Vaccine 37 (2019) 6039–6047

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Optimization of frequency and targeting of measles supplemental immunization activities in Nigeria: A cost-effectiveness analysis

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ARTICLE INFO

Article history:
Received 7 May 2019
Received in revised form 19 August 2019
Accepted 20 August 2019
Available online 27 August 2019

Keywords:
Cost-effectiveness
Measles
Routine immunization
Sub-national
Supplemental immunization activities

ABSTRACT

Background: Measles causes significant childhood morbidity in Nigeria. Routine immunization (RI) coverage is around 40% country-wide, with very high levels of spatial heterogeneity (3–86%), with supplemental immunization activities (SIAs) at 2-year or 3-year intervals. We investigated cost savings and burden reduction that could be achieved by adjusting the inter-campaign interval by region.

Methods: We modeled 81 scenarios; permuting SIA calendars of every one, two, or three years in each of four regions of Nigeria (North-west, North-central, North-east, and South). We used an agent-based disease transmission model to estimate the number of measles cases and ingredients-based cost models to estimate RI and SIA costs for each scenario over a 10 year period.

Results: Decreasing SIAs to every three years in the North-central and South (regions of above national-average RI coverage) while increasing to every year in either the North-east or North-west (regions of below national-average RI coverage) would avert measles cases (0.4 or 1.4 million, respectively), and save vaccination costs (save $19.4 or $5.4 million, respectively), compared to a base-case of national SIAs every two years. Decreasing SIA frequency to every three years in the South while increasing to every year in the just the North-west, or in all Northern regions would prevent more cases (2.1 or 5.0 million, respectively), but would increase vaccination costs (add $3.5 million or $34.6 million, respectively), for $1.65 or $6.99 per case averted, respectively.

Conclusions: Our modeling shows how increasing SIA frequency in Northern regions, where RI is low and birth rates are high, while decreasing frequency in the South of Nigeria would reduce the number of measles cases with relatively little or no increase in vaccination costs. A national vaccination strategy that incorporates regional SIA targeting in contexts with a high level of sub-national variation would lead to improved health outcomes and/or lower costs.

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1. Introduction

Measles causes a significant burden of disease in Nigeria. Estimates suggest nearly one million disability-adjusted life-years (DALYs) lost and over ten-thousand deaths in 2016 [1]. The burden of measles is not evenly distributed throughout the country, with over 80% of the reported cases occurring in the Northern states.

A measles vaccine that is safe, effective, and inexpensive has been available since 1963 [2]. This vaccine successfully reduces measles incidence and severity. According to the National Program on Immunization in Nigeria, children should be immunized against measles as part of routine immunization (RI) with a single dose at 9 months of age. However, RI coverage in Nigeria remains low at 42% as of 2017 [3], and is heterogeneous by region (52% in the North-central region, 36% in the North-east, 22% in the North-west, and 71% in the South [3]). These values remain largely unchanged from 2013 [4,5].

Nigeria is currently one of only a few countries implementing a single dose (MCV1) immunization strategy without the World Health Organization recommended second dose of vaccine (MCV2) [6]. The canonical role of MCV2 in RI is to seroconvert

Abbreviations: CFR, case fatality ratio; DALY, disability adjusted life years; DHS, Demographic and Health Survey; EMOD, Epidemiological Modeling; LMIC, low and middle income countries; MCV, measles containing vaccine; NC, North-central; NE, North-east; NW, North-west; S, South; RI, routine immunization; SIA, supplemental immunization activities; WHO, World Health Organization.

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https://doi.org/10.1016/j.vaccine.2019.08.050
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children who failed to respond to an MCV1 dose [7–9], which is estimated to be 5–15% when MCV1 is delivered at 9 months. The introduction of MCV2 is not expected to substantially reduce burden when MCV1 coverage is poor. Burden is dominated by the unvaccinated, not children who failed to respond to MCV1. A second routine dose is unlikely to reach children who fail to receive a first routine dose through existing systems.

In addition to routine immunization services, Nigeria is currently conducting national supplemental immunization activities (SIAs) every two to three years. During these activities, all children in a specified age range are targeted for vaccination. Due to logistical constraints, these campaigns are organized and conducted serially in different regions, though not with independently variable frequency. SIAs have the greatest impact when they reach susceptible children after inconsistent or insufficient routine immunization delivery, and before they are naturally infected. As such, targeting the frequency of SIAs to reflect subnational variation in birth rates and routine coverage has the potential to further reduce measles burden.

The health effects and costs of changing SIA strategy to a subnational campaign frequency are not currently known. This study aims to evaluate the potential health outcomes and costs of implementing SIAs sub-nationally and with region-dependent frequencies in Nigeria.

2. Methods

2.1. Scenarios

We modeled SIAs every one, two, or three years, in each of four regions in Nigeria: North-west (NW), North-central (NC), North-east (NE), and South (S). The South region is an aggregation of South-west, South-east, and South-south zones, which were considered jointly because of the relatively better rates of routine immunization compared to Northern regions. This produced a total of 81 scenarios for evaluation. For each of these scenarios, we analyzed health outcomes at current coverage rates, as well as outcomes for SIA coverage rates improved by 25%. We analyzed cost outcomes at current coverage rates only, as the costs to increase SIA coverage are unknown. The time horizon for this model was 10 years. Here, SIA coverage is defined as the fraction of the targeted population receiving a dose of measles containing vaccine (MCV) during the SIA.

We chose annual campaigns as the upper limit for frequency due to concerns of feasibility for any more frequent campaigns, particularly in North Nigeria. The WHO recommends 9–12 months of preparation for an SIA, indicating that SIAs every year would be feasible given that preparation time [10].

2.2. Target population

Simulations of the Nigerian population reflected age-based demography of each of the regions, and included all ages. However, more than 95% of measles incidence occurred in children under the age of 10 years, which is in line with the reported distribution of ages-at-infection for measles in Nigeria.

2.3. Outcomes

Our primary health outcome for this analysis was the number of measles cases. We also evaluated health outcomes using DALYs. For cost outcomes, we evaluated RI costs, SIA costs, measles treatment costs, and total costs.

2.4. Epidemiological model

Measles transmission in Nigeria was simulated using the generic branch of EMOD [11], a stochastic agent-based model of disease transmission. Input parameter values for known disease properties (e.g., infectious period), demographic variables (e.g., birth rate), and interventions (e.g., calendar of past SIAs) were fixed; latent quantities (e.g., infectivity) were inferred from disease incidence time series and age-at-infection data (Additional file 1). A constant low-level of disease importation ensured that the re-introduction of disease was possible in the event of local elimination.

SIA coverage was incorporated as a latent variable. Published estimates of coverage (i.e., proportion of the target population receiving a dose of MCV) can vary widely [12,13]. As a result, a distribution for possible values of SIA coverages, as well as other latent variables, was used to create an ensemble of input parameterizations (Additional file 2). This ensemble was calibrated to best match reported time-series and age-of-infection data over the period from 2009 to 2015. These were important factors in the calibration of our model, and were driving factors in the final results. Calibrated simulation outcomes and reference values for the incidence time-series are depicted in Fig. 1.

Simulations provided state-level resolution, and incidence was subsequently aggregated into the four regions depicted in Fig. 1. The three Northern regions used in the simulation are the three Northern regions as identified by the Nigerian Demographic and Health Survey (DHS), while the single Southern region is a union of the three Southern DHS regions. These four regions are relevant to SIA implementation because planning for the 2017–2018 Nigerian measles SIA used these four regions, with implementation occurring in the following order: NW, NE, NC, and S. A summary of descriptors for these four regions is given in Table 1. These descriptors include the estimated total population in 2006, rate of population growth, average percentage of children receiving a dose of MCV through RI, median percentage of SIA targeted population receiving a dose of MCV (i.e. SIA coverage), and amplitude of seasonality in measles infectivity. Calculation of these values is described in detail in additional files 1 and 2. Seasonality magnitudes in Table 1 are most-probable-point-estimates from posterior distributions of simulations based on a uniform prior; sampled ranges and uncertainty are included in additional file 2. The seasonality in the South region is much lower than in any other region, and (unlike the three other regions) is not significantly different from zero.

Future SIAs were scheduled using 2019 as a base year, with implementation occurring every third year (2019, 2022, 2025, etc.), every second year (2019, 2021, 2023, etc.) or every year. The effective coverage of future SIAs in a given simulation is assumed to be constant and equal to the mean effective coverage of previous SIAs in that simulation.

For each scenario, we also evaluated the impact of an improvement of SIA coverage. This SIA coverage increase was calculated as a 25% reduction in the fraction not receiving a dose of MCV (e.g., 20% coverage improves to 40%, 60% coverage improves to 70%) relative to the mean values calibrated from the 2009 to 2015 period. Modeling the improvement of SIA coverage in this manner reflects the increased difficulty of reaching previously missed children when approaching 100% coverage.

Measles-specific mortality was not explicitly incorporated into the epidemiological model; only non-specific, all-cause mortality was included. A measles-specific case fatality ratio (CFR) of 2.1% was applied post-hoc to each of the simulated cases in the 10-year time horizon used for evaluating outcomes [14–17]. DALYs were calculated by combining total measles deaths with a disutility for each measles case of 0.5 per-day for 13.8 days [18].

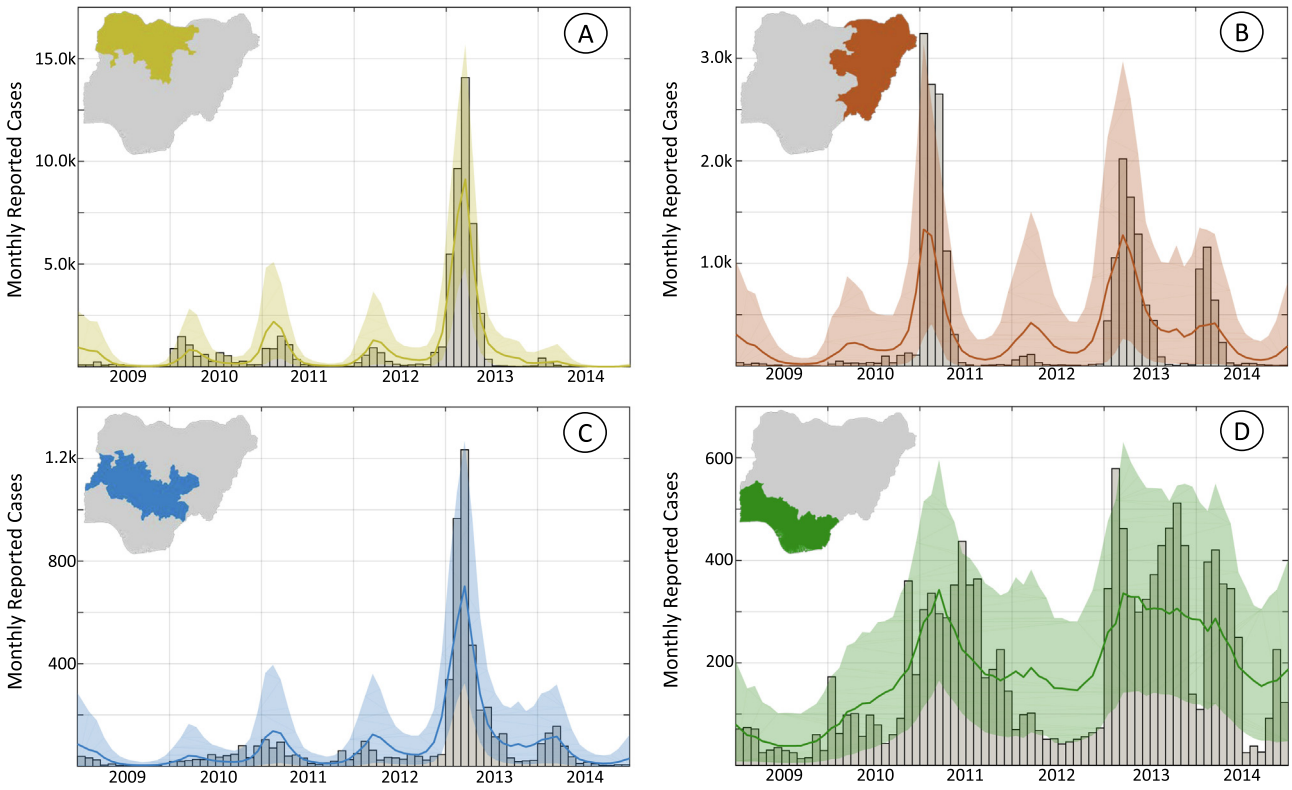

Fig. 1. Monthly reported measles cases for the four regions of Nigeria used in this study: North-west (A), North-east (B), North-central (C), and South (D). Gray bars represent observed data; solid lines represent mean simulation outcomes; shaded patches contain 90% of all simulation outcomes. Note that the vertical scale varies substantially between regions.

Table 1
Representative values for several metrics in the four SIA regions.

	North-west (NW)	North-central (NC)	North-east (NE)	South (S)
Population	36 M	20 M	19 M	66 M
Growth rate	2.8%	1.7%	2.6%	1.7%
RI average coverage	22%	48%	27%	69%
SIA average coverage	50%	44%	44%	23%
R0 seasonality	0.93	0.62	0.66	0.16

2.5. Costs

We used two perspectives for this analysis, a vaccination program perspective and a health system perspective. The vaccination program perspective was used to estimate the cost of running the vaccination program, including direct operational costs of vaccine delivery as well as indirect infrastructure and management costs. The health system perspective incorporated direct medical costs of measles treatment as well as vaccination costs. All costs are presented in 2018 US dollars.

We created ingredients-based cost models separately for the RI and SIA programs. The models were built at the lowest possible level of detail without compromising on the integrity of the data sources. The cost models captured costs within the major cost component categories of consumables, labor, infrastructure, and supply chain (Table 2). Each component was either included as a number of units or a percentage relative to another cost component. Those components included as a number of units were included per dose (as defined by per dose given, planned, or opened), per day (as defined by vaccination-day or team-day), or per area (as defined by ward, local government area (LGA), state, or zone). We excluded surveillance costs specific to case reporting and laboratory testing, since these activities should occur regardless of vaccination activity, and we would therefore expect little to no marginal differences with changes in vaccination frequency. Prices were collected from a variety of published sources and each cost component was calculated individually and then aggregated by state and by year. The calculations were done independently for the RI and SIA programs.

Consumable costs were based on published UNICEF pricing tables [19,20]. We assumed continued use of 10-dose measles vials. Total number of required vaccine vials, administration and reconstitution syringes, and waste boxes were calculated based on the number of MCV doses required for each scenario per the epidemiological model. We used an average wastage rate of 25% [21] for SIA campaigns and an average wastage rate of 40% for RI based on rates of open-vial wastage in low and middle income countries (LMIC) [22].

Direct labor costs for RI were estimated based on the number of doses delivered, an average time to deliver a dose, and the daily pay rate of $38.11 for a Nigerian nurse [23–25]. Delivery times per dose were based on expert opinion and were assumed to be an average of 6 min per dose in-clinic for all dose-related activities including vaccine retrieval, reconstitution, delivery, and documentation. During RI outreach, we assumed a slightly faster 5 min per dose due to having the support of a recorder and the ability to

Table 2
Ingredients-based cost model components for RI and SIA estimations, which were either modeled directly as number of units (per vaccine, per ward, per state, etc.) or estimated as a percentage of another cost category, as appropriate and data allowed. pw = per ward, pl = per LGA, ps = per state, pr = per region, pc = per campaign. GNI = gross national income per capita. ToT = training of trainers. Ntl = national. SIA = supplementary immunization activity. RI = routine immunization.

Component	Cost value	Reference details
Consumables		
Vaccines	$0.2674 per dose planned (SIA) or given (RI)	Average UNICEF price of a 10-dose vial of measles vaccine [20]
Administration Syringes	$0.037 per dose planned (SIA) or given (RI)	Average UNICEF price for a 0.5 mL AD syringe [19]
Reconstitution Syringes	$0.040 per dose planned (SIA) or given (RI)	Average UNICEF price for a 5 mL RUP syringe [19]
Waste Boxes	$0.494 per box planned (SIA) or used (RI)	Average UNICEF price for a 5 L safety box [19]
Direct Labor		
SIA Vaccinator	$7.61 per person-day	L04 federal service employee salary, mean per day, inflated using GNI [28]
RI Vaccinator	$37.28 per person-day	CONHESS level 8, 3 years of experience, inflated using GNI [23]
Record Keeper	$5.54 per person-day	L01 federal service employee salary, entry, per day, inflated using GNI [28]
RI Driver (Outreach)	$5.54 per person-day	L01 federal service employee salary, entry, per day, inflated using GNI [28]
SIA Town Crier	$5.54 per person-day	L01 federal service employee salary, entry, per day, inflated using GNI [28]
SIA Team Supervision	$8.67 per person-day	L05 federal service employee salary, mean per day, inflated using GNI [28]
SIA Local Leader	$10.57 per person-day	L06 federal service employee salary, mean per day, inflated using GNI [28]
Indirect Labor		
SIA Microplanning	Micro-Planning: $71 pw	Author calculations from Nigeria's 2015 Gavi-funded campaign [31]
SIA Social Mobilization	Events: $59 pw Jingles: $4622 pc Media: $969 ps Print: $299 pw	Author calculations from Nigeria's 2015 Gavi-funded campaign [31]
RI Social Mobilization	0.9% of direct labor plus consumables	Author calculations based on results from [30]
SIA Training	Implementation: $83.00 pw Implementation: $142 pl Implementation: $5871 ps Management: $298 pl Micro-Planning: $202 pl Micro-Planning: $5067 ps Micro-Planning: $30939 pr State Training: $714 ps ToT Implementation: $22347 pr ToT Implementation: $5083 pc	Author calculations from Nigeria's 2015 Gavi-funded campaign [31]
SIA Oversight & Management	Coverage Eval: $2339 pr Management: $250 pl Management: $300 ps Materials: $873 ps Materials: $2 per team-day Monitoring: $375 pl Monitoring: $45 ps Ntl. Supervision.: $2118 pc Review: $101 pl Technical Facilitator: $6537 ps Verification: $5.46 pw Ward Supervisors: $45 pw	Author calculations from Nigeria's 2015 Gavi-funded campaign [31]
RI Oversight & Management	Operational support: 20.3% of direct labor cost General management: 11.1% of direct labor cost National and sub-national overhead: 8.3% of facility-level costs	Author calculations based on results from [29]
Supply Chain		
SIA Delivery & Logistics	Transportation: $312 pw Transportation: $118 pl Warehouse: $29762 pc	Author calculations from Nigeria's 2015 Gavi-funded campaign [31]
RI Delivery & Logistics	Transportation: $0.1113 per dose (given + wasted)	Author calculations from Nigeria's 2015 Gavi-funded campaign [31]
Waste Management	$0.0834 per dose planned (SIA) or given (RI)	Author calculations from Nigeria's 2015 Gavi-funded campaign [31]
Infrastructure & Transport		
SIA Generators & Fuel	$10.47 per ward	Author calculations from Nigeria's 2015 Gavi-funded campaign [31]
SIA Vaccinator Transport	16.0% of direct labor	Author calculations from Nigeria's 2015 Gavi-funded campaign [31]
RI Outreach Transport	12.6% of outreach labor	Author calculations based on results from [29]
RI Building & Infrastructure	13.5% of direct labor	Author calculations based on results from [29]

recruit many children together and then quickly vaccinate them in series. Outreach recorder day rates were also included in RI costs at a pay rate of $4.21, the entry level salary for a high school graduate in the Nigerian civil service [26–28]. Indirect labor costs for RI were estimated by applying percentage rates to other cost categories (Table 2). For RI, operational support contributed an additional 20.3% of vaccinator labor costs [29], social mobilization was 0.9% of direct labor costs [30], and management and training was 11.1% of direct labor costs [29]. Supply chain costs for RI were $0.11 per vaccine for delivery and logistics, and $0.08 per vaccine dose for waste management [31]. Infrastructure and transport costs for RI were calculated as 13.5% of total labor costs for buildings and equipment, 12.6% of direct outreach vaccination labor cost for outreach transportation, and 8.3% of all other RI costs for national and subnational overhead [29].

Direct labor costs for SIAs were estimated based on the number of vaccination teams required to deliver the planned number of doses. We estimated the number of teams required and then applied daily pay rates obtained from the Nigerian federal civil service commission for comparable entry-level positions [26,27]. Each team was composed of two vaccinators and two recorders working together to deliver 250 vaccines per day, with each team supported by direct supervisors who oversaw six teams each [32]. To validate this methodology, we compared the resulting cost estimates to previous SIA budgets [31,33].

The remainder of the SIA costs were sourced from a proposed budget for the Gavi-funded measles SIA in Nigeria from 2015 [31]. Costs estimated in this way include SIA micro-planning, training, supervision, coordination, social mobilization, monitoring, supply chain, and facilities and equipment. That SIA budget was for a national campaign targeting ages nine months through ten years, and larger in scale than the SIAs considered in this paper. To account for this difference, we scaled the budget line items proportionately to match our simulated SIAs.

Cost to treat a measles case was $16.44, based on 75% of measles patients seeking care, of whom 80% are hospitalized for an average of 4 days with a cost of $6 per day, and 25% have an ambulatory visit with a total cost of $1.50 [34]. Because it seems unlikely that 75% of patients seek care in Nigeria, we also perfomed scenarios with 50%, 25%, 15%, and 5% of patients seeking care.

2.6. Analytic methods

Annual costs and health outcomes were calculated for each scenario. Means and standard deviations were calculated for each scenario based on an ensemble of 1000 model outcomes for that scenario, each of which resampled the latent model parameters (maternal protection, infectivity, coverage, routine immunity bias, reporting rate) for a new stochastic run of the parameter set. This incorporated both stochastic uncertainty and parameter uncertainty. We then calculated a cost-effectiveness frontier based on total costs and total measles cases of those scenarios that led to the fewest measles cases at equal of lower costs. We calculated this frontier from both the vaccine program and health system perspective. We used a 3% discount rate for costs and health outcomes.

3. Results

In aggregate, our cost model resulted in median per-dose SIA costs of $1.15 (range $0.82–$1.97) and median per-dose RI costs of $2.09 (range $1.83–$2.34). The marginal cost for increased coverage decreased with scope as seen in Fig. 2. Drivers of the cost variability were population size, density, number of LGAs and wards per state, and rurality. Cost results were similar to previously published SIA budgets.

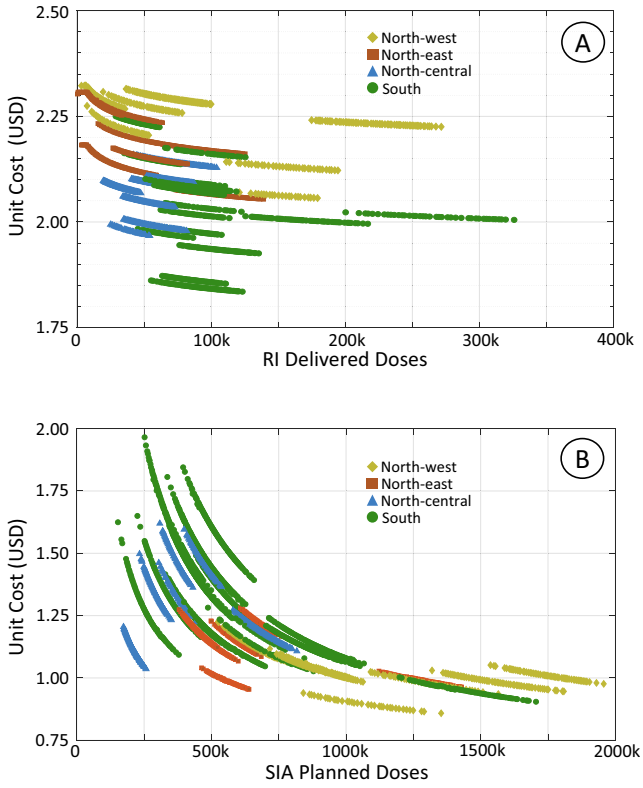

Fig. 2. Marginal unit costs for RI vaccines actually delivered (A), and marginal unit costs for SIA doses planned to be delivered (B). Each line segment represents a state. Variations between states are driven by population size, density, number of LGAs and wards per state, and rurality.

The impact of changing SIA frequency in terms of number of measles cases and vaccination costs, varied by region (Table 3). The length of each line in Fig. 3 top panel represents the total impact of changing SIA frequency in each region, which is driven primarily by population (populous regions require more vaccine and more staff, but also have more measles cases, as seen in Table 1), but also driven by vaccination unit costs (Fig. 2). In all regions, the impact over 10 years in terms of both measles cases and vaccination costs was greater for changing from SIAs every two to one year than changing from every three to two years.

The slope of each line in (Fig. 3) represents the relative value of changing SIA frequency in terms of measles cases prevented for the cost: when RI coverage is low and SIA coverage is high, there is more value to increasing SIA frequency. The greatest relative impact on value (slope magnitude) was for changing between SIAs every two or three years in the North-west. The least relative impact on value (slope magnitude) was for changing between SIAs every two or one year in the South. In all regions, the value was greater for changing from SIAs every two to one year than changing from every three to two years.

When scenarios combining all four regions were analyzed over a 10 year period, measles cases ranged from 23.2 million with SIAs nationwide every 3 years, to 9.4 million with SIAs nationwide every year (Additional file 3). Corresponding measles deaths over that period ranged from 489 thousand to 198 thousand. DALYs ranged narrowly from 351.4 million to 349.8 million over 10 years. Total RI costs were $60.1 million for all baseline scenarios, whereas SIA costs ranged from $88.2 million for nationwide SIAs every 3 years, to $257.5 million for nationwide SIAs every year (Additional file 3) over 10 years. Measles treatment costs ranged from $382.8 million with SIAs nationwide every 3 years, to $154.9 mil-

Table 3
Vaccination costs and measles incidence by region and SIA frequency. Cumulative values over 10 years, both total and per-population.

Region	SIA frequency	Vaccine costs	Vaccine costs per 1000 population	Measles cases	Measles cases per 1000 population
South	1	$557,040,941	$721	5,642,687	7.3
South	2	$300,819,008	$389	7,611,107	9.8
South	3	$241,854,901	$313	8,378,941	10.8
North central	1	$187,231,030	$776	615,850	2.6
North central	2	$99,498,202	$412	1,506,879	6.2
North central	3	$79,477,520	$329	2,217,662	9.2
North east	1	$168,093,329	$640	2,115,813	8.1
North east	2	$88,387,995	$336	4,031,505	15.3
North east	3	$69,054,048	$263	5,064,648	19.3
North west	1	$267,724,435	$526	1,046,637	2.1
North west	2	$144,364,471	$284	3,962,115	7.8
North west	3	$112,871,419	$222	7,623,350	15.0

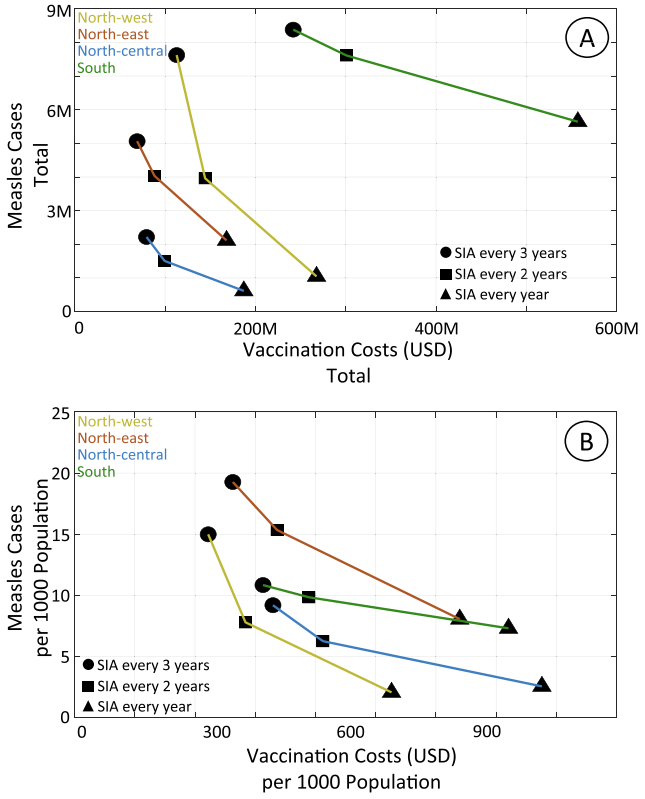

Fig. 3. Measles cases and vaccination costs by region. In each region, total measles cases and total vaccination costs (RI plus SIA) over 10 years (top), and per total 1000 total population size (bottom) for SIAs every one, two, or three years. Length of lines in top panel represents total maximum magnitude of impact of changing SIA frequency in each region. Slope of lines in both panels represents relative impact of changing SIA frequency on number of cases in each region.

lion with SIAs nationwide every year (Additional file 3) over 10 years.

When comparing the number of cases versus total vaccination program costs (RI and SIA), we found that seven scenarios were on the cost-effectiveness frontier (Fig. 4). These scenarios could yield the fewest measles cases for equal or less vaccination cost than alternatives. Nationwide SIAs every three years led to the lowest costs but also the highest number of cases, while SIAs every year led to highest costs with lowest cases (Fig. 5). When uncertainty was included, 95% credible ranges for many scenarios overlapped (ellipses Fig. 5). The cost per case averted ranged from $4.85 for scenario 81 to 80, to $25.92 for scenario 55 to 1.

The current strategy of national SIAs every two years led to 17.1 million cases and $212 million in vaccination costs over 10 years, but this scenario was not on the frontier. Scenario 62 on the cost-effectiveness frontier would cost less in vaccination costs and avert more cases (see Additional file 3, Table 1). This could avert an additional 0.4 million measles cases while saving $19.4 million in vaccination costs compared to the current strategy.

Decreasing SIA frequency to every three years in the South would save significant vaccination costs with relatively little impact on measles cases. Combining this with increased SIAs every year in northern regions provides value in several scenarios: SIAs every three years in the South with SIAs every year in the NW and NE (scenario 58), or in NW, NE, and NC (scenario 55), would cost an additional $20.2 million or $34.6 million in vaccination costs over 10 years, respectively, compared to the current strategy, but would prevent and additional 4.1 million or 5.0 million cases over 10 years. This results in a cost per case averted of $4.99 or $6.99. Most of the scenarios on the frontier with less than 17.1 million cases (results from the current strategy) required annual SIAs in the NW and NE regions, with reduced frequency to one SIA every three years in the South (Fig. 5).

If 75% of patients seek care, measles treatment costs ranged from $155 million with SIAs nationwide every year, to $383 million with SIAs nationwide every three years (Additional file 3) over 10 years. When we included measles treatment costs with vaccination costs, only two scenarios were on the cost-effectiveness frontier (Fig. 6). These scenarios had SIAs every year in the North-west, North-central, and North-east. As the percentage of patients seeking care decreased, more scenarios were on the cost-effectiveness frontier, with 4 and 6 scenarios on the frontier when 50% or 25% of patients seek care (Fig. 6). When only 15% or 5% of patients seek care, the frontier was equivalent to the frontier in Fig. 4 for vaccination costs only.

Improved SIA coverage led to an average decrease in measles cases of 38%, ranging from 21% for national SIAs every three years to 65% for national SIAs every year. This corresponded to an average of 6.0 million fewer cases, ranging from 3.8 million (for SIAs every year in the North-west and North-central and every three years in the North-east and the South), to 7.9 million (for SIAs every two years in Northern regions and every year in the South) over 10 years. The magnitude of the effect of improving SIA coverage varied by scenario dependent on frequency of SIAs, population, baseline coverage, and birth rate in each region. In general, improving SIA coverage had a large effect on scenarios with SIAs every year in the South, and a small effect in scenarios with SIAs every three years in the South. For the current strategy of national SIAs every two years, improved SIA coverage would prevent an additional 6.9 million cases over 10 years (Fig. 4). Though costs to increase coverage are unknown, the impact on cases indicates that improving SIA coverage would be a valuable strategy. As shown by the arrows in Fig. 4, it would be possible to spend up to $82.6 million to improve coverage with the current strategy and still have it be more cost-effective than changing SIA frequency.

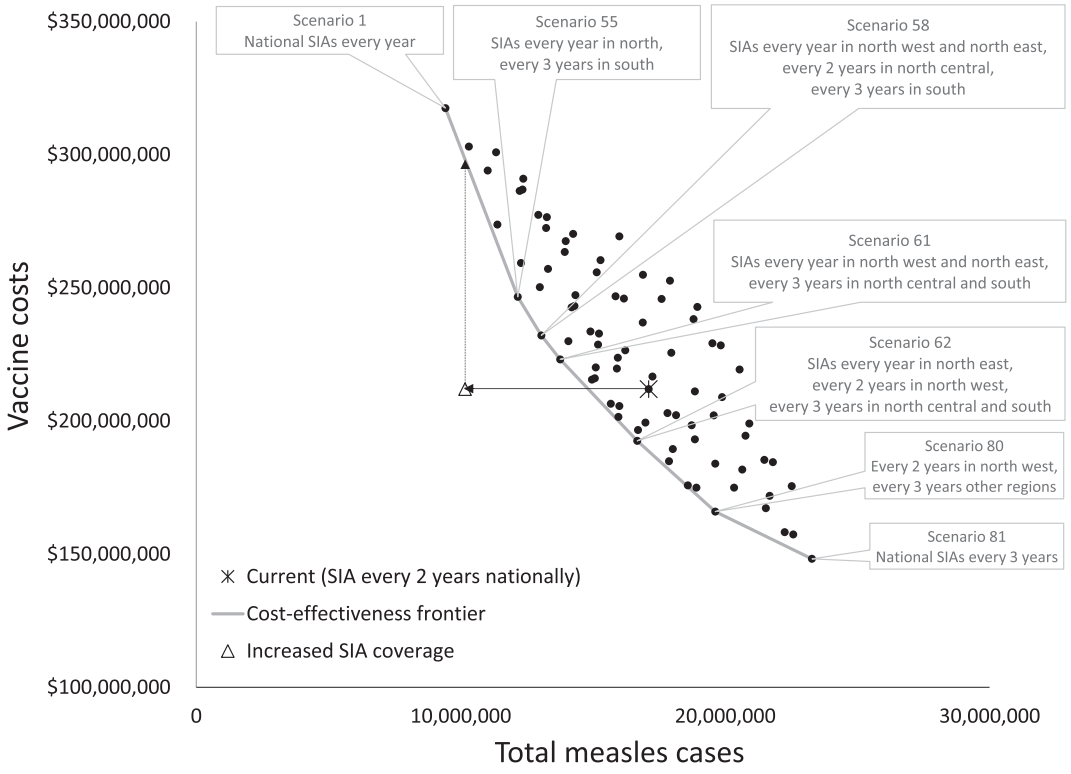

Fig. 4. Scenario results for vaccine costs. Total measles cases and vaccine costs, including all costs for RI and SIAs, for each scenario. Starred point represents the current strategy of SIAs every two years in all regions. Line represents the cost-effectiveness frontier, scenarios which prevent the most cases for equal or lesser cost. For the current strategy of national SIAs every two years, increasing SIA coverage by 25% would decrease the number of cases (solid arrow). Relative to the cost-effectiveness frontier of changing SIA frequencies, increased SIA coverage may provide added value if the cost to do so was less than the difference between the current cost and the frontier (dashed arrow).

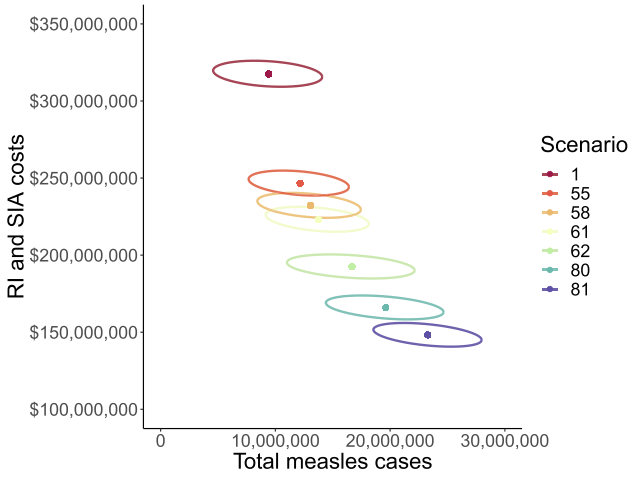

Fig. 5. Cost-effectiveness frontier for vaccine costs. Scenarios on the cost-effectiveness frontier which led to the fewest measles cases at equal of lower vaccine costs. Points represent mean and ellipses represent 95% credible ranges for each scenario on the frontier.

4. Discussion

We found several SIA scenarios that would decrease measles cases for equal or lesser cost than the current strategy in Nigeria. Compared to the current strategy of national campaigns every two years, increasing SIAs in the North-west while decreasing in the North-central and the South would avert measles cases with minimal added vaccination costs, or even cost savings, over 10 years. When taking measles treatment costs into account, annual SIAs throughout the North may be superior to the current strategy depending on the rate of care seeking.

In general, increasing SIA frequency in the North-west and North-east while decreasing frequency in the South tended to provide added value for relatively low cost. This pattern can be attributed to low RI coverage rates and high birth rates in the Northern regions relative to the South. Regions with low RI coverage such as the North-west have a high potential to decrease cases, while regions with higher RI coverage such as the South have a high potential to decrease costs with little impact on measles cases. This insight can be applied for countries other than Nigeria, or for different regions than the regions that we analyzed. Overall, targeting subnational regions rather than national strategies would provide value for money. It is important to note that vaccination efforts are complicated in northern Nigeria due to conflict and political instability, which often occurs in low-coverage regions and makes costs to improve vaccination unclear.

The cost to deliver vaccines varied by state depending on local characteristics, including the level of urbanization, density of population, level of healthcare infrastructure, geographic and security hindrances, and number of administrative units. There are also structural differences between an SIA and the RI program, which led to variance in delivery costs; for example SIA budgets included micro-planning and engaged much higher levels of social mobilization than RI. On the other hand, RI had more infrastructure and overhead cost, as well as higher pay rates for staff. There is also potential bias introduced through our choice not to allocate buildings or overhead costs to the SIA program, although they do in part rely on the RI infrastructure.

Though the costs to improve SIA coverage are not currently known, we found that such a strategy could have a significant impact on measles cases. Limited studies have documented how

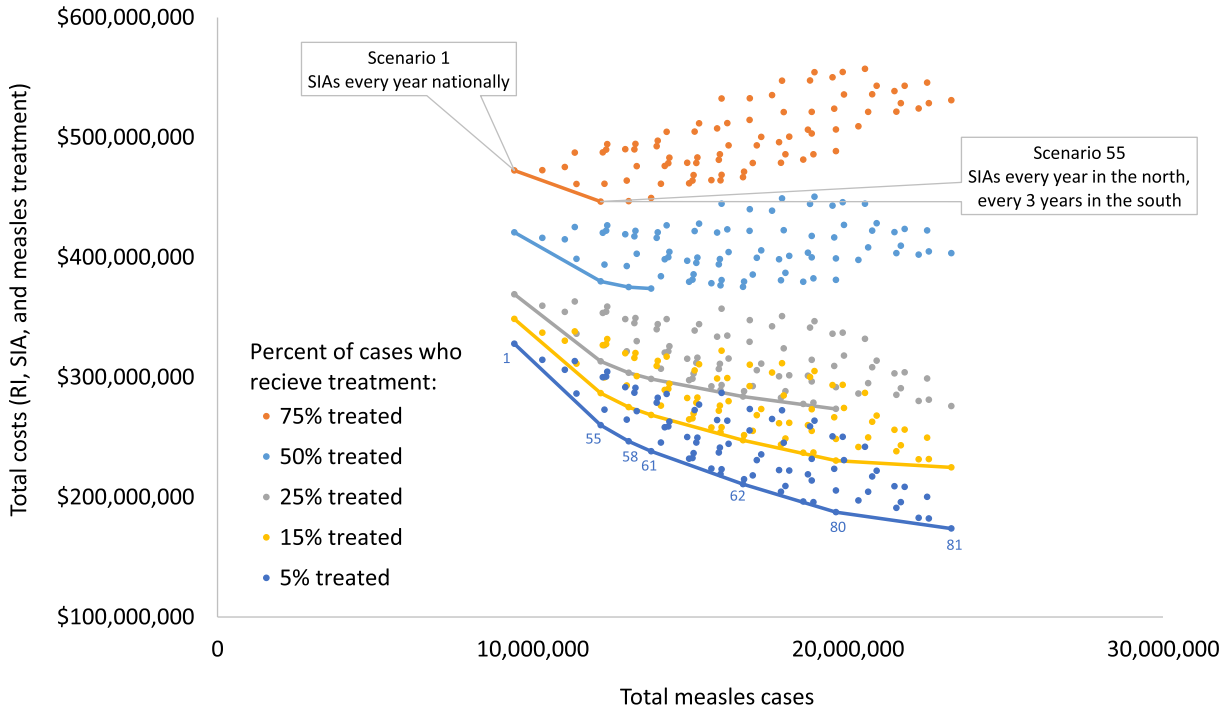

Fig. 6. Scenario results and cost-effectiveness frontiers for total costs with varying percentages of patients seeking care. Total cases and total costs for each scenario with 75%, 50%, 25%, 15%, or 5% of patients seeking care. Scenarios on the cost-effectiveness frontier which led to the fewest measles cases at equal of lower total costs including RI, SIA, and measles treatment.

to increase SIA coverage, but some evidence exists that improving RI coverage requires outreach, social mobilization, and maternal education, so it is likely that any efforts to improve SIA coverage would also be labor-intensive [35]. Improved vaccination communication and outreach would also likely be necessary [36].

This analysis had several limitations. First, data on the cost of treating measles in Nigeria are limited. Values used in this study are reasonable estimates, although the true costs may differ and bias our results for total treatment costs. Second, we have limited the time horizon to 10 years due to the difficulties of extrapolating epidemiological models into the future. This may bias our results by undervaluing the benefit of vaccination when calculating life-years or DALYs averted because not all years of life saved from an averted death would be included in the time horizon. However, this would not influence our estimation of measles cases or costs within the 10 years, which is a reasonable time frame for consideration of intervention or policy changes. Relatedly, we censored all cases and costs at the end of the time horizon, rather than including outcomes for the remaining population at that time point. Third, delivery of SIA doses relies partially on existing health infrastructure, including both logistical and cold chain capacity as well as trained healthcare workers. Therefore increasing SIA coverage would require investment in support systems. Typical SIA budgets represent Federal government contributions and do not incorporate the support from state or local administrative division. Additionally, surveillance data on measles incidence is limited. Finally, there was no explicit correlation between the regions in the disease transmission model.

5. Conclusions

Overall, we found that the current strategy of nationwide SIAs every 2 years in Nigeria is sub-optimal. Increasing SIA frequency in Northern regions (where RI coverage is low and birth rates are high) and decreasing frequency in the South (where RI coverage is higher and birth rates are lower) could significantly reduce measles incidence, and in some cases reduce the total vaccination cost. Additionally, increasing SIA coverage could significantly reduce measles incidence.

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.

Acknowledgements

The authors would like to acknowledge our colleagues at the National Primary Health Development Agency and NCDC (Ministry of Health of Nigeria), World Health Organization Nigeria office, and the World Health Organization Headquarters for collecting and providing the surveillance data for the model development, as well as review and feedback on the manuscript.

Funding

This work was funded by Bill and Melinda Gates through the Global Good Fund, Seattle, WA, USA.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2019.08.050.

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