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Exploring the subnational inequality and heterogeneity of the impact of routine measles immunisation in Africa

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ABSTRACT

Despite vaccination being one of the most effective public health interventions, there are persisting inequalities and inequities in immunisation. Understanding the differences in subnational vaccine impact can help improve delivery mechanisms and policy. We analyse subnational vaccination coverage of measles first-dose (MCV1) and estimate patterns of inequalities in impact, represented as deaths averted, across 45 countries in Africa. We also evaluate how much this impact would improve under more equitable vaccination coverage scenarios. Using coverage data for MCV1 from 2000–2019, we estimate the number of deaths averted at the first administrative level. We use the ratio of deaths averted per vaccination from two mathematical models to extrapolate the impact at a subnational level. Next, we calculate inequality for each country, measuring the spread of deaths averted across its regions, accounting for differences in population. Finally, using three more equitable vaccination coverage scenarios, we evaluate how much impact of MCV1 immunisation could improve by (1) assuming all regions in a country have at least national coverage, (2) assuming all regions have the observed maximum coverage; and (3) assuming all regions have at least 80% coverage. Our results show that progress in coverage and reducing inequality has slowed in the last decade in many African countries. Under the three scenarios, a significant number of additional deaths in children could be prevented each year; for example, under the observed maximum coverage scenario, global MCV1 coverage would improve from 76% to 90%, resulting in a further 363(95%CrI:299–482) deaths averted per 100,000 live births. This paper illustrates that estimates of the impact of MCV1 immunisation at a national level can mask subnational heterogeneity. We further show that a considerable number of deaths could be prevented by maximising equitable access in countries with high inequality when increasing the global coverage of MCV1 vaccination.

1. Introduction

Vaccination remains one of the most effective public health interventions globally, preventing an estimated 5.4 million vaccine-preventable deaths per year [1]. Efforts to improve global vaccination coverage over the last three decades have substantially increased global immunisation access and decreased inequities since 1974 [2]. These include strategies such as Reaching Every District-Reaching Every Child (RED-REC) [3], the implementation of the United Nations' Sustainable Development Goals (SDGs)[4], and the development of the Global Vaccine Action Plan (GVAP) [5]. High-level political commitment in the African Region, including the Addis Declaration on Immunisation [6] and the Regional Strategic Plan on Immunisation 2014–2020 (RSPI 2014-2020)[7], further set ambitious targets to reduce vaccine preventable diseases (VPDs) and improve immunisation service access.

However, despite progress towards the global and regional targets set by the GVAP, RSPI 2014, and SDGs, immunisation progress in the World Health Organisation African Region (WHO AFRO) has stagnated in recent years. Among all low- and middle-income countries (LMICs), African countries see more than 30 million under-five children with VPDs every year; of these, over half a mil-

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lion children die, accounting for 58% of all VPD child deaths [8]. In addition, goals and targets as stated in the AFRO RSPI 2014–2020 [9] have not been achieved. As of 2019, measles-containing vaccine (MCV1) coverage stagnated at 69%, and only 15[1] countries had achieved the RSPI 2014 target of ⩾90% coverage for MCV1, the same number as in 2013.

Well-documented inequalities and inequities in immunisation continue to persist and remain a key concern in LMICs, largely due to gaps in immunisation coverage among individuals living in rural areas or urban developments, families living in poverty, and individuals without formal education [10]. The African Region now contains 7.3 million zero-dose children, with 86% of them located in just 10 Member States [11]. In addition, the SARS-CoV-2 pandemic has deepened existing inequities, further highlighting the need for robust and equitable immunisation systems. For instance, existing initiatives addressing MCV1, including the Global Measles and Rubella Strategic Plan 2012–2020 [12] and Measles and Rubella Initiative [13], are anticipated to face increasing setbacks, especially in the Sub-Saharan African (SSA) Region [14].

As coverage remains an important indicator for progress towards the global targets noted above, and as national level estimates can miss important heterogeneity that prevents effective and efficient resource allocation, there has been an increasing need to understand the differences in subnational coverage to improve delivery mechanisms and immunisation policy, and to monitor and track the GVAP and RSPI 2014[2] progress. This is especially important in ensuring that disadvantaged populations meet the required coverage levels alongside continued improvement in national coverage levels. Monitoring outcomes, including inequality, between administrative regions within a country, which are the main units of resource allocation, further provides important evidence to develop and improve on equitable policies and health programs.

In the case of MCV1 coverage, even countries with high national vaccination coverage are at risk of outbreaks if there is a significant geographic disparity in vaccination. As such, measles is often used as a tracer for implementation progress, useful due to its epidemiological properties, including a high R0 and high vaccine efficacy. Nearly all countries offer MCV1 and MCV2 doses alongside supplementary immunisation activities (SIAs), meaning measles is capable of highlighting issues in systematically missed children and communities, including those among zero-dose children [15].

There is a current major deficiency in the availability of disaggregated data at a subnational level, with a wide geographical and temporal range, suitable to monitor inequalities throughout time. However, thanks to the development of transmission models projecting annual impact of routine coverage for vaccines [16,17], it is possible to translate those coverage estimates into estimates of vaccine impact (e.g., deaths averted) and evaluate the current inequality and changes of this inequality of impact through time.

This study presents a comprehensive analysis of the magnitude and patterns of inequalities in the impact of MCV1 routine immunisation across 45 countries of Africa. Specifically, it aims to: quantify the impact of vaccination of MCV1 represented as deaths averted at the subnational level in the African region; assess the changes in the impact of immunisation through time; evaluate how much this impact would improve under hypothetical scenarios of increased coverage while maximising the equality of vaccine impact among regions of a country; and finally, identify the countries and regions with the highest potential of increase in deaths averted under more equitable vaccination coverage scenarios.

2. Methods

2.1. Data sources

First administrative level measles-containing-vaccine first-dose (MCV1) coverage data was extracted for 45 African countries from 2000–2019 from the Institute for Health Metrics and Evaluation (IHME) data portal, the Global Health Data Exchange released in 2020 [18,19]. The first administrative level is the largest subdivision of each country which can vary in area both within and between countries.

We extracted subnational population data from www.worldpop.org by age (0–1, 1–4, and 5–80+), and gender for the first administrative level (admin1) for the 45 African countries with available coverage data between 2000–2019.The Worldpop for each region i in country k WP_{ki} was then adjusted, so the total population over all the regions matched the country's total population from the 2019 United Nations World Population Prospects (UNWPP) $UNWPP_k$ [20–22].

$$AP_{ki} = \frac{WP_{ki}}{\sum_j WP_{kj}} \times UNWPP_k$$

We then used this adjusted population AP_{ki} and the coverage estimates of MCV1 for region i from IHME $IHMEcov_i$ to calculate the number of fully vaccinated people (FVPs), which refers to the total number of doses provided by a vaccination activity. These estimates of FVPs were also adjusted $Afvps_{ki}$ to match the total number of FVPs $WUE - Fvps_k$ of a country k from WHO/UNICEF Estimates of National Immunisation Coverage (WUENIC) as published in July 2019 [23] $WUE - cov_k$, and the UNWPP population $UNWPP_k$.

$$Afvps_{ki} = \frac{WP_{ki} \times IHME_{ki}}{\sum_j WP_{kj} \times IHME_{kj}} \times (UNWPP_k \times WUE - cov_k)$$

From both the adjusted population and adjusted FVPs, we can calculate the adjusted values of coverage of a region i and country k as $ACov_{ki} = \frac{Afvps_{ki}}{AP_{ki}}$. This normalisation procedure ensures that the mean of subnational coverage estimates matches the national coverage estimates from WUENIC, the reference coverage of the latest impact estimates from the Vaccine Impact Modelling Consortium (VIMC) used in this study. Figures S1 and S2 illustrate the differences between the adjusted and unadjusted population and coverage estimates used in this study.

2.2. Impact calculation

The Vaccine Impact Modelling Consortium (VIMC) uses demographic data and vaccine coverage data from the World Health Organization (WHO), United Nations Children's Fund (UNICEF) and Gavi, the Vaccine Alliance, to calculate the impact of immunisation activities. The VIMC uses multiple mathematical models under different vaccination scenarios: no vaccination, routine immunisation of measles first-dose (MCV1), measles second-dose (MCV2) and supplementary immunisation activities (SIAs) to calculate the burden averted (death, DALYs and cases) by the vaccination against 12 pathogens (see [16,17] for more details). In this study, we used the latest immunisation impact estimates for measles available in [17]. These estimates are based on two vaccine impact models, the DynaMICE (DYNAmic Measles Immunisation Calculation Engine) [24], and Penn State model [25]. Using the mean of the burden estimates from these models, from the no vac-

[1] Botswana, Burundi, Cabo Verde, Comoros, Eritrea, Ghana, Lesotho, Malawi, Mauritius, Rwanda, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone and Zambia

[2] The RSPI 2014, developed in line with the GVAP at World Health Assembly in 2012, was replaced by IA2030 in 2020; on July 21st, 2021, the AFRO Region released a framework for the implementation of IA2030. The RSPI for 2021–2030 is still in progress.

Table 1
Summary characteristics of the vaccine impact models for measles used in this study as baseline estimates of national immunisation impact. Information taken from [28]

	Model 1	Model 2
Model name	DynaMICE [24]	Penn State [25]
Structure	Compartmental	Semi-mechanistic
Randomness	Deterministic	Stochastic
Time step	Weekly	Annual
Age stratification	Yes	Yes
Model fitting	Not fitted; uses country-specific R0 (basic reproduction number) for measles from fitted models	Fitted to observed annual WHO case data (1980–2017)
Validation	Validated through comparisons to the Penn State in two previous model exercises [16,26]. Has been reviewed by WHO's Immunization and Vaccines Implementation Research Advisory Committee (IVIR-AC)[27].	Model and performance of parameter estimation was validated through simulation experiments as described in Eilertson et al., 2019. Validated through comparisons to the DynaMICE in two previous model comparison exercises [16,26]. Has also been reviewed by WHO's Immunization and Vaccines Implementation Research Advisory Committee (IVIR-AC) in 2017 and 2019 [27].

cination and MCV1 vaccination scenario, we calculate the number of deaths averted by MCV1 in the 45 African countries used in this study. The mean and 95% credible interval (CrI) values of the deaths averted were computed from the distribution of input parameters and posterior distributions of fitted parameters. Summary model details are available in Table 1.

Whilst mathematical modelling of vaccine impact is essential to determine the effect of vaccination, updating these estimates with new coverage estimates, especially those at a subnational level, can be incredibly computationally expensive and time-consuming. Due to the constant changes in coverage and vaccine impact estimates, as well as their uncertainty, the VIMC developed an impact extrapolation (IE) method [29], which uses the deaths averted rates (deaths averted per fully vaccinated person) from the latest modelling estimates to extrapolate the impact calculation (see estimates in Table S4). In this study, we used this extrapolation method to calculate the impact of MCV1 vaccination at a subnational level. Using the deaths averted rates from the latest VIMC modelling estimates (i.e., from [17]), we calculate the impact of MCV1 vaccination $I(s,y)$, defined in this study as deaths averted in region s, at year y as:

$$I(s,y) = \rho(c,k) \times \mathrm{FVP}(s,k,y), \tag{1}$$

where $\rho(c,k)$ corresponds to the country (c) modelled deaths averted rate per birth cohort (k), and $\mathrm{FVP}(s,k,y)$ describes the number of fully vaccinated persons at year (y) in region s, which is calculated as the coverage in year (y) $\times$ the size of the cohorts (k) vaccinated in year (y). The final impact estimates $I(s,y)$ denote the total current and future deaths averted, due to long terms effects of MCV1 vaccination, attributed to the MCV1 vaccination activities occurring in the year (y).

Assuming that the deaths averted rates within a country vary proportionally with vaccination coverage, a factor that is highlighted in estimates of measles case fatality ratio [30], we calculate the deaths averted rates at the regional level using the range of the maximum and minimum rates achieved in a country for the year range 2000–2019 (see figure S6). As such we define the deaths averted rates for a region d to be:

$$eq: 2\rho_d = \rho \times \left(1 - \left(\frac{C_d - C_{mean}}{C_{mean}}\right)\Theta\right), \tag{2}$$

where ρ is the national deaths averted rates, ρ_d is the region deaths averted rates, C_d is the regional coverage, C_{mean} is the mean/national coverage and Θ is the maximum proportional change informed by the historic national extrema. For example, if a region has 60% coverage, the mean/national coverage is 80%, the maximum proportional change is 10% and the national impact ratio is 0.1; the regional impact ratio would be 0.1025. This means we assume that impact would be higher in areas of lower coverage.

2.3. Inequality measures

We used the index of disparity [31] to calculate the changes in inequality in vaccination through time. This index measures the degree of inequality a country experiences by comparing the differences between each region's vaccine impact and that of the entire country, with consideration towards the differences in population. This disparity index $DI(c,y)$ was calculated per country c and year y as:

$$DI(c,y) = \frac{\sum_r pop_{ry}\left|I_{ry} - \mu_{cy}\right|}{\mu_{cy}} \times 100, \tag{3}$$

where pop_{ry} is the population of the region r in year y, I_{ry} corresponds to the deaths averted in region r and year y, and μ_{cy} is the mean of deaths averted across all regions of country c and year y. The disparity index (DI) is a modified variation coefficient expressed as a percentage that describes the spread of the impact of vaccination and population across the regions of a country. This index is equal to zero if there are no inequalities among regions; larger values indicate higher levels of inequality.

2.4. Addressing inequality

We calculate the impact of vaccination of MCV1 under three scenarios of improved coverage with varying assumptions of reducing inequality, detailed below. We used these scenarios to illustrate the potential national improvement of vaccination's impact with coverage increases while assuming inequality declines.

1. At least national scenario: Assumes that none of the regions have a coverage that is lower than the one achieved at the national level, i.e., if inequalities were to be addressed, the goal would be to increase the coverage of all regions that are below the national average up to the level of the national average.
2. Regional max scenario: Assumes that the highest coverage among regions within a country in a specific year was achieved in all the regions. This scenario describes the total health improvement expected at national level if all regions had the same level of health as the reference, in this case the one with the highest coverage.
3. GVAP target scenario: Assumes that all regions achieve a specific target or threshold coverage. In this scenario, we describe the total health improvement expected at national level if all regions achieved at least 80% coverage, which is the subnational target coverage from the Global Vaccine Action Plan (GVAP) [32].

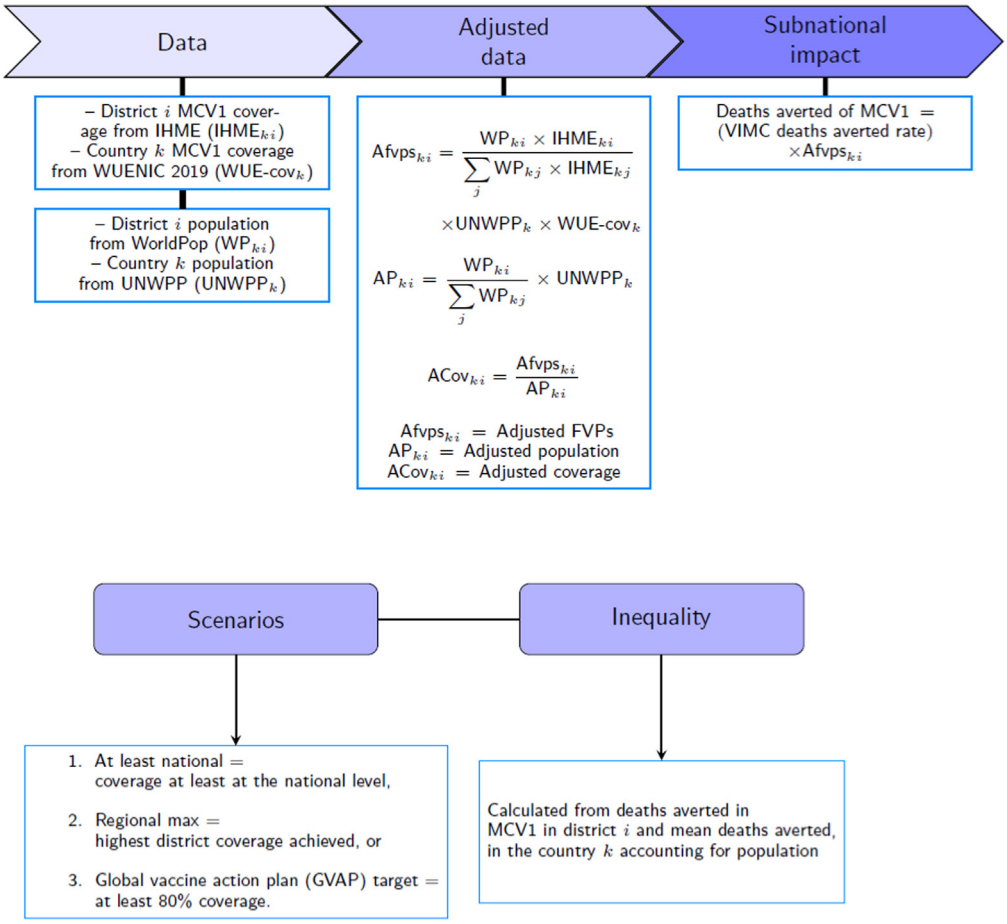

Fig. 1. Overall flow chart of the methods of this study. FVPs: fully vaccinated people. The impact is represented as deaths averted.

For an overall description of the methods see Fig. 1.

3. Results

3.1. Coverage and impact

Our adjusted MCV1 immunisation coverage estimates at the first administrative for 2019 ranged from 23% in Ennedi est, Chad (95% CrI: 10–44) to 100% in Eritrea and Cabo Verde in all their regions (95% CrI: 100–100). This coverage masks considerable variation over time and high regional heterogeneity (see Fig. 2), and is further reflected in the subsequent immunisation impact estimates as seen in Fig. 3a. For example, the national average of deaths averted per 100,000 live births in Nigeria in 2019 is 1,893 (see Table S3), but the impact among the regions ranges from 762 in Zamfara to 2,574 in Lagos.

Between 2000–2009, the national deaths averted for MCV1 immunisation ranged from 959 per 100,000 live births (95% CrI: 682–1,396) in Egypt and 3,674 deaths averted per 100,000 live births (95% CrI: 3,280–4,415) in Zambia. Between 2010–2019, the deaths averted ranged from 670 per 100,000 live births (95% CrI: 524–925) in Egypt and 2,545 deaths averted per 100,000 live births (95% CrI: 2,158–3,019) in Djibouti (see Table S2). Across regions, between 2000–2009, the deaths averted for MCV1 immunisation ranged from 603 per 100,000 live births (95% CrI: 288–827) in Sokoto, Nigeria, and 4,397 (95% CrI: 2,279–5,835) in Ekiti, Nigeria. Between 2010–2019, the deaths averted ranged from 540 per 100,000 live births (95% CrI: 258–742) in Sokoto, Nigeria, and 3,989 (95% CrI: 2,146–5,965) in Addis Abeba in Ethiopia.

3.2. Inequality Scenarios

Across the study countries, Angola, Nigeria, Chad, Somalia, and Ethiopia showed the most considerable subnational inequality in deaths averted in 2019 (see Fig. 3) as measured by the disparity index (see Eq. 3). In Fig. 3, Angola showed the highest disparity in deaths averted across regions in 2019. In this country, increasing the coverage in the total population by 36% when targeting neglected regions would eliminate the disparity in death averted across its regions.

There is a mixed picture of how the inequality of the impact of vaccination has changed through time. Although inequality has generally decreased in the last two decades, this varies from country to country. Some countries, including Burkina Faso, Cote d'Ivoire, Eritrea, Egypt, Malawi, Mozambique, and Namibia, have seen a considerable decrease in their inequality in the last decade. However, in several countries, inequality has stagnated — as evidenced in Chad, Congo, Ethiopia, Kenya, Morocco, Niger, Rwanda, and Sierra Leone, among others. Moreover, several countries have additionally experienced an increase in their inequality in the last decade, with Angola, Benin, Cameroon, Guinea, the Republic of the Congo, the Central African Republic, Sudan, and Uganda among them. In general, however, national coverage progress over time was accompanied by declines in the inequality of subnational impact (see Fig. 4).

Differences in the impact estimates under the different coverage scenarios presented in this study illustrate the potential of maximising equitable access when increasing the overall coverage of MCV1 vaccination. For example, under the at least national sce-

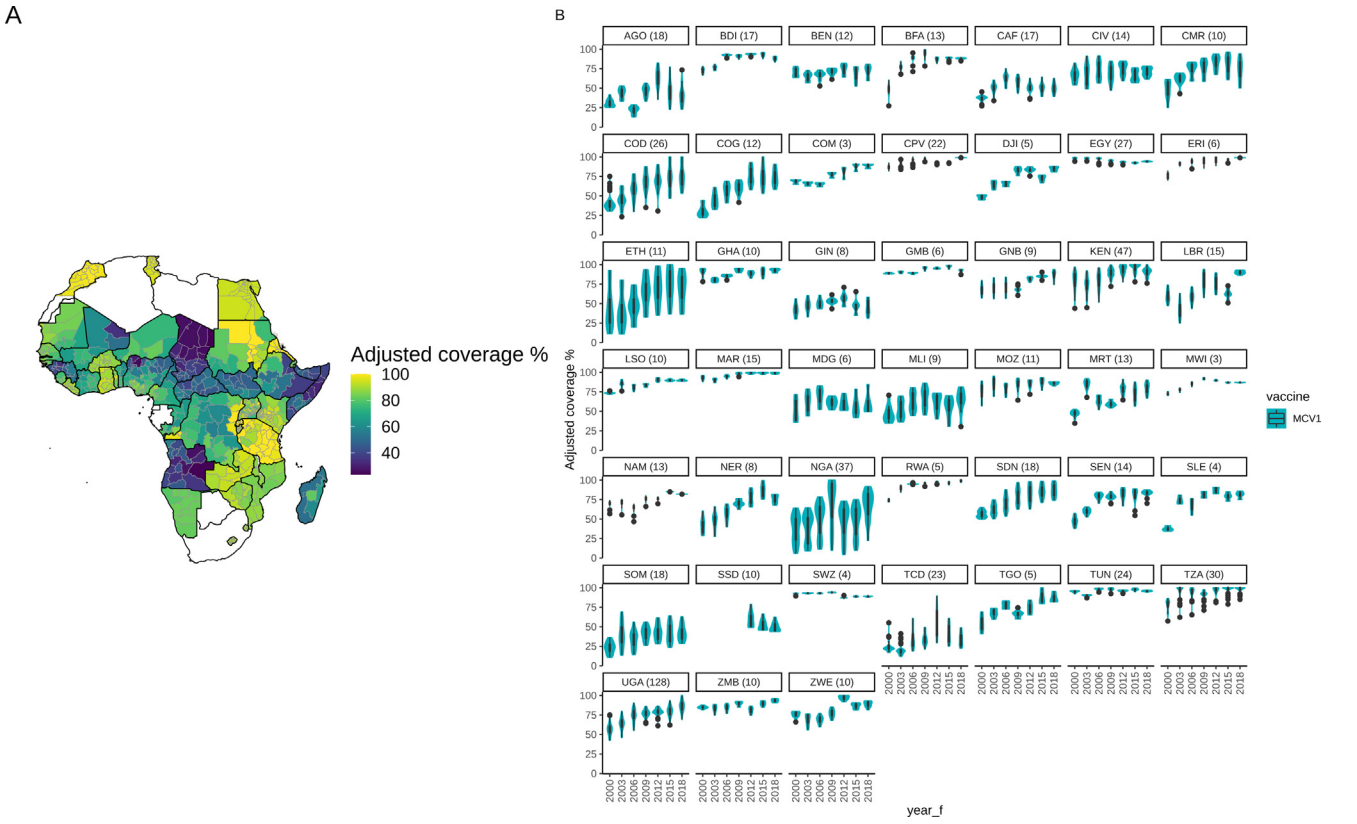

Fig. 2. A. Adjusted values of vaccine coverage at the first administrative level for the measles-containing-vaccine first-dose (MCV1) for 45 countries in Africa for 2019. B. Distribution of the adjusted values of vaccine coverage from 2000–2019. Numbers in parenthesis correspond to the number of first administrative regions within a country.

nario (see Fig. 5, S3 and Table 2), if Angola improved MCV1 coverage such that each region's coverage is at least as high as the national coverage level, it would improve the national average from 51% in 2019 to 59%, resulting in additional 230 (95% CrI: 159–356) deaths averted per 100,000 live births. For Ethiopia, a highly heterogeneous country, under the regional max scenario (see Fig. 5, S4, and Table 2), where MCV1 coverage is improved to that of the region with the highest coverage achieved in 2019, the national coverage would improve from 62% to 95%, resulting in a further 857 (95% CrI: 622–1,211) deaths averted per 100,000 live births. Finally, countries with historically low MCV1 coverage would benefit the most under the GVAP target scenario. Under this scenario (see Fig. 5, S5 and Table 2), in Chad, reaching at least 80% of MCV1 coverage in each region would increase the national coverage from 38% to 80%, increasing the MCV1 impact by 1,273 deaths averted per 100,000 live births (95% CrI: 776–2,072).

Globally, if the 45 countries in Africa in this study improved their MCV1 coverage for each region to their national coverage, the MCV1 coverage would improve overall from 77% to 80% in 2019, resulting in an additional 97(95% CrI: 80–128) deaths averted per 100,000 live births. Furthermore, under the regional max scenario, where MCV1 coverage is improved to that of the region with the highest coverage achieved in 2019, the total MCV1 coverage would improve from 76% to 90%, resulting in a further 363 (95% CrI: 299–482) deaths averted per 100,000 live births. Finally, if these regions reached at least 80% of MCV1 coverage, the total coverage of MCV1 would change from 76% to 86%, increasing the MCV1 impact by 255 deaths averted per 100,000 live births (95% CrI: 205–345).

Fig. 5 summarises the improvements in deaths averted in the vaccination activities of MCV1 in 2019 under the different scenarios for the top 10 countries with the highest values of inequality defined by the disparity index. This figure highlights the countries that would benefit the most from reducing the coverage gaps under the different scenarios in this study. Details of the improvement in deaths averted under the different scenarios are shown in Table 2 for 2019 and Table S1 for 2000–2009 and 2010–2019 periods. (See Table 3).

The top five countries with the most considerable boosts in deaths averted when using the national coverage as a focal point for the overall improvement in the impact of the MCV1 vaccination are Angola, Nigeria, Ethiopia, the Democratic Republic of the Congo, and Somalia. Within these countries, the regions with the biggest gain in deaths averted are the regions in northern Nigeria, eastern Ethiopia, the eastern Democratic Republic of the Congo, and most of the regions in Angola (see Figs. 6 and S3).

The countries with the highest field of opportunity to increase their impact of vaccination if the coverage among regions were equal to the region with the highest coverage are Ethiopia, the Democratic Republic of the Congo, Nigeria, and Angola. Within these countries, the regions with the highest increases in deaths averted are in northern Nigeria, eastern Ethiopia, the Moxico, Lunda Norte and Bie regions in Angola, and the Sankuru, Maniema, and Tshopo regions in the Democratic Republic of the Congo (see Figs. 6 and S5). Finally, the regions with the highest increase in deaths averted when increasing the MCV1 coverage to meet the GVAP threshold of 80% coverage are mainly localted in Chad, Somalia, the Central African Republic, Guinea, South Sudan, northern Nigeria, and eastern Ethiopia (see Fig. 6 and S5).

4. Discussion

These findings illustrate that despite the progress in expanding MCV1 coverage globally, there remain critical disparities in cover-

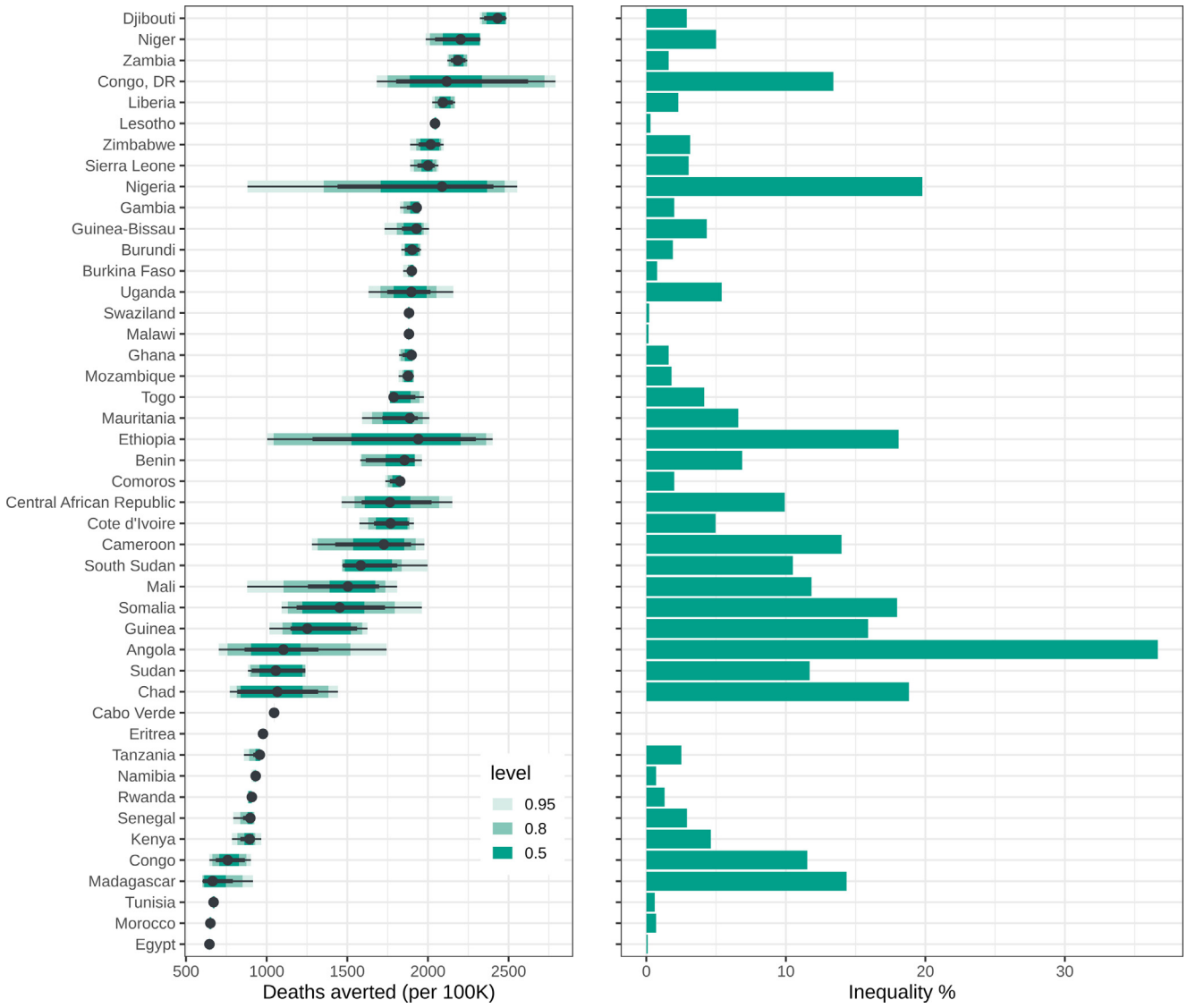

Fig. 3. A. Distribution of the mean of the deaths averted per 100,000 live births across all the regions in the countries of Sub-Saharan Africa in 2019. Legends correspond to the 95%, 80% and 50% credible intervals. B. Inequality in vaccine impact in 2019. Inequality is measured using the disparity index (see Eq. 3) which describes the spread of the impact of vaccination across the regions of a country, taking into account the differences in population. This index is equal to zero if there are no inequalities among regions, and larger values indicate higher level.s of inequality.

age, producing significant heterogeneity in the impact of MCV1 immunisation across the African region. Furthermore, we show that this inequality in impact has changed over time, contrasting the stagnation and, in some instances, increasing inequality in the last decade. Countries that show an improvement in the coverage and reduction of inequality over time between 2000–2009 include the Democratic Republic of Congo, Ethiopia, Kenya, Madagascar and Zimbabwe. This concurs with the results of a 2005 pilot where these countries participated in the Reaching Every District (RED) initiative [33]. Thanks to this initiative, countries under the RED approach improved their routine immunisation services considerably helping reduce the gaps in immunisation impact. However, since 2010, the coverage of MCV1 in several African countries has stagnated, resulting in increasing inequality in countries like Angola, Benin, Uganda, and even the Democratic Republic of Congo, despite its improvement between 2000–2009. Our results further highlight Angola, Nigeria, Chad, Somalia and Ethiopia as the countries with the highest heterogeneity in the impact of MCV1 immunisation in 2019; among these countries, Angola, Nigeria and Ethiopia were previously identified as having considerable values of heterogeneity in DTP3 vaccine coverage [34].

In this study, comparing the impact of MCV1 vaccination under the scenarios of increasing coverage while reducing inequality with the current national impact estimates allows us to assess the performance of vaccine delivery systems within each country. For instance, countries with low historical coverage and significant gains in deaths averted under the GVAP target scenario, such as Chad, Somalia, Guinea and Angola, would benefit the most from universal interventions to increase national routine immunisation across the whole population. In contrast, in countries with considerable heterogeneity, such as Nigeria, Ethiopia, Cameroon, Madagascar and Mali, targeting neglected and disadvantaged regions might be more effective to increase the overall coverage over the population and to maximise the equity in the impact of MCV1 immunisation.

Under the regional max scenario, the overall impact of MCV1 improves substantially in countries with significant regional variation. For example, in Nigeria, the current national coverage of

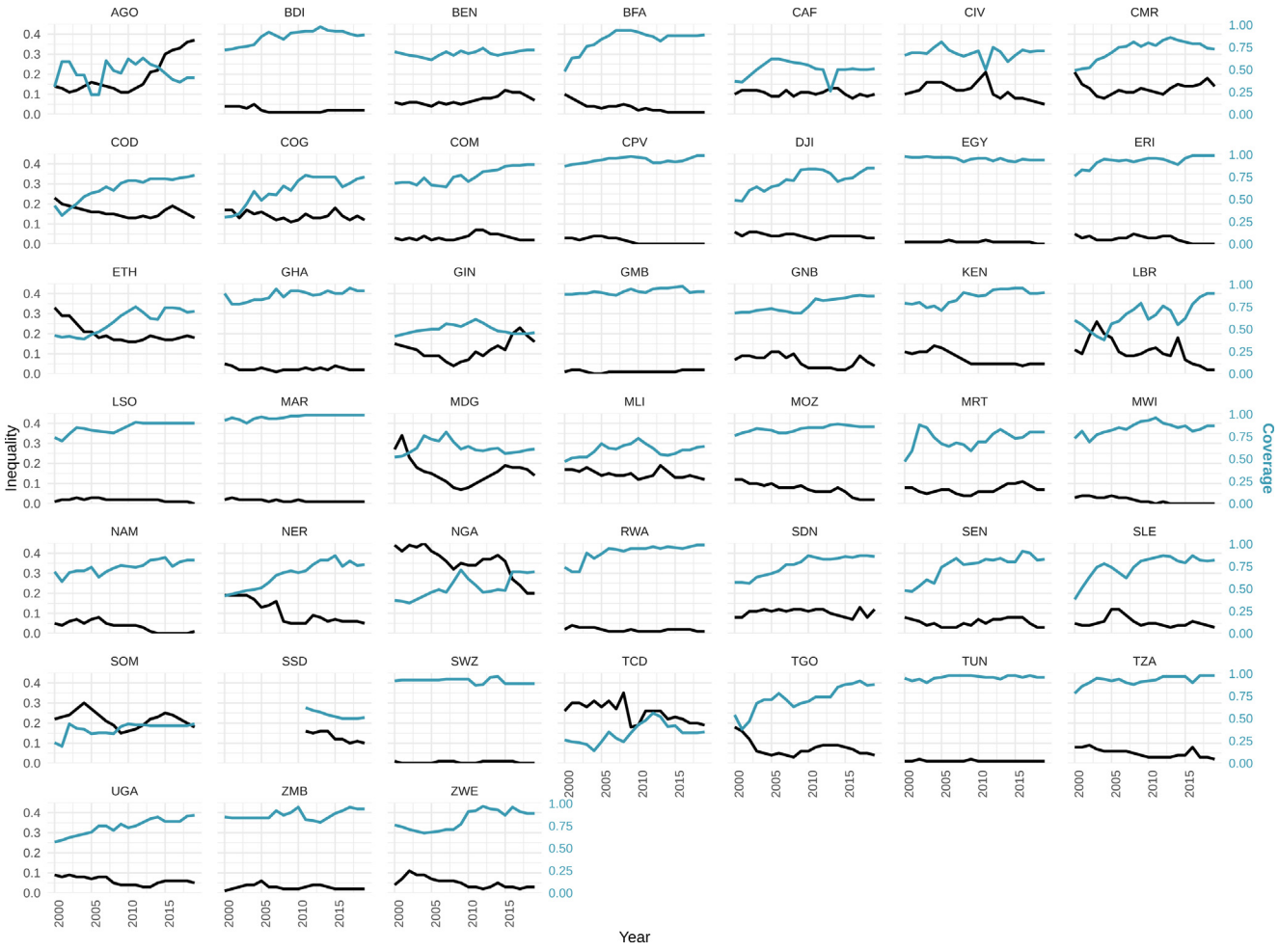

Fig. 4. Standardised inequality (black) and coverage (blue) of MCV1 over time. Inequality is measured using the disparity index (see Eq. 3) which describes the spread of the impact of vaccination across the regions of a country, also considering the differences in population. This index is equal to zero if there are no inequalities among regions, and larger values indicate higher level.s of inequality.

MCV1 ranges from 25% in Zamfara to 91% in Lagos in 2019 (after adjusting the coverage, see methods). However, if Nigeria improved coverage to that of Lagos in 2019, the wealthiest region, the national coverage would improve from 65% to 91%, gaining 743 more deaths averted per 100,000 live births (95% CrI: 610–963). Although this may be limited by other factors, this scenario helps us understand the field of opportunity to increase the impact of immunisation across a country using its most advantageous region as a reference.

Across Sub-Saharan Africa, much of the persistent inequality in vaccine coverage and impact can be explained by the low coverage, disparate progress in addressing targets and indicators, and issues in the timeliness of vaccination [2,14,35]. Stark inequalities, especially in MCV1 immunisation coverage, persist both globally and between or within countries in Sub-Saharan Africa, even when accounting for the SARS-CoV-2 pandemic; measles remains the 7th most prevalent infectious disease in the region, with children accounting 51% of acute respiratory infections globally (Inc. measles) [35,14]. Sub-Saharan Africa also faces issues with extensive data gaps with some of the lowest estimates of vaccination coverage, especially in conflict or post-conflict areas [3], [14,36].

Pockets of low vaccination coverage have further been suggested to be the result of low access to healthcare services and vaccine acceptance [37], though ongoing conflicts and forced displacements have further resulted in healthcare service disruptions, data gaps, and surveillance challenges. All of these factors continue to promote high levels of heterogeneity in vaccine coverage [14]. For example, the Democratic Republic of Congo has faced significant challenges in increasing and sustaining immunisation coverage. An investigation following a measles outbreak in 2010 showed the country faced an accumulation of susceptible children, driven by the poor implementation and follow-up of SIA campaigns and low overall coverage [38]. Nigeria and Ethiopia face similar issues, with gaps in DTP1 coverage and country-wide geographical divides, especially in rural areas. Conflict, lack of formal education or acceptance of vaccines among caregivers, and inadequate health infrastructure have all been thought to contribute to incomplete immunisation [37]. While the Democratic Republic of Congo, Nigeria, and Ethiopia currently contain 50% of the children not receiving MCV1 in the African Region, all show higher rates of MCV1 immunisation compared to DTP3, due primarily to successful SIA campaigns alongside routine immunisation programmes between 2011–2016 [37,15].

The inequities described have the potential to be addressed through changes in the financing of, organisation, and delivery of measles immunisation services, given current routine immunisation services often fail to reach children in high-risk regions, with socioeconomic, cultural, and health systems barriers predominant [39]. The COVID-19 pandemic has further exacerbated these

[3] the Central African Republic, the Democratic Republic of the Congo, Nigeria, Somalia, South Sudan, and Sudan

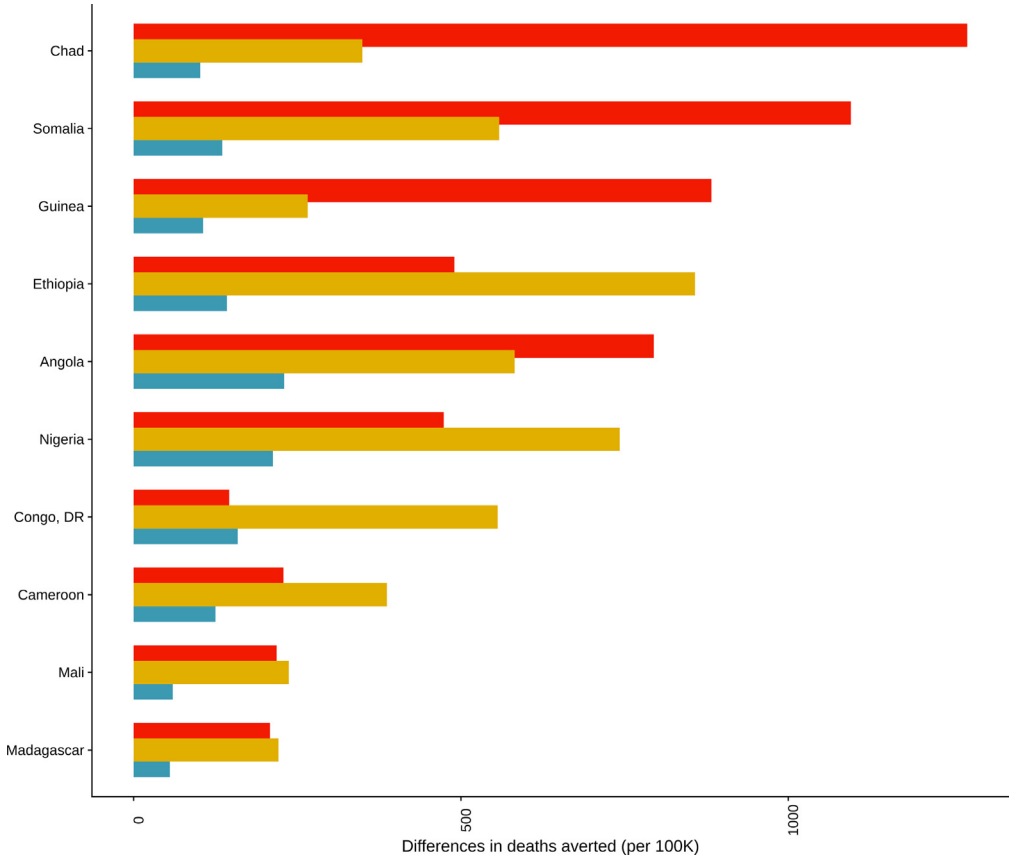

Fig. 5. Potential improvement in deaths averted per 100,000 live births in 2019 under the different scenarios of reducing inequality in MCV1 vaccination. Red represents the gain of deaths averted under the GVAP target scenario, which assumes that all regions have achieved at least a coverage of 80% of MCV1. Yellow represents the improvement in deaths averted under the regional max scenario, which assumes that all regions have achieved the highest coverage of a specific year. Finally, the blue represents the gains in deaths averted under the at least national scenario, which assumes that all regions have achieved at least the national coverage in a specific year. Only the top 10 countries with the most considerable disparities in the impact among regions are shown.

inequities at a time when national ownership and accountability of immunisation programmes was already threatened by sub-optimal political commitment [9,40]; efforts towards sustainable immunisation financing will remain essential to address and investigate missed opportunities for vaccination and to meet the targets set by the ambitious IA2030 goals. Further efforts to continue to coordinate and differentiate support, such as through community engagement and universal healthcare services, with consideration to the local demographic, will remain essential to improve reach, especially for those in rural or high-risk regions [39], while improvements to tracking demographic and health information will ensure all children are receiving access to essential and lifesaving immunisations [39].

As more subnational coverage data becomes available, subsequent analysis on evaluating inequality could consider multiple vaccines to have a more comprehensive panorama of the vulnerability of the disadvantaged populations in African countries; this analysis could additionally be extended to other countries and continents. In addition, to assess the full impact of vaccination on measles, it is vital to determine the heterogeneity and inequalities in MCV2 and SIAs once subnational coverage data becomes available.

The analyses in this study demonstrate the significant inequalities in the impact of MCV1 vaccination that some countries in Africa are facing. However, these analyses were limited by certain characteristics in the data (e.g., quality and availability) and the assumptions within the methodology used to calculate subnational impact estimates.

In the data, quality and availability constraints restricted our estimation of the impact of vaccination at the regional level when compared to national impact. Monitoring inequality in vaccine impact among regions within a country provides essential evidence to frame policies and health programs, especially when significant disparities exist. We use regions at the first administrative level as the primary units of analysis in this study, since these geographic units are usually the main target of resources allocation in vaccination activities [41]. With this, the main challenge that we encountered was the limited availability of disaggregated data. Although we managed to extract coverage data at the subnational level for several vaccine-preventable diseases, such as Hepatitis B 3rd dose, yellow fever, and MCV1, a lack of completeness and reporting biases resulted in the restriction of our analyses to only MCV1.

The values of subnational MCV1 coverage used in this paper are estimates provided by IHME, whose methodology and limitations are discussed in [19]. Accuracy of the MCV1 coverage estimates is constrained by the extent to which underlying household surveys are representative, relevant predictors of MCV1 coverage are available, and modelling assumptions (e.g. functional forms of geospatial models and choice of priors) are accurate.

In our data, and as reported in various studies [42–44], understanding the target population (i.e., denominator) was the most common problem in interpreting the vaccine coverage. One reason for these inherent errors might be differences in the estimation of the target population between regions. These errors could also occur because of changes in population and administrative capac-

Table 2
Gains in deaths averted (per 100,000 live births) in 2019 if all the regions of a country reach at least the national coverage of MCV1 (at least national); if all the regions of a country meet the highest coverage reached in 2019 (regional max); or if all regions a country reach at least the GVAP target threshold of 80% coverage in 2019. Values in parentheses correspond to the 95% credible interval in deaths averted. The national coverage column represents the national average coverage of MCV1 in 2019, and the regional max coverage represents the highest coverage achieved by a region in 2019. '–' indicates that coverage was already achieved.

Country	At least national	Regional max	GVAP target	National coverage	Max coverage
Angola	230 (159–356)	582 (402–900)	795 (550–1,224)	51.00	72.00
Benin	66 (51–87)	196 (153–260)	218 (170–289)	71.00	79.00
Burkina Faso	7 (6–10)	20 (16–26)	–	89.00	90.00
Burundi	18 (14–26)	67 (49–93)	–	89.00	92.00
Cabo Verde	–	–	–	99.00	99.00
Cameroon	125 (88–180)	387 (273–556)	229 (162–329)	71.00	88.00
Central African Republic	94 (74–118)	467 (366–585)	1,074 (843–1,345)	50.00	63.00
Chad	102 (61–168)	349 (211–572)	1,273 (776–2,072)	38.00	49.00
Comoros	7 (5–11)	11 (7–16)	–	91.00	91.00
Congo	46 (30–69)	146 (97–220)	69 (46–104)	76.00	90.00
Congo, DR	159 (137–186)	556 (478–648)	146 (125–170)	81.00	100.00
Cote d'Ivoire	45 (32–65)	165 (115–237)	215 (150–310)	71.00	78.00
Djibouti	30 (26–35)	46 (40–54)	–	86.00	88.00
Egypt	0 (0–1)	2 (1–3)	–	94.00	94.00
Eritrea	–	–	–	99.00	99.00
Ethiopia	142 (103–202)	857 (622–1,211)	490 (356–693)	62.00	95.00
Gambia	18 (13–25)	61 (45–84)	–	91.00	94.00
Ghana	15 (10–22)	51 (35–73)	–	92.00	95.00
Guinea	106 (69–156)	266 (174–390)	883 (578–1,295)	49.00	58.00
Guinea-Bissau	44 (31–60)	135 (97–187)	8 (6–12)	86.00	92.00
Kenya	21 (14–30)	104 (70–150)	1 (0–1)	89.00	100.00
Lesotho	3 (2–3)	10 (8–12)	–	90.00	91.00
Liberia	20 (17–25)	46 (39–57)	–	91.00	93.00
Madagascar	55 (38–82)	221 (153–328)	208 (144–308)	62.00	81.00
Malawi	1 (1–1)	2 (1–2)	–	87.00	87.00
Mali	60 (44–86)	237 (173–340)	218 (159–313)	71.00	81.00
Mauritania	64 (42–94)	249 (165–366)	78 (51–114)	79.00	90.00
Morocco	2 (1–3)	7 (4–10)	–	99.00	100.00
Mozambique	15 (10–21)	61 (41–87)	–	85.00	88.00
Namibia	3 (2–4)	6 (5–8)	–	82.00	83.00
Niger	56 (46–66)	124 (102–145)	77 (64–90)	78.00	83.00
Nigeria	213 (173–276)	743 (610–963)	474 (388–615)	65.00	91.00
Rwanda	7 (5–10)	12 (8–17)	–	99.00	100.00
Senegal	14 (10–19)	42 (31–59)	8 (6–11)	83.00	87.00
Sierra Leone	34 (27–46)	108 (85–143)	26 (21–35)	81.00	85.00
Somalia	135 (75–170)	558 (314–699)	1,096 (618–1,368)	47.00	64.00
South Sudan	86 (53–105)	359 (223–437)	896 (554–1,090)	52.00	63.00
Sudan	67 (52–73)	148 (116–162)	24 (19–27)	89.00	100.00
Swaziland	2 (1–3)	4 (3–6)	–	89.00	89.00
Tanzania	16 (13–21)	21 (16–27)	–	99.00	100.00
Togo	34 (23–49)	183 (123–264)	–	86.00	95.00
Tunisia	2 (1–3)	8 (5–12)	–	96.00	97.00
Uganda	54 (35–79)	299 (197–439)	11 (7–16)	86.00	100.00
Zambia	18 (15–22)	51 (43–62)	–	94.00	96.00
Zimbabwe	32 (22–45)	116 (81–164)	–	88.00	93.00

ity due to civil conflict. Mobility can also produce critical mismatches between the number of doses administered (i.e., numerator) and the target population (i.e., denominator). These mismatches can create inequality in coverage between regions, especially in countries with significant population movement due to civil conflict, nomadic populations, or significant differences in health access between areas [42,44]. These challenges are common when reporting vaccine coverage at a national level, but exacerbated at a subnational level.

There are further data challenges that arise from using different datasets of vaccine coverage at the subnational level. One challenge is that the classification and the number of regions within a country may vary across datasets. These disparities might reflect the unstable delimitation of subnational boundaries in some countries. For example, due to a change in its constitution in 2010, Kenya has been divided administratively into 47 counties since 2013, replacing its eight former provinces. Changes in the number of administrative areas can affect the interpretation of inequality results over time since aggregating regions reduces the heterogeneity in general [41]. Cross-country comparisons of inequalities can be problematic when using a significant number of regions across countries (e.g., three regions of Comoros vs 47 regions in Kenya). The magnitude of the resulting inequality can change for the same population depending on whether the analysis is performed at the state or province level [45]. Given this resolution problem, comparing geographical inequalities between countries can be more informative by measuring disparities across smaller geographic and administrative units, depending on data availability.

To calculate the subnational impact estimates in this study, we used a simplified process that extrapolates published national impact estimates of vaccination into subnational estimates [29], given the computational effort and time required for a complete mathematical model run update. While this method allows us to calculate the impact estimates for the 737 regions used in this study on a short timescale, with the latest demographic and immunisation data available, it has several limitations. First, by linearly re-scaling the national baseline vaccine impact by the subnational vaccine coverage, we assumed that a proportional change in vaccine coverage results in a proportional change in vaccine impact. For epidemic diseases like measles, we recommend the full use of dynamic models; however, we consider our extrapolation

Table 3
Average national MCV1 coverage (%) in 2019, and changes of this coverage under the different scenarios of inequality reduction. At least national: coverage if all the regions of a country reach at least the national coverage; regional max: if all the regions of a country reach the highest coverage in 2019; GVAP target: if all regions a country reach at least the GVAP target threshold of 80% coverage in 2019.

Country	National coverage	At least national	Regional max	GVAP target
Angola	51	59	72	80
Benin	71	74	79	80
Burkina Faso	89	89	90	89
Burundi	89	90	92	89
Cabo Verde	99	99	99	99
Cameroon	71	77	88	81
Central African Republic	50	52	63	80
Chad	38	41	49	80
Comoros	91	91	91	91
Congo	76	80	90	83
Congo, DR	80	86	100	86
Cote d'Ivoire	71	73	78	80
Djibouti	86	87	88	86
Egypt	94	94	94	94
Eritrea	99	99	99	99
Ethiopia	62	68	95	81
Gambia	91	92	94	91
Ghana	92	93	95	92
Guinea	49	53	58	80
Guinea-Bissau	86	88	92	87
Kenya	89	91	100	89
Lesotho	90	90	91	90
Liberia	91	92	93	91
Madagascar	62	67	81	80
Malawi	87	87	87	87
Mali	71	73	81	80
Mauritania	79	82	90	82
Morocco	99	99	100	99
Mozambique	85	86	88	85
Namibia	82	83	83	82
Niger	78	80	83	81
Nigeria	65	73	91	81
Rwanda	99	100	100	99
Senegal	83	84	87	84
Sierra Leone	81	82	85	82
Somalia	47	51	64	80
South Sudan	52	55	63	80
Sudan	88	93	100	90
Swaziland	89	89	89	89
Tanzania	99	100	100	99
Togo	86	88	95	86
Tunisia	96	96	97	96
Uganda	86	89	100	87
Zambia	94	95	96	94
Zimbabwe	88	90	93	88

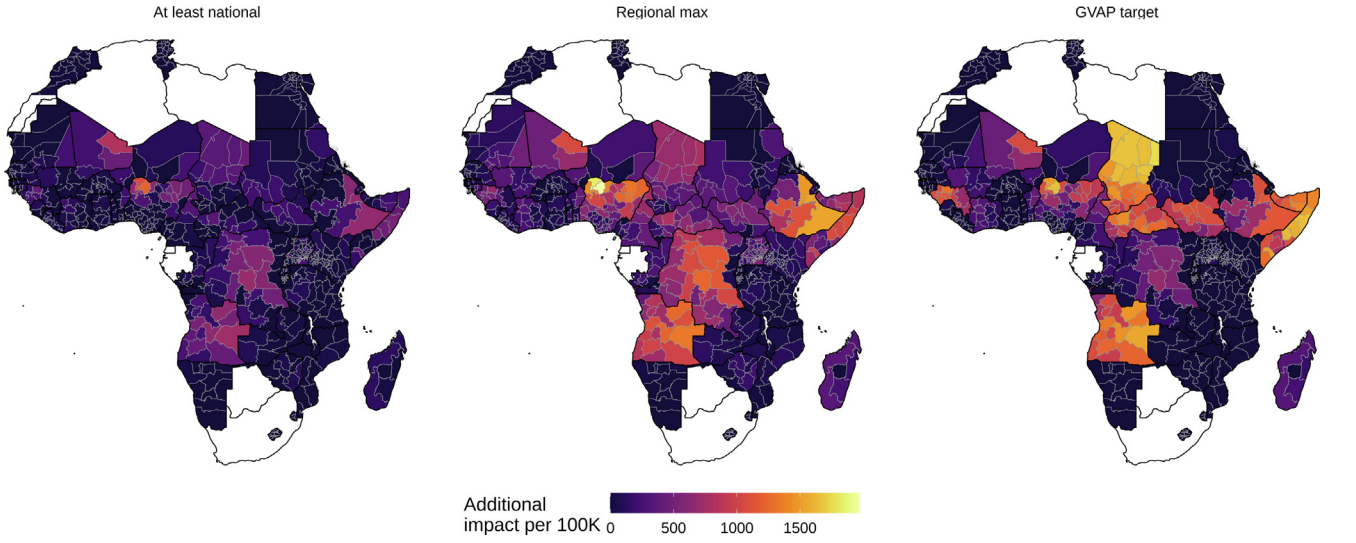

Fig. 6. Change of deaths averted per 100,000 live births in 2019 under the different scenarios of inequality reduction. At least national: assuming all regions have achieved at least the national coverage; regional max: assuming all regions have achieved the highest coverage; and GVAP target: assuming all regions have achieved at least a coverage of 80%.

method as a complementary approach to understanding the impact of vaccination when there is a constant update of vaccine coverage and when modelling the impact of vaccination at the subnational level in large geographic extent.

Additionally, we assumed that the deaths averted rates vary proportionally to the coverage across the regions within a country but treat them independently, i.e., we assume that the burden averted per fully vaccinated person is affected by coverage differences across the areas and do not consider interactions between regions. We acknowledge that these two assumptions may not be realistic in most settings. Even though the deaths averted rates used in this study change over time and by coverage, we do not include other key determinants of measles vaccine impact, such as case-fatality risk, contact patterns, and age-dependent vaccine efficacy, which can vary subnationally [46]. Similarly, we may expect low coverage to be clustered which can affect policy recommendations [47]. Thus, as more model parameters and coverage estimates are available at finer scales, an update of the model runs of measles that calculate the baseline estimates used in this study could provide a more accurate picture of the impact estimates of MCV1 immunisation. Aside from these limitations, we consider that the gains in deaths averted under our scenarios are rather conservative, since we expect the benefit of vaccination in regions with historically low coverage to be more prominent [48].

5. Conclusion

In this study, we illustrate that the estimates of the impact of immunisation at national level can mask considerable subnational heterogeneity and highlight the regions where boosts in coverage will save the lives of a substantial number of children dying from preventable diseases. The coverage of MCV1 in these overlooked regions have lagged disproportionately behind the others and warranted extra attention; this remains true despite efforts to increase the national coverage of MCV1. Further research using subnational coverage estimates for MCV2 and SIAs is necessary to understand the entire inequality of vaccination impact on measles. In addition, subsequent analysis on evaluating inequality could consider multiple vaccines to have a more comprehensive panorama of the vulnerability of the disadvantaged populations in African countries.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.vaccine.2022.09.049.

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