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Assessing the cost-effectiveness of different measles vaccination strategies for children in the Democratic Republic of Congo

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ABSTRACT

Introduction: One of the goals of the Global Measles and Rubella Strategic Plan is the reduction in global measles mortality, with high measles vaccination coverage as one of its core components. While measles mortality has been reduced more than 79%, the disease remains a major cause of childhood vaccine preventable disease burden globally. Measles immunization requires a two-dose schedule and only countries with strong, stable immunization programs can rely on routine services to deliver the second dose. In the Democratic Republic of Congo (DRC), weak health infrastructure and lack of provision of the second dose of measles vaccine necessitates the use of supplementary immunization activities (SIAs) to administer the second dose.

Methods: We modeled three vaccination strategies using an age-structured SIR (Susceptible-Infectious-Recovered) model to simulate natural measles dynamics along with the effect of immunization. We compared the cost-effectiveness of two different strategies for the second dose of Measles Containing Vaccine (MCV) to one dose of MCV through routine immunization services over a 15-year time period for a hypothetical birth cohort of 3 million children.

Results: Compared to strategy 1 (MCV1 only), strategy 2 (MCV2 by SIA) would prevent a total of 5,808,750 measles cases, 156,836 measles-related deaths and save U.S. $199 million. Compared to strategy 1, strategy 3 (MCV2 by RI) would prevent a total of 13,232,250 measles cases, 166,475 measles-related deaths and save U.S. $408 million.

Discussion: Vaccination recommendations should be tailored to each country, offering a framework where countries can adapt to local epidemiological and economical circumstances in the context of other health priorities. Our results reflect the synergistic effect of two doses of MCV and demonstrate that the most cost-effective approach to measles vaccination in DRC is to incorporate the second dose of MCV in the RI schedule provided that high enough coverage can be achieved.

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1. Introduction

Measles is a highly infectious disease that can lead to severe illness, lifelong complications and death [1]. The disease remains one of the major causes of childhood vaccine preventable diseases globally, despite the fact that an effective and inexpensive vaccine exists. To meet measles mortality and morbidity reduction goals outlined in the Global Measles and Rubella Strategic Plan

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(2012–2020), WHO recommends high vaccination coverage with two doses of measles containing vaccines (MCV) [2]. Since 2000, vaccination has led to a 79% reduction in measles mortality [2]. 2015, there were still an estimated 132,200 measles-related deaths, the majority among children under the age of five [2]. More than 95% of these deaths occur in resource-limited countries with weakened public health infrastructures [2].

In Sub-Saharan Africa, measles remains a major public health problem, with an estimated 28,000 deaths still occurring yearly [3]. Measles deaths generally occur due to complications, with infants and malnourished children at highest risk of death [4]. Measles immunization requires a two-dose schedule due to vaccine efficacy and competing maternal antibodies at younger ages [2]. One dose of measles vaccine at 9 months of age confers only 85% protection and children require 2 doses for the vaccine to be >99% effective [2]. The first dose of MCV should be offered through Routine Immunization (RI) services and only countries with strong, stable immunization programs are able to rely on routine services to deliver the second vaccine dose. Countries unable to achieve high and homogenous vaccine coverage through their routine systems must deliver the second dose in the form of supplementary immunization activities (SIAs) [5]. In these countries, special efforts must be undertaken to ensure that children missed during routine services are immunized, especially in hard-to-reach, poor communities [5].

The Democratic Republic of Congo (DRC) is struggling to recover from a devastating multi-year conflict. Limited roads, electricity and water continue to leave a significant portion of the country inaccessible. Coupled with a lack of human resources, these challenges have led to limited improvements in health infrastructure and difficulty implementing routine immunization services effectively. In 2010, DRC saw a resurgence of measles with large scale outbreaks occurring throughout the country [6]. In 2013, national RI coverage was still estimated at 71.6%, well below the WHO recommended 95% [7,8], and in 2015, WHO/UNICEF estimates of MCV1 coverage was 77% [9], which is the value used in the model analyses.

The country's effort to reduce measles mortality currently consists of 3 strategies; (1) increase routine immunization coverage of MCV1, administered at 9 to 11 months of age, (2) implement SIAs to provide a second opportunity for MCV, and (3) expand epidemiologic surveillance [6,10]. In 2012, DRC's Expanded Program on Immunization (EPI) committed to measles elimination by 2020. This plan proposed a shift in the administration of MCV2 from SIAs to the RI schedule.

Whereas several studies have assessed the cost-effectiveness of measles elimination or eradication, few studies have addressed the cost-effectiveness of differing vaccination strategies. The diversity of both measles epidemiology and health system infrastructure across countries make analyses context specific. A comparison of the costs and benefits of providing the second doses of measles vaccine through RI services and SIAs can guide the selection of the most appropriate measles immunization strategy for DRC.

Vaccination recommendations should be tailored to each country, offering a framework where countries can adapt to local epidemiological and economical circumstances in the context of other health priorities [11]. In DRC, interpretable data on what strategies are needed to effectively and efficiently control measles is critical. We utilized cost specific data from a DRC health care perspective to analyze and compare the costs and benefits of two different strategies for administering two doses of measles-containing vaccine (MCV) to one dose of MCV through routine immunization.

2. Methods

We modeled three vaccination strategies using an age-structured SIR (Susceptible-Infectious-Recovered) model to simulate natural measles dynamics along with the effect of immunization. Strategy 1 (baseline): One dose of measles vaccine delivered through the routine immunization services at 9 months of age at the most recent reported coverage rate.

Strategy 2: One dose of measles vaccine delivered through routine immunization services at 9 months of age with multiple opportunities for immunization through national SIAs up to the age of five years (SIAs doses are independent of the dose received through the routine system).

Strategy 3: Two doses of measles vaccine delivered through routine immunization services at 9 months and 18 months of age.

The population was divided into five age cohorts: 0–9 months, 9–18 months, 18 months-5 years, 5–15 years, and 15+ years. Aging from one cohort to the next happens at a rate inversely proportional to the age width of the cohort, and the birth rate into the first cohort is based on the 2014 estimates for annual births [12]. In addition to the aging from one cohort to the next, individuals are removed from each cohort at a cohort-specific rate so that the overall age structure matches the 2015 UN Population Division estimates.

Upon the transition from the first to the second age cohort, individuals have a chance of being immunized with a first RI dose, with coverage and vaccine efficacy specified. Similarly, upon transition from the second to the third age cohort, children have a chance of being immunized with a second RI dose, with coverage specified by second-dose RI coverage and the vaccine efficacy corresponding to the efficacy in those over 12 months of age. Children in the second and third age cohorts are eligible for SIA vaccination doses, which have the older-child efficacy and are distributed at a specified rate. The SIA coverage rate is the probability of receiving an SIA dose over a 4-year interval.

The system is initialized and allowed to burn-in for 40 years with the scenario-specific immunization rates, so that the population distribution and disease dynamics reach equilibrium. During the burn-in, a steady additional force of infection is applied to avoid disease fade-out. Then the system is simulated for 15 years with dynamics that approximate 2015 dynamics. The number of infections and immunizations over these 15 years are then normalized to get an annual value. The annual incidence across the population as a function of first-dose RI coverage can be seen in Fig. 1.

The equations for propagating the system are as follows:

$$F_{inf}(t_j) = (R_0/\tau_{inf})(\Sigma I_i/(\Sigma(S_i + I_i + R_i)) + \beta_{intro}(t_j < T_{burn} * 365)$$

$$S_1(t_{j+1}) = S_1(t_j) + \Delta t(B/365 - F_{inf}(t_j)S_1(t_j) - a_1 S_1(t_j) - d_1 S_1(t_j))$$

$$I_1(t_{j+1}) = I_1(t_j) + \Delta t(F_{inf}(t_j)S_1(t_j) - I_1(t_j)/\tau_{inf} - a_1(I_1(t_j) - d_1 I_1(t_j))$$

$$R_1(t_{j+1}) = R_1(t_j) + \Delta t(I_1(t_j)/\tau_{inf} - a_1 R_1(t_j) - d_1 R_1(t_j))$$

$$S_2(t_{j+1}) = S_2(t_j) + \Delta t((1 - c_{RI1} k_{eff1})a_1 S_1(t_j) - r_{SIA} k_{eff2} S_2(t_j) - F_{inf}(t_j)S_2(t_j) - a_2 S_2(t_j) - d_2 S_2(t_j))$$

$$I_2(t_{j+1}) = I_2(t_j) + \Delta t(a_1 I_1(t_j) + F_{inf}(t_j)S_2(t_j) - I_2(t_j)/\tau_{inf} - a_2(I_2(t_j) - d_2 I_2(t_j))$$

$$R_2(t_{j+1}) = R_2(t_j) + \Delta t(c_{RI1} k_{eff1} a_1 S_1(t_j) + a_1 R_1(t_j) + r_{SIA} k_{eff2} S_2(t_j) + I_2(t_j)/\tau_{inf} - a_2 R_2(t_j) - d_2 R_2(t_j))$$

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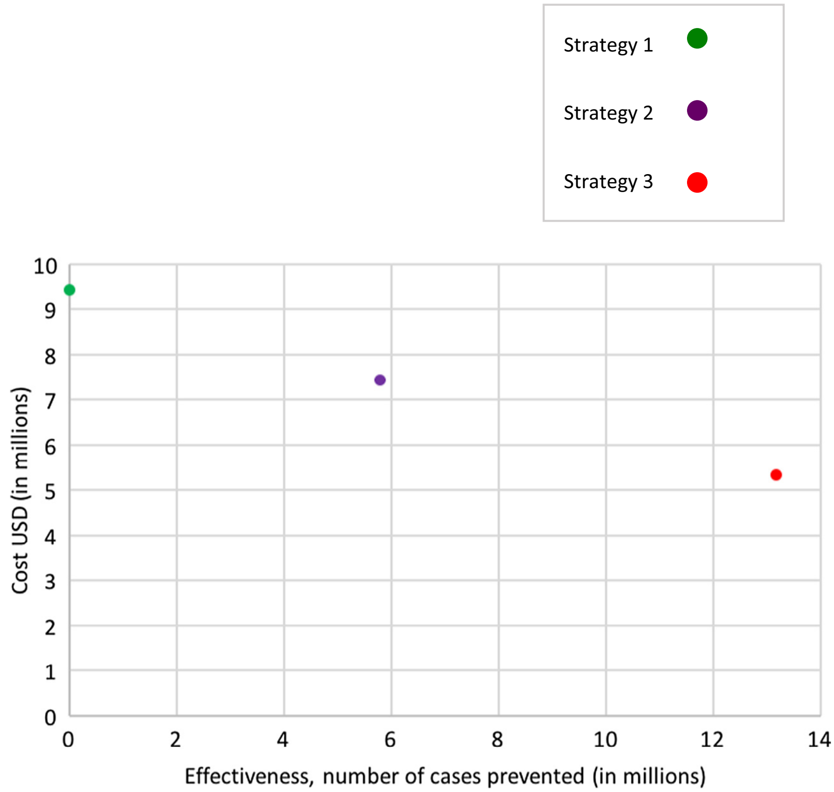

Fig. 1. Cost Effectiveness Analysis for three strategies of measles immunization.

$$S_3(t_{j+1}) = S_3(t_j) + \Delta t((1 - c_{RI2}k_{eff2})a_2S_2(t_j) - r_{SIA}k_{eff2}S_3(t_j) - F_{inf}(t_j)S_3(t_j) - a_3S_3(t_j) - d_3S_3(t_j))$$
$$I_3(t_{j+1}) = I_3(t_j) + \Delta t(a_2I_2(t_j) + F_{inf}(t_j)S_3(t_j) - I_3(t_j)/\tau_{inf} - a_3(I_3(t_j) - d_3I_3(t_j))$$
$$R_3(t_{j+1}) = R_3(t_j) + \Delta t(c_{RI2}k_{eff2}a_2S_2(t_j) + a_2R_2(t_j) + r_{SIA}k_{eff2}S_3(t_j) + I_3(t_j)/\tau_{inf} - a_3R_3(t_j) - d_3R_3(t_j))$$

$$S_4(t_{j+1}) = S_4(t_j) + \Delta t(a_3S_3(t_j) - F_{inf}(t_j)S_4(t_j) - a_4S_4(t_j) - d_4S_4(t_j))$$
$$I_4(t_{j+1}) = I_4(t_j) + \Delta t(a_3I_3(t_j) + F_{inf}(t_j)S_4(t_j) - I_4(t_j)/\tau_{inf} - a_4(I_4(t_j) - d_4I_4(t_j))$$
$$R_4(t_{j+1}) = R_4(t_j) + \Delta t(a_3R_3(t_j) + I_4(t_j)/\tau_{inf} - a_4R_4(t_j) - d_4R_4(t_j))$$

$$S_5(t_{j+1}) = S_5(t_j) + \Delta t(a_4S_4(t_j) - F_{inf}(t_j)S_5(t_j) - a_5S_5(t_j) - d_5S_5(t_j))$$
$$I_5(t_{j+1}) = I_5(t_j) + \Delta t(a_4I_4(t_j) + F_{inf}(t_j)S_5(t_j) - I_5(t_j)/\tau_{inf} - a_5(I_5(t_j) - d_5I_5(t_j))$$
$$R_5(t_{j+1}) = R_5(t_j) + \Delta t(a_4R_4(t_j) + I_5(t_j)/\tau_{inf} - a_5R_5(t_j) - d_5R_5(t_j))$$

In these equations, S_i, I_i, R_i are the Susceptible, Infectious, and Recovered population in age group i. B is the birth rate, a_i is the rate of aging from age group i to i+1, and d_i is the rate of dying while in age group i. F_{inf} is the force of infection, R_0 is the basic reproductive number, and τ_{inf} is the average duration of infection. c_{RI1} and c_{RI2} are the coverage with the first and second RI doses, with k_{eff1} and k_{eff2} the efficacy of MCV at 9 months and at over 12 months. r_{SIA} is the rate at which older children under-5 receive SIA doses, each with efficacy k_{eff2} at that age. Finally, Δt is the time step, and T_{burn} is the burn-in duration during which there is an additional force of infection β_{intro} to initialize the population immunity and prevent disease fade-out. All model parameter values can be found in Table 1 and all costs are presented in Table 2. Note that the 2-dose efficacy with one dose at 9 months of age and one dose at over 12 months old will be $1 - (1 - k_{eff1})(1 - k_{eff2})$, which at the values in Table 1 will be >99%.

2.1. Annual birth cohort

We used DRC's estimated annual birth cohort of 3,284,139 in our decision analysis [12].

2.2. Vaccine coverage

WHO/UNICEF estimates MCV1 coverage at 77% in 2015 [9], which we used as the value of MCV1 coverage in all three strategies. We assumed MCV2 RI coverage to be 77% as well for Strategy 3. Reported SIA coverage is variable across health zones, thus we assumed SIA coverage to be 80% in Strategy 2 based on published and unpublished MoH data [13].

2.3. Vaccine efficacy

Measles vaccine efficacy is expected to be 85% at 9–11 months of age and increases to 95% when administered at ≥ 12 months, therefore a percentage of children will always remain susceptible even after vaccination [14–17].

2.4. Wastage factor

The wastage factor represents the proportion of vaccine not used in a program. SIAs generally have a smaller wastage factor than RI. In DRC, the SIA wastage factor was estimated to be 1.15 for SIAs and 3.43 (based on data from other countries) for RI [18].

Table 1
Variables included in the decision analysis with sources.

Variable	Value	Source
Annual birth cohort	3,000,000	[1]
Vaccine Coverage		
Routine		
MCV1	77%	[2]
MCV2	77%	Assumption
SIAs	80.0%	Assumption
Vaccine Efficacy		
MCV1 at 9–11 months	85%	[3,4]
MCV1 at $\geq$ 12 months	95%	[3,4]
MCV2 at $\geq$ 12 months	98%	[3,4]
Wastage Factor		
RI	3.42	[5]
SIAs	1.15	[6,7]
Adverse events	5%	[8]
Measles attack rate	21.87 per 1000	[9]
Proportion of cases seeking care[*]	40%	[10]
Hospitalization Rate	10%	Assumption
Duration of hospital stay	4 days	Assumption
Number of Hospital visits	1	Assumption
Case-Fatality ratio	2.7%	[9]

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[*] Fever, malaria, diarrhea, and respiratory illness reporting rates are were estimated at 40%, assumptions are based on surveys of key organizations and health care personnel interviewed throughout DRC.

Table 2
Vaccination program costs by routine immunization and Supplementary immunization activities.

Variables	Cost per Dose	Source
Routine Immunization		
Vaccine w/freight	. 31	[1,2]
Injection Equipment[a]	0.17	[1,3]
Cold Chain	0.57	[4]
Transportation	0.11	[5]
Personnel	0.04	[5]
Stationary	0.02	[6]
Total costs RI	*1.21*	
Supplementary Immunization Activities		
Transportation	0.13	[6]
Cold Chain[b]	0.02	[7]
Personnel	0.20	[1]
Social Mobilization		
Supplies	0.02	[6]
Personnel	0.03	[6]
Planning/Training	0.07	[6]
Supervision	0.04	[6]
Total Additional Costs (SIAs)	*0.51*	
Total costs[c]	**1.72**	

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[a] Injection equipment includes syringes, biosafety boxes, and measles vaccine diluent.
[b] Cold chain costs for additional support were assumed to be 0.5 the cost of the RI program.
[c] Total costs include routine immunization, additional costs of SIAs through routine system, excluding wastage.

2.5. Adverse events post-vaccination

Minor adverse events post vaccination occur in 5–15% of individuals [19]. We assumed that only 5% of those vaccinated would suffer an adverse event requiring a health center visit. This was determined based on literature in other countries [18].

2.6. Adjusted estimated measles incidence

In 2013, national incidence was estimated at 14.88 per 1000 persons. We calculated an adjusted incidence for children aged 6 to 59 months. To correct the denominator (susceptible population), we multiplied the population of children aged 6 to 59 months by the vaccine coverage (71.6%) and expected vaccine efficacy (95%) [13]. Our adjusted attack rate was 21.87 per 1000 persons.

2.7. Medical care

The DRC-DHS 2013 estimated that 40% of mothers would seek medical care for children sick with diarrhea, fever, or a respiratory illness [20]. Based on this information we assumed that the proportion seeking medical care for measles was similar due to shared symptoms.

2.8. Case-fatality rate

We assumed the case-fatality rate to be 2.6%. This was based on assessments during measles outbreaks between 2010 and 2013 [21].

2.9. Costs

Cost determinants were identified through unpublished data from the DRC-EPI microplans, reviews of the literature, and interviews with key stakeholders and local health workers.

2.10. Vaccine costs

Costs of RI and SIAs were estimated using an *ingredients* approach by assigning a value to each dose of MCV administered through either routine services or an SIA [22]. Costs associated with RI were incorporated into each of the 3 strategies. Injection equipment included the cost of auto-disable syringes and safety boxes. Cold chain costs include vaccine carriers, cold boxes, ice packs, refrigerator parts and fuel. Transportation represented the distribution of vaccines, repair of vehicles, and other logistical considerations between the district, health zone, and health centers. Personnel included health workers and other vaccinators, while stationary represented the use of printing supplies for vaccination documentation.

For vaccine administered through an SIA, additional costs were included to complement the routine immunization program. Social mobilization was divided into personnel (mobilizers) and supplies, which included printed materials, megaphones, and radio announcements. Supervision, planning and training included the use of workshops, meetings, training of staff, and printing of vaccination tools. Finally, we included additional costs for transportation and personnel for vaccine administered through SIAs using 2013 EPI budgets as SIAs target hard-to-reach populations generally missed by routine services.

2.11. Disease costs

Information on average costs of hospitalization and medical care for measles cases was collected using interviews with local health care workers. Mild cases of measles were estimated at $30 and cases with complications were estimated at $110. Severe cases requiring an average 4-day hospital stay were estimated at $290 including hospitalization and medication costs.

3. Results

3.1. Cost-Effectiveness

Strategy 3 was the most cost-effective scenario and dominated strategy 1 and 2 (Fig. 1). Over 15 years, strategy 1 would result in 19,398,000 measles cases, 775,920 hospitalizations and 523,746 deaths (Table 3a). Compared to strategy 1, strategy 2 would prevent a total of 5,808,750 measles cases, 232,350 hospitalizations, and 156,836 deaths (Table 3b). Compared to strategy 1, strategy 3 would prevent a total of 13,232,250 measles cases, 529,290 hospitalizations, and 357,271 deaths. We also calculated Incremental cost-effectiveness ratio (ICER), defined as the cost per death averted. Strategy 3 had the lowest ICER at 1144 compared to strategy 2 ICER of 1275.

A single dose vaccination program (strategy 1) would cost a total of $942.31 million: $143.12 million in vaccination costs and $799.20 million in disease expenses. A vaccination program using strategy 3 would result in $279.42 million in vaccination costs and $254.03 million in disease expenses, resulting in a 15-year decrease of $408.87 million compared to strategy 1. A vaccination program using strategy 2 would result in a total of $182.53 million in vaccination costs and $559.88 million in disease expenses, resulting in $199.91 million decrease over 15 years compared to strategy 1. Comparing strategy 2 and strategy 3, strategy 3 would result in a total savings of $208.96 million, 7.42 million cases of measles and 200,435 deaths over a 15-year period. Therefore, strategy 3 dominated both other strategies, yielding the fewest deaths at the lowest total program costs.

3.2. Sensitivity analysis

3.2.1. MCV1 Coverage

We performed a Sensitivity analysis for resulting measles incidence as a function of RI coverage in Strategy 1, 2, and 3 (Fig. 2). In all strategies, effectiveness increased with higher rates of MCV1 coverage. Even with 100% MCV1 coverage, strategy 1 would

Table 3
Results of the cost-effectiveness analysis comparing strategies 1–3 over 15 years, Democratic Republic of Congo.

a. Summary of costs associated with three vaccination strategies[1,2]

	Strategy 1	Strategy 2	Strategy 3
No. Of Cases	19,398,000	13,589,250	6,165,750
No. Of Deaths	523,746	366,910	166,475
Hospitalizations	775,920	543,570	246,630
Avg. Hospitalization Days	3,103,680	2,174,280	986,520
Avg. number of adverse events	969,900	679,463	308,288
Disease Costs (US$)			
Hospitalization	225,016,800	7157,635,300	71,522,700
General Medication	574,180,800	402,241,800	182,506,200
Total Disease Costs	*799,197,600*	*559,877,100*	*254,028,900*
Vaccination Costs (US$)			
Vaccine	35,483,522	47,547,482	69,276,911
Injection Equipment	20,107,329	26,943,573	39,256,916
Cold Chain	67,418,691	68,222,955	131,626,130
Transport	13,010,625	18,238,341	25,401,534
Personnel	4,731,136	12,773,776	9,236,921
Stationary	2,365,568	2,365,568	4,618,461
SIA social mobilization	0	2,010,660	0
SIA supervision	0	1,608,528	0
SIA planning/training	0	2,814,924	0
Total Vaccination Costs	*143,116,870*	*182,525,806*	*279,416,872*
Total Costs	$942,314,470	$742,402,906	$533,445,772

b. Summary of the cost-effectiveness analysis comparing strategies 2 and 3 to strategy 1

Strategy	Total Costs Over 15 Years (US$)				Effectiveness				Incremental cost-effectiveness ratio ($ per death averted)
	Disease Costs	Vaccination Costs	Total Costs (Disease + Vaccination)	Additional costs	Measles Cases	Cases averted	Measles Deaths	Deaths averted	
1	799,197,600	143,116,870	942,314,470	–	19,398,000	–	523,746	–	–
2	559,877,100	182,525,806	742,402,906	−199,911,564	13,589,250	5,808,750	366,910	156,836	1275
3	254,028,900	279,416,872	533,445,772	−408,868,698	6,165,750	13,232,250	166,475	357,271	1144

[1] Strategy 1: one dose at 9 to 11 months old, Strategy 2: MCV1 through RI services, MCV2 through SIA, Strategy 3: two doses.
[2] All costs were rounded to the nearest dollar.

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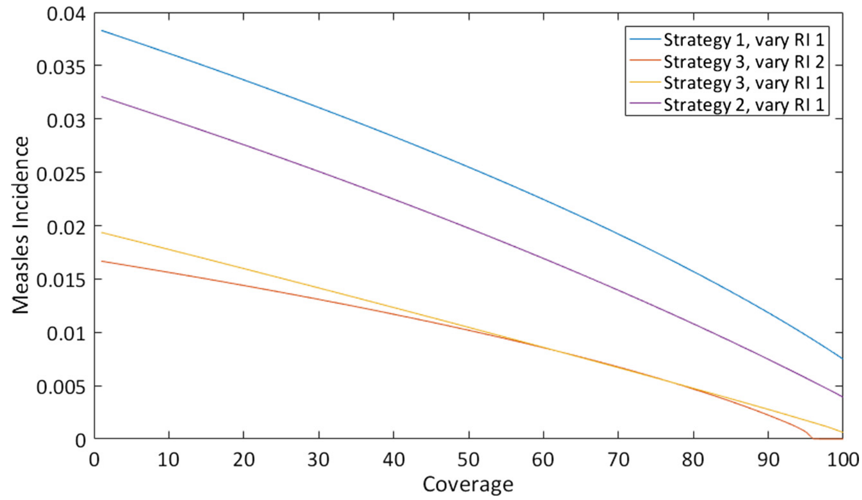

Fig. 2. Sensitivity analysis for resulting measles incidence as a function of RI coverage in Strategy 1, 2, and 3. [1]Strategy 1 (1 dose of RI only), the RI first-dose coverage is varied; strategy 3 (1 dose of RI at a coverage of 0.77, and a second dose of RI at a coverage of 0.77), the coverage of RI first dose and RI second dose are varied from 0 to 1, with the other held constant at 0.77; single SIA in a four-year interval on top of a single dose of RI (Strategy 2), the RI first dose coverage is varied from 0 to 1.

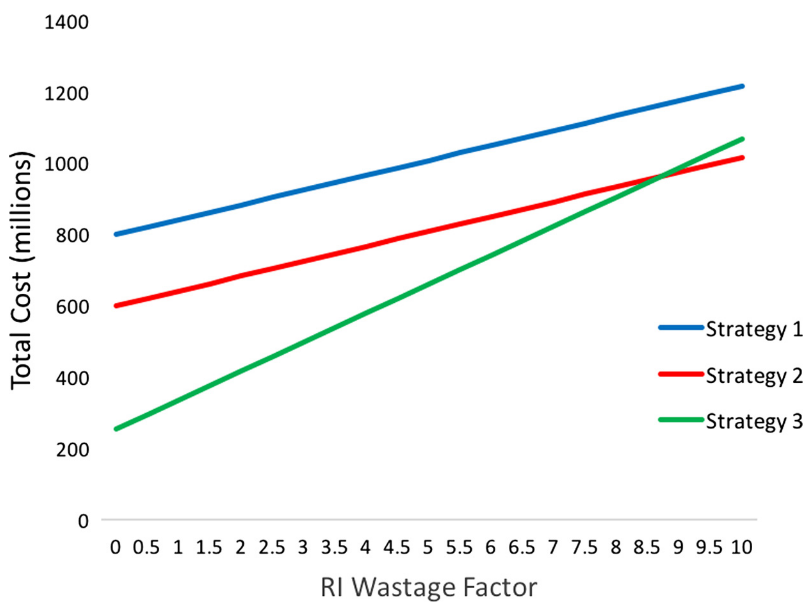

Fig. 3a. Sensitivity Analyses varying the routine immunization wastage factor by vaccination strategy.

be unable to provide the measles control that strategy 2 or 3 could achieve with lower MCV1 coverage. This is a result of the lower efficacy of the MCV1 dose at 9-months; even 100% coverage with an 85% effective vaccine is insufficient to counter the transmission potential of measles. Thus, receiving two doses of MCV would be necessary to achieve the optimal level of measles control.

3.2.2. Wastage factor

We varied the RI wastage factor from no wastage (1.0) to extreme wastage (10.0) (Fig. 3a). As the wastage factor increased, the total vaccination costs increased for all strategies. Strategy 3 was generally lower in costs, except when the RI wastage factor was extremely high (>8.0).

3.2.3. Cold chain

We measured the impact of varying cold chain costs on all vaccination strategies (Fig. 3b). Even with high cold chain costs, strategy 3 remained the most cost-effective option.

4. Discussion

Our results reflect the synergistic effect of two doses of MCV and demonstrate that the most cost-effective approach to measles vaccination in DRC is to incorporate the second dose of MCV into the routine immunization program, provided that high enough coverage can be achieved through routine immunization.

Vaccination with a single dose of MCV has resulted in substantial reductions in disease incidence and mortality from the pre-vaccination era; however, countries using a single dose of MCV are still unable to achieve true herd immunity even with high levels of vaccine coverage. While past studies have yielded high benefit-cost ratios from a single MCV dose, our simulations indicated that the number of projected measles cases and deaths were lower with a second dose of MCV by either routine or SIA services when compared to one dose of MCV [18,23,24]. The accumulation of susceptibles in areas of low vaccine coverage coupled with a 15% vaccine failure rate of one dose at 9 months of age, compared to

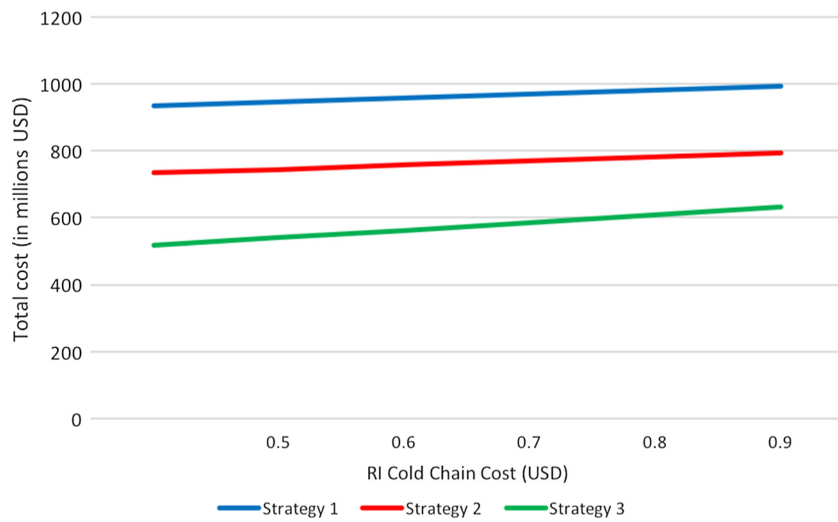

Fig. 3b. Sensitivity analyses varying the routine immunization cold chain cost by vaccination strategy.

just a 1% vaccine failure rate with two doses, has resulted in outbreaks worldwide [14]. These outbreaks underscore the importance of a two-dose vaccination program, particularly in DRC, where vaccine coverage remains low**.**

In terms of projected advantages, cost savings and/or improved health outcomes, strategy 3 outweighs the projected advantages of strategy 2 [25]. While strategy 3 would result in an estimated $96.8 million more in vaccination costs than strategy 2, strategy 3 would prevent 7,423,500 measles cases and 200,435 deaths.

In DRC, routine immunization remains sub-optimal and estimated RI coverage is low [7,26]. A 2013 serosurvey conducted among children aged 6–59 months indicated that only 66% were seropositive for measles antibodies [unpublished data]. Our results clearly illustrate the absolute importance of coverage, and if RI coverage does not increase sufficiently or if RI leaves large sub-national under-immunized pockets, then measles transmission will continue. Presently, the role of SIAs is essential to increase coverage when RI has not attained high-enough levels. However, in the long-term, a transition to two doses through RI delivered at sufficiently high coverage will be both more cost-effective and more effective overall at reducing measles incidence.

Our assumption of RI (77%) and SIA (80%) coverage may represent overestimates. Sensitivity analyses with the addition of more frequent SIA (two in a four year timeframe) still indicated that demonstrated that strategy 3 would prevent more measles cases compared to strategy 2, However, WHO recommends that countries with weak routine immunization systems implement targeted SIAs every 3 years to ensure high coverage among new birth cohorts [8]. This strategy should be adopted until RI coverage exceeds 80% in each heath zone [27,28].

We assumed that SIA vaccine coverage was slightly higher than RI coverage and offered one opportunity for additional vaccination during a four-year timeframe. During SIAs, children of different age ranges, who may not have access to regular health services, are targeted regardless of their previous vaccination history. These should be implemented every 2–4 years to prevent the build-up of susceptibles [28]. The Pan American Health Organization (PAHO) has successfully implemented SIAs since the 1990 s, which significantly contributed to the elimination of endemic measles in most Latin American countries [29]. The use of SIAs in sub-Saharan African countries has significantly contributed reductions in measles cases and deaths in that region [3,30,31]. Moreover, SIAs often incorporate the delivery of other health interventions including vitamin A supplementation, the distribution of deworming medicines, other vaccines, and insecticide-treated bed nets (ITNs) [32]. SIAs provide an opportunity to increase community awareness of good health practices and strengthen and build capacity within RI programs through improvements in the cold chain, logistics, and local partnerships with stakeholders [33].

Vaccination program costs include a number of variables, some of which represent more substantial expenses. While one dose of measles vaccine costs only $0.30, additional vaccine must be available and wastage must be accounted for. We estimated the wastage factor to be 1.15 for SIAs and 3.43 for RI services. While vaccination only costs were high with strategy 3, it still performed better in terms or case prevention compared to strategy 2. In countries planning to incorporate the second dose into the routine system, targeting a reduction in RI waste can result in substantial cost reductions.

A review of the literature suggests a wide range of cold chain costs, thus for the purpose of our analyses, we assumed the cost in DRC to be $0.57 per dose of vaccine, with an additional $0.02 per dose during an SIA [34,35]. Other countries have estimated cold chain costs to be substantially lower; therefore, our assumption may represent an overestimate. Nevertheless, limited resources in DRC lead to higher costs for most health activities [36]. Our sensitivity analysis demonstrated that reducing cold chain costs could lead to substantial reductions in overall vaccination program costs, especially in strategy 3.

Our analyses are subject to a number of limitations. While our simulations were based on DRC specific costs and probabilities, our data represents a national average. Accurate information on cold chain costs specific to DRC was not available. We included additional costs for transportation and personnel for vaccine administered through SIAs using 2013 EPI budgets, however accessibility across health zones varies and there may be increased costs associated with travel to more remote areas that we were unable to account for. Disease costs were obtained through interviews with local health workers, but the large heterogeneity seen across provinces, health zones, and villages cannot be accounted for in our model. We estimated that 40% of measles cases seek some form of treatment; however, the availability of medications and health services in rural areas is often insufficient and may be overestimated [7]. We were unable to include all costs associated with measles complications including costs associated with pain and suffering, loss of productivity, time off taken by caregivers, and rare and severe complications such as encephalitis or sub-acute sclerosing panencephalitis, which would have increased the overall disease costs and increased the cost-effectiveness of strategy 2. Moreover, there are a number of additional costs that may be difficult to quantify and include in our analyses. For example, the cost of social mobilization was included in the RI strategies. Additionally, implementation of a vaccination campaign could detract attention and resources from other health programs, leading to inaccurate disease costs.

Since the dependence of MCV1 and MCV2 is unknown and there is no specific country-level data to determine the probability of an individual receiving a second dose of vaccine, our model assumes independence of vaccine doses [37]. Additionally, the effect of vaccination on the epidemiology is difficult to model accurately and while we assumed a dynamic population, we were unable to perfectly account for the change in age structure across the 15-year period of analysis, resulting in possible overestimates in the reduction of measles cases and deaths [18]. The higher attack and death rates we utilized throughout the 15-year time period may have resulted in overestimates of measles cases and deaths in each strategy.

Administration of a second dose via RI appears to be the most cost effective strategy in DRC, provided RI coverage rates are high. SIAs provide children unable to access routine immunization services, the opportunity to obtain the vaccine, especially in hard-to-reach areas, and continuing support SIAs will be important until the RI program can effectively administer two doses with high coverage. Thus, preferences around these two approaches are a function of more than just costs and policymaker preference, and will also be influenced by practical limitations such as short-term affordability and resource constraints.

Targeted efforts focused on reaching previously unvaccinated children are needed to ensure high coverage in RI services and through SIAs.

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Conflict of interest

The authors do not have a commercial or other association that might pose a conflict of interest.

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