

## Measles control in Sub-Saharan Africa: South Africa as a case study

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### ABSTRACT

**Background:** Due to intensified measles immunization efforts, measles mortality has decreased substantially worldwide, particularly in Sub-Saharan Africa (SSA). The World Health Organization (WHO) estimated a 92% decrease in measles-related deaths in the WHO AFRO region for the period 2000–2008. Recently, the AFRO region established a measles pre-elimination goal and experts have suggested engaging in a measles eradication campaign at the global level. However, recent large-scale outbreaks in many Sub-Saharan African countries present a challenge to measles control efforts. This paper examines measles immunization and the impact of measles supplemental immunization activities (SIAs) on routine immunization coverage in South Africa (SA).

**Methods:** We reported on immunization coverage trends in SA for the period 2001–2010 at the province and district levels. The data included routine immunization for 1st and 2nd doses of measles vaccine (MCV1, MCV2), SIAs, 1st dose of Bacille Calmette–Guérin vaccine, 1st and 3rd doses of oral polio vaccine (OPV1, OPV3), 3rd dose of Diphtheria–Tetanus–Pertussis–Haemophilus–influenzae–B vaccine (DTP–Hib3), and the number of under-one-year-olds having completed a primary course of immunization (Imm1). A regression model looked at the SIA impact on routine coverage.

**Results:** Over the past decade, MCV1 and MCV2 coverage have increased nationally from 68% and 57% in 2001 to 95% and 83% in 2010, respectively. SIA coverage has remained at high levels, around 90%, over the same period. Substantial heterogeneity in MCV1 and MCV2 coverage is present across SA districts, with differences in coverage of 56% (MCV1) and 51% (MCV2) in 2010. In any given year, occurrence of SIAs was associated with a decrease in routine immunization coverage of MCV1, MCV2, OPV1, OPV3, DTP–Hib3, and Imm1, at the district level.

**Conclusions:** The heterogeneity in measles vaccination coverage across SA districts challenges the goal of measles elimination in SA and SSA. The reduction in routine immunization coverage associated with the occurrence of SIAs raises the legitimate concern that SIAs may negatively impact health systems' functioning.

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### 1. Introduction

The burden of disease attributed to measles throughout history is considerable. Before the introduction of a live attenuated measles vaccine in 1963, measles was an unavoidable risk in early life [1]. Prior to the 1960s, 135 million cases and 7–8 million deaths were

assumed to occur each year globally [2]. In 2000, measles-related deaths accounted for 1–5% of under-five deaths worldwide [3–6].

Responding to the momentum of the Millennium Development Goal 4 (MDG 4), the World Health Assembly (WHA) in 2003 adopted a resolution to reduce deaths attributable to measles by 50% from 1999 levels, by 2005 [7]. Shortly thereafter, UNICEF and the World Health Organization (WHO), in defining a Global Immunization Vision and Strategy (GIVS) for 2006–2015 [8], set the goal to further reduce measles-related deaths by 90% from 2000 levels, by 2010, which was officially endorsed by the WHA in 2005. Drawing on the WHO's Expanded Programme on Immunization (EPI) [9], the UNICEF's Universal Childhood Immunization by 1990 Initiative (UCI) [10], and with the benefit of momentum developed by the Global Alliance for Vaccines and Immunization (GAVI) [11],

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the Measles Initiative [12] has emerged. The Measles Initiative is a consortium of global health agencies which provides support to measles-burdened countries in order to achieve the measles-mortality reduction goal. The focus has been on sustaining high coverage of routine immunization of children at around 9 months and to supplement it with a recommended second dose [13]. In high-income nations, the second dose is included in the routine vaccination schedule and usually administered to children before school entry [13]. In low- and middle-income countries, a second dose of measles vaccine is offered through supplemental immunization activities (SIAs) [13]. During SIAs, children are targeted for vaccination regardless of their previous history of measles vaccination. This approach, implemented by the Pan American Health Organization (PAHO) since the 1990s, is thought to have contributed to the elimination of the endemic transmission of measles in the Americas [14].

The same strategy has been exported and adapted to Sub-Saharan Africa and may explain the reported drop in measles deaths and incidence in Africa in the last decade [15–17]. WHO researchers have reported achievement of the 2005 measles mortality reduction goal [18] as well as continued downward trends in worldwide measles mortality toward the 2010 measles mortality reduction target [19]. The Africa WHO (AFRO) region saw a 92% decrease in measles-related deaths from 2000 to 2008, with an estimated 28,000 deaths attributable to measles in the AFRO region in 2008 [19]. Most recently, the AFRO region measles technical advisory group has recommended establishing a pre-elimination goal by the end of 2012 [20,21]. Experts at the global level have even been considering the feasibility of engaging in measles eradication [22,23]. However, 28 out of the 46 AFRO countries reported laboratory-confirmed measles outbreaks in 2009–2010 [24]. These outbreaks present challenges to the recent successes against measles-mortality and to the goal of measles elimination in the AFRO region.

In South Africa (SA), a first and a second dose of measles vaccine are given to children at 9 and 18 months. Since 1996, SA has been at the forefront of implementing regular national or sub-national SIAs [25,26]. These SIAs are executed in each of the country's nine provinces and fifty-two districts. However, a measles outbreak which started in Gauteng province in 2009 spread to the whole country in 2010 [27], an example of one of the outbreaks which challenge measles mortality reduction goals and even basic measles control.

The analysis presented here is intended to inform the measles control policies of Sub-Saharan African countries by using SA as a case study. We analyzed coverage levels of the first and second doses of measles routine vaccination, and supplemental immunization activities for the period 2001–2010 at both the district and province levels in SA. We also analyzed the association between the implementation of a supplementary immunization campaign and its impact on the coverage of routine immunization services in a given year. This analysis will assist policy makers in evaluating how best to fill gaps in coverage in order to achieve successful measles control in SA, and elsewhere in Sub-Saharan Africa.

## 2. Material and methods

### 2.1. Data

We used district-level routine immunization data for the years 2001–2010 sourced from the District Health Information System (DHIS), SA. This included coverage data for the first and second doses of measles vaccine (MCV1, MCV2). We also had routine immunization coverage data for the 1st dose of Bacille Calmette-Guérin vaccine (BCG), the 1st and 3rd doses of oral polio vaccine (OPV1, OPV3), the 3rd dose

of Diphtheria–Tetanus–Pertussis–Haemophilus-influenzae-B vaccine (DTP-Hib3), and the number of under-one-year-olds having completed their primary course of immunization (Imm1).

SIAs have been held in SA since 1996 [25,26]. The most recent campaign was held in April–May 2010. Coverage numbers for 2010 were obtained from DHIS, SA, and other years were extracted from other sources [15,28].

Population estimates were sourced from Statistics SA. They were based on annual projections from the last census conducted in 2001 [29]. The immunization coverage indicators were calculated in the DHIS from the number of doses of vaccine given, divided by the target population (the age groups varied for the different vaccines).

### 2.2. Methods

Coverage numbers for MCV1, MCV2, and for the SIAs for the years 1996–2010 were analyzed at the national, province and district level. Within each province  $P$ , we aimed at capturing the degree of heterogeneity in the coverage among the province's districts. For that purpose, we defined an inequality index  $I_{P,v}$ :

$$I_{P,v} = \frac{\sigma(C_{P,d,v})}{\mu(C_{P,d,v})} \quad (1)$$

where  $\mu$  and  $\sigma$  were respectively the average coverage of province  $P$  and the standard deviation of coverage  $C_{P,d,v}$  in the districts  $d$  of province  $P$ , for  $v = \text{MCV1, MCV2, SIA}$ .

We analyzed quantitatively the association between the introduction of an SIA in a given year and the potential increase/decrease at the district level for each of the following routine vaccination coverage indicators: MCV1, MCV2, OPV1, OPV3, DTP-Hib3, BCG, and Imm1. We used a linear model where the dependent variable was one of the latter coverage indicators  $\text{Cov}$ . For each  $\text{Cov}$ , for each year  $t$  of 2001–2010, for each district  $d$ , we estimated the model:

$$\text{Cov}_{d,t} = \beta_0 + \beta_1 \text{Year}_t + \beta_2 \text{SIA}_t + \beta_d + e_{d,t} \quad (2)$$

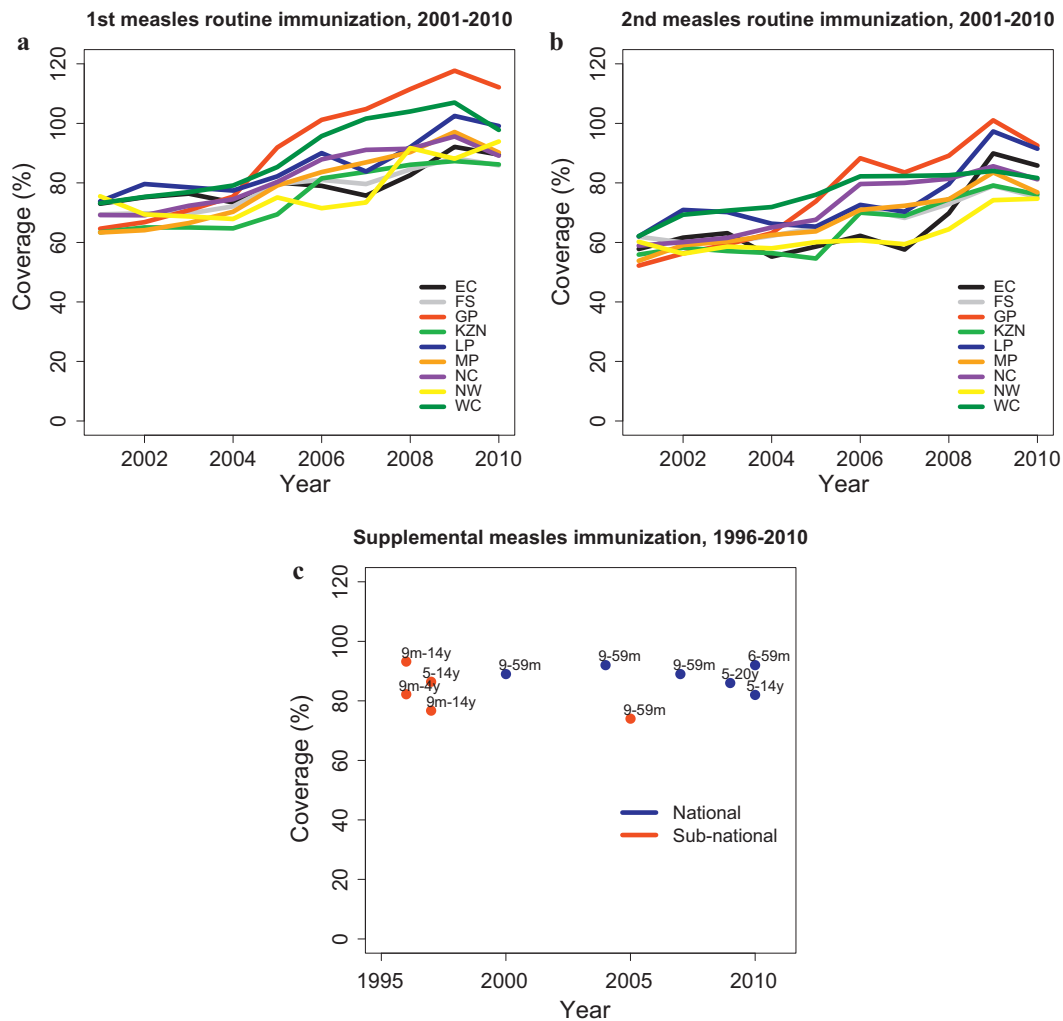
$\text{Year}_t$  is the number of years since 2001,  $\text{SIA}_t = 1$  when an SIA occurred in a given year (0 otherwise),  $e_{d,t}$  is an error term.  $\beta_d$  is a district level random effect.  $\beta_1$  is controlling for time trends.  $\beta_2$ 's sign, if significant, indicates a increase/decrease in the coverage  $\text{Cov}$  associated with the SIA implementation in a given year. For this quantitative analysis using model (2), the years 2007 and 2010 were excluded to avoid any confounding due to the two large public sector strikes that occurred in SA in June 2007 and August 2010, respectively. The year 2009 was also excluded as there was a change in the vaccination schedule in April 2009 in SA, which affected both OPV3 and DTP-Hib3.

The analysis was conducted with R statistical package (<http://www.r-project.org/>).

## 3. Results

The trend in coverage over the last decade for MCV1 and MCV2 implemented by routine immunization services at the province level, and for SIAs at the national level, is plotted in Fig. 1.

Fig. 1 shows that, nationally, coverage of MCV1 and MCV2 have increased by 27% and 26% from 68% and 57% in 2001 to 95% and 83% in 2010, respectively. Comparatively, SIA coverage (Fig. 1) has remained at high levels, around 90%, over the years 1996–2010. In 2010, SIA coverage reached about 92% of children aged 6–59 months and 82% of children aged 5–14 years of SA (total average of 85%). Fig. 2 presents coverage for MCV1, MCV2 and SIA (2010), at the district level. Table 1 collates the coverage for MCV1 and MCV2 (2010), SIA (2010) at the province level and corresponding inequality indices as defined above.



**Fig. 1.** Trends in measles immunization coverage for: 1st dose of measles routine immunization (2001–2010) at the province level (panel a); 2nd dose of measles routine immunization (2001–2010) at the province level (panel b); supplementary immunization activities (SIA) (1996–2010) at the national level (the labels indicate the targeted age group, the colors indicate whether the campaigns were national or sub-national) (panel c). EC, Eastern Cape; FS, Free State; GP, Gauteng; KZN, KwaZulu-Natal; LP, Limpopo; MP, Mpumalanga; NC, Northern Cape; NW, North West; WC, Western Cape.

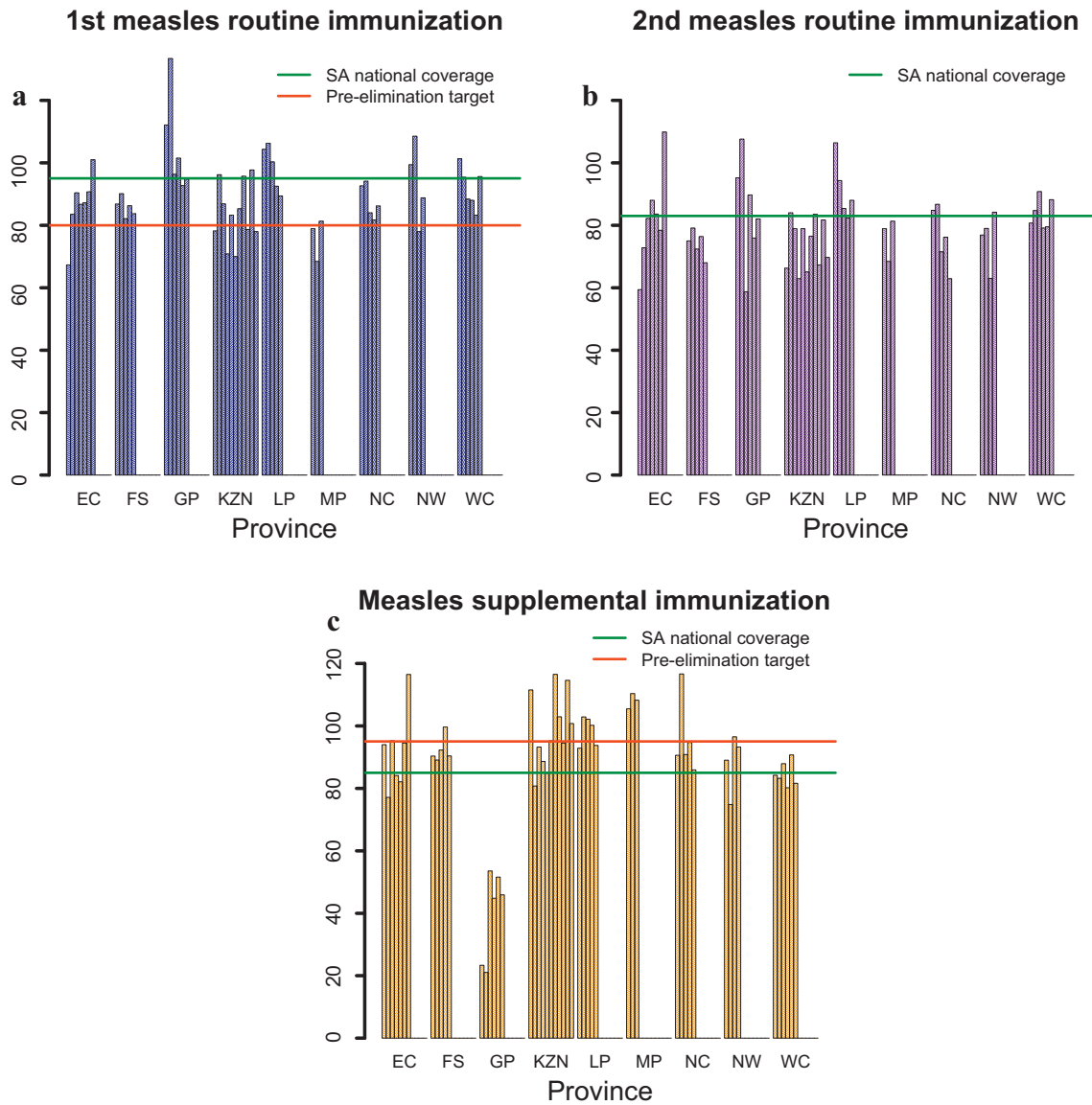
We observe that some provinces present high coverage of MCV1 and MCV2 combined with low coverage of SIA (Table 1). For example, the Western Cape presents high coverage of MCV1 and MCV2 (98% and 82%), but presents one of the lowest coverage percentages of SIA (84%). Gauteng presents the highest coverage of MCV1 and MCV2 (112% and 93%), and presents the lowest coverage of SIA (33%).<sup>1</sup> In contrast, some provinces present low coverage of MCV1 and MCV2 combined with high coverage of SIA. For example, the province with the largest population, KwaZulu-Natal, presents the lowest coverage for MCV1 (86%) and the second to lowest coverage for MCV2 (76%), but the second highest coverage number in SIA (100%). Similarly, Mpumalanga presents intermediate numbers for MCV1 and MCV2 (90% and 77%), but presents the highest coverage of SIA (107%).

The heterogeneous nature of the measles coverage picture reveals itself at the province level (Fig. 1; Table 1) but is even

more striking at the district level (Fig. 2). For example, MCV1 coverage ranges from 67% in a district in the Eastern Cape to 133% in a district in Gauteng. Despite presenting very high coverage of MCV1 and MCV2, Gauteng has high inequality indices, meaning that there is high variability in measles immunization coverage between districts. The Eastern Cape is even more pronouncedly heterogeneous, with one district presenting low coverage of MCV1 and MCV2 (67% and 59%), but another with MCV1 and MCV2 coverage at 101 and 110%, respectively. In contrast, the Free State presents a relatively homogeneous picture with all five districts' coverage in a small range, between 82% and 90% for MCV1 coverage, and 68% and 79% for MCV2 coverage.

Based on this analysis, for the period 2001–2010 there was a statistically significant decrease of 3.8% in the coverage of fully immunized children under-one year associated with SIA implementation (Table 2). The impact of SIAs on routine immunization services in a given year at the district level was associated with a significant decrease of 4.1% and 5.5% in the coverage of MCV1 and MCV2, respectively. Similarly, SIA was associated with a significant decrease in the coverage of OPV3 (2.6%) and DTP-Hib3 (2.6%). The presence of SIA in a given year did not affect OPV1 and BCG coverage.

<sup>1</sup> It should be noted that 33% coverage is an artifact of 2010: the province implemented an emergency campaign in late 2009 in response to a measles outbreak, and since the national campaign followed six months after the emergency campaign, the province only conducted a mop-up of the children not reached in 2009. In 2009, SIA coverage was 87%, which is also relatively low.



**Fig. 2.** 2010 coverage at the district level for: 1st dose of measles routine immunization (panel a); 2nd dose of measles routine immunization (panel b); measles supplemental immunization (panel c). EC, Eastern Cape; FS, Free State; GP, Gauteng; KZN, KwaZulu-Natal; LP, Limpopo; MP, Mpumalanga; NC, Northern Cape; NW, North West; WC, Western Cape; SA, South Africa.

**4. Discussion**

This analysis provides evidence of the trends in measles immunization coverage in SA for routine and supplemental

immunizations over the last decade at province and district levels. It points to the successes that have been achieved in scaling up immunization coverage but also highlights the challenges facing the country's effort toward the control and elimination

**Table 1**

Mean coverage and inequality index for each province for routine measles 1st dose, routine measles 2nd dose and supplementary immunization activity, and corresponding rankings among the nine provinces; 2010.

Province	$\mu_{MCV1}$	$R\mu_{MCV1}$	$I_{MCV1}$	$RI_{MCV1}$	$\mu_{MCV2}$	$R\mu_{MCV2}$	$I_{MCV2}$	$RI_{MCV2}$	$\mu_{SIA}$	$R\mu_{SIA}$	$I_{SIA}$	$RI_{SIA}$
Eastern Cape	90	5	0.11	5	86	3	0.18	8	89	6	0.15	8
Free State	86	8	0.04	1	75	8	0.06	1	96	4	0.04	2
Gauteng	112	1	0.14	8	93	1	0.18	8	33	9	0.43	9
KwaZulu-Natal	86	8	0.11	5	76	7	0.10	5	100	2	0.12	6
Limpopo	99	2	0.07	3	92	2	0.10	5	99	3	0.05	3
Mpumalanga	90	5	0.11	5	77	6	0.09	4	107	1	0.02	1
Northern Cape	89	7	0.06	2	81	5	0.08	3	96	4	0.13	7
North West	94	4	0.14	8	75	8	0.12	7	87	7	0.11	5
Western Cape	98	3	0.07	3	82	4	0.06	1	84	8	0.05	3

$\mu$ , mean coverage;  $I = \sigma/\mu$ , inequality index ( $\sigma$ , standard deviation); MCV1, 1st dose of measles routine immunization; MCV2, 2nd dose of measles routine immunization; SIA, supplementary immunization activity; R, ranking among the 9 provinces.



**Table 2**

Association between the occurrence of supplementary immunization activity in a given year and routine immunization coverage of: measles 1st dose under 1 year, measles 2nd dose of one-year olds, oral polio vaccine 1st dose under 1 year, oral polio vaccine 3rd dose under 1 year, Diphtheria/Tetanus/Pertussis–Haemophilus influenzae B vaccine 3rd dose under 1 year, Bacille Calmette–Guérin under 1 year, under-one year olds who have completed primary course of immunization. Number of observations:  $N = 364$ .

Variable	Coefficient	Standard error	P-value
MCV1	−4.1	1.2	<0.001
MCV2	−5.5	1.0	<0.001
OPV1	−2.1	1.4	0.071
OPV3	−2.6	1.4	0.032
DTP–Hib3	−2.6	1.4	0.029
BCG	0.9	1.4	0.258
Imm1	−3.8	1.2	0.001

MCV1, measles 1st dose under 1 year; MCV2, measles 2nd dose of one-year olds; OPV1, oral polio vaccine 1st dose under 1 year; OPV3, oral polio vaccine 3rd dose under 1 year; DTP–Hib3, Diphtheria/Tetanus/Pertussis–Haemophilus influenzae B vaccine 3rd dose under 1 year; BCG, Bacille Calmette–Guérin under 1 year; Imm1, under-one year olds who have completed primary course of immunization.

of measles. The coverage estimates are consistent with prior estimates [30–33]. For the period 2001–2010, coverage of MCV1 has increased. This is consistent with the reported increase from 56% in 2001 to 69% in 2009 in the AFRO region [21]. Over the period 1996–2010, SIA coverage in SA has remained at high levels, similar to the average in the AFRO region [28], which reflects a consistent commitment of resources to the SIA policy.

The seemingly adequate overall country level data masks the coverage picture in MCV1, MCV2 and SIA, which shows substantial heterogeneity across the 52 districts in SA. Whereas 2010 national coverage for MCV1 was more than 90% as recommended by pre-elimination goals [20,21], 8 districts presented MCV1 coverage below 80%, five of which were in KwaZulu–Natal (Fig. 2). Among the 8 districts with MCV1 coverage below 80%, 3 were among the 18 priority districts identified by the National Department of Health, SA based on poor health outcomes and health care needs [34]. In addition, only 17 districts had 2010 SIA coverage higher than 95% as recommended by pre-elimination goals [20,21] (Fig. 2). The heterogeneity in measles coverage among the nine provinces and fifty-two districts of SA remains a concern. Large pockets of low coverage prevent reaching the very high threshold required for population-level immunity to measles [13]. This ultimately facilitates the resurgence of outbreaks.

Coverage for the first dose of immunizations in SA is generally adequate but this is not the case for most boosters. Care is provided free to all children under age six in SA so cost to the parents is probably not a major barrier. There is a need to study other possible barriers to subsequent targeted vaccinations and boosters. This should be addressed from both the supply side, such as stock-outs, and the demand side such as parental understanding of vaccine protective effects. While incomplete booster vaccination is not confined to measles in SA, UNICEF is supportive of measles elimination in Sub-Saharan Africa. To enable this to occur, the National Department of Health in SA is once again engaging in WHO's "Reaching Every District" (RED) strategy [35]. The goal is to achieve at least 80% coverage in all districts. The potential improvement in routine coverage over several years from the implementation of a successful RED strategy could well supersede the need for SIAs, as well as provide potential cost savings.

Significantly, our analysis at the district level showed that the presence of SIAs was associated with decreases in coverage of routine MCV1 and MCV2. Part of the decrease may be because some routine immunizations get counted as campaign immunizations. However, our analysis shows that SIAs can compromise routine measles immunization services. This goes against a fundamental WHO objective of sustaining high coverage of routine

immunization [13]. Furthermore, the introduction of SIAs in SA is associated with a similar reduction in coverage of other routine immunization services including OPV3 and DTP–Hib3. This evidence reinforces the suggestion that SIAs may affect routine services [36]. It also calls for study of the opportunity costs of SIAs for health systems, in particular the potentially negative impact of the mobilization of the primary health care workforce to deliver supplemental vaccinations, with a corresponding reduction in routine activities beyond measles immunization. Mass immunization campaigns can promote the development of health systems, but they can also disrupt regular function and divert resources from other health activities [37,38]. We note that the impact of polio eradication on routine immunization coverage was found to be equivocal at national levels: strengthening of routine vaccine delivery was shown in the Western Pacific [39], while non-improvement or decrease was identified in several Sub-Saharan African/South Asian countries [40]. A Southern African study showed that national routine immunization rates had decreased since introduction of the National Immunization Days in 1996 [41]. A recent study on the impact of measles elimination activities on immunization services and health systems in six countries [42] found no decrease of DTP3 (3rd dose of combined Diphtheria/Tetanus/Pertussis) coverage in years of SIAs at the national level, but reported significant negative impacts from these activities in Cameroon and Ethiopia. Notably, SIAs may interfere with delivery of other health services, which may be interrupted during SIAs because of staff shortages and inadequate preparation [42].

The data we used presents several limitations. First, administrative data can reflect weaknesses in monitoring systems, and measurement errors [43]. Second, the coverage numbers often surpass 100%, likely reflecting inaccuracies in the determination of the denominators of the targeted population. Underestimation of the denominators may be related to several factors, one of which is migration. SA is a destination for migrants, legal and illegal, from neighboring countries such as Zimbabwe, Lesotho, and Mozambique [44,45]. The children of illegal immigrants may be omitted from the census but still receive immunizations. The use of primary health care services in border districts by residents of neighboring countries can also be significant. Internal migration in SA is the legacy of an apartheid-era migrant labor system establishing social networks and transport systems [46]. It is characterized by migration between rural villages and metropolitan areas [47], combined with rapid urbanization, resulting in the movement of people back and forth across districts/provinces [45,47]. This is hard to capture in national figures [47], yet affects access to health services. Migration therefore becomes a source of inflation of the estimates, contributing to numerators but not accounted for in denominators, for which a district's patient attraction and catchment zones do not overlap [48]. Underestimation can occur with outflows of users in search of better vaccination services [48]. Another limiting factor is that the most recent SA census was conducted in 2001 [29]. Denominators can be sensitive to fertility rates at the district level. If the same fertility rate is used in the census projections of all districts, denominators will not reflect locally observed demographic variations [48]. Finally, the routine data probably overlooks the substantial number of vaccinations carried out in the private sector which are not reported to the National Department of Health.

Future work should focus on the distribution of measles and other vaccine coverage in SA. Analysis of the coverage of all routinely provided vaccines can be useful in the assessment of the effectiveness of the health system at the district level. In particular, vaccination coverage is often higher among children living in areas with community health workers [49] or with a higher density of health workers such as nurses [50]. In addition, HIV-positive mothers and measles vaccinations for their children deserve specific

consideration. Positive maternal HIV status reduces the probability of receiving childhood vaccinations [51]. Also, children born to mothers infected with HIV have a higher risk of contracting measles early (before 9 months), independently of whether they are HIV positive or not. This may be due to lower levels of passively acquired antibodies at birth [52]. Hence, the current recommended vaccination schedule to eliminate measles might need to be adjusted in SA and other countries with a high prevalence of HIV positive adults and children.

## 5. Conclusions

High national rates of measles vaccination coverage can mask the important underlying sub-national heterogeneity/inequality seen in districts presenting low rates of immunization coverage. This situation prevents effective disease control, which in turn affects potential for disease elimination. In the case of measles, SIAs can reduce some of this heterogeneity while raising overall coverage in all districts, and addressing the promise of equity in targeting those not reached by health care systems [53,54]. Yet, SIAs can also create perverse effects such as lowering levels of routine coverage and, moreover, affecting performance of the health system as a whole.

Effective disease control can only occur when accurate and timely monitoring of progress or setbacks is implemented. In that respect, measles control policy in Sub-Saharan Africa should be designed using proper census tools that account for the populations to target. Planning for corrective interventions in low coverage areas requires analysis of disaggregated immunization data at district and sub-district levels. Taking regional demographic features into account, such as internal and cross-border migration, is essential in order to quantify their impact on population immunity. Understanding these dynamics will enable not only measles control in Sub-Saharan Africa, but will provide greater accuracy for a broad range of comprehensive immunization indicators.

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