023; Chromy et al., 2024; Brosius et al., 2025). However, Chromy et al. (2024) found that 43 percent of scars persisted at 15 months, and Jezek et al. (1987) found that about half of scars persist 2–4 years later. Therefore, overall we assume the probability of long-term scarring in Africa to be 40 percent in ascertained cases and 10 percent in unascertained infections. The rate in unascertained infections is lower because we assume having a high symptom burden leads people to attend healthcare.

Probability of vision loss

Ocular scarring, pitting, and general corneal complications have been increasingly associated with severe mpox cases (Zong et al., 2023; Titanji et al., 2024). A cohort study in the DRC found reduced visual acuity occurs in approximately 5 percent of cases, with 1 percent leading to blindness (Brosius et al., 2025). In an earlier DRC outbreak, (Jezek et al., 1987) cited a 4 percent visual impairment rate, having documented several cases of blindness and vision loss among both vaccinated and unvaccinated individuals. A more recent literature review found that 4.3 percent of mpox cases experienced visual impairment (Rohilla et al., 2025). However, the geographical disparity is stark – Gandhi et al. (2023) identified vision loss in 7.7 percent of cases and vision changes in 2.3 percent, yet notably, not a single non-African patient reported vision loss. The long-term consequences can be devastating; Jezek et al. (1988) found that serious sequelae, including blindness, severe scarring, and lasting vision defects, affected up to 10 percent of primary mpox cases. The risk is significantly higher among unvaccinated individuals, with 74 percent suffering severe complications compared to 39.5 percent of those who had been vaccinated (Damavandi et al., 2023). Overall, research supports the potential for long-term visual impairment in patients in Africa; we assume long-term impairment in 2.5 percent of infections experiencing minor visual impairment and 0.5 percent experiencing moderate visual impairment.

Case hospitalisation rate

Hospitalisation rates are important for understanding the cost implications of mpox. Brosius et al. (2025) reported a hospitalisation rate of 73 percent in their DRC study of 407 confirmed mpox cases.

A median of other studies done in African countries estimates a case hospitalisation rate of 43 percent (DeWitt et al., 2022; Ogoina et al., 2023). A study of global estimates based on WHO data reported a hospitalisation rate of 14 percent, noting the discrepancy in case hospitalisation reporting is influenced by available hospitalisation data and varying definitions (Hoxha et al., 2023). Therefore, we assume an overall case hospitalisation rate in African countries of 50 percent, and we assume only ascertained cases receive hospital treatment. We assume ascertained cases not receiving hospital treatment to attend outpatients at least once, and for 10 percent of unascertained infections to attend outpatient healthcare but not be recorded as cases due to misdiagnosis or failure to input data into a surveillance system.

Length of hospital stay

Length of hospital stay is a helpful indicator to estimate healthcare costs. A cohort study in the DRC and a cross-sectional study in Nigeria provided median estimates of 7 and 14 day stays, respectively, in hospitals when admitted with mpox (Brosius et al., 2025; Ogoina et al., 2023). Another observational study in the DRC reported a longer median stay in hospital of 22 days (Pittman et al., 2023). Patients with compromised immune systems who experienced more intense symptoms experienced longer hospital stays (Ogoina et al., 2023; Pittman et al., 2023). However, length of stay may be longer in research and teaching hospitals than other settings, with patients kept for longer observation as studies standardise data collection periods, and research hospitals having more resources to increase treatment intensity. Therefore, we assume a 7–14 day median length of hospital stay for admitted mpox patients.

Cost of hospitalisation

We were unable to identify estimates of the cost of hospitalisation within Africa, so we use WHO-Choice to estimate the cost of a hospitalisation based on length of stay. These estimates are inflated to 2022 USD, which is our reference price year.

Infection fatality rate

The true infection fatality rate (IFR) of mpox is highly uncertain, historic estimates of case fatality rates (CFRs) markedly overestimated the fatality rate observed in countries with higher levels of case ascertainment. The true level is probably much closer to 0.1 percent than the historic estimates of case fatality which were often reported to be 4–20 percent (Hoff, 2014; Beer and Rao, 2019). CFRs for endemic provinces of the DRC (where cases are more likely to be caused by clade Ia) are around 2.5 percent, whereas CFRs for other province with more clade Ib are considerably lower between 0.1 and 0.4 percent (WHO, 2025a); however, case ascertainment and case mix mean these populations may not be comparable, therefore we assume IFR for ascertained infections from clade Ib are likely to be 50–90 percent lower. We assume clade II (IIa and IIb) are somewhere in between with 0–70 percent lower IFR than clade Ia. The wide ranges we include on these adjustments

reflects the fact that the clinical characteristics of the clades are uncertain (Hoffmann, 2024; UKHSA, 2024c). Unascertained infections will tend to be less severe, because severity will lead people to attend treatment; however, severe infections that are not properly diagnosed and treated may disproportionately experience the most adverse outcomes, therefore we conservatively assume the IFR in unascertained cases is 90 percent lower. This assumption implicitly assumes that there could be underreporting of deaths from mpox, but given the challenges of diagnosis, testing, and registering deaths in Sub-Saharan Africa, this is a reasonable assumption.

Within-Africa vaccination costs

Because previous vaccine procurement has not been done in these quantities for low- and middle-income countries (LMICs), it is uncertain what price per dose an organisation like Gavi could negotiate. Therefore, we use an illustrative assumption of US$10 per dose and then have sensitivities for between US$2 a dose (an inexpensive global health price) all the way to US$100 a dose (a realistic HIC price assuming the buyer can negotiate based on quantity). Here a dose merely means half an immunisation schedule for a person, so we are not making assumptions about whether intradermal fractional doses are used. We use illustrative values of low-income country costs of vaccinating a child at US$1.50 and assume the cost is higher for catch-up programmes in adults at US$4.50.

Maximum ICER threshold

This modelling investigates whether pandemic mitigation might lead to higher global cost-effectiveness of mpox vaccine than evaluating the vaccine from a domestic perspective. Therefore, in our global pandemic modelling scenarios, we assume vaccine rollout past the point of cost-effectiveness in Africa, up to the ICER of US$10,000 per DALY. This cut-off is chosen to be a round number that is well above the point of national cost-effectiveness. Other values are tested in sensitivity analyses.

Onward transmission suppression impact of vaccination

For the following reasons, we deemed it out of scope to estimate a dynamic transmission model:

1. **Uncertainty in the contribution of different groups and behaviours to disease transmission:** During the 2022 outbreak in some HICs, it was clear that close contact between GBMSM (that could have reflected sexual interaction) was a primary route of disease transmission, so several infectious disease modellers concluded that explicitly capturing this form of transmission in a network model was appropriate (Brand et al., 2023; Murayama et al., 2024; UKHSA, 2024). In Africa, the relative contributions between zoonotic transmission in live animals, zoonotic transmission in food, human to human contact in households, human to human transmission during sexual activity, and other human to human transmission is unclear (UKHSA, 2025c).

2. **Lack of available data on behaviour:** In HICs reliable survey data on sexual contact made it possible to calibrate more sophisticated network models. Though even in these data-rich settings, it was still necessary to make many assumptions which were challenging to fully evidence.
3. **Low rates of case ascertainment:** The large variance between cases and infections reduce the signal from case data and make fitting any type of complex model in a defensible way considerably more challenging.

Due to the lack of evidence for which transmission routes are most important for mpox transmission in Africa, and the scope of this model to provinces, we did not build a dynamic transmission model (e.g., a susceptible-exposed-infectious-recovered (SEIR) type model).

A study published after ours had begun, Jin et al., (2025), make these transmission dynamics the main focus of their study. They attempt to include some of these features in a next-generation model; in spite of the impressive scope of their evidence summary, they have to make many simplifying assumptions. Most materially, they assume contact only happens in households or sexually, and that there is no zoonotic transmission. Depending on the exact assumptions they make about sexual contact, their estimates of the effective reproduction number move from just below 1 to around 2, leading to completely different conclusions about the benefit and necessary coverage of vaccination to mitigate transmission.

To somewhat capture the impact of the vaccine on onward transmission, we take a simple approach of assuming for every infection mitigated directly through vaccination there is an indirect impact averting 0.5 additional infections within Africa. A dynamic transmission model done in Africa finds this value to be considerably higher (1.7–2.2) for low levels of vaccine coverage (Peter et al., 2025). HIC modelling on mpox suggests that low levels of immunity, particularly of high contact individuals, has a disproportionate impact on transmission (Brand et al., 2023; Murayama et al., 2024; UKHSA, 2024). Therefore, the value of 0.5 is highly conservative and so understates the benefit of vaccination.

Global deaths and DALYs

We include the impact of deaths and disability on DALYs estimated outside of Africa. For deaths, we compare an estimated infection number to the number of laboratory confirmed deaths to get an IFR, and this IFR is then held constant in simulations. Where this outside-of-Africa IFR is estimated primarily based on clade IIb cases and deaths, we adjust it according to assumptions about the relative severity of clade Ia and clade Ib, using the same assumptions as we apply to the IFR within Africa. Our focus on laboratory confirmed deaths outside of Africa assumes there is no underreporting of deaths in these countries to be conservative. We assume 30 DALYs per

death because the average age at death was 34; with conditional life expectancy into the 80s, the discounted years of life lost (YLL) is approximately 30. For disability, we include a 10 percent probability of lifetime scarring and 0.2 percent probability of minor lifetime vision impairment, which is considerably lower than the values for Africa because timely access to healthcare likely averts considerable long-term impacts. The disability weights applied are the same as those in Table A9.1, because disability weights are universal.

Healthcare spending outside of Africa

We cost healthcare spending in response to an mpox pandemic based on three main components: inpatient hospital costs, testing costs, and responsive vaccination costs. We assume an infection hospitalisation rate of 5 percent, where higher case hospitalisation rates are often observed in lower-income countries due to lower case ascertainment (so a more severe mix of cases). Hospital costs of US$5,000 are assumed for the UK based on Zhang et al. (2024); this is then scaled by estimates of the EcoAMR study for bacterial skin and soft tissue infections. Producing more detailed country-level estimates of this cost is outside the scope of this study, and EcoAMR was a large dedicated effort to make comparable infection admission costs across countries using advanced modelling techniques (McDonnell et al., 2024; Laurence et al., 2025). We assume US list prices for vaccine costs because vaccines were procured when demand outstripped supply, so it is assumed that the manufacturer had pricing power. The US deployed a majority of mpox vaccine doses, so this price covers most doses, even if not most countries that deployed some vaccines. The cost of testing depends on tests delivered rather than confirmed cases, so we adjusted confirmed cases for tests delivered using an assumed positivity of 25 percent (where total tests are confirmed cases divided by test positivity). We assume only one PCR test is run per suspected case to be conservative, where in practice multiple swabs are generally taken and tested (CDC, 2024a; WHO, 2024a; UKHSA, 2025b). We assume an illustrative PCR test cost of US$60, which will be most appropriate for HICs which did most testing (because they are more likely to use testing to confirm infections).

TABLE A9.1. Within-Africa health parameters

Model Parameter	Value	Underpinning Evidence
Probability of long-term scarring	Assumed probability of long-term minor scarring: **40 percent** in ascertained cases, **10 percent** in unascertained infections	(Jezek et al., 1987; Iroezindu et al., 2023; Prasad et al., 2023; Titanji et al., 2024; Brosius et al., 2025)
Probability of vision loss	Estimated **2.5 percent** of infections experiencing minor visual impairment; **0.5 percent** experiencing moderate visual impairment	(Jezek et al., 1987, 1988; Damavandi et al., 2023; Gandhi et al., 2023; Zong et al., 2023; Titanji et al., 2024; Brosius et al., 2025; Rohilla et al., 2025)
Case hospitalisation rate	In African countries, we assume a case hospitalisation rate of **50 percent**, and assume that all ascertained cases receive inpatient or outpatient treatment	(DeWitt et al., 2022; Hoxha et al., 2023; Ogoina et al., 2023; Brosius et al., 2025)
Infection fatality rate	**0.25 percent** to **2.5 percent** in ascertained cases depending on clade, **90 percent** lower for each clade in unascertained cases	WHO dashboard case fatality rate for DRC (for ascertained cases) and then a much lower value for infections not ascertained Ascertained outcomes are assumed to be worse because more severe cases tend to present at healthcare and so are ascertained. However, severe cases that do not present at healthcare are more likely to die when untreated, so we include some mortality for this group.
DALY burden of adverse events per vaccine	0.0004	See Appendix 8
Disability weight minor scarring	0.011	(WHO, 2020)
Disability weight vision loss	0.005 (minor vision loss) 0.089 (moderate vision loss)	(WHO, 2020)

TABLE A9.2. Within-Africa economic parameters

Model Parameter	Value	Underpinning Evidence
Length of hospital stay	Median **7–14** days hospital stay for admitted mpox cases	(Ogoina et al., 2023; Pittman et al., 2023; Brosius et al., 2025)
Cost of hospitalisation	Cost of hospitalisation not available, will be estimated based on length of stay	(WHO-Choice, 2021) - inpatient cost per day
Price of vaccine per dose	US$10 – in the base case. Sensitivities: US$2, US$5, US$22, US$100	US$2 assumption based on low negotiated price by Gavi long-run, US$5 negotiated price medium-run, US$22 lower end of Gavi-assumed stockpile price, US$100 upper end of Gavi-assumed stockpile price
Cost per dose of routine vaccine delivery	US$1.50	(Laurence and McDonnell, 2025)
Cost per dose of older age vaccine delivery	US$4.50	Assumed an average of influenza and HPV vaccination collected by immunisation economics (ThinkWell, 2024)
Vaccine coverage	80 percent	Purely illustrative, not necessarily achievable for mpox, but approximately the WUENIC estimate of coverage for other vaccines in DRC

Note: WUENIC = WHO/UNICEF Estimates of National Immunization Coverage.

TABLE A9.3. Outside-of-Africa and onward transmission parameters

Model Parameter	Value	Underpinning Evidence
Maximum local ICER below which allocate vaccination	US$10,000	Illustrative cut-off to allow for vaccination to be rolled out well passed national cost-effectiveness in Africa
Indirect impact in Africa of averting one infection	0.5 additional infections	Peter et al. (2025) report results form a range of 1.7–2.3, so use 0 to 1 out of conservatism because this parameter is so uncertain
Total confirmed cases before pandemic confirmed	**58** confirmed cases outside of Africa 1970 to pre-2022 breakout, of which 17 were exported cases and 41 were cases from exported animals	(McCollum et al., 2023)
Deaths	Global reported cases of human mpox-related deaths 1970–2021 **(547)**; Total reported deaths since 2022 **(410)**	(McCollum et al., 2023; WHO, 2025a)
DALY loss per death outside Africa	30	The average age of mpox related death 2022–2023 is 34 years old (Riser et al., 2023)
Probability scarring HIC	10 percent	Average six month follow-up between studies (Prasad et al., 2023; Chromy et al., 2024; Titanji et al., 2024)
Probability vision loss HIC	0.2 percent	(Cash-Goldwasser et al., 2022; Gandhi et al., 2023; Pazos et al., 2023) CDC estimates 5 percent of mpox cases in US experience eye complications (only 1 of the 5 people described had significant vision loss)
IHR outside of Africa	5 percent	Ward et el. (2024) report around 4 percent for England.
Cost per hospitalisation	US$5,000 This is scaled by consistent estimates of bacterial skin hospitalisations to other countries in the world	(Zhang et al., 2024; Laurence and McDonnell, 2025)
Number of doses delivered outside Africa	2 million	(PAHO, 2022; European Centre for Disease Prevention and Control, 2023; Charles et al., 2024; GT staff reporters, 2024; Kang et al., 2024; Public Health Agency of Canada, 2024; Silva et al., 2024; Department of Health, Disability, and Ageing, Australia, 2025)
Vaccine dose cost outside Africa	US$200	£160 (Zhang et al., 2024); US$229.50 (CDC, 2025b)
Cost per dose delivered outside Africa	US$40	£36.85 first dose administration, £25.78 second dose administration (Zhang et al., 2024)
Testing positivity	24.5 percent	(WHO, 2023; CDC, 2024b)
Testing cost	US$50	(Moloney et al., 2019; Minhas et al., 2023; Bonnet et al., 2024; Sharfstein, 2025)

TABLE A9.4. All parameters uncertainty distribution

Model Parameter	Mean	Lower	Upper	Distribution
Proportion scarring ascertained	0.4	0.3	0.5	beta
Proportion scarring unascertained	0.1	0.05	0.2	beta
Proportion vision loss minor	0.05	0.01	0.1	beta
Proportion vision loss major	0.01	0.005	0.02	beta
Case hospitalisation rate	0.5	0.25	0.75	beta
Infection fatality rate ascertained Ia	0.025	0.0125	0.05	beta
Infection fatality rate reduction ascertained Ib	70%	90%	50%	beta
Infection fatality rate reduction ascertained II	50%	70%	0%	beta
Infection fatality rate reduction for unascertained infections	90%	95%	80%	beta
DALY burden of adverse events per vaccine	0.0004	0.0001	0.001	lognorm
Disability weight minor scarring	0.011	0.005	0.02	beta
Disability weight minor vision loss	0.005	0.002	0.01	beta
Disability weight major vision loss	0.089	0.05	0.314	beta
Length of hospital stay	10	7	14	gamma
Cost per hospital day	WHO choice	WHO choice	WHO choice	not varied prob.
Price of vaccine per dose	10	same as mean	same as mean	not varied prob.
Cost per dose of routine vaccine delivery	1.5	0.5	3	gamma
Cost per dose of older age vaccine delivery	4.5	3 (3.73)	6 (5.61)	gamma
Vaccine coverage	0.8	same as mean	same as mean	not varied prob.
Maximum local ICER below which allocate vaccination	10000	same as mean	same as mean	not varied prob.
Indirect impact in Africa of averting one infection	0.5	0	1	uniform
Total confirmed cases before pandemic confirmed	17	5	50	gamma
Lower expected size of a clade Ia pandemic	70%	90%	50%	beta
Deaths	derived from IFR (ascertained, unascertained)		-	
DALY loss per death outside Africa	40	30	50	gamma
Probability scarring outside Africa	0.1	0.05	0.2	beta
Probability minor vision loss outside Africa	0.002	0.001	0.005	beta
IHR outside Africa	0.04	0.03	0.05	beta
Cost per hospitalisation	5000	4000	7000	gamma
Number of doses delivered outside Africa	2000000	1500000	2500000	norm
Vaccine dose cost outside Africa	200	100	300	gamma
Cost per dose delivered outside Africa	40	20	60	gamma
Testing positivity	0.25	0.15	0.5	beta
Testing cost	50	25	100	gamma

Appendix 10: Results of the case ascertainment regression analysis

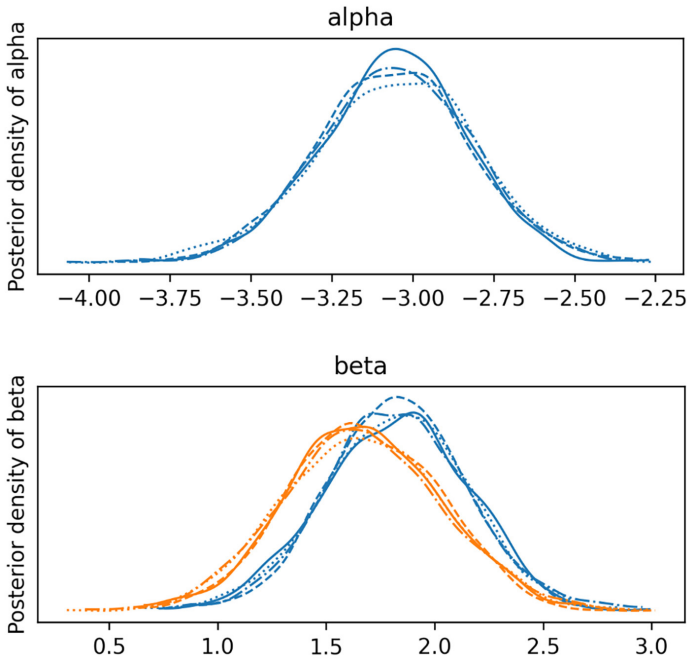
Diagnostics suggest good convergence and stable posterior estimates across the model. All parameters have R-hat values of 1.0, suggesting that the Markov chains mixed well. The effective sample sizes (ESS) for both bulk and tails are sufficiently high. The value of α implies that the lowest ascertainment country would be expected to have between 2.8 percent and 7.1 percent case ascertainment for mpox. The values of β_1 and β_2 imply that case ascertainment would be expected to increase to 21.2 percent for a country with 0.5 for each of these covariates (which are highly correlated), and the country with the maximum value of these covariates would have case ascertainment of 60.7 percent. The overdispersion parameter indicates that there is considerable variation in resulting estimates, likely because of the large range in estimates used to estimate the model.

TABLE A10.1. Estimated coefficients of the case ascertainment regression (equation A5.1)

Parameter	Mean	SD	ESS Bulk	ESS Tail	R-hat
α (intercept)	−3.058	0.241	4794.0	4436.0	1.0
β_1 (HAQ coeff.)	1.822	0.328	4708.0	4269.0	1.0
β_2 (healthcare spend coeff.)	1.672	0.361	4361.0	4185.0	1.0
λ (overdispersion)	25.883	1.770	5525.0	3559.0	1.0

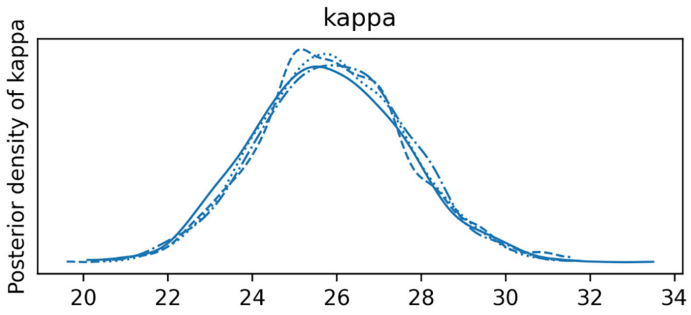
Note: ESS = effective sample size.

FIGURE A10.1. Posterior densities of the parameter values (where each line represents a different MCMC chain)



Notes: MCMC = Markov Chain Monte Carlo. The blue lines are β_1 and the orange lines are β_2.

FIGURE A10.1. (Continued)



Appendix 11: Additional charts and tables

TABLE A11.1. Estimated ICERs for routine and catch-up vaccination for the provinces and age groups with the lowest estimated ICERs

Country (ISO3)	Province (admin-one)	Age Range	Estimated ICER (90 Percent Credible Interval)	Base Case Scenarios Receiving Vaccine
COD	SANKURU	00–09	433 (186, 939)	Both
COD	TSHUAPA	00–09	628 (270, 1,367)	Both
COD	EQUATEUR	00–09	771 (332, 1,684)	Both
COD	SANKURU	10–19	793 (340, 1,751)	Routine and catch-up only
COD	BAS UELE	00–09	914 (393, 2,000)	Both
COD	TSHUAPA	10–19	1,215 (519, 2,699)	Routine and catch-up only
COD	SUD UBANGI	00–09	1,386 (594, 3,111)	Both
COD	SANKURU	20–29	1,613 (689, 3,618)	Routine and catch-up only
COD	TSHOPO	00–09	1,760 (751, 4,009)	Both
COD	EQUATEUR	10–19	1,828 (782, 4,125)	Routine and catch-up only
COD	BAS UELE	10–19	1,905 (814, 4,302)	Routine and catch-up only
COD	TSHUAPA	20–29	2,106 (898, 4,773)	Routine and catch-up only
COD	SANKURU	30–39	2,138 (912, 4,851)	Routine and catch-up only
COD	SUD UBANGI	10–19	2,564 (1,092, 5,906)	Routine and catch-up only
COD	SUD KIVU	00–09	2,695 (1,078, 6,591)	Both
COD	TSHUAPA	30–39	2,845 (1,210, 6,582)	Routine and catch-up only
COD	MAI NDOMBE	00–09	2,882 (1,215, 6,605)	Both
COD	MONGALA	00–09	2,931 (1,235, 6,719)	Both
COD	BAS UELE	20–29	3,464 (1,473, 8,107)	Routine and catch-up only
COD	TSHOPO	10–19	3,693 (1,569, 8,674)	Routine and catch-up only
COD	SUD UBANGI	20–29	3,882 (1,646, 9,137)	Routine and catch-up only
COD	EQUATEUR	20–29	3,911 (1,657, 9,209)	Routine and catch-up only
COD	SUD KIVU	10–19	4,329 (1,729, 11,205)	Routine and catch-up only
COD	BAS UELE	30–39	4,715 (1,981, 11,254)	Routine and catch-up only
COD	MAI NDOMBE	10–19	5,121 (2,148, 12,269)	Routine and catch-up only
COD	SUD UBANGI	30–39	5,311 (2,226, 12,773)	Routine and catch-up only
COD	EQUATEUR	30–39	5,362 (2,247, 12,908)	Routine and catch-up only

TABLE A11.1. Estimated ICERs for routine and catch-up vaccination for the provinces and age groups with the lowest estimated ICERs (Continued)

Country (ISO3)	Province (admin-one)	Age Range	Estimated ICER (90 Percent Credible Interval)	Base Case Scenarios Receiving Vaccine
COD	SUD KIVU	20–29	6,160 (2,419, 16,405)	Routine and catch-up only
BDI	BUJUMBURA MAIRIE	00–09	6,745 (1,523, 22,169)	Both
COD	SUD KIVU	30–39	7,100 (2,776, 19,317)	Routine and catch-up only
COD	MONGALA	10–19	7,211 (2,998, 17,913)	Routine and catch-up only
COD	TSHOPO	20–29	7,418 (3,084, 18,523)	Routine and catch-up only
COD	KASAI	00–09	7,438 (3,036, 20,002)	Both
SLE	WESTERN	20–29	7,529 (2,225, 23,210)	Routine and catch-up only
COD	MANIEMA	00–09	7,953 (3,243, 22,033)	Both
COD	NORD UBANGI	00–09	8,953 (3,634, 25,353)	Both
COD	TSHOPO	30–39	10,244 (4,162, 28,041)	Neither
BDI	BUJUMBURA MAIRIE	20–29	10,822 (2,539, 38,774)	Neither
SLE	WESTERN	30–39	11,070 (3,178, 37,037)	Neither
COD	KASAI	10–19	14,073 (5,518, 42,224)	Neither
SLE	WESTERN	10–19	14,801 (4,138, 59,509)	Neither
BDI	GITEGA	20–29	14,900 (3,428, 60,887)	Neither
BDI	GITEGA	00–09	15,123 (3,194, 68,786)	Neither
COD	MANIEMA	10–19	15,402 (6,011, 47,448)	Neither
COD	TANGANYIKA	00–09	17,323 (6,247, 68,013)	Neither
BDI	BUJUMBURA MAIRIE	30–39	18,025 (4,112, 82,292)	Neither
COG	LIKOUALA	00–09	18,154 (6,417, 66,339)	Neither
COD	NORD KIVU	00–09	19,377 (6,913, 83,233)	Neither

FIGURE A11.1. Additional spend on vaccination has a diminishing impact on infections directly averted (routine and catch-up)

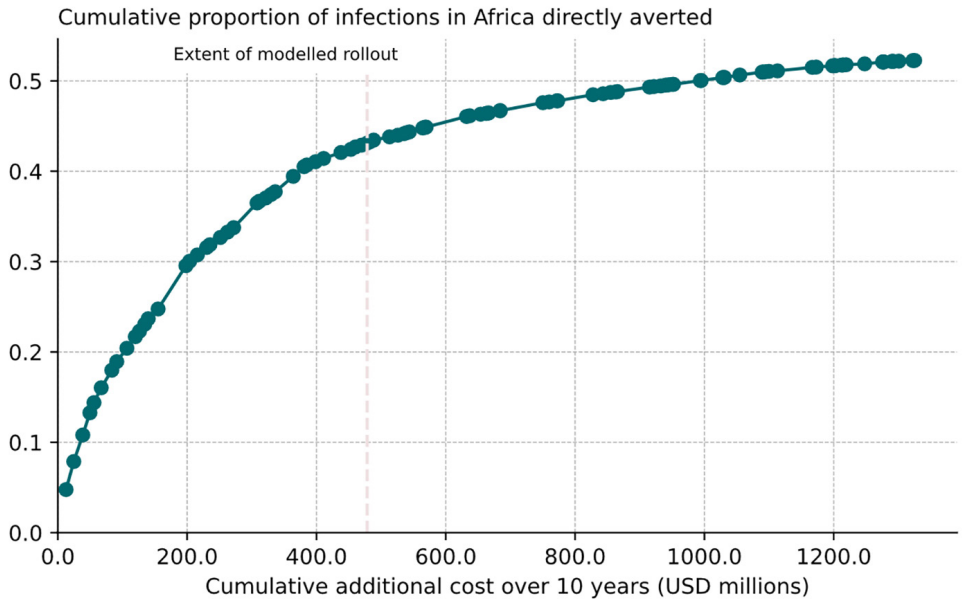
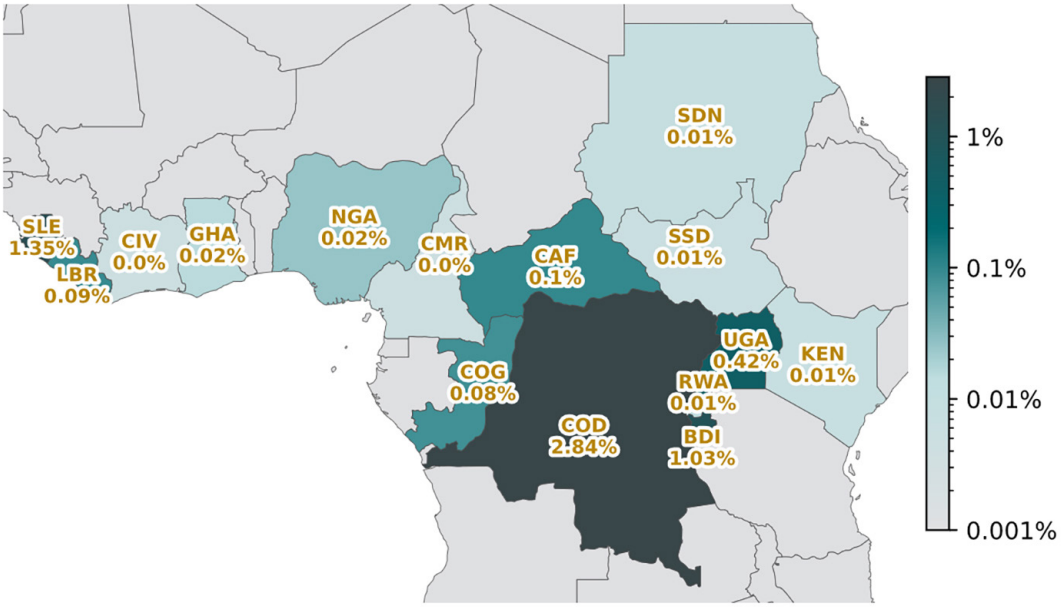


FIGURE A11.2. Cumulative probability of having been infected with mpox for an adult turning 30 years old in 2025 (colour log scaled)



Appendix 12: Detailed discussion of study strengths and limitations

Strengths and limitations of case ascertainment regression modelling

We assess the confidence in the estimates resulting from this analysis as **low** for countries within Africa and **medium** for HICs.

The strengths of this approach to estimate case ascertainment through regression modelling are:

1. The best available estimates of case ascertainment are built directly into this regression, so our resulting estimates are broadly consistent with the weight of evidence from the literature.
2. Using covariates allows us to estimate case ascertainment (and so understand the true infection burden) for countries for which there are no existing estimates.

The five key limitations of our estimates resulting from our case ascertainment modelling are:

1. The underlying studies which form our *observed* values are generally the results of modelling studies themselves. This means they should not be interpreted as true values themselves, but rather as evidence-based estimates of the actual value, not direct

measurements of it. This increases the chance that they are structurally biased, rather than subject to random error, and any structural bias would be replicated in our model.
2. There are few estimates of this parameter within Africa, so many countries in our modelling are solely dependent on the relationship we estimate through this modelling.
3. Sometimes we had to make assumptions to transform the results of studies reporting related variables (such as the number of cases found through enhanced testing) to estimate case under-ascertainment. Different analysts may have made different assumptions and estimates.
4. This purely statistical approach has no mechanism for assessing the potential feasibility of the upper and lower bounds of the resulting estimates.
5. We were not able to estimate whether this parameter is changing over time in Africa.

Strengths and limitations of simple infection modelling

We assess the confidence in the estimates resulting from this analysis are **low**.

The main strengths of our simple infection modelling and resulting estimates are:

1. It allows us to try to quantify the burden of mpox imposed by the majority of infections that are not reported as cases.
2. It is highly transparent and easy to understand the methodology and drivers of resulting estimates.
3. Partly due to its simplicity, the method yields results that look sensible because there are no unexpected non-linearities in an underlying model mechanism.

The main limitations of the method are:

1. Some of the reported case data are very weak, with suspected case reporting in the DRC varying widely between different areas, and levels of laboratory confirmation very low for some areas. We did not systematically estimate case ascertainment subnationally, so our application of national estimates to specific geographies may be inappropriate.
2. It does not incorporate serology data, which is discussed in detail in Appendix 7. Without a data source like serology, there is not a mechanism to constrain potentially infeasible values of case ascertainment.
3. It does not force basic constraints, for instance stopping the probability someone is infected (which should be bounded between 0 and 1) from going above 1, though this does not happen in practice.
4. It does not allow places with no cases in a given year to have any estimated infections. This is fine for the purpose of our study of routine vaccination, because areas that report no cases are highly unlikely to represent sensible regions to roll out routine vaccination unless further evidence of burden is collected.

5. It does not allow case ascertainment to change over time: our regression results only apply to current case ascertainment, but are applied historically. In particular, the scale of the outbreak in the DRC in 2024 and 2025 may have led to higher case ascertainment than our estimates suggest, and so lower total infection numbers. Case ascertainment in the DRC is also likely to have been considerably lower before the introduction of the ISDR surveillance system including mpox in 2000.

Strengths and limitations of within-Africa cost-effectiveness modelling

While our findings represent a valuable contribution to the literature, we think our within-Africa modelling is subject to considerable limitations, and the results and findings should be regarded as **low confidence**.

Some of the strengths of the approach and estimates are:

1. Focusing on provinces, while uncertain, allows the modelling to better articulate the value of mpox vaccination for those areas with the highest burden.
2. It represents a comprehensive assessment of the healthcare costs and burden relevant to mpox vaccination.

Some of the key limitations of the approach and estimates are:

1. There are considerable uncertainties on the epidemiology of mpox, as set out in the simple infection modelling section above.
2. The transmission dynamics of MPXV in Africa are very uncertain. This means fitting more complex model structures that better account for transmission dynamics was deemed out of scope, particularly given that our analysis spans provinces across multiple countries. We discuss this in Appendix 9.
3. Building on point 2), without capturing these complex transmission dynamics, simpler compartmental model structures were deemed inappropriate because they may overestimate attack rates (Brand et al., 2023; Murayama et al., 2024; UKHSA, 2024).
4. To estimate the DALY loss from the AEs caused by mpox vaccination, we had to rely on evidence from adults in HICs because safety data in children is still being gathered (CEPI, 2024).
5. There is a lack of standard health economics evidence for mpox in Africa; specifically there are a lack of patient-reported outcomes for people suffering from mpox sequelae and healthcare cost estimates. We used the best available evidence based on length of stay and WHO-Choice, along with disability weights deemed analogous to the sequelae mentioned in clinical studies.

Strengths and limitations of the pandemic modelling

Due to inherent uncertainties in pandemic modelling, and other limitations that could be reduced by better quality data, we assess the results of our pandemic modelling to be **very low confidence**.

Strengths of our pandemic modelling:

1. Our results are the first to demonstrate the significant potential health gains globally from using vaccination in the highest burden regions of Africa to reduce transmission both inside and outside the African continent.
2. Our results demonstrate that the impact outside of Africa may be large in terms of healthcare costs and monetised health benefits.
3. Our results are an internally consistent end-to-end model that would directly answer questions of a pandemic prevention policymaker.

Limitations of our pandemic modelling:

1. Pandemic prevention models are inherently uncertain because pandemics do not occur often enough to have large sample datasets to predict their frequency and size.
2. The epidemiological impact of exported mpox cases from Africa on the geographical reach of pandemics outside of Africa is highly uncertain.
3. One particular limitation of our pandemic prevention work is not incorporating international travel data explicitly into the model. While flight data are available, the extent to which people are travelling from regions to major airport hubs would be uncertain. Future work that seeks to build on this analysis should better characterise the unequal risk to global transmission posed by mpox transmission in different geographies in Africa.
4. Previous limitations on uncertainties around mpox in Africa also apply here.
5. We do not adjust for whether a future pandemic is more or less likely to occur, which is discussed below.

Assumption 5) may be challenged because MPXV transmission in countries outside of Africa has been reduced since the peak of the 2022 pandemic. While it is clear that transmission dynamics changed over the course of 2022, the drivers of this remain unclear. Potential drivers include:

1. Build up of natural immunity in GBMSM at higher-risk
2. Build up of vaccine-derived immunity in GBMSM at higher-risk
3. Greater knowledge of mpox vigilance in GBMSM at higher-risk
4. Changes in sexual behaviour in GBMSM at higher-risk

(Endo et al., 2022; Brand et al., 2023; De Vos et al., 2024; Guzzetta et al., 2024; Murayama et al., 2024; UKHSA, 2024)

It is clear that drivers 3 and 4 can change relatively quickly, to revert to much nearer baseline (pre-2022) levels. For drivers 1 and 2, the group of GBMSM with the highest number of sexual contacts is not a fixed group, as people break and form partnerships (Mercer et al., 2004, 2013; Anderson et al., 2021; Ogaz et al., 2024). People can enter and leave this group, so in a short number of years the level of immunity in GBMSM at higher-risk of mpox transmission might be markedly lower (as immune GBMSM reduce behaviours that increase the risk of mpox transmission, and non-immune GBMSM adopt these behaviours). The size of this group can also grow relatively rapidly as sexual behaviour is not fixed. The potential for a growing population of sero-naive GBMSM is greater because immunity from vaccination may wane, and vaccine uptake across the broader GBMSM population was far from universal in many countries. Finally, while the 2022 pandemic disproportionately affected GBMSM, data in Africa shows mpox can also spread through heterosexual networks sufficiently to sustain human-to-human transmission (Ndembi et al., 2024; Kangbai et al., 2025; WHO, 2025c).

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