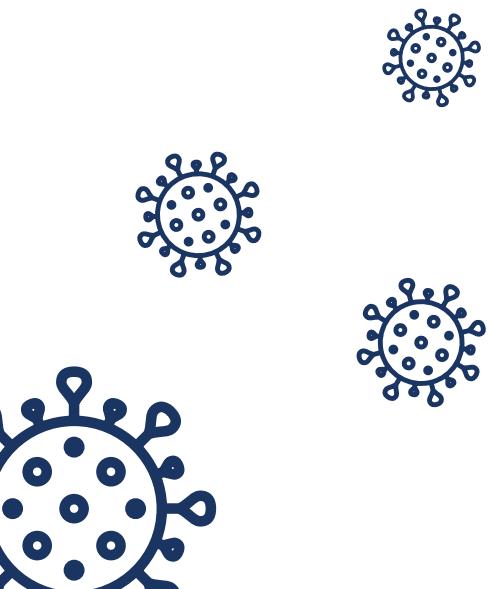


# Vaccine Impact Assessment Modelling

Phase 1 – Chikungunya and Chikungunya-X



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## Acronyms

<b>AFRO</b>	WHO Regional Office for Africa
<b>AMRO</b>	WHO Regional Office for the Americas
<b>CEPI</b>	Coalition for Epidemic Preparedness Innovations
<b>CHIK</b>	Chikungunya disease
<b>CHIK-X</b>	Chikungunya-X disease
<b>CFR</b>	Case Fatality Ratio
<b>DALYs</b>	Disability-Adjusted Life Years
<b>EMRO</b>	WHO Regional Office for the Eastern Mediterranean
<b>EVI</b>	Enhanced Vegetation Index
<b>FoI</b>	Force of Infection
<b>GDP</b>	Gross Domestic Product
<b>GNI</b>	Gross National Income
<b>HIC</b>	High-Income Country
<b>IFR</b>	Infection Fatality Ratio
<b>LIC</b>	Low-Income Country
<b>LMIC</b>	Lower Middle-Income Country
<b>NTD</b>	Neglected Tropical Disease
<b>NPIs</b>	Non-Pharmaceutical Interventions
<b>OOP</b>	Out-of-Pocket
<b>PAHO</b>	Pan American Health Organisation
<b>PPP</b>	Purchasing Power Parity
<b>I\$</b>	International Dollars

<b>R&amp;D</b>	Research and Development
<b>SEARO</b>	WHO Regional Office for South-East Asia
<b>TPC</b>	Target Product Characteristics
<b>UI</b>	Uncertainty Interval
<b>UMIC</b>	Upper Middle-Income Country
<b>USD</b>	United States Dollar
<b>VE</b>	Vaccine Efficacy
<b>VSL</b>	Value of Statistical Life
<b>WHO</b>	World Health Organisation
<b>WPRO</b>	WHO Regional Office for the Western Pacific
<b>YLL</b>	Years of Life Lost

## Key Terms

<b>100 Days Mission investment:</b>	CEPI's "moonshot" initiative that aims to enable global response to the next pandemic pathogen with a new vaccine ready for initial authorisation (vaccine rollout into humans) and manufacturing at scale within 100 days of genetic sequencing of the virus causing the outbreak.
<b>Attack rate:</b>	The proportion of new infections in an at-risk population over a given time period.
<b>Cases:</b>	Infections that are symptomatic.
<b>Case fatality ratio (CFR):</b>	Disease severity can be represented by the case fatality ratio (CFR), which estimates the proportion of deaths among all cases.
<b>Catastrophic healthcare expenditure:</b>	The number of cases for which out-of-pocket (OOP) expenses were greater than or equal to 10% of an individual's annual income.
<b>Chikungunya (CHIK):</b>	A mosquito-borne viral disease caused by the chikungunya virus, an alphavirus in the <i>Togaviridae</i> family.
<b>Chikungunya-X (CHIK-X):</b>	A mosquito-borne viral disease caused by a hypothetical, novel chikungunya virus (originating from a single outbreak event) characterized by higher spread potential and more severe clinical characteristics compared to CHIK.
<b>Cost of hospitalisations:</b>	The costs attributed to hospitalised cases.
<b>Disability-adjusted life years (DALYs):</b>	A metric for measuring disease burden that consists of the sum of years lived with a disability due to a disease and the years of life lost due to disease-induced mortality.
<b>DALYs expressed in monetary values:</b>	A monetised estimate of the sum of years lived with a disability due to a disease and the years of life lost due to disease-induced mortality.
<b>Detection:</b>	The isolation of viral antigens or nucleic acid in clinical samples to identify the presence of a specific virus.
<b>Discount rate:</b>	The rate at which future costs and outcomes are discounted to account for time preference.

<b>Disease X:</b>	A new, currently unknown pathogen that could emerge and cause a serious international epidemic.
<b>Force of infection (FoI):</b>	The rate at which susceptible individuals in a population acquire an infectious disease in a given unit of time. Also known as the incidence rate or hazard rate.
<b>Health systems investment:</b>	An assumption that global investments in health systems and infrastructure result in the reduction of in-country vaccine delivery constraints such that all countries are able to deliver vaccines at the same rate as high-income countries (HICs).
<b>Impoverishment:</b>	The case where OOP expenses resulting from CHIK caused individuals/households to fall below the \$2.15 poverty line.
<b>Infection:</b>	The invasion of a person's body by the chikungunya or chikungunya-X virus following a mosquito bite.
<b>Life years lost (also called years of life lost; YLL):</b>	The number of expected life years lost due to early mortality using age-specific life expectancies.
<b>Lineage:</b>	A group of related viruses with a common ancestor.
<b>Manufacturing investment:</b>	An assumption that global investments in vaccine manufacturing systems result in the reduction of introduction delays and supply stockouts due to production constraints.
<b>Non-pharmaceutical interventions (NPIs):</b>	Actions, apart from getting vaccinated and taking medicines, used to reduce the spread of an illness.
<b>Out-of-pocket (OOP) expenses:</b>	The individual OOP expenditures for CHIK treatment.
<b>Productivity losses:</b>	The economic impact of lost productivity due to 1) absence of work during the acute phase of disease and 2) premature mortality.
<b>Societal Costs:</b>	Costs that include both direct healthcare costs and lost resources in consequence of disease.
<b>Sequelae:</b>	A condition or complication stemming from a previous illness or disease.
<b>Sequencing:</b>	The analysis of a virus' genetic material.

<b>Seroprevalence:</b>	The number of individuals containing antibodies from previous chikungunya or chikungunya-X infections.
<b>Suitability:</b>	The fitness of a geographical area for the presence of CHIK or CHIK-X in humans.
<b>Target Product Characteristics (TPC):</b>	Outlines the desired profile or characteristics of a target product aimed at a particular disease or diseases and states its intended use, target populations, and other desired attributes including safety and efficacy-related characteristics.
<b>Value of statistical life (VSL):</b>	The monetary value a typical individual places on reductions in mortality risk.

# Executive Summary

Chikungunya (CHIK) is a mosquito-borne disease caused by the chikungunya virus. Spread to humans primarily by the bites of infected *Aedes aegypti* and *Aedes albopictus* mosquitoes, the virus has become widely distributed across the world, causing significant health and economic impacts. Due to this emerging public health and economic burden, CHIK was identified as a neglected tropical disease (NTD) that will be addressed in WHO's 2030 disease strategy<sup>1</sup>.

In addition to climate change, globalization, and other factors that threaten to further the global spread of chikungunya, viral evolution could also lead to the emergence of chikungunya-X, a novel chikungunya-related virus with pandemic potential that is more transmissible and/or more pathogenic than currently circulating lineages of chikungunya. While chikungunya-X is purely hypothetical, the recent emergence and global spread of novel lineages of chikungunya and other arboviruses highlights a need to prepare for a potential pandemic caused by a future chikungunya-related virus.

Vaccination will be a vital tool to mitigate the current global health-economic burden of chikungunya and to prepare against the potential future emergence of chikungunya-X. As the COVID-19 pandemic has made clear, there is a critical need for future investments that enable the more rapid availability and equitable global distribution of vaccines, particularly for those against diseases with pandemic potential. The Coalition for Epidemic Preparedness Innovations (CEPI) has been an important investor in the development and recent approval of the first vaccine against CHIK. CEPI has also proposed its 100 Days Mission, which aims to

reduce the development time for new vaccines against novel pathogens with pandemic potential to 100 days.

The models presented in this report were developed to estimate the value of investments in CHIK vaccination, alongside those made in support of vaccine development, manufacturing, and delivery in line with the 100 Days Mission. In this report, in the event of chikungunya-X emerging, it was assumed there is a need for a novel vaccine due to chikungunya-X escaping potential immunity provided by chikungunya infection and vaccination.

To that end, two main questions were addressed:

1. What is the potential impact of a CHIK vaccine in limiting the health-economic burden caused by CHIK?
2. In the event of the emergence of CHIK-X—a disease caused by a hypothetical, novel chikungunya-like virus with pandemic potential—what is the potential impact of achieving the 100 Days Mission for a new CHIK-X vaccine?

To address the first question, global chikungunya suitability was estimated using machine learning techniques, recorded disease occurrence, and environmental covariates. Average annual infection incidence was then projected using four different approaches based on the relationship between suitability and historical patterns of the force of infection (F0I) and compared to estimated incidence from an existing model<sup>2</sup>. From these incidence estimates, country-specific health and health economic impacts were calculated with and without a

<sup>1</sup> WHO, 2021. Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021–2030.

<sup>2</sup> Salje et al., 2023. The global burden of chikungunya virus and the potential benefit of vaccines.

CHIK vaccine. Using this approach, the results indicated that the most expansive vaccination scenario was the most effective strategy considered—covering 30–40% of people ages 12–99 with preventative campaigns and 60–65% of 12-year-olds with routine vaccination in 37 countries (including high, medium, and low countries). Under baseline assumptions<sup>3</sup>, this scenario prevented approximately 22.3 million symptomatic cases, 11.4 million cases of persistent post-acute arthralgia/arthritis, 752 thousand hospitalisations, 49 thousand deaths, and 14.3 million disability-adjusted life years (DALYs) over a 16-year period. In turn, this vaccination strategy averted \$2.3 billion in societal costs<sup>4</sup>, preventing 410 thousand patients from suffering catastrophic healthcare expenditures and 136 thousand of them from falling into poverty as a result.

Important factors limiting the potential impact of the vaccination strategies were the assumptions that the vaccines only prevented disease and were not available to children under 12. Furthermore, the same average location-specific FoI was used for each year of the simulated 16-year period due to the difficulty of predicting future CHIK outbreaks. CHIK epidemiology is more volatile, and the true impact of vaccines depends on a timely response to these outbreaks.

To address the second question, chikungunya-X emergence was modelled such that the probability of emergence was more likely in areas where estimates of CHIK incidence were higher. International CHIK-X spread was then modelled using human mobility data and reports of cases in different countries in the Pan American Health Organisation (PAHO) region over the last decade. Three disease severity scenarios (Scenarios A–C) were proposed to

estimate health and health economic impacts. Scenario A assumed similar hospitalisation and death risks as CHIK, whereas Scenario B and C assumed these risks were five and 10 times greater, respectively, for CHIK-X than CHIK. A CHIK-X pandemic was estimated to reach on average 32 countries over 5.6 years, resulting in approximately 22 million infections before naturally subsiding due to the accumulation of immunity. Further assuming that the age- and sex-specific health risks associated with CHIK-X in Scenario B (5 times the risk of hospitalisation and death than CHIK), it was estimated that this outbreak could result in 10.1 million symptomatic cases, 2.7 million outpatient visits, 2.0 million hospitalisations, and 113 thousand deaths globally, for a total estimated 7.9 million DALYs.

A vaccination campaign seeking to have a vaccine ready for initial authorisation and manufacturing at scale within 100 days of detection was estimated to have a large impact on mitigating the burden of CHIK-X. Assuming 60 days to detect the outbreak and 100 days to vaccine approval and rollout initiation, from which point populations were vaccinated at a daily rate of 0.1% per day evenly distributed by age and sex (i.e. resulting in 40% vaccine coverage after one year and 80% after the end of two-year vaccination campaigns), a vaccine with 70% efficacy against disease and no impact on infection averted an estimated 2.7 million symptomatic cases, 537.1 thousand hospitalisations, 29.7 thousand deaths, and 2.1 million DALYs. These health gains in turn averted \$1.1 billion in societal costs. The rate of vaccine delivery to affected countries (5%, 20%, or 40% of the population per year) was by far the greatest driver of vaccine impact. However, the global reactivity of vaccine

<sup>3</sup> Baseline assumption: CHIK infection incidence sourced from OxLIV 1, mean 18% of infections symptomatic, 70% vaccine efficacy against disease, minimum 16-year duration of protection (the time horizon of the simulation).

<sup>4</sup> Societal costs are the sum of healthcare costs, productivity losses, and out-of-pocket expenses, where the largest proportion of the economic burden was caused by productivity losses.

administration was also important, largely driven by the assumption that CHIK-X outbreak dynamics would have a similar explosive nature as observed during CHIK outbreaks in the PAHO region. These results suggest robust surveillance, rapid manufacturing at scale, and efficient allocation are critical to benefit non-origin countries in a CHIK-X pandemic.

While it is impossible to predict what a future CHIK-X pathogen might look like, or when such a pathogen might arise, the results here showed that to maximize the impact of vaccination strategies for this type of pathogen, it is crucial to invest in resources that would enable the availability of a vaccine as soon as possible after the pathogen is detected.

# 1. Introduction

The Coalition for Epidemic Preparedness Innovations (CEPI) was launched in 2017 as an international coalition of government, academic, philanthropic, private, public, and intergovernmental institutions. CEPI's mission is twofold: 1) accelerate the development of vaccines and other biologic countermeasures against epidemic and pandemic threats and 2) ensure these countermeasures are accessible to all people in need. Since its inception, the organisation has invested over \$2.3 billion into vaccine research and development (R&D) and other projects focused on tackling CEPI's priority emerging infectious diseases<sup>5</sup>.

One of CEPI's priority diseases is chikungunya (CHIK), an emerging mosquito-borne disease caused by the chikungunya virus. Spread to humans primarily by the bites of infected *Aedes aegypti* and *Aedes albopictus* mosquitoes, the virus has become widely distributed with over one billion people living in areas where CHIK is endemic<sup>6</sup>. While about 8 million CHIK cases were reported between 2004-2017, some estimates suggest the true burden could be as high as 100 million during that period<sup>7</sup>. In the Americas alone, CHIK's economic impact has been estimated to be about \$185 billion—a large portion of which can be attributed to certain types of long-term sequelae following acute disease<sup>8</sup>. Due to the emerging public health and economic challenges CHIK poses, it was also identified as a neglected tropical disease (NTD) that will be addressed in WHO's 2030 NTDs strategy<sup>7</sup>. Despite large outbreaks and significant consequences of the disease, the first

CHIK vaccine was approved only recently—Valneva's live attenuated single-dose shot won U.S. FDA approval in 2023<sup>9</sup>. With support from the European Commission, CEPI has been an important investor in CHIK vaccine R&D and was a major investor in Valneva's recently approved vaccine. Another CEPI-backed CHIK vaccine is currently in late-stage trials.

In addition, CEPI articulated its “moonshot” 100 Days Mission in 2021—an initiative to cut vaccine development time to 100 days for new pandemics, about a third of the time required to deliver the first COVID-19 vaccine. Under this mission, a vaccine against an unknown virus with pandemic potential (“Disease X”) would be ready for authorisation, manufacturing at scale, and initial delivery within 100 days of the viral sequence becoming available. The undertaking aims to enable the containment of a future Disease X outbreak before it spreads to become a global pandemic. Coupled with improved surveillance and effective use of non-pharmaceutical interventions (NPIs), vaccine delivery within 100 days would give the world a better chance of containing a future pandemic threat and averting the catastrophic global public health and socio-economic impacts of pandemics, such as those caused by COVID-19. Part of this initiative involves the ability to develop a pathogen-specific vaccine during an outbreak by adapting previously developed and well-characterised prototype vaccines against closely related viruses, including those CEPI has named as priority R&D areas<sup>10</sup>.

5 CEPI, 2021. 2022-2026 Strategy: Objectives and ambitions for the second 5-year cycle.

6 CEPI, 2023. Priority diseases.

7 WHO, 2021. Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021–2030.

8 Bloch, 2016. The cost and burden of chikungunya in the Americas.

9 Valneva, 2023. Valneva announces U.S. FDA approval of world's first Chikungunya vaccine, IXCHIQ®.

10 CEPI, 2022. Delivering pandemic vaccines in 100 days.

This report describes the models, scenarios, and results of impact assessment modelling designed to estimate the potential health and economic benefits of a CEPI-supported vaccine on current CHIK incidence and the 100 Days Mission on a hypothetical novel, chikungunya-like virus with Disease X pandemic potential.

## 1.1. Why is CEPI conducting impact assessment modelling?

Climate change, virus evolution, and globalisation threaten to further the spread of CHIK and amplify its already substantial global public health and economic consequences—highlighting the pandemic potential of the chikungunya virus and the urgent need for effective vaccines. As the world learned from COVID-19, delayed and reactive investments in pandemic response can lead to devastating consequences. These lessons make proactive investments in vaccine R&D for diseases such as CHIK more important than ever. To prioritise global health investments that deliver the greatest benefit and level of preparedness for future pandemic threats, CEPI has commissioned independent experts to develop mathematical models to assess the potential health, health economic, and economic impacts of CEPI’s CHIK investments, target product characteristics (TPCs) for vaccines, and the 100 Days Mission. Quantifying these potential impacts will help inform CEPI decision-making, mobilise engagement for the 100 Days Mission, and support advocacy within the international and global health communities.

## 1.2. CHIK and CHIK-X background

Impact assessment modelling was conducted on two viruses: 1) chikungunya virus, a globally distributed arbovirus which causes disease hereafter referred to as CHIK, and 2) chikungunya-X virus, a hypothetical, novel, chikungunya-related arbovirus with pandemic potential, which causes CHIK-X, a disease assumed to be more severe than regular CHIK. Chikungunya-X is assumed to be sufficiently antigenically distinct from chikungunya so as to evade any immunity conferred by previous chikungunya infection or vaccination. This section provides an overview of these diseases and a summary of CEPI’s contribution to CHIK vaccine development.

### Overview of diseases

CHIK is a mosquito-borne viral disease caused by the chikungunya virus, an alphavirus in the *Togaviridae* family. The chikungunya virus has four distinct geographical lineages, each with a distinct genotype (Figure 1)<sup>11</sup>. First identified in Tanzania in the 1950s, the disease caused sporadic outbreaks across Africa and Asia over the next several decades. Beginning in the early 2000s, CHIK outbreaks became more frequent and widespread, in part due to viral adaptations allowing the chikungunya virus to be spread more easily by its mosquito vector<sup>12</sup>. Since then, the chikungunya virus has caused over 3.4 million cases in over 43 countries; however, the true incidence may be underestimated, as CHIK shares clinical presentations with infections from other arboviruses, including dengue and Zika<sup>13</sup>. Disease outbreaks can be both unpredictable and explosive—causing attack rates of up to 68%—and can place a sudden, heavy burden on health systems<sup>14</sup>. CHIK hospitalisation rates range

<sup>11</sup> CEPI, 2023. Report of the meeting with National Regulatory Authorities of Regional Reference: “Regulatory preparation for vaccines of chikungunya in the Americas”.

<sup>12</sup> WHO, 2022. Chikungunya fact sheet.

<sup>13</sup> Márquez et al., 2022. A chikungunya outbreak in dengue-endemic region in rural northern coastal Ecuador.

<sup>14</sup> WHO, 2021. Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021–2030.

from 0.6% to 13% and estimates of CHIK-related mortality range from 0.024% to 0.7%<sup>15</sup>.

While the mortality rate is low, morbidity can be substantial and persistent, with critical quality of life implications<sup>16</sup>. Available evidence suggests that immunity against chikungunya virus re-infection is lifelong<sup>17</sup>.

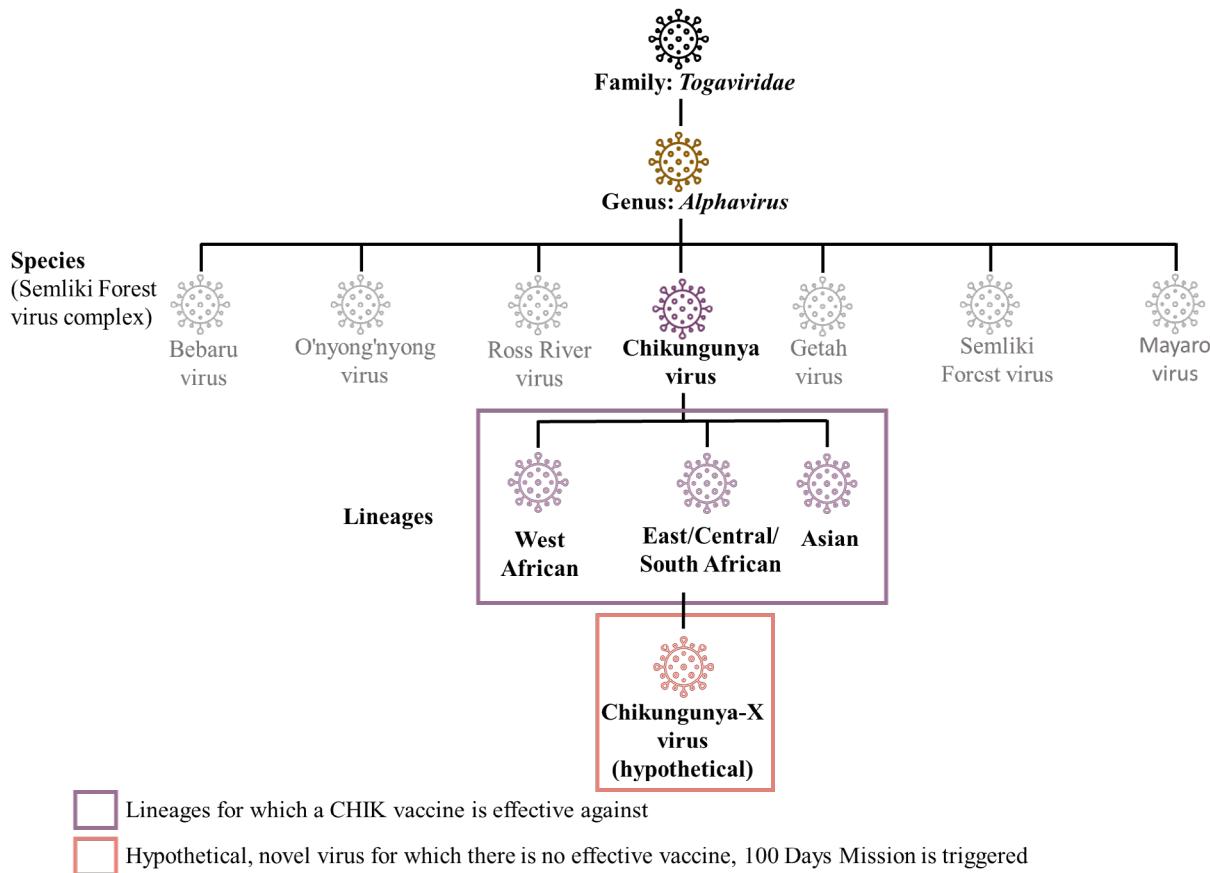


Figure 1: Illustrated classification tree highlighting the three main lineages of chikungunya virus, as well as the hypothetical virus chikungunya-X, which is assumed to emerge from one of the currently circulating chikungunya lineages. It was assumed chikungunya-X had a higher probability of emerging in countries with higher chikungunya infection incidence. CHIK vaccination is assumed to have equal efficacy in preventing CHIK caused by any extant chikungunya lineage, but no efficacy against CHIK-X, motivating the development of a new vaccine in line with the timelines of the 100 Days Mission as a reactive response to an emerging CHIK-X pandemic. This schematic is only intended to be illustrative and does not reflect the evolution of lineages.

15 Surbier, 2019. Rheumatic manifestations of chikungunya: Emerging concepts and interventions.

16 Lima Neto et al., 2019. Chikungunya-attributable deaths: A neglected outcome of a neglected disease.

17 Auerswald et al., 2018. Broad and long-lasting immune protection against various chikungunya genotypes demonstrated by participants in a cross-sectional study in a Cambodian rural community.

Chikungunya-X represents a potential future virus characterised by higher spread potential. CHIK-X, the disease stemming from a chikungunya-X infection, was assumed to have a higher risk of symptomatic infection, hospitalisation, and death compared to CHIK. It was assumed this virus originates from a single outbreak event, defined as the transmission of a zoonotic pathogen from the same mosquito that spreads CHIK to a human. While it doesn't exist yet, CHIK-X was assumed in this analysis to have similar outbreak dynamics as CHIK, and, in line with previous CEPI impact assessment modelling analyses, it was assumed that chikungunya and chikungunya-X are antigenically distinct viruses. Thus, the current CHIK vaccine would be ineffective against CHIK-X.

### **CEPI's contribution to disease response and preparedness**

CHIK is one of CEPI's seven priority diseases<sup>18</sup>, and as of 2024, CEPI has invested up to \$59.7 million in CHIK vaccine R&D<sup>19</sup>. CEPI has backed the development of the only currently approved vaccine against the virus (\$24.6 million, Valneva)<sup>20</sup> and supported another candidate in late-stage trials (\$14.1 million, International Vaccine Institute and Bharat Biotech)<sup>19</sup>. The coalition is also supporting effectiveness studies to help expand the potential use of licensed CHIK vaccines for children, people who are immunocompromised, and pregnant women<sup>21</sup>.

### **1.3. How was impact assessment modelling conducted?**

Impact assessment modelling was conducted considering two separate modelling approaches for CHIK and CHIK-X, assuming that the vaccines introduced would only have a direct impact on disease and not on transmission.

The approach for CHIK assessed the potential impact of a vaccine against modelled incidence of the disease. This analysis estimated the health and health economic impacts of different vaccination strategies and vaccine characteristics.

The approach for CHIK-X considered the potential use and benefits of delivering a novel vaccine following timelines from the 100 Days Mission. This analysis estimated the health and health economic impacts across a range of simulations for the spread of CHIK-X, vaccination scenarios, detection timelines, and vaccine characteristics.

The main research questions and model-related details for these two approaches are summarised in Table 1.

<sup>18</sup> CEPI, 2024. Priority diseases.

<sup>19</sup> CEPI, 2024. Our portfolio.

<sup>20</sup> CEPI, 2023. Accelerating access to the world's first chikungunya vaccine.

<sup>21</sup> CEPI, 2023. Licensed chikungunya vaccines are on the horizon.

Table 1: Main research questions and additional details on the modelling approach for the analyses assessing the potential impact of CEPI's investments on CHIK and CHIK-X.

Approach	Question	Details of Modelling Approach
1) CHIK	What is the potential impact of a CHIK vaccine in limiting the burden of CHIK?	<p>This scenario-based analysis assessed the potential impact of a CHIK vaccine by first estimating global suitability and patterns of the force of infection (FoI). The relationship between the two was then used to project annual CHIK incidence using logistic growth curves.</p> <p>Health and health economic impacts were then estimated from this incidence, along with the impact of vaccine rollout strategies and characteristics as detailed in Table 4.</p>
2) CHIK-X	In the event of the emergence of CHIK-X, what is the potential impact of achieving the 100 Days Mission for a CHIK-X vaccine?	<p>This hypothetical, scenario-based analysis assessed the potential impact of vaccines on a CHIK-X outbreak. The suitability and incidence estimates from CHIK were used to inform where CHIK-X was likely to emerge, the relative size of outbreaks, and the relative probability of establishment in different countries. This analysis assumed no cross-protection against CHIK-X from natural- or vaccine-acquired immunity against CHIK.</p> <p>The model incorporated two scenarios for the timing of a CHIK-X vaccine introduction: 1) 100 days after detection, assuming the first case is detected and sequenced immediately or 2) 160 days after CHIK-X detection, allowing for 60 days between the first case and detection/sequencing. Further details on vaccination scenarios are provided in Table 2.</p>

#### 1.4. Outputs from impact assessment modelling

Mathematical models were used to estimate health and health economic impacts by comparing scenarios with and without delivery of vaccines. The outputs from the models are summarised in Table 2.

Table 2: Health and health economic impact outputs for all models. Additional information on the metrics and how they were calculated can be found in Appendix 3.

Category	Metric	Description
Health	Cases, hospitalisations, and deaths averted	<ul style="list-style-type: none"> <li>The number of symptomatic cases, cases seeking care in the community, hospitalisations<sup>22</sup>, and deaths averted by age group</li> <li>Estimated based on the probability of becoming a symptomatic case, probability of seeking treatment, and the probability of severe disease distributed based on age and sex group</li> </ul>
	Chronic sequelae secondary to hospital discharge	<ul style="list-style-type: none"> <li>The number of cases experiencing complications from CHIK or CHIK-X</li> <li>Estimated based on the probability of sequelae</li> </ul>
	Life years lost (YLL)	<ul style="list-style-type: none"> <li>The number of expected life years lost due to early mortality using age-specific life expectancies</li> <li>Estimated based on the modelled age of individuals that die due to infection</li> </ul>
	Disability-adjusted life years (DALYs) averted	<ul style="list-style-type: none"> <li>A metric for measuring disease burden that consists of the sum of years lived with a disability due to a disease and the years of life lost due to disease-induced mortality</li> <li>Estimated by assigning disability weights to each clinical sign of CHIK identified in two systematic reviews<sup>23,24</sup></li> </ul>
Health Economic	Societal Costs	<ul style="list-style-type: none"> <li>Both direct healthcare costs and lost resources in consequence of disease</li> <li>Estimated as the sum of direct healthcare costs and productivity costs</li> </ul>
	Cost of hospitalisations averted	<ul style="list-style-type: none"> <li>The costs saved due to the lower number of monetised cases</li> <li>Estimated from a cost-of-illness study in Colombia<sup>25</sup>, scaling to each country by first adjusting to 2021 international dollars (I\$) using the purchasing power parity (PPP) conversion factor and gross domestic product (GDP) deflation factor from 2021 to the time at which cost data was collected, and second scaling to each country using World Bank country-specific unit costs and percent out-of-pocket (OOP) estimates</li> </ul>
	Direct healthcare costs	<ul style="list-style-type: none"> <li>Costs of hospitalisation and outpatient care</li> <li>Estimated by inflating all-cause outpatient costs from a systematic review<sup>26</sup> to 2021 I\$</li> </ul>

22 All hospitalised cases were considered severe disease.

23 Puntasecca et al., 2021. Measuring the global burden of chikungunya and Zika viruses: A systematic review.

24 Mora-Salamanca et al., 2020. Estimating the burden of arboviral diseases in Colombia between 2013 and 2016.

25 Alvis-Zakzuk et al., 2018. Economic costs of chikungunya virus in Colombia.

26 Moses et al., 2018. Funding and services needed to achieve universal health coverage: Applications of global, regional, and national estimates of utilisation of outpatient visits and inpatient admissions from 1990 to 2016, and unit costs from 1995 to 2016.

Category	Metric	Description
Health Economic cont.	Productivity losses averted	<ul style="list-style-type: none"> <li>The economic impact of lost productivity due to 1) absence of work during the acute phase of disease and 2) premature mortality</li> <li>Estimated by multiplying the number of productive days lost from work absences due to symptomatic disease or years lost from premature mortality by daily or annual gross national income (GNI), respectively</li> </ul>
	Out-of-pocket (OOP) expenses averted	<ul style="list-style-type: none"> <li>The individual OOP expenditures for CHIK treatment</li> <li>Estimated from a cost-of-illness study in Colombia<sup>27</sup> which included an estimate of the proportion of treatment costs that were OOP and scaling these to each country using World Bank OOP estimates</li> </ul>
	Catastrophic healthcare expenditure prevented	<ul style="list-style-type: none"> <li>The number of cases for which OOP expenses were greater than or equal to 10% of an individual's annual income</li> <li>Calculated based on estimated country-specific per capita OOP expenditure for CHIK treatment and World Bank data on the number of individuals that live below the income threshold for which the OOP expenditure would be 10% or more of their income</li> </ul>
	Impoverishment prevented	<ul style="list-style-type: none"> <li>The number of cases for which OOP expenses resulted in individuals/households falling below the \$2.15 poverty line</li> <li>Estimated by calculating the proportion of the population that live under the threshold of \$2.15 plus OOP expenditure</li> </ul>
	DALYs expressed in monetary values averted	<ul style="list-style-type: none"> <li>A monetised estimate of the sum of years lived with 1) a disability due to the acute phase of symptomatic disease and to long-term sequelae in a percentage of survivors, and 2) the years of life lost due to disease-induced mortality</li> <li>Estimated based on country-specific threshold values of the cost per DALY (the additional cost required to avert one DALY) that reflect the likely health opportunity costs (i.e., the improvement in health that would have been possible if any additional resources required had been made available for other healthcare activities)</li> </ul>
	Value of statistical life (VSL) savings	<ul style="list-style-type: none"> <li>The monetary value a typical individual places on reductions in mortality risk</li> <li>Monetary values are averaged over a population to estimate the value of saving one life</li> <li>Estimated by multiplying the total number of lives saved by the monetary values of a statistical life</li> </ul>

27 Alvis-Zakzuk et al., 2018. Economic costs of chikungunya virus in Colombia.

## 2. Mathematical Models and Scenarios

Two sets of mathematical models and scenarios were developed for the CHIK and CHIK-X approaches. This section provides a high-level overview of these models and describes the scenarios used to assess various vaccine rollout strategies, vaccine characteristics, and global health investments.

For impact assessment modelling, scenarios were created by combining assumptions on suitability-FoI relationships, vaccine rollout strategies, sequencing delays (for CHIK-X), and vaccine characteristics (minimal and preferred CEPI TPCs). The impacts of a CHIK or CHIK-X vaccine were estimated by comparing these scenarios to the baseline in which there were no vaccines.

### 2.1. CHIK model

To estimate the potential health and health economic impacts of a CHIK vaccine, a four-step approach was used as follows (Figure 2):

1. Estimate global CHIK suitability using machine learning techniques, recorded disease occurrence, and environmental covariates
2. Estimate historical patterns of the FoI in different areas of the world from age-stratified seroprevalence data
3. Project average annual incidence of CHIK based on the relationship between suitability, FoI, and the population at risk using four separate approaches<sup>28</sup>
4. Estimate the associated, country-specific health and health economic impacts from the global incidence estimates modelled

in the previous step with and without a CHIK vaccine

Health economic outcomes (Table 2) were estimated over a 16-year period (2025-2040) with and without implementation of vaccination. These results are aggregated at the national and global level over the 16-year period. Vaccination uptake was simulated for 37 countries selected for recent evidence of CHIK outbreaks (between 2010 and 2022) and interest in the CHIK vaccine. Additional information on country awareness of and interest in introducing a CHIK vaccine can be found in Appendix 3.

<sup>28</sup> Average annual incidence results were compared to estimates from a different approach produced by Salje et al., 2023. The global burden of chikungunya virus and the potential benefit of vaccines.

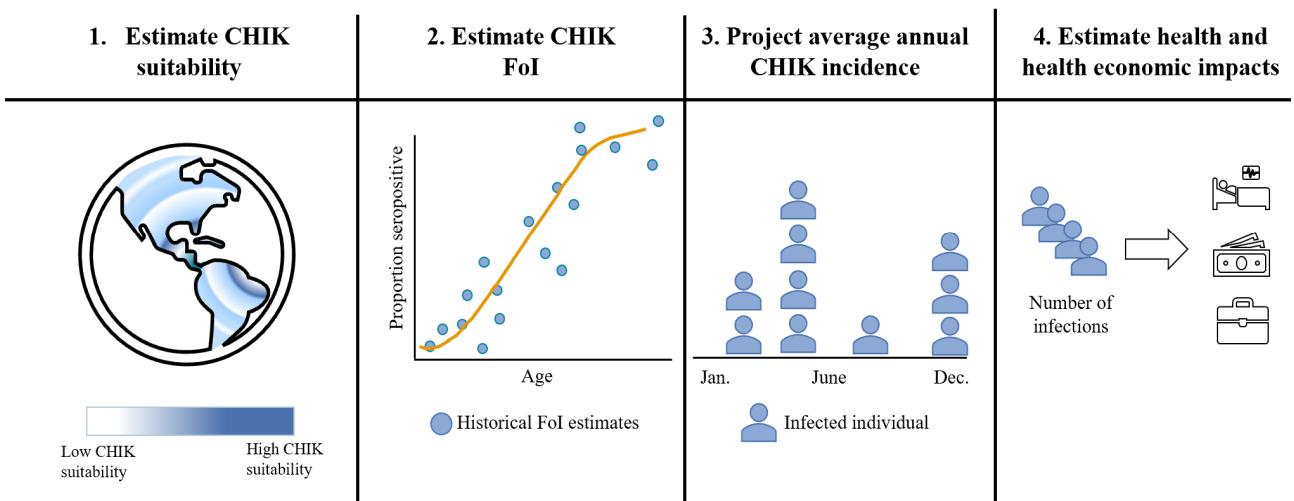


Figure 2: Four-step approach for estimating the potential health and health economic impact of a CHIK vaccine. Estimates of CHIK suitability and historical patterns of FoI were used to project annual incidence of CHIK. Average annual incidence data were then used to generate estimates of health and health economic metrics with and without a CHIK vaccine (listed in Table 2).

### Estimating CHIK suitability

The global suitability surface for CHIK was estimated by establishing a relationship between the known presence of disease occurrence, the artificial absence of occurrence, and predictor variables known to be biologically relevant for the vector species or the pathogen. CHIK suitability represents the fitness of a geographical area for the presence of disease in humans. It does not represent the suitability for the mosquito vector species (*Aedes aegypti* and *Aedes albopictus*), as there are areas where the primary species are present, but no disease has ever been recorded.

Known presence data were gathered from an occurrence database with point (e.g., town or city) or polygon (e.g., country or province) locations of confirmed chikungunya virus infections, excluding polygons greater than 2500 square kilometer due to corresponding large uncertainty around locations of the occurrence. An occurrence was defined as one or more reports of infections within a unique location in one year. Pseudo-absences—areas of potentially unsuitable environmental conditions at unsampled locations—were generated and

weighted based on a surface of temperature suitability for *Aedes aegypti* (the primary mosquito vector of CHIK).

Six explanatory covariates were chosen based on factors known or hypothesised to contribute to suitability for human CHIK occurrence. These included:

1. Annual mean precipitation
2. Minimum land surface temperature
3. Maximum annual Enhanced Vegetation Index (EVI)
4. Population density
5. Elevation
6. Environmental suitability for known mosquito vectors *Aedes aegypti* and *Aedes albopictus*

A boosted regression tree model established a relationship between the occurrence and covariate datasets described above. The relationship was established at each occurrence at the administrative- or point-level or averaged across each polygon-level occurrence. The final suitability surface was generated by averaging the suitability across all models for each 5 km x

5 km pixel.

## Estimating FoI and projecting annual CHIK incidence

The suitability surface was translated into incidence estimates using georeferenced, time-varying FoI estimates obtained from age-stratified seroprevalence data. FoI was defined as the annual probability of the susceptible population becoming infected. Because CHIK induces long-lasting antibodies, the proportion of seropositive individuals as a function of age can be used to reconstruct historical infection patterns<sup>29</sup>.

FoI was estimated from each seroprevalence dataset (34 locations from 12 countries) using a model that made the following assumptions:

1. The risk of infection was not age-dependent
2. The risk of infection was potentially time-varying
3. There was no seroreversion (i.e., once a person tests positive for CHIK antibodies, they will continue testing positive for life)
4. There was no migration due to CHIK disease status

Because seroprevalence studies are likely preferentially, or potentially even exclusively, performed in areas where there is a known (recent) history of substantial transmission of CHIK, seroprevalence data for areas with no suggestion of outbreaks or substantial endemic transmission were not available. The relationship between FoI and suitability was estimated using a logistic growth curve that used the global suitability surface as the only covariate and the estimated FoI as the outcome. Besides including datapoints based on the

seroprevalence studies, additional FoI estimates were imputed by assuming that the FoI was zero in the following countries with strong evidence of the absence of local CHIK transmission: Austria, Belgium, Canada, Denmark, Faroe Islands, Finland, Germany, Iceland, Latvia, Liechtenstein, Lithuania, Netherlands, Norway, Poland, Sweden, and Switzerland. The modelled relationship between FoI and suitability was used to predict the FoI at all locations of interest. Given significant uncertainties about true global and country-level numbers of CHIK cases, four separate approaches were used to generate the average number of infections in each country (Table 3). These approaches (OxLiv 1-4) estimated FoI and suitability using the methods described previously but varied the following:

1. FoI or suitability datapoints included in the modelled relationship
2. Accumulated immunity due to infections in previous years

<sup>29</sup> Lim et al., 2023. Seroepidemiological reconstruction of long-term chikungunya virus circulation in Burkina Faso and Gabon.

Table 3. The four OxLiv approaches used to generate the average number of infections in each country.

Model	Characteristics
OxLiv 1	<ul style="list-style-type: none"> <li>Predicted FoI from suitability, including all datapoints (Figure 12)</li> <li>Accounted for WHO region-specific averages of preexisting antibody levels and accumulating immunity due to infections occurring over successive years</li> </ul>
OxLiv 2	<ul style="list-style-type: none"> <li>Predicted FoI from suitability but excluded datapoints with suitability &gt; 0.75 and FoI &lt; 0.005 (Figure 13)</li> <li>Accounted for WHO region-specific averages of preexisting antibody levels and accumulating immunity due to infections occurring over successive years</li> </ul>
OxLiv 3	<ul style="list-style-type: none"> <li>Predicted FoI from suitability, including all datapoints (Figure 12)</li> <li>Accounted for WHO region-specific averages of preexisting antibody levels only</li> </ul>
OxLiv 4	<ul style="list-style-type: none"> <li>Predicted FoI from suitability but excluded datapoints with suitability &gt; 0.75 and FoI &lt; 0.005 (Figure 13)</li> <li>Accounted for WHO region-specific averages of preexisting antibody levels only</li> </ul>

In the absence of detailed country-specific data on antibody levels, existing immunity was estimated by subtracting WHO-region specific antibody levels from one. Predicted FoI (on a 5km x 5km pixel scale) was related to the population at risk for each pixel by multiplying the FoI with the corresponding population sizes<sup>30</sup> to get the estimated mean annual number of infections in each pixel. Subsequently, country-specific annual number of chikungunya virus infections were estimated by summing the relevant pixel values within each country. This was done both for the scenario with (OxLiv 2 & 4) and without (OxLiv 1 & 3) the exclusion of datapoints with simultaneously high suitability and low FoI estimates.

Results from these approaches were compared to a fifth approach<sup>31</sup> that was based on an existing model which classified countries into different suitability categories (endemic, epidemic, and no transmission) and used age-specific seroprevalence data to generate two estimates for the probability of infection among the population at risk for epidemic and endemic countries, respectively. For India, China, and the U.S., Salje et al. set predicted infections

to zero in areas for which there is no reported evidence of sustained transmission through seroprevalence data (for India) or case reporting (China and U.S.), regardless of predicted suitability. Therefore, in those countries only a proportion of the population was considered to be at risk of infection (China 13%, India 59%, and U.S. 7%). In addition, Salje et al. overruled the FoI-based predictions of incidence in all countries with a Healthcare Access and Quality<sup>32</sup> index > 82.2 (20<sup>th</sup> percentile) and used reported case data to obtain estimates of incidence instead.

### CHIK vaccine characteristics and vaccination scenarios

Various assumptions regarding CHIK vaccine characteristics and rollout strategies were applied to CHIK incidence estimates to evaluate the health and health economic impacts of a CHIK vaccine.

All scenarios assumed a CHIK vaccine would offer protection against symptomatic infection of 70%, 80%, and 90%, respectively. The vaccine was assumed to have the same protective effect against symptomatic infections regardless of

30 World Pop, 2024. Unconstrained, 1km resolution, UN-adjusted population counts ([www.worldpop.org](http://www.worldpop.org)).

31 Salje et al., 2023. The global burden of chikungunya virus and the potential benefit of vaccines.

32 Fullman et al., 2018. Measuring performance on the Healthcare Access and Quality Index for 195 countries and territories and selected subnational locations: A systematic analysis from the Global Burden of Disease Study 2016.

severity, and no impact on CHIK transmission. The duration of protection was assumed to be at least 16 years (the time horizon of the simulation).

The vaccine's potential impact was estimated using two categories of vaccine rollout scenarios (Table 4):

1. **Target-based:** Optimistic scenarios including both preventative and routine vaccination strategies requiring major demand generation from current market interest
2. **Market-based:** Realistic scenarios including only preventative vaccination strategies reflecting current market demand and interest in introducing the vaccine

The vaccination scenarios were built off a CHIK vaccine demand forecast previously conducted for CEPI<sup>33</sup>. This forecast focused on 39 countries with recent CHIK outbreaks (between 2010 and 2022), organizing them into three levels (high, medium, and low) based on their awareness of and interest in introducing a CHIK vaccine. For this analysis, 37 of the original 39 countries were included to align with the countries in the Salje et al. study<sup>34</sup>. The countries excluded from the original list were Grenada and Micronesia. Their exclusion had negligible impact on the results due to low infection numbers (about 0.002% of global CHIK cases). Country inclusion in each level was based on its recent CHIK outbreak frequency, its region's interest in a CHIK vaccine (derived from country stakeholder interviews), and its participation in a CHIK vaccine clinical trial. A country with numerous recent outbreaks, expressed interest in a CHIK vaccine, and/or participation in a clinical trial was placed in the “high” level,

meaning it was highly likely to introduce the vaccine. In contrast, a country with infrequent outbreaks, expressed ambivalence in a CHIK vaccine, and no participation in a clinical trial was placed in the “low” level, meaning it was unlikely to introduce the vaccine unless in the most optimistic scenario. Due to the presence of recent outbreaks, any country in the WHO Regional Office for the Americas (AMRO) region that wasn't already in the “high” level was placed in the “medium” level (see Appendix 3 for more details on this method).

The target-based scenarios incorporated assumptions from the high scenario of the demand forecast (including high, medium, and low countries), while the market-based strategies were informed by the low and medium demand forecast scenarios (including only high and medium countries). For vaccination scenarios in both categories, it was assumed that the target population was spread equally across age groups for all campaigns.

For all allocation scenarios, cholera was used as a proxy for assumptions regarding target coverage in preventative campaigns. Cholera was chosen for preventative campaigns because of similarities in target age, vaccination strategies, and geographical distribution. Historical data on doses administered in cholera campaigns for an approximate coverage value per country were used to inform the target coverages and campaign lengths<sup>35</sup>. Human papillomavirus (HPV) was used as a proxy for the routine vaccination campaigns because of the similar target age (12). Global coverage was used to inform the target coverage during routine vaccination<sup>36</sup>.

33 CEPI, 2023. Chikungunya vaccine introduction: Understanding LMIC perspectives. (Not public).

34 Salje et al., 2023. The global burden of chikungunya virus and the potential benefit of vaccines.

35 WHO, 2024. International Coordinating Group (ICG): Cholera dashboard.

36 WHO, 2022. Human papillomavirus vaccines: WHO position paper (2022 update).

Table 4. Vaccination scenarios for CHIK. Two categories of scenarios were run: target-based (Scenarios 1-3) and market-based (Scenarios 4-5). Target-based scenarios included preventative campaigns followed by routine vaccination, while market-based scenarios incorporated only preventative campaigns. Target coverages over the multi-year preventative campaigns and annual coverage for routine vaccination are provided.

Scenario	Title	Countries covered with preventative campaigns (target coverage over multiple years)	Countries covered with routine vaccination (annual coverage)
Target-based			
1	Target High	High, Medium, Low (30-40%)	High, Medium, Low (60-65%)
2	Target Medium	High, Medium (30-40%)	High, Medium (60-65%)
3	Target Low	High (30-40%)	High (60-65%)
Market-based			
4	Market High	High, Medium (20-30%)	None
5	Market Low	High (10-20%)	None

The target-based scenarios (Scenarios 1-3, Figure 3, Table 4) assumed equal uptake per year for preventative campaigns with multi-age cohort introductions occurring for two years followed by routine vaccination five years after campaign introduction. Campaigns included in the target-based scenarios covered people ages 12-99. Routine vaccination for all scenarios under the target-based strategy aimed to reach 60-65% of 12-year-olds. The number of

countries included in the target-based scenarios ranged from 37 (Scenario 1) to 7 (Scenario 3). Countries with high outbreak burden (a recent outbreak since 2018 and history of > 2 outbreaks) and interest in the CHIK vaccine reached the higher end of the coverage range provided. The other countries—those at the “medium” or “low” level or participants in a clinical trial—remained at the lower end of the assumed coverage range.

### Target-based scenarios

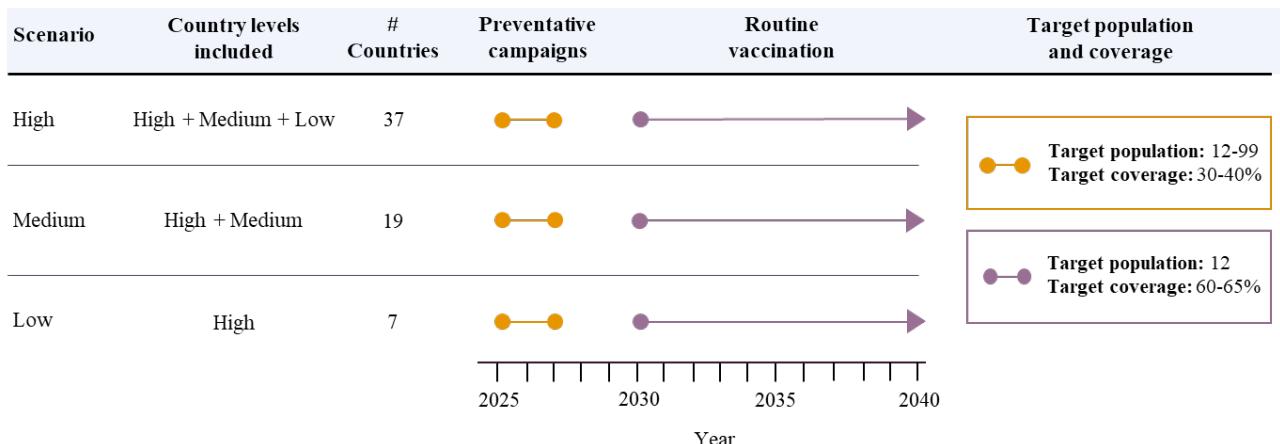


Figure 3: Country levels and number of countries included in preventative campaigns and routine vaccination under the target-based vaccination scenarios. The target population for preventative campaigns was 12-99 with a target coverage of 30-40%. This target coverage was achieved over a two-year campaign. Routine vaccination targeted 60-65% of people age 12.

The market-based scenarios included three-year preventative campaigns only, targeting people ages 18-99 in the high scenario (Scenario 4, Figure 4, Table 4) and people ages 50-99 for the low scenario (Scenario 5). Target coverage ranged from 20-30% in the high scenario to 10-20% in the low scenario.

### Market-based scenarios

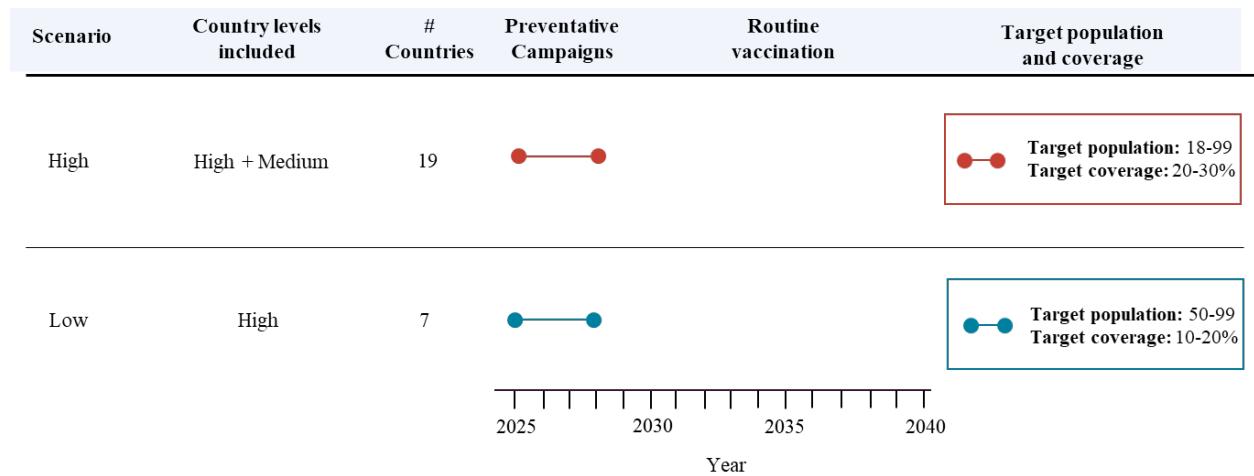


Figure 4: Country levels and number of countries included in three-year preventative campaigns under the market-based vaccination scenarios. Campaigns targeted people ages 18-99 in the high scenario (20-30% coverage) and those ages 50-99 in the low scenario (10-20% coverage).

## **Health economic impacts of a CHIK vaccine**

Lastly, health economic outcomes (listed in Table 2) were estimated using projected annual CHIK incidence generated by the five models (OxLiv 1-4 and Salje et al.) and the vaccination scenarios. Only the mean infection number from the Salje et al. model was used as an input for the health economic model. Parameters and methods to produce symptomatic cases and all other clinical and economic outcomes were consistent across all model inputs (Figure 5). The probability of symptomatic infection was assumed to be 18%, and the mean probability of hospitalisation was assumed to be 4% of total symptomatic infections—which varied according to age and sex, informed by observations from an outbreak in Paraguay<sup>37</sup>. The probability of symptomatic infection varied in a sensitivity analysis.

The probability of death was assumed to be age- and sex-specific among cases informed by case fatality ratios (CFR) in Brazil<sup>38</sup>. The resulting mean CFR aggregated over age and sex groups was approximately 2.6 in 1000. The probability of suffering sequelae after symptomatic infection was assumed to be 51%<sup>39</sup>.

Future costs were discounted using a discount rate of 3% per year to account for consumer preference for present consumption rather than later. Additional information on the health economic model can be found in Appendix 3.

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37 Torales et al., 2023. Notes from the field: Chikungunya outbreak — Paraguay, 2022–2023.

38 Souza et al., 2023. Spatiotemporal dynamics and recurrence of chikungunya virus in Brazil: An epidemiological study.

39 Kang et al., 2024. Chikungunya seroprevalence, force of infection, and prevalence of chronic disability in endemic and epidemic settings: Systematic review, meta-analysis, and modelling study.

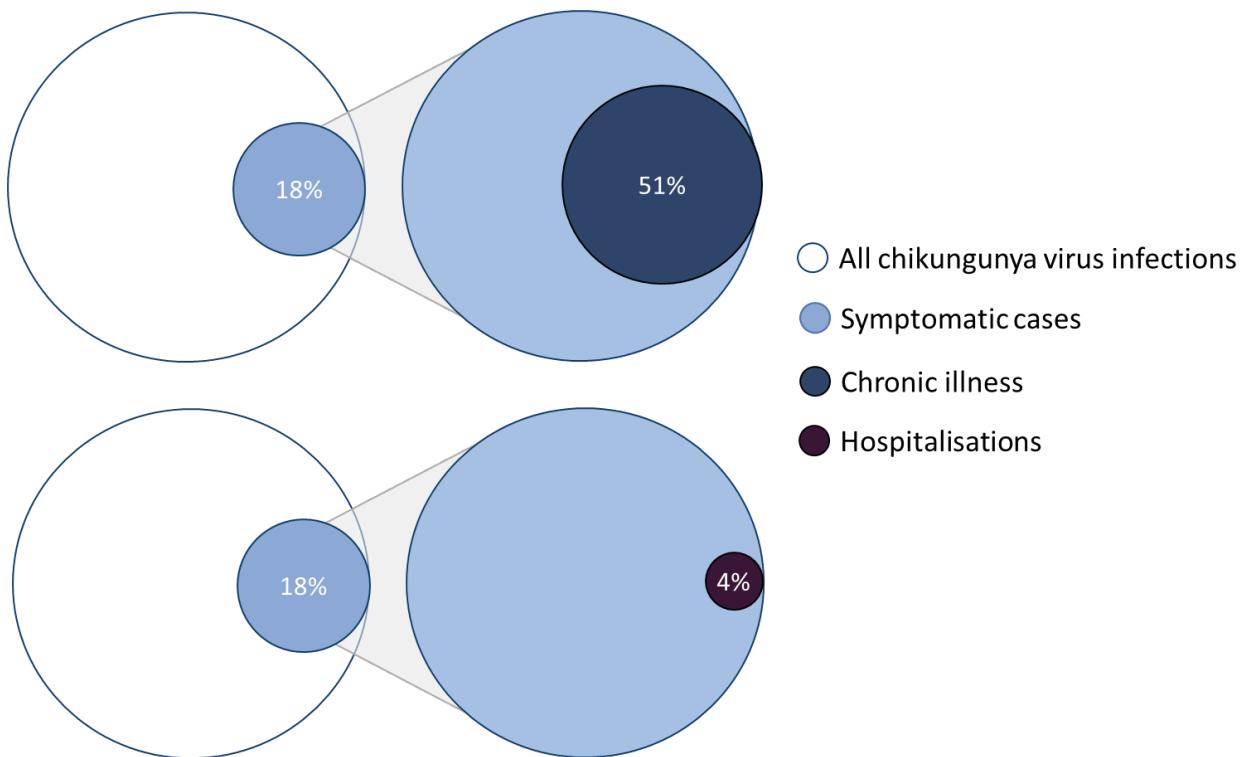


Figure 5: Illustrative figure showing the proportion of chikungunya virus infections that result in symptomatic cases and the proportion of symptomatic cases that result in chronic illness or hospitalisation. The probability of death given symptomatic illness was assumed to be age- and sex-specific.

## 2.2. CHIK-X model

Simulating CHIK-X is necessarily a speculative exercise as it pertains to a hypothetical scenario in which a new chikungunya-related virus emerges and spreads internationally. It could be argued that the expansion of CHIK in 2013 to the Americas represents one such scenario, but it will likely not be the last such event. As such, a series of pragmatic assumptions were made to formulate a set of scenarios for how such a variant could spread.

Three disease severity scenarios for CHIK-X were considered:

1. **Scenario A:** The probability of an infection becoming symptomatic was 46% (based on the Carillo et al.

alternative estimate used in CHIK sensitivity analyses<sup>40</sup>), and the probability of hospitalisation and death were the same of those for CHIK

2. **Scenario B:** The probability of an infection becoming symptomatic was 46%, and the probability of hospitalisation and death were 5 times that of CHIK
3. **Scenario C:** The probability of an infection becoming symptomatic was 100%, and the probability of hospitalisation and death were 10 times that of CHIK

40 Carrillo et al., 2022. Epidemics of chikungunya, Zika, and COVID-19 reveal bias in case-based mapping.

The health and health economic outcomes of a CHIK-X outbreak and the potential impact of various vaccine allocation assumptions were modelled using a country-level simulation of larger outbreaks (with increased transmissibility) and spread through global mobility patterns. The dynamics were simulated using the following four-step approach (Figure 6):

1. Model the emergence of CHIK-X, with the probability of emergence more likely in areas where there were estimates of higher CHIK incidence
2. Model the pattern of international spread using human mobility data, where the probability of a CHIK-X outbreak

- stemming from a single infected individual travelling from an outbreak country to a country where there was no outbreak was based on a scaling of the estimates of suitability for CHIK transmission
3. Simulate the shape of CHIK-X outbreaks (i.e. incident infections over time in any one country) by scaling reports of cases in different countries in the PAHO region over the last decade
  4. Estimate health economic outcomes by post-processing outbreak data in a similar way to the CHIK process described previously, with different assumptions on relative severity

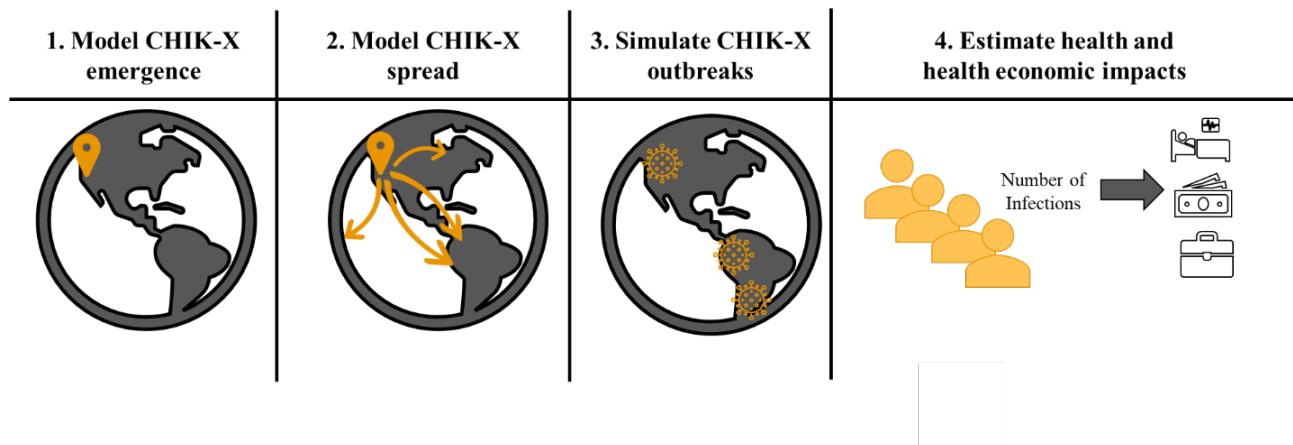


Figure 6: Four-step approach for estimating the potential health and health economic impacts of a CHIK-X vaccine. CHIK-X emergence was modelled using estimates of incidence predicted from CHIK suitability maps. From the point of introduction, human movement data were used to model CHIK-X spread, and subsequent outbreaks were simulated. Daily infection rates per country were then used to generate estimates of health and health economic metrics (listed in Table 2).

## **CHIK-X emergence**

The estimates of average yearly country-level incidence predicted from CHIK suitability maps were used to estimate the probability of a CHIK-X outbreak and its potential point of introduction. This relationship reflected an underlying assumption that the opportunities for mutation of a new lineage would increase as the number of new infections in a country increased. Further, it was assumed that there were no subsequent CHIK-X emergences after the initial outbreak event. While CHIK-X incidence and spread was assumed to be more likely to occur where CHIK occurs, the model did not account for previous natural or vaccine-induced CHIK immunity in the population, reflecting an assumption that this was an antigenically distinct virus.

## **Modelling the spread of CHIK-X**

From the point of emergence, the probability of CHIK-X spread from one country to another was modelled based on published human movement data<sup>41</sup>, where the probability of a person travelling from one location to another was combined with the probability they were infected with CHIK-X—i.e., the prevalence of infection in that country on that day.

In order to account for variation in both vector-abundance and suitability for transmission, the probability of establishment in a new country was given by the population-weighted suitability of the country for CHIK transmission (estimated in the main CHIK section).

## **CHIK-X outbreak dynamics**

A CHIK-X outbreak was simulated in each country where CHIK-X emerged or spread so that the impact of vaccination at different times in the epidemic could be estimated. The CHIK-X outbreak dynamics in each country were simulated based on extant CHIK outbreak data to capture their explosive dynamics. The outbreak data was sourced from country-level reported case numbers between 2013-2017 from the Pan American Health Organisation (PAHO; Figure 7)<sup>42</sup>. These data were smoothed using a 30-day rolling average and adjusted to start the outbreak from the beginning of the simulation in that country—to simulate daily rather than monthly incidence—and to exclude cases where the increase was extreme. A monthlong lag of a single daily infection was added to each curve to attenuate the rate of spread. For each outbreak, a random epidemic shape was picked from this group.

As noted previously, CHIK underreporting presents a significant challenge. Whilst the PAHO outbreak shapes were used, the total number of infections was scaled to match the country-level estimates of CHIK incidence as calculated using the CHIK suitability-FoI model. The CHIK-X model used this scaled incidence as a mean, with a noise of 10% around this mean. The choice of scaling factor is discussed below.

41 Recchi et al., 2019. Estimating transnational human mobility on a global scale.

42 PAHO, 2018. Chikungunya fever in the Americas: Number of reported cases.

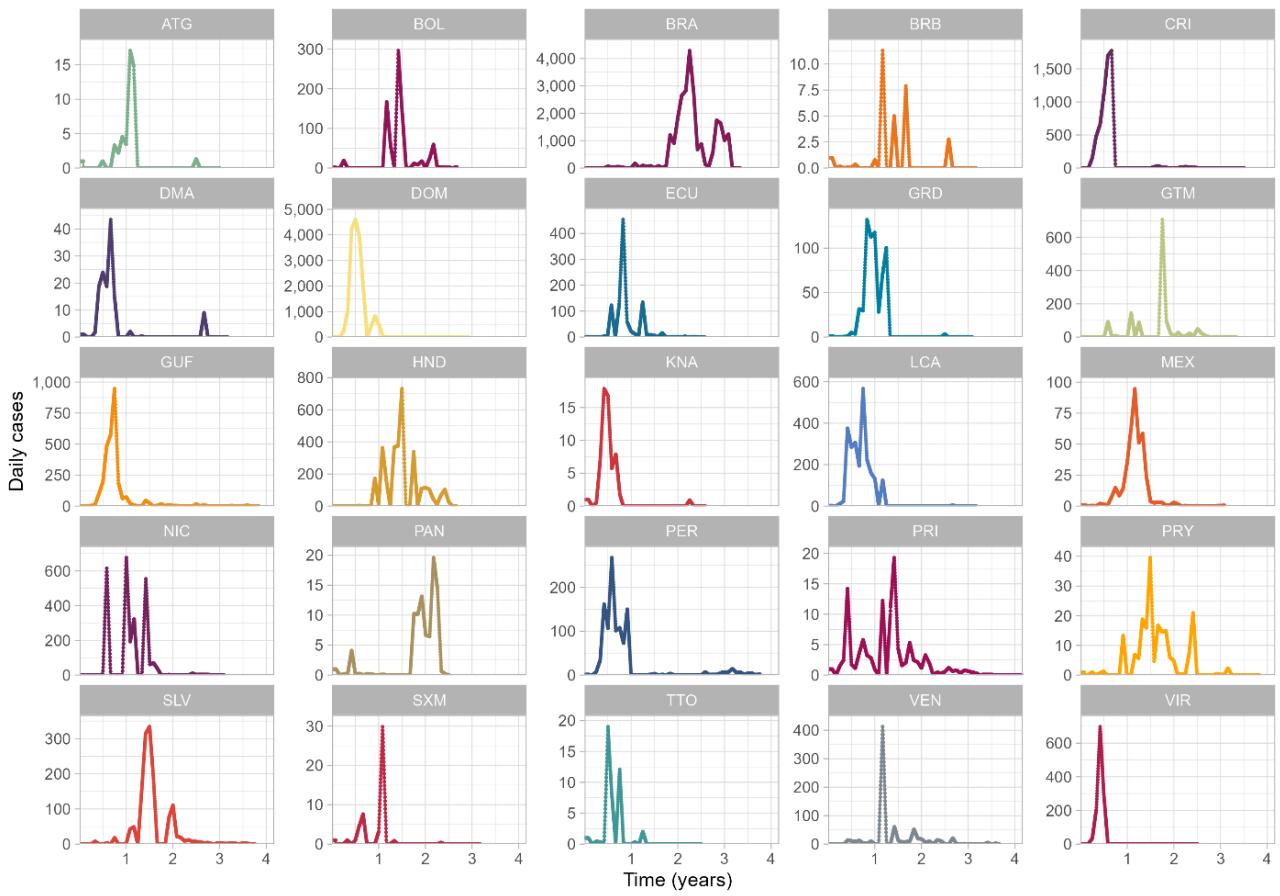


Figure 7: Smoothed reported CHIK case incidence by country aligned so that each outbreak starts at time zero, adapted from data reported by PAHO<sup>43</sup>. The country name for each ISO code is provided in Appendix 3.

### Tuning the parameters of CHIK-X

There were several parameters in the model description which could be varied. Previous global spread events from chikungunya or similar viruses were sought to ground-truth the transmission parameters in real-world data. However, there was limited genetic information on the spread of CHIK to the Americas from 2013 onwards (62% of sequences are still from Brazil with much of the remainder from the U.S.)<sup>44</sup>. Therefore, data from the global spread of Zika was used to tune the model. Publicly available analyses from Nextstrain gave the number of countries affected during

the expansion of Zika in the mid-2010s<sup>45,46</sup>. The two-year period from July 2014 to July 2016 was used to reflect the fact that the initiating outbreak in the simulation was an explosive outbreak and highly likely to spread. The estimated date of introduction in each country from this genetic analysis was used to generate a number of countries affected over time.

To emulate this rate of spread, we varied the incidence rate and the extent of variation in outbreak sizes and compared the median number of countries infected over time to the data from the genetic analysis of Zika data (Figure 8).

<sup>43</sup> PAHO, 2018. Chikungunya fever in the Americas: Number of reported cases.

<sup>44</sup> de Souza et al., 2024. Chikungunya: A decade of burden in the Americas.

<sup>45</sup> Hadfield et al., 2018. Nextstrain: Real-time tracking of pathogen evolution.

<sup>46</sup> Nextstrain, 2024. Real-time tracking of Zika virus evolution (<https://nextstrain.org/zika/>).

This was to reflect the fact that part of the remit for the CHIK-X simulations was to simulate outbreaks from a more transmissible pathogen. As is shown in the figure, the model which most appropriately reflected the data was to multiply

mean incidence by 0.7 and to introduce 10% noise, allowing more simulations that affected only a few countries initially before spreading more quickly globally.

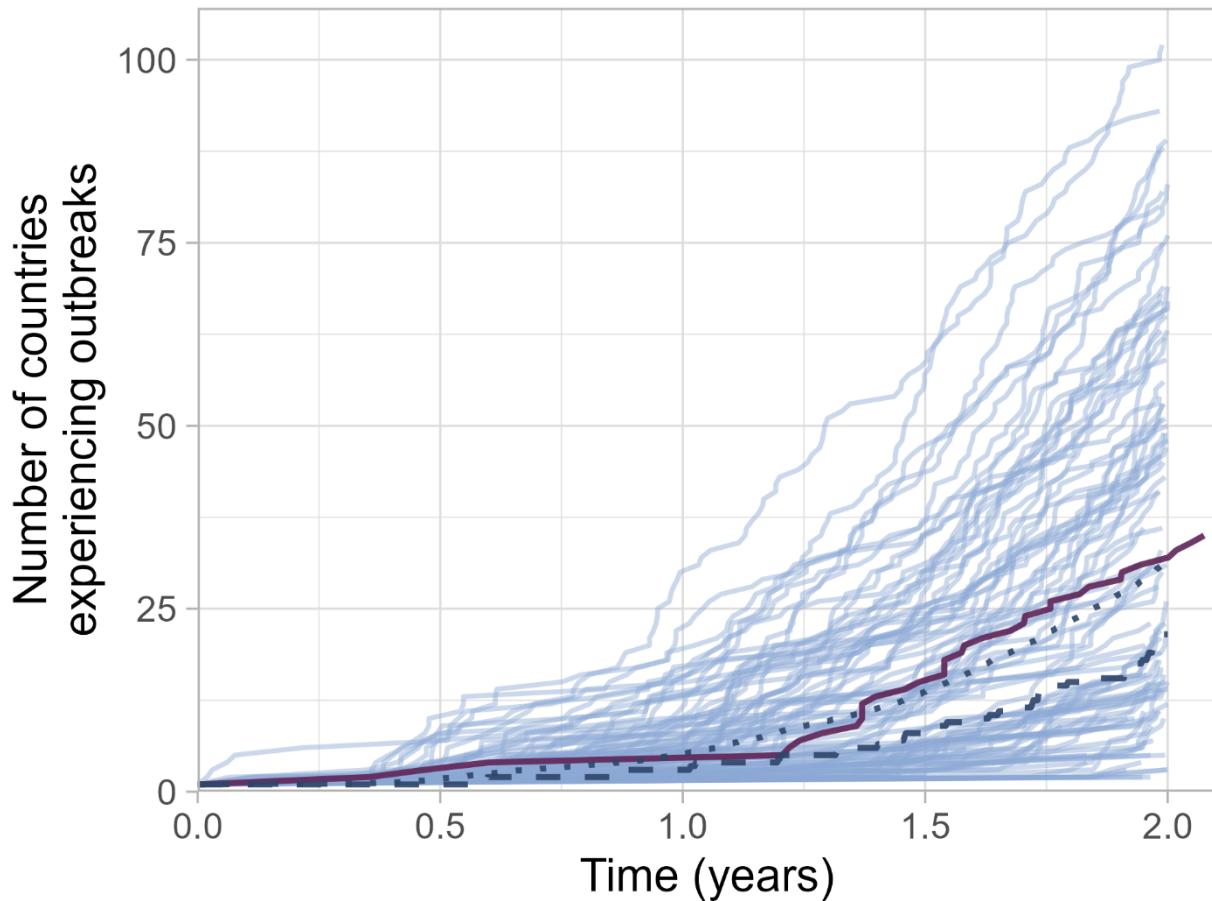


Figure 8: Cumulative number of countries affected by CHIK-X outbreaks over a spread period of two years. Light blue lines show individual simulations ( $n=100$ ). Solid line shows the rate of Zika spread between 2014 and 2016; dotted line shows the mean cumulative number of countries with a CHIK-X outbreak over time; dashed line shows the median cumulative number of countries with a CHIK-X outbreak over time.

## **CHIK-X vaccine characteristics and vaccination scenarios**

Several vaccination scenarios were run to assess the potential impact of CEPI's 100 Days Mission on CHIK-X infections (Table 5). The scenarios had varying levels of surveillance, coverage, country scope, vaccination timing, and investments in manufacturing and health systems.

Similar to the CHIK vaccine, all scenarios assumed a CHIK-X vaccine would have 70%, 80%, or 90% efficacy against disease and offered protection through at least the length of the simulation (10 years).

Two main assumptions were made for vaccine rollout. First, it was assumed that vaccines were rolled out in a country-specific manner only after CHIK-X had arrived. Thus, secondary spread countries were assumed to wait to initiate vaccination campaigns until CHIK-X arrived. Second, there was assumed to be a longer delay from the first infection to vaccine rollout in the outbreak country compared to any secondary spread countries. In the outbreak country, vaccine rollout initiation was timed to accommodate the 100 days after detection/sequencing required for a CHIK-X vaccine to be ready for initial authorization and manufacturing at scale (according to CEPI's 100 Days Mission). In secondary spread countries, vaccine rollout after the first infection took less than 100 days because the vaccine was already developed, with additional delays reflecting time needed to mount a vaccination campaign in a newly affected country.

Based on these two assumptions, rollout varied depending on three parameters:

1. The surveillance timing of CHIK-X detection/sequencing after emergence in

the outbreak

2. The trigger that initiated vaccination in secondary spread countries
3. The rate of annual vaccine uptake

On surveillance timing, each scenario evaluated one of two CHIK-X detection/sequencing assumptions for the 100 Days Mission. In the first assumption, it was assumed that there was no delay between when CHIK-X first arrived in an outbreak country and when detection/sequencing took place. Thus, CHIK-X vaccination in the outbreak country began 100 days after the first infection was detected. In the second, more realistic assumption, it was assumed that it would take 60 days after CHIK-X emerged in the outbreak country for the virus to be detected/sequenced, which would then trigger the 100 Days Mission. Under this assumption, vaccination would start in the outbreak country 160 days after CHIK-X arrived. For both assumptions, once vaccination was initiated in any given country, the rate of vaccine uptake was assumed to be stable throughout the CHIK-X pandemic, resulting in linear increases in the share of the population vaccinated over time. Once CHIK-X vaccination was initiated, it was assumed that either 5%, 20%, or 40% of the country's total population was vaccinated after one year, up to a maximum of 80%. These annual uptake rates translate to weekly vaccination coverages of approximately 0.1%, 0.4%, and 0.8% of the population, respectively. Vaccinations were evenly distributed by age and sex across the total population.

In secondary spread countries, it was assumed that vaccination would not begin before vaccination had started in the outbreak country (Figure 9). That is, secondary spread countries would start vaccinating at whatever time was later: the initial lag in the outbreak country

(i.e., vaccination starting 100 days after CHIK-X arrival or 160 days after CHIK-X arrival) or the time to reach the trigger that initiated vaccination in the secondary spread country. Two triggers were assumed in different scenarios. The first trigger modelled vaccine rollout starting 50 days after the first case was detected in the secondary spread country. The second trigger assumed vaccine rollout started after the 20<sup>th</sup> infection<sup>47</sup>.

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<sup>47</sup> This trigger is equivalent to 10 cases because it was assumed 50% of infections led to symptomatic cases. In one sensitivity analysis, the trigger was 20 cases since it was assumed 100% of infections were symptomatic.

Table 5: Vaccination scenarios for CHIK-X. Six scenarios were run based on varying levels of surveillance, annual vaccination coverage (uptake), country scope, the time lag to vaccine introduction, and investments in manufacturing and health systems. Low scenarios aimed to reach 5% of people annually, while medium and high scenarios reached 20% and 40%, respectively. Sequencing—and subsequent initiation of manufacturing of the CHIK-X vaccine—was assumed to take place either right away (no delay) or 60 days after the virus was detected. Outbreak countries were assumed to introduce a CHIK-X vaccine 100 days after detection. Secondary spread countries introduced the vaccine at 50 days after the virus was detected or at a threshold of 20 infections. Vaccine uptake was assumed to be stable throughout the pandemic with linear increases in the share of the population vaccinated over time.

Scenario	Title	Manufacturing investment	Health systems investment	Annual coverage	Country scope	Lag to vaccine introduction
No Delay (Initiation of 100 Days Mission occurs immediately after detection/sequencing of CHIK-X virus)						
1	Low no delay	Yes	No	5%	Outbreak	100 days after detection
					Secondary spread	50 days after detection, or at case threshold
2	Medium no delay	Yes	Yes	20%	Outbreak	100 days after detection
					Secondary spread	50 days after detection, or at case threshold
3	High no delay	Yes	Yes	40%	Outbreak	100 days after detection
					Secondary spread	50 days after detection, or at case threshold
60-Day Delay (Initiation of 100 Days Mission occurs 60 days after detection/sequencing of CHIK-X virus)						
4	Low delay	Yes	No	5%	Outbreak	160 days after detection
					Secondary spread	50 days after detection, or at case threshold
5	Medium delay	Yes	Yes	20%	Outbreak	160 days after detection
					Secondary spread	50 days after detection, or at case threshold
6	High delay	Yes	Yes	40%	Outbreak	160 days after detection
					Secondary spread	50 days after detection, or at case threshold

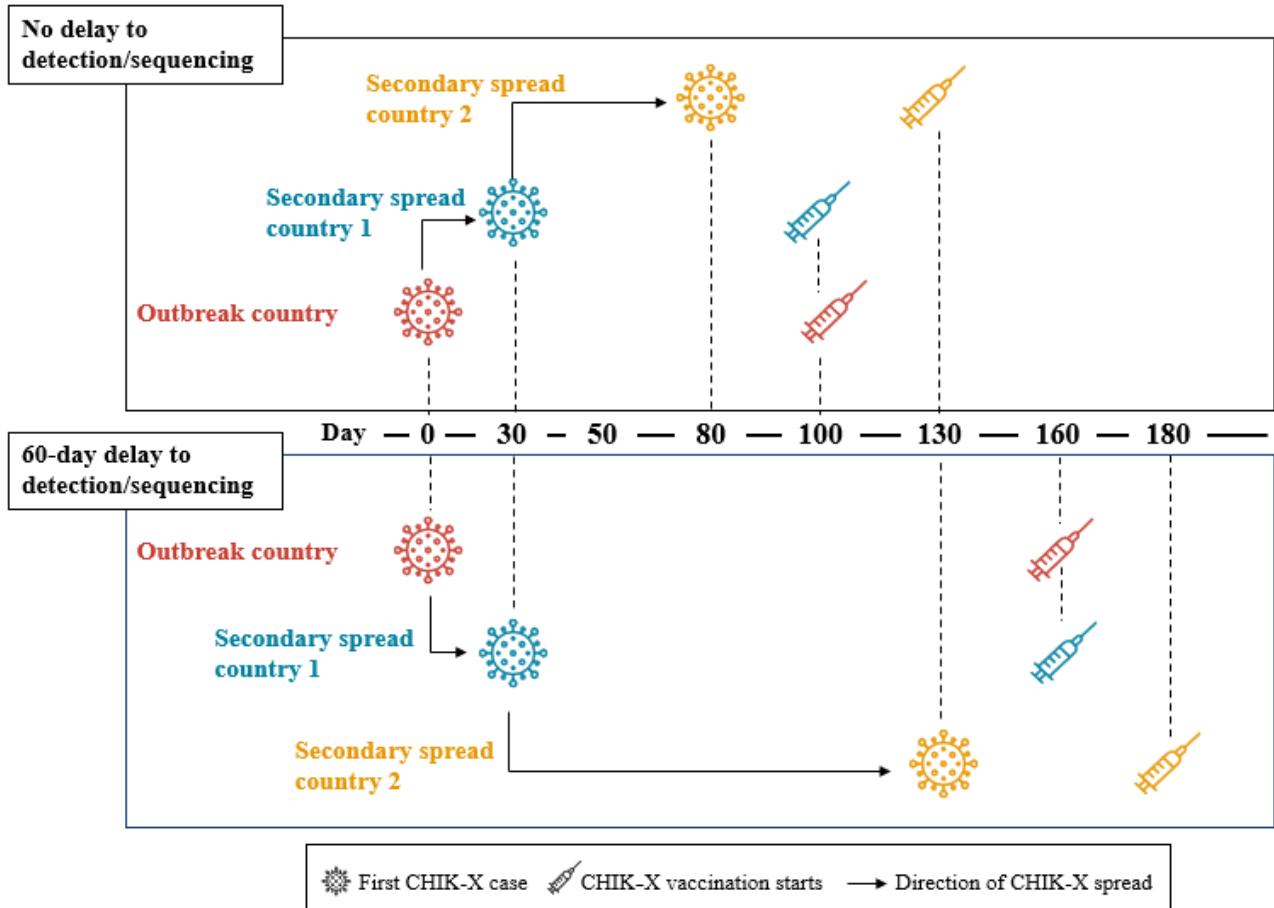


Figure 9: Illustrative example of CHIK-X detection and subsequent vaccination initiation in a scenario where there is no delay between when CHIK-X is first detected in the outbreak country and the 100 Days Mission is initiated (e.g., vaccination begins 100 days after the first case, Scenarios 1-3) and when there is a 60-day delay (Scenarios 4-6). This example shows varying timelines for CHIK-X vaccine introduction in the secondary spread countries. In the no-delay scenario, secondary spread country 1 begins vaccination at the same time as in the outbreak country (day 100) because that occurs after the 50-day or infection-threshold triggers. In secondary spread country 2, however, vaccination begins 50 days after the first CHIK-X infection (i.e., the country does not have to wait as long as secondary spread countries 1, since CHIK-X vaccination began in those countries and the outbreak country on day 100). Similarly in the 60-day delay scenario, the outbreak country and secondary spread country 1 can introduce CHIK-X vaccines on the same day (day 160), while the secondary spread country 2 only has to wait 50 days for CHIK-X vaccination to begin.

The annual 5% coverage rate for the low scenario followed the guidance for reaching critical workers set by WHO and COVAX during early stages of vaccine allocation in the COVID-19 pandemic. Similarly, target coverage for the medium scenario was based on guidance for the first year of COVAX (20% in first year)<sup>48</sup> and for containing a yellow fever outbreak (80%)<sup>49</sup>. After two years, coverage for the medium scenario would be half of the target coverage for a yellow fever campaign (40%). In the high scenario, annual coverage (40%) was set to reach the yellow fever target coverage after two years. In all scenarios, an upper coverage limit of 80% was set to account for individuals unable or unwilling to vaccinate.

It was assumed that investments in manufacturing and health systems were made to support the additional CHIK-X vaccine doses that would be needed to meet the demand in the scenarios with medium and high coverage assumptions (Figure 10). Investing in manufacturing would help alleviate vaccine supply constraints such that there would be no stockouts or introduction delays, while investing in health systems would remove constraints on slower vaccine rollout to enable all countries to deliver vaccines at the same rate.

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48 WHO, 2020. Fair allocation mechanism for COVID-19 vaccines through the COVAX Facility.

49 WHO, 2016. Global strategy to eliminate yellow fever epidemics (EYE).

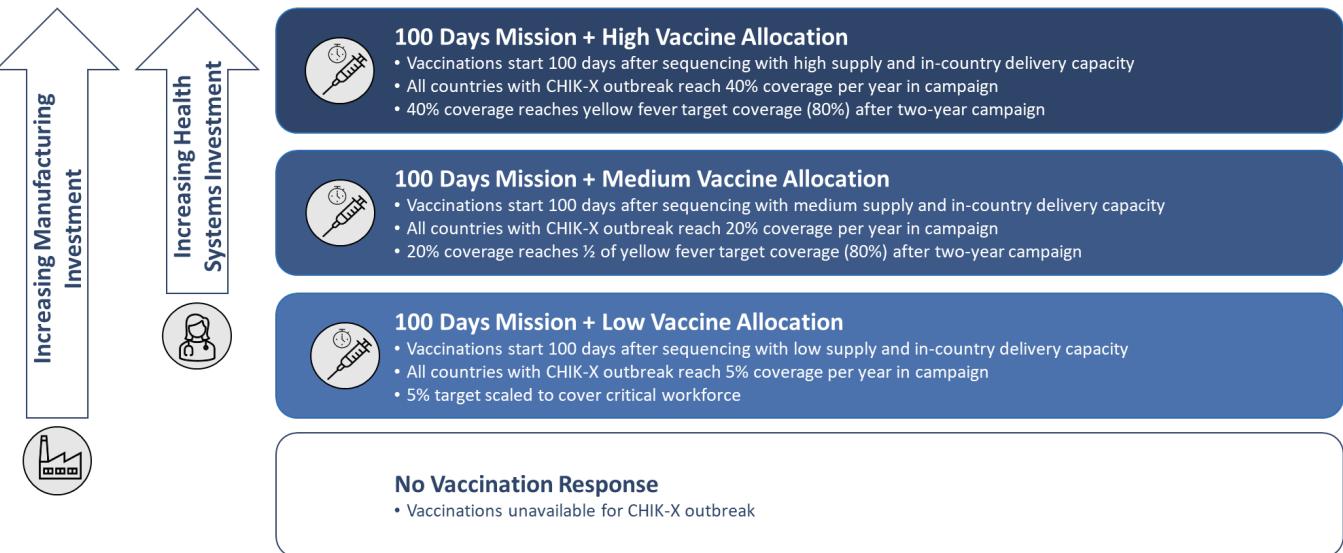


Figure 10: Schematic showing how manufacturing and health systems investments would increase with increasing coverage assumptions. Increasing manufacturing investments would help increase vaccine supply, while increasing health systems investments would help boost in-country delivery capacity.

### Health economic impacts of a CHIK-X vaccine

Lastly, the data generated by the CHIK-X outbreak dynamics model were post-processed to estimate health economic outcomes and potential benefits of the 100 Days Mission vaccination scenarios. Future costs were discounted using a discount rate of 3% to account for consumer preference for present consumption rather than later. Additional information can be found in Appendix 3.

### 2.3. Uncertainties and assumptions

While uncertainties exist in the infection numbers underlying the different models, these have not been propagated into the final results for CHIK as it was infeasible to take all uncertainties (e.g., the global suitability, the FoI estimates, the relationship between the suitability and FoI, and existing and accumulating immunity through antibody levels)

into account in a model that runs fast enough to deliver the results in time.

Instead, we used different scenario and sensitivity analyses to explore the impact of different assumptions around estimated infection numbers. All analyses took into account uncertainties in relevant clinical parameters and the age-sex distribution of infections.

Due to data availability and quality, clinical parameters have been informed by data from PAHO countries, which are assumed representative of all other countries. While all available data has been reviewed from sources believed to be the most reliable, this may result in some biases. Where possible, for instance with distribution of cases among age- and sex- specific groups, adjustments were made to the Brazil distribution using other countries' population pyramids. However, there is uncertainty about whether these age-specific incidences are indeed typical for other countries.

Furthermore, results from an investigation into CHIK mortality in Brazil notes that our assumed mean CFR of approximately 2.6 in 1000<sup>50</sup> may be at least twice<sup>51</sup> as low as true mortality risk due to underreporting, suggesting that our estimates of deaths might be conservative.

Similarly, there is an assumption that treatment costs, which rely on a study from Colombia<sup>52</sup>, are representative of treatment costs in other affected countries, and while adjustments were made using country-specific per capita OOP expenditure as a percentage of total healthcare expenditure, there is nevertheless considerable uncertainty about the true, current OOP expenses related to chikungunya hospitalisations globally.

For the CHIK-X analyses, certain key assumptions drove much of the outbreak dynamics, including the assumption of a single emergence of a new strain, the use of Zika outbreak data to estimate likely subsequent spread to other countries, and the timing of spread to other countries. In addition, we assumed no existing previous natural or vaccine-induced immunity in the population that would be effective against CHIK-X. Finally, there are some countries included in the CHIK-X analysis in particular for which data to inform economic parameters are not readily available (e.g., North Korea). As such, less established sources than the World Bank and UN data were relied on in these instances to reach a feasible estimate.

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50 de Souza et al., 2023. Spatiotemporal dynamics and recurrence of chikungunya virus in Brazil: an epidemiological study.

51 Frutuoso et al., 2020. Estimated mortality rate and leading causes of death among individuals with chikungunya in 2016 and 2017 in Brazil.

52 Alvis-Zakzuk et al., 2018. Economic costs of chikungunya virus in Colombia.

### 3. Results and Discussion

This section provides the main results, figures, and tables from the CHIK and CHIK-X analyses described in the previous sections. Supplementary results are provided in Appendix 4. For CHIK, these include the health economic processing of all five epidemiological models (OxLiv 1, OxLiv 2, OxLiv 3, OxLiv 4, and Salje et al.) considering 70%, 80%, and 90% vaccine efficacy against disease. The main results for CHIK include health economic processing of OxLiv 1 infection numbers. Key assumptions include “low” probability of being symptomatic (18%), mean hospitalisation risk of 4%, and age- and sex-dependent mortality risk. Unless stated otherwise, vaccine efficacy is assumed to be 70%.

For CHIK-X main results, outputs of 100 simulations were processed, with each simulation producing varying infection numbers in varying countries. The probability of symptomatic cases was assumed to be 46% in the main analysis and 100% in a sensitivity analysis. Mean hospitalisation and death risks were both five times greater for CHIK-X than for CHIK. Vaccine efficacy against disease was assumed to be 70% unless stated otherwise. Additional results for CHIK-X consider severity scaled by 1x and 10x, as well as 80% and 90% vaccine efficacy. The full breakdown of health and health economic metrics by country are provided in Appendix 4.

#### 3.1. CHIK results

##### **Estimating mean annual infections in absence of vaccination**

###### *CHIK suitability*

To estimate predicted infections, OxLiv models 1-4 relied on estimated suitability of CHIK occurrence. Predicted environmental suitability for CHIK occurrence is shown in Figure 11. Suitability was predicted to be particularly high in India, Southeast Asia, Central America, parts of South America (particularly in Brazil), and various parts of sub-Saharan Africa. However, elevated suitability was also observed in parts of Europe, the U.S., Australia, North Africa, and parts of China.

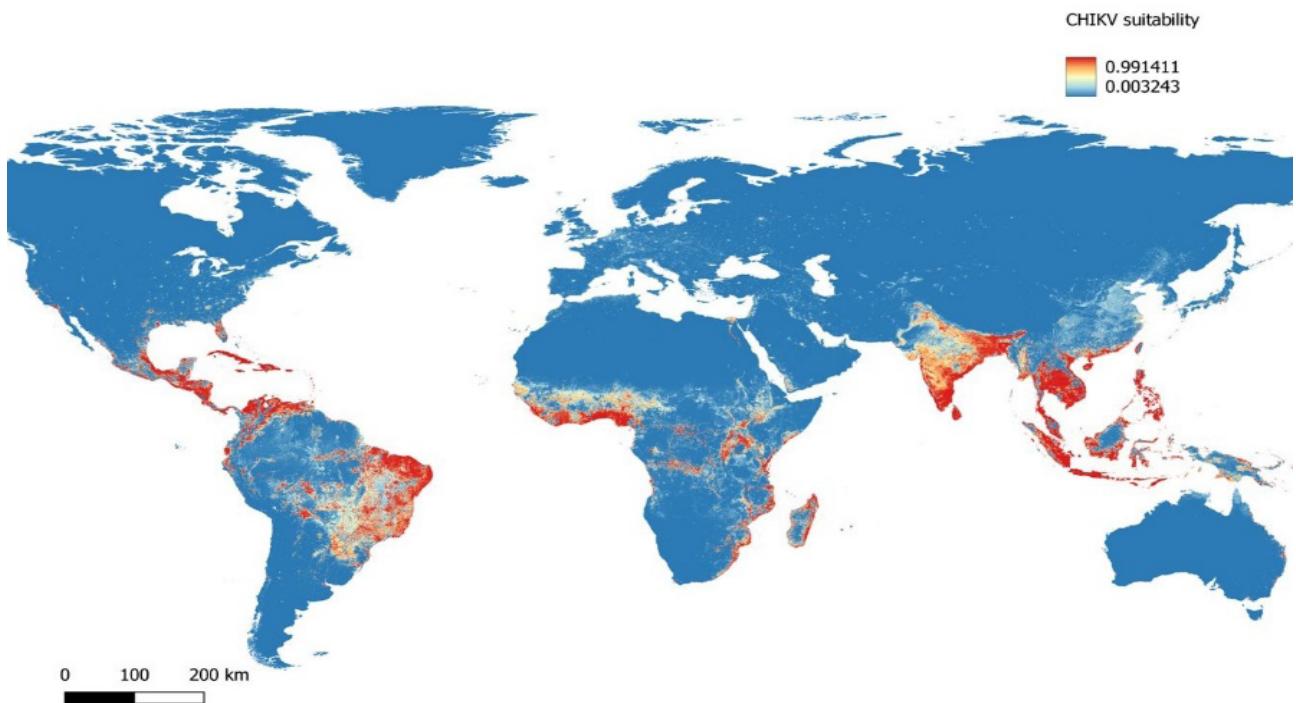


Figure 11: Predicted suitability for CHIK. Values mapped are predicted probability of disease presence.

#### *CHIK force of infection (FoI)*

OxLiv models 1-4 also relied on estimates of FoI, which were generated from cross-sectional age-stratified seroprevalence data from countries in different WHO regions, including the African Region (AFRO: Benin, Cameroon, Ethiopia, Kenya, and Senegal); Eastern Mediterranean Region (EMRO: Djibouti); Region of the Americas (AMRO: Brazil, Guadeloupe, and Martinique); South-East Asian Region (SEARO: India); and Western Pacific Region (WPRO: Malaysia, Singapore, and Vietnam). Cross-sectional age-stratified data can only provide information on FoI estimates varying by age or time alone, not about how FoI might vary over

time in different age groups. Given evidence from several countries that CHIK incidence varies substantially over time<sup>53, 54, 55</sup>, it was assumed that FoI would be time-varying but remain the same across all ages at each time point. The long-term average across all years and locations was estimated at 0.7%—identical to a recent systematic review that included a re-analysis of datasets using catalytic models with slightly different modelling assumptions<sup>56</sup>. However, the FoI started to substantially increase around 2000 in several locations. CHIK epidemiology has been reported to dramatically change with the emergence of a new strain from the East/Central/South Africa enzootic

53 Bettis et al., 2022. The global epidemiology of chikungunya from 1999 to 2020: A systematic literature review to inform the development and introduction of vaccines.

54 Grabenstein and Tomar, 2023. Global geotemporal distribution of chikungunya disease, 2011–2022.

55 Eneh et al., 2023. Chikungunya outbreak in Africa: a review of the literature.

56 Kang et al., 2024. Chikungunya seroprevalence, force of infection, and prevalence of chronic disability in endemic and epidemic settings: Systematic review, meta-analysis, and modelling study.

lineage, leading to outbreaks in different countries. Furthermore, the age categories in the underlying data were not sufficiently narrow to pinpoint the exact timing of real changes in the FoI. Therefore, FoI estimates in subsequent modelling were restricted to those for the year 2000 and onwards, reflecting the possibility that this more recent period could reflect what will happen in the next 10-15 years. Restricting estimates to this time period yielded an average FoI of 1.6% across all years and locations.

The relationship between suitability and average annual FoI was used to estimate FoI in the 37

countries of interest. A logistic growth curve model with suitability as the only covariate revealed that low suitability was associated with low FoI estimates, whereas areas with high suitability (e.g., above 0.75 on a scale of 0-1) tended to have higher FoI estimates. This model was subsequently used to predict the potential average annual FoI in all areas (Figure 12). Based on this relationship, the predicted unweighted average FoI at the country-level ranged from < 0.001 in several countries to 0.0193 in El Salvador.

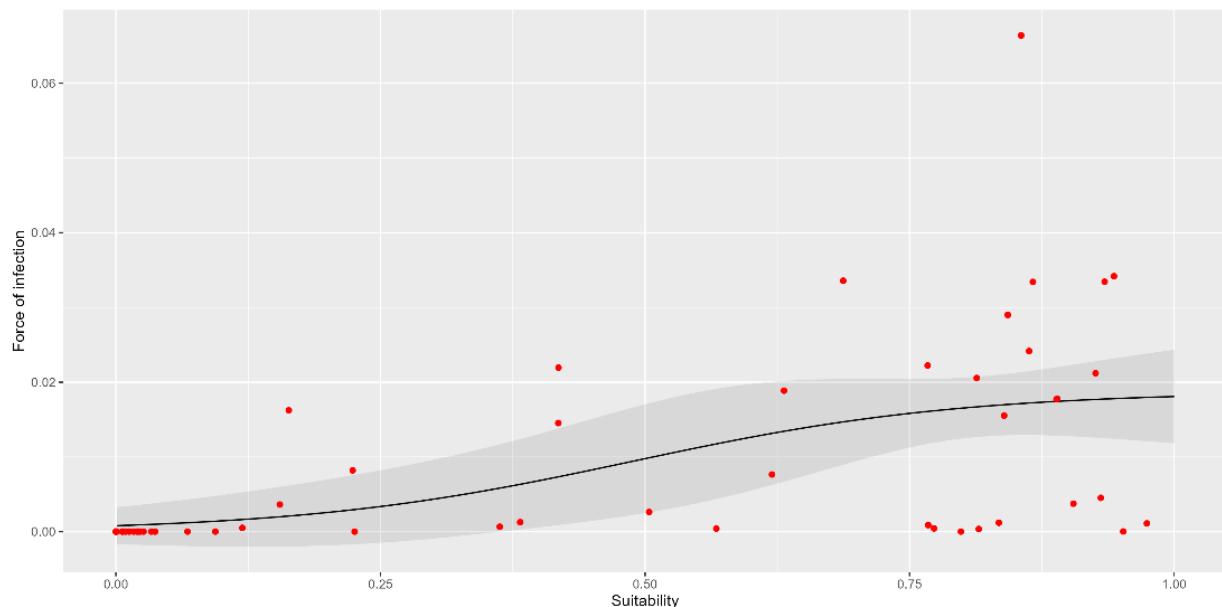


Figure 12: Relationship between modelled suitability and estimated FoI using data from all areas with age-stratified seroprevalence data. The shaded area represents the confidence intervals of the logistic growth model.

Given that there is temporal variation in which areas are experiencing the highest incidence, it is possible that some areas with high suitability (> 0.75) and a low FoI (< 0.005) had not experienced a significant outbreak between the year 2000 and the year the cross-sectional seroprevalence survey was performed. Therefore, to avoid potential underestimation of the average annual incidence in the next 15 years, the model was refitted after excluding data from these areas. Applying this rule, data from one area from Brazil (Cabrobo), four areas

from India (Assam, Bihar, Odisha, and Tripura), Singapore, and Vietnam were excluded. After this exclusion, the FoI in areas with high suitability was estimated to result in higher FoI estimates, with estimates of approximately 3% at the higher end of suitability instead of remaining below 2% across the entire range of possible suitability estimates. Based on this relationship, the predicted unweighted average FoI at the country-level ranged from < 0.001 in several countries to 0.0272 in El Salvador (Figure 13).

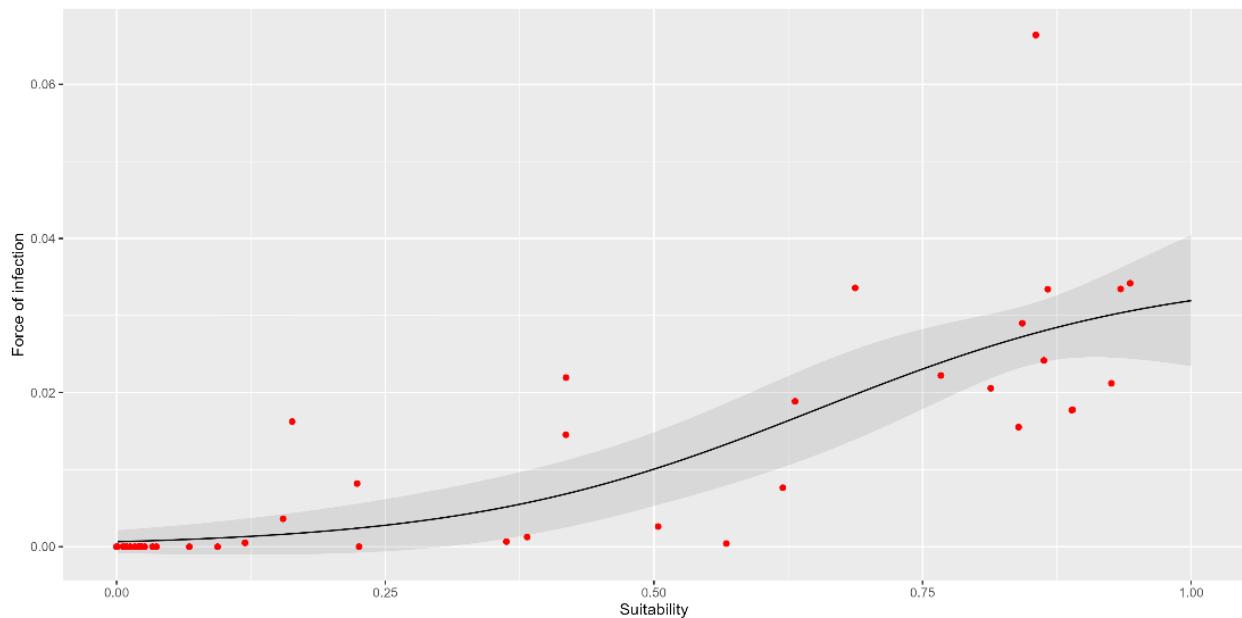


Figure 13: Relationship between modelled suitability and estimated FoI after excluding age-stratified seroprevalence data in areas with a suitability  $> 0.75$  and a FoI  $< 0.005$ . The shaded area represents the confidence intervals of the logistic growth model.

Two approaches were used to account for immunity in the population when estimating FoI. These approaches used WHO region-specific averages of preexisting antibody levels as baseline levels of infection immunity in 2025, either 1) with (OxLIV 1 & 2) or 2) without (OxLIV 3 & 4) accumulating immunity due to infections occurring each year to 2040 (Table 3). FoI estimates were weighed by the respective population sizes for each age and country, resulting in WHO-region specific antibody levels of 31% for AFRO, 28% for AMRO, 2% for EMRO, 21% for SEARO, and 55% for WPRO. In sensitivity analyses, WHO region-specific estimates from a recent systematic review<sup>57</sup> were used that also included non-age-stratified seroprevalence data (Table 6). The estimated population-average antibody levels were consistent with each other in most regions, except for WPRO, for which the systematic review estimated an antibody prevalence of 18%, whereas the catalytic models used on the age-stratified seroprevalence data suggested

an average prevalence of 55%. As a result, the sensitivity analysis using the estimated prevalence from the systematic review had higher incidence estimates in this region.

<sup>57</sup> Skalinski et al., 2023. Chikungunya seroprevalence in population-based studies: A systemic review and meta-analysis.

Table 6: Estimated seroprevalence by WHO region using (1) catalytic models fitted to age-stratified seroprevalence data and (2) non-age-stratified data from a meta-analysis. The meta-analysis from Skalinski et al. also includes sero-prevalence data that is not age-stratified<sup>58</sup>.

WHO region	Estimated seroprevalence from catalytic models (main analysis)	Estimated seroprevalence from meta-analysis (sensitivity analysis)
African (AFRO)	31%	31%
Americas (AMRO)	28%	29%
Eastern Mediterranean (EMRO)	2%	5%
South-East Asian (SEARO)	21%	24%
Western Pacific (WPRO)	55%	18%

### *Comparison between models*

Under the baseline scenario, which considered the cumulative CHIK burden over a 16-year simulation period, the four methods used to generate mean annual incidence of infections across countries estimated 513.2, 595, 785.1 million, and 1 billion infections for OxLIV 1, OxLIV 2, OxLIV 3 and OxLIV 4, respectively. Estimated mean infections for the Salje et al. approach was 372.9 million.

### **Health metrics**

A comparison of the baseline cumulative burden of symptomatic cases, hospitalisations, deaths, years of lives lost, sequelae, and DALYs over the full 16-year simulation period across all five models is shown in Figure 14. Note that only mean infection numbers from the Salje et al. model were used as an input for the health economic model. Parameters and methods to produce symptomatic cases and all other clinical and economic outcomes were consistent across all model inputs.

Using the baseline estimate for probability of symptomatic infection (18%), these infection incidence estimates translated to an estimated cumulative mean of 93, 107.8, 137.3, 187.8, and 67.5 million symptomatic cases in OxLIV 1, OxLIV 2, OxLIV 3, OxLIV 4, and Salje et al., respectively; 3.8, 4.3, 5.5, 7.6, and 2.7 million hospitalisations, respectively; and 208.3, 243.2, 307.7, 423.6, and 152 thousand deaths, respectively. Across OxLIV 1-4, infection estimates under the baseline scenario showed that the highest burden was in India, China, Indonesia, Brazil, and Bangladesh (Figure 15).

<sup>58</sup> Skalinski et al., 2023. Chikungunya seroprevalence in population-based studies: A systemic review and meta-analysis.

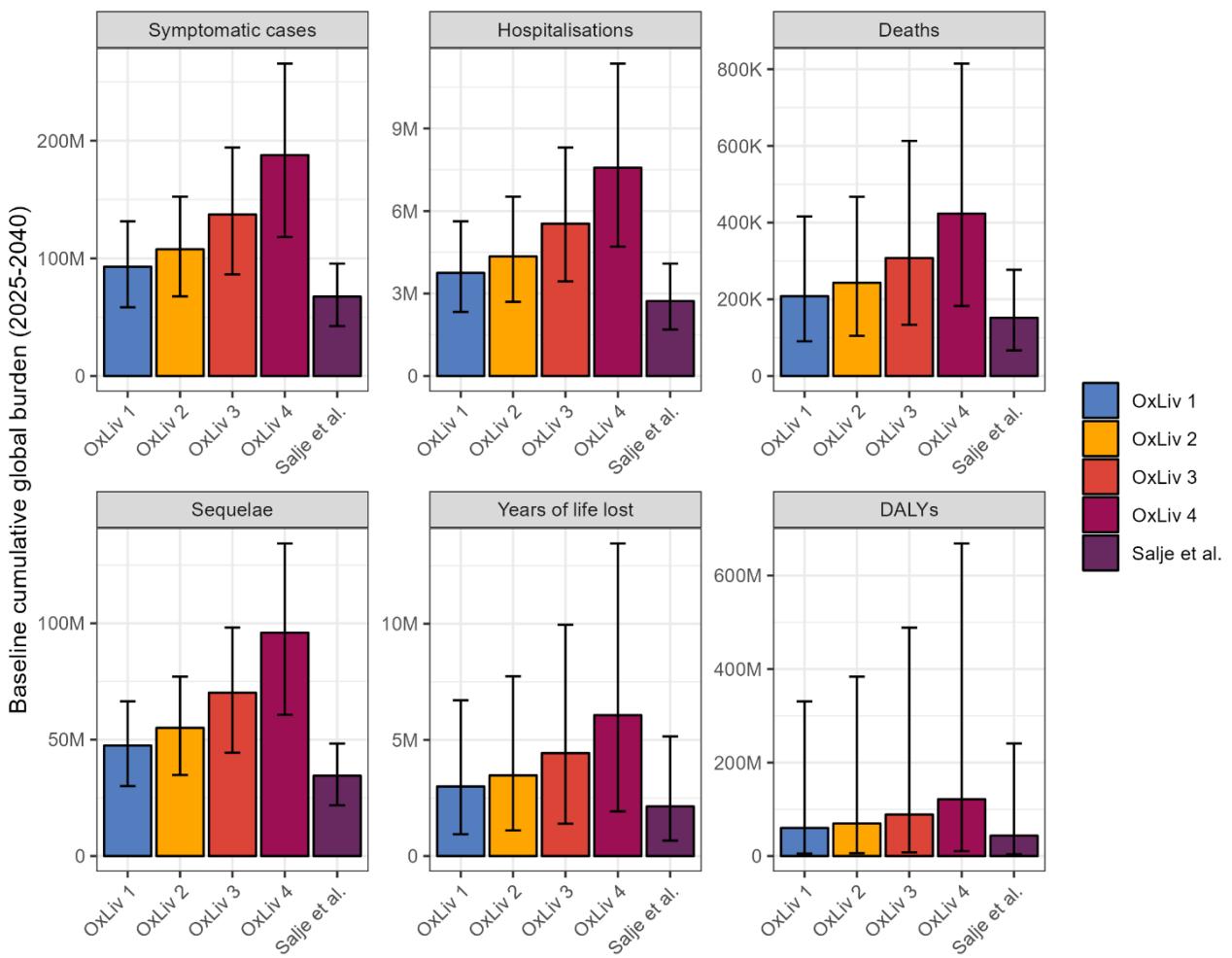


Figure 14: Cumulative global health burden of chikungunya virus infections without vaccination considered over 16 years (y-axis) according to each model's infection incidence estimates (x-axis). Panels correspond to each health outcome. DALYs are undiscounted. Bar height represents mean estimates and error bars represent 95% uncertainty intervals (UI).

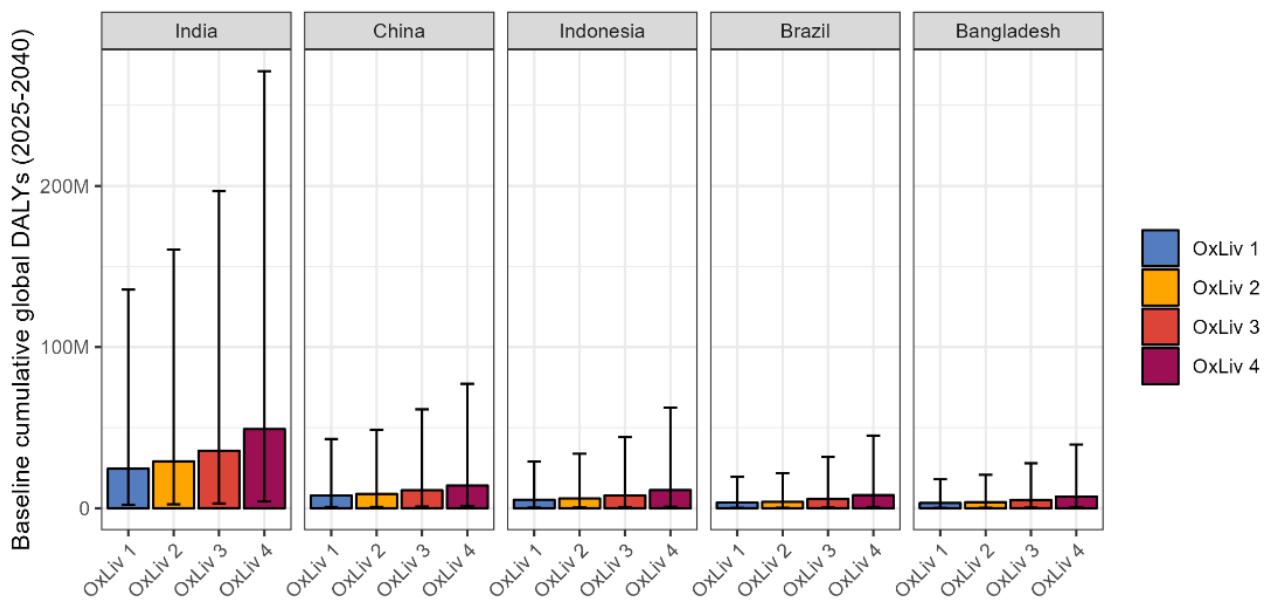


Figure 15: Cumulative DALYs of chikungunya virus infections without vaccination considered over 16 years (y-axis) according to OxLIV 1-4 models' infection incidence estimates (x-axis). Panels correspond to highest burden countries. DALYs are undiscounted. Bar height represents mean estimates and error bars represent 95% UI.

Aggregated hospitalisation results were sensitive to age- and sex-specific distributions of infections, as only a population-average estimate of hospitalisation risk (4%) was available in Kang et al<sup>59</sup>. However, mortality estimates further control for age- and sex-specific CFRs observed in Brazil<sup>60</sup>. More detailed estimates for all health burden metrics are in Table 7.

The impact of all vaccination scenarios on global cases (A) and deaths (B) over 16 years under the OxLIV 1 model is shown in Figure 16. The target-based vaccination scenarios had a greater combined impact on key health economic metrics globally, given that these scenarios were more ambitious in terms of the number of countries and age groups included, and also included routine vaccinations covering 60-65% of 12-year-olds following the initial campaign.

<sup>59</sup> Kang et al., 2024. Chikungunya seroprevalence, force of infection, and prevalence of chronic disability in endemic and epidemic settings: Systematic review, meta-analysis, and modelling study.

<sup>60</sup> de Souza et al., 2023. Spatiotemporal dynamics and recurrence of chikungunya virus in Brazil: An epidemiological study.

Table 7: Estimated cumulative health outcomes (Mean, 2.5% - 97.5% UI) of chikungunya virus infection at baseline over 16 years. For all five models, estimates for each outcome represent the combined total across all countries included in vaccination scenarios. Future DALYs are undiscounted.

Health outcome	OxLiv 1	OxLiv 2	OxLiv 3	OxLiv 4	Salje et al.
Symptomatic cases	93.0M (58.5M-131.5M)	107.8M (67.8M-152.4M)	137.3M (86.4M-194.2M)	187.8M (118.1M-265.6M)	67.5M (42.5M-95.5M)
Number of patients seeking care at primary care level	24.6M (14.8M-36.9M)	28.5M (17.2M-42.8M)	36.3M (21.9M-54.5M)	49.6M (29.9M-74.5M)	17.9M (10.8M-26.8M)
Hospitalisations	3.8M (2.3M-5.6M)	4.3M (2.7M-6.5M)	5.5M (3.4M-8.3M)	7.6M (4.7M-11.4M)	2.7M (1.7M-4.1M)
Deaths	208.3K (90.5K-416.1K)	243.2K (104.8K-467.4K)	307.7K (133.7K-613.0K)	423.6K (182.8K-814.7K)	152.0K (66.9K-277.1K)
Sequelae	47.5M (30.1M-66.5M)	55.1M (34.8M-77.1M)	70.2M (44.4M-98.2M)	96.0M (60.7M-134.3M)	34.5M (21.8M-48.3M)
Years of life lost	3.0M (939.1K-6.7M)	3.5M (1.1M-7.7M)	4.4M (1.4M-10.0M)	6.1M (1.9M-13.5M)	2.1M (664.6K-5.1M)
Years of life with sequelae	62.5M (12.5M-191.0M)	72.4M (14.5M-221.5M)	92.3M (18.5M-282.1M)	126.2M (25.3M-385.9M)	45.4M (9.1M-138.8M)
DALYs	60.1M (5.2M-330.7M)	69.7M (6.0M-383.6M)	88.8M (7.7M-488.5M)	121.4M (10.5M-668.4M)	43.6M (3.6M-240.7M)

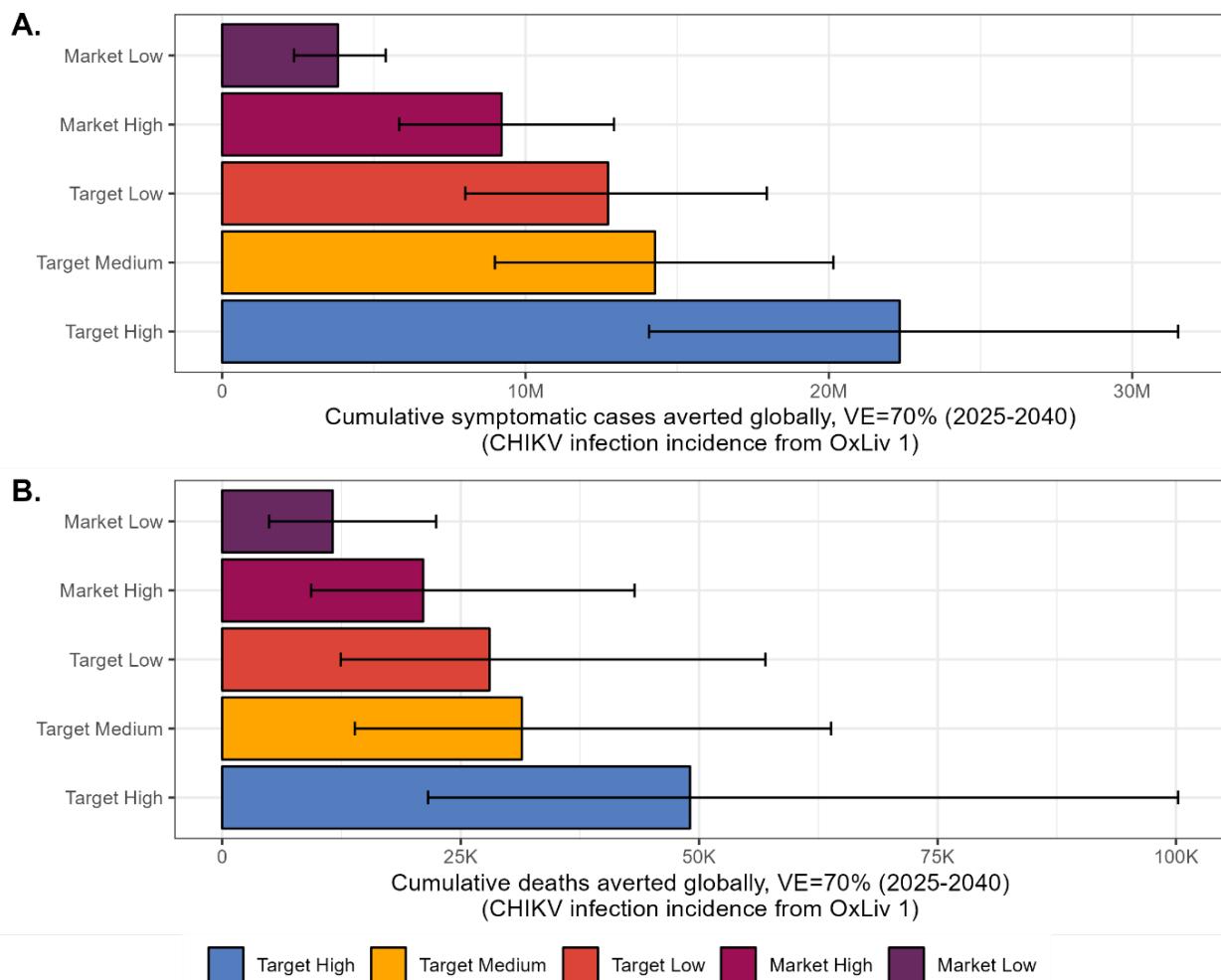


Figure 16: (A) Cumulative number of symptomatic cases averted globally over 16 years (x-axis) as a result of each vaccination scenario (y-axis). (B) Cumulative number of deaths averted globally over 16 years (x-axis) as a result of each vaccination scenario (y-axis). Both estimates assume OxLIV 1 infection incidence and 70% vaccine efficacy. Bar length represents mean estimates and error bars represent 95% UI.

The main health outcomes averted due to CHIK vaccination are summarised in Table 8. This includes a comparison of outcomes using OxLIV 1 infection estimates across all five vaccine scenarios and with assumed vaccine efficacy ranging from 70-90%.

Table 8: Estimated health outcomes (Mean, 2.5% - 97.5% UI) averted due to five considered CHIK vaccination scenarios over the 16-year period. Assuming OxLiv 1 infection incidence, combined estimates for all countries considered in vaccination scenarios are presented for three assumptions of vaccine efficacy (VE): 70%, 80%, and 90%.

Health outcome	VE (%)	Target Low	Target Medium	Target High	Market Low	Market High
Symptomatic cases	70	12.7M (8.0M-18.0M)	14.3M (9.0M-20.1M)	22.3M (14.1M-31.5M)	3.8M (2.4M-5.4M)	9.2M (5.8M-12.9M)
	80	14.5M (9.2M-20.5M)	16.3M (10.3M-23.0M)	25.5M (16.1M-36.0M)	4.4M (2.7M-6.2M)	10.5M (6.7M-14.8M)
	90	16.4M (10.3M-23.1M)	18.3M (11.6M-25.9M)	28.7M (18.1M-40.5M)	4.9M (3.0M-6.9M)	11.8M (7.5M-16.6M)
Hospitalisations	70	427.8K (267.6K-640.1K)	479.9K (300.2K-718.0K)	752.5K (470.8K-1.1M)	114.0K (69.7K-170.9K)	294.0K (183.5K-441.0K)
	80	488.9K (305.8K-731.5K)	548.4K (343.1K-820.6K)	860.0K (538.0K-1.3M)	130.3K (79.7K-195.3K)	336.0K (209.7K-504.0K)
	90	550.0K (344.1K-822.9K)	617.0K (386.0K-923.2K)	967.5K (605.3K-1.4M)	146.6K (89.6K-219.7K)	378.0K (235.9K-567.0K)
Deaths	70	28.0K (12.4K-56.9K)	31.4K (13.9K-63.8K)	49.0K (21.6K-100.2K)	11.6K (4.9K-22.4K)	21.1K (9.3K-43.2K)
	80	32.0K (14.2K-65.1K)	35.9K (15.9K-73.0K)	56.1K (24.7K-114.5K)	13.2K (5.6K-25.6K)	24.1K (10.7K-49.4K)
	90	36.0K (16.0K-73.2K)	40.4K (17.9K-82.1K)	63.1K (27.7K-128.8K)	14.9K (6.3K-28.8K)	27.1K (12.0K-55.6K)
Sequelae	70	6.5M (4.1M-9.1M)	7.3M (4.6M-10.2M)	11.4M (7.2M-16.0M)	2.0M (1.2M-2.7M)	4.7M (3.0M-6.6M)
	80	7.4M (4.7M-10.4M)	8.3M (5.3M-11.7M)	13.0M (8.3M-18.3M)	2.2M (1.4M-3.1M)	5.4M (3.4M-7.5M)
	90	8.4M (5.3M-11.7M)	9.4M (5.9M-13.1M)	14.7M (9.3M-20.6M)	2.5M (1.6M-3.5M)	6.1M (3.9M-8.5M)
DALYs	70	8.2M (643.4K-45.4M)	9.1M (721.6K-50.9M)	14.3M (1.1M-79.8M)	2.4M (189.2K-13.8M)	5.9M (461.9K-32.4M)
	80	9.3M (735.4K-51.8M)	10.5M (824.7K-58.2M)	16.4M (1.3M-91.2M)	2.8M (216.2K-15.8M)	6.7M (527.9K-37.0M)
	90	10.5M (827.3K-58.3M)	11.8M (927.7K-65.5M)	18.4M (1.5M-102.6M)	3.1M (243.2K-17.8M)	7.6M (593.9K-41.6M)

When considering infection incidence under the OxLIV 1 model, the mean number of symptomatic cases averted in the most ambitious scenario (Target High) ranged from 22.3-28.7 million for vaccine efficacy assumptions ranging from 70-90%, respectively. In turn, 752.5-967.5 thousand hospitalisations were averted, along with 49.0-63.1 thousand deaths, 11.4-14.7 million sequelae, and 14.3-18.4 million DALYs, respectively. For the Market High scenario, across all vaccine efficacy assumptions, an estimated 9.2-11.8 million symptomatic cases, 294.0-378.0 thousand hospitalisations, 21.1-27.1 thousand deaths, 4.7-6.1 million sequelae, and 5.9-7.6 million DALYs were averted. The order and relative impact of the five vaccination scenarios were conserved across all vaccine

efficacy assumptions, with Target High being most ambitious and Market Low being least ambitious.

Figure 17 shows hospitalisations averted in the highest burden countries across all vaccination scenarios and vaccine efficacy assumptions, demonstrating the impact of classifying China, Indonesia, and Bangladesh as "low". Under both market scenarios and in the Target Medium and Low scenarios, no hospitalisations were averted in these countries, representing a missed opportunity to prevent disease and associated health and economic outcomes.

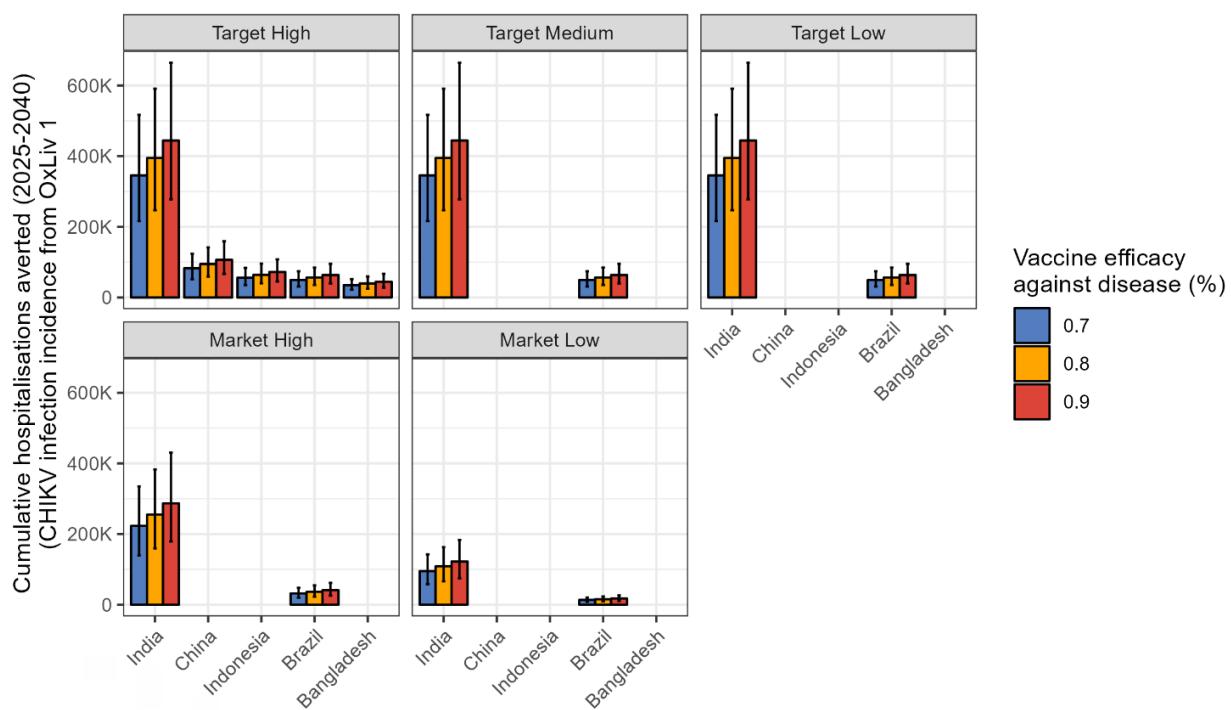


Figure 17: Cumulative number of hospitalisations averted over 16 years (y-axis) for highest burden countries (x-axis) over 16 years assuming OxLIV 1 infection incidence. Panels correspond to each of the five vaccination scenarios, and bar colours correspond to vaccine efficacy assumptions (70%, 80%, and 90%). Bar height represents mean estimates and error bars represent 95% UI.

## Health economic metrics

A comparison of the baseline cumulative burden of the costs of CHIK over the simulated 16-year period across all five models is found in Table 9. Societal costs include direct healthcare costs and productivity losses. The economic value of

DALYs and VSL are distinct. Detailed estimates of baseline health and cost burdens experienced by each country included in vaccination scenarios are found in Appendix 4.

Table 9: Estimated health economic costs (Mean, 2.5% - 97.5% UI) of chikungunya infections at baseline over 16 years for comparison to vaccination scenarios. Results are presented for all five models. For all models, estimates for each outcome represent the combined total across the 37 countries included in vaccination scenarios. All outcomes apart from instances of ‘catastrophic healthcare expenditure’ and ‘impoverishing healthcare expenditure’ are in I\$ 2021. Future costs are discounted at 3% per year.

Health economic outcome	OxLiv 1	OxLiv 2	OxLiv 3	OxLiv 4	Salje et al.
Societal costs	9.7B (4.1B-17.8B)	11.1B (4.7B-20.7B)	14.6B (6.1B-26.7B)	19.9B (8.5B-36.9B)	6.4B (2.7B-12.0B)
Government health expenditure	452.2M (256.8M-743.0M)	520.0M (295.6M-853.7M)	676.9M (383.6M-1.1B)	924.6M (524.1M-1.5B)	318.2M (181.6M-520.5M)
OOP health expenditure	500.0M (313.7M-704.7M)	572.7M (359.2M-807.1M)	753.4M (472.8M-1.1B)	1.0B (645.5M-1.5B)	345.2M (216.5M-486.4M)
Productivity costs	8.8B (3.5B-16.7B)	10.0B (4.1B-18.9B)	13.2B (5.2B-25.1B)	17.9B (7.3B-33.8B)	5.8B (2.3B-11.2B)
Monetised DALYs	115.2B (9.3B-624.8B)	131.7B (10.6B-714.1B)	171.6B (13.8B-930.7B)	230.8B (18.5B-1.3T)	63.5B (5.0B-345.0B)
VSL	251.9B (107.9B-496.2B)	290.4B (128.1B-557.1B)	378.4B (162.0B-744.8B)	517.9B (228.3B-987.5B)	162.3B (71.5B-295.7B)
Catastrophic healthcare expenditure	2.0M (1.2M-3.0M)	2.3M (1.5M-3.5M)	2.9M (1.8M-4.3M)	3.9M (2.4M-5.9M)	1.5M (948.0K-2.3M)
Impoverishing healthcare expenditure	649.4K (403.3K-973.9K)	764.4K (474.8K-1.1M)	937.4K (582.2K-1.4M)	1.3M (800.0K-1.9M)	513.2K (318.7K-769.6K)

Figure 18 shows the health economic impact of vaccination from a societal perspective (built on baseline OxLiv 1 infection estimates). Societal costs averted account for direct healthcare costs and productivity costs averted, and the economic value of DALYs and VSL averted are considered separately. Productivity costs accounted for the greater share of the societal economic burden imposed by CHIK. When considering

70% vaccine efficacy under the target-based scenarios, \$1.1-\$2.3 billion I\$ in societal costs could be averted and a further \$11.3-\$26.6 billion I\$ in terms of monetised DALYs. In terms of VSL, \$27.3-\$57.8 billion I\$ could be averted. For market-based scenarios, \$231.5-\$841.1 million I\$ in societal costs, \$3-\$9 billion I\$ in monetised DALYs, and \$10.8-\$21.6 billion I\$ in VSL costs could be averted.

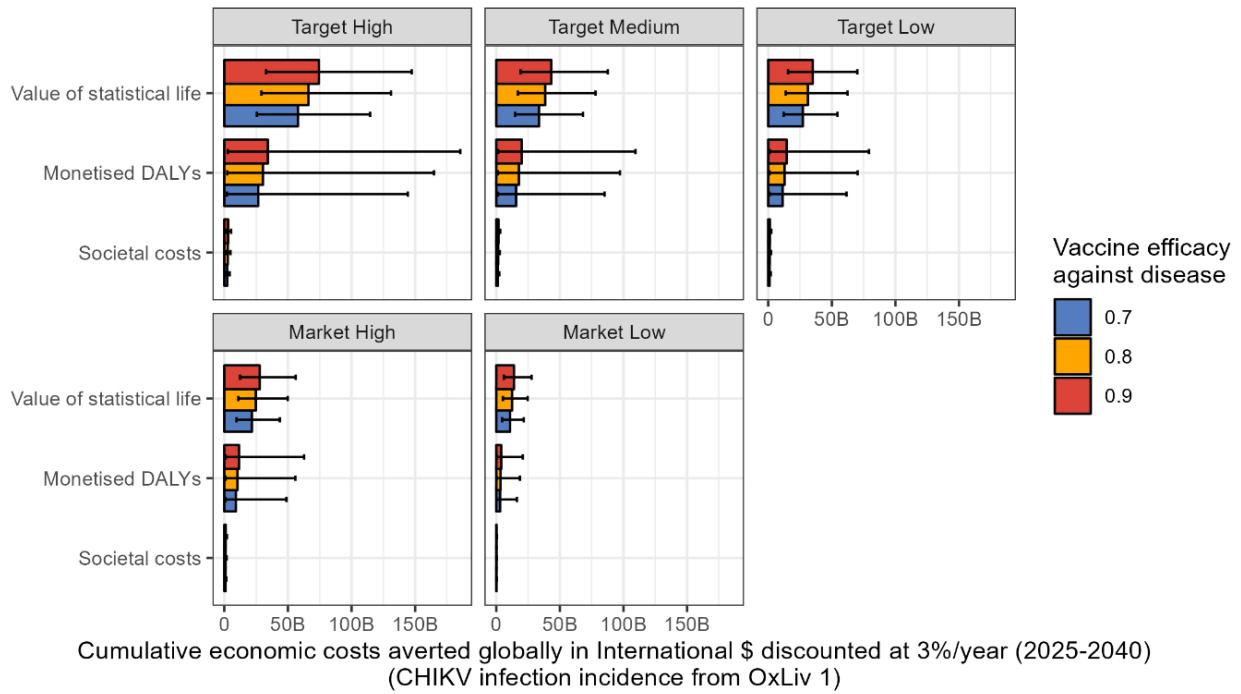


Figure 18: Cumulative economic costs (I\$ 2021) averted over 16 years (x-axis) for three outcomes: VSL, economic value of DALYs, and societal costs (y-axis) assuming OxLiv 1 infection incidence. Panels correspond to each of the five vaccination scenarios, and bar colours correspond to vaccine efficacy assumptions (70%, 80%, and 90%). Bar width represents mean estimates and error bars represent 95% UI.

The main economic costs averted due to CHIK vaccination are summarised in Table 10 for the OxLiv 1 model, across vaccine efficacies of 70%, 80%, and 90%. When considering 70% vaccine efficacy, the target-based scenarios were estimated to save individuals combined OOP costs of between \$56.8-\$115.5 million I\$. These savings would prevent an estimated 280-410.2 thousand individuals from suffering catastrophic healthcare expenditures, and 95.9-135.5 thousand individuals would be prevented from falling below the poverty line. For the market-based scenarios, \$16.2-\$44.6 million I\$ in OOP

costs would be averted, preventing 76.8-184.6 thousand instances of catastrophic healthcare expenditures and 26.2-63.6 thousand instances of impoverishment. Alternative estimates accounting for a higher risk of disease and lower estimates of seroprevalence are presented in Appendix 4.

Table 10: Estimated economic costs (Mean, 2.5% - 97.5% UI) averted due to five CHIK vaccination scenarios over the 16-year period. Assuming OxLiv 1 infection incidence, combined estimates for all countries considered in vaccination scenarios are presented for three assumptions of vaccine efficacy (VE): 70%, 80%, and 90%. All outcomes apart from instances of ‘catastrophic healthcare expenditure’ and ‘impoverishing healthcare expenditure’ are in I\$ 2021. Future costs are discounted at 3% per year.

Health economic outcome	VE (%)	Target Low	Target Medium	Target High	Market Low	Market High
Societal costs	70	1.1B (458.1M-2.0B)	1.3B (566.3M-2.4B)	2.3B (954.2M-4.2B)	231.5M (103.3M-405.7M)	841.1M (356.3M-1.5B)
	80	1.2B (523.6M-2.2B)	1.5B (647.2M-2.8B)	2.6B (1.1B-4.8B)	264.5M (118.0M-463.6M)	961.3M (407.2M-1.7B)
	90	1.4B (589.0M-2.5B)	1.7B (728.1M-3.1B)	2.9B (1.2B-5.4B)	297.6M (132.8M-521.6M)	1.1B (458.1M-2.0B)
Monetised DALYs	70	11.3B (854.6M-61.6B)	15.6B (1.2B-85.1B)	26.6B (2.0B-144.3B)	3.0B (248.8M-16.2B)	9.0B (680.6M-48.8B)
	80	12.9B (976.6M-70.4B)	17.9B (1.3B-97.3B)	30.4B (2.3B-164.9B)	3.4B (284.4M-18.5B)	10.3B (777.8M-55.8B)
	90	14.6B (1.1B-79.2B)	20.1B (1.5B-109.5B)	34.1B (2.6B-185.5B)	3.9B (319.9M-20.8B)	11.6B (875.1M-62.7B)
VSL	70	27.3B (12.1B-54.6B)	33.7B (14.9B-68.2B)	57.8B (25.5B-114.6B)	10.8B (4.6B-21.6B)	21.6B (9.5B-43.6B)
	80	31.2B (13.9B-62.4B)	38.5B (17.0B-78.0B)	66.1B (29.1B-131.0B)	12.4B (5.2B-24.6B)	24.7B (10.9B-49.8B)
	90	35.1B (15.6B-70.1B)	43.3B (19.1B-87.7B)	74.4B (32.8B-147.4B)	13.9B (5.9B-27.7B)	27.8B (12.2B-56.0B)
Catastrophic healthcare expenditure	70	280.0K (175.1K-418.9K)	290.0K (181.4K-433.9K)	410.2K (256.6K-613.7K)	76.8K (46.9K-115.1K)	184.6K (115.2K-277.0K)
	80	320.0K (200.2K-478.8K)	331.4K (207.3K-495.8K)	468.8K (293.2K-701.3K)	87.7K (53.7K-131.5K)	211.0K (131.7K-316.6K)
	90	360.0K (225.2K-538.6K)	372.8K (233.2K-557.8K)	527.3K (329.9K-789.0K)	98.7K (60.4K-148.0K)	237.4K (148.2K-356.1K)
Impoverishing healthcare expenditure	70	95.9K (60.0K-143.5K)	100.4K (62.8K-150.2K)	135.5K (84.8K-202.8K)	26.2K (16.0K-39.3K)	63.6K (39.7K-95.4K)
	80	109.6K (68.6K-164.0K)	114.8K (71.8K-171.7K)	154.9K (96.9K-231.7K)	30.0K (18.3K-44.9K)	72.7K (45.4K-109.0K)
	90	123.3K (77.2K-184.5K)	129.1K (80.8K-193.2K)	174.2K (109.0K-260.7K)	33.7K (20.6K-50.5K)	81.8K (51.0K-122.7K)

### 3.2. CHIK-X results

#### Health metrics

In each simulation of a CHIK-X outbreak, infection spread to varying countries following a unique transmission pattern based on suitability, FoI, and mobility data. Across all simulations, CHIK-X was estimated to reach on average 32 countries over 5.6 years, resulting in approximately 22 million (95% UI: 235K-56M) infections before naturally subsiding due to the accumulation of immunity. Figure 19 shows highest burden countries in terms of (A) percentage of 100 simulations with a

CHIK-X outbreak, (B) the cumulative number of CHIK-X infections per country among simulations in which that country experienced an outbreak, and (C) the cumulative number of CHIK-X infections per country across all simulations. While Bangladesh, Brazil, China, India, and Indonesia were the highest burden countries (both among simulations in which they experience an outbreak and across all simulations), the countries with the highest percentage of simulated outbreaks were Bangladesh, Brazil, India, Indonesia, and Vietnam.

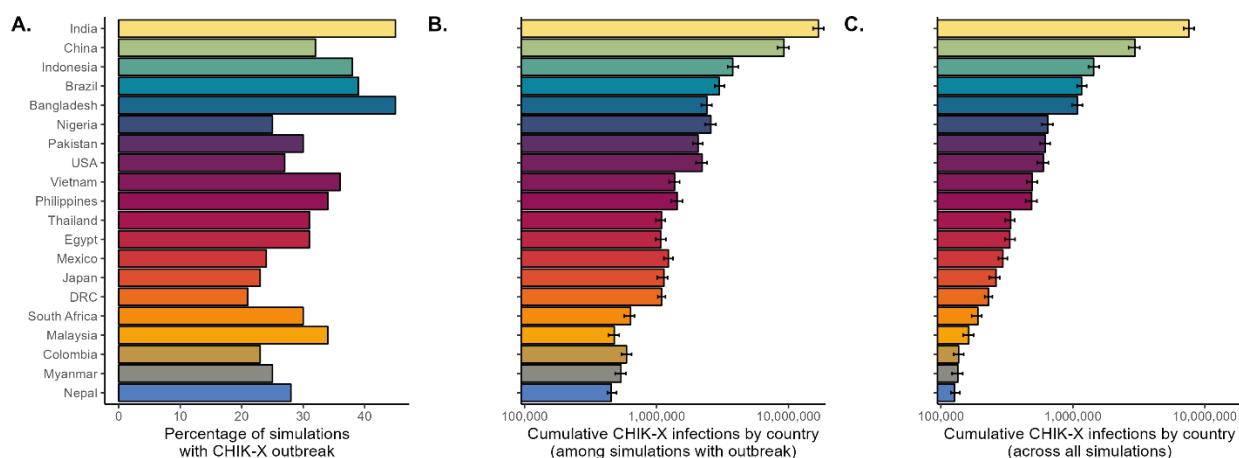


Figure 19: (A) Countries experiencing highest percentage of simulations with CHIK-X outbreaks across all simulations; (B) Countries experiencing highest infection numbers among simulations with outbreaks; and (C) Countries experiencing highest numbers of infections across all 100 simulations. (B) and (C) infection numbers are plotted on a log-scale for easy comparison across countries. Bar width represents mean estimates and error bars represent 95% UI.

Figure 20 shows the mean cumulative global burden of CHIK-X for 100 simulations across severity scenarios. The combined mean symptomatic caseload was 10.1 million for both Scenario A and B. In Scenario C, the combined mean symptomatic caseload was 22.2 million. Mean hospitalisations were 408.6 thousand in

Scenario A, 2 million in Scenario B, and 4.1 million in Scenario C, which corresponded to 22.6, 113.1, and 226.1 thousand deaths, respectively. More detailed estimates for health burden metrics across all three scenarios are in Table 11. Unless stated otherwise, results presented below focus on Scenario B.

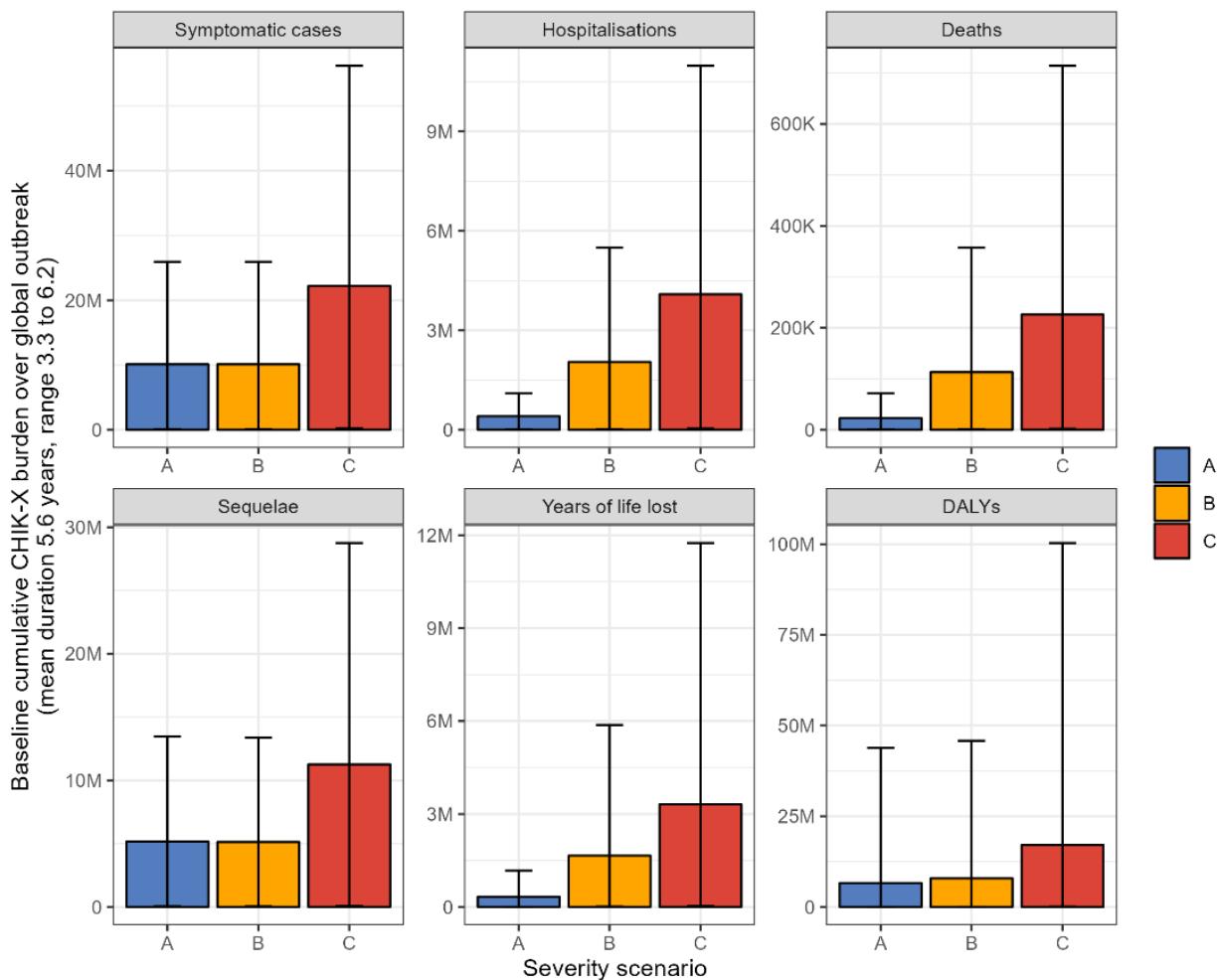


Figure 20: Cumulative global health burden of chikungunya-X virus infections without vaccination (y-axis) according to each disease severity scenario (x-axis). Disease Scenarios A and B assumed the probability of infection becoming symptomatic was 46%. The probability of hospitalisation and death were either the same as for CHIK (Scenario A) or 5 times that of CHIK (Scenario B). Scenario C assumed the probability of an infection becoming symptomatic was 100% and the probability of hospitalisation and death were 10 times that of CHIK. Panels correspond to each health outcome. DALYs are undiscounted. Bar height represents mean estimates and error bars represent 95% UI.

Table 11: Estimated cumulative health outcomes (Mean, 2.5% - 97.5% UI) of chikungunya-X virus infections without vaccination. For all three severity scenarios, estimates for each outcome represent the mean combined global total across all simulations. Future DALYs are undiscounted.

Health outcome	Scenario A	Scenario B	Scenario C
Symptomatic cases	10.1M (84.9K-25.9M)	10.1M (84.9K-25.9M)	22.2M (186.5K-56.2M)
Number of patients seeking care at primary care level	2.7M (22.5K-7.0M)	2.7M (22.5K-7.0M)	5.8M (49.0K-15.1M)
Hospitalisations	408.6K (3.5K-1.1M)	2.0M (17.5K-5.5M)	4.1M (35.0K-11.0M)
Deaths	22.6K (194.9-71.4K)	113.1K (974.3-357.0K)	226.1K (1.9K-714.1K)
Sequelae	5.2M (43.7K-13.5M)	5.1M (43.4K-13.4M)	11.3M (94.6K-28.8M)
Years of life lost	331.2K (2.8K-1.2M)	1.7M (13.9K-5.9M)	3.3M (27.8K-11.7M)
Years of life with sequelae	6.8M (53.8K-28.5M)	6.8M (53.4K-28.2M)	14.9M (116.5K-62.3M)
DALYs	6.6M (32.6K-43.8M)	7.9M (46.9K-45.8M)	17.1M (99.5K-100.3M)

Health economic burden estimates for top burden countries in the absence of vaccination are detailed in Tables A4.5 and A4.6 in Appendix 4.

Figure 21 shows two plots demonstrating the extent of global chikungunya-X transmission and impacts of three vaccine uptake scenarios. First, it shows the number of daily chikungunya-X infections globally over the simulated outbreak period. The mean daily number of infections peaked at a mean of 32,715 after approximately 2.4 years, although

the maximum daily peak across all simulations was 343,761 infections. Second, it shows the proportion of chikungunya-X infections occurring in vaccinated individuals for three scenarios: high vaccine uptake (40%), medium (20%), and low (5%). By the time the simulation ended under the low uptake scenario, most chikungunya-X infections had occurred in non-vaccinated individuals. Under the high uptake scenario, most chikungunya-X infections had occurred in vaccinated individuals, allowing for most health economic outcomes of the simulated outbreak to be averted.

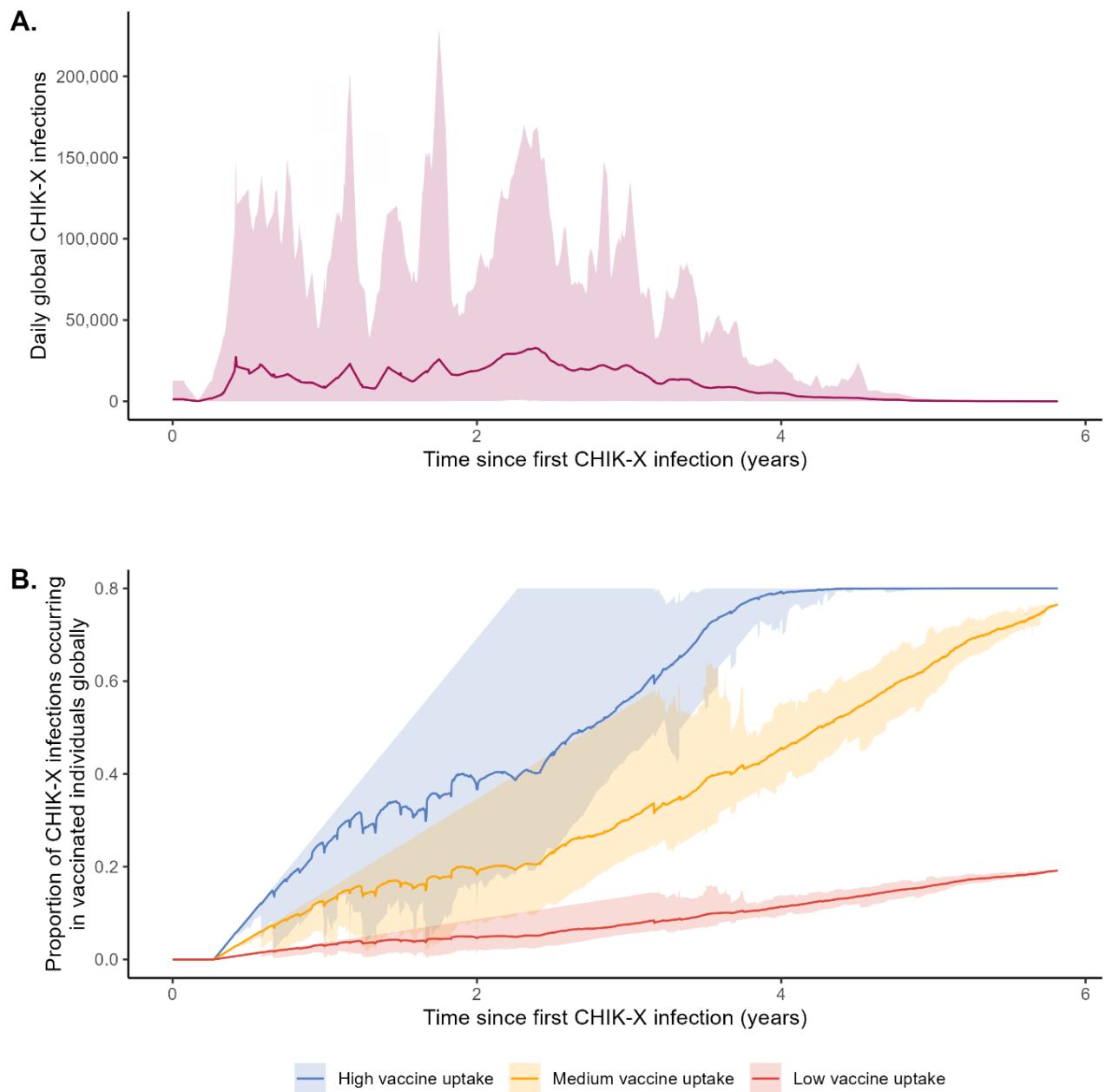


Figure 21: Impact of three vaccination scenarios on daily global chikungunya-X infections over the total simulated outbreak period (A), and the proportion of chikungunya-X infections occurring globally in vaccinated individuals over the total simulated outbreak period (B). Solid lines represent means and shaded areas represent 95% UI. Annual vaccine uptake was 5% of each country's population for the low scenario, 20% for the medium scenario, and 40% for the high scenario, up to a maximum 80% of the population. Here, the vaccination scenarios assumed no delay to vaccination initiation after the initial 100 days of vaccine development in the outbreak country, and assumed vaccination was initiated in secondary spread countries after 20 chikungunya-X infections.

The mean impact of all vaccination uptake scenarios on global cases (A) and deaths (B) for all simulated outbreaks under disease severity Scenario B is shown in Figure 22. For each vaccination scenario, affected countries were classified either as outbreak countries (countries initiating an outbreak) or secondary spread countries. The rate of vaccine delivery to affected countries (5%, 20%, or 40% of the population per year) was by far the greatest

driver of vaccine impact. However, the global reactivity of vaccine administration was also important. Although the difference was modest between administering first vaccines 100 days versus 160 days since CHIK-X's identification in the origin country, substantial differences were observed in non-origin countries between starting vaccination after the first 20 infections versus after 50 days from the first infection.

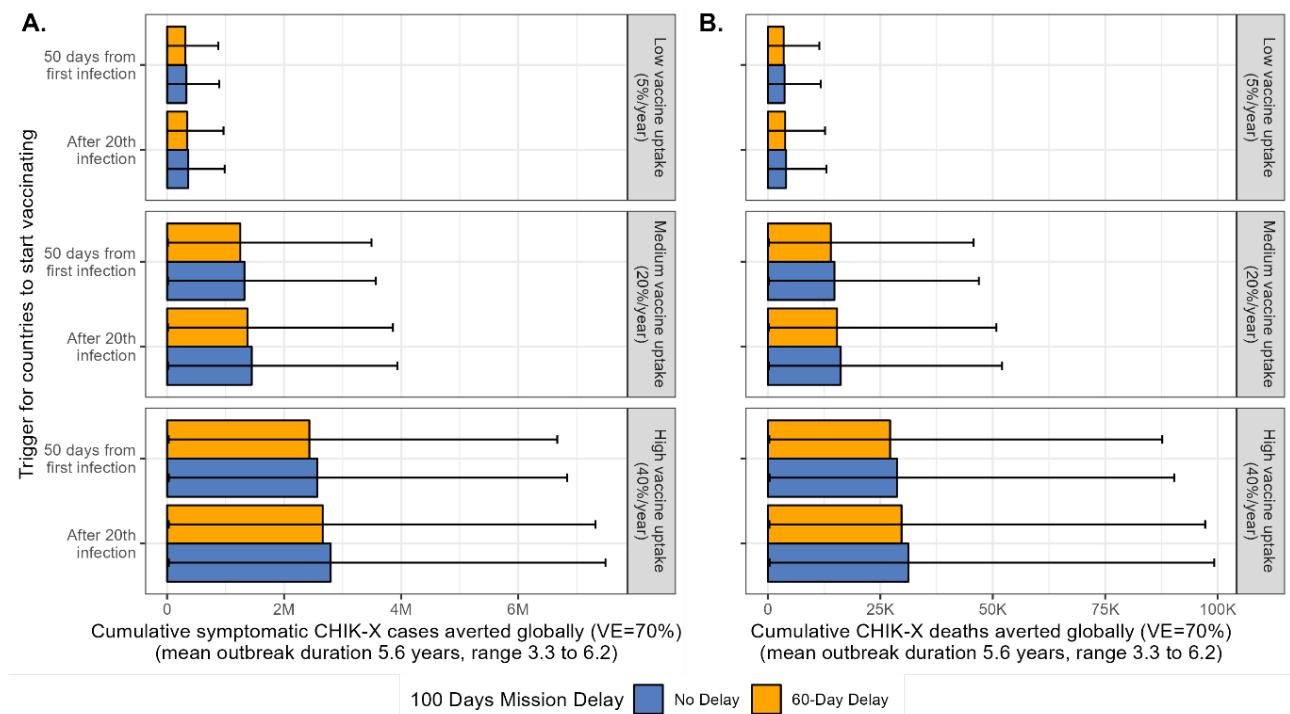


Figure 22: Cumulative number of symptomatic cases (A) and deaths (B) averted globally by vaccination over the simulation period (x-axis) as depending on different vaccination triggers (y-axis). Panels correspond to vaccine uptake rates (the proportion of the population vaccinated over 1 year), and bar colours correspond to the delay assumption (no delay or 60-day delay to initiation of the 100 Days Mission). These estimates assume CHIK-X disease Scenario B and 70% vaccine efficacy. Bar width represents mean estimates and error bars represent 95% UI.

For each simulation, only countries experiencing CHIK-X outbreaks due to outbreak initiation or secondary spread were targeted in vaccination scenarios. Therefore, given that some countries were affected in some simulations and not in others, vaccination campaigns would only be initiated in simulations in which countries had CHIK-X burdens to prevent. In addition, Figure 23 shows hospitalisations averted in the highest-burden countries under the no-delay vaccination

uptake scenario and 50 days from the first infection trigger. In India alone, which had the greatest CHIK-X burden and vaccination gains, 48 thousand hospitalisations were averted given low vaccine uptake, 193 thousand given medium uptake, and 373 thousand given high uptake. When assuming 90% vaccine efficacy instead of 70%, these numbers increased, respectively, to 62 thousand, 248 thousand, and 480 thousand hospitalisations averted.

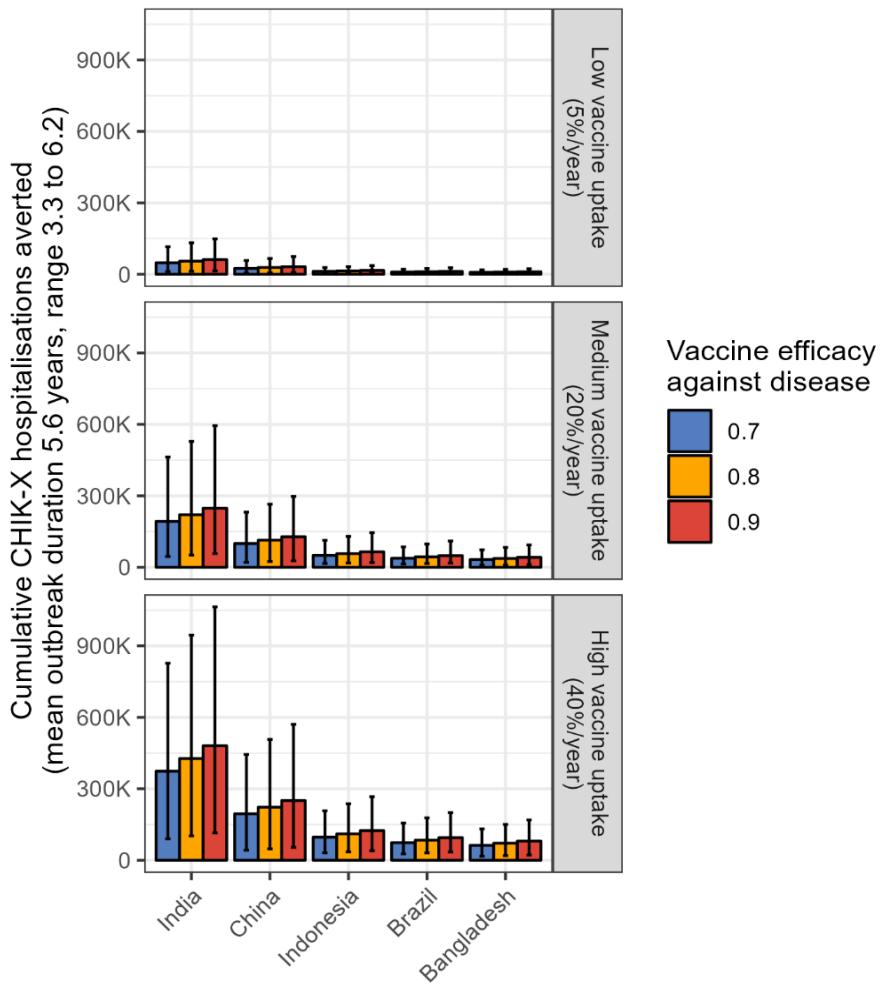


Figure 23: Cumulative number of hospitalisations averted (y-axis) over all simulations in which an outbreak occurred for highest-burden countries (x-axis) considering no delay and an outbreak trigger of 50 days from the first infection. Panels correspond to vaccination uptake scenarios, and bar colours correspond to vaccine efficacy assumptions (70%, 80%, and 90%). All estimates assume disease Scenario B. Bar height represents mean estimates and error bars represent 95% UI.

Detailed estimates of CHIK-X health outcomes averted due to vaccination are provided in Table 12 considering disease Scenario B. Outcomes were estimated for each uptake, delay, trigger, and vaccine efficacy scenario. Under the medium vaccine uptake scenario with 60-day delay, there were between 1.3-1.4 million symptomatic cases averted depending on the trigger and assuming 70% vaccine

efficacy. In turn, between 252.2-278 thousand hospitalisations, and 14-15 thousand deaths were averted under this same scenario. Under the high vaccine uptake scenario with 60-day delay, there were between 2.4-2.7 million symptomatic cases averted, depending on the trigger, resulting in 491.1-537.1 thousand hospitalisations averted and 27.2-29.7 thousand deaths averted.

Table 12: Estimated health outcomes (Mean, 2.5% - 97.5% UI) averted under three CHIK-X uptake vaccination scenarios, each of which contains two trigger scenarios and two delay scenarios. Assuming disease Scenario B, combined estimates for all countries are presented for three assumptions of vaccine efficacy (VE): 70%, 80%, and 90%.

Health outcome	Trigger	VE (%)	Low vaccine uptake (5%/year)		Medium vaccine uptake (20%/year)		High vaccine uptake (40%/year)	
			No Delay	60-Day Delay	No Delay	60-Day Delay	No Delay	60-Day Delay
Symptomatic cases	After 20 <sup>th</sup> infection	70	362.0K (4.0K-983.6K)	344.1K (3.7K-964.8K)	1.4M (15.9K-3.9M)	1.4M (14.7K-3.9M)	2.8M (31.4K-7.5M)	2.7M (29.1K-7.3M)
		80	413.7K (4.6K-1.1M)	393.2K (4.2K-1.1M)	1.7M (18.2K-4.5M)	1.6M (16.8K-4.4M)	3.2M (35.9K-8.6M)	3.0M (33.2K-8.4M)
		90	465.4K (5.1K-1.3M)	442.4K (4.7K-1.2M)	1.9M (20.5K-5.1M)	1.8M (18.9K-5.0M)	3.6M (40.4K-9.6M)	3.4M (37.4K-9.4M)
	50 days from first infection	70	330.8K (3.9K-891.7K)	312.9K (3.5K-873.4K)	1.3M (15.4K-3.6M)	1.3M (14.2K-3.5M)	2.6M (30.5K-6.8M)	2.4M (28.1K-6.7M)
		80	378.0K (4.4K-1.0M)	357.6K (4.1K-998.2K)	1.5M (17.6K-4.1M)	1.4M (16.2K-4.0M)	2.9M (34.8K-7.8M)	2.8M (32.1K-7.6M)
		90	425.3K (5.0K-1.1M)	402.4K (4.6K-1.1M)	1.7M (19.8K-4.6M)	1.6M (18.2K-4.5M)	3.3M (39.2K-8.8M)	3.1M (36.2K-8.6M)
Hospitalisations	After 20 <sup>th</sup> infection	70	73.1K (810.2-206.6K)	69.5K (747.7-202.7K)	292.4K (3.2K-826.6K)	278.0K (3.0K-810.9K)	564.5K (6.4K-1.6M)	537.1K (5.9K-1.5M)
		80	83.6K (925.9-236.2K)	79.4K (854.5-231.7K)	334.2K (3.7K-944.6K)	317.7K (3.4K-926.7K)	645.2K (7.3K-1.8M)	613.8K (6.8K-1.8M)
		90	94.0K (1.0K-265.7K)	89.4K (961.3-260.6K)	376.0K (4.2K-1.1M)	357.4K (3.8K-1.0M)	725.8K (8.2K-2.0M)	690.6K (7.6K-2.0M)
	50 days from first infection	70	66.8K (783.2-187.2K)	63.2K (720.7-183.7K)	267.3K (3.1K-748.9K)	252.8K (2.9K-734.7K)	518.6K (6.2K-1.4M)	491.1K (5.7K-1.4M)
		80	76.4K (895.1-214.0K)	72.2K (823.7-209.9K)	305.4K (3.6K-855.8K)	289.0K (3.3K-839.6K)	592.6K (7.1K-1.6M)	561.3K (6.5K-1.6M)
		90	85.9K (1.0K-240.7K)	81.3K (926.6-236.1K)	343.6K (4.0K-962.8K)	325.1K (3.7K-944.6K)	666.7K (8.0K-1.8M)	631.5K (7.3K-1.8M)

Health outcome	Trigger	VE (%)	Low vaccine uptake (5%/year)		Medium vaccine uptake (20%/year)		High vaccine uptake (40%/year)	
			No Delay	60-Day Delay	No Delay	60-Day Delay	No Delay	60-Day Delay
Deaths	After 20 <sup>th</sup> infection	70	4.0K (44.4-13.0K)	3.8K (40.2-12.7K)	16.2K (177.5-52.1K)	15.4K (160.8-50.8K)	31.2K (346.3-99.2K)	29.7K (312.0-97.2K)
		80	4.6K (50.7-14.9K)	4.4K (45.9-14.5K)	18.5K (202.8-59.5K)	17.6K (183.8-58.1K)	35.7K (395.8-113.4K)	33.9K (356.5-111.1K)
		90	5.2K (57.0-16.7K)	4.9K (51.7-16.3K)	20.8K (228.2-66.9K)	19.8K (206.7-65.3K)	40.2K (445.2-127.6K)	38.2K (401.1-125.0K)
	50 days from first infection	70	3.7K (43.6-11.7K)	3.5K (39.0-11.4K)	14.8K (174.3-46.9K)	14.0K (155.9-45.7K)	28.7K (340.1-90.3K)	27.2K (302.4-87.7K)
		80	4.2K (49.8-13.4K)	4.0K (44.5-13.1K)	16.9K (199.2-53.6K)	16.0K (178.2-52.3K)	32.8K (388.7-103.3K)	31.0K (345.6-100.2K)
		90	4.8K (56.0-15.1K)	4.5K (50.1-14.7K)	19.0K (224.1-60.3K)	18.0K (200.5-58.8K)	36.9K (437.3-116.2K)	34.9K (388.8-112.7K)
Sequelae	After 20 <sup>th</sup> infection	70	183.5K (2.0K-506.6K)	174.4K (1.9K-497.8K)	733.8K (8.1K-2.0M)	697.6K (7.5K-2.0M)	1.4M (15.9K-3.8M)	1.3M (14.8K-3.8M)
		80	209.7K (2.3K-578.9K)	199.3K (2.1K-568.9K)	838.7K (9.2K-2.3M)	797.3K (8.5K-2.3M)	1.6M (18.2K-4.4M)	1.5M (16.9K-4.3M)
		90	235.9K (2.6K-651.3K)	224.2K (2.4K-640.1K)	943.5K (10.4K-2.6M)	896.9K (9.6K-2.6M)	1.8M (20.5K-4.9M)	1.7M (19.0K-4.9M)
	50 days from first infection	70	167.7K (2.0K-459.4K)	158.6K (1.8K-450.0K)	670.7K (7.8K-1.8M)	634.5K (7.2K-1.8M)	1.3M (15.5K-3.5M)	1.2M (14.3K-3.4M)
		80	191.6K (2.2K-525.0K)	181.3K (2.1K-514.2K)	766.5K (8.9K-2.1M)	725.1K (8.2K-2.1M)	1.5M (17.7K-4.0M)	1.4M (16.3K-3.9M)
		90	215.6K (2.5K-590.6K)	203.9K (2.3K-578.5K)	862.3K (10.0K-2.4M)	815.7K (9.3K-2.3M)	1.7M (19.9K-4.5M)	1.6M (18.3K-4.4M)

Health outcome	Trigger	VE (%)	Low vaccine uptake (5%/year)		Medium vaccine uptake (20%/year)		High vaccine uptake (40%/year)	
			No Delay	60-Day Delay	No Delay	60-Day Delay	No Delay	60-Day Delay
DALYS	After 20 <sup>th</sup> infection	70	282.8K (2.1K-1.6M)	268.8K (1.9K-1.6M)	1.1M (8.6K-6.5M)	1.1M (7.4K-6.2M)	2.2M (16.6K-12.6M)	2.1M (14.5K-12.0M)
		80	323.2K (2.5K-1.9M)	307.2K (2.1K-1.8M)	1.3M (9.8K-7.5M)	1.2M (8.5K-7.1M)	2.5M (19.0K-14.4M)	2.4M (16.5K-13.7M)
		90	363.5K (2.8K-2.1M)	345.6K (2.4K-2.0M)	1.5M (11.1K-8.4M)	1.4M (9.6K-8.0M)	2.8M (21.4K-16.2M)	2.7M (18.6K-15.4M)
	50 days from first infection	70	258.4K (2.2K-1.5M)	244.5K (1.8K-1.4M)	1.0M (8.6K-6.0M)	977.9K (7.2K-5.6M)	2.0M (16.4K-11.6M)	1.9M (14.1K-10.9M)
		80	295.3K (2.5K-1.7M)	279.4K (2.1K-1.6M)	1.2M (9.9K-6.8M)	1.1M (8.2K-6.4M)	2.3M (18.8K-13.3M)	2.2M (16.1K-12.5M)
		90	332.2K (2.8K-1.9M)	314.3K (2.3K-1.8M)	1.3M (11.1K-7.7M)	1.3M (9.3K-7.2M)	2.6M (21.1K-14.9M)	2.4M (18.1K-14.0M)

## Health economic metrics

A comparison of the baseline cumulative health economic burden of CHIK-X across three disease severity scenarios are found in Table 13. Societal costs include direct healthcare costs and productivity losses. The economic value of DALYs and VSL are distinct. Under Scenario B, the burden of CHIK-X on OOP health expenditure was \$113.2 million I\$, resulting in 1 million instances of catastrophic

healthcare expenditure and 371.7 thousand instances of impoverishing healthcare expenditure. Under Scenario C, where the risk of hospitalisation and death were double that of Scenario B, OOP health expenditure was \$242.5 million I\$, resulting in 2 million instances of catastrophic healthcare expenditure and 743.4 thousand instances of impoverishing healthcare expenditure.

Table 13: Estimated economic costs (Mean, 2.5% - 97.5% UI) of chikungunya-X virus infections at baseline across the entire duration of all simulations. Results are presented for three disease severity scenarios. All outcomes apart from instances of ‘catastrophic healthcare expenditure’ and ‘impoverishing healthcare expenditure’ are in I\$ 2021. Future costs are discounted at 3% per year.

Economic outcome	Scenario A	Scenario B	Scenario C
Societal costs	1.7B (15.0M-5.4B)	4.0B (33.5M-14.9B)	8.1B (69.0M-30.2B)
Government health expenditure	71.9M (630.6K-203.9M)	175.9M (1.5M-474.5M)	360.5M (3.1M-964.4M)
OOP health expenditure	88.8M (769.8K-248.8M)	113.2M (951.7K-309.1M)	242.5M (2.0M-661.2M)
Productivity costs	1.5B (13.9M-5.0B)	3.7B (31.0M-14.3B)	7.5B (64.3M-29.0B)
Monetised DALYs	23.8B (51.8M-163.8B)	27.6B (83.0M-168.7B)	59.9B (177.4M-369.5B)
VSL	38.9B (337.8M-129.1B)	194.4B (1.7B-645.6B)	388.8B (3.4B-1.3T)
Catastrophic healthcare expenditure	200.7K (217.7-552.9K)	1.0M (1.1K-2.8M)	2.0M (2.2K-5.5M)
Impoverishing healthcare expenditure	74.3K (79.8-210.8K)	371.7K (399.1-1.1M)	743.4K (798.1-2.1M)

Detailed estimates of each health economic outcome averted by vaccination scenarios are found in Table 14 considering disease Scenario B. Outcomes were estimated for each uptake, delay, trigger, and vaccine efficacy scenario. Under the medium vaccine uptake scenario with 60-day delay and 70% vaccine efficacy, \$492.2-\$543.9 million were averted in terms of societal costs, \$3.4-\$3.8 billion in terms of the economic value of DALYs, and \$24.6-\$27.2 billion in

terms of VSL, with these estimates varying depending on the trigger to vaccine initiation in secondary outbreak countries. Between 121.7-133 thousand individuals were protected from catastrophic health expenditure, and 45.3-49.7 thousand individuals were protected from impoverishing health expenditure. The relative impact of vaccine scenarios was constant across outcomes.

Table 14: Estimated health economic outcomes (Mean, 2.5% - 97.5% UI) averted due to three considered CHIK-X uptake vaccination scenarios (low, medium, high), two trigger scenarios (20 infections, 50 days) and two delay scenarios (no delay, 60-day delay to initiation of 100 Days Mission). Assuming disease severity Scenario B, combined estimates for all countries are presented for three assumptions of vaccine efficacy (VE): 70%, 80%, and 90%. All outcomes apart from instances of ‘catastrophic healthcare expenditure’ and ‘impoverishing healthcare expenditure’ are in I\$ 2021. Future costs are discounted at 3% per year.

Health economic outcome	Trigger	VE (%)	Low vaccine uptake (5%/year)		Medium vaccine uptake (20%/year)		High vaccine uptake (40%/year)	
			No Delay	60-Day Delay	No Delay	60-Day Delay	No Delay	60-Day Delay
Societal Costs	After 20 <sup>th</sup> infection	70	141.8M (1.8M-537.8M)	136.0M (1.7M-528.6M)	567.2M (7.3M-2.2B)	543.9M (6.7M-2.1B)	1.1B (13.7M-4.1B)	1.1B (12.9M-4.1B)
		80	162.1M (2.1M-614.6M)	155.4M (1.9M-604.1M)	648.2M (8.4M-2.5B)	621.6M (7.7M-2.4B)	1.3B (15.7M-4.7B)	1.2B (14.7M-4.6B)
		90	182.3M (2.3M-691.4M)	174.8M (2.2M-679.6M)	729.2M (9.4M-2.8B)	699.3M (8.6M-2.7B)	1.4B (17.7M-5.3B)	1.4B (16.5M-5.2B)
	50 days from first infection	70	128.9M (1.9M-479.2M)	123.0M (1.6M-470.0M)	515.4M (7.7M-1.9B)	492.2M (6.6M-1.9B)	1.0B (14.0M-3.7B)	956.0M (12.4M-3.6B)
		80	147.3M (2.2M-547.7M)	140.6M (1.9M-537.2M)	589.0M (8.8M-2.2B)	562.5M (7.5M-2.1B)	1.1B (16.0M-4.2B)	1.1B (14.2M-4.2B)
		90	165.7M (2.5M-616.2M)	158.2M (2.1M-604.3M)	662.7M (9.9M-2.5B)	632.8M (8.5M-2.4B)	1.3B (18.0M-4.8B)	1.2B (16.0M-4.7B)
Monetised DALYs	After 20 <sup>th</sup> infection	70	991.5M (4.3M-6.1B)	955.3M (4.1M-5.9B)	4.0B (17.3M-24.3B)	3.8B (16.5M-23.7B)	7.7B (32.9M-46.9B)	7.4B (31.4M-45.5B)
		80	1.1B (4.9M-7.0B)	1.1B (4.7M-6.8B)	4.5B (19.8M-27.8B)	4.4B (18.8M-27.1B)	8.8B (37.6M-53.6B)	8.4B (35.9M-52.0B)
		90	1.3B (5.6M-7.8B)	1.2B (5.3M-7.6B)	5.1B (22.2M-31.3B)	4.9B (21.2M-30.5B)	9.8B (42.3M-60.3B)	9.5B (40.4M-58.5B)
	50 days from first infection	70	898.3M (4.2M-5.5B)	862.2M (3.9M-5.3B)	3.6B (16.8M-22.0B)	3.4B (15.8M-21.3B)	7.0B (32.1M-42.9B)	6.7B (30.4M-41.4B)
		80	1.0B (4.8M-6.3B)	985.4M (4.5M-6.1B)	4.1B (19.2M-25.2B)	3.9B (18.0M-24.3B)	8.0B (36.7M-49.0B)	7.7B (34.8M-47.3B)
		90	1.2B (5.4M-7.1B)	1.1B (5.1M-6.8B)	4.6B (21.6M-28.3B)	4.4B (20.3M-27.4B)	9.0B (41.3M-55.1B)	8.6B (39.1M-53.2B)

Health economic outcome	Trigger	VE (%)	Low vaccine uptake (5%/year)		Medium vaccine uptake (20%/year)		High vaccine uptake (40%/year)	
			No Delay	60-Day Delay	No Delay	60-Day Delay	No Delay	60-Day Delay
VSL	After 20 <sup>th</sup> infection	70	7.1B (107.3M-24.4B)	6.8B (98.4M-24.0B)	28.3B (429.3M-97.4B)	27.2B (393.5M-96.0B)	54.5B (796.4M-186.5B)	52.5B (747.7M-184.2B)
		80	8.1B (122.6M-27.8B)	7.8B (112.4M-27.4B)	32.3B (490.6M-111.3B)	31.1B (449.7M-109.7B)	62.3B (910.2M-213.1B)	60.0B (854.5M-210.5B)
		90	9.1B (138.0M-31.3B)	8.7B (126.5M-30.9B)	36.4B (551.9M-125.3B)	35.0B (505.9M-123.5B)	70.1B (1.0B-239.8B)	67.5B (961.3M-236.8B)
	50 days from first infection	70	6.4B (111.5M-21.8B)	6.2B (98.4M-21.4B)	25.7B (446.2M-87.4B)	24.6B (393.5M-85.8B)	49.8B (815.1M-168.3B)	47.7B (747.7M-165.7B)
		80	7.3B (127.5M-25.0B)	7.0B (112.4M-24.5B)	29.4B (509.9M-99.8B)	28.1B (449.7M-98.0B)	56.9B (931.5M-192.3B)	54.6B (854.5M-189.3B)
		90	8.3B (143.4M-28.1B)	7.9B (126.5M-27.6B)	33.1B (573.7M-112.3B)	31.7B (505.9M-110.3B)	64.0B (1.0B-216.4B)	61.4B (961.3M-213.0B)
Catastrophic healthcare expenditure	After 20 <sup>th</sup> infection	70	35.4K (33.8-114.8K)	33.3K (32.1-113.9K)	141.5K (135.3-459.0K)	133.0K (128.6-455.6K)	273.0K (250.9-855.1K)	256.8K (240.8-848.6K)
		80	40.4K (38.6-131.2K)	38.0K (36.7-130.2K)	161.7K (154.6-524.6K)	152.1K (147.0-520.7K)	312.0K (286.8-977.2K)	293.5K (275.2-969.8K)
		90	45.5K (43.5-147.6K)	42.8K (41.3-146.5K)	181.9K (173.9-590.2K)	171.1K (165.3-585.8K)	350.9K (322.6-1.1M)	330.2K (309.6-1.1M)
	50 days from first infection	70	32.5K (33.2-104.7K)	30.4K (30.6-104.0K)	130.1K (132.9-418.8K)	121.7K (122.4-415.9K)	252.4K (242.4-796.1K)	236.3K (229.2-790.7K)
		80	37.2K (38.0-119.7K)	34.8K (35.0-118.8K)	148.7K (151.9-478.7K)	139.1K (139.9-475.3K)	288.4K (277.0-909.8K)	288.4K (277.0-909.8K)
		90	41.8K (42.7-134.6K)	39.1K (39.4-133.7K)	167.3K (170.9-538.5K)	156.4K (157.4-534.7K)	324.5K (311.6-1.0M)	303.8K (294.6-1.0M)

Health economic outcome	Trigger	VE (%)	Low vaccine uptake (5%/year)		Medium vaccine uptake (20%/year)		High vaccine uptake (40%/year)	
			No Delay	60-Day Delay	No Delay	60-Day Delay	No Delay	60-Day Delay
Impoverishing healthcare expenditure	After 20 <sup>th</sup> infection	70	13.1K (20.5-41.9K)	12.4K (17.9-41.5K)	52.4K (82.1-167.7K)	49.7K (71.7-166.1K)	101.3K (161.8-316.0K)	96.1K (141.7-310.5K)
		80	15.0K (23.5-47.9K)	14.2K (20.5-47.5K)	59.9K (93.8-191.7K)	56.8K (81.9-189.9K)	115.8K (184.9-361.1K)	109.8K (162.0-354.9K)
		90	16.9K (26.4-53.9K)	16.0K (23.0-53.4K)	67.4K (105.6-215.6K)	63.9K (92.2-213.6K)	130.3K (208.0-406.3K)	123.5K (182.2-399.3K)
	50 days from first infection	70	12.0K (20.5-38.4K)	11.3K (17.9-38.0K)	48.0K (82.1-153.5K)	45.3K (71.7-151.9K)	93.2K (161.8-293.7K)	88.0K (141.7-288.3K)
		80	13.7K (23.5-43.9K)	12.9K (20.5-43.4K)	54.9K (93.8-175.5K)	51.7K (81.9-173.6K)	106.6K (184.9-335.6K)	100.5K (162.0-329.5K)
		90	15.4K (26.4-49.4K)	14.6K (23.0-48.8K)	61.8K (105.6-197.4K)	58.2K (92.2-195.3K)	119.9K (208.0-377.6K)	113.1K (182.2-370.7K)

## 4. Key Takeaways and Policy Implications

This section summarises the key takeaways and policy implications for CHIK and CHIK-X from the impact assessment modelling.

### 4.1. CHIK takeaways

CHIK currently causes a substantial number of symptomatic infections resulting in chronic sequelae, hospitalisations, and deaths, thereby resulting in large healthcare expenditures and productivity losses. Although estimating the annual number of CHIK infections using different approaches and assumptions, results were comparable between the OxLiv models and the model developed previously by Salje et al<sup>61</sup>. In particular, crudely assuming only 13% of the population of China and 59% of the population of India is at risk (similar to Salje et al.) would reduce overall symptomatic infection numbers for the OxLiv 1 model by almost 26 million over the 16-year period, narrowing the original difference of 25.5 million between models.

The results presented in this report show that the Target High scenario was the most effective vaccination strategy considered. This scenario covered 30-40% of people ages 12-99 in 37 countries (including high, medium, and low country levels) with preventative campaigns and 60-65% of 12-year-olds in those countries with routine vaccination. Under baseline assumptions<sup>62</sup>, this scenario prevented approximately 22.3 million symptomatic cases, 11.4 million cases of persistent post-acute arthralgia/arthritis, 752 thousand hospitalisations, 49 thousand deaths, and 14.3

million DALYs over a 16-year period. In turn, this vaccination strategy averted \$2.3 billion in societal costs<sup>63</sup>, preventing 410 thousand patients from suffering catastrophic healthcare expenditures and 136 thousand of them from falling into poverty as a result. If more optimistic vaccine efficacy assumptions were made (80% or 90% effective against disease instead of 70%), societal costs averted over 16 years increased to \$2.6 billion and \$2.9 billion, respectively.

An important factor limiting the potential impact of the considered vaccination strategies is that we conservatively assumed that the vaccines would only prevent disease and have no impact on transmission. Furthermore, the considered vaccination scenarios did not include vaccination of children under 12 years old, whereas we estimated a substantial proportion of hospitalisation to occur in young children, further limiting the potential impact of the vaccination strategies.

Given that it is difficult to predict when CHIK outbreaks will occur in the future, we used the same average location-specific FoI each year of the simulated 16-year period. In practice, CHIK epidemiology is more volatile, and the true impact of vaccination will depend on the timing of vaccine uptake relative to potentially explosive outbreaks.

### 4.2. CHIK-X takeaways

Our simulations for chikungunya-X represented a hypothetical but plausible scenario for the emergence and global spread of a novel, highly pathogenic chikungunya-related virus. Assuming previous exposure to CHIK does not protect

<sup>61</sup> Salje et al., 2023. The global burden of chikungunya virus and the potential benefit of vaccines.

<sup>62</sup> Baseline assumptions: CHIK infection incidence sourced from OxLiv 1, mean 18% of infections symptomatic, 70% vaccine efficacy against disease, and minimum 16-year duration of protection (the time horizon of the simulation).

<sup>63</sup> Societal costs are the sum of healthcare costs, productivity losses, and out-of-pocket expenses, where the largest proportion of the economic burden was caused by productivity losses.

against CHIK-X and global spread follows a similar trajectory to Zika virus from 2014 to 2016, a CHIK-X pandemic was estimated to reach on average 32 countries over a duration of 5.6 years and result in approximately 22 million infections before naturally subsiding due to the accumulation of immunity. Further assuming that the age- and sex-specific health risks associated with CHIK-X (risks of hospitalisation and death) are approximately five times greater than CHIK, we estimated that this outbreak could result in 10.1 million symptomatic cases, 2.7 million outpatient visits, 2.0 million hospitalisations, and 113 thousand deaths globally, for a total estimated 7.9 million DALYs. Due to the hypothetical nature of this scenario, these simulations were associated with a high degree of uncertainty, with the 95% UI for global CHIK-X DALYs ranging from 47 thousand to 46 million.

Vaccination following 100 Days Mission targets was estimated to have a large impact on mitigating the burden of CHIK-X. Assuming 70% efficacy against disease, no impact on infection, and a 60-day detection delay, the most ambitious vaccine rollout scenario—covering 40% of affected countries’ population annually in two-year campaigns—vaccination averted an estimated 2.7 million symptomatic cases, 537 thousand hospitalisations, 29.7 thousand deaths, and 2.1 million DALYs. These health gains in turn averted \$1.1 billion in societal costs, although this estimate is likely conservative, as we do not account for potential pandemic externalities including the destabilisation of global tourism and trade and the potential collapse of healthcare services.

Across CHIK-X vaccine scenarios, assumptions were varied on the delay from CHIK-X identification to initial vaccine delivery, the country-level trigger for vaccine initiation (time since the first identification or number of cases), and the total volume of vaccine delivery (as a

proportion of national population estimates). The rate of vaccine delivery to affected countries (5%, 20%, or 40% of the population per year) was by far the greatest driver of vaccine impact, as expected. However, the global reactivity of vaccine administration was also important, largely driven by the assumption that CHIK-X outbreak dynamics would have a similar explosive nature as observed during CHIK outbreaks in the PAHO region. Although the difference was modest between administering the first vaccines 100 days versus 160 days since CHIK-X’s identification in the origin country, substantial differences were observed in non-origin countries between starting vaccination after the first 20 infections versus after 50 days from the first infection. These results suggest robust surveillance, rapid manufacturing at scale, and efficient allocation are critical to benefit non-origin countries in a CHIK-X pandemic.

## **5. Appendix**

Further details on the following topics are included for reference:

Appendix 1. Frequently Asked Questions

Appendix 2. Project Teams and Governance

Appendix 3. OxLiv Consortium Lassa and Lassa-X Models, Scenarios, and Data Sources

Appendix 4. Supplementary Results

## **Appendix 1. Frequently Asked Questions**

This section provides answers to frequent questions asked from internal and external working groups providing feedback on the development of the models, scenarios, and results.

### ***What was the assumed ratio between total infections, symptomatic cases, chronic cases, and hospitalisations for CHIK and CHIK-X?***

In the main analysis for CHIK, the following assumptions were made:

1. The probability of infections being symptomatic was 18%
2. The probability of a symptomatic infection (i.e. case) leading to chronic sequelae was 51%
3. The probability of a symptomatic infection (i.e. case) leading to hospitalisations and deaths varied by age and sex but were on average approximately 4% and 0.2%, respectively

Three disease severity scenarios for CHIK-X disease were considered:

1. **Scenario A:** The probability of an infection becoming symptomatic was 46%, and the probability of hospitalisation and death were the same of those for CHIK
2. **Scenario B:** The probability of an infection becoming symptomatic was 46%, and the probability of hospitalisation and death were 5 times that of CHIK
3. **Scenario C:** The probability of an infection becoming symptomatic was 100%, and the probability of hospitalisation and death were 10 times that of CHIK

### ***What was the assumed effectiveness and duration of protection for the CHIK and CHIK-X vaccines?***

The vaccine effectiveness against disease was varied over 70%, 80%, and 90% for both CHIK and CHIK-X. For CHIK we assumed protection lasted at least 16 years (the time horizon of the simulation). For CHIK-X we assumed a duration of protection of 10 years (the time horizon of the simulation).

### ***Why was suitability, FoI, and populations at risk used to project CHIK incidence?***

Given that there is likely significant under-reporting of CHIK, we cannot simply rely on reported cases to accurately capture CHIK epidemiology. Instead, the FoI—the annual probability of getting infected for the population that is still susceptible—was estimated from age-stratified seroprevalence data. Given that age-stratified seroprevalence data was available in a limited number of countries, the relationship between FoI and CHIK suitability was estimated from locations having data on both. Combining our global predictions of CHIK suitability generated using boosted regression trees with this estimated relationship between suitability and FoI, we predicted FoI globally to estimate CHIK infection incidence. A similar approach was not possible for FoI given that there were insufficient datapoints to do this directly with the FoI without using the suitability.

### **Why was Zika used to tune the CHIK-X model?**

There was limited genetic information on the spread of CHIK to the Americas from 2013 onwards (62% of sequences are still from Brazil and much of the remainder from the U.S.)<sup>64</sup>. Therefore, data from the global spread of Zika was used to tune the model. Publicly available analyses from Nextstrain gave the number of countries affected during the expansion of Zika in the mid-2010s<sup>65,66</sup>.

### **Why was the cholera vaccine used as an analog for the preventative vaccination campaigns against CHIK?**

The cholera vaccine was the best fit to inform assumptions on target age, coverage goals, vaccination strategies, and geographical distribution. Arbovirus vaccines (yellow fever and Japanese encephalitis) were first considered as analogs but were excluded for use as proxies due to significant differences with the CHIK vaccine. Yellow fever and Japanese encephalitis are better-established vaccines that are mostly given to infants in endemic countries through routine immunization. Since a CHIK vaccine was developed for ages 12+, yellow fever and Japanese encephalitis weren't appropriate. Finally, yellow fever and Japanese encephalitis had very high coverage, which was not in line with the global interest gathered in country interviews in the CHIK demand forecast. The cholera vaccine is one of the few vaccines given in campaigns to anyone eligible, aligning better with what countries were looking for as an introduction campaign. The geographical distribution of burden for cholera also aligned well with CHIK burden in the AFRO, WPRO, and SEARO regions. Historical data on doses administered in cholera campaigns for an approximate coverage value per country were used to inform the target coverages and campaign lengths.

### **Was climate change incorporated into the modelling?**

Climate change was not explicitly incorporated into the modelling. Relatively recent data used (e.g., for precipitation, land surface temperature, EVI, and environmental suitability for CHIK mosquito vectors) reflects currently observed temperatures and consequences of climate change on vector suitability and vegetation. To predict the impact of future climate change, the suitability surfaces could be updated with modelled climate change driven changes in the considered covariates in future work.

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<sup>64</sup> de Souza et al., 2024. Chikungunya: A decade of burden in the Americas.

<sup>65</sup> Hadfield et al., 2018. Nextstrain: Real-time tracking of pathogen evolution.

<sup>66</sup> Nextstrain, 2024. Real-time tracking of Zika virus evolution (<https://nextstrain.org/zika/>).

***Were any aspects of vector control (e.g., mosquito nets, indoor residual spraying) incorporated into the modelling?***

Vector control was not incorporated into the modelling for several reasons. First, vector control can contribute to a build-up of susceptible people. If vector control measures fail, they can ultimately lead to larger outbreaks than would have happened without any vector control measures in place. Therefore, human vaccines are largely the most impactful way to prevent CHIK. Second, while the use of bed nets for other vector-borne diseases such as malaria have been successful, the primary vector of chikungunya (*Aedes* species) is typically daytime biting, potentially rendering bed nets less effective. Third, and related to the prior point, *Aedes* species are also peridomestic, meaning they are more often found around homes compared to *Anopheles* species (the main vector of malaria). Different ecology between these primary vectors can make vector control measures that may work well for malaria less practical for preventing CHIK.

## Appendix 2. Project Teams and Governance

CEPI's Impact Assessment Modelling project required the contribution and coordination across several teams inside and outside CEPI. This consortium included CEPI's Project Team, CEPI's Investment Team, Linksbridge, and the OxLiv Team. The OxLiv team combined researchers from the University of Oxford and Liverpool School of Tropical Medicine.

This section describes the approach used for this project, each team's roles, and the project governance structure.

The consortium aimed to achieve this project's goals by dividing the impact assessment modelling into three modules. These modules were designed to build on each other, where the output from one informed the models in the next (Table A2.1).

Table A2.1: Consortium approach for achieving the goals for this impact assessment modelling.

Module	Lead	Outputs Generated
<b>1. CEPI Input Data</b> <ul style="list-style-type: none"> <li>Design scenarios to evaluate CEPI investments (e.g., 100 Days Mission, vaccine products, TPCS)</li> <li>Provide necessary input data for all scenarios to run in the Infectious Disease Module</li> </ul>	<b>CEPI &amp; Linksbridge</b>	<ul style="list-style-type: none"> <li>Number of people vaccinated by CEPI-supported vaccines per year, country for each scenario</li> <li>Other assumptions needed by the infectious disease models</li> </ul>
<b>2. Disease Incidence</b> <ul style="list-style-type: none"> <li>Model disease incidence within a population for each scenario</li> <li>Uses input from CEPI Input Data module to inform vaccinations and other assumptions in the model</li> </ul>	<b>OxLiv</b>	<ul style="list-style-type: none"> <li>Infections, deaths, and hospitalisations for each disease and scenario</li> </ul>
<b>3. Outputs</b> <ul style="list-style-type: none"> <li>Quantifies impact of vaccines in standardised set of metrics</li> <li>Uses output from Infectious Disease module to calculate health, health economic, and economic metrics</li> </ul>	<b>OxLiv</b>	<ul style="list-style-type: none"> <li>Standardised health, health economic, and economic metrics across all diseases</li> <li>Specific metrics per disease an option on case-by-case basis</li> </ul>

Each module was led by a subset of the overall project team. The responsibilities for each of these teams are summarised in Table A2.2.

Table A2.2: Project teams and their respective roles.

<b>CEPI Project Team</b>	<b>CEPI Investment Team</b>	<b>Linksbridge/MSH</b>	<b>OxLiv Modelling Team</b>
<ul style="list-style-type: none"> <li>• CEPI point of contact for all other teams</li> </ul>	<ul style="list-style-type: none"> <li>• Provide investment information and other necessary inputs for scenario design</li> </ul>	<ul style="list-style-type: none"> <li>• Design scenarios and generate input data to evaluate specific investments</li> <li>• Coordinate across teams and diseases to standardise model inputs (investments and scenarios) and outputs (metrics)</li> </ul>	<ul style="list-style-type: none"> <li>• Build disease model as agreed with CEPI's project team</li> <li>• Build models needed for calculating output metrics</li> </ul>

The project governance is illustrated in Figure A2.1. The CEPI Project Team was responsible for the day-to-day project management, providing updates to the CEPI Leadership Team, coordinating across all modelling teams, and acting as the point of contact for all teams. The CEPI Investment Team was primarily involved in the early stages of the project when scenarios were designed to evaluate specific investments. They worked closely with Linksbridge to provide information, data, and assumptions needed to generate input data for the disease models. Linksbridge worked with the CEPI Investment Team on scenario design and coordinated across modelling teams to standardise scenarios and outputs where possible. The modelling teams were responsible for building the disease models. OxLiv also built any other models required for calculating the output metrics.

An internal working group at CEPI and an external advisory group were also presented with updates on the project's progress and the proposed methods. The internal working group provided feedback and guidance throughout the project and ensured key investments from their relevant departments were included. The external advisory group provided independent, high-level feedback and advice on the project during two meetings throughout the project.

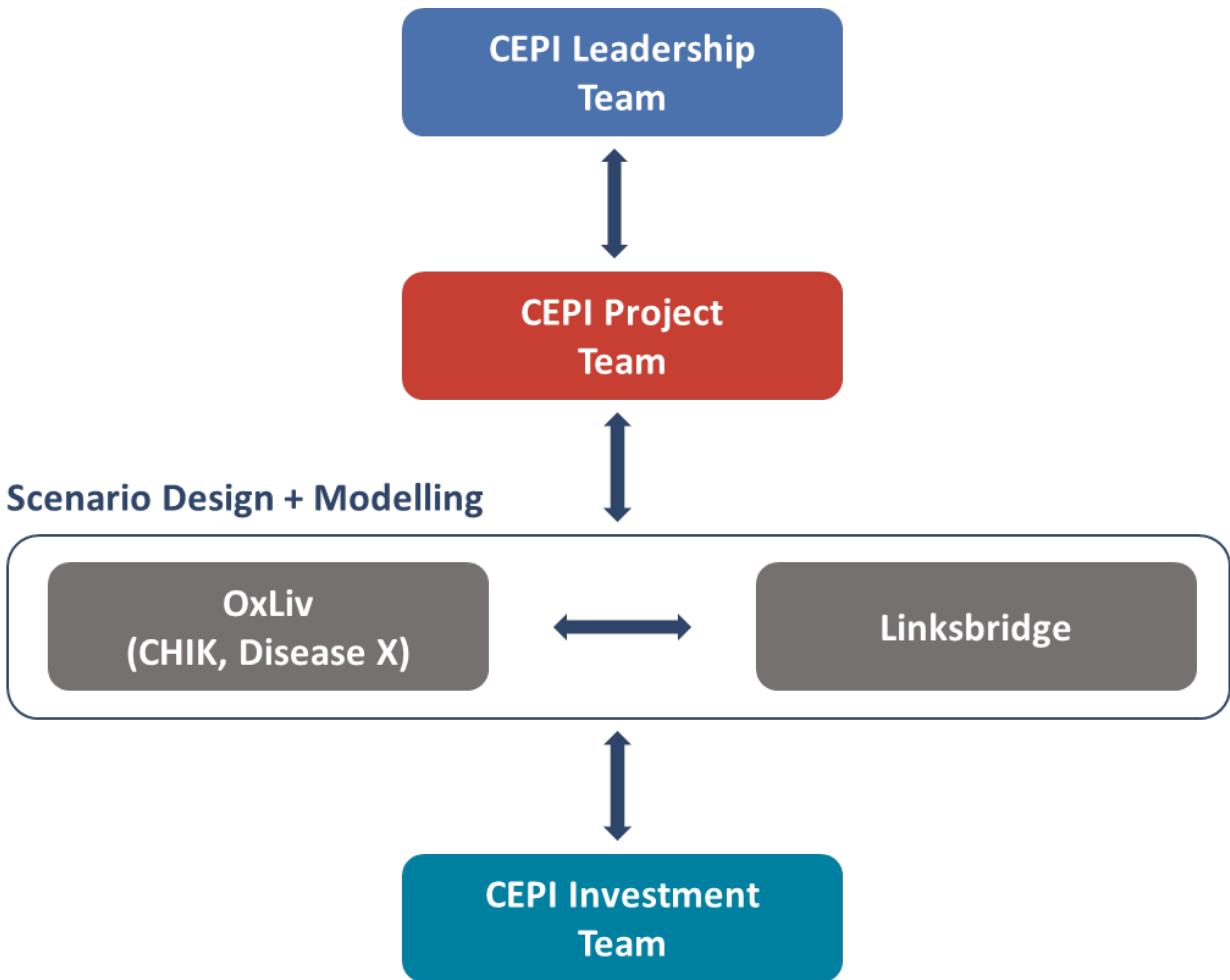


Figure A2.1: Project governance across the teams in the consortium.

## **Appendix 3. OxLiv Consortium CHIK and CHIK-X Models, Scenarios, and Data Sources**

This section provides more details on the mathematical models, CHIK and CHIK -X analyses, and data sources.

### ***CHIK vaccine demand forecast and vaccination scenario assumptions***

A demand forecast for the CHIK vaccine was commissioned by CEPI in 2023<sup>67</sup>. This forecast focused on 39 countries where CHIK outbreaks have happened. The goal was to collect country stakeholder feedback on awareness of and interest in the CHIK vaccines before they enter the market. These responses clarified country plans to introduce the CHIK vaccine, providing the assumptions behind the vaccination scenarios in this impact assessment.

The demand forecast used outbreak frequency data, interview feedback, and participation in clinical trials to sort the 39 countries into “low”, “medium”, and “high” categories based on their likelihood of introduction. The next three subsections will describe how countries were sorted into their introduction categories.

#### *Outbreak frequency data*

First, countries were selected and then categorized by their outbreak frequency. Outbreak frequency was used as a selection criteria because global case burden data was very limited. Countries were grouped into outbreak burden categories following the criteria in Table A3.1<sup>68, 69, 70, 71</sup>.

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67 CEPI, 2023. Chikungunya vaccine introduction: Understanding LMIC perspectives. (Not public).

68 Bettis et al., 2022. The global epidemiology of chikungunya from 1999 to 2020: A systematic literature review to inform the development and introduction of vaccines.

69 U.S. CDC, 2023. Areas at risk for chikungunya.

70 European CDC, 2023. Chikungunya worldwide overview.

71 PAHO, 2024. Chikungunya cases by country or territory: Cumulative cases.

Table A3.1: Criteria for categorizing 39 countries by their outbreak burden.

Category	Criteria	Number of Countries	Example Countries
High	<ul style="list-style-type: none"> <li>Has had CHIK outbreak since 2018</li> <li>Historically had a high number of outbreaks (2+)</li> </ul>	6/91	Brazil India Colombia
Medium	<ul style="list-style-type: none"> <li>Has had CHIK outbreak since 2018</li> <li>Historically had more infrequent outbreaks (only 1)</li> </ul>	16/91	Paraguay Malaysia Kenya
Low	<ul style="list-style-type: none"> <li>Has had 1 CHIK outbreak between 2010-2017</li> </ul>	17/91	Indonesia Viet Nam Haiti
Very Low	<ul style="list-style-type: none"> <li>Historically has had CHIK outbreak, but not since 2010</li> </ul>	52/91	Tanzania Bahamas United States
Not included	<ul style="list-style-type: none"> <li>Never had CHIK outbreak (as of 2022)</li> </ul>	N/A	N/A

The results of this outbreak burden categorization are included in Figure A3.1.

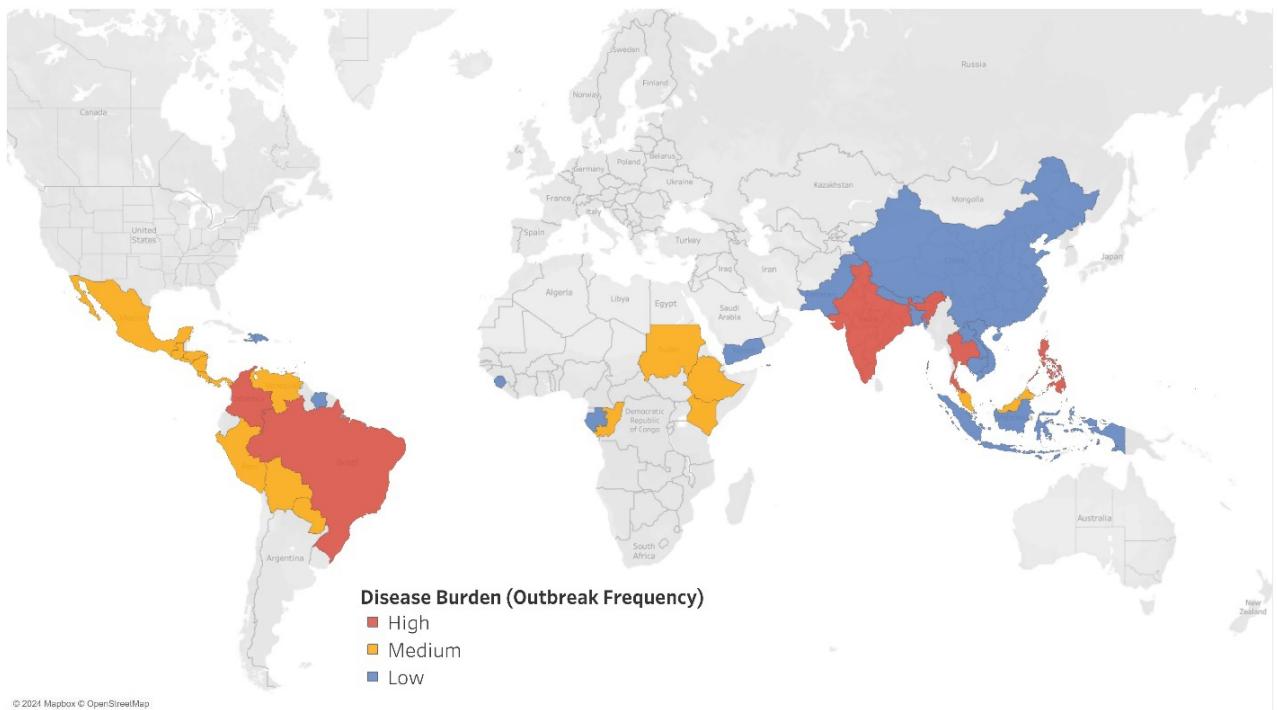


Figure A3.1: Results from the country CHIK burden categorization.

### *Country stakeholder interviews and likelihood of introduction*

Second, in-depth interviews were conducted with key stakeholders in countries of interest. These interviews were conducted with representatives from ministries of health, academia, and national or international technical agencies and advisory groups. The interviews were designed to gather information from these stakeholders on the following:

1. Level of knowledge of CHIK and CHIK vaccines
  2. Level of public health and political priority of the virus and vaccine
  3. Strategies for vaccine introduction and use (including age, geographical targeting, and financing strategies)

10 target countries—including Brazil, Colombia, Ethiopia, Guatemala, India, Indonesia, Kenya, Malaysia, Paraguay, and Vietnam—were selected based on their history of CHIK outbreaks, regional diversity, and availability of in-country contacts. 15 interviews were conducted in total, with 13 at the country level and two at the regional level. National stakeholders came from the following regions and countries<sup>72</sup>:

1. African region (Kenya, Ethiopia)
  2. Asian region (India, Indonesia)
  3. Region of the Americas (Brazil, Colombia, Guatemala, Paraguay)

The key findings from these interviews are included in Table 3.2.

<sup>72</sup> Representatives from Malaysia and Vietnam did not respond to requests for interviews.

Table A3.2: Findings from stakeholder interviews for eight target countries.

Country	Current likelihood of intro	KII Awareness of vaccine	Priorities	Introduction decision-making factors	Introduction deployment preferences	Financing factors	Other
Brazil	Possible	Yes	Dengue vaccine introduction; Wolbachia scale up	Local capacity and technology transfer for local production	Routine at national level	Government financing	Concerns around adherences to CHIK vaccine after dengue vaccine introduction
Colombia	Low	Yes	Malaria and dengue	Enhanced immunity (provides protection against other arboviruses)	Routine for high-risk populations in targeted geographic areas	Government financing with inclusion in PAHO's revolving fund	Data on international experiences essential to evaluate alternatives for introduction
Ethiopia	Very low	No	Crowded vaccine pipeline (malaria Hep B, meningitis, yellow fever)	Ease of delivery within current system; disease burden	Outbreak response	Reliant on Gavi	Needs increased awareness and better disease burden data
Guatemala	Very low	No	Malaria and dengue	Significant immunity after vaccination (>10 years)	Outbreak response	Government financing with inclusion in PAHO's revolving fund	Needs increased awareness
India	Possible	Yes	Dengue; multiple other vaccines waiting for addition to National Immunization Schedule	Availability of data and comparative mortality	High-risk populations then scaled nationally	Pilot to prove efficacy/safety then taken on and scaled by govt	Needs better disease burden data
Indonesia	Low	No	Japanese Encephalitis vaccine, Wolbachia scale-up; future Dengue vaccine introduction	Ease of delivery within current system	High-risk populations	Pilot through private sector/donor financing then taken on and scaled by govt	Needs increased awareness
Kenya	Low	No	Malaria and typhoid vaccines	Ease of delivery within current system	High-risk populations then scaled nationally	Reliant on Gavi	Needs increased awareness and better disease burden data
Paraguay	Low	Yes	Dengue	Level of immunity among population after current outbreak	Routine at national level	Government financing with inclusion in PAHO's revolving fund	Priority given to update the current national plan; no new vaccines in pipeline

For the vaccination scenarios, these findings were summarized by the following introduction assumptions for each target country or region:

1. **Brazil:** CHIK is a high priority with the government tracking vaccine development
2. **India:** There is interest in CHIK with the plan to pilot introduction and then scale with the government
3. **Colombia/Paraguay/Guatemala:** CHIK awareness is high because of the recent outbreak in Paraguay, but the vaccine is a moderate priority
4. **Indonesia:** CHIK is a low priority
5. **Kenya and Ethiopia:** CHIK is a low priority
6. **Malaysia and Vietnam:** The lack of response was assumed to indicate low priority for CHIK

The demand forecast contained 39 countries in total, but the country stakeholder interviews only covered 10 of them. A clustering analysis was then conducted to extrapolate the introduction assumptions from the 10 target countries to the other 29 countries. This analysis was conducted following two steps:

1. Non-target countries (i.e., “followers”) were clustered with the 10 target countries (i.e., “leads”) based on variables representing their decision factors
2. The “follower”, non-target countries were then assumed to adopt the same introduction decision as the “lead”, target country they were clustered with

The cluster analysis was conducted using the K-means algorithm with the following variables:

1. WHO region
2. 5-year median cases/100,000
3. Vaccine adoption speed, based on historical speed of introduction for other vaccines
4. Number of outbreaks since 2010
5. Planned vaccine introductions in the next five years
6. Health spending as a percentage of GDP

Results from this clustering analysis are included in Table A3.3.

Table A3.3: Results from the clustering analysis to extrapolate vaccine introduction assumption from 10 target countries to 29 countries without interview data.

Cluster	Country	Region	Cases/100K	# Outbreaks	# Vaccine Introductions	Speed	Health Expenditure	Lead or Follower	Introduction Assumption
1	Malaysia	WPRO	4.22	1	1	Moderate	4.12	Lead	Low
	Viet Nam	WPRO	0.00	1	3	Slow	4.68	Lead	Low
	China	WPRO	0.00	1	2	Very Slow	5.59	Follower	Low
	Micronesia	WPRO	0.00	1	0	Fast	11.56	Follower	Low
	Cambodia	WPRO	0.00	1	3	Moderate	7.51	Follower	Low
	Laos	WPRO	0.00	1	1	Slow	2.69	Follower	Low
	Philippines	WPRO	0.48	4	0	Fast	5.11	Follower	Low
2	Colombia	AMRO	0.31	3	0	Fast	8.99	Lead	Medium
	Guatemala	AMRO	4.59	1	0	Fast	6.47	Lead	Medium
	Paraguay	AMRO	4.66	1	0	Fast	7.58	Lead	Medium
	Bolivia	AMRO	7.60	1	0	Moderate	7.86	Follower	Medium
	Barbados	AMRO	9.59	1	0	Fast	7.2	Follower	Medium
	Costa Rica	AMRO	0.98	1	0	Slow	7.86	Follower	Medium
	Dom. Rep.	AMRO	0.20	1	0	Fast	4.94	Follower	Medium
	Grenada	AMRO	0.00	1	1	Slow	5.82	Follower	Medium
	Honduras	AMRO	0.53	1	0	Moderate	9.04	Follower	Medium
	Haiti	AMRO	0.00	1	1	Slow	3.31	Follower	Medium
	Mexico	AMRO	0.00	2	0	Fast	6.24	Follower	Medium
	Nicaragua	AMRO	0.24	1	1	Fast	8.63	Follower	Medium
	Panama	AMRO	0.05	1	0	Fast	9.66	Follower	Medium
	Peru	AMRO	1.00	1	0	Fast	6.3	Follower	Medium
	El Salvador	AMRO	2.43	1	0	Fast	9.85	Follower	Medium
3	Suriname	AMRO	0.00	1	0	Fast	6.77	Follower	Medium
	Venezuela	AMRO	0.64	1	1	Fast	3.82	Follower	Medium
	Indonesia	SEARO	0.00	4	1	Slow	3.41	Lead	Low
	Bangladesh	SEARO	0.00	2	4	Moderate	2.63	Follower	Low
	Bhutan	SEARO	0.00	1	2	Slow	4.37	Follower	Low

Cluster	Country	Region	Cases/100K	# Outbreaks	# Vaccine Introductions	Speed	Health Expenditure	Lead or Follower	Introduction Assumption
3 cont.	Nepal	SEARO	0.00	1	1	Slow	5.17	Follower	Low
	Thailand	SEARO	1.55	2	2	Slow	4.36	Follower	Low
4	India	SEARO	5.78	19	2	Slow	2.96	Lead	High
5	Brazil	AMRO	61.58	7	0	Fast	10.31	Lead	High
6	Ethiopia	AFRO	0.25	1	5	Moderate	3.48	Lead	Low
	Kenya	AFRO	0.69	1	1	Moderate	4.29	Lead	Low
	Congo	AFRO	0.00	2	1	Moderate	4.47	Follower	Low
	Gabon	AFRO	0.00	1	2	Slow	3.43	Follower	Low
	Pakistan	EMRO	0.00	1	1	Moderate	2.79	Follower	Low
	Sudan	EMRO	0.01	1	1	Moderate	3.02	Follower	Low
	Sierra Leone	AFRO	0.00	1	0	Slow	8.76	Follower	Low
	Yemen	EMRO	0.00	1	1	Fast	4.25	Follower	Low

### *Participation in a clinical trial*

A country's participation in a clinical trial was the final factor considered when grouping countries into "low", "medium", and "high" categories for the vaccination scenarios. CEPI-supported CHIK vaccines were only considered for this step. The two manufacturers and their clinical trial sites included the following:

1. **Valneva/ Instituto Butantan:** Brazil, United States
2. **International Vaccine Institute / Bharat Biotech:** Colombia, Costa Rica, Guatemala, India, Panama, and Thailand

For each country participating in a clinical trial, it was assumed they had a high interest in introducing the CHIK vaccine. Therefore, these countries were placed in the "high" category regardless of the results from the clustering analysis.

### *Final categorization*

The final categorization combined the results from the outbreak frequency data, stakeholder interviews, clustering analysis, and clinical trial list to generate the country levels used in the vaccination scenarios. Results from this analysis are included in Figure A3.2 and Table A3.4.

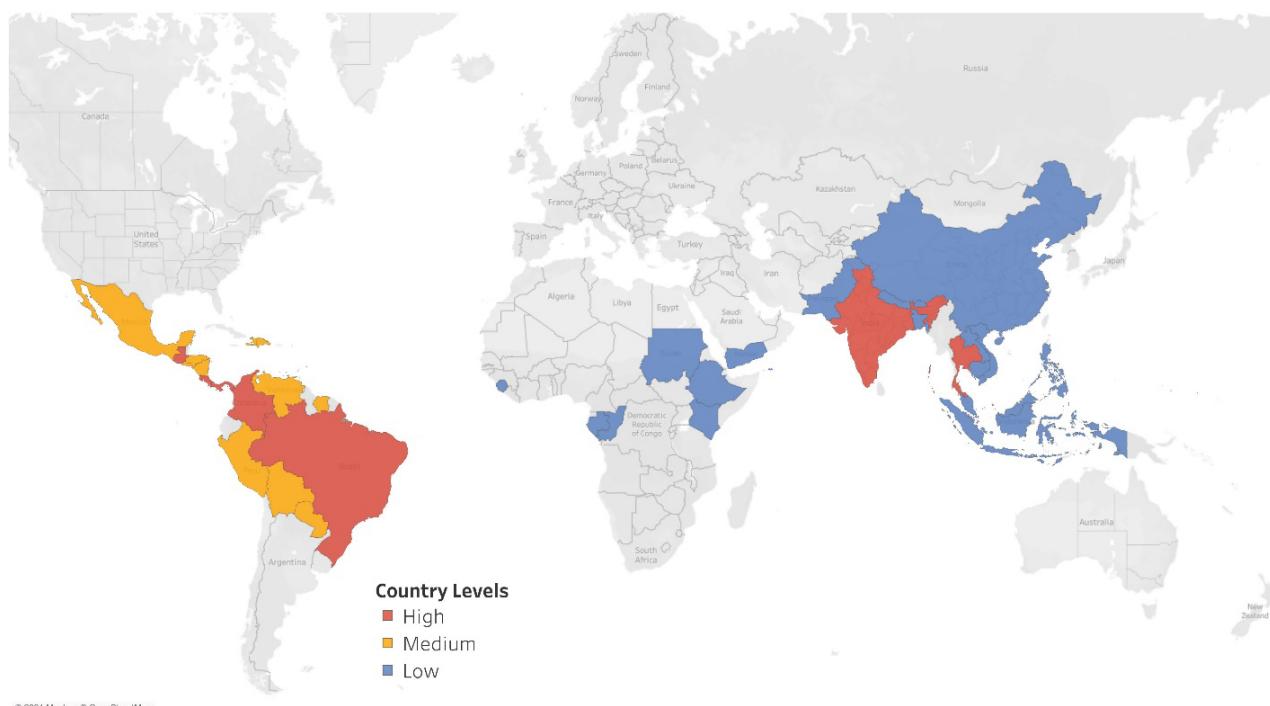


Figure A3.2: Countries in the "high", "medium", and "low" categories used in the vaccination scenarios.

Table A3.4: Final categorization of 37 countries for the vaccination scenarios. Micronesia and Grenada were excluded to align with the countries in the Salje et al. analysis<sup>73</sup>. Their exclusion had negligible impact on the results as their incidence was low, accounting for 0.002% of global CHIK cases.

Cluster	Country	Region	Burden	Lead Intro	Clinical Trial	Country Level
1	Malaysia	WPRO	Medium	Low	FALSE	Low
	Viet Nam	WPRO	Low	Low	FALSE	Low
	China	WPRO	Low	Low	FALSE	Low
	Cambodia	WPRO	Low	Low	FALSE	Low
	Laos	WPRO	Low	Low	FALSE	Low
	Philippines	WPRO	High	Low	FALSE	Low
2	Colombia	AMRO	High	Medium	TRUE	High
	Guatemala	AMRO	Medium	Medium	TRUE	High
	Paraguay	AMRO	Medium	Medium	FALSE	Medium
	Bolivia	AMRO	Medium	Medium	FALSE	Medium
	Barbados	AMRO	Medium	Medium	FALSE	Medium
	Costa Rica	AMRO	Medium	Medium	TRUE	High
	Dominican Republic	AMRO	Low	Medium	FALSE	Medium
	Honduras	AMRO	Medium	Medium	FALSE	Medium
	Haiti	AMRO	Low	Medium	FALSE	Medium
	Mexico	AMRO	Medium	Medium	FALSE	Medium
	Nicaragua	AMRO	Medium	Medium	FALSE	Medium
	Panama	AMRO	Medium	Medium	TRUE	High
	Peru	AMRO	Medium	Medium	FALSE	Medium
	El Salvador	AMRO	Medium	Medium	FALSE	Medium
3	Suriname	AMRO	Low	Medium	FALSE	Medium
	Venezuela	AMRO	Medium	Medium	FALSE	Medium
4	Indonesia	SEARO	Low	Low	FALSE	Low
	Bangladesh	SEARO	Low	Low	FALSE	Low
	Bhutan	SEARO	Low	Low	FALSE	Low
5	Nepal	SEARO	Low	Low	FALSE	Low
	Thailand	SEARO	High	Low	TRUE	High
6	India	SEARO	High	High	TRUE	High
5	Brazil	AMRO	High	High	TRUE	High
6	Ethiopia	AFRO	Medium	Medium	FALSE	Low
	Kenya	AFRO	Medium	Medium	FALSE	Low
	Congo	AFRO	Medium	Medium	FALSE	Low
	Gabon	AFRO	Low	Medium	FALSE	Low
	Pakistan	EMRO	Low	Medium	FALSE	Low
	Sudan	EMRO	Medium	Medium	FALSE	Low
	Sierra Leone	AFRO	Low	Medium	FALSE	Low
	Yemen	EMRO	Low	Medium	FALSE	Low

73 Salje et al., 2023. The global burden of chikungunya virus and the potential benefit of vaccines.

Table A3.5: Assumptions for the target-based and market-based vaccination scenarios.

Assumptions or Scenarios		Market-Based Scenarios	Target-Based Scenarios
<b>Year of introduction</b>		• 2025	• 2025
<b>Time horizon</b>		• 2025-2040	• 2025-2040
<b>Vaccination strategy (Country levels included)</b>			
<i>High</i>		• High: Preventative campaigns • Medium: Preventative campaigns • Low: none	• High: Preventative campaigns followed by routine vaccination • Medium: Preventative campaigns followed by routine vaccination • Low: Preventative campaigns followed by routine vaccination
<i>Medium</i>			• High: Preventative campaigns followed by routine vaccination • Medium: Preventative campaigns followed by routine vaccination • Low: none
<i>Low</i>		• High: Preventative campaigns • Medium: none • Low: none	• High: Preventative campaigns followed by routine vaccination • Medium: none • Low: none
<b>Target population</b>			
<i>Assumption</i>		• Assume equal spread across age groups in campaigns	• Assume equal spread across age groups in campaigns
<i>High</i>		• Campaigns: 18-99 years	• Routine: 12 years • Campaigns: 12-99 years
<i>Medium</i>			• Routine: 12 years • Campaigns: 12-99 years
<i>Low</i>		• Campaigns: 50-99 years	• Routine: 12 years • Campaigns: 12-99 years
<b>Coverage</b>			
<i>High</i>		• Campaign: Reach 20-30%	• Routine: 60-65% annual • Campaign: Reach 30-40%
<i>Medium</i>			• Routine: 60-65% annual • Campaign: reach 30-40%
<i>Low</i>		• Campaign: Reach 10-20%	• Routine: 60-65% annual • Campaign: reach 30-40%
<b>Uptake curve</b>			
<i>Assumption</i>		• Assume equal uptake for preventative campaigns (33.3% of total each year for 3-year campaigns)	• Assume equal uptake for preventative campaigns (50% of total each year for 2-year campaigns)
<i>High</i>		• Multi-age cohort introduction for 3 years	• Multi-age cohort introduction for 2 years • Routine vaccination 5 years after campaign introduction

Assumptions or Scenarios		Market-Based Scenarios	Target-Based Scenarios		
<i>Medium</i>		<ul style="list-style-type: none"> <li>• Multi-age cohort introduction for 2 years</li> <li>• Routine vaccination 5 years after campaign introduction</li> </ul>			
<i>Low</i>		<ul style="list-style-type: none"> <li>• Multi-age cohort introduction for 3 years</li> <li>• Multi-age cohort introduction for 2 years</li> <li>• Routine vaccination 5 years after campaign introduction</li> </ul>			
<b>Countries in scope</b>					
<i>High</i>	<ul style="list-style-type: none"> <li>• All high and medium countries (n=19)</li> </ul>	<ul style="list-style-type: none"> <li>• All countries with very low-high CHIK burden (n=37)</li> <li>• All high and medium countries (n=19)</li> <li>• All high, all countries with clinical trials, none of medium and low burden countries (n=7)</li> </ul>			
<i>Medium</i>					
<i>Low</i>	<ul style="list-style-type: none"> <li>• All high and all countries with clinical trials (n=7)</li> </ul>				
<b>Wastage</b>					
<i>High</i>	<ul style="list-style-type: none"> <li>• 5% wastage</li> </ul>	<ul style="list-style-type: none"> <li>• 5% wastage</li> </ul>			
<i>Medium</i>					
<i>Low</i>	<ul style="list-style-type: none"> <li>• 5% wastage</li> </ul>				
<b>Vaccine Details</b>					
<i>High</i>	<ul style="list-style-type: none"> <li>• 1 Dose per Course</li> </ul>	<ul style="list-style-type: none"> <li>• 1 Dose per Course</li> </ul>			
<i>Medium</i>					
<i>Low</i>	<ul style="list-style-type: none"> <li>• 1 Dose per Course</li> </ul>	<ul style="list-style-type: none"> <li>• 1 Dose per Course</li> </ul>			

## CHIK model

### CHIK Force of Infections (FoI)

The methods to derive the CHIK infection numbers are described in detail in the main text. However, this section provides some additional detail on how the FoI was estimated using the age-stratified seroprevalence data. FoI was defined as the annual probability of the susceptible population becoming infected. Because CHIK induces long-lasting antibodies, the proportion of seropositive individuals as a function of age can be used to reconstruct historical infection patterns<sup>74</sup>.

FoI was estimated from each seroprevalence dataset (33 locations from 10 countries) using a model that made four assumptions:

1. The risk of infection was not age-dependent
2. The risk of infection was potentially time-varying
3. There was no seroreversion (i.e., once a person tests positive for CHIK antibodies, they will continue testing positive for life)
4. There was no migration due to CHIK disease status

The Bayesian catalytic model has been built in Stan using the Hamiltonian Monte Carlo (HMC) algorithm for Markov chain Monte Carlo (MCMC) sampling. The model applied was inspired by the so-called ‘time-varying fast epidemic model – from the serofoi R package<sup>75</sup>. This model relies on a normal prior distribution for the FoI in the logarithmic scale in order to capture fast changes in CHIK epidemiology that is often observed in practice. The following priors were used for estimating the FoI:

$$\lambda(t=1) \sim \text{normal}(-6,4)$$

$$\lambda \sim \text{normal}(\log(\lambda(t-1)), \sigma)$$

$$\sigma \sim \text{half-Cauchy}(0,1)$$

where  $\lambda$  represents the FoI and denotes the standard deviation.

<sup>74</sup> Lim et al., 2023. Seroepidemiological reconstruction of long-term chikungunya virus circulation in Burkina Faso and Gabon.

<sup>75</sup> Carrera et al., 2020. Endemic and Epidemic Human Alphavirus Infections in Eastern Panama: An Analysis of Population-Based Cross-Sectional Surveys.

## CHIK-X model

CHIK-X was modelled on a global scale at the country level using an adapted metapopulation model which aimed to capture the explosiveness and unpredictable nature of CHIK with the intended disease-X modifications. CHIK-X spread was limited to two years after the initial outbreak.

Assumptions:

1. Similar transmission dynamics and geospatial constraints were assumed for this novel alphavirus
2. No immunity from previous CHIK vaccination or infection. Since CHIK-X is a sister group to the extant CHIK viruses, no immunity against it was assumed
3. No repeated outbreaks in countries. For every simulation, CHIK-X could cause one outbreak per country

### CHIK-X introduction

The probability of CHIK-X emergence was proportional to the estimates of global country-level CHIK incidence. The covariates from suitability (annual mean precipitation, minimum land surface temperature, maximum EVI, population density, elevation, and vector presence) were used to drive the incidence estimates. It was assumed that a greater abundance of virus would render the mutation giving rise to CHIK-X more likely. While estimates of historic incidence drove the probability of CHIK-X emergence, the population immunity was not taken into account. Higher vector density would make it more likely to pass the new variant. The starting location of the first outbreak was sampled with these weights (Figure A3.3).

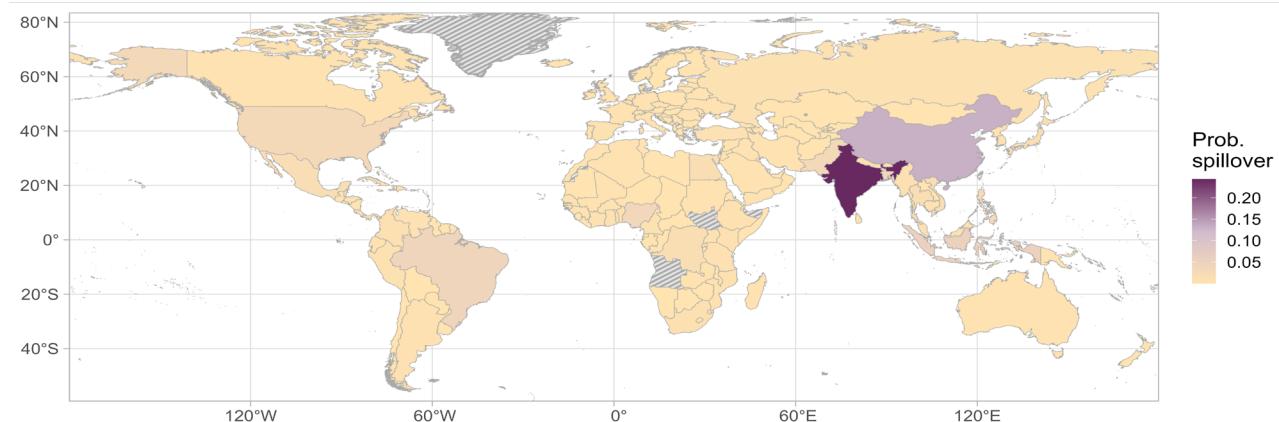


Figure A3.3: Probability of CHIK-X emergence was proportional to geospatially estimated annual CHIK incidence aggregated to country level.

### *CHIK-X spread between countries*

The number of infectious people in every country with an ongoing outbreak was calculated for every day of simulation. Infectiousness was assumed to last for seven days<sup>76</sup>. For every country where an outbreak has already started, the possibility of spread to other countries was evaluated as proportional to the number of infectious people who are travelling from a source to a destination. This was obtained by computing the proportion of infectious population (prevalence of the last seven days divided by populations size) and the number of trips per day between the source of CHIK-X and susceptible destination countries. The daily number of trips between a pair of countries was calculated from the annual number of trips from a data set of the Global Mobilities Project<sup>77</sup>. A random draw from the binomial distribution determined whether CHIK-X successfully spread to the potential destination.

### *CHIK-X outbreak establishment*

If CHIK-X was carried to a new country, the probability of an outbreak starting was given by the geospatial estimates of CHIK suitability (see main text). Similarly, to spread above, outbreak establishment was accepted or rejected based on a random draw from the binomial distribution. Figure A3.4 illustrates the variability in CHIK-X spread, with most simulations showing CHIK-X spread to fewer than 25 countries, while some outbreaks reached > 50 countries.

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76 Schwartz et al. 2010. Biology and pathogenesis of chikungunya virus.

77 Recchi et al., 2019. Estimating transnational human mobility on a global scale.

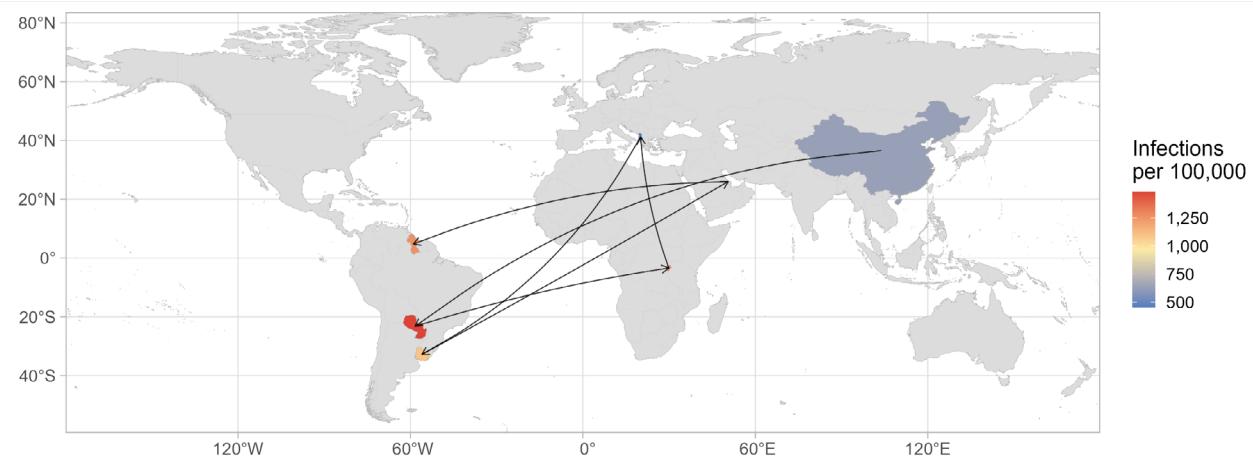
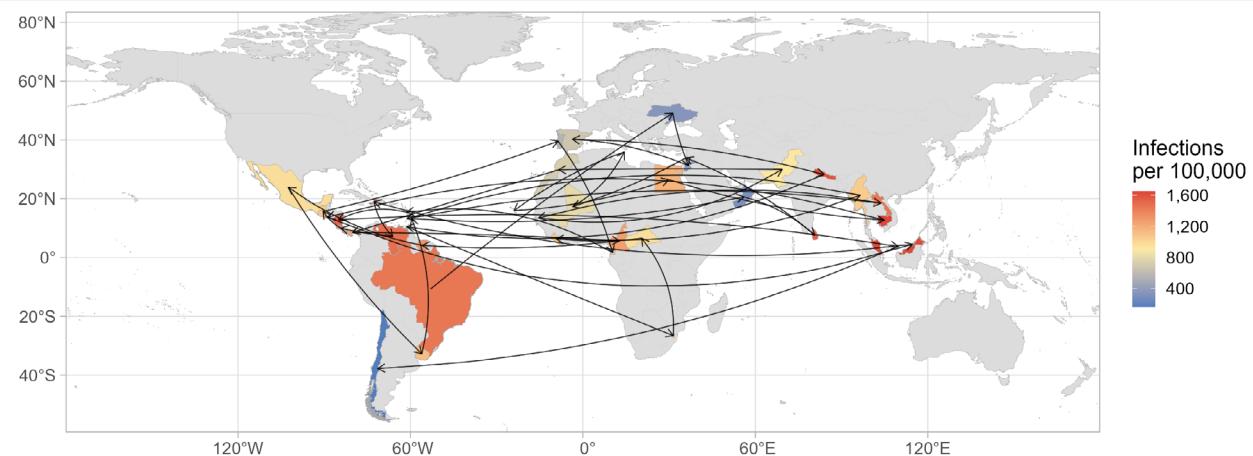
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Figure A3.4: Variability in global CHIK-X spread. Arrows indicate the temporal sequence of CHIK-X spread (not necessarily source-destination). Colors show the size of the outbreak as the number of infections per 100,000 population. (A) A simulation in which CHIK-X spreads to seven countries. (B) A simulation in which CHIK-X spreads to 41 countries.

### CHIK-X outbreak dynamics

CHIK-X transmission dynamics were not modelled in every country explicitly; instead, we used case reporting data from the Pan American Health Organization<sup>78</sup>. For every country, the outbreak size was scaled to match geospatial CHIK incidence estimates. The simulation resolution was daily and covered two years in total. However, individual outbreak duration, depending on the underlying PAHO curve shape, could exceed two years. Examples of the simulation output can be seen in Figure A3.5 below. Country names for the ISO codes given in Figure 7 are listed in Table A3.6.

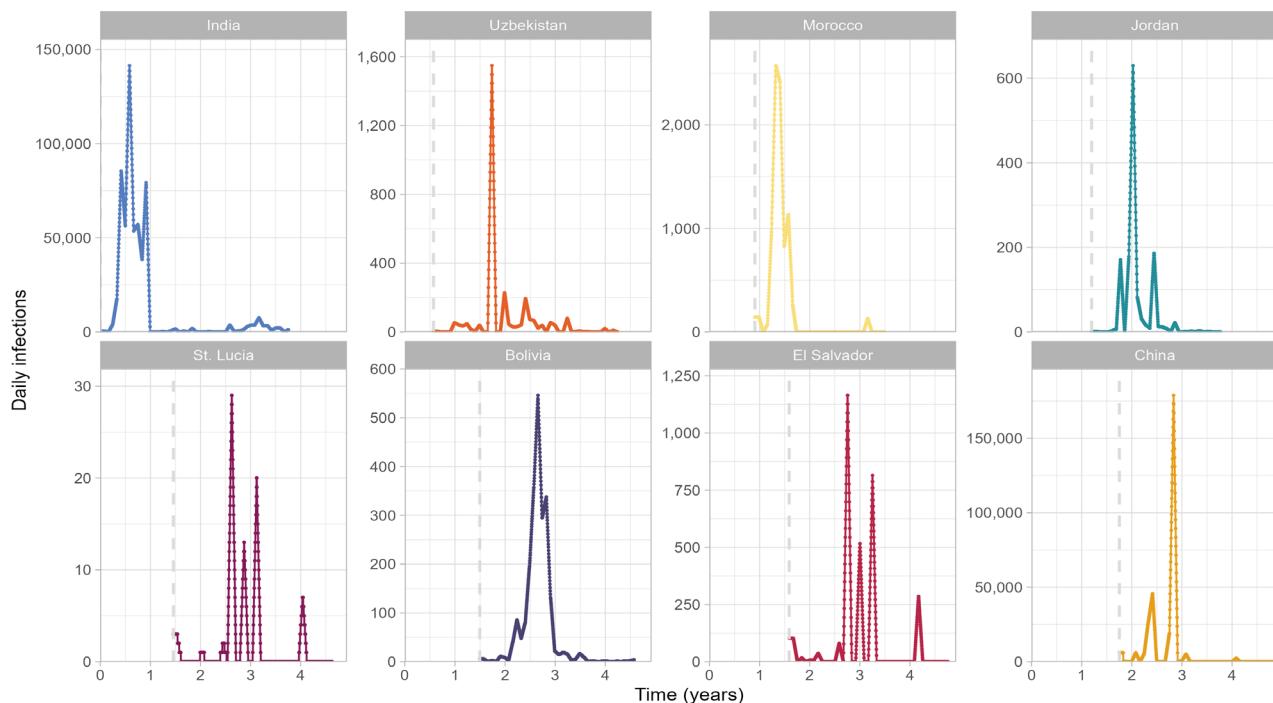


Figure A3.5: An example of a single CHIK-X simulation outbreak results. In this simulation, CHIK-X originated in India on day 0 and spread to seven other countries. Every panel shows the simulated daily infections (y-axis) over time (in years, x-axis). The grey dotted vertical line indicates the introduction of CHIK-X in a given country.

78 PAHO, 2018. Chikungunya fever in the Americas: Number of reported cases.

Table A3.6: Countries and ISO codes included in country-level reported case numbers between 2013-2017 from PAHO.

ISO	Country
ATG	Antigua and Barbuda
BOL	Bolivia
BRA	Brazil
BRB	Barbados
CRI	Costa Rica
DMA	Dominica
DOM	Dominican Republic
ECU	Ecuador
GRD	Grenada
GTM	Guatemala
GUF	French Guiana
HND	Honduras
KNA	St. Kitts and Nevis
LCA	St. Lucia
MEX	Mexico
NIC	Nicaragua
PAN	Panama
PER	Peru
PRI	Puerto Rico
PRY	Paraguay
SLV	El Salvador
SXM	Sint Maarten
TTO	Trinidad and Tobago
VEN	Venezuela
VIR	U.S. Virgin Islands

#### *Tuning the rate of spread to 2014-2016 Zika virus transmission*

According to Nextstrain data<sup>79</sup>, Zika virus spread to 35 countries between July 2014 and August 2016. We tuned the baseline spread rate to reflect this rate. To this end, the annual incidence was varied to modify outbreak sizes and, therefore, spread dynamics. As seen in Figure A3.6, outbreaks 0.7 times the CHIK burden estimates allowed for spread comparable to Zika virus spread. These outbreaks had the smallest mean absolute error (dotted line vs darker solid line, MAE = 2.45). The final outbreak size was determined by varying the new incidence values with 10% uniform noise. The amount of noise was fine-tuned similarly to before (Figure A3.6). This approach was preferred, as propagating the uncertainty around the annual CHIK incidence estimates and the suitability map coherently was not feasible.

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79 Hadfield et al., 2018. Nextstrain: Real-time tracking of pathogen evolution.

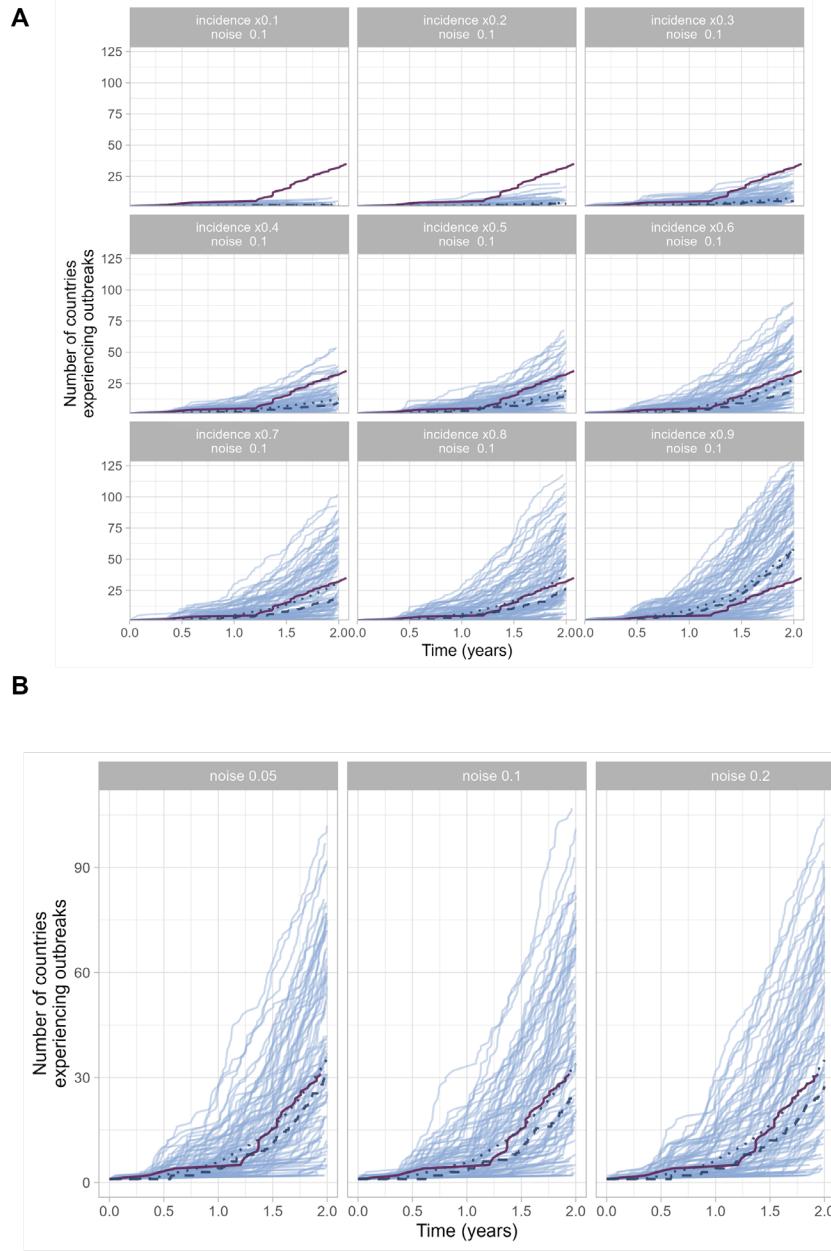


Figure A3.6: Every panel shows the number of countries affected over time across 100 different simulations. Zika virus spread over time shown as dark solid line. Lighter lines show the spread dynamics for an individual simulation. Dotted lines show mean cumulative number of countries experiencing outbreaks over time. Dashed lines show median cumulative number of countries experiencing outbreaks over time. (A) Outbreak size was varied by multiplying the estimated CHIK incidence by factors from 0.1 to 0.9. (B) Outbreak size was varied uniformly and symmetrically with window size indicated on panel.

### Selecting optimal number of simulations

To capture the variability underlying spread reasonably well, 100 simulations were run for every transmissibility scenario. Figure A3.7 shows that fewer than 100 simulations are susceptible to noise, while 1,000 simulations show saturation and redundancy.

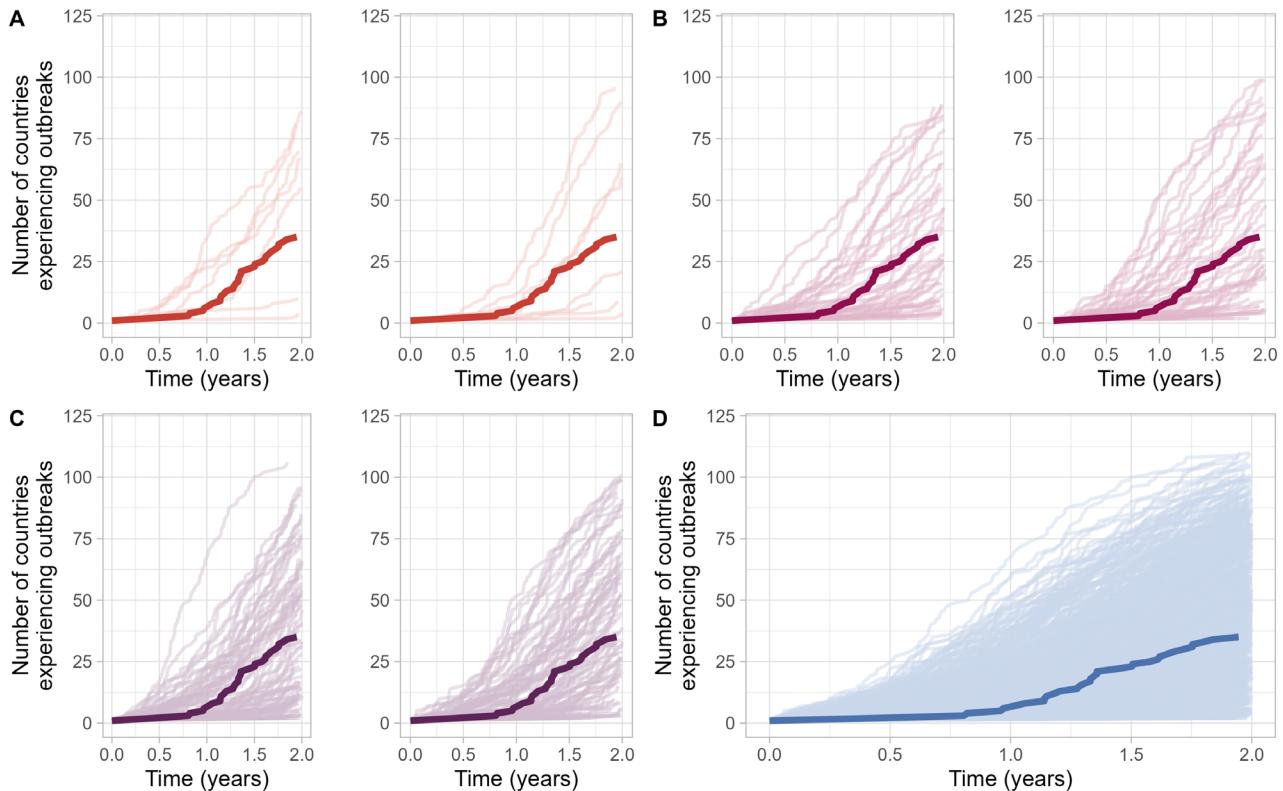


Figure A3.7: Selecting an optimal number of CHIK-X simulations to run. Cumulative number of infections (y-axis) over time (x-axis). Lighter lines show (A) 10 simulations, (B) 50 simulations, (C) 100 simulations, and (D) 1,000 simulations. Solid dark line shows the rate of Zika spread between 2014 and 2016.

## Health economics

Infection numbers produced by each of the five models were distributed into age- and sex-specific groups by applying a Dirichlet distribution to the observed case numbers during a CHIK outbreak in Brazil<sup>80</sup>. The uncertainty produced by the Dirichlet distribution was then scaled to each country's population pyramid and applied to their overall infection numbers ensuring total number of infections remain the same.

### *Chikungunya symptoms, disability weights, and the estimation of monetised disability-adjusted life years*

The disability-adjusted life year (DALY) is a synthetic indicator for measuring health effects generically, ranging from 0 to 1 (1 equals one year of healthy life lost). Developed by the World Bank in the early 90s, it is one of the most common metrics for estimating health impacts<sup>81</sup>. The DALY incorporates a measure of disease burden, in the form of disability and associated health disutility, and years of life lost prematurely<sup>82</sup>. For the estimation of CHIK-related health effects, we first reviewed the literature for evidence on clinical symptoms. Here, Silva et al. and Puntasecca et al. offered good insight into the symptoms that distinguish CHIK<sup>83, 84</sup>. We utilised the proportions of patients suffering mild, moderate, and severe CHIK in both acute and chronic phases in order to properly weight disability weights from Puntasecca et al. For the disutility of hospitalisation, we applied the weighting from Mora Salamanca et al. in order to capture the severity of chikungunya requiring hospitalisation<sup>85</sup>. Patients who have symptoms but don't go to hospital are assigned a disability weight associated with fever and a 90% likelihood of severe arthralgia (0.525) for a mean duration of 6.28 days. Patients who have symptoms and do go to hospital are assigned a mean disability weight of 0.808 for a mean duration of 6.28 days pre-hospitalisation and a mean hospital stay of 5.19 days. Of all those CHIK patients who survive symptoms, independent of hospitalisation, 51% suffer from rheumatoid arthritis symptoms associated with a mean disability weight of 0.476 for a mean of 1.32 years.

Additionally, non-survivors were assigned a full DALY for each year of their remaining age-specific life expectancy. Two separate approaches were used to estimate the cost per DALY based on the income group of each country. One approach for low and lower middle-income countries was based on the methodology used in Ochalek et al. where DALYs averted for a 1% change in health expenditure are calculated by the product of the estimated DALY burden for that country and the estimated elasticity<sup>86</sup>. The estimates produced in Ochalek et al. of the cost per DALY averted for each country expressed as a percentage of GDP per capita was then multiplied by GDP per capita of each country to reach a 2021 estimate of cost per DALY. For countries not relevant to the Ochalek

80 de Souza et al., 2023. Spatiotemporal dynamics and recurrence of chikungunya virus in Brazil: an epidemiological study.

81 Berkley et al., 1993. World development report 1993: investing in health.

82 Disability-Adjusted Life-Years (DALYs) [online], 2016. York; York Health Economics Consortium; 2016. <https://yhec.co.uk/glossary/disability-adjusted-life-years-dalys>

83 Silva et al., 2021. Risk of chronic arthralgia and impact of pain on daily activities in a cohort of patients with chikungunya virus infection from Brazil.

84 Puntasecca et al., 2021. Measuring the global burden of chikungunya and Zika viruses: A systematic review.

85 Mora-Salamanca et al., 2020. Estimating the burden of arboviral diseases in Colombia between 2013 and 2016.

86 Ochalek et al., 2020. Valuing health outcomes: Developing better defaults based on health opportunity costs.

et al. approach given their income status as high or upper middle income, a simpler approach to calculate monetised DALYs was used where the cost of a DALY was estimated to be 50% of GDP per capita, based on an analysis that finds that this method is relatively accurate for higher income countries than for lower income countries. Future monetised DALYs were discounted at a rate of 3%.

#### *Hospital treatment costs*

In our analysis, hospitalisations costs were based on a study in Colombia by Alvis-Zakzuk et al. which reported treatment costs in 2014 I\$<sup>87</sup>. These were adjusted to 2021 PPP I\$. The cost-adjustment was done using the PPP conversion factor and the GDP deflator based on World Bank data<sup>88</sup>.

#### *Out-of-pocket treatment costs*

The estimation of individual OOP expenditures for chikungunya treatment is based on Alvis-Zakzuk et al., who reported the medical cost of treatment in four hospitals in Colombia<sup>87</sup>. We took the total direct cost of \$71.6 in 2014 I\$, and then adjusted to 2021 PPP I\$ using the same method employed for adjusting treatment cost estimates. Second, we sourced World Bank data on current health expenditure per capita (in 2019 PPP I\$) and OOP expenditure (as a percentage of current health expenditure), which were equally adjusted to 2021 PPP I\$, and compared the estimated per capita OOP expenditure with the OOP expenditure from Alvis-Zakzuk et al<sup>87,88</sup>.

#### *Risk of catastrophic/impoverishing healthcare expenditures*

An important consideration when vaccinating individuals is to optimise overall population health, a target underpinning cost-effectiveness analyses focusing on how to best allocate a limited healthcare budget. Also, it is important to increasingly recognise the importance of tackling inequality and the occurrence of large OOP expenses that can be classified as catastrophic healthcare expenditures or lead to impoverishment. The estimation of the number of individuals at risk of either catastrophic or impoverishing healthcare expenditures is based on estimated country-specific per capita out-of-pocket expenditure for Lassa fever treatment. Catastrophic healthcare expenditures are defined based in the Sustainable Development Goal 3.8.2 (catastrophic health spending), which outlines that a “population with household expenditures on health greater than 10% of total household expenditure or income” are at risk of experiencing catastrophic health spending<sup>89</sup>.

First, we extrapolated from the above, that given catastrophic healthcare expenditure is 10% (or more) of income, then if OOP expenditure divided by an individual’s income is greater than 10%, that individual is at risk of catastrophic healthcare expenditure. We assumed that healthcare expenditure would be divided over a month and utilised the *pipr* package in R which scrapes data from the World Bank Poverty and Inequality Platform (WB PIP) to estimate the number of individuals that live below the calculated country-specific income thresholds under which an individual would be at risk of catastrophic health expenditure<sup>90</sup>. Scraping the WP PIP database for ‘headcount’ gives the proportion of the population at risk. Second, we repeated this exercise

<sup>87</sup> Alvis-Zakzuk et al., 2018. Economic costs of chikungunya virus in Colombia.

<sup>88</sup> World Bank, 2023. World Bank Open Data [online]; <https://data.worldbank.org>

<sup>89</sup> WHO, 2023. The Global Health Observatory. SDG 3.8.2 Catastrophic health spending (and related indicators).

<sup>90</sup> Fujs et al. 2022. pipr: Client for the PIP API (<https://worldbank.github.io/pipr/>).

with an altered threshold of OOP/30 + 2.15 PPP I\$ (i.e., the international poverty line), to estimate the number of individuals who if forced to pay estimated OOP expenditure would fall below the poverty line. The proportion of individuals at risk of impoverishing expenditure is the proportion of the population that falls below this country-specific threshold.

#### *Productivity losses*

Productivity loss due to CHIK was estimated for non-hospitalised, hospitalised, and deceased working age (16-64 years) individuals using data on labour force participation (International Labour Organisation data<sup>91</sup>) and 2021 PPP I\$ estimates on GNI (World Bank data<sup>94</sup>). Total productivity loss equated to the product of the probability of participating in the labour force, the daily GNI, and the number of sick leave days, which were assumed given the duration parameters of acute disease and hospitalisation. For deceased individuals, total productivity loss was estimated by the product of the probability of participating in the labour force, the annual GNI, and the number of years left to work. The number of years left to work were estimated based on the difference between the maximum age (retirement age) and the weighted country-specific average age in the working age cohort. Due to the lack of data on projected wage growth in the countries of interest, wages (proxied through GNI) were held constant over the time horizon of the analysis.

#### *Value of Statistical Life*

The conceptual idea underlying the value of statistical life (VSL) method is to estimate an individual's willingness to pay for a reduction in the probability of dying, which is then averaged across all individuals to estimate the value of preventing one death. To produce global estimates of the VSL, we applied the methodology developed in 2019 by a global expert group of benefit-cost researchers<sup>92</sup>. This methodology is also available in a special issue of the *Journal of Benefit-Cost Analysis*<sup>93</sup>. The reference point of this approach is the recently updated U.S. Department of Health & Human Services VSL estimate of \$12.3 million (2022 US\$). Due to the limited availability of direct VSL estimates in LMICs, we applied the value-transfer method outlined in the Reference Case Guidelines for Benefit-Cost Analysis in Global Health and Development.

We used the following formula to compute the VSL of all non-U.S. countries:

$$VSL_x = VSL_{USA} \times (GNI\ pC_x \div GNI\ pC_{USA})_E$$

where VSL<sub>x</sub> is the unknown VSL of country x, VSL USA is the VSL of the United States (\$12.3 million), and GNI pC is the 2021 gross national income per capita (PPP) of country x or the United States, as applicable. GNI pC data were obtained from the World Bank<sup>94</sup>. E denotes the income elasticity of VSL, i.e., the percentage change in VSL associated with a 1% change in real income. The value-transfer method adjusts VSL from the US setting to lower-income settings based on the income ratio between the target and reference countries.

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91 ILO, 2023. ILOSTAT. Labour Force Statistics.

92 Robinson et al., 2019. Reference case guidelines for benefit-cost analysis in global health and development.

93 Robinson et al., 2019. Special Issue – Benefit-cost analysis in low- and middle- income countries: Methods and case studies.

94 World Bank, 2023. World Bank Open Data [online]; <https://data.worldbank.org>.

The ratio is raised to the income elasticity for the value of reducing mortality risk, which is estimated at 1.2 for middle-income countries, 1.5 for low-income countries, and 1.0 for other high-income countries. World Bank 2021 definitions of country income group classifications were used throughout our analysis.

## Data Sources

Data for economic analyses were obtained from the sources listed in below Tables A3.6 and A3.7, which include values for specific parameters, and sources and descriptions for economic parameters. Where economic parameters for particular countries could not be sourced through below sources, data was sourced from peer reviewed literature, or proxy countries were used.

Table A3.7: Disease-specific parameter values and data sources.

Parameter	Mean, UI	Author	Source
Probability symptomatic (base case)	0.18 (0.12, 0.25)	Yoon et al., 2015	High rate of subclinical chikungunya virus infection and association of neutralizing antibody with protection in a prospective cohort in the Philippines. <i>PLoS Negl Trop Dis</i>
Probability symptomatic (sensitivity analysis)	0.46 (0.39, 0.53)	Carrillo et al., 2022	Epidemics of chikungunya, Zika, and COVID-19 reveal bias in case-based mapping. <i>medRxiv</i>
Probability chronic	0.51 (0.58, 0.45)	Kang et al., 2024	Chikungunya seroprevalence, force of infection, and prevalence of chronic disability in endemic and epidemic settings: Systematic review, meta-analysis, and modelling study. <i>Lancet Infectious Dis</i>
Probability seeking any treatment	0.26 (0.22, 0.31)	Paul et al., 2020	Comparing insights from clinic-based versus community-based outbreak investigations: a case study of chikungunya in Bangladesh. <i>Intern J of Infectious Dis</i>
Of any treatment, probability seeking govt treatment	0.53 (0.44, 0.62)	Paul et al., 2020	Comparing insights from clinic-based versus community-based outbreak investigations: a case study of chikungunya in Bangladesh. <i>Intern J of Infectious Dis</i>
Probability of death	Age- and sex-dependent Mean across groups: 0.0022 (range: 0.0004 - 0.0073)	de Souza et al., 2023	Spatiotemporal dynamics and recurrence of chikungunya virus in Brazil: an epidemiological study. <i>Lancet Microbe</i>
Probability hospitalisation (aggregated across all age groups)	0.04 (0.03, 0.05)	Kang et al., 2024	Chikungunya seroprevalence, force of infection, and prevalence of chronic disability in endemic and epidemic settings: Systematic review, meta-analysis, and modelling study. <i>Lancet Infectious Dis</i>

Parameter	Mean, UI	Author	Source
Probability of hospitalised cases belonging to different age- and sex- groups	Age- and sex-dependent Mean across groups: 0.056 (range: 0.022 - 0.120)	Torales et al., 2023	Notes from the field: Chikungunya Outbreak — Paraguay, 2022–2023. <i>MMWR Morb Mortal Wkly Report</i>
Duration of acute (days)	6.30 (4.29, 13.31)	Sharp et al., 2016.	Surveillance for chikungunya and dengue during the first year of chikungunya virus circulation in Puerto Rico. <i>J Infect Dis</i> .
Duration of hospitalisation (days)	5.22 (2, 12)	Soumahoro et al., 2011	The chikungunya epidemic on La Réunion Island in 2005–2006: A cost-of-illness study. <i>PLoS Negl Trop Dis</i>
Duration chronic (years)	1.48 (0.29, 3.8)	Kang et al., 2024	Chikungunya seroprevalence, force of infection, and prevalence of chronic disability in endemic and epidemic settings: Systematic review, meta-analysis, and modelling study. <i>Lancet Infectious Dis</i>
Disability weight acute	0.518 (0.040, 0.771)	Puntasecca et al., 2021 weighted by Monaíse et al., 2021	Puntasecca: Measuring the global burden of chikungunya and Zika viruses: A systematic review. <i>PLoS Negl Trop Dis</i>  Monaíse: Risk of chronic arthralgia and impact of pain on daily activities in a cohort of patients with chikungunya virus infection from Brazil. <i>Intern J of Infectious Dis</i>
Disability weight hospitalisation	0.81 (0.6, 0.92)	Mora-Salamanca et al., 2020	Estimating the burden of arboviral diseases in Colombia between 2013 and 2016. <i>Intern J of Infectious Dis</i>
Disability weight chronic	0.478 (0.21, 0.729)	Puntasecca et al., 2021 weighted by Monaíse et al., 2021	Puntasecca: Measuring the global burden of chikungunya and Zika viruses: A systematic review. <i>PLoS Negl Trop Dis</i>  Monaíse: Risk of chronic arthralgia and impact of pain on daily activities in a cohort of patients with chikungunya virus infection from Brazil. <i>Intern J of Infectious Dis</i>

Table A3.8: Country-specific economic parameter and population data sources.

Parameter	Source	Description
Proportion of population working	ILO, 2023	ILOSTAT. Labour Force Statistics
Monetised DALY parameters	Ochalek et al., 2018	Estimating health opportunity costs in low-income and middle-income countries: A novel approach and evidence from cross-country data
Monetised DALY parameters	Ochalek et al., 2021	Estimating health opportunity costs by income group.
Hospitalisation cost	Alvis-Zakzuk et al., 2018	Estimating the economic impact of chikungunya
Age and life expectancy parameters	UN, 2023	World Population Prospects 2022. Department of Economic and Social Affairs. Population Division.
Outpatient costs	WHO, 2021	WHO-CHOICE estimates of cost for inpatient and outpatient health service delivery
Proportion of population living below poverty line and ‘catastrophic health expenditure line’	World Bank, 2023	Poverty and Inequality Platform
Other economic parameters including GDP per capita, GINI per capita and health expenditure.	World Bank, 2023	World Bank Open Data
Population	World Pop	Unconstrained, 1km resolution, UN-adjusted population counts

## Appendix 4. Supplementary Results

This section provides supplementary results from the CHIK and CHIK-X analyses.

### Chikungunya supplementary results

Table A4.1: Considering OxLIV 1 infection incidence estimates, the estimated health outcomes (Mean, 2.5% - 97.5% UI) of chikungunya at baseline over 16 years for countries included in vaccination scenarios.

<b>Country</b>	<b>Symptomatic cases</b>	<b>Hospitalisations</b>	<b>Deaths</b>	<b>Sequelae</b>	<b>DALYs</b>
Bangladesh	5.1M (3.2M-7.1M)	203.8K (126.6K-305.6K)	11.2K (4.8K-23.1K)	2.6M (1.6M-3.6M)	3.3M (284.0K-18.0M)
Bolivia	160.4K (100.9K-226.9K)	6.5K (4.0K-9.7K)	355.0 (151.1-744.4)	82.0K (51.9K-114.7K)	102.7K (8.3K-569.2K)
Brazil	5.5M (3.4M-7.7M)	220.9K (137.2K-331.3K)	12.2K (5.3K-23.4K)	2.8M (1.8M-3.9M)	3.6M (308.7K-19.5M)
Barbados	6.7K (4.2K-9.5K)	271.9 (168.8-407.7)	15.1 (5.8-30.1)	3.4K (2.2K-4.8K)	4.4K (408.1-24.1K)
Bhutan	18.0K (11.3K-25.4K)	725.2 (450.4-1.1K)	40.4 (17.7-80.3)	9.2K (5.8K-12.9K)	11.6K (986.6-63.9K)
China	12.0M (7.6M-17.0M)	485.6K (301.6K-728.3K)	27.4K (11.0K-54.5K)	6.2M (3.9M-8.6M)	7.9M (739.4K-43.0M)
Republic of Congo	78.9K (49.7K-111.7K)	3.2K (2.0K-4.8K)	174.3 (62.3-376.6)	40.4K (25.5K-56.4K)	50.7K (3.9K-280.0K)
Colombia	1.3M (799.9K-1.8M)	51.3K (31.9K-77.0K)	2.8K (1.2K-5.6K)	650.1K (411.2K-909.6K)	825.4K (71.8K-4.5M)

<b>Country</b>	<b>Symptomatic cases</b>	<b>Hospitalisations</b>	<b>Deaths</b>	<b>Sequelae</b>	<b>DALYs</b>
Costa Rica	123.0K (77.4K-174.0K)	5.0K (3.1K-7.4K)	277.0 (121.5-541.2)	62.9K (39.8K-88.0K)	80.1K (7.2K-438.7K)
Dominican Republic	306.0K (192.5K-432.9K)	12.3K (7.7K-18.5K)	684.2 (289.5-1.4K)	156.4K (98.9K-218.8K)	199.5K (18.2K-1.1M)
Ethiopia	963.0K (605.7K-1.4M)	38.9K (24.1K-58.3K)	2.1K (742.8-4.6K)	492.2K (311.4K-688.4K)	620.6K (49.9K-3.4M)
Gabon	52.1K (32.8K-73.7K)	2.1K (1.3K-3.2K)	116.1 (43.1-242.0)	26.6K (16.8K-37.2K)	33.6K (2.7K-184.9K)
Guatemala	401.9K (252.8K-568.5K)	16.2K (10.1K-24.3K)	882.8 (353.4-1.9K)	205.4K (129.9K-287.3K)	260.3K (22.0K-1.4M)
Honduras	239.9K (150.9K-339.3K)	9.7K (6.0K-14.5K)	529.6 (213.0-1.2K)	122.6K (77.6K-171.5K)	154.7K (12.6K-851.9K)
Haiti	358.9K (225.8K-507.7K)	14.5K (9.0K-21.7K)	790.2 (325.5-1.7K)	183.5K (116.1K-256.6K)	230.7K (18.7K-1.3M)
Indonesia	8.2M (5.1M-11.5M)	329.1K (204.4K-493.5K)	18.3K (7.6K-36.4K)	4.2M (2.6M-5.8M)	5.2M (438.2K-29.0M)
India	38.2M (24.0M-54.0M)	1.5M (956.4K-2.3M)	85.8K (36.3K-170.9K)	19.5M (12.3M-27.3M)	24.6M (2.1M-135.6M)
Kenya	890.6K (560.1K-1.3M)	35.9K (22.3K-53.9K)	1.9K (682.4-4.2K)	455.2K (287.9K-636.5K)	573.5K (46.1K-3.2M)
Cambodia	198.4K (124.8K-280.7K)	8.0K (5.0K-12.0K)	438.8 (177.3-870.1)	101.4K (64.2K-141.9K)	128.2K (10.9K-705.6K)

<b>Country</b>	<b>Symptomatic cases</b>	<b>Hospitalisations</b>	<b>Deaths</b>	<b>Sequelae</b>	<b>DALYs</b>
Laos	86.1K (54.2K-121.8K)	3.5K (2.2K-5.2K)	190.7 (78.2-409.5)	44.0K (27.8K-61.6K)	55.5K (4.6K-305.8K)
Mexico	2.7M (1.7M-3.8M)	107.9K (67.0K-161.9K)	6.0K (2.6K-12.0K)	1.4M (864.9K-1.9M)	1.7M (151.6K-9.5M)
Malaysia	357.9K (225.1K-506.2K)	14.4K (9.0K-21.7K)	804.7 (347.5-1.6K)	182.9K (115.7K-255.9K)	232.4K (20.4K-1.3M)
Nicaragua	173.2K (109.0K-245.0K)	7.0K (4.3K-10.5K)	381.7 (162.4-805.4)	88.5K (56.0K-123.9K)	112.4K (9.6K-616.1K)
Nepal	1.1M (676.9K-1.5M)	43.4K (27.0K-65.1K)	2.4K (992.1-5.2K)	550.1K (348.0K-769.5K)	692.8K (57.1K-3.8M)
Pakistan	6.7M (4.2M-9.5M)	271.7K (168.7K-407.4K)	14.9K (5.7K-32.0K)	3.4M (2.2M-4.8M)	4.3M (351.9K-23.9M)
Panama	102.0K (64.2K-144.3K)	4.1K (2.6K-6.2K)	229.0 (98.1-457.3)	52.1K (33.0K-72.9K)	66.8K (6.3K-363.8K)
Peru	675.5K (424.8K-955.4K)	27.3K (16.9K-40.9K)	1.5K (649.9-3.0K)	345.2K (218.4K-483.0K)	437.9K (38.8K-2.4M)
Philippines	1.1M (711.2K-1.6M)	45.6K (28.3K-68.4K)	2.5K (1.1K-5.1K)	578.0K (365.6K-808.5K)	727.5K (59.4K-4.0M)
Paraguay	196.3K (123.4K-277.6K)	7.9K (4.9K-11.9K)	436.8 (184.6-890.2)	100.3K (63.5K-140.3K)	126.8K (10.9K-697.7K)
Sudan	650.6K (409.2K-920.2K)	26.2K (16.3K-39.4K)	1.4K (515.6-3.1K)	332.5K (210.4K-465.1K)	419.7K (33.7K-2.3M)

<b>Country</b>	<b>Symptomatic cases</b>	<b>Hospitalisations</b>	<b>Deaths</b>	<b>Sequelae</b>	<b>DALYs</b>
Sierra Leone	161.0K (101.3K-227.7K)	6.5K (4.0K-9.7K)	354.3 (125.5-768.2)	82.3K (52.1K-115.1K)	103.4K (8.2K-571.0K)
El Salvador	173.9K (109.4K-246.0K)	7.0K (4.4K-10.5K)	380.9 (159.8-795.5)	88.9K (56.2K-124.4K)	112.6K (9.8K-619.2K)
Suriname	15.6K (9.8K-22.1K)	631.3 (392.1-946.8)	34.9 (15.0-69.8)	8.0K (5.1K-11.2K)	10.1K (881.5-55.7K)
Thailand	2.3M (1.4M-3.2M)	90.8K (56.4K-136.2K)	5.1K (1.9K-10.2K)	1.2M (728.0K-1.6M)	1.5M (151.7K-8.1M)
Venezuela	796.2K (500.8K-1.1M)	32.1K (20.0K-48.2K)	1.8K (757.2-3.6K)	406.9K (257.5K-569.3K)	515.4K (45.1K-2.8M)
Vietnam	1.0M (642.9K-1.4M)	41.2K (25.6K-61.8K)	2.3K (953.8-4.2K)	522.4K (330.5K-731.0K)	664.4K (59.2K-3.6M)
Yemen	725.5K (456.3K-1.0M)	29.3K (18.2K-43.9K)	1.6K (539.9-3.5K)	370.8K (234.6K-518.6K)	466.5K (37.0K-2.6M)

Table A4.2: Considering OxLiv 1 infection incidence estimates, the estimated economic costs (\$I\$ 2021) of chikungunya at baseline over 16 years for countries included in vaccination scenarios. Future costs are discounted at 3% per year.

<b>Country</b>	<b>Societal cost</b>	<b>Monetised DALYs</b>	<b>VSL</b>
Bangladesh	316.6M (134.5M-606.6M)	740.9M (57.3M-4.0B)	7.8B (3.4B-16.2B)
Bolivia	17.2M (7.7M-33.1M)	240.7M (16.8M-1.3B)	328.0M (139.6M-687.7M)
Brazil	970.4M (421.4M-1.8B)	19.2B (1.5B-104.3B)	23.0B (10.1B-44.1B)
Barbados	1.4M (614.3K-2.6M)	28.9M (2.3M-156.8M)	26.7M (10.2M-53.2M)
Bhutan	2.2M (896.8K-4.1M)	8.2M (622.9K-44.3M)	51.4M (22.5M-102.1M)
China	2.4B (964.2M-4.6B)	46.0B (3.7B-249.1B)	66.1B (26.4B-131.3B)
Republic of Congo	2.5M (1.2M-4.9M)	77.7M (5.4M-423.9M)	52.7M (18.9M-113.9M)
Colombia	224.6M (91.1M-419.2M)	6.1B (479.9M-32.9B)	5.7B (2.5B-11.2B)
Costa Rica	30.6M (13.5M-56.6M)	1.1B (91.6M-6.2B)	779.5M (342.0M-1.5B)
Dominican Republic	65.7M (28.9M-120.2M)	724.6M (58.7M-3.9B)	1.7B (709.8M-3.4B)
Ethiopia	28.4M (13.7M-55.1M)	158.7M (11.3M-864.4M)	449.4M (157.6M-983.9M)
Gabon	5.2M (2.4M-10.1M)	80.2M (5.6M-436.5M)	172.4M (64.0M-359.3M)
Guatemala	38.1M (17.3M-69.2M)	421.4M (30.9M-2.3B)	927.0M (371.1M-2.0B)
Honduras	14.4M (6.6M-26.9M)	296.2M (21.2M-1.6B)	292.8M (117.8M-645.5M)
Haiti	11.4M (5.6M-21.3M)	68.1M (4.8M-371.7M)	219.0M (90.2M-469.5M)

Country	Societal cost	Monetised DALYs	VSL
Indonesia	1.1B (477.9M-2.1B)	3.7B (270.8M-20.0B)	26.8B (11.2B-53.5B)
India	2.4B (1.0B-4.4B)	9.4B (708.0M-51.1B)	63.1B (26.7B-125.8B)
Kenya	50.1M (22.9M-94.2M)	431.6M (30.3M-2.3B)	964.9M (338.2M-2.1B)
Cambodia	11.7M (5.5M-21.5M)	33.6M (2.5M-182.7M)	187.8M (75.9M-372.4M)
Laos	6.8M (3.0M-13.1M)	30.3M (2.2M-164.8M)	163.5M (67.0M-351.2M)
Mexico	545.7M (235.6M-971.8M)	11.5B (912.6M-62.4B)	14.9B (6.4B-29.9B)
Malaysia	103.1M (42.6M-190.0M)	1.2B (94.1M-6.4B)	3.7B (1.6B-7.2B)
Nicaragua	11.0M (4.9M-20.5M)	202.4M (15.1M-1.1B)	219.2M (93.2M-462.5M)
Nepal	33.9M (16.4M-60.7M)	237.9M (17.6M-1.3B)	927.5M (390.1M-2.0B)
Pakistan	325.9M (147.6M-643.1M)	601.7M (43.5M-3.3B)	8.3B (3.2B-17.9B)
Panama	31.5M (12.9M-59.2M)	827.8M (69.2M-4.5B)	1.1B (475.5M-2.2B)
Peru	99.7M (41.5M-184.8M)	1.9B (151.7M-10.4B)	2.2B (963.2M-4.4B)
Philippines	96.9M (44.1M-183.9M)	599.3M (42.4M-3.3B)	2.5B (1.1B-5.1B)
Paraguay	34.1M (15.2M-62.5M)	625.0M (47.1M-3.4B)	759.4M (321.0M-1.5B)
Sudan	21.8M (10.5M-42.2M)	38.8M (2.8M-211.0M)	512.6M (184.5M-1.1B)
Sierra Leone	3.0M (1.5M-5.6M)	8.0M (559.6K-43.7M)	15.9M (5.6M-34.6M)
El Salvador	19.2M (9.1M-33.9M)	318.3M (25.1M-1.7B)	391.5M (164.2M-817.6M)

<b>Country</b>	<b>Societal cost</b>	<b>Monetised DALYs</b>	<b>VSL</b>
Suriname	2.3M (1.1M-4.1M)	18.9M (1.5M-102.8M)	58.1M (25.0M-116.3M)
Thailand	479.2M (202.0M-928.4M)	7.4B (669.9M-40.0B)	11.4B (4.4B-22.9B)
Venezuela	106.1M (44.8M-196.3M)	322.1M (24.9M-1.8B)	3.0B (1.3B-6.0B)
Vietnam	139.6M (57.6M-260.0M)	535.0M (43.0M-2.9B)	2.8B (1.2B-5.3B)
Yemen	14.3M (7.5M-25.9M)	40.2M (2.8M-219.2M)	21.3M (7.2M-46.7M)

Table A4.3: Key health economic outcomes averted in the Market High vaccine scenario across all five models at vaccine efficacy 70%. The table shows the sensitivity of these outcomes to the probability symptomatic parameter, by comparing the ‘higher’ estimate with the ‘lower’ baseline estimate.

Health Outcome	Probability Symptomatic	OxLiv 1	OxLiv 2	OxLiv 3	OxLiv 4	Salje et al.
Symptomatic cases	0.46 (Carillo et al.) <sup>95</sup>	23.2M (20.1M-26.6M)	27.2M (23.7M-31.0M)	34.1M (29.5M-39.2M)	47.2M (41.1M-53.8M)	17.2M (14.8M-19.6M)
	0.18 (Yoon et al.) <sup>96</sup>	9.2M (5.8M-12.9M)	10.8M (6.9M-15.3M)	13.6M (8.6M-19.0M)	18.8M (11.9M-26.5M)	6.8M (4.3M-9.6M)
DALYs	0.46 (Carillo et al.)	15.0M (1.3M-90.9M)	17.6M (1.5M-107.3M)	22.1M (1.9M-133.8M)	30.5M (2.6M-186.0M)	11.1M (931.3K-66.4M)
	0.18 (Yoon et al.)	5.9M (461.9K-32.4M)	6.9M (540.6K-38.0M)	8.7M (680.7K-47.7M)	12.0M (940.3K-65.9M)	4.4M (346.7K-24.3M)
Societal costs	0.46 (Carillo et al.)	2.1B (956.4M-3.8B)	2.5B (1.1B-4.5B)	3.2B (1.4B-5.7B)	4.4B (2.0B-8.0B)	1.7B (779.9M-3.2B)
	0.18 (Yoon et al.)	841.1M (356.3M-1.5B)	982.3M (427.4M-1.8B)	1.3B (531.3M-2.3B)	1.7B (757.2M-3.2B)	673.3M (280.1M-1.3B)

<sup>95</sup> Carrillo et al., 2022. Epidemics of chikungunya, Zika, and COVID-19 reveal bias in case-based mapping.

<sup>96</sup> Yoon et al., 2015. High rate of subclinical chikungunya virus infection and association of neutralizing antibody with protection in a prospective cohort in the Philippines.

Table A4.4: Key health economic outcomes averted in the Market High vaccine scenario across OxLiv models 2 and 4 at vaccine efficacy (VE) 80% and 90%. The table shows the sensitivity of these outcomes to the seroprevalence estimate, by comparing the ‘baseline’ estimate with the ‘Skalinski’ estimate<sup>97</sup>.

<b>Health economic outcome</b>	<b>Seroprevalence estimate</b>	<b>VE (%)</b>	<b>OxLiv 2</b>	<b>OxLiv 4</b>
Symptomatic cases	Baseline	80	10.5M (6.7M-14.8M)	12.4M (7.9M-17.5M)
		90	11.8M (7.5M-16.6M)	13.9M (8.8M-19.6M)
	Skalinski	80	9.9M (6.3M-13.9M)	11.5M (7.3M-16.3M)
		90	11.2M (7.1M-15.7M)	13.0M (8.2M-18.3M)
DALYs	Baseline	80	6.7M (527.9K-37.0M)	7.9M (617.9K-43.4M)
		90	7.6M (593.9K-41.6M)	8.9M (695.1K-48.8M)
	Skalinski	80	6.4M (498.2K-34.9M)	7.4M (577.2K-40.5M)
		90	7.2M (560.5K-39.3M)	8.3M (649.3K-45.6M)
Societal costs	Baseline	80	961.3M (407.2M-1.7B)	1.1B (488.5M-2.1B)
		90	1.1B (458.1M-2.0B)	1.3B (549.6M-2.3B)
	Skalinski	80	917.3M (388.6M-1.7B)	1.1B (461.8M-2.0B)
		90	1.0B (437.2M-1.9B)	1.2B (519.5M-2.2B)

<sup>97</sup> Skalinski et al., 2023. Chikungunya seroprevalence in population-based studies: A systemic review and meta-analysis.

## CHIK-X supplementary results

Table A4.5: Considering disease severity scenario B, the estimated health outcomes (Mean, 2.5% - 97.5% UI) of CHIK-X at baseline over all simulations, with each country adjusted for the proportion of outbreaks experienced in all simulations.

Country	Symptomatic Cases	Hospitalisations	Deaths	Sequelae	DALYs
India	3.4M (2.9M-4.1M)	695.9K (502.7K-910.7K)	38.7K (18.2K-71.4K)	1.7M (1.4M-2.1M)	2.6M (470.2K-14.1M)
China	1.3M (1.1M-1.6M)	271.8K (195.4K-355.4K)	15.3K (6.7K-27.5K)	681.9K (537.7K-834.0K)	1.1M (222.7K-5.7M)
Indonesia	654.3K (542.3K-781.2K)	132.2K (95.3K-173.4K)	7.3K (3.4K-13.5K)	331.6K (261.4K-407.9K)	497.5K (86.0K-2.7M)
Brazil	530.6K (442.1K-629.3K)	107.2K (77.8K-139.9K)	5.9K (2.7K-10.3K)	268.9K (212.9K-328.6K)	418.4K (80.4K-2.2M)
Bangladesh	493.8K (410.2K-589.6K)	99.7K (71.9K-130.5K)	5.5K (2.5K-10.4K)	250.3K (198.1K-307.9K)	391.5K (74.7K-2.0M)
Nigeria	294.0K (242.3K-350.4K)	59.4K (42.6K-77.8K)	3.3K (1.2K-7.0K)	149.1K (117.3K-182.3K)	219.6K (37.0K-1.2M)
Pakistan	282.1K (234.8K-334.7K)	57.0K (41.3K-74.3K)	3.1K (1.3K-6.2K)	143.0K (113.3K-174.5K)	216.7K (38.6K-1.1M)
USA	272.7K (223.6K-327.2K)	55.1K (39.2K-72.3K)	3.1K (1.3K-5.9K)	138.2K (108.0K-170.8K)	224.6K (46.9K-1.2M)
Vietnam	224.5K (186.5K-268.5K)	45.3K (32.7K-59.5K)	2.5K (1.1K-4.4K)	113.8K (89.8K-140.2K)	178.7K (35.3K-936.1K)
Philippines	221.9K (182.4K-266.2K)	44.8K (32.1K-59.0K)	2.5K (1.1K-4.7K)	112.5K (87.9K-138.5K)	169.2K (29.2K-914.0K)
Thailand	153.9K (127.4K-182.4K)	31.1K (22.5K-40.4K)	1.7K (731.3-3.3K)	78.0K (61.7K-95.2K)	128.8K (27.9K-652.2K)
Egypt	151.8K (125.8K-181.4K)	30.7K (22.1K-40.3K)	1.7K (727.1-3.2K)	76.9K (60.6K-94.7K)	116.2K (20.8K-615.8K)
Mexico	134.4K (112.4K-159.3K)	27.1K (19.7K-35.3K)	1.5K (689.3-2.6K)	68.1K (54.2K-83.3K)	105.3K (20.1K-556.8K)
Japan	119.1K (98.2K-141.1K)	24.1K (17.4K-31.2K)	1.3K (436.2-3.1K)	60.4K (47.8K-73.3K)	101.5K (19.2K-513.9K)
DRC	104.3K (87.9K-123.3K)	21.1K (15.4K-27.3K)	1.1K (408.1-2.5K)	52.9K (42.4K-64.3K)	79.0K (13.9K-424.4K)
South Africa	86.9K (71.4K-103.2K)	17.6K (12.6K-22.8K)	949.5 (432.5-1.7K)	44.1K (34.7K-53.6K)	66.0K (12.0K-353.7K)
Malaysia	74.1K (61.1K-88.5K)	15.0K (10.7K-19.6K)	831.7 (396.2-1.5K)	37.5K (29.5K-46.2K)	58.7K (11.1K-310.4K)
Colombia	62.0K (51.8K-74.1K)	12.5K (9.1K-16.4K)	690.3 (321.5-1.2K)	31.4K (24.9K-38.7K)	49.1K (9.4K-258.5K)
Myanmar	61.3K (50.7K-72.7K)	12.4K (9.0K-16.2K)	681.3 (314.2-1.3K)	31.1K (24.5K-38.0K)	46.7K (8.1K-249.8K)
Nepal	57.9K (48.5K-69.0K)	11.7K (8.5K-15.3K)	633.8 (277.8-1.2K)	29.3K (23.3K-36.0K)	44.3K (7.9K-235.9K)

Table A4.6: Considering disease severity scenario B, the estimated health economic costs (Mean, 2.5% - 97.5% UI), (\$ I\$ 2021) of CHIK-X at baseline over all simulations, with each country adjusted for the proportion of outbreaks experienced in all simulations.

<b>Country</b>	<b>Societal costs</b>	<b>Monetised DALYs</b>	<b>VSL</b>
India	638.4M (244.9M-1.5B)	1.2B (185.8M-6.3B)	28.4B (13.4B-52.6B)
China	757.6M (263.8M-2.0B)	7.2B (1.3B-38.2B)	36.8B (16.2B-66.3B)
Indonesia	253.3M (90.5M-639.0M)	390.0M (61.4M-2.1B)	10.7B (5.0B-19.8B)
Brazil	256.0M (93.8M-634.6M)	2.5B (430.8M-13.4B)	11.1B (5.2B-19.4B)
Bangladesh	92.3M (33.9M-225.6M)	97.8M (16.7M-521.6M)	3.8B (1.8B-7.3B)
Nigeria	44.2M (16.5M-120.0M)	43.5M (7.1M-238.5M)	1.6B (603.0M-3.5B)
Pakistan	41.3M (15.6M-103.5M)	33.7M (5.6M-183.6M)	1.7B (713.1M-3.5B)
USA	612.3M (211.7M-1.7B)	6.6B (1.2B-35.2B)	35.3B (15.0B-68.4B)
Vietnam	86.1M (31.0M-212.6M)	430.6M (75.7M-2.3B)	3.1B (1.4B-5.5B)
Philippines	54.4M (19.9M-132.4M)	154.7M (24.2M-853.9M)	2.5B (1.1B-4.7B)
Thailand	89.6M (30.7M-232.7M)	706.1M (132.7M-3.7B)	3.9B (1.6B-7.4B)
Egypt	35.6M (12.8M-89.1M)	132.4M (21.7M-717.5M)	2.4B (1.0B-4.6B)
Mexico	74.9M (27.3M-187.0M)	777.2M (136.0M-4.2B)	3.7B (1.7B-6.5B)
Japan	174.8M (49.2M-539.9M)	1.6B (269.1M-8.6B)	9.6B (3.2B-22.8B)
DRC	4.9M (2.5M-11.7M)	5.9M (1.0M-32.4M)	26.1M (9.3M-57.5M)
South Africa	34.5M (13.4M-82.2M)	224.4M (37.2M-1.2B)	1.6B (736.0M-2.9B)
Malaysia	60.5M (20.5M-150.9M)	331.3M (56.5M-1.8B)	3.8B (1.8B-7.0B)
Colombia	30.9M (10.7M-77.1M)	398.0M (69.3M-2.1B)	1.4B (649.4M-2.5B)
Myanmar	8.4M (3.5M-19.7M)	17.5M (2.8M-95.1M)	274.0M (126.3M-508.4M)
Nepal	5.4M (2.4M-12.4M)	17.0M (2.7M-92.4M)	249.2M (109.2M-485.2M)

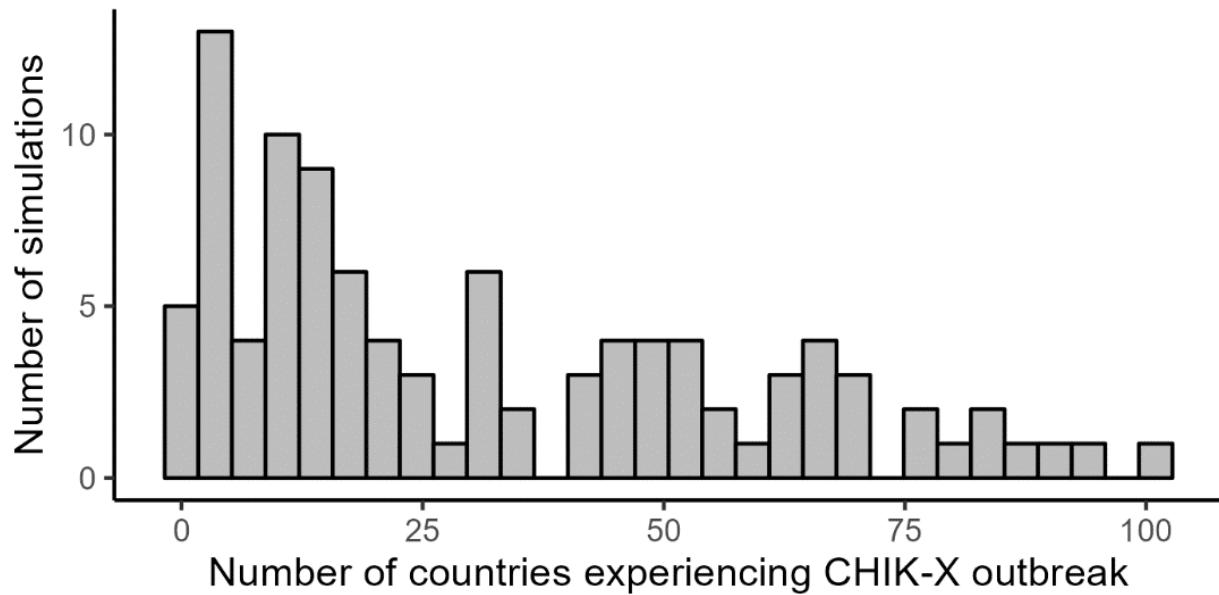


Figure A4.1: Number of countries experiencing CHIK-X outbreaks (x-axis) in the number of simulations as per y-axis.

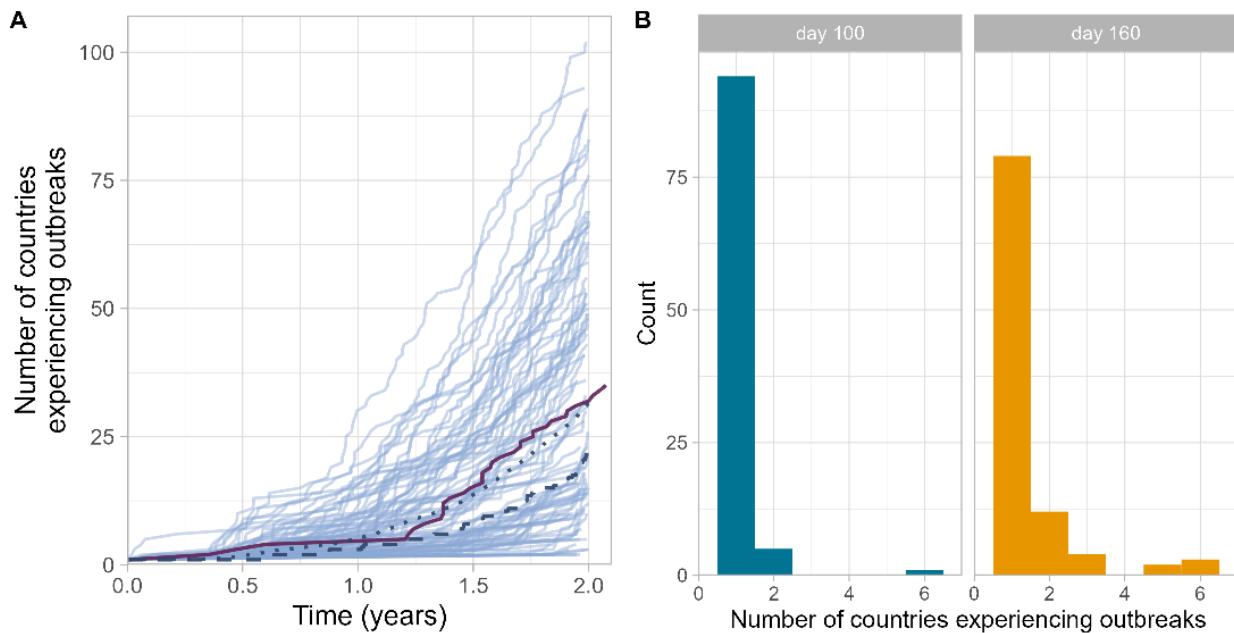


Figure A4.2: (A) The cumulative number of countries with CHIK-X spread (y-axis) over time (x-axis). (B) The number of countries experiencing outbreaks by days 100 and 160, respectively.

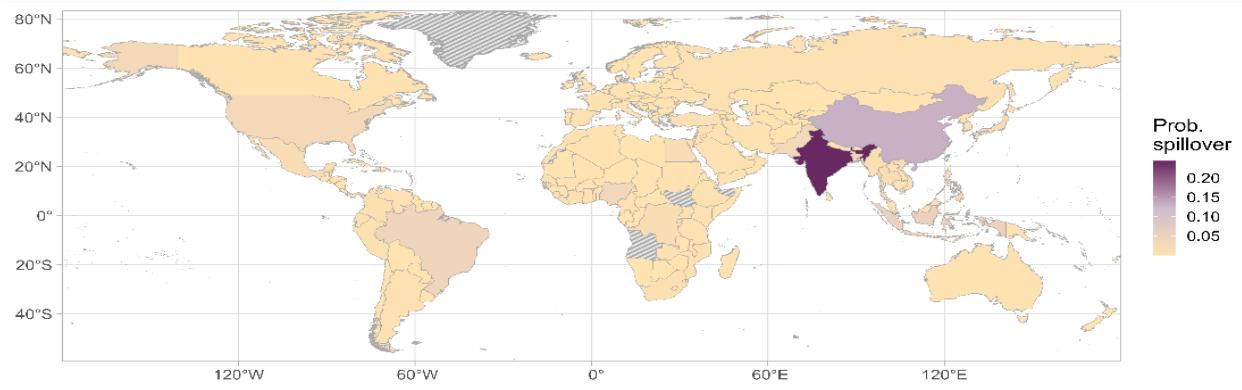


Figure A4.3: The probability of spillover (i.e., country-level incidence / total incidence) for each country in the analysis.

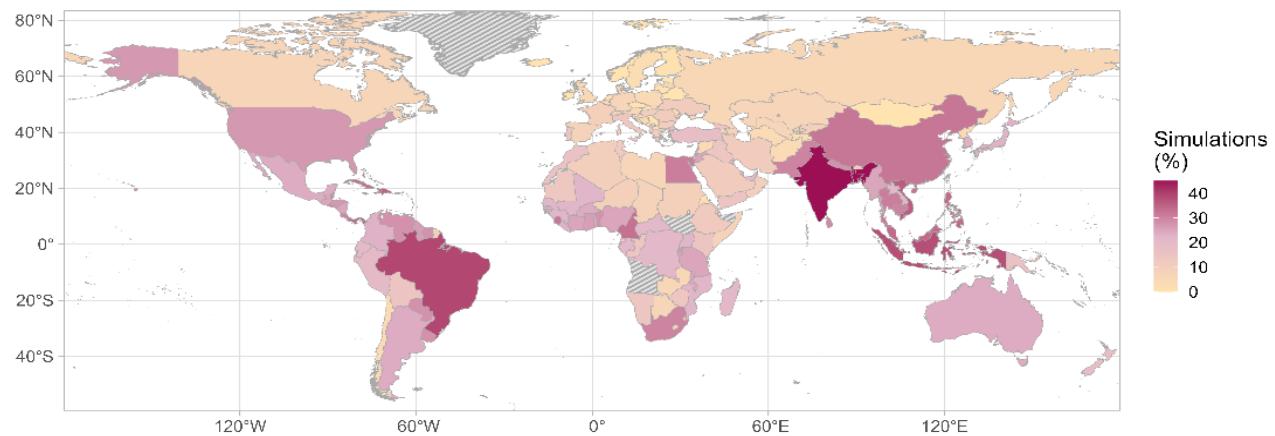


Figure A4.4: The percentage of simulations (n=100) that include each country in the analysis.

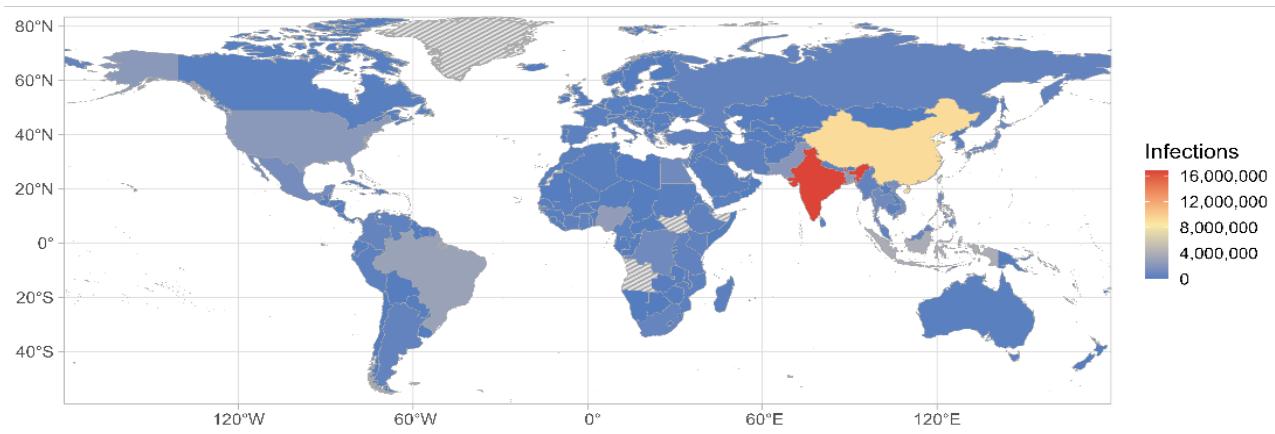


Figure A4.5: The mean cumulative infections for each country in the analysis.

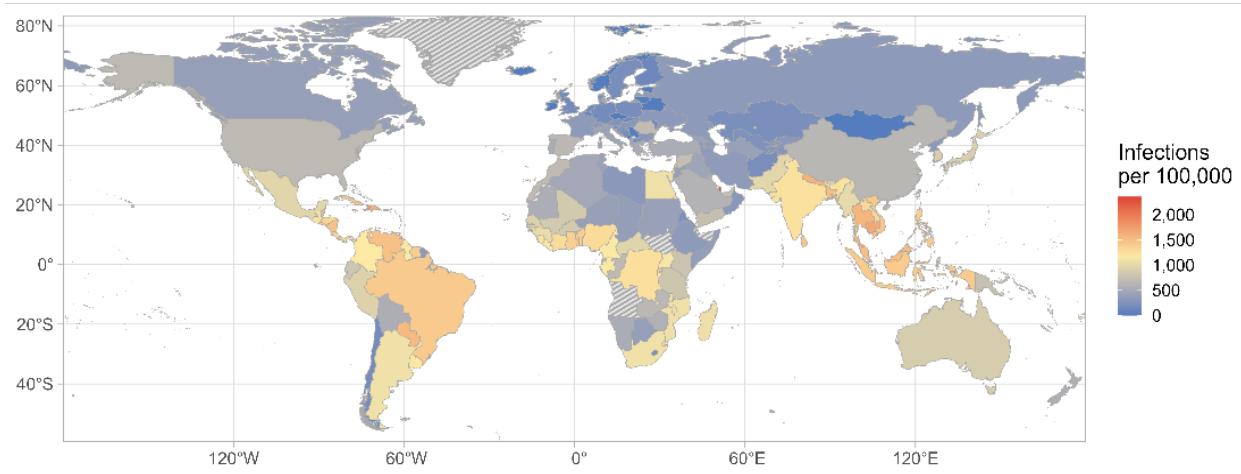


Figure A4.6: The mean cumulative infections per 100,000 population for each country in the analysis.

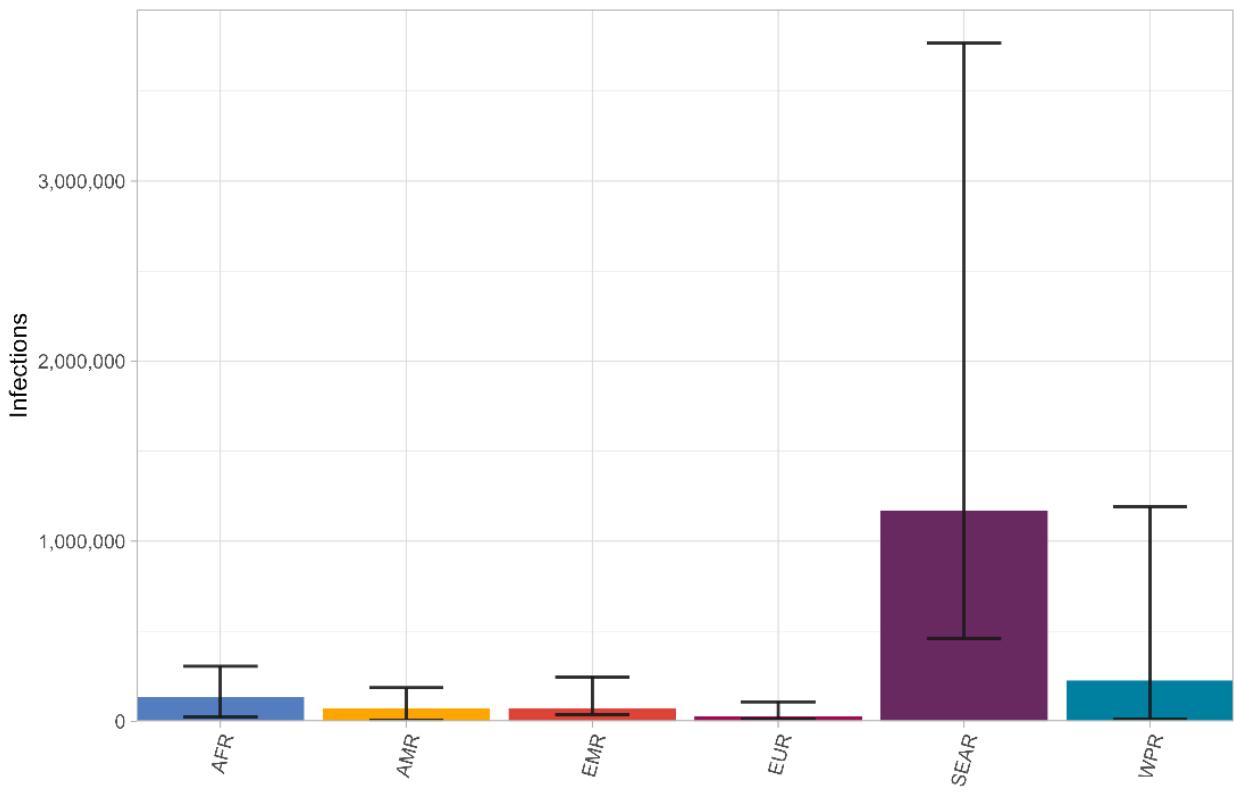


Figure A4.7: The cumulative incidence from 100 simulations by WHO region. The spread duration was 2 years, but the outbreak duration approximates the PAHO shape. Data includes countries with no outbreaks when aggregating WHO region population.

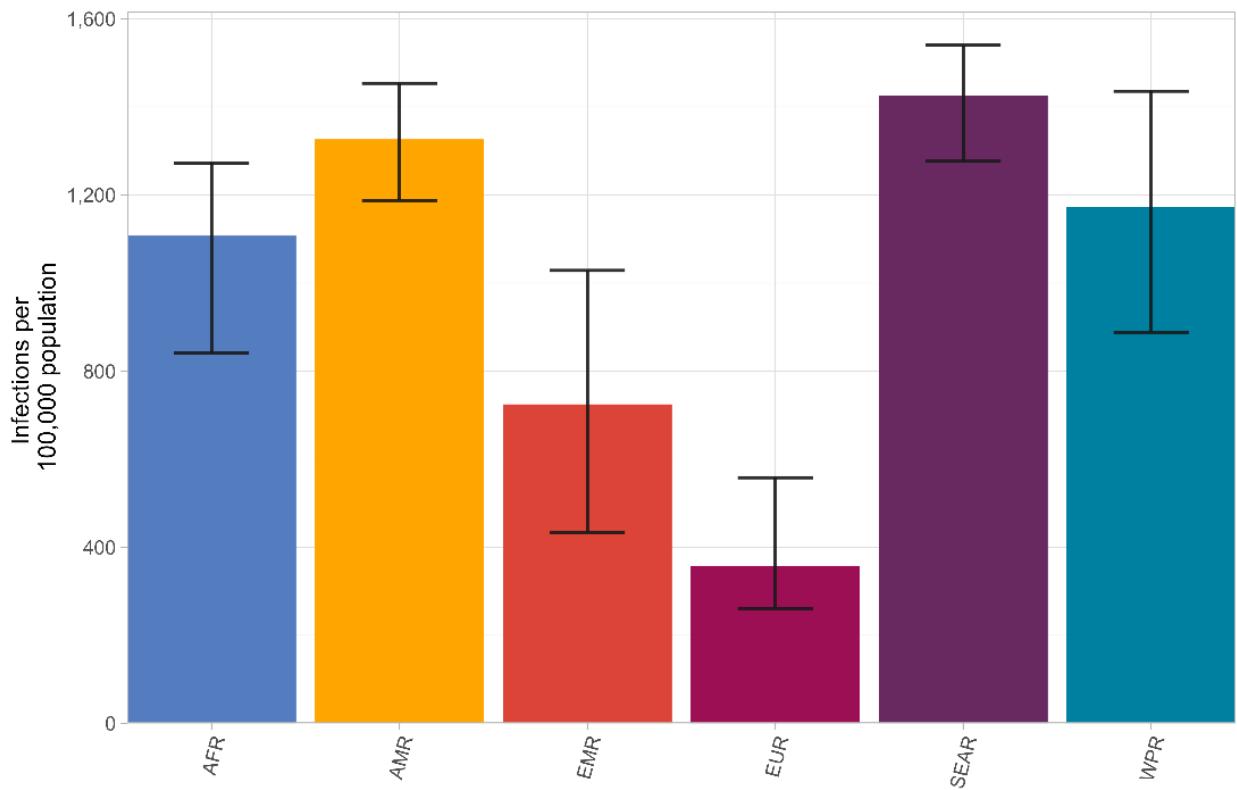


Figure A4.8: The cumulative incidence per 100,000 population from 100 simulations by WHO region. The spread duration was 2 years, but the outbreak duration approximates the PAHO shape. Data includes countries with no outbreaks when aggregating WHO region population.