Risks and benefits of sustaining routine childhood immunisation programmes in Africa during the Covid-19 pandemic

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Executive summary

Aim: To weigh the health benefits of continued routine infant immunisation delivery in Africa against the risk of acquiring coronavirus infections through visiting vaccination services.

Methods: We used previously reported country-specific child mortality impact estimates of childhood immunisation for DTP, HepB, Hib, PCV, RotaC, MCV, MenA, RCV and YFV to approximate the deaths averted by the continuation of vaccination during a 6-month Covid-19 risk period. The excess number of infections due to additional Covid-19 exposure during an immunisation visit assumes that contact reducing interventions flatten the outbreak curve during the Covid-19 risk period, that 60% of the population will have been infected after 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 estimates are then applied to calculate the number of deaths attributable to the vaccine clinic visits. We present benefit-risk ratios for sustaining routine childhood immunisation alongside 95% uncertainty range of a parametric probabilistic sensitivity analysis.

Key findings: For one excess Covid-19 death attributable to an infection acquired during a child vaccination visit, there would be 128 (34 - 1,247) future deaths in children prevented from the time of vaccination to 5 years of age by sustaining the routine childhood vaccination programmes. If only the risk to the vaccinated child is considered, the benefit-risk ratio increases to 51,755 (3,041 - 46,486,749). Measles and pertussis containing vaccines each contribute about one-third of the vaccine preventable mortality in these estimates.

Limitations: By approximating the benefit of sustaining routine vaccination with the risk of acquiring coronavirus infections through visiting vaccination services, we make a number of simplifying assumptions: (i) we assume that the potential cohort of unvaccinated children during the Covid-19 risk period would be at similar risk for infection with any of the included vaccine preventable disease as children in a completely unvaccinated cohort would be; (ii) we assume that no catch-up would be administered once the pandemic ends and (iii) we assume that the contact reducing measures in place to flatten the pandemic curve will have limited effect on at least the highly transmissible pathogens, measles and pertussis. Addressing these shortcomings systematically will need a more extensive dynamic modelling framework, however, this is unlikely to qualitatively change our findings.

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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, but has stagnated over the last decade. 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 [4]. 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 [5]. This progress is now challenged by the coronavirus disease 2019 (Covid-19) pandemic [6], which has necessitated measures to minimise physical contact between individuals to avert or delay a 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 [7]. As of April 4, 2020, there were 1,056,159 confirmed cases and 57,206 confirmed deaths affecting 208 countries and territories [8]. Almost all African countries have now reported cases with the majority reporting local transmission and rapidly rising case numbers [8]. The prevention and control measures to suppress and mitigate the Covid-19 outbreak in Africa during the upcoming months will place an immense pressure on the national health systems in their provision of essential health services, including the Expanded Programme on Immunization (EPI) and routine vaccination of infants. On March 26, 2020, the World Health Organization (WHO) and the Pan American Health Organization (PAHO) have issued guidance on the operation of immunisation programmes during the Covid-19 pandemic, and have recommended for mass vaccination campaigns to be temporarily suspended [9,10].

Our aim is to weigh the health benefits of continued routine infant immunisation delivery against the risk of acquiring coronavirus infections through visiting vaccination service delivery points. Specifically, we conducted a benefit-risk analysis of Covid-19 deaths averted by suspending immunisation programmes to prevent new SARS-CoV-2 infections acquired by attending vaccination clinics in comparison to vaccine-preventable deaths averted by sustaining childhood immunisation programmes in Africa.

Methods

Assumptions

We assess the benefit-risk trade off for continuing routine childhood immunisation in the presence of a Covid-19 epidemic 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), *Neisseria meningitidis* serogroup A (MenA), *Streptococcus pneumoniae*, rotavirus (hereafter called EPI-1) and (ii) 9 months and in the second year of life for measles, rubella and yellow fever (EPI-2 and EPI-3, respectively). We did not consider Bacillus Calmette–Guérin (BCG) or HepB birth dose because they are recommended for administration shortly after birth and hence would not 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 infection with SARS-CoV-2. We assume that the risk from Covid-19, and hence the potential disruption to the health services including vaccination lasts for 6 months. The main analyses consider the impact of suspension of all five immunisation clinic visits without a catch up campaign at the point where services are reinstated in comparison with keeping them; we assume that in the latter case, vaccine coverage remains the same as observed in each country in 2018. We also include a probabilistic sensitivity analysis to assess the impact of parametric assumptions on our findings.

Benefits of continued routine infant immunisation

We base our analyses on model-based country- and antigen-specific vaccine impact estimates for <5 y old children in low and middle income countries [3]. We use the estimates for 2020 to approximate the number of vaccine preventable deaths attributable to the potential suspension of the national routine childhood immunisation programmes. Using this crude approximation implies some underlying key assumptions: (i) 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 (ii) their vulnerability persists until they are 5 years old (no catch-up campaign will be conducted at the end of the SARS-CoV-2 outbreak). While in reality pathogen resurgence will happen gradually due to herd protection from the rest of the population, this could be compensated for by unvaccinated children of this and other cohorts continuing to be at risk of disease until herd immunity can be established again. 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.

No estimate for the impact of vaccines against Diphtheria, Tetanus and Pertussis (DTP) was included in the work by Li et al [3]. Hence 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 [11]. Also, polio was not included in the estimates by Li et al, despite oral polio vaccine and inactivated polio vaccine being part of EPI-1. However, despite a substantial burden of disease polio is rarely fatal for children and hence we did not include polio mortality into our estimates.

Risk of continued routine infant immunisation for additional Covid-19 disease

We assume that in the months to come all of Africa 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 [12,13].

The risk of Covid-19 depends on both exposure probability to SARS-CoV-2 and progression to disease. For this analysis we only consider the fatality risk for Covid-19 and ignore other potentially severe health outcomes.

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 make the simplification that the exposure risk is constant during that time due to contact-reducing interventions successfully mitigating sharp peaks in disease (Table 1) [14]. We assume a basic reproduction number (R_0) of 2.5 [15] 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 infant vaccination. Furthermore, if after 6 months 60% of the population was infected then, assuming a duration of infectiousness (ψ) of one week [16] and a reasonably flat epidemic curve, then on any given day about $p_0 = 2\%$ of the population would be infected and potentially transmitting. We assume that vaccinators are at twice that risk of being infected ($p_v = 2p_o$) because of their higher frequency of exposure to other people, but at half the risk of onward transmission ($t_v = t_0/2$) because most of their contacts with vaccinees are extremely brief, 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 and the caregiver child and her mother each have another $n = 2$ potentially infectious contacts during the travel or in the waiting room. For each of the potentially infectious contacts we assume a $t_0 = 6\%$ probability of a transmission event occurring (see Table 1 for equations); which corresponds for example to an average of R_0 secondary infections for someone with 5 contacts per day during their infectious period (i.e., a community member), or R_0 secondary infections for someone with 18 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 infant and the caregiver, assumed to be one of the parents, 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 [17]. We ignore any additional secondary infections outside the household, which are likely to be minimal due to physical distancing measures.

Hence, 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: $P = 1 - (1 - p_v)^{2\nu t_v}(1 - p_o)^{2\nu t_o n}$, with ν 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. However, children receiving their measles/measles and rubella-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 and half of the children aged 12-23 months.

We use the country-specific household age composition as reported by the United Nations [18] 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. 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 relatives 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. We apply age-stratified infection fatality risk (IFR) 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 [19]. For children we use the reported risks for age 0 to 9, for adults the risk for age 20-29, and for adults over 60 the risk for age 60-69.

Sensitivity analyses

To account for the considerable uncertainty around the majority of our parameter assumptions we conduct a probabilistic sensitivity analysis (PSA). We include uncertainty

ranges around parameters governing the SARS-CoV-2 infection model (Table1), as well as the reported uncertainty ranges for the IFR estimates (modelled using a gamma distribution) and the vaccine preventable mortality estimates (modelled using a lognormal distribution). We report the 95% uncertainty range of the PSA alongside the central estimates.

The program code 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 [20].

Results

The benefit of sustaining EPI

We estimate that the current routine childhood immunisation programme (DTP, HepB, Hib, PCV, RotaC, MCV, RCV, MenA, YFV) in Africa prevents 809,991 (692,699 - 6,962,385) future deaths in children from the time of vaccination until 5 years of age. About one third of those are attributable to measles and another third to pertussis. One in three of the deaths are prevented in Nigeria, Ethiopia, Democratic Republic of Congo, and Tanzania.

The excess Covid-19 risk of sustaining EPI

We estimate that for visits for EPI-1 and EPI-2 & 3 the added probability of a SARS-Cov-2 infection in the household is 1.75% and 0.60%, respectively. Thus, continuation of routine childhood immunisation in Africa may lead to 7,069 (1,914 - 24,964) additional deaths attributable to additional SARS-CoV-2 infections associated with the immunisation visits of children. About 18 (0 - 294) of these are expected to be among the vaccinated children and 6,400 (1,696 - 22,786) among elders in the household.

The benefit-risk ratio of sustaining EPI

We estimate that for every extra death caused by an additional household exposure to SARS-CoV-2 attributable to a routine childhood immunisation visit, unimpaired continuation of the African routine childhood immunisation programme would prevent 128 (34 - 1,247) future deaths in children from the time of vaccination to 5 years of age. More than 90% of the excess risk is due to the high fatality rate in elders. Considering only the risk for the vaccinated infants, the benefit-risk ratio is that for every one excess Covid-19 death among vaccinated children, 51,755 (3,041-46,486,749) future deaths in children from the time of vaccination to 5 years of age would be prevented.

The findings were largely similar across Africa (Figure 1). The lowest benefit-risk ratio was estimated for Tunisia, Morocco and Eswatini, although each with a central estimate of more than 40 child deaths averted per excess Covid-19 death and a lower estimate of more than 10 child deaths averted per excess Covid-19 death.

The benefit of continuation of both the three EPI-1 immunisation visits in early infancy as well as the visit for EPI-2 at about 9 months was substantial with 105 (29 - 402) and 214 (53 - 4,342) future deaths averted among children (from the time of vaccination to 5 years of age) per Covid-19 excess death, respectively. Continuing EPI-3 visit at 15-18 months results in an incremental benefit of 6 (2 - 22) future deaths averted among children (from the time of vaccination to 5 years of age) per excess Covid-19 death.

Conclusion & Limitations

In summary, our analysis suggests that the benefit from routine childhood immunisation far outweighs the excess risk of Covid-19 deaths due to the additional risk for infection during the vaccination visit, particularly for the child that is to be vaccinated.

The analyses come with a number of key limitations. Given the constraints of the available data on vaccine preventable childhood disease burden in Africa the results need to be interpreted in the context that all children in the cohorts normally eligible for vaccination during the suspension of the EPI would be completely unprotected for the duration of the cessation of immunisation services and until they are 5 years of age. For many vaccine-preventable infections with relatively low transmissibility, indirect protection from cohorts vaccinated before the pandemic will help to limit circulation in the community before immunisation can continue, although those unvaccinated cohorts will remain at higher risk throughout their lifetime. For highly transmissible pathogens like pertussis or measles, however, a 6 months interruption of routine immunisation may well be sufficient for a resurging disease burden extending to those missed for vaccination among previous cohorts and those too young to be vaccinated. For measles, indeed rapid resurgence has been observed before the West African Ebola outbreak and the accompanying disruption of routine immunisation had ended [21–23]. In a country with 80% routine MCV uptake and an inter-epidemic period of 4 years, 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. This would yield a 25% chance that an outbreak starts during the 6 months of suspension and a further 25% in the 6 months following, all else being equal.

Similarly, we have not considered catch-up campaigns that help to cap the risk period as soon as vaccination services can resume function. While these are logistically challenging and for some vaccines impossible to conduct due to licensing age restrictions, they would reduce the currently considered risk period for vaccine preventable diseases of about 5 years to the 6 months during which we assume health services are disrupted. This would reduce the risk from suspending routine childhood immunisation but is unlikely to qualitatively change our findings, particularly since much of the vaccine preventable disease risk in children is concentrated within the first two years of life.

Contact reducing interventions aimed at mitigating SARS-CoV-2 will also reduce the transmission of other pathogens. However, larger household sizes and higher daily dependency on income and food supplies may make contact reducing measures less effective than observed elsewhere [24,25]. Furthermore, these interventions may curb transmission by up to 50% or, during a lockdown, temporarily even by 70% but for measles or pertussis with an estimated basic secondary attack rate of at least 12 and 5.5, respectively [26,27], these interventions are unlikely to substantially limit their spread in the community if routine vaccination is suspended.

To calculate the number of Covid-19 associated fatalities, we used infection fatality rates (IFRs) 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 help with mitigating some of the burden of Covid-19, IFRs 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 coinfection in some parts of Africa.

Given these limitations we cannot completely rule out the possibility that some African countries with (i) high pre-pandemic vaccine coverage that ensures robust herd immunity, (ii) stringent contact reducing interventions during the pandemic that would delay resurgence of vaccine preventable diseases and (iii) immediate large-scale catch-up campaigns following the pandemic, may experience a substantially smaller number of vaccine preventable fatalities. Pathogen specific dynamic modelling approaches would be needed to account for such effects and particularly for measles and pertussis would substantially add to the robustness to our results. However, for our findings to qualitatively change, the risk for infection with the vaccine-preventable antigens during the vaccine suspension period would need to be more than 100 times smaller than with our crude estimates, and more than 50,000 times smaller if the Covid-19 risk only to the vaccinated child is considered.

Our estimates are aimed at the strategic consideration of whether childhood immunisation should be suspended to limit the risk of Covid-19 mortality. Specifically, we do not consider logistical constraints that factor into such decisions, including a partial break down of the vaccine supply or delivery cold chain, the necessity of re-allocation of doctors and nurses to prioritised health services or staff shortages because of ill-health or because of underlying health conditions that put them at increased risk for severe Covid-19 disease.

Tables

Table 1. Simulation parameters. 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
ν	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	[28]
R_0	Basic reproduction number for SARS-CoV-2*	$\underset{\Gamma(2.5,25)}{2.5}$	[15]
T	Duration of period at risk for SARS-CoV-2	$6 * 30 days$	[14]
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.	$1 - \frac{1}{R_0}$	calculated
ψ	Duration of infectiousness*	$\underset{\Gamma(7,14)}{7 days}$	[16]
$p_0 = \frac{p_v}{\iota_1}$	Prevalence of infectiousness among other community members at any one day (and that of vaccinators)	$\frac{\theta\psi}{T}$	calculated
ι_1	Risk ratio of a vaccinator being infected and infectious vs another community member	$\underset{U(1,4)}{2}$	assumption
ι_2	Risk ratio per potentially infectious contact of a vaccinator transmitting vs another community member	$\underset{U(0.25,1)}{0.5}$	assumption
N	Average number of transmission relevant contacts of a community member per day	$\underset{U(2,10)}{5}$	[29]
$t_0 = \iota_2 t_v$	Probability of transmission given potentially infectious contact for other community members (and vaccinators)	$\frac{R_0}{N\psi}$	calculated
n	Number of non-vaccinator contacts of child and carer during their travel to the vaccine clinic and in the waiting room	$\underset{U(1,10)}{2}$	assumption
P	Probability for a SARS-CoV-2 infection for the whole household of a child who gets vaccinated	See manuscript	calculated
P_E	Probability for excess a SARS-CoV-2 infection for the whole household of a child who gets vaccinated	$P(1-\theta)$	calculated

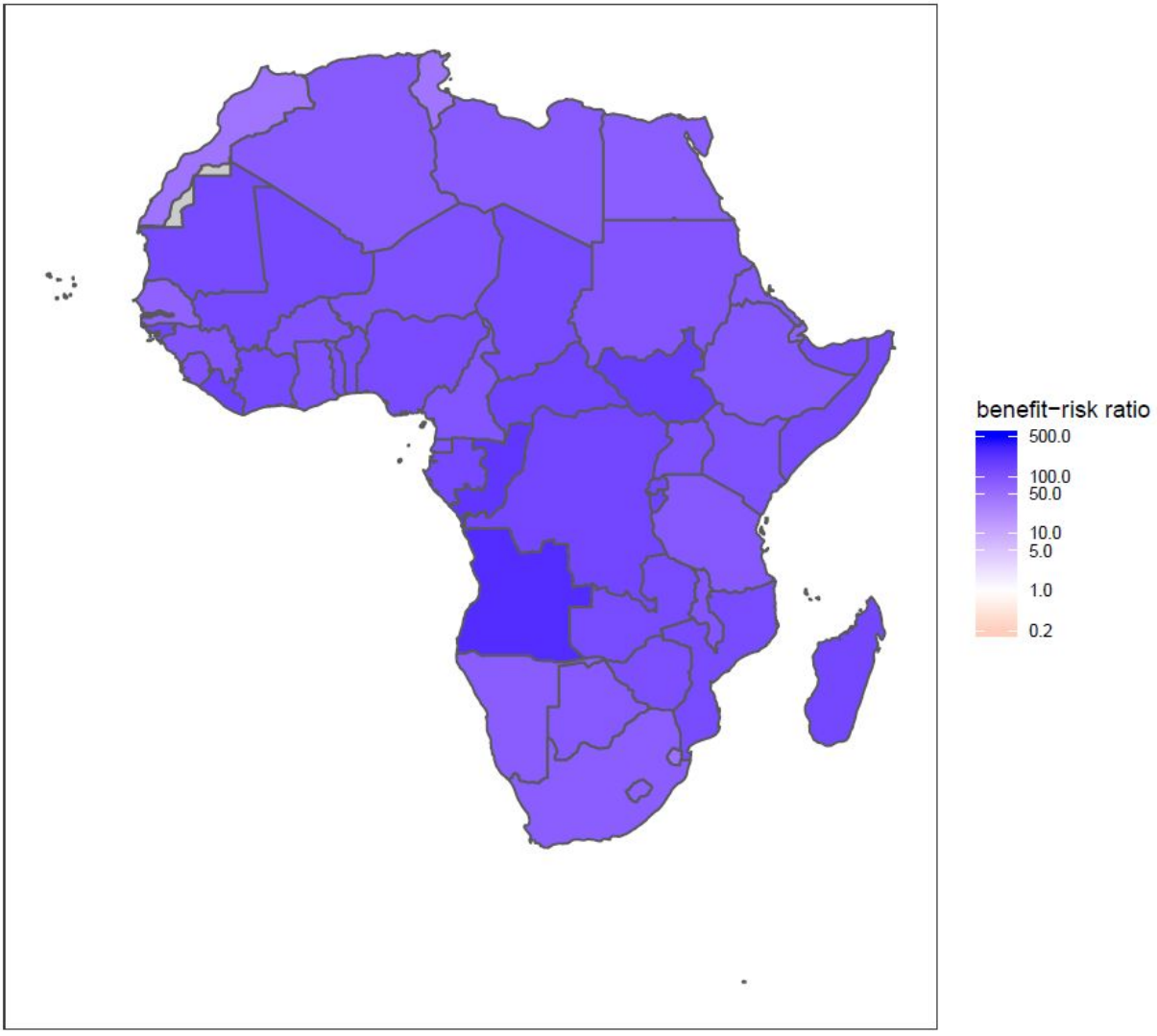
* Gamma distributions are parameterised as (mean,shape)

Table 2: Vaccine antigen specific risks and benefits of sustaining routine childhood vaccination. The benefit-risk ratio estimates (median estimates and 95% uncertainty intervals) show the child deaths averted by continuing the routine childhood immunisation programmes per one Covid-19 death attributable to an excess SARS-CoV2 infection acquired in the process of attending vaccine delivery. Note that while the vaccine preventable deaths estimates are vaccine antigen specific, the excess deaths are dependent on the number of required visits. As vaccination visits are grouping delivery of several vaccines these have a superior 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	13,228 (10,352-17,908)	4,778 (1,308-16,476)	3 (1-10)
Tetanus	6, 10, 14 weeks	70,983 (55,478-94,928)	4,778 (1,308-16,476)	15 (4-56)
Pertussis	6, 10, 14 weeks	279,663 (217,097-368,354)	4,778 (1,308-16,476)	58 (16-213)
HepB	6, 10, 14 weeks	7,351 (3,327-232,326)	4,780 (1,308-16,483)	2 (0-58)
Hib	6, 10, 14 weeks	57,056 (48,089-70,166)	4,797 (1,313-16,541)	12 (3-44)
PCV	6, 10, 14 weeks	47,154 (39,570-57,939)	4,256 (1,164-14,690)	11 (3-40)
RotaC	6, 10 weeks	10,770 (9,569-12,374)	2,031 (548-7,265)	5 (2-20)
MCV1	9 months	241,356 (203,199-4,951,052)	1,617 (431-5,926)	169 (43-2,867)
RCV	9 months	5,486 (855-433,910)	637 (170-2,333)	10 (1-796)
MenA	9 months	2,031 (244-211,221)	240 (64-879)	9 (1-1,139)
YFV	9 months	24,242 (17,866-34,027)	748 (199-2,743)	32 (9-127)
MCV2	15-18 months	3,569 (2,733-6,160)	639 (171-2,342)	6 (2-22)
EPI-1 (DTP, HepB, Hib, PCV, RotaC)	6, 10, 14 weeks	495,183 (422,180-716,605)	4,797 (1,313-16,541)	105 (29-402)
EPI-2 (MCV1, RCV1, MenA, YFV)	9 months	294,487 (235,672-6,138,958)	1,617 (431-5,926)	214 (53-4,342)
EPI (DTP3, HepB3, Hib3, PCV3, RotaC, MCV1, RCV1, MenA, YFV, MCV2)	6, 10, 14 weeks; 9 months; 15-18 months	808,991 (692,699-6,962,385)	7,069 (1,914-24,964)	128 (34-1,247)

Figures

Figure 1: Spatially disaggregated benefit-risk ratio of continuing routine infant immunisation. The number of vaccine preventable deaths averted among <5y old children by sustaining routine childhood vaccination of DTP, HepB, Hib, PCV, RotaC, MCV, RCV, MenA and YFV per one Covid-19 death attributable to the excess risk of infection from attendance of a vaccination clinic for respective vaccine delivery. 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 based on the number of deaths averted (and not the number of life years gained).



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Supplement

Table S1: 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. Note that in the columns only the risk is disaggregated across the different age groups in the household.

Vaccine	Benefit-risk ratios				
	Household	Vaccinated children	Siblings	Parents	Grandparents
Diphtheria (DTP3)	3 [1-10]	1,086 [67-656,030]	954 [59-576,075]	38 [8-220]	3 [1-11]
HepB3	2 [0-58]	794 [29-758,820]	697 [26-666,250]	25 [4-971]	2 [0-66]
Hib3	12 [3-44]	4,715 [304-2,966,714]	4,136 [267-2,602,381]	168 [36-937]	13 [4-50]
MCV1	169 [43-2,867]	72,072 [3,777-69,486,337]	63,270 [3,316-61,000,114]	2,398 [470-51,010]	185 [46-3,040]
MCV2	6 [2-22]	2,232 [136-1,474,443]	2,148 [131-1,418,901]	80 [16-487]	6 [2-25]
PCV3	11 [3-40]	4,442 [279-2,650,622]	3,843 [241-2,293,433]	162 [35-900]	12 [3-45]
Pertussis (DTP3)	58 [16-213]	23,061 [1,453-15,591,982]	20,251 [1,276-13,691,691]	823 [174-4,786]	64 [18-249]
RCV1	10 [1-796]	4,551 [94-11,610,421]	4,026 [84-10,270,037]	140 [10-14,170]	11 [1-835]
RotaC	5 [2-20]	2,241 [133-1,417,240]	2,008 [119-1,269,965]	79 [17-442]	6 [2-22]
Tetanus (DTP3)	15 [4-56]	5,860 [355-3,774,725]	5,146 [312-3,314,676]	211 [43-1,264]	16 [5-62]
YFV	32 [9-127]	13,112 [785-7,864,815]	10,326 [618-6,193,910]	468 [92-2,821]	36 [10-142]
MenA	9 [1-1,139]	5,153 [87-11,080,453]	3,989 [67-8,576,506]	135 [8-18,276]	10 [1-1,326]
DTP3, HepB3, Hib3, PCV3, RotaC	105 [29-402]	42,207 [2,605-28,070,496]	37,024 [2,285-24,623,247]	1,475 [320-9,148]	115 [32-459]
MCV1, RCV1, MenA, YFV	214 [53-4,342]	91,152 [4,649-88,871,390]	80,020 [4,081-78,017,710]	3,054 [566-72,442]	236 [58-4,563]
DTP3, HepB3, Hib3, PCV3, RotaC, MCV1, RCV1, MenA, YFV, MCV2	128 [34-1,247]	51,755 [3,041-46,486,749]	45,778 [2,691-41,119,838]	1,834 [363-21,314]	141 [37-1,441]

Table S2: 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. Note that in the columns only the risk is disaggregated across the different age groups in the household.

Country	Benefit-risk ratios				
	Household	Vaccinated children	Siblings	Parents	Grandparents
Angola	254 [65-1,672]	60,124 [3,245-61,104,552]	48,300 [2,606-49,086,961]	2,123 [387-21,354]	303 [76-2,069]
Burundi	151 [38-867]	46,188 [2,592-36,921,693]	41,631 [2,336-33,278,851]	1,636 [317-14,047]	173 [44-1,012]
Benin	121 [33-507]	50,877 [2,872-33,391,655]	40,232 [2,271-26,405,031]	1,841 [360-11,764]	132 [35-550]
Burkina Faso	104 [26-449]	45,312 [2,586-31,788,975]	31,592 [1,803-22,163,365]	1,559 [301-10,737]	113 [28-498]
Botswana	85 [21-332]	36,128 [1,951-21,529,325]	42,751 [2,308-25,475,779]	1,328 [255-7,831]	92 [23-368]
Central African Republic	147 [40-588]	47,673 [2,743-30,510,179]	36,998 [2,129-23,678,178]	1,698 [344-9,786]	168 [44-681]
Cote d'Ivoire	126 [34-509]	56,225 [3,198-34,243,032]	47,582 [2,706-28,979,004]	1,897 [393-11,749]	139 [37-573]
Cameroon	97 [25-516]	47,499 [2,637-42,342,422]	36,900 [2,048-32,893,869]	1,665 [307-12,730]	105 [27-559]
Congo - Kinshasa	139 [38-590]	44,943 [2,702-30,752,292]	33,544 [2,017-22,952,423]	1,605 [314-9,637]	158 [42-690]
Congo - Brazzaville	205 [54-794]	55,555 [3,297-35,099,169]	56,459 [3,351-35,670,158]	1,977 [394-11,475]	238 [63-960]
Comoros	71 [19-295]	41,722 [2,498-27,198,293]	35,868 [2,147-23,381,912]	1,510 [301-8,899]	77 [21-322]
Cape Verde	68 [17-416]	29,315 [1,628-25,568,517]	25,062 [1,392-21,859,317]	1,062 [197-8,942]	74 [18-458]
Djibouti	68 [18-310]	28,592 [1,837-21,415,406]	24,444 [1,571-18,308,693]	1,062 [213-6,486]	75 [19-349]
Algeria	82 [22-339]	35,527	30,373	1,260	90 [23-378]

		[2,190-19,909,837]	[1,873-17,021,536]	[256-7,580]	
Egypt	77 [17-360]	20,728 [1,121-14,439,265]	28,470 [1,539-19,832,173]	702 [122-4,849]	89 [20-411]
Eritrea	88 [24-363]	38,674 [2,169-24,873,087]	33,064 [1,855-21,264,772]	1,338 [267-8,290]	97 [25-413]
Ethiopia	90 [23-360]	42,157 [2,560-27,753,338]	41,627 [2,528-27,404,440]	1,508 [311-9,603]	98 [26-400]
Gabon	132 [34-539]	44,160 [2,630-29,439,280]	40,691 [2,424-27,126,071]	1,605 [302-10,031]	149 [37-611]
Ghana	104 [28-424]	41,904 [2,281-26,275,814]	49,993 [2,721-31,348,070]	1,500 [289-9,583]	116 [30-477]
Guinea	98 [25-371]	61,734 [3,713-39,589,421]	42,401 [2,551-27,191,458]	2,279 [438-13,318]	103 [26-405]
Gambia	69 [18-283]	51,560 [3,069-32,461,006]	24,057 [1,432-15,145,326]	1,826 [363-10,968]	73 [18-304]
Guinea-Bissau	142 [37-545]	58,859 [3,468-40,514,896]	50,321 [2,965-34,637,438]	2,146 [433-12,343]	157 [40-616]
Equatorial Guinea	104 [27-429]	44,298 [2,589-34,457,528]	37,872 [2,214-29,458,807]	1,581 [318-10,266]	114 [29-474]
Kenya	105 [28-436]	35,359 [2,061-23,464,096]	41,127 [2,398-27,292,030]	1,252 [247-7,908]	119 [31-512]
Liberia	152 [38-644]	63,604 [3,392-39,930,289]	56,007 [2,987-35,160,850]	2,200 [425-14,241]	168 [41-710]
Libya	82 [21-345]	35,592 [2,079-21,655,801]	30,429 [1,777-18,514,214]	1,262 [256-8,009]	90 [23-379]
Lesotho	71 [19-279]	38,321 [2,282-26,941,636]	56,303 [3,353-39,583,509]	1,377 [268-8,446]	77 [20-308]
Morocco	42 [10-186]	20,968 [1,151-14,510,601]	22,864 [1,255-15,823,036]	770 [139-5,317]	45 [10-203]
Madagascar	134 [37-543]	41,324 [2,461-26,017,772]	36,703 [2,186-23,108,297]	1,503 [312-8,639]	153 [42-630]
Mali	128 [32-692]	64,185 [3,451-48,665,442]	46,716 [2,512-35,420,480]	2,195 [409-16,951]	140 [34-796]
Mozambique	123 [32-483]	36,811 [2,312-22,692,539]	36,488 [2,292-22,492,929]	1,359 [262-7,842]	140 [36-558]
Mauritania	125 [31-661]	55,663 [2,998-39,822,926]	47,588 [2,563-34,045,852]	1,950 [345-14,617]	137 [33-739]
Mauritius	84 [22-337]	35,178 [2,050-27,585,189]	30,075 [1,753-23,583,432]	1,281 [250-7,642]	93 [24-373]
Malawi	96 [24-608]	35,562	36,197	1,216	107 [26-685]

		[1,926-28,087,090]	[1,960-28,588,329]	[220-10,154]	
Namibia	77 [20-320]	38,568 [2,437-25,831,318]	38,166 [2,411-25,562,214]	1,398 [280-8,632]	83 [21-361]
Niger	104 [27-403]	48,973 [2,832-31,632,145]	32,823 [1,898-21,200,773]	1,696 [324-10,081]	113 [29-445]
Nigeria	119 [32-452]	47,584 [2,801-31,004,230]	40,046 [2,357-26,092,889]	1,706 [342-10,107]	132 [35-507]
Rwanda	129 [32-681]	41,435 [2,412-25,425,982]	48,502 [2,824-29,762,497]	1,441 [272-11,742]	148 [35-764]
Sudan	95 [23-625]	41,683 [2,132-26,321,820]	33,038 [1,690-20,862,526]	1,391 [251-13,565]	105 [25-719]
Senegal	68 [14-521]	60,267 [2,930-50,471,809]	27,374 [1,331-22,924,795]	2,090 [335-22,011]	72 [14-538]
Sierra Leone	101 [26-385]	58,359 [3,352-33,895,593]	45,451 [2,610-26,398,490]	2,136 [425-12,928]	107 [27-413]
Somalia	119 [32-454]	52,106 [3,040-37,635,838]	44,547 [2,599-32,176,042]	1,840 [366-10,984]	131 [36-507]
South Sudan	175 [27-142,550]	101,335 [2,314-516,409,057]	72,162 [1,648-367,744,327]	2,319 [257-2,344,844]	197 [30-159,407]
São Tomé and Príncipe	117 [29-521]	38,027 [2,146-24,352,562]	42,065 [2,374-26,938,641]	1,343 [241-9,341]	132 [32-581]
Swaziland	46 [12-190]	23,292 [1,389-17,422,214]	18,064 [1,077-13,511,672]	822 [163-5,576]	50 [12-208]
Seychelles	90 [23-359]	38,072 [2,269-24,885,241]	32,549 [1,940-21,275,162]	1,366 [256-8,026]	98 [25-400]
Chad	124 [31-761]	48,253 [2,677-33,567,311]	30,713 [1,704-21,365,390]	1,630 [331-13,539]	140 [35-840]
Togo	114 [29-471]	51,189 [2,801-30,652,956]	46,895 [2,566-28,082,090]	1,816 [335-11,287]	125 [31-517]
Tunisia	41 [10-192]	17,267 [905-12,332,882]	14,762 [773-10,543,762]	615 [108-4,429]	45 [11-207]
Tanzania	86 [20-618]	38,974 [1,947-25,860,588]	34,366 [1,717-22,803,319]	1,355 [232-12,330]	95 [22-675]
Uganda	108 [28-434]	37,220 [2,145-24,697,355]	32,095 [1,850-21,296,635]	1,335 [258-8,045]	122 [31-492]
South Africa	75 [19-308]	36,285 [2,131-22,605,407]	54,133 [3,179-33,725,035]	1,288 [266-7,832]	81 [20-339]
Zambia	122 [31-589]	41,682 [2,341-29,204,525]	33,093 [1,859-23,186,883]	1,446 [276-11,404]	137 [34-688]

Zimbabwe	108 [29-571]	44,271 [2,569-32,924,068]	51,480 [2,988-38,285,296]	1,553 [293-12,142]	120 [31-659]

Figure S1: 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 programme during the Covid-19 pandemic.

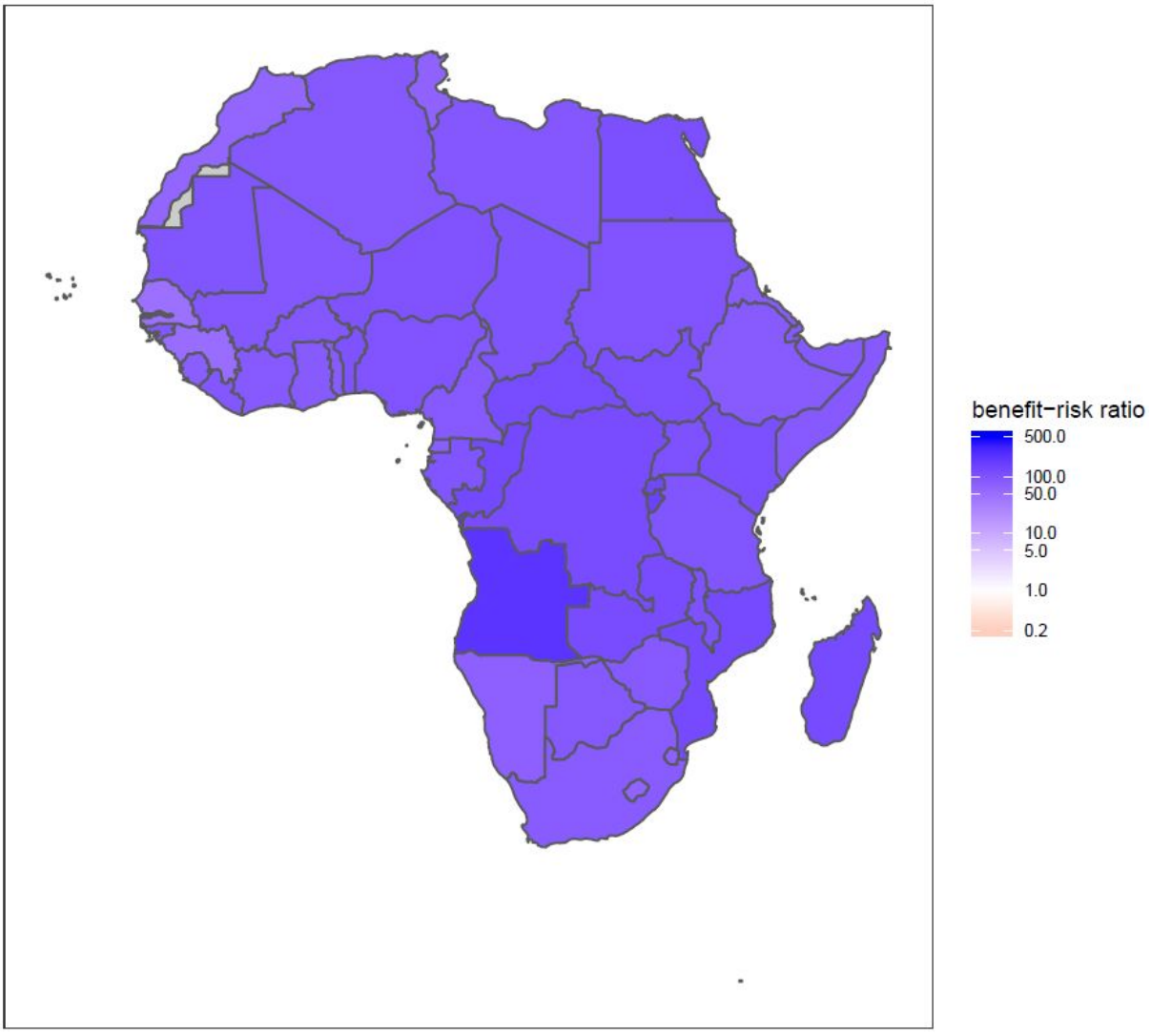

Figure S2: Benefit-risk ratio of vaccines delivered in the fourth vaccination-related clinical visit (1-dose MCV1, RCV1, MenA, YFV) for children at 9-months of age during the Covid-19 pandemic in Africa. The central estimates for benefit-risk ratio at the household level show the child deaths averted 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 programme during the Covid-19 pandemic.

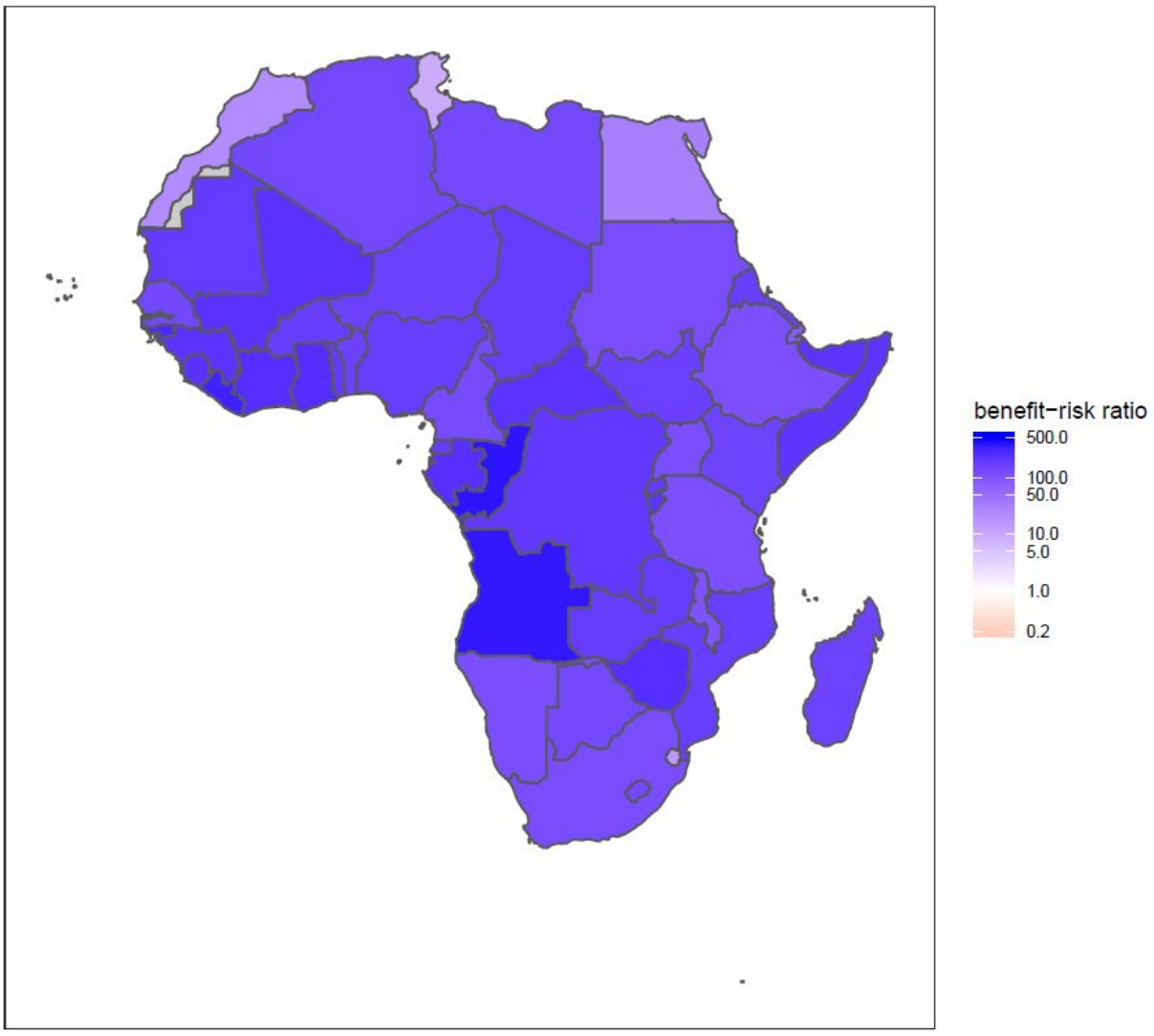

Figure S3: Benefit-risk ratio of vaccines delivered in the fifth vaccination-related clinical visit (1-dose MCV2) for children at 15-18 months of age during the Covid-19 pandemic in Africa. The central estimates for benefit-risk ratio at the household level show the child deaths averted by continuing 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 programme during the Covid-19 pandemic.