

1 **Informing an mpox stockpile investment case:** 2 **epidemiological modelling and cost-benefit analysis**

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17 **Abstract**

18 **Background:** In response to ongoing mpox outbreaks, Gavi, The Vaccine Alliance (Gavi) was
19 considering funding the establishment of an mpox vaccine stockpile. To support their decision-
20 making, Gavi commissioned the Johns Hopkins University Center for Outbreak Response
21 Innovation to estimate the optimal size, impact, health benefits, and monetized net benefits of
22 different mpox vaccine stockpile sizes for an effective global stockpile to support outbreak
23 containment and prevention of widespread mpox transmission.

24 **Methods:** A deterministic compartmental model of mpox transmission with vaccine
25 interventions was developed, including intervening at 20 or 100 cases reported. The findings
26 from this model were incorporated into a Monte-Carlo cost-benefit analysis.

27 **Findings:** Rapid response using a single-dose vaccination strategy provided the greatest cost
28 benefits compared to a two-dose strategy. Using a one-dose strategy, expected net benefits are
29 estimated to be over \$81 million to \$220 million higher when responding to outbreaks rapidly
30 (after 20 cases) than when responding after 100 cases. Total cost per DALY averted for one-dose
31 vaccine strategy ranges from roughly 18% to 53% lower than the two-dose strategy. A stockpile
32 of 1,000,000 doses had the highest ratio of benefits to costs.

33 **Interpretation:** At a large enough size, a stockpile can be effective in controlling outbreaks and
34 reducing overall negative health impacts. The cost-effectiveness of mpox vaccine stockpiles
35 could be further maximized with reduced vaccine pricing and dose-sparing strategies.

36 **Funding:** Gavi, The Vaccine Alliance (Gavi).

37 **Key words:** Mpox; Vaccine stockpile; Outbreaks; Epidemiological modeling; Cost-Benefit
38 Analysis

39 **1. Introduction**

40 Mpox is a viral zoonotic disease that is endemic to West and Central Africa. The causative viral
41 agent of mpox disease (MPXV) is classified into two clades, clade I and clade II, with further
42 subdivisions into subclades a and b.¹ Clade I is associated with a higher case fatality ratio (1.4%
43 to ~10%) compared with clade II (0.1% to 3.6%).^{2,3} Furthermore, clade I is more commonly
44 endemic to Central Africa, and clade II is typically identified in West Africa, although, since
45 2022, clade II has been circulating globally.⁴ Although mpox has mostly remained endemic in
46 several African countries since its identification in 1970, outbreaks in recent years have been
47 reported in both endemic and non-endemic countries globally, which continue to circulate with
48 ongoing clade II and clade Ib outbreaks originating in 2022 and 2023, respectively.⁵ These
49 outbreaks, and the global circulation of clade II, led to a public health emergency of international
50 concern (PHEIC) being declared in 2022, which ended in 2023.^{4,6} A second PHEIC was declared
51 from August 2024 to September 2025 due to increasing mpox cases and the spread of the
52 emerging clade Ib on the African continent.^{4,7}

53 The World Health Organization's (WHO) vaccination recommendations for mpox primarily
54 focus on vaccination in outbreak settings, with preventive vaccination currently recommended
55 only for laboratory personnel working with Orthopoxviruses in non-outbreak contexts.¹ In
56 outbreak settings, the WHO's Strategic Advisory Group of Experts on Immunization (SAGE)
57 recommends vaccinating target populations, such as high-risk groups, contacts of confirmed
58 cases, and healthcare workers for mpox vaccination during an ongoing outbreak.¹ Populations at
59 higher risk for the virus include men who have sex with men, female sex workers, and children,
60 particularly under the age of 5 years.⁸ Currently, two mpox vaccines, MVA-BN (non-replicating,
61 prequalified (PQ) by WHO in September 2024) and LC16m8 (minimally replicating, granted
62 WHO Emergency Use Listing (EUL) in November 2024), are used in response to mpox
63 outbreaks to reduce mpox transmission with varying vaccine efficacy based on the dosing
64 schedule.⁹ The rapid deployment of vaccines can assist in preventing a small outbreak from
65 progressing to a larger epidemic.¹⁰

66 Globally, stockpiles have been a key approach to enable rapid vaccine deployment to support
67 outbreak containment and prevent widespread transmission.¹¹ Gavi, the Vaccine Alliance,
68 (Gavi), already funds four existing stockpiles for meningitis vaccine, Ebola virus disease
69 vaccine, cholera vaccine, and yellow fever vaccine, with the aim of preventing vaccine-
70 preventable deaths and protecting national and global health security. These vaccine stockpiles
71 are formally managed by the International Coordinating Group (ICG) on Vaccine Provision.^{12,13}
72 This study aimed to enhance the evidence base to support Gavi's decision-making for investing
73 in an mpox vaccine stockpile, with the primary use intended to be for Gavi-eligible countries to
74 have equitable and timely access to mpox vaccines during outbreaks, using epidemiological
75 modelling and cost-benefit analysis.

76 **S1.1 Research in Context**

77 **a) Evidence before this study**

78 Since first being detected in the Democratic Republic of the Congo (DRC) in 1970,
79 intermittent outbreaks of mpox disease have occurred, mostly in West and Central Africa,
80 until the global spread of the disease in 2022.⁵ In July 2022, the World Health
81 Organization (WHO) declared the global transmission of mpox as a Public Health
82 Emergency of International Concern (PHEIC), which was ended in May 2023. This was
83 followed by a second PHEIC declaration from August 2024 to September 2025, due to
84 the increase of mpox cases in Africa and the emergence and spread of the clade Ib
85 MPXV.^{4,14} With the rise in mpox transmission in recent years, there has been an increase
86 in utilizing various forms of modelling to investigate and forecast mpox transmission
87 dynamics.^{15,16} A recent study by Savinkina et al. (2025) utilized epidemiological
88 modelling of vaccine approaches for containing mpox transmission in the DRC to inform
89 future vaccination policies.¹⁶ Despite the increased incorporation of epidemiological
90 modelling to inform cost-benefit analyses (CBAs) of prevention strategies, only a limited
91 number of studies have incorporated results from mpox epidemiological models of
92 disease transmission and mitigation strategies into CBAs to inform public health
93 preparedness policies.^{17,18} In this study, we aimed to quantify the potential impact of
94 vaccination on future mpox outbreaks to inform Gavi's decision-making for investing in
95 an effective mpox vaccine stockpile.

96
97 **b) Added value of this study**

98 This study expands on previous use of epidemiological models to investigate various
99 vaccination strategies for responding to an mpox outbreak in Gavi-eligible African
100 countries across three different archetypal settings. The findings from the Monte Carlo
101 simulations of mpox transmission dynamics across these settings in Africa were
102 incorporated into a mpox stockpile simulation and cost-benefit analysis. This analysis
103 contextualizes the benefits of various stockpile sizes of the MVA-BN vaccine, vaccine
104 delivery times, and dosing strategies with varying vaccine efficacy (76% for one-dose
105 regimen; 82% for two-dose regimen). To support Gavi's evidence-based decision-
106 making, this study applied various modelling techniques to estimate the required quantity
107 for an mpox stockpile and model the health impacts of stockpile options for outbreaks in
108 various contexts and population groups.

109
110 **c) Implication of all the available evidence**

111 The results from this study suggest cost-effectiveness is maximized at a relatively large
112 stockpile size, with use of a single dose of the MVA-BN mpox vaccine compared to a
113 two-dose strategy, and a rapid vaccine delivery time. Additional research is needed to
114 understand how cost-effectiveness might change with other mpox vaccines, such as
115 LC16m8, and dose-sparing strategies such as fractional dosing, and to compare the costs

116 and benefits of outbreak response vaccination strategies versus preventative
117 immunization strategies.

118 **2. Methods**

119 *2.1. Epidemiological Model*

120 To explore potential vaccine-based mitigation strategies for mpox outbreaks in Gavi-eligible
121 countries, we constructed a deterministic compartmental Susceptible, Exposed, Infected,
122 Recovered, Dead, and Vaccinated (SEIRD-V) model to simulate disease transmission and
123 control dynamics within target populations for vaccination, given two vaccination strategies
124 (one-dose and two-dose), compared to no intervention. The model was developed based on a
125 series of ordinary differential equations and inputs from the literature, as well as consultation
126 with an external steering committee comprised of country representatives and representatives
127 from international organizations involved in the latest mpox PHEIC response.¹⁹⁻²⁶ The model was
128 implemented in Python (version 3.13.5) to simulate mpox transmission dynamics in four distinct
129 sub-populations, to approximate true transmission dynamics based on the SAGE
130 recommendations for vaccination of specific high-risk groups.²⁷ The modeled sub-populations
131 included:(1) Children under 5 years of age, (2) men who have sex with men (MSM), (3) female
132 sex workers (FSW), and (4) the remaining general population.²⁰ To simulate transmission within
133 each subpopulation, risk factors were used as multipliers of the baseline transmission rate to
134 represent higher transmission risks among high-risk groups compared to the general population.
135 The risk factors featured in Table 1 were selected based on discussion among the authors and the
136 study's external steering committee.

137 *2.1.1 Model dynamics*

138 In the model, disease transmission dynamics among each of the four sub-populations are tracked
139 as susceptible individuals move through the eight possible compartments: susceptible (S),
140 exposed (E), infected (I), recovered (R), deceased (D), vaccinated (V), under contact tracing, but
141 not yet infectious (C), and contact-traced individuals eligible for vaccination (C_V) (Figure S1).
142 These compartments were used to construct the three main model dynamics of the unvaccinated
143 disease pathway, contact tracing and vaccination of contacts pathway, and targeted preventative
144 vaccination of high-risk groups. To understand the dynamics of transmission between high-risk
145 groups and the general population, the SEIRD-V model was modified to include crossover
146 transmission effects (see Table S1 for model differential equations). The crossover transmission
147 effect simulates transmission from high-risk groups (MSM, sex workers, and children under 5) to
148 the general population, implemented as an additional force of infection term where infectious
149 individuals in high-risk groups contribute to new infections in the general population. The model
150 implements vaccine efficacy as the proportion of vaccination attempts conferring complete
151 protection (all-or-nothing model), with efficacy levels of 75% and 82% corresponding to one vs.

152 two doses of MVA-BN, respectively. We also include extinction factors to represent outbreaks
 153 that burn out naturally.

154 *2.1.2. Model Assumptions & Parameters*

155 To represent the potential variability in outbreak recognition and response, the epidemiological
 156 model assumes two thresholds for when vaccination would begin. The first threshold is 20 cases
 157 (about 5 days), which is an optimistic estimate agreed by the authors as an early response
 158 threshold. The second threshold is at 100 cases (about 3-8 weeks, depending on the model run).
 159 The 100-case threshold represents input from the Steering Committee that it may take 3 weeks or
 160 more to acquire vaccines and implement vaccination in-country.

161 A baseline transmission rate parameter beta varied throughout the Monte Carlo simulations
 162 (1,000 runs) with a mean of 0.086 (SD: 0.013) (approximating an R_0 of ~ 1.2) and a coefficient of
 163 variation of 15% during the simulated outbreak. The outbreak was simulated for 180 days
 164 (approximately 6 months) to balance capturing epidemic dynamics through the initial outbreak
 165 wave while avoiding artifacts from long-term parameter assumptions. A stochastically varying
 166 beta was used to capture the epidemiological uncertainty in mpox transmission dynamics and
 167 reflect real-world epidemic variability. The model also assumed that group-specific risk factors
 168 modify the base beta value to simulate heterogeneous transmission patterns within different
 169 subgroups. In the model, susceptible individuals were exposed over the course of an 8.6-day
 170 incubation period and infected individuals remained contagious for 21 days (Table 1). Each
 171 specific population group had a distinct case-fatality ratio.^{16,26,28}

172 **Table 1.** Primary parameters and assumptions for the SEIRD-V epidemiological model.

Summary of Key Epidemiological Model Parameters

Parameter	Value
Transmission rate (β)	0.086
Risk factors (multipliers to represent higher transmission risk faced by high-risk groups compared)	Children <5 years old: 1.5 Men who have sex with men: 2.0 Female Sex Workers: 4.0 Remaining General Population: 1.0
Case Fatality Ratio (CFR) – Setting 1 (Kamituga Health Zone, South Kivu, DRC (clade I)) ^{16,26,28}	Children <5 years old: 0.085 Men who have sex with men: 0.05 Female Sex Workers: 0.05 Remaining General Population: 0.03
Case Fatality Ratio (CFR) – Setting 2 (Kawempe Division, Kampala, Uganda (clade I)) ^{16,26,28}	Children <5 years old: 0.085 Men who have sex with men: 0.05 Female Sex Workers: 0.05 Remaining General Population: 0.03
Case Fatality Ratio (CFR) – Setting 3 (Mushin Local Government Area, Lagos, Nigeria (clade II)) ^{16,26,28}	Children <5 years old: 0.0336 Men who have sex with men: 0.011 Female Sex Workers: 0.011 Remaining General Population: 0.001
Coefficient of variation for β (β_{CV})	0.15
Time horizon	180 days

Incubation rate (Σ) ^b	1/8.6
Recovery rate (Γ) ^b	1/21
Vaccine delay for contacts ^c	5 days
Contact vaccination rate (C -> V)	1/ VACCINE_DELAY
Vaccine efficacy ^d	0.75 for one-dose; 0.82 for two-doses (for clades I and II)
Detection rate (% of cases detected and contact traced)	50% - varied between 20% and 100% in Monte Carlo simulations
Contact rate multiplier (average number of contacts per case)	15
Contact tracing rate (% of contacts traced)	50%, varied between 20% and 100% in Monte Carlo simulations

^aThe remaining general population excludes the high-risk populations of: children <5 years old, men who have sex with men, and female sex workers.

^bIncubation period and recovery period were derived from WHO Global Trends data¹⁹

^c Vaccine delay parameter was derived from data provided by Gavi on DRC outbreak response average time from contact identification to contact vaccination

^dVaccine efficacy parameters derived from the Introduction to the mpox session, Meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization presentation on March 12, 2025²⁰

173 Among the cases, each case was assumed to have 15 contacts, and the percentage of contacts
174 traced varied from 20% to 100% in the Monte Carlo simulations. The number of contacts was
175 determined through consultation with the Steering Committee and discussion of outbreak
176 response experiences and country data. All contacts were assumed to be eligible for vaccination,
177 with each contact receiving vaccination after a 5-day delay period. This delay between case
178 identification and contact tracing was derived from country-level data provided to Gavi from an
179 ongoing mpox outbreak in a Gavi-eligible country. The 5-day delay was the mean time between
180 case identification and contact tracing from that data set. The case detection rate varied
181 stochastically from 30% to 100% in the simulations. For the vaccination strategies tested in the
182 model, vaccine efficacy for only the MVA-BN vaccine was applied. Other vaccines (LC16m8
183 and ACAM2000) licensed for prevention of mpox were excluded from the analysis for a number
184 of reasons: 1) LC16m8 and ACAM2000 had not been granted WHO PQ; 2) LC16m8 and
185 ACAM2000 are not recommended for use in immunocompromised or pregnant populations
186 because they are replicating vaccines; 3) published data on vaccine efficacy for LC16m8 were
187 limited at the time of the analysis; and 4) the steering committee noted expressed preference for
188 MVA-BN by public health authorities and populations in affected countries.^{20,29} For MVA-BN,
189 vaccine efficacy was assumed to be 0.75 for one-dose of the vaccine, and 0.82 for two-doses.^{20,29}

190 2.1.3. Model Archetypal Settings

191 To inform Gavi's decision-making to invest in an mpox stockpile, three archetypal settings were
192 modeled separately to simulate an array of post-2022 mpox outbreak dynamics, population
193 characteristics, and response capabilities across Gavi-eligible countries in Sub-Saharan Africa
194 (Table S2-S4).^{16,19,21-26,30} The Kamituga Health Zone, South Kivu in the Democratic Republic of
195 the Congo (DRC) was selected as it represents a clade I mpox outbreak in a non-endemic, more
196 rural area, with low availability and access to response resources. Similarly, the Kawempe

197 Division in Kampala, Uganda, was selected because it represents a clade I mpox outbreak in a
198 non-endemic area characterized by a rapidly urbanizing population and moderate availability of
199 healthcare and response resources. Clade II mpox outbreaks in endemic areas were represented
200 by the archetypal setting of Mushin Local Government Area, Lagos, Nigeria. Lagos also
201 represents a highly urbanized population with greater access to healthcare and response
202 resources.

203 With these archetypes, the number of similar locations across Gavi-eligible countries that might
204 experience mpox outbreaks over the next 5 years was estimated. The total population in 2030 in
205 Gavi-eligible countries in areas at risk of mpox outbreaks was estimated, considering the
206 literature on how the endemic regions may change due to climate change, expected population
207 growth, and expected division of population into different types of areas. The 90% uncertainty
208 interval (UI) of population at risk of mpox outbreaks in Gavi-eligible countries is 250 to 420
209 million.³¹ In each simulation run of the cost-effectiveness model, a total population number and a
210 per-location population number were drawn. The number of locations is the total population
211 divided by the per-location population, rounded to the nearest integer. Based on this approach,
212 across all Gavi-eligible countries, there were an average of 21 locations or geographic areas with
213 a situation similar to South Kivu, 47 places with a situation similar to Kampala, and 6 places
214 with a situation similar to Lagos.

215 *2.2. Cost-Benefit Analysis*

216 As early analysis showed that there was a small difference in mpox cases and deaths averted
217 between a one and two-dose strategy with the same timing of vaccination initiation, as well as
218 the operational complexity and added cost of a two-dose regimen, we conducted a CBA of the
219 effects and impact of different stockpiles with a one-dose vaccination strategy initiated at either
220 20 or 100 cases. Specifically, the CBA investigated the likelihood that a given stockpile size
221 would be sufficient to respond to expected outbreaks, and the impact it has on cases prevented,
222 deaths prevented, and disability-adjusted life years (DALYs) averted. For this analysis, we
223 conducted a simulation of future 5-year periods, starting in 2030, with 1,000 Monte Carlo runs.
224 Each run of the simulation tracks outbreaks and vaccines used and compares the outcomes to a
225 no-vaccine baseline to determine the benefits of the stockpile.

226 *2.2.1. Cost-Benefit Analysis Inputs & Key Assumptions*

227 Due to the shift in mpox transmission dynamics and subclade mutations, pre-2022 outbreak
228 frequencies do not offer reliable guidance for the frequency of future outbreaks. Prior to the 2022
229 multi-country outbreak, significant outbreaks occurred about once every 10 years.³² Based on a
230 review of the literature, post-2022 case reporting, interviews, and expert understanding, we
231 assumed that future outbreaks will be at least 3.5 times, and up to 16 times more likely in the
232 future. We applied this rate distribution, with an average annual probability of an mpox outbreak
233 of 44% and some years having multiple outbreaks. The outbreak sizes (with and without
234 vaccines) used in each Monte Carlo simulation for the CBA were selected from one of the 1,000

235 epidemiological modelling outputs for each archetypal setting. Additional inputs and
 236 assumptions for the CBA are provided in Table 2.³³⁻³⁶

237 **Table 2.** Details of the assumptions for the CBA of the mpox stockpile size simulation.

Stockpile Simulation and CBA Assumptions (All money values are 2025 USD)		
Parameter	Assumption	Reference
Vaccine doses purchased	50% of the total purchases have been made at the start of the simulation, and 10% of the total target is purchased each year thereafter	Input from Gavi based on historical experiences in establishing new stockpiles
DALY Loss Per Case (due to 5.2-5.9% CFR)	Each fatality results in the loss of 30-60 DALYs	³³
	There is a Lognormal (10%,10%) chance of sequelae ¹⁴ with a Lognormal (0.219,0.5) disability weight ¹⁵ for Lognormal (2,2) years ¹⁶	³⁴
	The DALY loss from the rash is negligible ¹⁷ but was included in the simulation	³⁴
	Average DALY loss per case is 2.6, with a 90% CI of 1.7 to 3.7.	Calculated from previous variables
Value per DALY in Gavi-eligible countries	Mean of \$12,000; 90% CI \$4,000 to \$19,000	Derived from USA value per DALY, adjusted for income difference at elasticity of 1
Monetized DALY harm per case	Mean of \$33,000, 90% CI of \$7,000 to \$68,000	Calculated from previous variables
Monetized chance per case of causing a mutation that leads to global pandemic	Mean of \$10,000, 90% CI of \$600-\$45,000 (The cost of global pandemic is 1×10^{14} and the probability per case of causing it is 1×10^{-10})	^{35,36}
Average harm per case (summing DALY, mutation, medical, and economic costs)	Mean of \$46,000, 90% CI of \$8,000 to \$110,000	Calculated from previous variables
Estimated vaccine procurement cost per dose	\$65	Public price of Gavi-funded mpox vaccines in current outbreak
Response cost	Mean of \$23, 90% CI of \$10-\$45	Hours required (mean 5, SD 2) and wage rate (mean \$2, SD \$0.5) from interviews, plus logistics cost (mean \$5.6, SD \$0.5) and overhead (mean 40%, SD 5%)
Estimated vaccine delivery cost per dose administered	\$10.60	Input from Gavi based on historical outbreak response data
HCW vaccination	HCW as a Proportion of the Population (multiplied by the local population used in each scenario) DRC: 0.00050094 Nigeria: 0.00344303 Uganda: 0.00165331	

238

239 2.2.2. Analysis Scenarios

240 The mpox vaccine stockpile simulation for the CBA used a scenario that assumed half of the
241 stockpile was available initially, with further planned purchases of 10% of the total per year.
242 Under this simulation, the CBA investigated the impact, cost value for money, and benefits
243 across various numbers of doses purchased over five years (300,000; 500,000; 1,000,000; and
244 2,000,000 doses) of creating a stockpile assuming a single-dose vaccination strategy responding
245 at 20 vs. 100 cases. The CBA measured impact via the number of vaccinated persons, cases
246 prevented, deaths prevented, and DALYs averted. Cost and value for money were analyzed
247 through gauging the costs to Gavi, total costs, and cost per death and DALYs averted. Similarly,
248 benefits were measured by monetized DALYs, medical and other costs averted, and the value of
249 reducing opportunity for the virus to mutate in ways that could result in new, more transmissible,
250 or more severe infections.

251 2.3. Data Collection

252 The data used to inform both the epidemiological model and the CBA were collected from peer-
253 reviewed and grey literature and expert opinion (Tables S2 and S5). A literature review was
254 conducted to obtain key model parameters and information about mpox transmission dynamics
255 in the three selected archetypal settings. Expert opinions were solicited through key informant
256 interviews and meetings with the external steering committee to gather insights into
257 epidemiological and operational dynamics of ongoing outbreaks and assess face validity of the
258 model parameters and assumptions.

259 2.4 Use of AI

260 The SEIRD-V model was implemented in Python using Claude (Anthropic) as an AI coding
261 assistant. AI assistance was limited to: (1) translating our epidemiological model design into
262 functional code; (2) resolving numerical integration issues for small population groups; (3)
263 implementing stochastic dynamics and Monte Carlo frameworks; and (4) debugging solver
264 compatibility issues. All model structure, parameters (e.g., transmission rate $\beta=0.086$, case
265 fatality ratios, risk factors, vaccine efficacy 75%/82%), intervention strategies, and scientific
266 interpretations were independently determined by the authors. Authors reviewed and validated
267 all code and take full responsibility for the model and results. Additional details about the AI
268 model version and user prompts can be found in the Acknowledgments section.

269 2.5 Role of the Funder

270 The funder of this research (Gavi) played a facilitative and collaborative role in this work. Gavi
271 provided input to decisions about model structure and assumptions, and in some cases, assisted
272 in gaining access to data and expertise. Gavi provided the requirements for the work and
273 approved the initial scope but relied on the Johns Hopkins-led project team to determine

274 appropriate methods and conduct and interpret the analysis. Gavi provided input and editing to
 275 the manuscript and gained institutional approval internally for their authorship. The decision to
 276 submit the manuscript was made by the first and senior authors from Johns Hopkins.

277 3. Results

278 3.1. Epidemiological Modelling Results

279 In the absence of vaccination, the simulated mean cases and deaths were several orders of
 280 magnitude higher than with a vaccine strategy in place. The epidemiological modelling for
 281 settings such as Kamituga (clade I, non-endemic, rural, low healthcare and response access)
 282 estimated a mean of 11,331 mpox cases (95% uncertainty interval UI): 10,778, 11,883) and 821
 283 (95% UI: 784, 858) mpox-associated deaths over the span of a 180-day outbreak. The model for
 284 settings such as Kawempe (clade I, non-endemic, semi-urban, moderate healthcare and response
 285 access) resulted in 12,040 mean cases (95% UI: 11,221, 12,860) and 862 mean deaths (95% UI:
 286 806, 918). Although the simulation involving settings such as Mushin (clade II, endemic, urban,
 287 moderately-high healthcare and response access) exhibited the lowest mean mpox deaths (464;
 288 95% UI: 427, 500), because of the parameters associated with clade II mpox, these settings had
 289 the highest projected mean cases (17,807; 95% CI: 16,494, 19,121) (Table 3).

290 **Table 3.** Model outcomes of mean cases, deaths, and individuals vaccinated for each scenario
 291 and archetypal setting using a one-dose vaccination strategy.

Mean Cases By Vaccination Strategy and Country (*n* (95% Uncertainty Interval))

	Kamituga, South Kivu, DRC (clade I)	Kawempe, Kampala, Uganda (clade I)	Mushin, Lagos, Nigeria (clade (II)
No Vaccine	11,331 (10,778, 11,883)	12,040(11,221, 12,860)	17,807 (16,494, 19,121)
One-Dose – 20 cases	950 (920 979)	1,678 (1,611, 1,746)	2,389 (2,264, 2,515)
One-Dose – 100 cases	1,679 (1,643, 1,715)	2,840 (2,757, 2,922)	4,355 (4,191, 4,519)

Mean Deaths By Vaccination Strategy and Country (*n* (95% Uncertainty Interval))

	Kamituga, South Kivu, DRC (clade I)	Kawempe, Kampala, Uganda (clade I)	Mushin, Lagos, Nigeria (clade (II)
No Vaccine	821 (784, 858)	862(806, 918)	464 (427, 500)
One-Dose – 20 cases	29 (28, 30)	51 (49, 53)	3 (3, 3)
One-Dose – 100 cases	56 (55, 57)	89 (86, 91)	7 (7, 7)

Mean Number of Individuals Vaccinated by Vaccination Strategy and Country (*n* (95% Uncertainty Interval))

	Kamituga, South Kivu, DRC (clade I)	Kawempe, Kampala, Uganda (clade I)	Mushin, Lagos, Nigeria (clade (II)
No Vaccine	0	0	0
One-Dose – 20 cases	109,165 (107,085, 111,245)	201,260 (195,930, 206,590)	347,725(337,427, 358,023)

One-Dose - 100 cases	154,671 (152,612, 156,730)	285,040 (278,870, 291,211)	495,978 (482,601, 509,355)
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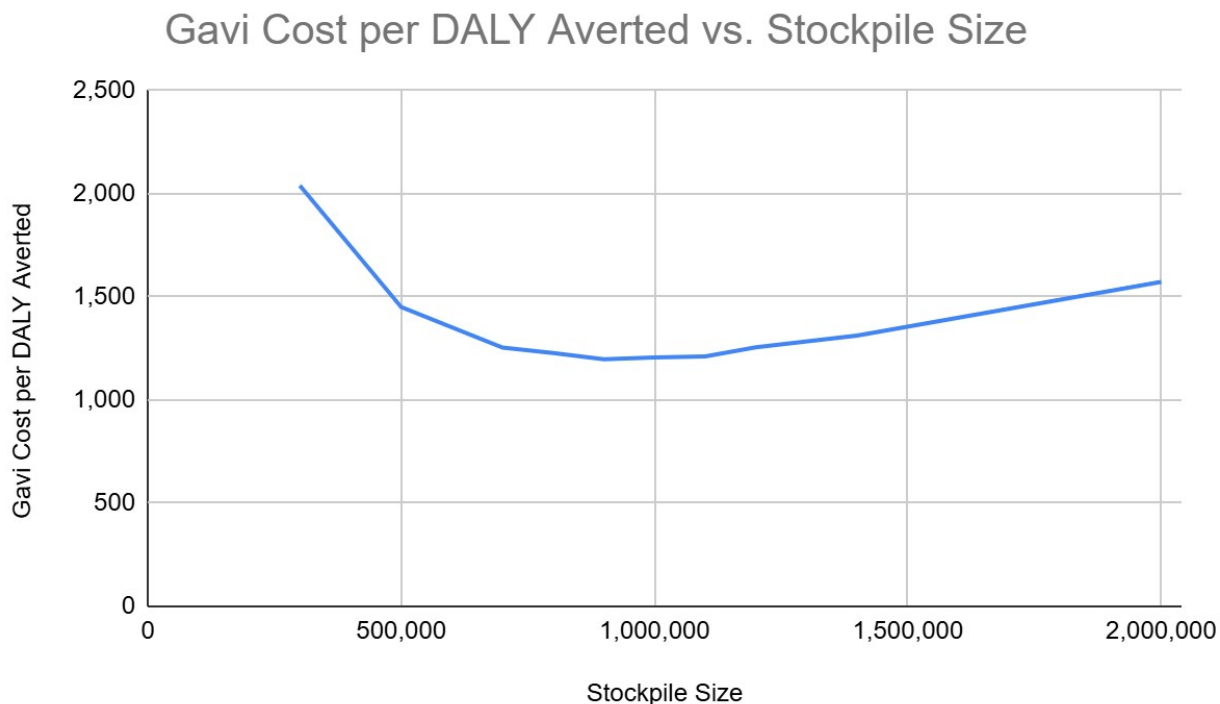
292 Across the modeled outcomes, implementation of vaccination at a threshold of 20 accumulated
 293 cases, regardless of the number of doses, resulted in lower mean cases, deaths, and number of
 294 individuals vaccinated compared to responding at a threshold of 100 cases (Figure S2 A-C). The
 295 difference in mean cases between one- and two-dose strategies (with the same vaccination
 296 timing) was less than 1%, with an average difference of 0.5% (SD: 0.5%). No estimated
 297 difference was projected in mean deaths between the one and two-dose strategies for the same
 298 vaccine timing strategy. When the dose strategy was held constant, delaying implementation
 299 resulted in substantial increases in average percentage difference in mean cases (92.8%; SD:
 300 34.7%), deaths (135.9%; SD: 70.4%), and individuals vaccinated (44.1%, SD: 15.2%) across all
 301 three settings. In each outcome, when the dose strategy was constant, response at a threshold of
 302 20 cases resulted in fewer mean cases, deaths, and individuals vaccinated. The Monte Carlo
 303 results of the epidemiological model yielded the highest estimated mean cases (4,355) and
 304 individuals vaccinated (495,978) for settings such as Mushin. In contrast, the highest mean
 305 deaths were projected for settings such as Kawempe under late implementation of both dosing
 306 strategies. Given the less than 1% difference in outcomes across dose strategies, the one-dose
 307 strategy was recommended for the additional stockpile simulation and analysis to investigate the
 308 benefit of vaccination implementation at 20 vs. 100 accumulated cases.

309 3.2. Cost-Benefit Analysis Results

310 In the no vaccine baseline, the CBA simulation results showed an average of 4.5 outbreaks in
 311 Gavi-eligible regions in the 5-year period, resulting in 54,000 cases and 3,000 deaths. Across
 312 these outcomes, response at 20 cases had the highest averted adverse outcomes and chance of
 313 responding to all mpox outbreaks in Gavi-eligible countries (Table 3). Furthermore, among these
 314 outcomes, the early timing strategy with a stockpile size of 2,000,000 mpox vaccine doses
 315 resulted in the highest averted medical and other costs, cases, and deaths compared to the other
 316 stockpile sizes and timing strategies. This stockpile size and response strategy are sufficient to
 317 respond to 95% of outbreaks, which is much greater than the predicted 38% of outbreaks that a
 318 300,000-dose vaccine stockpile can respond to. Similarly, a stockpile of 2,000,000 doses with a
 319 rapid response time is estimated to increase the chance of responding to all mpox outbreaks in
 320 Gavi-eligible countries in Africa over five years to 81% compared to 12% provided by the
 321 smallest simulated stockpile size of 300,000. Total cost per death and DALY averted is estimated
 322 to be lowest at a stockpile of 1,000,000 vaccines across both response strategies, with the
 323 response at 20 cases having lower costs compared to response at 100 cases. At this size, with a
 324 response at 20 accumulated cases, Gavi's expected average cost per DALY averted has a 90%
 325 uncertainty interval of \$360 to \$9,400 (Table 4) and cost per death averted is \$18,000 to
 326 \$360,000. The use of other licensed (e.g. LC16m8) or cheaper vaccines, or the use of fractional

327 doses of MVA-BN could reduce the cost per DALY averted if vaccine effectiveness remains
 328 high.

329 **Figure 1.** A graph of Gavi’s estimated mean cost per DALY by mpox stockpile size.



330

331 Overall, the analysis found that regardless of size, the establishment of an mpox stockpile would
 332 bring higher benefits in monetized DALY (\$59M – \$200M) and net benefits (\$81M – \$220M)
 333 compared to a delayed response. Comparatively, a response initiated after 100 accumulated cases
 334 has a lower estimated percentage of outbreaks responded to, chance of responding to all
 335 outbreaks, and impact on disease burden compared to responding at 20 cases for all considered
 336 stockpile sizes (Table 4). See Table S5 for additional results.

337 **Table 4.** The results of the cost-benefit analysis (CBA) at 20 and 100 cases. Presenting mean and
 338 90% uncertainty interval, the 5th and 95th percentile of simulation results.

Key Cost-Benefit Analysis Results of Responding at 20 Cases*				
# of Doses Purchased over 5 Years	300,000 Doses	500,000 Doses	1,000,000 Doses	2,000,000 Doses
% of outbreaks adequately responded to*:	38%	52%	74%	95%
Chance of responding to all outbreaks:	12%	20%	43%	81%
Impact				
Vaccinated Persons	300K (280K – 300K)	500K (370K – 500K)	1M (600K – 1M)	1.6M (1M – 2M)
Cases Prevented	4.2K	10K	24K	36K

Deaths Prevented	(760 – 23K) 230	(2.1K – 44K) 570	(3.7K – 77K) 1.3K	(3.7K – 120K) 2.1K
DALYs Averted	(43 – 1.3K) 11K (1.7K – 66K)	(110 – 2.4K) 26K (4.6K – 110K)	(200 – 4.3K) 62K (7.6K – 210K)	(200 – 6.8K) 92K (7.7K – 350K)
Grand Total Cost(US\$) ^b	\$25M (23M – 33M)	\$42M (38M – 54M)	\$82M (74M – 110M)	\$160M (150M – 200M)
Value for Money** (US\$)^b				
Gavi Cost per death averted	\$98K (18K – 530K)	\$66K (16K – 330K)	\$56K (18K – 360K)	\$71K (22K – 710K)
Gavi Cost per DALY averted	\$2K (340 – 13K)	\$1.5K (340 – 8.1K)	\$1.2K (360 – 9.4K)	\$1.6K (430 – 18K)
Total Cost per death averted	\$110K (21K – 600K)	\$77K (18K – 390K)	\$65K (20K – 430K)	\$80K (24K – 780K)
Total Cost per DALY averted	\$2.4K (440 – 14K)	\$1.7K (390 – 8.6K)	\$1.4K (420 – 9.7K)	\$1.8K (530 – 19K)
Benefits (US\$)^b				
Monetized DALY	\$110M (0 – 820M)	\$250M (0 – 1500M)	\$590M (0 – 3100M)	\$810M (0 – 5200M)
Medical + Other Costs Averted	\$630K (0 – 4.5M)	\$1.4M (0 – 8.6M)	\$3.2M (0 – 17M)	\$4.5M (0 – 28M)
Net Benefits	\$120M (-21M – 1200M)	\$280M (-35M – 2200M)	\$640M (-71M – 4500M)	\$ 850M (-140M – 7400M)
Key Cost-Benefit Analysis Results of Responding at 100 Cases^a				
# of Doses Purchased over 5 Years :	300,000 Doses	500,000 Doses	1,000,000 Doses	2,000,000 Doses
% of outbreaks adequately responded to*:	30%	44%	65%	88%
Chance of responding to all outbreaks:	8%	15%	32%	66%
Impact				
Vaccinated Persons	300K (300K – 300K)	500K (420K – 500K)	1M (640K – 1M)	1.8M (1.1M – 2M)
Cases Prevented	1.9K (130 – 14K)	5.5K (550 – 33K)	16K (2K – 59K)	30K (2.2K – 110K)
Deaths Prevented	100 (7 – 760)	310 (30 – 1.8K)	910 (110 – 3.3K)	1.7K (120 – 5.9K)
DALYs Averted	4.8K (290 – 39K)	14K (1.3K – 87K)	41K (4.3K – 170K)	75K (5.3K – 280K)
Grand Total Cost(US\$) ^b	\$25M (23M – 33M)	\$42M (38M – 54M)	\$82M (74M – 110M)	\$160M (150M – 200M)
Value for Money** (US\$)^b				
Gavi Cost per death averted	\$200K (21K – 1.6M)	\$120K (17K – 810K)	\$81K (22K – 570K)	\$87K (23K – 850K)
Gavi Cost per DALY averted	\$4.3K (380 – 38K)	\$2.6K (350 – 22K)	\$1.8K (420 – 14K)	\$1.9K (490 – 20K)
Total Cost per death averted	\$240K (25K – 1.9M)	\$140K (19K – 950K)	\$95K (24K – 630K)	\$98K (27K – 960K)
Total Cost per DALY	\$5.1K	\$3.1K	\$2.1K	\$2.2K

averted	(500 – 42K)	(410 – 23K)	(510 – 15K)	(600 – 22K)
Benefits (US\$) ^b				
Monetized DALY	\$51M (0 – 490M)	\$140M (0 – 1200M)	\$390M (0 – 2400M)	\$670M (0 – 4200M)
Medical + Other Costs	\$270K	\$750K	\$2.1M	\$3.8M
Averted	(0 – 2.5M)	(0 – 6.5M)	(0 – 13M)	(0 – 23M)
Net Benefits	\$39M (-23M – 630M)	\$130M (-37M – 1600M)	\$410M (-73M – 3600M)	\$670M (-150M – 6100M)

^aCBA results for impact, cost, value for money, and benefits provided in thousands (K) and millions (M).

^bEstimates for cost, value for money, and benefits provided in US dollars.

*% of outbreaks adequately responded to means the % of outbreaks that had enough vaccine doses for the modeled response strategy.

**Impact and Value for Money results ignore the 5.4% of simulations where there are no outbreaks.

339 4. Discussion

340 This study combined epidemiological modelling with cost-effectiveness analysis to inform
341 decisions regarding the establishment of and investment in a global mpox vaccine stockpile. The
342 goal in establishing a stockpile is to improve equitable and timely access to vaccines, to ensure
343 that communities most affected by mpox can respond effectively to outbreaks, and to limit
344 morbidity, mortality, and long-term health and economic consequences.³⁷ Inclusion of
345 probabilistic cost-effectiveness analysis alongside epidemiological modelling provided a more
346 comprehensive picture for policy and investment decisions than epidemiological results alone.

347 The findings from the study confirm that a rapid response strategy would result in a lower mpox
348 disease burden and higher averted impacts compared to a more delayed response when more
349 cases have accumulated. For a 300,000-dose stockpile procured over five years, the difference in
350 expected net benefits of launching a response at 20 cases compared to 100 cases is likely to be at
351 least tens of millions, with greater net benefit differences for larger stockpiles. Calculating the
352 costs of fully implementing a reliable rapid response strategy is beyond the scope of this paper,
353 but our results can inform these capacity decisions. The differences in projected mean cases,
354 deaths, and people vaccinated were minimal between the one-dose vs. two-dose strategies.

355 The CBA demonstrated that rapid detection and timely request of vaccines from the largest
356 stockpile investigated (2,000,000 doses procured over 5 years) resulted in the highest benefit
357 scenario and percentage of outbreaks responded to. The monetized benefit of responding to more
358 outbreaks (i.e. reducing the probability that the vaccine is depleted) is higher than the increased
359 costs of the larger stockpile. However, this stockpile did not have the lowest cost per both deaths
360 and DALYs averted. Rather, a stockpile of 1,000,000 doses procured over 5 years combined with
361 a response at 20 cases resulted in the lowest estimated cost per deaths averted and DALYs
362 averted (74% of outbreak responded to). In other words, the second million doses are less cost-
363 effective than the first million, even though they have positive expected value. Given the context,
364 these results provided valuable insights to support Gavi and the ICG's decision-making on

365 establishment of an mpox vaccine stockpile. This study further demonstrates how the
366 combination of an epidemiological model and a CBA can be used to support evidence-based
367 decision-making to positively impact countries at elevated risk for mpox outbreaks.

368 *4.1. Limitations*

369 These results have several limitations given the nature of the involved modelling and the limited
370 timeframe to inform the Gavi Board's decision about funding an mpox vaccine stockpile in the
371 6.0 (i.e., 2026-2030) strategic period.^{38,39} First, the epidemiological model was limited to a 180-
372 day outbreak to reflect the focus on short-term impacts and the expectation that interventions
373 would prevent epidemics from extending beyond 180 days. Second, the model assumed
374 heterogeneous transmission across population groups through risk multipliers rather than entirely
375 separate transmission rates. While this simplification maintains parsimony and biological
376 consistency (the virus itself has constant transmissibility; contact patterns vary), it may not
377 capture all sources of transmission heterogeneity. Due to data limitations and other reasons noted
378 in the methods, the model does not include the use of mpox vaccines other than MVA-BN.
379 Additionally, the model did not account for translocation of cases, ongoing zoonotic spillover
380 events, waning immunity over time, and variations in surveillance detection capacity depending
381 on the location. While the three archetypal settings were carefully selected to represent a range of
382 settings across Gavi-eligible countries in Africa, they were all located in sub-Saharan Africa;
383 thus, some countries or communities may not be reflected in the profile of these settings, which
384 could limit the generalizability of the results.

385 The CBA was built upon static assumptions about the cost and monetary benefits of establishing
386 a stockpile, which could vary at the local level during an outbreak. However, these assumptions
387 were made utilizing the literature and guided by consultation with the steering committee and
388 other experts/practitioners. The stockpile simulation did not consider the possibility of other
389 vaccines and funding sources, fractional dosing, or the development of a more cost-effective
390 single-dose vaccination option, as these estimates are based on the only WHO-Prequalified
391 vaccine available at the time and its current cost. Both the epidemiological modelling and CBA
392 were limited by data scarcity in highly impacted and endemic countries; thus, expert judgment
393 informed by existing literature was required to fill these gaps.

394 Results are heavily influenced by the future outbreak probability, which is unknown. Many
395 simulation runs showed zero benefits of the stockpile because there were zero outbreaks. Results
396 should be treated as an expected-value prediction of an insurance policy against future events of
397 unknown probability, not an investment that generates reliable returns in all future states of the
398 world.

399 With regards to uncertainty in the model, we acknowledge the distinction between parameter
400 uncertainty, which our Monte Carlo framework addresses, and structural uncertainty, which
401 remains unquantified. This choice reflects a trade-off between analytical comprehensiveness and
402 policy timeliness. Finally, the modelling and analysis in this work were confined to addressing

403 vaccine stockpiling for response to future mpox outbreaks. It did not address the possible
404 application of the mpox vaccine for prevention. Savinkina et al. (2025) have begun to examine
405 how mpox vaccines used preventatively before an outbreak would impact transmission, but this
406 question was out of scope for our analysis.¹⁶

407 *4.2. Recommendations for Future Work*

408 There is a need for increased mpox surveillance in highly impacted and endemic countries. We
409 acknowledge that this recommendation requires significant dedication of resources; however,
410 increasing available epidemiological data for outbreaks would help models and analyses reflect
411 the current mpox dynamics and therefore better guide decision-making. A major uncertainty and
412 limitation in our model is the probability of future outbreaks after the state change caused by the
413 recent mpox outbreaks, and surveillance will give us this data. Additionally, there is potential for
414 future modelling to dynamically assess surveillance/detection capacity, zoonotic transmission,
415 and additional factors affecting mpox transmission not reflected in this model. While previously
416 published studies have successfully demonstrated modelling of mpox vaccination strategies to
417 inform policy decisions, few studies have incorporated these results into a CBA to further
418 contextualize the cost-effectiveness of different strategies for decision-makers.^{17,18} Thus, we
419 advocate for the increased integration of CBA into epidemiological modelling studies to improve
420 the decision-making utility of these models for policymakers.

421 While this study did not address the question of whether it would be a more effective use of
422 stockpiled vaccine to prevent outbreaks versus respond to outbreaks, one next logical step for
423 modelling and analysis would be to construct models that examine the epidemiological and cost
424 effectiveness of procuring vaccines for preventive use compared to a stockpile used for outbreak
425 response. Additionally, it is clear that cost and availability of vaccine are very important for
426 effective mpox stockpiling. We are hopeful that data will be generated in the near future that will
427 better enable models to investigate the impact of fractional dosing of MVA-BN and use of other
428 vaccines, that might be available at a lower price-points.

429 In terms of practical recommendations, the study findings support the use of early detection and
430 timely access to vaccines as crucial aspects of ensuring the effectiveness of a stockpile in
431 achieving the aim of reducing the potential of a large-scale mpox epidemic. Diagnostic and
432 implementation strategies that enable faster detection and vaccine delivery should be considered,
433 where possible, based on the location and characteristics of future outbreaks. In addition, defined
434 thresholds for outbreak response vaccination in both mpox endemic and non-endemic areas
435 would be helpful to guide response as well as inform modelling of mpox outbreaks.

436 Contributors

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469 via claude.ai web interface

470 Representative prompts used during model development included:

- 471 • Initial model implementation:

- 472 o "I need to create an SEIRD-V epidemiological model for mpox in Sud Kivu, DRC
473 with 4 population groups (MSM, sex workers, children <5, general population)
474 and 8 compartments per group including contact tracing compartments. Can you
475 help me implement this in Python using `scipy.integrate`?"
- 476 • Addressing numerical precision issues:
 - 477 o "The model runs are showing no cases or deaths in the MSM and SW high-risk
478 groups, even with the no-vaccination strategy. Why is that?" [followed by
479 diagnostic discussions]
 - 480 o "How do I fix this error: `RuntimeWarning: invalid value encountered in divide`
481 `c /= stddev[:, None]`"
 - 482 o "Can you explain the changes to Higher Precision ODE Solver? And if there is a
483 way to increase processing speed?"
 - 484 • Implementing stochastic dynamics:
 - 485 o "How can I create more variability in parameters so that it is more realistic that
486 some outbreaks burn themselves out"
 - 487 o "What exactly is option 1 [stochastic transmission dynamics] doing?"
 - 488 • Refining intervention strategies:
 - 489 o "Why are the number of people vaccinated in the crossover group and the mass
490 vaccination group the same?"
 - 491 o "How do I fix the contact tracing component which is missing in the crossover
492 vaccination strategy"
 - 493 o "Can you make sure that the crossover strategy logic is working? Here is how the
494 crossover logic should work: an interaction term between the high-risk cases and
495 the general population..."
 - 496 • Model validation and output:
 - 497 o "Can you go through each section of the code and explain what is going on in the
498 model?"
 - 499 o "Going back to the model with the contact tracing compartment, how would I add
500 an output of a table that shows the cases, deaths, and vaccinated for each of the
501 1000 model runs for the no-vax and the crossover strategy"
 - 502 • Final implementation refinements:
 - 503 o "Right now, I am running this code twice (once for 75% vaccine efficacy; and
504 once for 82%) then saving all the documents in folder. However, it would save me
505 a lot of time if you gave me one file Sud Kivu that has the projected cases with no
506 vaccines, the cases at 75% efficacy with all other input parameters the same, and
507 the cases at 82% efficacy, again with the same parameters. This would require
508 changing the code... It would involve changing the larger outer loop and using the
509 same randomly generated parameters for all three models."

510 Each prompt was followed by iterative refinement based on our review of outputs, with multiple
511 rounds of debugging and validation. The complete prompt history demonstrates that all scientific
512 and epidemiological decisions (model structure, parameters, intervention designs, interpretation)
513 originated from the authors, while AI assistance was confined to technical implementation and
514 coding support. All AI-generated code was reviewed, tested, and validated by the authors before
515 inclusion in the final model.

516

517 **Data sharing**

518 All code used in this analysis are available at: https://github.com/JHU-CORI/mpox_vaxstockpile

519 The full code of the cost-benefit analysis is available online at:

520 <https://docs.google.com/spreadsheets/d/12w0c6HulREJGXg85ITgtJwT8TeYOmPlXy3mUAoC>

521 <KfT4/edit?usp=sharing>

522

523 **Declaration of interests**

524 Alison Kelly is a paid consultant for Renaissance Philanthropy.

525 Caitlin Rivers has received personal payments for writing projects, including a trade book,
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527 Richard Bruns is a paid consultant for the Centre for Long-Term Resilience, RAND Europe,
528 Renaissance Philanthropy, and Sentinel Bio, has received personal payments for forecasting and
529 red teaming, and is an ARPA-H subcontractor.

530

531 **Declaration of generative AI and AI-assisted technologies in the manuscript preparation** 532 **process**

533

534 During the preparation of this work the author(s) used Claude 3.5 Sonnet (Anthropic) in order to:

535 1) translate our epidemiological model design into functional code; (2) resolve numerical
536 integration issues for small population groups; (3) implement stochastic dynamics and Monte
537 Carlo frameworks; and (4) debug solver compatibility issues. After using this tool, the authors
538 reviewed and edited the content as needed and take full responsibility for the content of the
539 published article.

540

541 **References**

- 542 1 World Health Organization. Smallpox and Mpox (Orthopoxviruses) Vaccines Position Paper.
543 2024. <https://iris.who.int/bitstream/handle/10665/378522/WER9934-eng-fre.pdf> (accessed
544 Aug 5, 2025).
- 545 2 Pittman PR, Martin JW, Kingebeni PM, *et al.* Clinical characterization and placental
546 pathology of mpox infection in hospitalized patients in the Democratic Republic of the Congo.
547 *PLoS Negl Trop Dis* 2023; **17**: e0010384.
- 548 3 Bunge EM, Hoet B, Chen L, *et al.* The changing epidemiology of human monkeypox—A
549 potential threat? A systematic review. *PLoS Negl Trop Dis* 2022; **16**: e0010141.
- 550 4 World Health Organization. Mpox. 2024; published online Aug 26.
551 <https://www.who.int/news-room/fact-sheets/detail/mpox> (accessed Aug 25, 2025).
- 552 5 Srivastava S, Kumar S, Jain S, *et al.* The Global Monkeypox (Mpox) Outbreak: A
553 Comprehensive Review. *Vaccines* 2023; **11**: 1093.
- 554 6 World Health Organization. Fifth Meeting of the International Health Regulations (2005)
555 (IHR) Emergency Committee on the Multi-Country Outbreak of mpox (monkeypox). 2023;
556 published online May 11. [https://www.who.int/news/item/11-05-2023-fifth-meeting-of-the-
557 international-health-regulations-\(2005\)-\(ihr\)-emergency-committee-on-the-multi-country-
558 outbreak-of-monkeypox-\(mpox\)](https://www.who.int/news/item/11-05-2023-fifth-meeting-of-the-international-health-regulations-(2005)-(ihr)-emergency-committee-on-the-multi-country-outbreak-of-monkeypox-(mpox)) (accessed Nov 6, 2025).
- 559 7 World Health Organization. Fifth meeting of the International Health Regulations (2005)
560 Emergency Committee regarding the upsurge of mpox 2024. 2025; published online Oct 30.
561 [https://www.who.int/news/item/30-10-2025-fifth-meeting-of-the-international-health-
562 regulations-\(2005\)-emergency-committee-regarding-the-upsurge-of-mpox-2024](https://www.who.int/news/item/30-10-2025-fifth-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-upsurge-of-mpox-2024) (accessed
563 Nov 6, 2025).
- 564 8 World Health Organization. Vaccines and Immunization for Monkeypox: Interim Guidance.
565 2022; published online Dec 16. [https://www.who.int/publications/i/item/WHO-MPX-
566 Immunization](https://www.who.int/publications/i/item/WHO-MPX-Immunization) (accessed Aug 25, 2025).
- 567 9 World Health Organization. Strategic Advisory Group of Experts (SAGE) on Immunization
568 Evidence to recommendations framework Outbreak response. 2024; published online Nov 14.
569 [https://cdn.who.int/media/docs/default-source/immunization/sage/vpp-background-
570 documents/mpox/mpox_grade_and_evidence_to_decision_tables.pdf?sfvrsn=7a10ca01_1
571](https://cdn.who.int/media/docs/default-source/immunization/sage/vpp-background-documents/mpox/mpox_grade_and_evidence_to_decision_tables.pdf?sfvrsn=7a10ca01_1) (accessed Aug 25, 2025).
- 572 10 Shankar M, Hartner A-M, Arnold CRK, *et al.* How mathematical modelling can inform
573 outbreak response vaccination. *BMC Infect Dis* 2024; **24**: 1371.
- 574 11 Yen C, Hyde TB, Costa AJ, *et al.* The development of global vaccine stockpiles. *The Lancet*
575 *Infectious Diseases* 2015; **15**: 340–7.
- 576 12 Gavi. Vaccine stockpiles. VaccinesWork. n.d. [https://www.gavi.org/vaccineswork/vaccine-
577 stockpiles-guide](https://www.gavi.org/vaccineswork/vaccine-stockpiles-guide) (accessed Aug 25, 2025).

- 578 13 Gavi. About our Alliance. 2025; published online May 27. [https://www.gavi.org/our-](https://www.gavi.org/our-alliance/about)
579 alliance/about (accessed Aug 25, 2025).
- 580 14 Yadav R, Chaudhary AA, Srivastava U, *et al.* Mpox 2022 to 2025 Update: A Comprehensive
581 Review on Its Complications, Transmission, Diagnosis, and Treatment. *Viruses* 2025; **17**: 753.
- 582 15 Molla J, Sekkak I, Mundo Ortiz A, Moyles I, Nasri B. Mathematical modeling of mpox: A
583 scoping review. *One Health* 2023; **16**: 100540.
- 584 16 Savinkina A, Kindrachuk J, Bogoch II, *et al.* Modelling vaccination approaches for mpox
585 containment and mitigation in the Democratic Republic of the Congo. *The Lancet Global*
586 *Health* 2024; **12**: e1936–44.
- 587 17 Acheneje GO, Omale D, Atokolo W, Bolaji B. Modeling the transmission dynamics of the co-
588 infection of COVID-19 and Monkeypox diseases with optimal control strategies and cost-
589 benefit analysis. *Franklin Open* 2024; **8**: 100130.
- 590 18 Idisi IO, Oshinubi K, Yusuf TT, Adeniji A. Comparative Cost-Effectiveness Analysis of
591 Awareness and Treatment Strategies for Controlling Mpox in Diverse Epidemiological
592 Settings. 2025; published online July 8. DOI:10.20944/preprints202507.0661.v1.
- 593 19 World Health Organization. Global Mpox Trends. 2025; published online Aug 23.
594 https://worldhealthorg.shinyapps.io/mpx_global/_w_fd030bc5/_w_fea5322c/#sec-lit
595 (accessed Aug 25, 2025).
- 596 20 World Health Organization. Meeting of the Strategic Advisory Group of Experts on
597 Immunization, March 2025: Conclusions and recommendations. 2025; published online June
598 6. <https://www.who.int/publications/i/item/who-wer10023-219-238> (accessed March 13,
599 2025).
- 600 21 World Health Organization. Mpox: Multi-country External Situation Report. World Health
601 Organization, 2025 [https://cdn.who.int/media/docs/default-source/documents/emergencies/
602 mpox-sitrep_-48.pdf?sfvrsn=41abc9e9_1&download=true](https://cdn.who.int/media/docs/default-source/documents/emergencies/mpox-sitrep_-48.pdf?sfvrsn=41abc9e9_1&download=true) (accessed March 13, 2025).
- 603 22 Macrotrends. Lagos, Nigeria Metro Area Population (1950-2025). n.d.
604 [https://www.macrotrends.net/global-metrics/cities/22007/lagos/population#:~:text=The
605 %20metro%20area%20population%20of%20Lagos%20in%202022%20was,a
606 %203.54%25%20increase%20from%202021.](https://www.macrotrends.net/global-metrics/cities/22007/lagos/population#:~:text=The%20metro%20area%20population%20of%20Lagos%20in%202022%20was,a%203.54%25%20increase%20from%202021.) (accessed March 13, 2025).
- 607 23 World Health Organization. Uganda [Country Overview]. WHO Data. 2025.
608 <https://data.who.int/countries/800> (accessed March 13, 2025).
- 609 24 United Nations Department of Economic and Social Affairs. Demographic Yearbook 74th
610 Issue. 2023. <https://unstats.un.org/unsd/demographic-social/products/dyb/dybssets/2023.pdf>
611 (accessed March 13, 2025).

- 612 25 Femi-Adebayo T, Adeleke M, Adebayo B, *et al.* Application of the UNAIDS Incidence
613 Patterns Model to Determine the Distribution of New HIV Infection in Lagos State, Nigeria. *J*
614 *Int Assoc Provid AIDS Care* 2024; **23**: 23259582241238653.
- 615 26 Johns Hopkins Center for Health Security. Situation Update Mpox Virus: Clade I and Clade
616 IIb. 2024. [https://centerforhealthsecurity.org/sites/default/files/2024-06/20240610-](https://centerforhealthsecurity.org/sites/default/files/2024-06/20240610-mpoxsituationreport.pdf)
617 [mpoxsituationreport.pdf](https://centerforhealthsecurity.org/sites/default/files/2024-06/20240610-mpoxsituationreport.pdf) (accessed March 13, 2025).
- 618 27 Python Software Foundation. Python Language Reference, version 3.13.5.
619 <http://www.python.org> (accessed April 29, 2025).
- 620 28 Kunnuji M, Schmidt-Sane M, Adegoke O, *et al.* Mpox and the men who have sex with men
621 (MSM) community in Nigeria: Exploratory insights from MSM and persons providing
622 healthcare services to them. *Global Public Health* 2025; **20**: 2433725.
- 623 29 World Health Organization. WHO prequalifies the first vaccine against mpox. 2024;
624 published online Sept 13. [https://www.who.int/news/item/13-09-2024-who-prequalifies-the-](https://www.who.int/news/item/13-09-2024-who-prequalifies-the-first-vaccine-against-mpox)
625 [first-vaccine-against-mpox](https://www.who.int/news/item/13-09-2024-who-prequalifies-the-first-vaccine-against-mpox) (accessed Aug 25, 2025).
- 626 30 Gavi. Eligibility policy. 2025; published online Sept 5. [https://www.gavi.org/programmes-](https://www.gavi.org/programmes-impact/programmatic-policies/eligibility-policy)
627 [impact/programmatic-policies/eligibility-policy](https://www.gavi.org/programmes-impact/programmatic-policies/eligibility-policy) (accessed Sept 19, 2025).
- 628 31 Thomassen HA, Fuller T, Asefi-Najafabady S, *et al.* Pathogen-Host Associations and
629 Predicted Range Shifts of Human Monkeypox in Response to Climate Change in Central
630 Africa. *PLoS ONE* 2013; **8**: e66071.
- 631 32 Institut Pasteur. The history of mpox: from the very first cases to new findings. 2024
632 <https://www.pasteur.fr/en/research-journal/reports/history-mpox-very-first-cases-new-findings>
633 (accessed Oct 28, 2025).
- 634 33 Hoffmann C. Mpox—is there a more dangerous new clade? *The Lancet Infectious Diseases*
635 2024; **24**: e667.
- 636 34 World Health Organization. Annex Table C Health state weights used in WHO Global Health
637 Estimates. 2020.
- 638 35 Ghazy RM, Yazbek S, Gebreal A, *et al.* Monkeypox Vaccine Acceptance among Ghanaians:
639 A Call for Action. *Vaccines* 2023; **11**: 240.
- 640 36 Iliyasu Z, Kwaku AA, Nass NS, *et al.* Risk perception and mpox vaccine acceptability among
641 people living with HIV in northern Nigeria. *Transactions of The Royal Society of Tropical*
642 *Medicine and Hygiene* 2025; **119**: 487–97.
- 643 37 Berman A, Caballero-Anthony M. It takes a global village: advancing equitable access to
644 mpox vaccines. *bmjph* 2024; **2**: e002040.

645 38 Okumura N, Morino E, Nomoto H, *et al.* LC16m8 for Pre-exposure Prophylaxis Against
646 Mpox in a High-Risk Population: An Open-Label Randomized Trial. *Clinical Infectious*
647 *Diseases* 2025; : ciaf074.

648 39 Grabenstein JD, Hacker A. Vaccines against mpox: MVA-BN and LC16m8. *Expert Review of*
649 *Vaccines* 2024; **23**: 796–811.