

# First 5 years of measles elimination in southern Africa: 1996–2000

Robin Biellik, Simon Madema, Anne Taole, Agnes Kutsulukuta, Ernestina Allies, Rudi Eggers, Ntombenhle Ngcobo, Mavis Nxumalo, Adelaide Shearley, Egleah Mabuzane, Erica Kufa, Jean-Marie Okwo-Bele

## Summary

**Background** Measles is the leading cause of vaccine-preventable death in Africa. Regional measles elimination is considered feasible using current vaccines and a series of WHO-recommended strategies. We aimed to interrupt transmission of measles, and to use case-based surveillance to show the effect of such interruption.

**Methods** In southern Africa from 1996, seven countries with a total population of approximately 70 million and with relatively high routine vaccination coverage implemented measles elimination strategies. In addition to routine measles immunisation at 9 months of age, these included nationwide catch-up campaigns among children aged 9 months to 14 years, then follow-up campaigns every 3–4 years among children aged 9–59 months, and the establishment of case-based measles surveillance with serological diagnostic confirmation.

**Results** Nearly 24 million children aged 9 months to 14 years were vaccinated, with overall vaccination coverage of 91%. Reported clinical measles cases declined from 60 000 in 1996 to 117 laboratory-confirmed measles cases in 2000. Reported measles deaths declined from 166 in 1996 to zero in 2000. No increase in adverse events was noted after the measles vaccination campaign.

**Conclusion** A reduction in measles mortality and morbidity can be achieved in very low-income countries, in countries that split their vaccination campaigns by geographical area or by age-group of the target population, and where initial routine measles vaccination coverage among infants was <90%, even when prevalence of HIV/AIDS was extremely high. Continued high-level national commitment will be crucial to implementation and maintenance of proven strategies in southern Africa.

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**WHO, Harare, Zimbabwe** (R Biellik PhD, E Kufa, J-M Okwo-Bele MD); **Ministry of Health, Gabarone, Botswana** (S Madema); **Ministry of Health and Social Services, Maseru, Lesotho** (A Taole); **Ministry of Health and Population, Lilongwe, Malawi** (A Kutsulukuta); **Ministry of Health, Windhoek, Namibia** (M Allies); **Department of Health, Pretoria, South Africa** (R Eggers MD, N Ngcobo MD); **Ministry of Health, Mbabane, Swaziland** (M Nxumalo); and **Ministry of Health and Child Welfare, Harare, Zimbabwe** (A Shearley MPH, E Mabuzane)

**Correspondence to:** Dr Robin Biellik, WHO, PO Box 5160, Harare, Zimbabwe  
(e-mail: biellikr@who.co.zw)

## Introduction

Measles is the most contagious disease known to man. Globally, although national immunisation programmes are estimated to prevent 80 million cases and 4·5 million deaths due to measles yearly, it is estimated that more than 30 million cases and 0·9 million deaths still occur every year.<sup>1</sup> Approximately half of these deaths occur in Africa.<sup>2</sup> Measles is the leading cause of death in children in Africa, even though it is preventable by a vaccine that is currently in widespread use in developing countries. The measles vaccine is highly effective and safe; the major reason for the remaining measles disease burden is failure to vaccinate, not vaccine failure.<sup>3</sup>

In 1989 and 1990, respectively, the World Health Assembly<sup>4</sup> and the World Summit for Children<sup>5</sup> set specific goals for the reduction in measles morbidity by 90% and of measles mortality by 95%, as major milestones towards measles eradication in the long-term. Measles elimination is considered technically feasible<sup>6,7</sup> because: current vaccines are sufficiently efficacious; measles is primarily a disease of man—there is no non-human reservoir; there is no carrier state and very few symptom-free cases; and measles immunity acquired by vaccination or natural disease is of very long, possibly life-long, duration.

Strategies currently recommended by WHO to achieve measles elimination include: routine vaccination coverage of 95% or more, with one dose of measles vaccine administered at 9 months of age to immunise most children; implementation of a national catch-up measles vaccination campaign in children aged 9 months to 14 years with coverage of 90% or more, to reduce the residual number of susceptible children; implementation of periodic national follow-up measles campaigns in children aged 9 months to 59 months with coverage of 90% or more, and frequency every 3–4 years depending upon the rate of accumulation of new susceptible children in the population; and the establishment of case-based measles surveillance with laboratory confirmation to monitor and assess impact.

Routine vaccination coverage with one dose of standard measles vaccine at 9 months of age is associated with a vaccine efficacy of approximately 85%.<sup>8</sup>

A mass vaccination activity lends itself better to reaching children that were not reached by the routine vaccination programme, to immunise measles susceptibles in the population. Therefore, it is more effective to provide a second opportunity for measles vaccination through a single nationwide mass measles catch-up campaign. This campaign should be done among an epidemiologically determined target group, usually children 9 months to 14 years of age regardless of vaccination or disease history.<sup>9</sup> Experience in the WHO Americas Region shows that if catch-up campaign coverage of more than 90% can be achieved, measles transmission will be significantly reduced or interrupted.<sup>10</sup>

Unvaccinated children and children born after the measles catch-up campaign who do not respond to vaccination at 9 months of age will contribute to the gradual accumulation of measles susceptible individuals in the population. This new accumulation is then reduced with periodic mass follow-up campaigns. The timing of follow-up campaigns necessarily depends on coverage achieved during both the routine programme and the catch-up campaign. To achieve maximum effect on measles transmission, all catch-up and follow-up vaccination campaigns should be done in the low season of measles transmission, usually the drier winter months.

During the decade preceding the launching of measles elimination initiatives in the seven southern African countries of Botswana, Lesotho, Malawi, Namibia, South Africa, Swaziland, and Zimbabwe, average routine vaccination coverage with one dose of measles vaccine administered at 9 months of age of approximately 80% was achieved and sustained. This stable high routine coverage had a substantial effect on measles epidemiology.<sup>11</sup> Measles morbidity declined substantially, the interval between epidemics lengthened, the average age of measles cases increased, the proportion of primary vaccine failures among measles cases rose, with measles mortality reduced to very low levels.

With these epidemiological pre-conditions in place, and building upon experience gained in implementing the vaccination campaigns and case-based surveillance strategies associated with the polio eradication initiative, political commitment and operational support was obtained for launching measles elimination in the seven countries, in accordance with WHO/African Regional Office recommendations, and with advocacy and technical assistance provided by the WHO Southern African Expanded Programme on Immunisation (EPI) Unit.

The national prevalence rates of HIV-1 infection in southern African countries are among the highest in the world. At present, roughly a third of fertile-age adults in southern Africa are HIV-positive, although prevalence is often much higher in certain high-risk groups such as sex workers, soldiers, and long-distance drivers. From available data, we can therefore assume that up to 10% of newborns in southern African countries become HIV infected perinatally or through breastfeeding.

## Methods

### Country information

Catch-up vaccination campaigns in each country were planned and implemented by national Ministries of Health, with technical assistance from WHO/African Regional Office. The South African government funded its measles campaign in full; in the other countries, campaigns received primary financial support from Ministries of Health, the UK Department for International Development (DFID), UNICEF, and the US Centers for Disease Control and Prevention (CDC). Particular emphasis was placed on the implementation of three important operational strategies: safe injection practices (all countries used disposable syringes—Lesotho, Malawi and Swaziland used auto-destruct disposable syringes); safe disposal of used injection equipment (all countries packed used injection equipment in disposal boxes for incineration or deep burial); and monitoring systems for adverse events following vaccination. Furthermore, vitamin A supplementation for children 6–59 months of age was included in the catch-up measles campaigns in Lesotho, Malawi, and Namibia. Doses were consistent with WHO recommendations: 100 000 IU to infants 6–11 months of age, and 200 000 IU to children 12–59 months of age.

In accordance with the availability of logistical and human resources, particularly qualified vaccinators, and especially where measles vaccination was combined with polio National Immunisation Days (NIDs), national catch-up measles campaigns were divided by geographical area or target population. The national measles campaign in South Africa was combined with polio NIDs and divided over 2 years between 1996 and 1997; six of nine provinces targeted all children age 9 months to 14 years in 1 year, either 1996 or 1997, and the remaining three provinces targeted children age 9 months to 4 years in the first year and children age 5–14 years in the second year. Botswana divided the campaign geographically in 1997–98, whereas Swaziland and Lesotho opted to split the campaign by age-group in 1998–99 and 1999–2000, respectively, in combination with polio NIDs in Swaziland. The remaining three countries, Malawi, Namibia, and Zimbabwe, completed the campaign in 1 year. By the time Malawi and Zimbabwe had done their measles catch-up campaigns in 1998, they were no longer doing polio NIDs and provided measles vaccine only.

Measles vaccination campaigns cost approximately US\$0.85 to US\$1.10 per child vaccinated, depending mainly on variations in transport costs. Costs were lower where population density is higher, for example in Malawi and Swaziland, and higher where population density is lower, for example in Botswana and Namibia. Included in that estimate was approximately US\$0.25 per child vaccinated, for vaccine, injection equipment, and disposal boxes.

Simultaneous with, or soon after the catch-up campaigns, we initiated case-based surveillance of suspected measles cases in all of the seven countries, using the WHO-recommended case definition (any case with rash and fever and at least one of the three symptoms: cough, coryza, and conjunctivitis) and surveillance guidelines.<sup>10,12</sup> We trained key surveillance staff at national and provincial levels. They, in turn, developed country-specific measles surveillance guidelines, including standardised case investigation forms and procedures, which have been integrated into national vaccine-preventable and infectious disease surveillance guidelines. These guidelines then served as the basis for the large-scale training of provincial and district level medical and public-health workers.

After training for national laboratory technicians in six of the seven countries was done in July, 1998, laboratory investigation of suspected measles cases was established in six countries. Laboratory investigation in Lesotho was initiated in January, 2001. The African Regional Office (AFRO) designated the National Institute of Virology (NIV) in Johannesburg as the African Regional Measles Reference Laboratory.

In view of the high (>95%) sensitivity and specificity and simplicity of use, AFRO recommends testing single serum specimens collected during the first 30 days after rash onset with measles IgM enzyme-linked immuno-assay (ELISA) kits for the confirmation of acute measles infection.<sup>13</sup> Measles IgM-negative serum samples are further tested, where possible, for the presence of rubella IgM antibody using a similar ELISA kit. Since 1999, AFRO has supported measles surveillance activities and supplied measles and rubella ELISA kits to all seven countries except South Africa, using funds provided by the CDC.

AFRO also recommended collecting urine specimens from suspected measles cases during the first 7 days following rash onset. Urine specimens from measles IgM-positive cases are sent to NIV for measles virus isolation. When genomic sequencing of wild-type measles virus

	Dates of campaign	Target age-group	Target population	Population vaccinated	Vaccination coverage campaign	1996 routine coverage
<b>South Africa</b>						
4 provinces	Aug 96	9M-14Y	3 559 252	3 317 400	93.2%	..
3 provinces*	Aug 96	9M-4Y	2 173 753	1 786 048	82.2%	..
	May 97	5-14Y	4 045 498	3 495 415	86.4%	..
2 provinces	May 97	9M-14Y	4 278 598	3 281 321	76.7%	..
Total	..	..	14 057 101	11 880 184	84.5%	82%
<b>Botswana</b>						
	July-Aug 97	9M-14Y†	344 280	347 265	100.9%	..
	May 98	9M-14Y‡	234 960	246 420	104.9%	..
Total	..	..	579 240	593 685	102.5%	82%
<b>Namibia</b>						
	June 97	9M-14Y	737 977	677 538	91.8%	61%
<b>Zimbabwe</b>						
	June 98	9M-14Y	5 279 248	4 929 475	93.40%	77%
<b>Swaziland</b>						
	June 98	9-59M	147 545	146 626	99.4%	..
	May 99	5-14Y	276 732	244 739	88.4%	..
Total	..	..	424 277	391 365	92.2%	70%
<b>Malawi</b>						
	Oct 98	9M-14Y	4 179 229	4 747 452	113.6%	90%
<b>Lesotho</b>						
	Oct 99	9-59M	266 329	159 933	60.1%	..
	Oct 00	5-14Y	624 994	469 005	75.0%	..
Total	..	..	891 323	628 938	70.6%	82%

M=months. Y=years. \*Some provinces vaccinated some children twice (both in August, 1996, and May, 1997), but no gaps occurred. Vaccination coverage calculated here is best estimate based on one dose only; one province continued vaccinating for 3 months beyond May, 1997. †14 of 22 districts in 1997. ‡Remaining eight of 22 districts in 1998.

Table 1: Coverage achieved during measles catch-up vaccination campaigns and routine vaccination

isolates from laboratory-confirmed cases is more firmly established in the future, it will be possible to distinguish the origin of measles viruses as indigenous or imported and, thus, to confirm definitively when the transmission of indigenous measles strains has been fully eliminated.

#### Role of the funding source

The study sponsor had no role in study design, data collection, data analysis, data interpretation, or in the writing of the report.

#### Results

A total of nearly 24 million children were vaccinated during the catch-up measles campaigns. Overall, reported coverage was 91% in the seven countries that have completed their campaigns (table 1). Coverage was not independently verified. Namibia and South Africa implemented mopping-up vaccination activities in selected districts where initial coverage of less than 70% was achieved. No deaths or cases with persisting sequelae associated with vaccination were reported. In Zimbabwe, four children died within 30 days after vaccination; however, an independent review of the case histories of these four children done by the Johns Hopkins University School of Public Health determined that none of the deaths were attributable to vaccination.

The achievement of 93% coverage in Zimbabwe in 1998 appears to have partially overcome resistance by the minority of parents who refuse to have their children vaccinated on religious grounds. This was attributed largely to the use of a private sector marketing company that developed a professional social mobilisation strategy and

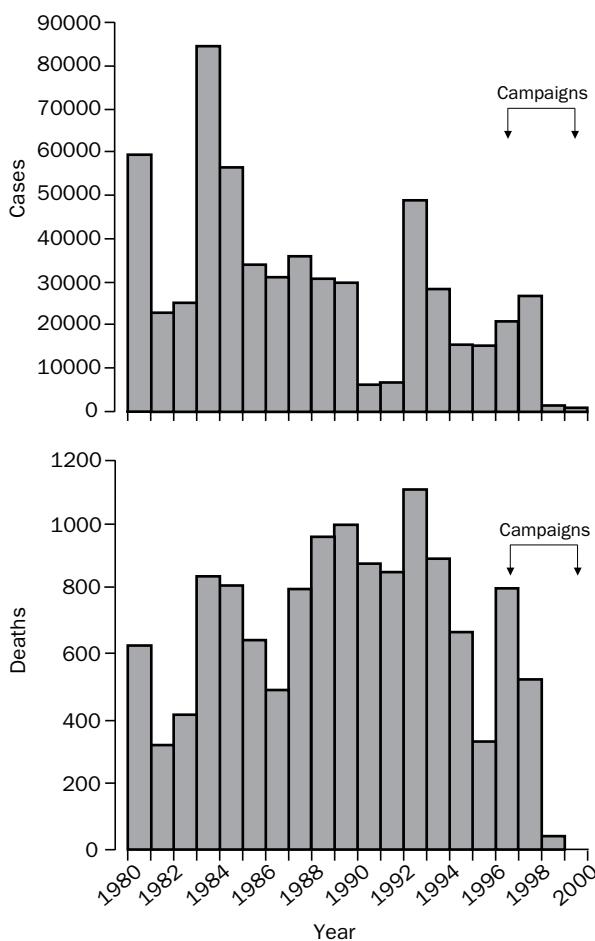


Figure 1: Reported measles cases and deaths by year, in seven southern African countries, 1983–2000

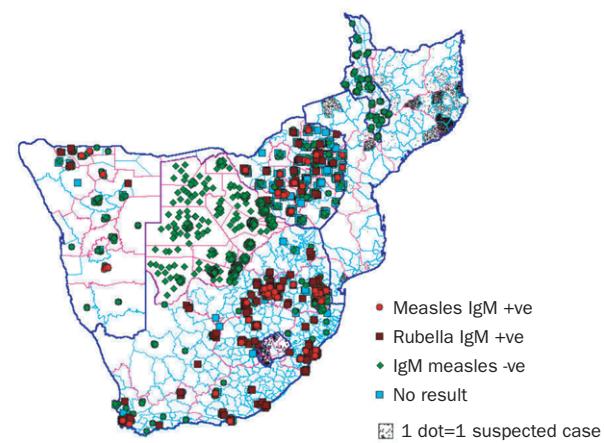


Figure 2: Geographical distribution of suspected measles cases investigated, southern Africa 2000

	Number of reported measles cases	Investigated measles	Reported cases with specimens taken	Specimens taken with results available	Measles IgM positive*	Measles IgM negative	Measles IgM indeter	Rubella IgM positive
Country								
Botswana	1666	678 (41%)	856 (126%)	210 (25%)	0	210	0	170
Lesotho	660	0	0	0	0	0	0	0
Malawi	303	303 (100%)	303 (100%)	287 (95%)	0	287	0	0
Namibia	261	261 (100%)	237 (91%)	173 (73%)	13 (8%)	158	2	43
South Africa	1449	1449 (100%)	1303 (90%)	1303 (100%)	77 (6%)	1166	9	471
Swaziland	230	230 (100%)	230 (100%)	229 (100%)	10 (4%)	219	0	115
Zimbabwe	1090	1090 (100%)	971 (89%)	275 (28%)	17 (6%)	247	11	12
<b>Total</b>	<b>5659</b>	<b>4011 (71%)</b>	<b>3900 (97%)</b>	<b>2477 (64%)</b>	<b>117 (5%)</b>	<b>2287</b>	<b>22</b>	<b>811</b>

Data are number (%). Indeter=indeterminate. \*Zero deaths.

Table 2: Results of measles case-based surveillance, southern Africa, 2000

also to the promulgation of a statutory instrument, based on a similar instrument in effect in Botswana, which sought to discourage religious refusal of vaccination on public-health grounds. More recently, South Africa adopted similar legislation.

After the implementation of measles catch-up vaccination campaigns in the seven countries, the number of reported measles cases and deaths decreased substantially (figure 1). To calculate the percentage reduction in reported morbidity and mortality between 1996 and 2000, data from Lesotho could not be included because the catch-up campaign was not completed in that country until 2000 and laboratory confirmation of measles was not established until 2001. A total of 60 000 clinical measles cases were reported by the six remaining countries in 1996, whereas 117 laboratory-confirmed measles cases were reported in 2000; that is, a reduction in reported morbidity of 99·8%. Reported measles deaths decreased from 166 in 1996 to zero in 2000, that is, a reduction in mortality of 100%.

By the end of 1999, case-based surveillance of suspected measles was fully established in all elimination countries except Lesotho, where laboratory support was not established until the beginning of 2001. The distribution of case detection in 2000 was consistent with the pattern of human settlement in southern Africa (figure 2).

A total of 1730 suspected measles cases were reported in southern Africa during 1999, and 5659 cases in 2000 (table 2). In 1999, 50 cases were laboratory confirmed with origin in Namibia, South Africa, and Zimbabwe, and in 2000, 117 cases were laboratory confirmed with origins in the same three countries plus Swaziland. No laboratory confirmed measles cases were reported from Botswana or Malawi in either 1999 or 2000. Four laboratory confirmed measles deaths (two in South Africa and Zimbabwe) were reported from the seven measles elimination countries in 1999 and zero measles deaths in 2000.

Using the definition of clustering among laboratory confirmed measles cases as all cases occurring in the same district with onset during a period of 30 days, analysis of cases in 1999 and 2000 showed very few clusters, all less than five cases. Secondary measles transmission beyond a single generation appeared to be very limited. However, the practice of doing a detailed search for additional cases in communities where laboratory-confirmed measles cases occur was not implemented routinely until 2001, particularly in Namibia and South Africa.

Specific epidemiological investigations in Namibia show that measles transmission occurred in pockets of unvaccinated or partially-vaccinated children. This included families with high socioeconomic status whose private physicians incorrectly advised parents that there was no need to participate in the catch-up campaign. In Gauteng Province in South Africa, nosocomial transmission primarily among infants younger than 9 months of age born to HIV-positive mothers occurred in three tertiary hospitals in 1999,

resulting in two deaths and 22 cases.<sup>14,15</sup> However, nosocomial transmission was halted effectively when measures to vaccinate all admitted infants aged 6 months or older against measles were instituted.<sup>14,15</sup>

A hospital-based study in two provinces of South Africa comparing admissions due to clinically-diagnosed measles before and after implementation of the catch-up measles vaccination campaign demonstrated a 96% reduction in cases and 100% reduction in deaths.<sup>16</sup> Furthermore, it was reported that in Malawi, hospital measles wards have been closed now that measles cases are not being admitted.<sup>17</sup>

## Discussion

To sustain the gains achieved through the measles elimination initiative in the long-term, the seven southern African countries are continuing to implement WHO-recommended measles elimination strategies. Firstly, the Ministries of Health in the seven countries are committed to identifying and implementing innovative operational and promotional steps to raise routine vaccination coverage to more than 95% in each district, including the elimination of missed opportunities for vaccination, to introduce defaulter tracing and follow-up where it does not currently exist, and to revitalise or reorganise outreach services to reach communities not routinely covered.

Efforts are currently in progress in all seven measles elimination countries to incorporate experience from measles campaigns into routine vaccination services with regards to safe injection practices, adequate disposal of used injection equipment, monitoring of adverse events following immunisation, and vitamin A supplementation.

Epidemiological analysis of district-specific routine measles vaccination coverage plus coverage achieved during catch-up vaccination campaigns has permitted Ministries and their EPI partner agencies to ascertain where mopping-up vaccination is required to ensure that no low-coverage pockets persist. Analysis has also permitted countries to estimate the accumulation of new susceptibles in the population and to plan the appropriate timing and target population for the implementation of follow-up vaccination campaigns (table 3), although in practice, countries have opted to target children 9–59 months of age.

Country	Catch-up year		Follow-up year interval (years)	
	Phase 1	Phase 2		
Botswana	1997	1998	2001*	4
Lesotho	1999	2000	2002	3
Malawi	1998	NA	2002	4
Namibia	1997	NA	2000*	3
South Africa	1996	1997	2000*	4
Swaziland	1998	1999	2002	4
Zimbabwe	1998	NA	2002	4

NA=not available. \*Completed.

Table 3: Timing of follow-up measles vaccination campaigns, southern Africa, 2000–02

All seven measles elimination countries must do follow-up measles vaccination campaigns during the period 2000–02, to sustain the interruption of measles transmission that has been achieved to date. Namibia and South Africa did their follow-up campaigns in June, 2000, and Botswana did its follow-up campaign in May, 2001. The follow-up campaigns were done in the same winter (low transmission) season as the catch-up campaigns, and all operational strategies remained the same except that the target group for follow-up campaigns was substantially smaller.

Case-based surveillance of severe measles cases has been strengthened and WHO-recommended indicators were developed and introduced to monitor routinely elimination status in each country. In principle, the number of laboratory-confirmed measles cases and duration of transmission associated with secondary spread around an index laboratory-confirmed measles case will permit countries to determine if elimination has been achieved.<sup>18</sup>

WHO-recommended strategies including the implementation of catch-up campaigns among children 9 months to 14 years of age are shown here to be operationally feasible and extraordinarily effective in an African setting in significantly reducing morbidity and virtually eliminating mortality due to measles. This impact was achieved in very low income countries such as Lesotho, Malawi, and Zimbabwe; in countries that split their catch-up campaigns by geographical area or age-group of the target population such as Botswana, South Africa, and Swaziland; in Namibia where routine measles vaccination coverage among infants was only 61% at the time of the campaign; and in South Africa where the measles catch-up campaign coverage among the target age-group achieved was only 85%.

We were particularly pleased to note that measles mortality and morbidity reduction was achieved in countries with extremely high HIV/AIDS prevalence rates such as Botswana, South Africa, and Zimbabwe. No significant increase in adverse events following measles campaign vaccination was noted. Furthermore, HIV-positive individuals 15 years of age or older who are likely to have had measles disease during their infancy or childhood, appear to continue to be protected by persisting immunity derived from natural infection, despite exposure to isolated measles cases.

To sustain this reduction in measles mortality and morbidity in southern Africa, continued high-level national commitment will be crucial in support of ongoing implementation of WHO-recommended strategies. Maintenance of high levels of vaccination coverage, complete and timely surveillance of all suspected measles cases including the timely processing of serum specimens and dissemination of results by national measles laboratories, and careful community investigation around laboratory-confirmed measles cases to assess the extent of secondary spread, will permit southern African countries to monitor and, where necessary, take corrective action to sustain measles elimination. Through these measures, countries will continue to benefit from the important investment that has been made in an attempt to permanently protect the population from this highly infectious disease.

#### Contributors

Robin Biellik coordinated the development and implementation of measles elimination strategies, assisted in securing funding, directed data analysis, and drafted the paper. The nine former and current National EPI Managers implemented measles elimination strategies, assisted in securing funding, and collected national data. Erica Kufa compiled and analysed all data. Jean-Marie Okwo-Bele supervised all activities. All investigators were involved in finalising the paper.

#### Conflict of interest statement

None declared.

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