Benefit-risk analysis of health benefits of routine childhood immunisation against the excess risk of SARS-CoV-2 infections during the Covid-19 pandemic in Africa

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Summary

Background: National immunisation programmes globally are at risk of suspension due to the severe health system constraints and physical distancing measures in place to mitigate the ongoing COVID-19 pandemic. Our aim is to compare the health benefits of sustaining routine childhood immunisation in Africa against the risk of acquiring SARS-CoV-2 infections through visiting routine vaccination service delivery points.

Methods: We used two scenarios to approximate the child deaths that may be caused by immunisation coverage reductions during COVID-19 outbreaks. First, we used previously reported country-specific child mortality impact estimates of childhood immunisation for diphtheria, tetanus, pertussis, hepatitis B, *Haemophilus influenzae* type b, pneumococcal, rotavirus, measles, meningitis A, rubella, and yellow fever (DTP3, HepB3, Hib3, PCV3, RotaC, MCV1, MCV2, MenA, RCV, YFV) to approximate the future deaths averted before completing five years of age by routine childhood vaccination during a 6-month Covid-19 risk period without catch-up campaigns. Second, we analysed an alternative scenario that approximates the health benefits of sustaining routine childhood immunisation to only the child deaths averted from measles outbreaks during the Covid-19 risk period. The excess number of infections due to additional SARS-CoV-2 exposure during immunisation visits assumes that contact reducing interventions flatten the outbreak curve during the Covid-19 risk period, that 60% of the population will have been infected by the end of that period, that children can be infected by either vaccinators or during transport and that upon child infection the whole household would be infected. Country specific household age structure estimates and age dependent infection fatality rates are then applied to calculate the number of deaths attributable to the vaccination clinic visits. We present benefit-risk ratios for routine childhood immunisation alongside 95% uncertainty range estimates from probabilistic sensitivity analysis.

Findings: For every one excess Covid-19 death attributable to SARS-CoV-2 infections acquired during routine vaccination clinic visits, there could be 140 (37 - 549) deaths in children prevented by sustaining routine childhood immunisation in Africa. The benefit-risk ratio for the vaccinated children, siblings, parents or adult care-givers, and older adults in the households of vaccinated children are 53,000 (3,400 - 21,865,000), 47,000 (3,000 - 19,340,000), 2,000 (410 - 12,000), and 154 (40 - 617) respectively. In the alternative scenario that approximates the health benefits to only the child deaths averted from measles outbreaks, the benefit-risk ratio to the households of vaccinated children is 5 (1 - 21) under these highly conservative assumptions and if the risk to only the vaccinated children is considered, the benefit-risk ratio is 2,000 (131 - 839,000).

Interpretation: Our analysis suggests that the health benefits of deaths prevented by sustaining routine childhood immunisation in Africa far outweighs the excess risk of Covid-19 deaths associated with vaccination clinic visits. However, there are other factors that must be considered for strategic decision making to sustain routine childhood immunisation in African countries during the Covid-19 pandemic. These include logistical constraints of vaccine supply chain problems caused by the

Covid-19 pandemic, reallocation of immunisation providers to other prioritised health services, healthcare staff shortages caused by SARS-CoV-2 infections among the staff, decreased demand for vaccination arising from community reluctance to visit vaccination clinics for fear of contracting SARS-CoV-2 infections, and infection risk to healthcare staff providing immunisation services as well as to their households and onward SARS-CoV-2 transmission into the wider community.

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Research in context

Evidence before the study

National immunisation programmes globally are at risk of disruption due to the severe health system constraints caused by the ongoing COVID-19 pandemic and the physical distancing measures to mitigate the outbreak. The decrease in vaccination coverage increases the proportion of susceptible children at risk of increased morbidity and mortality from vaccine-preventable disease outbreaks. Outbreaks of vaccine preventable disease have been observed during previous interruptions to routine immunisation services during an ongoing infectious disease epidemic, such as during the 2013-2016 Ebola outbreak in West Africa, when most health resources were shifted towards the Ebola response which led to decreasing vaccination coverage and consequently outbreaks of measles and other vaccine-preventable diseases.

Added value of this study

We estimated the benefit-risk ratio by comparing the deaths prevented by sustaining routine childhood immunisation for diphtheria, tetanus, pertussis, hepatitis B, *Haemophilus influenzae* type b, pneumococcal, rotavirus, measles, meningitis A, rubella, and yellow fever vaccines with the excess Covid-19 deaths associated with vaccination clinic visits. The benefit of routine childhood immunization programmes in all the 54 countries of Africa is higher than the COVID-19 risk associated with these vaccination clinic visits.

Implications of all the available evidence

Routine childhood immunisation programmes should be safeguarded for continued service delivery and prioritised for the prevention of infectious diseases, as logistically possible, as part of delivering essential health services during the Covid-19 pandemic in Africa. The current immunisation service models will require adaptation, including physical distancing measures, personal protective equipment, and good hygiene practices for infection control at the vaccination clinics, and have to be complemented by new immunisation service models for sustaining routine childhood immunisation in the African countries during the Covid-19 risk period.

Introduction

Vaccines have substantially improved health and reduced mortality, particularly among children in low-income countries [1–3]. Access to vaccines in these countries accelerated after the formation of Gavi, the Vaccine Alliance in 2000 [4]. This access needs to be sustained to further advance the public health gains and maintain progress towards goals such as the elimination of polio, measles, rubella, and maternal tetanus [5]. The World Health Organization has launched its Immunization Agenda 2030 strategy in order to accelerate progress towards equitable access and use of vaccines over the new decade [6]. However, ensuring everyone has access to immunization services has proved challenging, with a quarter of children in the Africa region not receiving three doses of diphtheria-tetanus-pertussis (DTP3) in 2018 [7]. This is now further challenged by the coronavirus disease 2019 (Covid-19) pandemic [8], which has necessitated physical distancing measures to mitigate or delay the coronavirus epidemic that threatens to overwhelm health care systems.

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in December 2019 causing cases of Covid-19 in Wuhan, China [9]. As of April 30, 2020, there were 3,059,642 confirmed cases and 211,028 confirmed deaths affecting 213 countries and territories [10]. Almost all African countries have now reported cases with the majority reporting local transmission and rapidly rising case numbers [11]. The prevention and control measures to suppress and mitigate the Covid-19 outbreak in Africa during the upcoming months will place immense pressures on the national health systems in their provision of essential health services, including the Expanded Programme on Immunization (EPI) and routine vaccination of infants [12].

On March 26, 2020, the World Health Organization and the Pan American Health Organization issued guidance on the operation of immunisation programmes during the Covid-19 pandemic [13,14]. The guidance advises for temporary suspension of mass vaccination campaigns and a risk-benefit assessment to decide on conducting outbreak response mass vaccination campaigns, while routine immunisation programmes should be sustained in places where essential health services have operational capacity of adequate human resources and vaccine supply while maintaining physical distancing and other infection control measures.

Our aim is to compare the health benefits of sustaining routine childhood immunisation in Africa against the risk of acquiring SARS-CoV-2 infections through visiting routine vaccination service delivery points. Specifically, we conducted a benefit-risk analysis of vaccine-preventable deaths averted by sustaining routine childhood immunisation in comparison to excess Covid-19 deaths from SARS-CoV-2 infections acquired by visiting routine vaccination service delivery points.

Methods

Assumptions

We assess the benefit and risk of continued routine childhood immunisation during the Covid-19 pandemic in all 54 African countries. We focus on the delivery of infant immunisation at: (i) 6, 10 and 14 weeks of age for diphtheria, tetanus and pertussis (DTP), polio, hepatitis B (HepB), *Haemophilus influenzae* type b (Hib), *Streptococcus pneumoniae*, rotavirus (hereafter called EPI-1); (ii) 9 months for measles (MCV1), rubella (RCV1), *Neisseria meningitidis* serogroup A (MenA), yellow fever (YFV) (hereafter EPI-2); and (iii) 15-18 months for the second dose of measles (MCV2; EPI-3). The target age for MenA routine immunization varies by country and is given along with the first or second dose of measles – 9 months in Central African Republic, Chad, Côte d'Ivoire, Mali, Niger, and Sudan; 15 months in Burkina Faso; and 18 months in Ghana [15]. We did not consider Bacillus Calmette-Guérin (BCG) or HepB birth dose because they are recommended for administration shortly after birth and thus were assumed not to require an additional vaccination visit, albeit home births or delayed administration may be common in some parts of Africa.

During the period of SARS-CoV-2 circulation, we assume that contact-reducing measures are in place and that while those measures fail to contain the outbreak, they will be able to substantially flatten the epidemic curve. In both other qualitatively different scenarios (uncontrolled epidemic or successful containment) sustaining vaccination as far as possible would be the largely obvious choice as doing so would not substantially affect the risk of SARS-CoV-2 infection.

We assume that the risk from Covid-19, and hence the potential disruption to the health services including routine childhood vaccination lasts for 6 months. The main analyses consider the impact of continuation of all five immunisation clinic visits in comparison with the risk for Covid-19 disease in the vaccinees household as a result of attending the vaccine clinic, tracking the health benefits from immunisation among the vaccinated children until five years of age.

Benefits of sustained routine childhood immunisation

We used the health impact estimates provided by Li et al for vaccines against hepatitis B, *Haemophilus influenzae* type b, measles, *Neisseria meningitidis* serogroup A, *Streptococcus pneumoniae*, rotavirus, rubella, and yellow fever [3]. For the health impact of vaccines against diphtheria, tetanus and pertussis (DTP), we calculated crude estimates for the annual number of deaths averted per 1000 vaccinated children by DTP in Africa based on global annual DTP3 vaccine impact estimates from 1980 to 2013 [16]. Polio is rarely fatal for children and hence we did not include polio vaccine preventable mortality into our estimates. Antigen-specific estimates of per-capita deaths averted by vaccination were unavailable for 9 countries, and were approximated to the mean estimates of other countries with available data. Country and antigen-specific levels of routine vaccination coverage are assumed to be the same level as 2018 for 2020.

The child deaths averted by routine vaccination during a 6-month suspension period of immunisation are the product of country and antigen-specific estimates of per-capita deaths averted by vaccination from the time of vaccination until 5 years of age [3,16], country-specific population estimates of the vaccinated cohort [17], country and antigen-specific official country reported estimates of vaccination coverage [18], and the suspension period of immunisation.

We considered two scenarios – high-impact and low-impact, for approximating the impact of sustained routine childhood immunisation. In the high-impact scenario, we approximate the impact of sustained routine childhood immunisation with the estimates for impact of vaccination of a 6-month cohort in 2020. Hence, this scenario assumes that the suspension of immunisation will result in a cohort of unvaccinated children who have the same risk of disease as children in a completely unvaccinated population, and their vulnerability persists until they are 5 years old, i.e. no catch-up campaign will be conducted at the end of the SARS-CoV-2 outbreak. Because of herd protection and likely catch-up activities at the end of a potential disruption of immunisation services, this high-impact scenario very likely overestimates the negative impact of suspending immunisation services for a short period of time.

In contrast, the low-impact scenario attempts to estimate a lower bound on the expected number of deaths due to disruptions to routine childhood immunisation services. We assume that in the absence of immunisation, herd immunity would protect children missing out on vaccination from all diseases with the exception of measles, and that vaccination through catch-up campaigns would close measles immunity gaps immediately following the 6 month Covid disruption period. This scenario is implemented as illustrated by the following example. In a country with 80% routine measles vaccine coverage, the inter-epidemic period of measles outbreaks is about 4 years [19]. The suspension of the routine vaccination programme for 6 months would correspond to an accumulation of susceptibles equivalent to 30 months in normal times, thus shrinking the inter-epidemic period to 2 years. In the absence of supplementary immunisation activities this would yield a 25% chance that an outbreak starts during the 6 months of suspension. Further, the physical distancing interventions in place to mitigate the Covid-19 risk may decrease that outbreak probability by an additional 50%. Thereby, there is a 12.5% (25% * 50%) chance of a measles outbreak during the 6-month suspension period.

Excess risk of Covid-19 disease from sustained routine childhood immunisation

We assume that in the coming months that African countries will experience SARS-CoV-2 spread similar to that observed in non-African countries affected earlier in the pandemic which were unable to contain the virus. Particularly, we assume that climatic or other Africa specific factors will not notably reduce the transmissibility of SARS-CoV-2 [20,21].

The risk of Covid-19 depends on exposure probability to SARS-CoV-2 and progression to disease. For this analysis, we only consider the case-fatality risk for Covid-19 and ignore other potentially severe health outcomes. We model the additional SARS-CoV-2 exposure risk for the vaccinated child, their

carer, and household members as a result of contact with the vaccinator and other community members during travel to the vaccine clinic. The Covid-19 risk model is described in more detail in Appendix A1, and the simulation parameters for SARS-CoV-2 infection dynamics are shown in Appendix A2 based on the Reed-Frost epidemic model [22]. We use the country-specific household age composition to approximate the age distribution in households at risk of SARS-CoV-2 infection given that one of the household members is a child who has been vaccinated, and is further elaborated in Appendix A3 [23]. We apply age-stratified infection fatality risk for SARS-CoV-2 using estimates obtained from reported cases and their severity in China in combination with the proportion of asymptomatic infections estimated among international residents repatriated from China [24]. For children, we used the reported risks for ages 0-9 years, for adults the risk for ages 20-29 years, and for older adults over 60 the risk for ages 60-69 years.

Sensitivity analyses

We conducted a probabilistic sensitivity analysis by conducting 4000 simulation runs to account for the uncertainty around the parameters governing the SARS-CoV-2 infection model, as well as the reported uncertainty ranges for the infection fatality rate estimates (modelled using a gamma distribution), and the vaccine preventable mortality estimates (modelled using a lognormal distribution), and assessed their impact on our findings.

The program code and data for the benefit-risk analysis conducted in this study is accessible on GitHub (https://github.com/vaccine-impact/epi_Covid). All analyses were done using R 3.6.3 [25]. All data were from secondary sources in the public domain, and ethics approval was thereby not required.

Role of the funding source

The funders were involved in the study design; collection, analysis, and interpretation of data; writing of the paper; and the decision to submit it for publication. All authors had full access to data in the study, and final responsibility for the decision to submit for publication.

Results

In the high-impact scenario, we estimate that the current routine childhood immunisation programme (DTP, HepB, Hib, PCV, RotaC, MCV, RCV, MenA, YFV) in Africa during a 6 months period in 2020 would prevent 715,000 (652,000 - 801,000) deaths in children from the time of vaccination until they are 5 years old. About one third of averted deaths are attributable to measles and another third to pertussis. Immunisation during the three EPI-1 visits for DTP3, HepB3, Hib3, PCV3, and RotaC will prevent 471,000 (411,000 - 554,000) deaths, immunisation during EPI-2 visit for MCV1, RCV1, MenA, and YFV will prevent 241,000 (224,000-258,000) deaths, and immunisation during EPI-3 for MCV2 will prevent 3,200 (3,000-3,500) deaths among children until they are 5 years old (see Table 1). One-third of the deaths prevented by routine childhood vaccination are in Nigeria, Ethiopia, Democratic Republic of Congo, and Tanzania (see Table 2).

We estimate that the three immunisation visits for EPI-1 add 2.3% altogether and each immunisation visit of EPI-2 and EPI-3 add 0.8% to the probability of a SARS-CoV-2 infection in the household. As a result, continuation of routine childhood immunisation in Africa may lead to 5,100 (1,300 - 19,300) additional deaths attributable to additional SARS-CoV-2 infections associated with the immunisation visits of children. About 14 (0 - 214) of these are expected to be among the vaccinated children, 15 (0 - 241) among their siblings, 358 (59 - 1,700) among their parents or adult carers, and 4,700 (1,200 - 17,600) among older adults in the household.

For every one excess Covid-19 death attributable to additional household exposure to SARS-CoV-2 infections due to routine childhood immunisation visits, we estimate that the routine childhood immunisation programme would prevent 140 (37 - 549) deaths in children until 5 years of age in Africa (see Table 1). The benefit of the three EPI-1 immunisation visits in early infancy and the visit for EPI-2 at 9 months were 136 (36-528) and 207 (53-819) deaths averted among children per excess Covid-19 death, respectively. The incremental benefit of the second dose of measles vaccination during EPI-3 visit at 15-18 months was 7 (2 - 27) deaths averted among children per excess Covid-19 death. More than 90% of the excess covid-19 risk is due to the high fatality rate in older people. If only the risk to vaccinated infants is considered, the benefit-risk ratio is substantially higher at 53,000 (3,400 - 22,000,000) (see appendix A4). Our findings were largely similar across countries (see Figure 1, Table 2, and appendix A5). Country-specific benefit-risk ratios for EPI-1, EPI-2, and EPI-3 are presented in the appendix (see A6, A7, A8). The overall benefit risk-ratio of sustaining routine childhood immunisation ranged from 55 (13 - 245) in Morocco to 305 (80 - 1,200) in Angola, and the number of child deaths averted through vaccination substantially exceeded the number of excess Covid-19 deaths for all the 54 countries of Africa.

In the low-impact scenario that approximates the health benefits to only the child deaths averted from measles outbreaks, the benefit-risk ratio to the households of vaccinated children is 5 (1 - 21). When the risk to only the vaccinated children is considered, the benefit-risk ratio is 2,000 (131 - 839,000). Even under these highly conservative assumptions, the benefit ratios for most countries in

Africa are larger than 1 and indicates in favour of sustaining the routine childhood immunisation programme during the Covid-19 pandemic (see Figure 2). Tunisia, Eswatini, and Morocco have benefit-risk ratios lower than 1, since measles vaccination impact is relatively at the lower end in these three countries in comparison to other countries in Africa.

We evaluated the contribution of the uncertainty in the model parameters to the uncertainty in the benefit-risk ratio estimates (Figure 3). The main factors influencing our estimates of the benefit-risk ratio were the average number of contacts of the child and their carer during a visit to the vaccine clinic, the average number of transmission relevant contacts of a community member per day and hence the risk for transmission given a potentially infectious contact, and the infection-fatality rate for SARS-CoV-2 infected older adults aged above 60 years.

Discussion

Our analysis suggests that the benefit from sustaining routine childhood immunisation in Africa far outweighs the excess risk of Covid-19 deaths due to the additional risk for SARS-CoV-2 infections during the child's vaccination visit, particularly for the vaccinated children. This reinforces the guidance and statement issued by the World Health Organization and the Measles & Rubella Initiative respectively to sustain routine childhood immunisation programmes where essential health services have operational capacity of adequate human resources and vaccine supply while maintaining physical distancing and other infection control measures to ensure the safety of communities and health workers [13,26].

We base our analyses on model-based country and antigen-specific vaccine impact estimates in low and middle income countries for 2020 [3,16]. There is considerable uncertainty in the impact suspending immunisation activities for a period of about 6 months and whether a timely and high-coverage catch-up campaign can be conducted soon after. Therefore, we presented two extreme scenarios – high-impact and low-impact, for the potential benefits from sustaining routine childhood vaccination.

In the high-impact scenario, we approximate the impact of sustained routine childhood immunisation with the estimates of vaccination impact for a 6-month cohort in 2020. While pathogen resurgence will happen gradually due to herd protection from the rest of the population, this could be counterbalanced by unvaccinated children of this and other cohorts continuing to be at risk of disease beyond the 6-month window. In the presence of social distancing measures, the exposure to non-coronavirus pathogens will also likely be reduced but those who may remain susceptible as a result of immunisation service suspension may get infected once distancing measures are relaxed. In the low-impact scenario, we approximate the impact of sustaining vaccination by the number of child deaths as a result of potential measles outbreaks during the Covid-19 risk period while also accounting for catch-up campaigns to be delivered at the end of the Covid-19 risk period. We show that in both scenarios that continuation of routine childhood immunisation is beneficial and outweighs the excess risk of Covid-19 deaths due to the additional risk for SARS-CoV-2 infections during the immunisation visits.

To calculate the number of Covid-19 associated fatalities, we used infection fatality rates that were derived based on a combination of estimates from Chinese surveillance for Covid-19 cases and fatalities and the proportion of asymptomatic cases observed on repatriation flights from China. While the younger African age-demographic may mitigate some of the Covid-19 disease burden, infection fatality rates in Africa may be substantially higher because of the prevalence of likely risk factors including HIV, tuberculosis, and malnutrition as well as lack of access to antibiotics to limit the risk for bacterial coinfections in some parts of Africa. However, our uncertainty analysis illustrates that while the uncertainty of the Covid-19 infection fatality rate is a key factor in the overall uncertainty of our estimates, even at the upper mortality bounds, continuation of routine

childhood vaccination is beneficial. Furthermore, the effects of a potentially higher Covid-19 fatality ratio in Africa may be balanced by a higher fatality ratio of measles and the other vaccine preventable diseases in times when the healthcare system is stretched and vitamin A supply is suspended.

Because of high transmissibility of measles, routine childhood immunisation coverage in many countries is insufficient to prevent outbreaks. To aid routine vaccination coverage, supplementary immunisation activities (SIAs) are conducted regularly, many of them scheduled for this year, at a point shortly before sufficient population immunity has built up to prevent measles outbreaks [27]. Supplementary immunisation activities have recently been postponed to reduce the risk for Covid-19 infections during mass vaccination [13], further enhancing the likelihood and impact of measles outbreaks if routine childhood vaccination is suspended. Because SIAs tend to be timed at the right interval to avoid outbreaks, our low-impact scenario is likely to underestimate the risk of an outbreak occurring due to SIA suspension.

We conducted a probabilistic sensitivity analysis to assess the impact of parameter uncertainty on the estimated benefit-risk ratios. We found that the biggest contribution to the uncertainty around the benefit of sustaining routine childhood immunisation during the Covid-19 pandemic in Africa are the transmission probability and the number of contacts during a vaccination visit. This highlights the need for personal protective equipment for vaccinators, the need to implement physical distancing measures including the avoidance of crowded waiting rooms for vaccination visits, and the importance of good hygiene practices to reduce the risk of SARS-CoV-2 acquisition and transmission at the vaccination clinics. It will be challenging to implement some of these infection prevention and control measures in many African countries due to resource constraints.

We estimated the benefit-risk trade-off for sustaining routine childhood immunisation during the Covid-19 pandemic in Africa and found that the benefits substantially outweigh the risks. However, there are other factors that must be considered for strategic decision making to sustain routine childhood immunisation in African countries during the Covid-19 pandemic. These include logistical constraints of vaccine supply and delivery cold chain problems caused by the Covid-19 pandemic, reallocation of doctors and nurses to other prioritised health services, healthcare staff shortages caused by SARS-CoV-2 infections among the staff or staff shortages because of ill-health or underlying health conditions that put them at increased risk for severe Covid-19 disease, and decreased demand for vaccination arising from community reluctance to visit vaccination clinics for fear of contracting SARS-CoV-2 infections. Also, the opportunity risk of SARS-CoV-2 infection for the vaccinated children and healthcare staff involved in immunisation activities as well as to their households and onward SARS-CoV-2 transmission into the wider community should be considered (see appendix A11).

In conclusion, routine childhood immunisation programmes should be safeguarded for continued service delivery and prioritised for the prevention of infectious diseases, as logistically possible, as part of delivering essential health services during the Covid-19 pandemic in Africa.

Tables

Table 1: Vaccine antigen specific benefits and risks of sustaining routine childhood vaccination. The benefit-risk ratio estimates (median estimates and 95% uncertainty intervals) show the child deaths averted by sustaining routine childhood immunisation in Africa per Covid-19 death attributable to excess SARS-CoV2 infections acquired through visiting routine vaccination service delivery points. Note that the vaccine preventable deaths estimates are vaccine antigen specific, while the excess deaths are dependent on the number of required visits. As vaccination visits group delivery of several vaccines, these have a higher benefit-risk ratio than that for individual antigens.

Vaccine antigen	Vaccination schedule	Deaths averted by vaccination	Excess Covid-19 deaths	Benefit-risk ratio
Diphtheria	6, 10, 14 weeks	12,954 (10,298-16,690)	3,492 (895-12,838)	4 (1-15)
Tetanus	6, 10, 14 weeks	69,219 (55,406-89,950)	3,492 (895-12,838)	20 (5-79)
Pertussis	6, 10, 14 weeks	271,466 (213,445-352,635)	3,492 (895-12,838)	78 (21-306)
HepB	6, 10, 14 weeks	3,824 (2,753-6,174)	3,494 (895-12,843)	1 (0-4)
Hib	6, 10, 14 weeks	54,882 (49,620-61,398)	3,506 (898-12,888)	16 (4-62)
PCV	6, 10, 14 weeks	46,532 (39,948-55,637)	3,109 (795-11,442)	15 (4-60)
RotaC	6, 10 weeks	10,685 (9,603-11,929)	1,475 (375-5,638)	7 (2-29)
MCV1	9 months	215,179 (200,259-231,691)	1,168 (296-4,591)	185 (47-729)
RCV	9 months	1,161 (800-1,815)	459 (116-1,805)	3 (1-11)
MenA	9 months	459 (342-688)	173 (44-682)	3 (1-11)
YFV	9 months	23,161 (17,624-31,316)	540 (137-2,126)	43 (11-174)
MCV2	15-18 months	3,192 (2,918-3,502)	462 (117-1,813)	7 (2-27)
EPI-1 (DTP3, HepB3, Hib3, PCV3, RotaC)	6, 10, 14 weeks	470,771 (410,736-554,206)	3,506 (898-12,888)	136 (36-528)
EPI-2 (MCV1, RCV1, MenA, YFV)	9 months	240,605 (223,580-258,446)	1,168 (296-4,591)	207 (53-819)
EPI (DTP3, HepB3, Hib3, PCV3, RotaC, MCV1, RCV1, MenA, YFV, MCV2)	6, 10, 14 weeks; 9 months; 15-18 months	714,862 (651,800-800,982)	5,132 (1,311-19,293)	140 (37-549)

Table 2. Benefits and risks of sustaining routine childhood vaccination at the national level. The benefit-risk ratio estimates (median estimates and 95% uncertainty intervals) show the child deaths averted by sustaining routine childhood immunisation in the African countries per Covid-19 death attributable to excess SARS-CoV2 infections acquired through visiting routine vaccination service delivery points. The combined impact of the routine childhood vaccination is shown for 3-dose DTP3, HepB3, Hib3, PCV3 for children at 6, 10 and 14 weeks, 2-dose RotaC for children at 6 and 10 weeks, 1-dose MCV1, RCV1, MenA, YFV for children at 9 months, and 1-dose MCV2 for children at 15-18 months of age.

Country	Deaths averted by vaccination	Excess Covid-19 deaths	Benefit-risk ratio
Angola	26,598 (20,284-40,066)	88 (23-327)	305 (80-1,243)
Burundi	8,695 (6,315-13,601)	49 (13-182)	182 (47-744)
Benin	7,511 (5,133-12,114)	48 (12-179)	160 (40-668)
Burkina Faso	14,326 (10,294-23,300)	111 (28-421)	132 (33-542)
Botswana	1,004 (696-1,637)	9 (2-34)	112 (29-475)
Central African Republic	2,423 (1,780-3,785)	12 (3-46)	201 (50-834)
Côte d'Ivoire	20,092 (14,053-31,482)	120 (30-449)	171 (43-672)
Cameroon	13,283 (9,501-21,692)	108 (28-407)	125 (32-519)
Congo - Kinshasa	62,965 (46,389-100,146)	345 (90-1,283)	189 (47-771)
Congo - Brazzaville	3,533 (2,559-5,400)	13 (3-48)	278 (72-1,150)
Comoros	440 (304-741)	5 (1-17)	97 (24-410)
Cape Verde	150 (94-276)	2 (0-7)	86 (21-369)
Djibouti	274 (186-467)	3 (1-11)	94 (23-394)
Algeria	18,188 (12,464-30,298)	165 (42-626)	112 (29-470)
Egypt	24,177 (13,097-51,938)	251 (66-936)	98 (23-437)
Eritrea	2,126 (1,473-3,402)	18 (5-69)	119 (31-501)
Ethiopia	62,756 (43,313-104,486)	534 (135-2,007)	118 (30-498)
Gabon	897 (619-1,479)	5 (1-19)	178 (45-737)
Ghana	18,690 (13,773-29,727)	135 (34-511)	141 (35-596)
Guinea	9,526 (6,874-14,266)	76 (19-284)	130 (33-522)
Gambia	2,243 (1,662-3,279)	24 (6-92)	93 (24-374)
Guinea-Bissau	1,404 (1,066-2,082)	8 (2-28)	188 (50-774)
Equatorial Guinea	378 (258-623)	3 (1-10)	141 (35-595)
Kenya	20,381 (14,030-35,068)	147 (38-554)	142 (36-585)
Liberia	4,116 (3,143-6,199)	21 (5-80)	197 (51-783)
Libya	2,341 (1,636-3,786)	21 (5-80)	114 (29-462)
Lesotho	836 (582-1,393)	9 (2-34)	95 (23-401)
Morocco	7,258 (4,163-14,746)	136 (34-519)	55 (13-245)
Madagascar	14,675 (10,511-24,043)	83 (22-310)	178 (45-756)

Mali	13,841 (10,124-20,581)	89 (23-335)	157 (40-637)
Mozambique	20,557 (14,718-33,187)	127 (33-478)	166 (42-681)
Mauritania	2,840 (2,029-4,439)	19 (5-70)	155 (40-629)
Mauritius	261 (183-426)	2 (1-9)	113 (29-474)
Malawi	8,972 (5,934-16,525)	80 (21-304)	115 (28-496)
Namibia	1,190 (841-1,927)	12 (3-44)	104 (26-438)
Niger	22,031 (16,788-32,355)	162 (41-612)	139 (36-580)
Nigeria	92,474 (68,042-143,363)	580 (148-2,174)	163 (41-660)
Rwanda	8,063 (5,607-13,235)	53 (14-200)	155 (39-635)
Sudan	22,536 (15,566-38,135)	206 (52-779)	112 (28-456)
Senegal	11,320 (8,418-16,918)	157 (39-593)	73 (19-308)
Sierra Leone	6,993 (5,331-10,051)	53 (13-201)	133 (34-543)
Somalia	10,134 (7,456-15,604)	63 (16-236)	166 (42-680)
South Sudan	3,245 (1,969-5,787)	21 (6-79)	155 (37-691)
São Tomé and Príncipe	121 (80-201)	1 (0-3)	149 (36-631)
Swaziland	345 (210-703)	6 (1-22)	63 (15-275)
Seychelles	34 (24-54)	0 (0-1)	120 (31-509)
Chad	9,328 (6,622-15,277)	60 (16-226)	157 (39-672)
Togo	5,173 (3,447-8,416)	34 (9-129)	154 (38-640)
Tunisia	1,822 (910-4,029)	33 (8-127)	56 (12-269)
Tanzania	36,645 (25,292-62,771)	360 (92-1,365)	103 (26-440)
Uganda	21,485 (14,155-36,882)	151 (39-563)	144 (36-611)
South Africa	18,957 (13,451-31,309)	191 (48-726)	102 (25-419)
Zambia	11,202 (7,750-18,338)	74 (19-279)	153 (39-634)
Zimbabwe	7,743 (5,670-12,102)	58 (15-221)	136 (34-560)

Figures

Figure 1. Spatially disaggregated benefit-risk ratio of continuing routine childhood immunisation. The number of vaccine preventable future deaths averted before completing five years of age by sustaining routine childhood vaccination of DTP, HepB, Hib, PCV, RotaC, MCV, RCV, MenA and YFV per Covid-19 death attributable to excess SARS-CoV2 infections acquired through visiting routine vaccination service delivery points. The routine childhood vaccines considered are 3-dose DTP3, HepB3, Hib3, PCV3 for children at 6, 10 and 14 weeks, 2-dose RotaC for children at 6 and 10 weeks, 1-dose MCV1, RCV1, MenA, YFV for children at 9 months, and 1-dose MCV2 for children at 15-18 months of age. A benefit-risk ratio larger than 1 indicates in favour of sustaining the routine childhood immunisation programme during the Covid-19 pandemic.

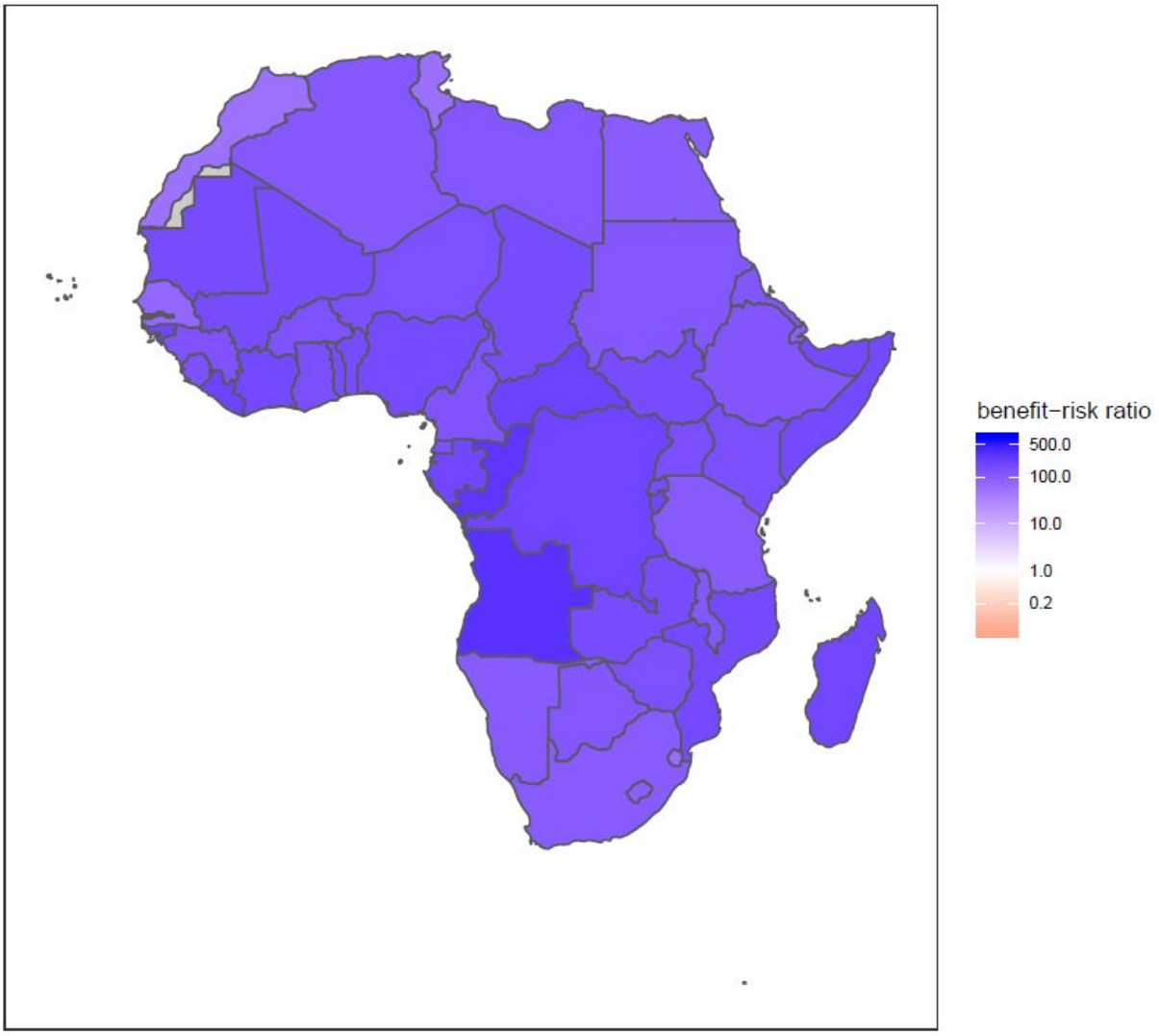


Figure 2. Scenario of measles-only vaccination impact during the Covid-19 pandemic. The number of vaccine preventable future deaths averted before completing five years of age by sustaining routine childhood vaccination of DTP, HepB, Hib, PCV, RotaC, MCV, RCV, MenA and YFV per Covid-19 death attributable to excess SARS-CoV2 infections acquired through visiting routine vaccination service delivery points. We consider a small chance (12.5%) of measles outbreaks while no other vaccine preventable disease outbreaks take place due to herd immunity.

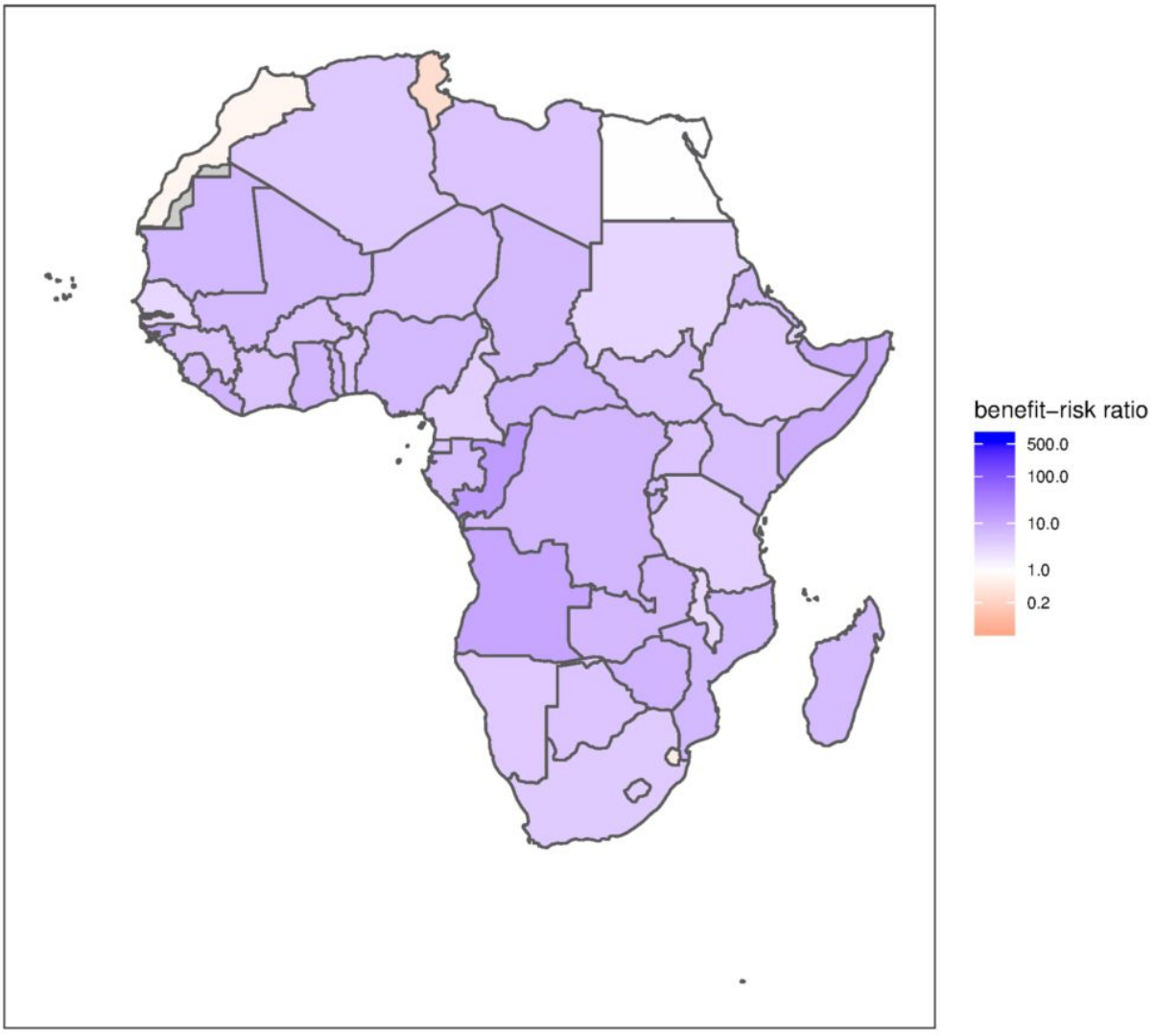
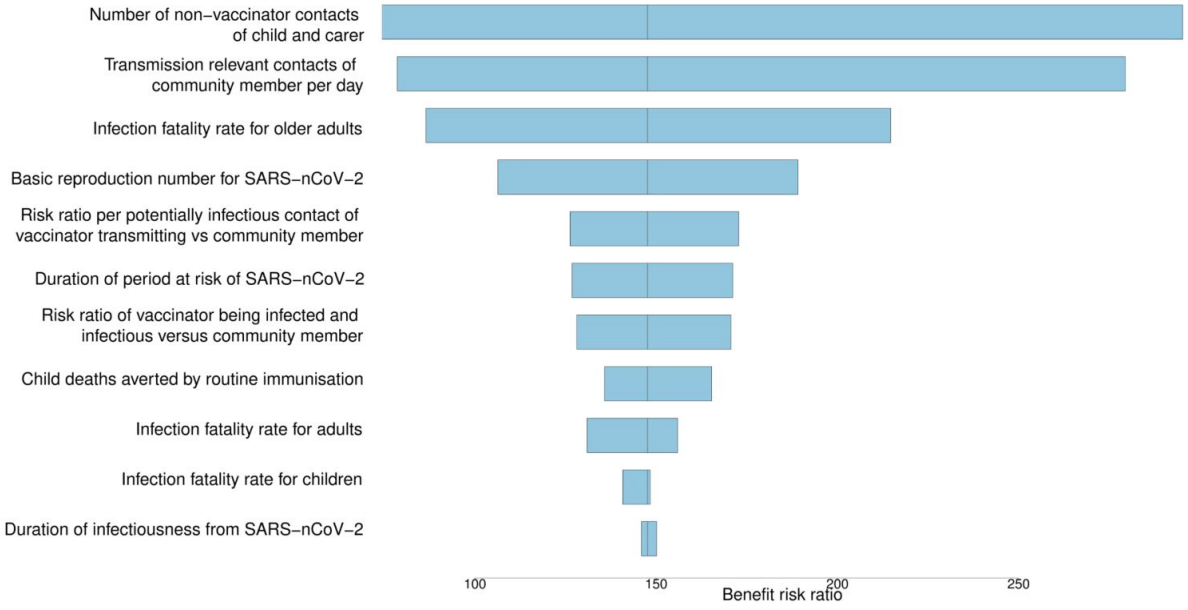


Figure 3. Sensitivity analysis for attributable impact of model parameters on uncertainty in the benefit ratio estimates. Sensitivity analysis shows the estimated contribution of different model parameters to the overall uncertainty in the benefit-risk ratio of continuing routine childhood immunisation during the Covid-19 pandemic in Africa. The tornado diagram was constructed using a multivariate Poisson regression model to the estimated posterior distribution of the benefit-risk ratio using our model input parameters as predictors, and treating total deaths averted by childhood immunisation as a single variable. The main factors influencing the benefit-risk ratio estimates were the average number of transmission relevant contacts of a community member per day, the average number of contacts of the child and their carer during a visit to the vaccination clinic, and the infection-fatality rate of SARS-CoV-2 infected older adults aged above 60 years.



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Supplementary appendix

A1. Covid-19 risk model

The risk of infection with SARS-CoV-2 depends on the stage of the epidemic. As a base case, we assume that through contact reducing interventions, community SARS-CoV-2 transmission will be spread over a period (T) of 6 months and the exposure risk is constant during that time due to contact-reducing interventions successfully mitigating sharp peaks in disease (Table A2) [28]. We assume a basic reproduction number (R_o) of 2.5 [29] and that the contact-reducing interventions enable the proportion of the population eventually infected to be approximately equal to the herd immunity threshold. Hence, we assume that in the absence of vaccination visits, $\Theta = 60\%$ of the population will have been infected with SARS-CoV-2 by the end of the epidemic. Hence, 40% of households would not have become infected with SARS-CoV-2 independent of whether or not the infant in the household had attended routine childhood vaccination. Furthermore, if after 6 months 60% of the population was infected then, assuming a duration of infectiousness (Ψ) of one week [30] and a reasonably flat epidemic curve, then on any given day about $p_o = 2\%$ of the population would be infected and potentially transmitting. In comparison to community members, we assume that vaccinators are at higher risk of being infected (between 1 and 4 times, $p_v = \iota_1 p_o$) because of their higher frequency of exposure to other people, but at lower risk of onward transmission (between 0.25 and 1 times, $t_v = \iota_2 t_o$) because most of their contacts with vaccinees are brief, and they have enhanced risk awareness and use corresponding protective measures including basic respiratory hygiene and personal protective equipment as available. Also, we assume that an infant child and the parent or adult carer each have between 1 and 10 ($n = U(1, 10)$) potentially infectious contacts during their travel to the vaccine clinic and in the waiting room.

For each of the potentially infectious contacts by the child and parent with community members, there is a probability of transmission ($t_o = R_o / N\Psi$), which for example corresponds to ($t_o = 6\%$) probability of a transmission event occurring for ($R_o = 2.5$) secondary infections for someone with 6 contacts per day during their infectious period of 7 days (i.e., a community member) or 21 potentially infectious contacts per day but who self isolates on symptom onset that occurred 2 days into their infectious period (i.e., a vaccinator).

Both the vaccinated child and the parent or caregiver, will be at additional risk of exposure during travel to the vaccine clinic, while waiting at the vaccine clinic and during vaccination. In addition, we assume that if either of them gets infected they will infect all other household members, owing to the high secondary attack rates observed for family gatherings [31]. We ignore any additional secondary infections outside the household, which are likely to be minimal due to physical distancing measures.

Based of the Reed-Frost epidemic model [22], the probability (P) for a SARS-CoV-2 infection for the whole household of a child who gets vaccinated is calculated as one minus the probability of either the infant or the mother not being infected by either the vaccinator or anyone else on any of the vaccination visits: $P = 1 - (1 - t_v)^{2\nu p_v}(1 - t_o)^{2\nu p_o n}$, with v the number of vaccine clinic visits.

Hence, the probability for such infection to be in excess of SARS-CoV-2 infections that would have occurred otherwise is $P_E = P\ (1 - \Theta)$.

We assume that during the 6 months of SARS-CoV-2 transmission, all children who get one dose of DTP will also get the other two doses. However, children receiving their measles containing vaccines will only get one dose during that time window because the two doses are given more than six months apart. The number of children who would normally get DTP during the considered time frame is approximated by half of the under one-year old population. Similarly, the number of children who will get either the first or the second measles-containing vaccine dose is half of the under 1-year old children or half of the children aged 12-23 months respectively.

A2. Simulation parameters for SARS-CoV-2 infection dynamics

Table A2. Parameters governing the estimation of SARS-CoV-2 infection probability during immunisation visits – baseline values and the uncertainty intervals for probabilistic sensitivity analyses.

Parameter	Description	Value	Source
v	Number of vaccine clinic visits: EPI-1: 3 visits for DTP3-HepB-Hib, PCV3, RotaC EPI-2: 1 visits for MCV1, RCV1, MenA, YF EPI-3: 1 visits for MCV2	3, 1 or 1	[32]
R_o	Basic reproduction number for SARS-CoV-2	$\Gamma(2.5, 25)^*$	[29]
T	Duration of period at risk for SARS-CoV-2	6 months $U(5, 7)$	[28]
Θ	Proportion of SARS-CoV-2 infected population at the end of the study period assuming neither (i) "overshooting" of the epidemic due to high rates of transmission or (ii) elimination of transmission prior to herd immunity being reached.	$1 - 1/R_o$	calculated
Ψ	Duration of infectiousness	7 days $\Gamma(7, 14)^*$	[30]
p_o	Prevalence of infectious community members on any given day	$\Theta\Psi / T$	calculated
p_v	Prevalence of infectious vaccinators on any given day	$\iota_1 p_o$	calculated
ι_1	Risk ratio of a vaccinator being infected and infectious versus another community member	$U(1, 4)$	assumption
ι_2	Risk ratio per potentially infectious contact of a vaccinator transmitting versus another community member	$U(0.25, 1)$	assumption
N	Average number of transmission relevant contacts of a community member per day	$U(2, 10)$	[33]
t_o	Probability of transmission given potentially infectious contact with community members	$R_o / N\Psi$	calculated
t_v	Probability of transmission given potentially infectious contact with vaccinators	$\iota_2\, t_o$	calculated
n	Number of non-vaccinator contacts of child and carer during their travel to the vaccine clinic and in the waiting room	$U(1, 10)$	assumption
P	Probability for SARS-CoV-2 infection for the whole household of a child who gets vaccinated	See manuscript	calculated
P_E	Probability for excess SARS-CoV-2 infection for the whole household of a child who gets vaccinated	$P(1 - \Theta)$	calculated

* Gamma distributions are parameterised as (mean, shape)

A3. Household structure and age composition

We use the country-specific household age composition to approximate the age distribution in households at risk of SARS-CoV-2 infection given that one of the household members is a child who has been vaccinated [23]. First, we estimate the number of siblings of an infant from the average number of household members aged less than 20 in households with at least one member aged less than 20. The number of siblings is adjusted to account for the effect of birth order by assuming that on average the infant would be the mid-born child. Secondly, we assume the average household will have two adults (parents or caregivers). Thirdly we assume that a proportion of households with vaccinated children will also have 2 older adults aged over 60 years. We estimate this proportion using the percentage of households that have both members aged less than 20 years and over 60 years old.

A4. Age and antigen specific benefit-risk ratios for Africa at the continental level

Table A4. Age-and antigen-specific benefit-risk ratios for childhood vaccination during the Covid-19 pandemic in Africa at the continental level. The benefit-risk ratio estimates (central estimates and uncertainty intervals) show the child deaths averted by continuing the routine childhood immunisation programmes per excess Covid-19 death caused by SARS-CoV2 infections acquired in the vaccination service delivery points in Africa. The routine childhood vaccines considered are 3-dose DTP3, HepB3, Hib3, PCV3 for children at 6, 10 and 14 weeks, 2-dose RotaC for children at 6 and 10 weeks, 1-dose MCV1, RCV1, MenA, YFV for children at 9 months, and 1-dose MCV2 for children at 15-18 months of age. Benefit-risk ratio above 1 indicates in favour of sustaining the routine childhood immunisation programme during the Covid-19 pandemic. The health benefits are accrued by the vaccinated children while the excess Covid-19 risk is disaggregated across the different age groups in the household.

Vaccine	Benefit-risk ratios				
	Household	Vaccinated children	Siblings (< 20 years of age)	Adults (20-60 years of age)	Older adults (> 60 years of age)
Diphtheria (DTP3)	4 (1-15)	1,433 (86-628,074)	1,258 (76-551,527)	54 (11-320)	4 (1-17)
HepB3	1 (0-4)	423 (26-189,236)	372 (23-166,151)	16 (3-101)	1 (0-5)
Hib3	16 (4-62)	5,929 (387-2,479,589)	5,201 (339-2,175,079)	227 (47-1,341)	17 (5-70)
MCV1	185 (47-729)	69,535 (4,492-28,777,172)	61,043 (3,943-25,262,675)	2,652 (522-16,053)	204 (51-832)
MCV2	7 (2-27)	2,560 (162-1,057,897)	2,464 (156-1,018,046)	98 (20-598)	8 (2-31)
PCV3	15 (4-60)	5,726 (367-2,342,643)	4,955 (317-2,026,956)	219 (45-1,337)	16 (4-67)
Pertussis (DTP3)	78 (21-306)	29,475 (1,933-12,668,931)	25,882 (1,697-11,124,890)	1,122 (226-6,621)	86 (22-346)
RCV1	3 (1-11)	980 (58-437,729)	867 (52-387,298)	37 (7-240)	3 (1-12)
RotaC	7 (2-29)	2,865 (187-1,200,594)	2,567 (168-1,075,831)	108 (23-651)	8 (2-33)
Tetanus (DTP3)	20 (5-79)	7,615 (497-3,368,467)	6,687 (436-2,957,931)	288 (58-1,740)	22 (6-89)
YFV	43 (11-174)	16,722 (1,004-7,625,307)	13,170 (790-6,005,286)	632 (122-3,893)	48 (12-199)
MenA	3 (1-11)	1,079 (68-488,665)	835 (52-378,237)	41 (8-245)	3 (1-12)
DTP3, HepB3, Hib3, PCV3, RotaC	136 (36-528)	50,982 (3,467-21,525,639)	44,721 (3,041-18,882,144)	1,949 (399-11,486)	149 (39-591)
MCV1, RCV1, MenA, YFV	207 (53-819)	77,958 (4,982-32,823,289)	68,437 (4,374-28,814,648)	2,958 (581-18,002)	227 (58-930)
DTP3, HepB3, Hib3, PCV3, RotaC, MCV1, RCV1, MenA, YFV, MCV2	140 (37-549)	52,892 (3,396-21,864,573)	46,785 (3,004-19,339,818)	2,014 (410-12,158)	154 (40-617)

A5. Country and age specific benefit-risk ratios for Africa at the national level

Table A5. Country and age specific benefit-risk ratios of vaccines delivered in the five vaccination-related clinical visits (3-dose DTP3, HepB3, Hib3, PCV3; 2-dose RotaC; 1-dose MCV1, RCV1, MenA, YFV, MCV2) during the Covid-19 pandemic in Africa at the country level. The benefit-risk ratio estimates (central estimates and uncertainty intervals) show the child deaths averted by continuing the routine childhood immunisation programmes per excess Covid-19 death caused by SARS-CoV2 infections acquired in the vaccination service delivery points in Africa. The routine childhood vaccines considered are 3-dose DTP3, HepB3, Hib3, PCV3 for children at 6, 10 and 14 weeks, 2-dose RotaC for children at 6 and 10 weeks, 1-dose MCV1, RCV1, MenA, YFV for children at 9 months, and 1-dose MCV2 for children at 15-18 months of age. Benefit-risk ratio above 1 indicates in favour of sustaining the routine childhood immunisation programme during the Covid-19 pandemic. The health benefits are accrued by the vaccinated children while the excess Covid-19 risk is disaggregated across the different age groups in the household.

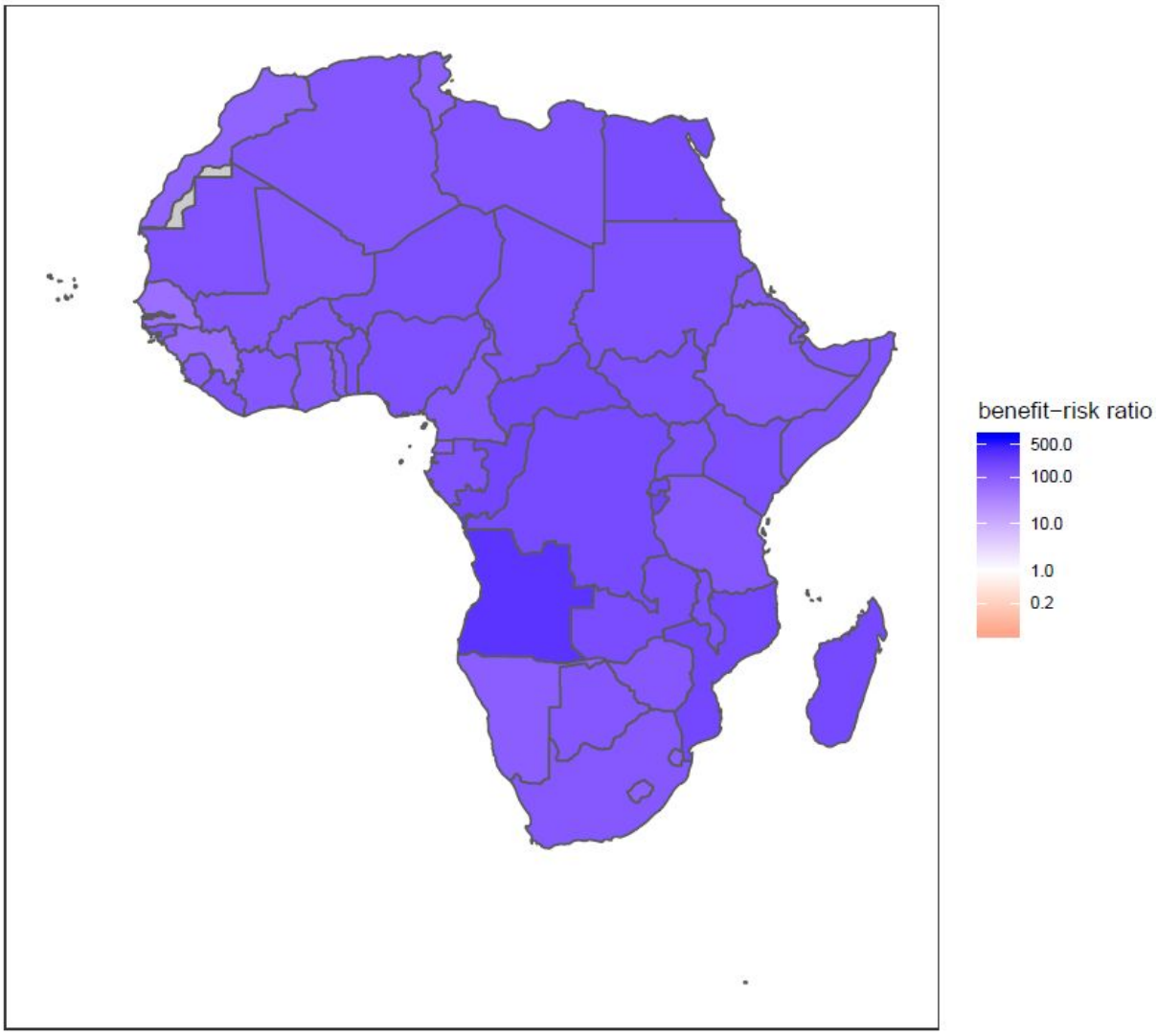
Country	Benefit-risk ratios				
	Household	Vaccinated children	Siblings (< 20 years of age)	Adults (20-60 years of age)	Older adults (> 60 years of age)
Angola	305 (80-1,243)	66,866 (4,224-27,158,503)	53,715 (3,394-21,817,169)	2,555 (508-15,908)	365 (93-1,526)
Burundi	183 (47-744)	53,293 (3,282-24,822,911)	48,035 (2,958-22,373,783)	2,042 (398-12,514)	207 (52-880)
Benin	159 (40-668)	64,884 (4,088-26,917,874)	51,308 (3,233-21,285,776)	2,453 (464-15,420)	175 (44-735)
Burkina Faso	132 (33-542)	54,631 (3,116-25,002,985)	38,089 (2,172-17,432,153)	2,024 (398-12,358)	144 (36-608)
Botswana	112 (29-475)	48,511 (2,991-19,335,900)	57,404 (3,539-22,880,286)	1,784 (346-11,366)	123 (31-517)
Central African Republic	201 (50-834)	62,605 (3,924-25,369,781)	48,586 (3,045-19,688,845)	2,332 (453-14,393)	229 (56-975)
Côte d'Ivoire	171 (43-672)	70,160 (4,207-29,176,617)	59,374 (3,560-24,691,426)	2,623 (519-15,585)	188 (47-757)
Cameroon	125 (32-519)	56,867 (3,406-23,015,625)	44,178 (2,646-17,879,774)	2,134 (420-13,603)	136 (34-581)
Congo - Kinshasa	189 (47-771)	56,445 (3,533-23,327,297)	42,129 (2,637-17,410,669)	2,184 (425-13,332)	212 (52-903)
Congo - Brazzaville	278 (72-1,150)	72,349 (4,462-30,515,926)	73,526 (4,535-31,012,355)	2,710 (542-16,833)	324 (82-1,403)
Comoros	97 (24-410)	56,080 (3,288-22,549,955)	48,211 (2,826-19,385,814)	2,044 (398-12,520)	103 (26-447)
Cape Verde	86 (21-369)	35,120 (2,019-15,084,921)	30,025 (1,726-12,896,565)	1,330 (258-8,640)	94 (22-412)
Djibouti	94 (23-393)	38,947 (2,353-17,439,519)	33,297 (2,012-14,909,585)	1,481 (282-9,146)	104 (25-443)
Algeria	112 (29-470)	45,914 (2,806-21,481,021)	39,253 (2,399-18,364,790)	1,764 (339-10,844)	123 (31-520)
Egypt	97 (23-437)	24,366 (1,461-11,159,928)	33,466 (2,007-15,328,039)	918 (164-6,267)	114 (26-526)

Eritrea	119 (31-501)	49,732 (3,016-20,122,825)	42,517 (2,578-17,203,626)	1,846 (370-11,700)	131 (33-561)
Ethiopia	118 (30-499)	54,444 (3,455-23,391,922)	53,760 (3,411-23,097,853)	2,060 (404-12,928)	129 (33-555)
Gabon	178 (45-737)	57,112 (3,514-23,288,805)	52,624 (3,238-21,458,874)	2,178 (410-13,608)	199 (49-856)
Ghana	141 (35-596)	54,001 (3,278-23,517,410)	64,426 (3,911-28,057,187)	2,017 (401-12,685)	156 (37-680)
Guinea	130 (33-522)	79,976 (5,078-32,322,999)	54,931 (3,487-22,200,614)	3,013 (605-18,429)	138 (35-562)
Gambia	93 (24-374)	66,859 (4,250-27,020,107)	31,194 (1,983-12,606,767)	2,517 (500-15,357)	99 (25-409)
Guinea-Bissau	187 (50-774)	77,096 (4,910-34,142,675)	65,912 (4,197-29,189,630)	2,949 (602-18,190)	206 (53-863)
Equatorial Guinea	141 (35-595)	58,970 (3,508-24,427,270)	50,415 (2,999-20,883,629)	2,183 (413-13,430)	154 (38-668)
Kenya	142 (36-585)	44,542 (2,828-19,723,254)	51,809 (3,290-22,940,907)	1,699 (323-10,652)	159 (40-665)
Liberia	197 (51-783)	79,867 (4,959-34,442,057)	70,327 (4,367-30,328,155)	2,978 (602-18,957)	216 (55-899)
Libya	114 (29-462)	47,088 (2,817-19,776,648)	40,257 (2,409-16,907,668)	1,747 (343-10,932)	125 (31-514)
Lesotho	95 (23-401)	50,224 (3,127-21,247,308)	73,791 (4,594-31,217,222)	1,866 (364-11,898)	101 (24-436)
Morocco	55 (13-245)	26,770 (1,516-11,694,817)	29,191 (1,653-12,752,575)	997 (187-6,489)	59 (14-268)
Madagascar	178 (45-756)	54,539 (3,229-23,001,882)	48,440 (2,868-20,429,664)	2,017 (395-12,962)	202 (51-864)
Mali	157 (40-637)	71,249 (4,422-29,676,026)	51,858 (3,219-21,599,292)	2,686 (530-16,453)	171 (43-698)
Mozambique	166 (42-681)	49,501 (2,949-21,454,299)	49,065 (2,923-21,265,581)	1,844 (360-11,693)	188 (47-823)
Mauritania	155 (39-629)	63,144 (4,092-26,210,165)	53,984 (3,498-22,407,881)	2,384 (474-15,191)	170 (43-705)
Mauritius	113 (29-474)	47,223 (2,919-19,377,286)	40,373 (2,495-16,566,241)	1,764 (355-11,377)	124 (32-530)
Malawi	115 (28-496)	39,187 (2,336-17,193,619)	39,886 (2,378-17,500,455)	1,439 (272-9,656)	128 (31-568)
Namibia	104 (26-438)	50,459 (3,122-21,820,461)	49,934 (3,089-21,593,141)	1,932 (363-11,825)	112 (27-480)
Niger	139 (36-580)	60,729 (3,854-24,577,522)	40,702 (2,583-16,472,562)	2,311 (463-14,404)	151 (39-640)
Nigeria	163 (41-660)	62,729 (3,956-30,387,692)	52,792 (3,329-25,574,016)	2,310 (459-14,899)	180 (44-742)
Rwanda	155 (39-635)	46,105 (2,916-19,248,915)	53,968 (3,414-22,531,903)	1,766 (351-11,117)	175 (43-737)
Sudan	112 (28-456)	43,412 (2,645-19,702,420)	34,408 (2,096-15,616,027)	1,683 (325-10,182)	123 (30-507)
Senegal	73 (19-308)	60,892 (3,774-29,176,828)	27,658 (1,714-13,252,404)	2,311 (468-14,265)	77 (20-327)

Sierra Leone	133 (34-543)	75,744 (4,858-31,662,721)	58,991 (3,783-24,659,489)	2,848 (564-17,245)	142 (36-593)
Somalia	166 (43-680)	66,816 (4,202-28,396,078)	57,123 (3,593-24,276,686)	2,529 (495-15,097)	181 (46-763)
South Sudan	155 (37-691)	52,263 (3,127-22,144,323)	37,217 (2,227-15,769,377)	1,975 (377-12,827)	174 (41-794)
São Tomé and Príncipe	149 (36-631)	46,248 (2,779-20,267,319)	51,159 (3,074-22,419,573)	1,749 (330-10,772)	169 (40-727)
Swaziland	63 (15-275)	31,447 (1,800-13,541,372)	24,389 (1,396-10,501,913)	1,179 (215-7,356)	68 (16-303)
Seychelles	120 (31-509)	50,162 (2,952-23,213,983)	42,885 (2,524-19,846,352)	1,833 (366-11,794)	131 (34-568)
Chad	157 (39-671)	54,757 (3,266-23,894,801)	34,853 (2,079-15,208,897)	2,086 (404-13,582)	175 (43-769)
Togo	154 (37-641)	65,380 (4,074-30,488,683)	59,897 (3,732-27,931,594)	2,454 (477-15,353)	167 (40-710)
Tunisia	56 (12-269)	23,472 (1,342-11,256,627)	20,067 (1,147-9,623,639)	843 (144-6,363)	61 (13-296)
Tanzania	103 (26-440)	42,346 (2,612-19,015,926)	37,340 (2,303-16,767,841)	1,599 (313-9,945)	114 (28-496)
Uganda	144 (36-611)	47,785 (2,880-19,708,740)	41,205 (2,483-16,994,931)	1,768 (353-11,635)	162 (40-693)
South Africa	102 (25-419)	46,001 (2,834-19,114,922)	68,630 (4,229-28,517,577)	1,771 (338-10,797)	111 (27-464)
Zambia	153 (39-634)	48,872 (2,973-21,373,497)	38,802 (2,360-16,969,452)	1,817 (352-11,250)	173 (43-727)
Zimbabwe	136 (34-560)	52,873 (3,252-22,320,779)	61,483 (3,782-25,955,409)	1,980 (392-12,259)	150 (37-636)

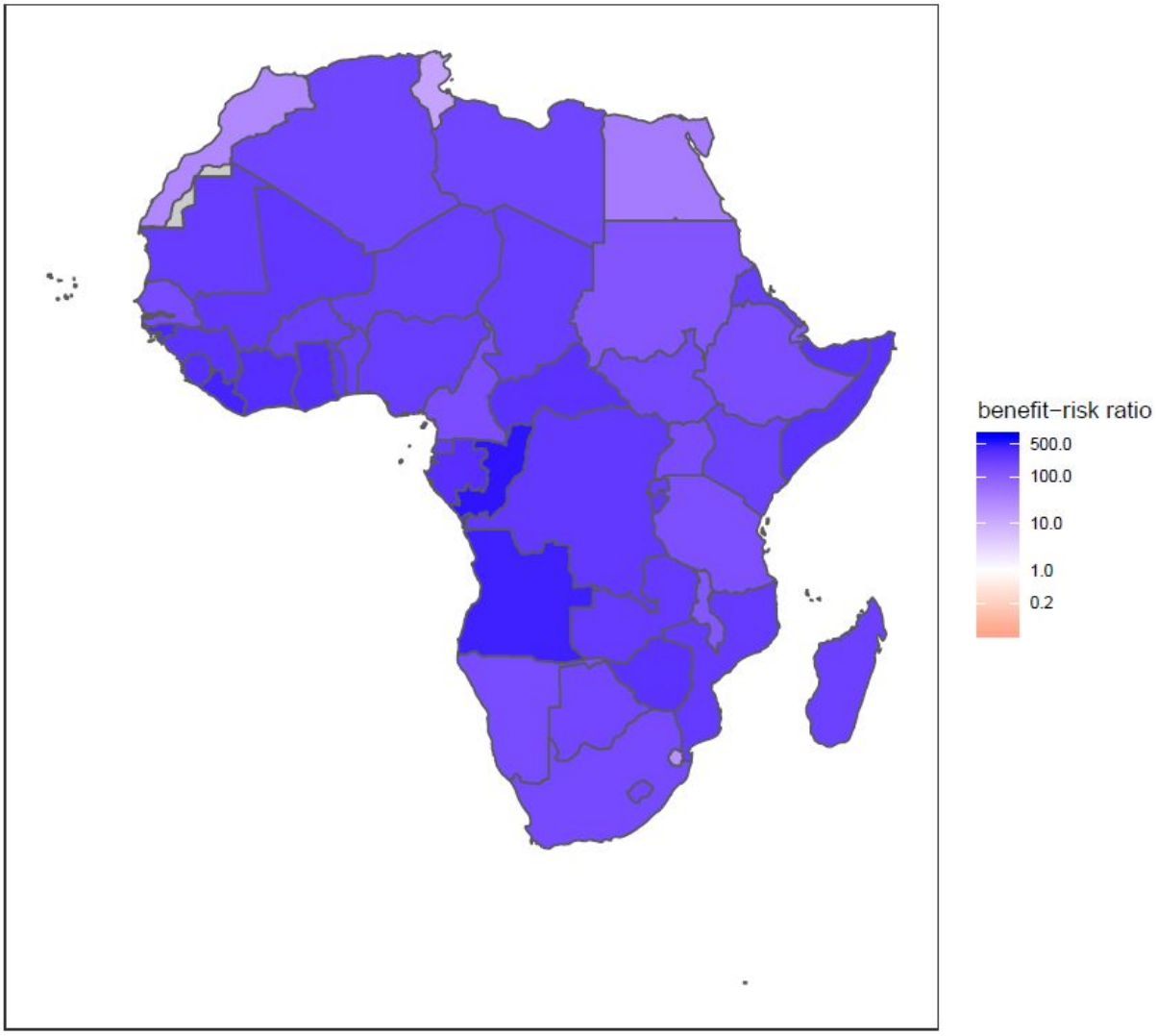
A6. Benefit-risk ratio of vaccines delivered in the first, second, and third vaccination-related clinical visits

Figure A6. Benefit-risk ratio of vaccines delivered in the first, second, and third vaccination-related clinical visits (3-dose DTP3, HepB3, Hib3, PCV3; 2-dose RotaC) for children at 6, 10, 14 weeks of age during the Covid-19 pandemic in Africa. The central estimates for benefit-risk ratio at the household level show the child deaths averted by continuing the routine childhood immunisation programmes (3-dose DTP3, HepB3, Hib3, PCV3 for children at 6, 10 and 14 weeks of age and 2-dose RotaC for children at 6 and 10 weeks of age) per excess Covid-19 death caused by SARS-CoV2 infections acquired in the vaccination service delivery points. Benefit-risk ratio above 1 indicates in favour of sustaining the routine childhood immunisation during the Covid-19 pandemic.



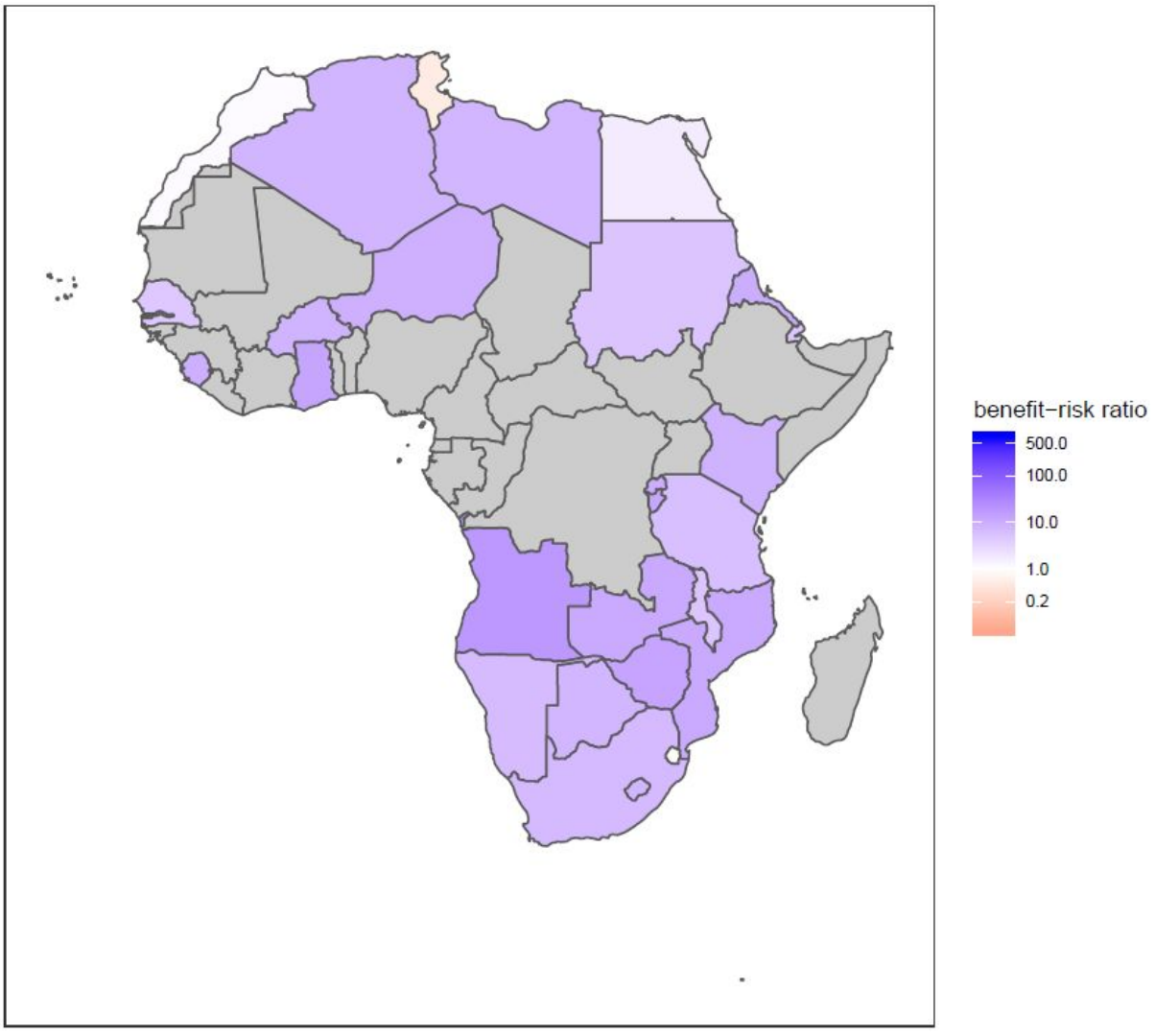
A7. Benefit-risk ratio of vaccines delivered in the fourth vaccination-related clinical visit

Figure A7. Benefit-risk ratio of vaccines delivered in the fourth vaccination-related clinical visit (1-dose MCV1, RCV1, MenA, YFV) for children at 9-months of age during the Covid-19 pandemic in Africa. The central estimates for benefit-risk ratio at the household level show the child deaths averted by continuing the routine childhood immunisation programmes (1-dose MCV1, RCV1, MenA, YFV for 9-month-old children) per excess Covid-19 death caused by SARS-CoV2 infections acquired in the vaccination service delivery points. Benefit-risk ratio above 1 indicates in favour of sustaining the routine childhood immunisation during the Covid-19 pandemic.



A8. Benefit-risk ratio of vaccines delivered in the fifth vaccination-related clinical visit

Figure A8. Benefit-risk ratio of vaccines delivered in the fifth vaccination-related clinical visit (1-dose MCV2) for children at 15-18 months of age during the Covid-19 pandemic in Africa. The central estimates for benefit-risk ratio at the household level show the child deaths averted by continuing the routine childhood immunisation programmes (1-dose MCV2 for children aged 15-18 months) per excess Covid-19 death caused by SARS-CoV2 infections acquired in the vaccination service delivery points. Benefit-risk ratio above 1 indicates in favour of sustaining the routine childhood immunisation during the Covid-19 pandemic. Grey shading indicates null MCV2 coverage.



A9. Age and antigen specific deaths averted by vaccination, excess deaths due to Covid-19, and benefit-risk ratios for Africa at the continental level

Age and antigen specific deaths averted by vaccination, excess deaths due to Covid-19, and benefit-risk ratios (central estimates and uncertainty intervals) for routine childhood vaccination are included in the dataset. The routine childhood vaccines considered are 3-dose DTP3, HepB3, Hib3, PCV3 for children at 6, 10 and 14 weeks, 2-dose RotaC for children at 6 and 10 weeks, 1-dose MCV1, RCV1, MenA, YFV for children at 9 months, and 1-dose MCV2 for children at 15-18 months of age. Note that the risk is disaggregated only across the different age groups in the household.

See supplementary appendix 2 (spreadsheet) for the dataset.

A10. Country, age, and antigen specific deaths averted by vaccination, excess deaths due to Covid-19, and benefit-risk ratios for Africa at the national level

Country, age and antigen specific deaths averted by vaccination, excess deaths due to Covid-19, and benefit-risk ratios (central estimates and uncertainty intervals) for routine childhood vaccination are included in the dataset. The routine childhood vaccines considered are 3-dose DTP3, HepB3, Hib3, PCV3 for children at 6, 10 and 14 weeks, 2-dose RotaC for children at 6 and 10 weeks, 1-dose MCV1, RCV1, MenA, YFV for children at 9 months, and 1-dose MCV2 for children at 15-18 months of age. Note that the risk is disaggregated only across the different age groups in the household.

See supplementary appendix 2 (spreadsheet) for the dataset.

A11. Opportunity risk for vaccinated children and healthcare staff involved in immunisation activities

The opportunity risk of SARS-CoV-2 infection for the vaccinated children and healthcare staff involved in immunisation activities as well as to their households and onward SARS-CoV-2 transmission into the wider community should be included in the decision-making process to sustain routine childhood immunisation.

First, we need to know the opportunity risk of SARS-CoV-2 infection for the healthcare staff. Similar to the concept of opportunity cost, what is the risk of SARS-CoV-2 infection to the healthcare staff engaged in alternative healthcare activities if not involved in immunisation activities? If the opportunity risk of alternative healthcare activities is lower than being involved in immunisation activities, then reallocation of healthcare staff from immunisation to alternative healthcare activities is a better risk-avoidance strategy. On the other hand, if the opportunity risk of alternative healthcare activities is higher than being involved in immunisation activities, then healthcare staff face relatively lower risk in continuing to provide the immunisation services, thereby posing relatively lower risk to their households and SARS-CoV-2 transmission into the wider community.

Second, we need to know the opportunity risk of SARS-CoV-2 infection to the vaccinated children. If the alternative activity that the children and their carers would be involved in had a higher risk of SARS-CoV-2 infection in comparison to the risk involved with the immunisation visits, then it is beneficial for the children and their carers to undertake the immunisation visits for the children to get vaccinated and thereby posing relatively lower risk to their households and SARS-CoV-2 transmission into the wider community.

Irrespective of the opportunity risk of SARS-CoV-2 infection for the healthcare staff providing immunisation services during the COVID-19 pandemic, to ensure their safety, health care practices will need to be adapted to minimise the risk of SARS-CoV-2 acquisition and transmission at vaccination clinics. This includes physical distancing measures, personal protective equipment, and good hygiene practices for infection control at the vaccination clinics.