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Cost-effectiveness of three different vaccination strategies against measles in Zambian children

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Abstract

The vaccination program in Zambia includes one dose of measles vaccine at 9 months of age. The objective of this study was to compare the cost-effectiveness of the current one-dose measles vaccination program with an immunization schedule in which a second dose is provided either through routine health services or through supplemental immunization activities (SIAs). We simulated the expected cost and impact of the vaccination strategies for an annual cohort of 400,000 children, assuming 80% vaccination coverage in both routine and SIAs and an analytic horizon of 15 years. A vaccination program which includes SIAs reaching children not previously vaccinated would prevent on additional 29,242 measles cases and 1462 deaths for each vaccinated birth cohort when compared with a one-dose program. Given the parameters established for this analysis, such a program would be cost-saving and the most cost-effective vaccination strategy for Zambia.

Keywords: Measles; Cost; Analysis

1. Background

Measles is one of the major causes of childhood vaccine-preventable disease in the world. Despite the progress made in its control after the introduction of measles vaccine, it is estimated that over 30 million measles cases and 777,000 deaths occur each year [1]. Of deaths attributable to measles, 98% occur in developing countries [2]. In addition to administration of measles vaccine at 9 months of age, the World Health Organization has recently recommended the provision of a second opportunity for measles immunization for all children through routine or supplemental immunization activities (SIAs) [3].

Zambia is a sub-Saharan African country with an estimated population of 9.5 million in 2000 [4]. Measles is one of the five major causes of childhood illness in Zambia [5]; in 2000, 30,930 cases were reported although underreporting exists. The current measles immunization schedule in Zambia consists of one dose of measles vaccine administered at 9 months of age through routine health services. Since 1999, a second opportunity for vaccination has been offered in some areas of the country through SIAs targeting children aged 9 months–4 years. In November 2002, 729,000 children aged 6 months–15 years were vaccinated in Southern Province as part of an emergency drought-relief effort [6].

This study compares, from the Zambian health-care system perspective, the costs and benefits of providing a single dose of measles vaccine to the costs and benefits of providing two opportunities for measles immunization. Since resources available for public health are scarce, analyses of cost-effectiveness may help guide the selection of measles vaccination strategies.

2. Methods

2.1. Design

A decision analysis model based on published and unpublished data was used to compare the economic impact of three vaccination strategies against measles in Zambia. The strategies considered are as follows:

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- *Strategy* 1: One dose of measles vaccine delivered through the routine health-care system at 9 months of age.
- *Strategy* 2: One dose of measles vaccine delivered through the routine health-care system at 9 months of age and a second opportunity for immunization through SIAs. Children who did not receive a dose through the routine health services have an equal chance of being vaccinated in the SIAs as children already vaccinated in the routine program (i.e. the SIAs dose is independent of the dose received through the routine system).
- *Strategy* 3: Two doses of measles vaccine delivered through the routine health-care system at 9 months and 18 months of age. Only children who have received a dose at 9 months are assumed to receive the second dose at 18 months of age.

A simplified version of the decision tree focusing on vaccination coverage and vaccine efficacy is shown in Fig. 1. The probability of contracting measles is directly related to susceptibility and the disease attack rate in the population. Susceptibility to measles is determined by vaccination coverage and vaccine efficacy. Because vaccine efficacy is less than 100%, some vaccinated children remain susceptible to infection and have a risk of contracting measles. Measles cases may be hospitalized and/or die. Additionally, vaccination may be associated with adverse events that may require medical care.

2.2. Program variables

The program variables used in our analysis were collected from published and unpublished sources and are summarized in Table 1.

2.2.1. Annual birth cohort

The population of children to be vaccinated was considered to be 1 year's birth cohort, or 400,000 [4].

2.2.2. Vaccination coverage

Since reported national one-dose vaccination coverage for the period 1995–2000 ranged from 93% in 1996 to 69% in 1997 [7], we assumed a vaccination coverage of 80% in all strategies (routine and SIAs).

2.2.3. Vaccine efficacy

Based on the age-specific incidence of measles and age-specific seroconversion rates to measles vaccine in developing countries, vaccination at age 9 months was predicted to elicit seroconversion in 85% of children [8]. Since measles vaccine results in a protective antibody response in 95% or more of susceptible vaccinees aged 12 months or older [9–12] and a high proportion of vaccinated persons lacking detectable antibody to measles will respond to the second dose [13–15], a vaccine efficacy of 95% was assumed for the second dose.

Table 1
Program variables included

Variable used	Value	Reference
Annual birth cohort	400,000	[4]
Vaccination coverage		
1st dose (routine)	80%	[7]
2nd dose (routine/SIAs)	80%	[7]
Vaccine efficacy		
One dose at 9 months of age	85%	[8]
One dose after 12 months of age	95%	[9–12]
Wastage multiplier		
Routine health services	3.42	[16]
SIAs	1.1	[5]
Adverse events in susceptible children	5%	[17–19]
Number of visits per child with adverse event	1	Assumption
Overall measles incidence rate		
≤5 years old	6.7/1000	Ministry of Health, Zambia, 1999, unpublished data
>5 years old	1.1/1000	Ministry of Health, Zambia, 1999, unpublished data
Measles attack rates among susceptible children		
≤5 years old	21/1000	[7,8]
>5 years old	3.5/1000	[7,8]
Reporting rate	40%	CBoH/CDC, Field Study, Zambia, August 2000, unpublished data
Proportion of measles case-patients seeking medical care	75%	[18]
Hospitalization rate	80%	[18]
Number of visits per ambulatory patient	1	Assumption
Duration of hospitalization (days)	4	CBoH/CDC, Field Study, Zambia, August 2000, unpublished data
Case–fatality ratio	5%	CBoH/CDC, Field Study, Zambia, August 2000, unpublished data

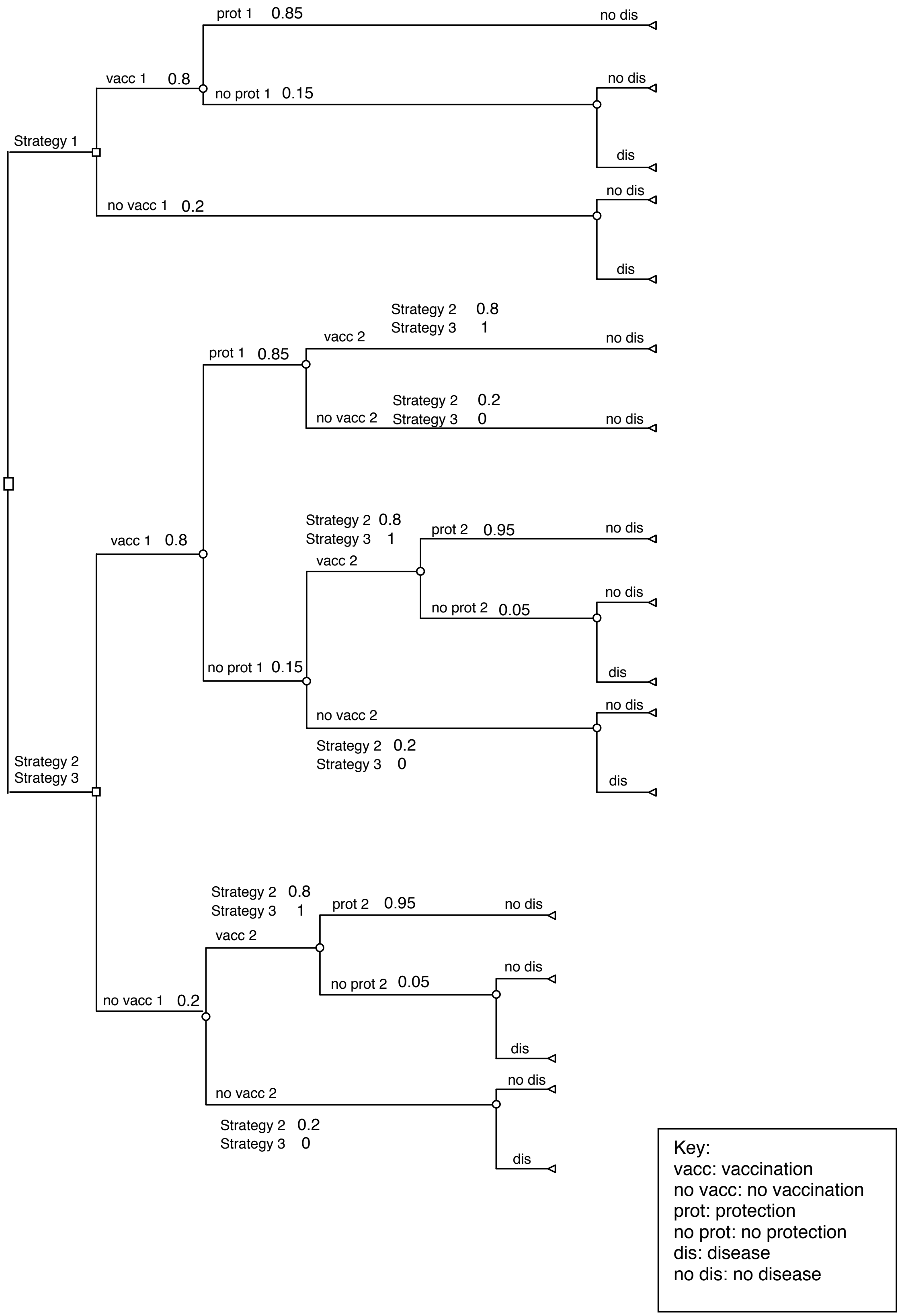

Fig. 1. Decision tree used to determine number of measles cases and deaths for strategies 1–3.

2.2.4. Wastage factor

The wastage multiplier estimates the proportion of vaccine wasted in a program. In SIAs the wastage factor is often less than that in routine health services. Based on experience in Zambia we used a wastage factor of 3.42 for the routine program [16] and 1.1 for SIAs [5].

2.2.5. Adverse events following vaccination

Fever and rash may occur 7–12 days after vaccination. Occurrence of fever is described in 5–15% and rash in 5% of individuals receiving vaccine [17]. In Zambia, the proportion of children having an adverse reaction to measles vaccination was estimated to be 9.1% [18]. Since not all adverse events following measles vaccination will result in visits to health-care facilities, we assumed that only 5% of vaccinees would have an adverse event requiring an outpatient visit. Since most of these adverse events will not occur in immune children receiving measles vaccine [19], we used the same rate (i.e. 5%) only for those remaining susceptible after the first dose who received a second dose.

2.2.6. Measles attack rate

The attack rate of measles was estimated from the annual incidence reported by the Ministry of Health of Zambia. According to this information, in 1999 the overall measles incidence rate was 6.7/1000 in children ≤5 years old and 1.1/1000 in the population aged >5 years [20]. Since these overall incidence rates are calculated dividing the number of cases by the total population in each age group, we adjusted the denominator to obtain the attack rate in the susceptible population. An average of 80% vaccination coverage [7] and a vaccine efficacy of 85% [8] were used to estimate the proportion of the population susceptible to measles. Therefore, attack rates of 21/1000 and 3.5/1000 were used to calculate the number of cases among susceptible persons under, and over 5 years of age, respectively. An estimate of the reporting efficiency (percentage of all measles cases notified to the Central Board of Health) of measles cases was used to adjust the reported incidence rates. A 40% reporting efficiency was assumed based on unpublished data from a field study carried out by the Zambian Central Board of Health (CBoH) and the US Centers for Disease Control and Prevention (CDC) in 2000.

2.2.7. Medical care/hospitalization

Based on a survey carried out among caretakers in Zambia, we assumed that medical care would be sought for 75% of measles cases and that 80% of patients seeking care would be hospitalized [18]. One outpatient visit was assumed for each measles case. The duration of hospitalization was estimated to be 4 days, based on unpublished data from a field study carried out by the CBoH and CDC in 2000. The total cost per hospital admission was calculated as the product of the estimated average duration of stay and the average cost per day.

2.2.8. Mortality of measles

For the purpose of our study we did not assign a monetary value to death because of difficulty in measuring its cost. However, we calculated the number of deaths for the different strategies. We used a case–fatality ratio of 5% to estimate the number of deaths based on unpublished data of hospitalized patients obtained from a field study conducted by CBoH and CDC in three regions of Zambia in 2000.

2.3. Costs

All costs used in our analysis are summarized in Table 2. Vaccination and disease-related costs were estimated in 2000 US dollars (US$). Because of the complex nature of valuing the costs of pain and suffering these were not included.

2.3.1. Vaccination costs

Vaccination costs were estimated by assigning a value to each dose of measles vaccine given based on the allocations for SIAs in Zambia in 2000 [21]. Although in Zambia in 2000 reusable injection equipment was common, in order to avoid underestimating program costs, bundled vaccine costs were based on the utilization of autodisable syringes and safety boxes both for vaccines administered through the routine health-care system and SIAs. Costs related to cold chain (e.g. vaccine carriers, cold boxes and refrigerator spare parts), transportation (e.g. distribution of vaccines and other logistics from central/district levels and costs of repairing vehicles), personnel (e.g. health workers and vaccinators) and stationery (e.g. photocopies, toner, diskettes) were incorporated into calculations of costs for all strategies.

Table 2
Cost variables

Variable	Costs per dose (costs in 2000) (US$)
Vaccination costs[a]	
Vaccine	0.15
Injection equipment	0.127
Cold chain	0.029
Transportation	0.024
Personnel	0.078
Stationery	0.002
Total routine vaccination costs	0.41
Social mobilization (SIAs)	0.073
Supervision (SIAs)	0.005
Planning/training (SIAs)	0.024
Administrative costs (SIAs)	0.005
Additional transportation (SIAs)	0.004
Additional personnel (SIAs)	0.014
Total vaccination costs (SIAs)	0.521
Direct costs of illness[b]	
Ambulatory visits and medication	1.5 per visit
Hospitalization	6 per day

US$ 1 = 3200 Zambian Kwacha in 2000.
[a] [21].
[b] Personal communication CBoH staff.

For vaccine doses administered through SIAs, some additional costs such as those for social mobilization (e.g. printed materials and radio announcements), supervision, planning and training (e.g. workshops/meetings, training of district staff and printing of field and vaccinator guides) and administration were included. Because SIAs may require greater expenditures for transportation/personnel to vaccinate hard-to-reach children, additional transportation costs to cover these expenditures were incorporated into strategy 2 [21].

2.3.2. Disease costs

The direct costs of outpatient medical care (i.e. professional services and medication) and hospitalization (i.e. professional services, medication and hospitalization costs) were based on the average costs to patients for medical services in Zambia. Information for calculation of these costs was based on personal communications from staff of the CBoH.

2.4. Analysis

The analysis was performed from the health-care system perspective. The primary outcome measure was the cost per averted case of measles; however, the costs per averted death were also calculated. Univariate sensitivity analysis was carried out to test the reliability of the model and the robustness of the results. Since coverage was one of the most important factors affecting both cost and program effectiveness and wastage was a major variable influencing cost of vaccination through routine services versus vaccination through SIAs, we conducted sensitivity analyses for these two variables. The effect of varying the total vaccination costs was also tested in our sensitivity analysis. Because disease incidence is an important factor affecting the costs related to the disease, we performed sensitivity analysis on the reporting efficiency rates. Because the proportion of previously unvaccinated children receiving a second opportunity for measles immunization is unknown in Zambia, we performed a sensitivity analysis on the percentage of children reached with the second opportunity. To further examine the robustness of the results we also performed sensitivity analysis on patient treatment costs for ambulatory visits and hospitalization. The analytical horizon for this analysis is 15 years, since the vast majority of cases occur under that age [22]. In order to estimate costs related to disease in the future, we used an annual discount rate of 3%.

3. Results

3.1. Base-case

In strategy 1, each annual birth cohort of 400,000 children would experience 38,476 measles cases and 1924 deaths between the ages 2 and 15 (Table 3). Measles disease would result in US$ 541,478 in medical costs. The cost of this vaccination program would be US$ 271,360.

Table 3
Summary of program strategy outcomes and costs of strategies 1–3[a]

	Strategy 1	Strategy 2	Strategy 3
Number of cases	38,476	9234	24,769
Number of deaths	1924	462	1238
Hospitalization days	92,342	22,162	59,446
Disease costs (costs in 2000) (US$)			
Direct costs			
Ambulatory visit costs	39,253	9421	25,269
Hospitalization costs	502,225	120,537	323,307
Total disease costs	541,478	129,958	348,576
Vaccination costs			
Vaccine cost	164,160	216,960	328,320
Injection equipment	40,640	81,280	81,280
Cold chain	9280	18,560	18,560
Transportation	7680	15,360	15,360
Personnel	24,960	49,920	49,920
Stationery	640	1280	1280
Social mobilization (SIAs)	0	23,360	0
Supervision (SIAs)	0	1600	0
Planning/training (SIAs)	0	7680	0
Administrative costs (SIAs)	0	1600	0
Additional transportation (SIAs)	0	1280	0
Additional personnel (SIAs)	0	4480	0
Adverse events	24,000	31,680	27,600
Total vaccination costs	271,360	455,040	522,320
Total	812,838	584,998	870,896

US$ 1 = 3200 Zambian Kwacha in 2000.

[a] Strategy 1: one dose at 9 months old. Strategy 2: two doses, second through SIAs. Strategy 3: two doses through routine system.

Compared with strategy 1, strategy 3 would prevent 13,707 measles cases and 686 deaths for each vaccinated birth cohort. However, vaccination using strategy 2 would prevent approximately 29,000 measles cases and 1460 deaths when compared with strategy 1. In the presence of a vaccination program using strategy 2, the numbers of both measles cases and deaths would be reduced by approximately 76 and 63% when compared to strategies 1 and 3, respectively (Table 3). Moreover, a total of approximately 70,000 hospitalization days would be saved when compared with strategy 1. A vaccination program following strategy 2 would be expected to cost US$ 455,040 including vaccine purchase, administration, treatment of adverse events and other SIAs costs. This would be US$ 67,280 less than strategy 3 (Table 3). Strategy 2 dominates the other strategies, as it is both more effective and less costly. In addition, it is the only strategy which results in savings per case and death prevented, when compared to the one-dose strategy (Table 4).

3.2. Sensitivity analysis

Even 100% vaccine coverage using strategy 1 would not reach the level of measles control achieved with strategy 2 at

Table 4
Results of the cost-effectiveness analysis comparing strategies 2 and 3 to strategy 1[a]

	Costs in 2000 (US$)				Total measles cases	Additional cases prevented[b]	Total measles deaths	Additional deaths prevented[b]
	Disease costs	Vaccination costs	Total disease and vaccination costs	Additional cost of program (US$)[b]				
Strategy 1	541478	271360	812838	0	38476	0	1924	0
Strategy 2	129958	455040	584998	−227840	9234	29242	462	1462
Strategy 3	348576	522320	870896	58058	24769	13707	1238	686

US$ 1 = 3200 Zambian Kwacha in 2000.
[a] Strategy 1: one dose at 9 months old. Strategy 2: two doses, second through SIAs. Strategy 3: two doses through routine system.
[b] All strategies are compared to strategy 1. Negative values represent savings.

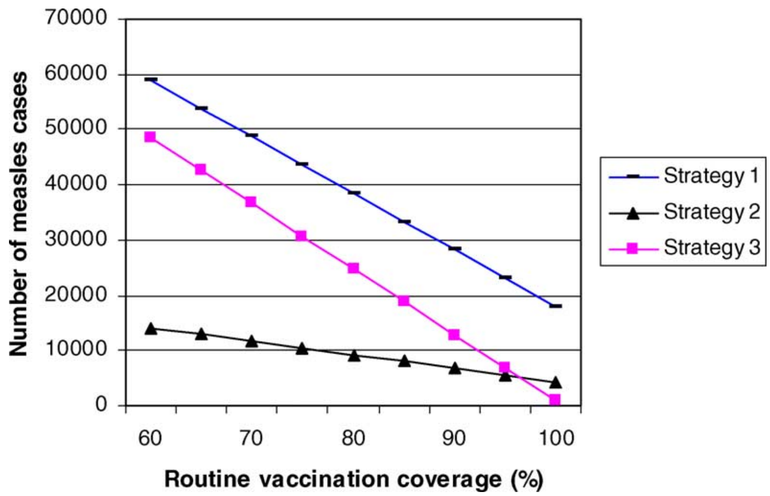

Fig. 2. Sensitivity analysis of relationship between number of measles cases and coverage with vaccine delivered through routine services according to strategy.

coverage of 80% for each of the two vaccine doses administered. Vaccination coverage for each dose using strategy 3 would have to increase from 80 to 99.5% to equal benefits in terms of disease prevented using strategy 2 (Fig. 2). As coverage for vaccine delivered through routine services increases, savings per averted case increases for strategy 3 but remains relatively unchanged for strategy 2. However, if 100% routine vaccination coverage were achieved, strategy 2 would still offer slight cost-savings while strategy 3 would approach being cost neutral (Fig. 3).

The impact of varying wastage factor in routine health services, vaccination costs and reporting efficiency of measles

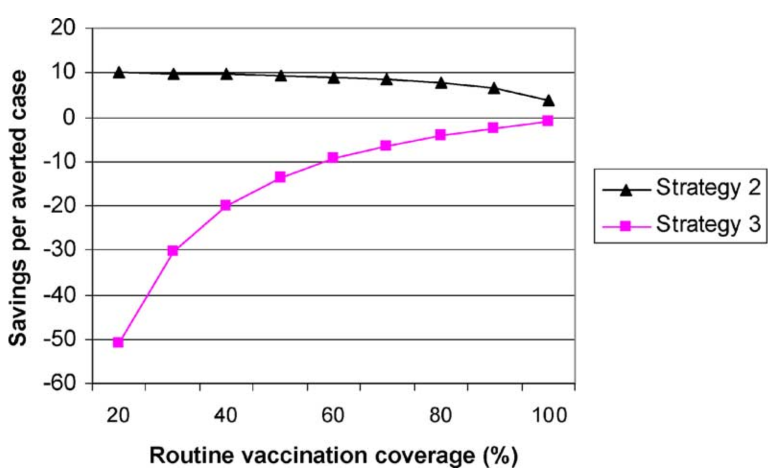

Fig. 3. Sensitivity analysis of relationship between savings per averted case and coverage with vaccine delivered through routine services according to strategy.

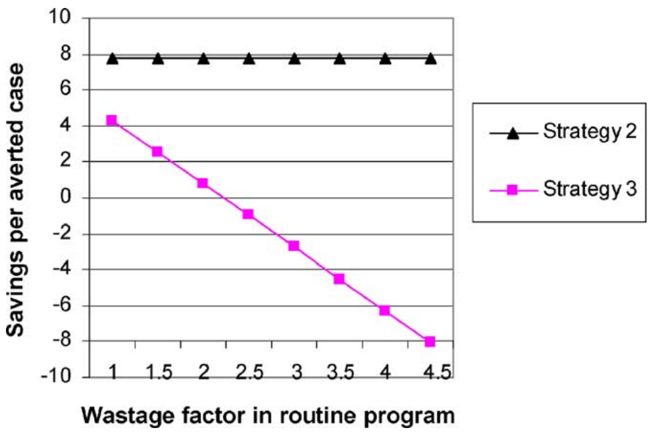

Fig. 4. Sensitivity analysis of relationship between savings per averted case and wastage factor for vaccine delivered through routine services according to strategy.

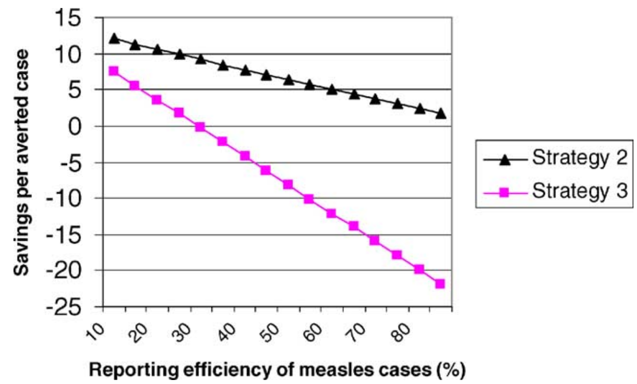

Fig. 6. Sensitivity analysis of relationship between savings per averted case and the reporting efficiency of measles cases according to strategy.

cases on savings per averted case is shown in Figs. 4–6, respectively. In each analysis, an increase in the variable resulted in a much greater and more rapid decrease in savings per averted case for strategy 3 than for strategy 2. We also performed sensitivity analysis on the percentage of children unvaccinated with the first dose reached with the second opportunity. As the percentage of children reached with the second opportunity increases, the savings per averted case uniformly increase for both strategies 2 and 3 (Fig. 7). The same is true when increasing ambulatory visit or hospitalization costs (Figures available from authors on request).

4. Discussion

The World Health Assembly [23] in 1989 and the World Summit for Children [24] in 1990 set specific goals for reduction in measles morbidity and mortality. In Zambia, the aim was to reduce measles mortality by 95% compared with pre-vaccine era levels.

One of the strategies to reduce measles mortality is to ensure that at least one dose of measles vaccine is given to all infants. Studies of single dose measles vaccination have found high benefit–cost ratios [25–29]. Although vaccination with one dose can substantially reduce disease from pre-vaccine era levels, outbreaks continue to occur even with high vaccination coverage rates due to accumulation of susceptible individuals who did not seroconvert after vaccination or were never vaccinated. Such outbreaks occurred in Romania [30], Sri Lanka [31], Canada [32] and the United States [33]. This underscores the importance of the WHO recommendation that a second opportunity for measles vaccination should be offered to achieve sustainable reduction of measles mortality [2]. When compared to a one-dose strategy, vaccination schedules that offer two opportunities for measles vaccination have been shown to improve measles control in developing and developed countries [34–38]. Moreover, a schedule that offers two opportunities for measles vaccination has been shown to be cost-effective [39]. Zambia is planning to offer a second opportunity for

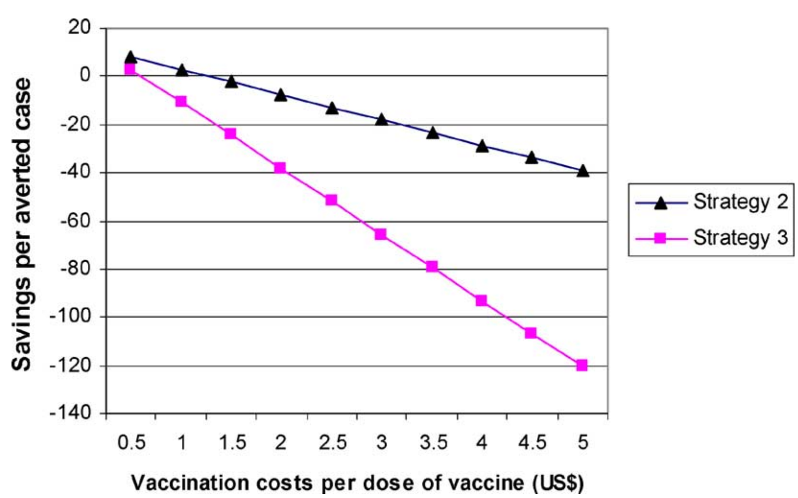

Fig. 5. Sensitivity analysis of relationship between savings per averted case and vaccination costs per dose of vaccine according to strategy.

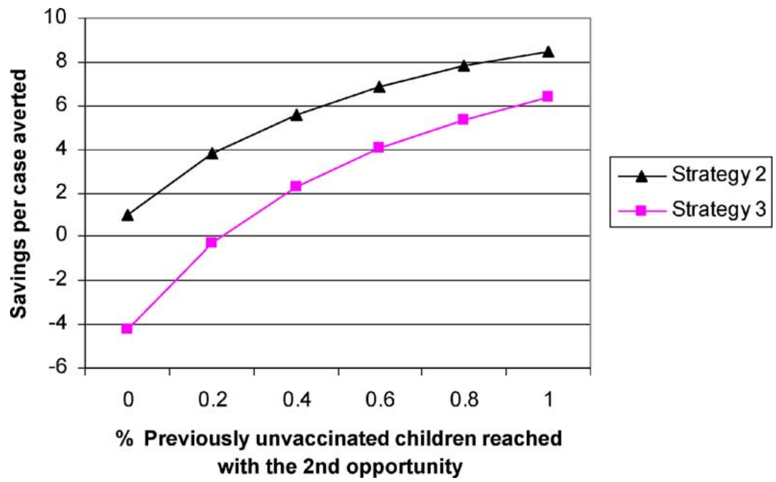

Fig. 7. Sensitivity analysis of relationship of savings per averted case and the percentage of previously unvaccinated children reached with the second opportunity.

measles vaccination delivered through SIA countrywide in mid-2003 [40].

Our analysis shows that in Zambia, a schedule that offers two opportunities for measles immunization results in a substantial decrease in measles cases and deaths compared with a one-dose strategy. In addition, a strategy that delivers the second opportunity through SIAs is the most cost-effective strategy because it reaches previously unvaccinated children and has low vaccine wastage.

Vaccination coverage was a factor critical to our results. One-dose vaccination, even achieving 100% coverage, could not prevent as many cases as those averted using strategy 2 with 80% coverage for each dose of vaccine. Moreover, strategy 3 would need to achieve almost 99.5% coverage with each dose of vaccine to result in the same reduction of disease as would be achieved with 80% coverage each for first and second doses in strategy 2. In fact, raising vaccination coverage for each dose from 80% to almost 99.5% may not be feasible and would require a disproportionate use of resources. In strategy 3 the main benefit of offering a second dose of measles vaccine is to immunize those children who have remained susceptible due to a failure to respond to the first dose of vaccine, since a second dose is only provided to previously vaccinated children. Strategy 2 offers a second opportunity for immunization both to previously vaccinated and previously unvaccinated children. Experience in countries with low to moderate coverage with vaccine delivered through routine services shows that offering a second opportunity for measles immunization through SIAs may be successful in reaching previously unvaccinated children [41]. Our assumption that about 80% of previously vaccinated and unvaccinated children were reached during SIAs is similar to the findings from a recent study in Burkina Faso [42]. However, special efforts in planning and implementation of SIAs are needed to achieve the highest coverage possible among previously unvaccinated children [43].

The current analysis had several limitations that may affect our results.

Due to lack of more accurate information, the costs for cold chain were considered to be similar for vaccines administered through SIAs and through routine health services. However, additional costs for transportation and personnel necessary to reach previously unvaccinated children were added to estimate the costs of vaccination through SIAs. We did not include additional costs related to routine health services (e.g. personnel, building, surveillance, training, etc.) because information on these items was not available. However, this makes our analysis more conservative (i.e. less likely to find a beneficial effect of delivering the second opportunity through SIAs). In our study, we did not consider that the implementation of a vaccination campaign would decrease attention to other health programs. Nor did we consider costs related to outbreak control, which would increase the benefits of strategy 2 [44].

Disease costs may not have been accurately estimated. We considered an average for the country; however, a cost–benefit analysis of measles immunization in Southern Zambia revealed that savings in rural areas can be insignificant due to the non-existence or insufficient availability of curative services [45]. Additionally, the number of cases occurring between the first and second doses in all two-dose strategies, which would increase the costs of disease, was not considered in our analysis. Increased costs which may have resulted from commonly found complications of measles such as otitis media [46] were also not included. Nor did we include the costs of rare but severe complications such as measles encephalitis or subacute sclerosing panencephalitis [47]; inclusion of these costs would increase the cost of disease, rendering strategy 2 more cost-effective. We did not attempt to assign monetary values to the intangible costs of pain or death. If these costs had been included, strategy 2 would have been even more cost-effective than in the present analysis. We may also have overestimated measles mortality. We used a case–fatality ratio from hospitalized patients, which may be higher than that experienced in the community as a whole [48]. However, case–fatality ratios above 25% have been reported in Africa during outbreaks [49] and in endemic settings with poor access to health services [50]. A case–fatality ratio of 5% is consistent with current WHO estimates for the region [51].

The effect of immunization on the epidemiology of measles was not considered in our model. In fact, after the introduction of vaccination programs attaining high vaccination coverage, a change in the age distribution of cases with a shift to older ages has been described due to the effect of herd immunity [3]. This can contribute to the reduction of measles-associated deaths, since the highest measles case–fatality ratios have been reported in children under 3 years old [52]. In Senegal it was estimated that this change in age distribution accounted for 20% of the decline in case–fatality ratios [53].

In conclusion, our analysis shows that a two-dose vaccination program which includes SIAs reaching children not previously vaccinated is the most cost-effective approach in Zambia. According to our analysis, including a second opportunity through SIAs is the best strategy for the implementation of future two-dose measles vaccination policies. Further studies to collect more detailed vaccination program costs and compare the cost-effectiveness of targeting different age groups should be considered.

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