# Using cost-effectiveness analysis to evaluate targeting strategies: the case of vitamin A supplementation

BENJAMIN P LOEVINSOHN, ROLAND W SUTTER2 AND MARIA OTELIA COSTALES3

<sup>1</sup>Asian Development Bank, Manila, Philippines, <sup>2</sup>Centers for Disease Control and Prevention (CDC), Atlanta, USA and <sup>3</sup>Philippine Department of Health, Manila, Philippines

Given the demonstrated efficacy of vitamin A supplements in reducing childhoood mortality, health officials now have to decide whether it would be efficient to target the supplements to high risk children. Decisions about targeting are complex because they depend on a number of factors; the degree of clustering of preventable deaths, the cost of the intervention, the side-effects of the intervention, the cost of identifying the high risk group, and the accuracy of the 'diagnosis' of risk.

A cost-effectiveness analysis was used in the Philippines to examine whether vitamin A supplements should be given universally to all children 6–59 months, targeted broadly to children suffering from mild, moderate, or severe malnutrition, or targeted narrowly to pre-schoolers with moderate and severe malnutrition. The first year average cost of the universal approach was US\$67.21 per death averted compared to \$144.12 and \$257.20 for the broad and narrow targeting approaches respectively. When subjected to sensitivity analysis the conclusion about the most cost-effective strategy was robust to changes in underlying assumptions such as the efficacy of supplements, clustering of deaths, and toxicity.

Targeting vitamin A supplements to high risk children is not an efficient use of resources. Based on the results of this cost-effectiveness analysis and a consideration of alternate strategies, it is apparent that vitamin A, like immunization, should be provided to all pre-schoolers in the developing world. Issues about targeting public health interventions can usefully be addressed by cost-effectiveness analysis.

#### Introduction

Targeting preventive health care interventions appears to be a sensible way of making better use of scarce resources, particularly in developing countries. It is, primarily, an attempt to increase the efficiency of services by withholding interventions from people who would be expected to get little benefit from them and focusing efforts instead on people at high risk of mortality or serious morbidity. The issue of targeting is ubiquitous. Growth monitoring of children, community diagnosis, and the 'risk' approach to prenatal care are examples of attempts to target health interventions.

The sine qua non of successful targeting is the existence of a health intervention of proven efficacy.

Hence, before consideration is given to targeting an intervention there should exist solid evidence of its efficacy, preferably coming from well-conducted, randomized community trials. Even in the presence of an efficacious intervention, however, the efficiency of targeting high risk individuals, communities, or geographical areas depends on: (i) whether the mortality or morbidity prevented by the intervention occurs primarily among an identifiable target group; (ii) the cost of the intervention; (iii) whether the intervention is associated with serious or frequent side-effects; (iv) the cost of identifying the high risk group or community; (v) whether the process of identifying ('diagnosing') people or communities as high risk is associated with serious or frequent side-effects; and (vi) the extent to which individuals or communities are misclassified.

Unfortunately, assessing the relative importance of these six factors is difficult to do simply by inspection. To what extent exactly does preventable mortality have to cluster in an identifiable group before targeting is warranted? How inexpensive does an intervention have to be before it is more efficient to simply use it universally? One way of evaluating all these factors is through the use of cost-effectiveness analysis.

According to a recent meta-analysis of eight randomized community trials in developing countries, vitamin A supplementation reduces overall child mortality by 23%. So compelling is the evidence that the authors of this meta-analysis conclude that it is unethical to conduct any further trials examining the effects of vitamin A on mortality in the age group 6 months to 5 years. The findings of this latest meta-analysis are consistent with those of two others. <sup>2,3</sup>

Given the weight of evidence in favour of vitamin A supplementation, health planners are now confronted with the issue of how to efficiently deliver vitamin A to children who could benefit from it. One approach to decreasing the costs of vitamin A programmes, whether supplementation or dietary diversification, would be to target efforts towards high risk groups, such as malnourished children or children living in areas where xerophthalmia rates are high. This article describes the application of cost-effectiveness analysis to evaluate approaches to targeting vitamin A supplementation to high risk children in the Philippines. It uses this specific case to illustrate general issues in targeting public health interventions.

#### Methods

#### **Background**

The Department of Health in the Philippines undertook to distribute high dose vitamin A capsules as a temporary measure until dietary diversification and food fortification ensured sufficient vitamin A intake by Filipino pre-schoolers. The managers in the Department of Health faced the decision of whether to target the vitamin A supplements to a particular high risk group, i.e. underweight children, or to give it universally.

Previous guidelines within the Department of Health called for vitamin A (100 000 IU for infants 6 to 12

months and 200 000 IU for children 12 to 59 months) to be given twice a year to pre-school children who were mildly, moderately, or severely undeweight (based on the Gomez classification), as well as children suffering from measles, chronic diarrhoea, acute respiratory tract infections, and clinically apparent vitamin A deficiency.

The programme managers decided to use the routine immunization programme to provide vitamin A to infants at the time they received measles vaccination (scheduled at nine months but sometimes given earlier). For older pre-schoolers mass campaigns were used to distribute vitamin A. Beginning in 1993 the Philippines launched a nation-wide polio eradication effort which relied on two annual immunization days focused on vaccinating children under 60 months of age against polio, but which also provided other vaccines. During the second immunization day vitamin A supplements were given to children of 12 to 59 months. Five months later a special micronutrient campaign was conducted to provide a second dose of vitamin A (and provide iodine to pregnant women).

#### The question addressed

The cost-effectiveness analysis was undertaken to decide whether high-dose vitamin A capsules should be given to all children 6–59 months (universal distribution), only to children who were mildly, moderately or severely underweight (broad targeting), or only those who were suffering from moderate and severe malnutrition (narrow targeting). The only difference between the universal and targeted approaches would be that during the latter, children would be weighed and classified prior to supplementation of those found to be malnourished.

For purposes of this study, effectiveness was defined as the number of deaths averted and the relative efficiency of the three approaches was defined as the cost per death averted by vitamin A supplementation given the current conditions in the Philippines. An initial analysis, using cost per 'healthy days of life saved' as the measure of cost-effectiveness, was undertaken to take into account days of illness due to consumption of vitamin A capsules. However, this showed that the side-effects from vitamin A were orders of magnitude less important than deaths prevented. This was because, based on the results of a randomized double-blinded study in the Philippines, 4 side-effects were minor and infrequent.

#### **Assumptions**

In this analysis the point of view adopted was that of the Department of Health. The costs examined were only those that would have to be borne directly by the Department of Health and did not include costs such as mothers' travelling time or money spent by families on transportation. All costs were calculated as the increase (incremental cost) in Department of Health expenditures due to the introduction of vitamin A supplementation, i.e. the costs calculated for each approach reflected the extra expenses incurred by classifying the children (for the two targeted approaches) and giving vitamin A, above what would be spent on the routine immunization and polio eradication efforts. Costs were measured for the first year of the programme only and were based on actual expenditures in the Philippines. The time needed to weigh and classify children and provide them with vitamin A supplements was based on direct observation by the authors in DOH clinics.

It was assumed that in the targeted approaches all children would have to be weighed because: (i) DOH statistics indicated that less than 50% of pre-schoolers were covered by the growth monitoring programme; (ii) not all mothers would bring existing growth monitoring cards with them during the vaccination campaigns; and (iii) sufficient time may have elapsed since the last weighing for nutritional status to have changed.

Included in the analysis were the costs of: (i) procurement and distribution of vitamin A capsules, (ii) training health workers, (iii) public information, education and communication, and (iv) the time the health workers spent weighing, classifying, and supplementing children. The analysis excluded the costs of volunteers' time because data were not available on the actual number that participated in routine immunization and the mass campaigns. It was also felt that the different approaches to targeting would use similar amounts of volunteer inputs.

In the calculation of benefits it was assumed that the coverage rates obtained would be the same regardless of the targeting strategy adopted and were based on the actual accomplishments during the 1993 National Immunization Days. Vitamin A supplementation was presumed to reduce overall mortality by 23% although no efficacy trials have been conducted in the Philippines. The other assumptions used in the analysis of costs and effects are described in Table

1. The effect of vitamin A distribution on blindness prevention and reduction in morbidity from infectious diseases was not taken into account.

Operational research carried out in the Philippines<sup>7</sup> has indicated that health workers are not very accurate in determining the weight of children. While this inaccuracy leads to both under- and over-estimation, over-estimation of weight would be a more serious error because it would mean that children might be denied the benefit of an effective intervention. The weights of children less than 3 years of age were often over-estimated because they were weighed while fully clothed. The average overestimate was 600 grams which meant that approximately 20% of malnourished children were misclassified as normal (i.e. were false negatives).

The proportion of deaths preventable by vitamin A that occurred among malnourished children had to be estimated due to a lack of data in the literature. The meta-analysis by Beaton et al. found no association between wasting (low weight for height) and the impact of vitamin A but did not examine the effect of low weight for age. Assuming that: (i) the 5% of children who were moderately and severely malnourished had an overall relative risk of dying of 3 compared to normal children; (ii) the 24.6% of children who were mildly malnourished had an overall risk of dying of 1.5 compared to normal children; and (iii) being malnourished did not add to the risk of dying from causes preventable by vitamin A; then moderately and severely malnourished children would comprise 12% of vitamin A preventable deaths and all malnourished children (mild, moderate and severe) would comprise 43%. However, if there was no interaction between nutritional status (as judged by anthropometry) and the risk of dying from causes preventable by vitamin A, there would be little justification in targeting malnourished children. Thus we assumed, for the sake of the analysis, that being moderately and severely malnourished doubled the relative risk of dying from causes preventable by vitamin A (i.e. the relative risk was 6 compared to normal children) and multiplied the relative risk for mildly malnourished children by 1.5. Based on these two assumptions, moderately and severely malnourished children would comprise 19% of all deaths preventable by vitamin A, and children who were mildly, moderately and severely malnourished would comprise 55% of the total.

**Table 1.** Variables and assumptions used in the calculation of the costs and effects of three strategies for distributing high-dose vitamin A capsules

Variable	Value/ estimates	Source of data/estimates
No. children aged 6 to 59 months	7 969 000	1990 Census
% children who are mild, moderate & severely malnourished	29.6%	National Nutrition Survey <sup>5</sup>
% children who are moderate & severely malnourished	5.0%	National Nutrition Survey <sup>5</sup>
Mortality rate among children 6 to 59 months (per 1000 live births)	36	1990 Census
Expected decrease in mortality due to vitamin A distribution	23 %	Meta-analysis of published trials
% preventable deaths occurring among mild, moderate & severely malnourished	55%	see text
% preventable deaths occurring among moderate & severely malnourished children	19%	see text
Coverage for vitamin A supplementation	90%	Household survey <sup>6</sup>
Mortality from vitamin A toxicity	1/100 000	see text
Sensitivity of weight classification done by midwives compared to 'expert'	80%	Operational research <sup>7</sup>
Specificity of weight classification done by midwives compared to 'expert'	90%	Operational research <sup>7</sup>
Cost of vitamin A capsule (US\$)	\$0.028	UNICEF price + 35% for freight and insurance
Time needed to give vitamin A and record it	1.25 Minutes	Observations in DOH health facilities
Time needed to weigh and classify child	3.0 Minutes	Observations in DOH health facilities
Midwives' hourly wage (US\$)	\$0.64	DOH salary scale
Information, Education, Communication	\$360 000	UNICEF, HKI costing <sup>8</sup>
Training costs for health staff (US\$)	\$40 000	UNICEF, HKI costing <sup>8</sup>
Number of births per year	1 998 000	1990 Census
Exchange rate (pesos per US\$)	25	Average 1994 rate

The mortality rate from vitamin A toxicity was estimated at 1 per 100 000 children given the supplement. This is likely a conservative (high) estimate since an early review of the topic<sup>9</sup> found no deaths reported in the literature.

To test how robust the results of this study were to these estimates and the other assumptions used, a sensitivity analysis was conducted. All the variables included in the cost-effectiveness equation (the original model) were varied over a wide range of values, one at a time, to see what affect the change would have on the overall results. Then key variables such as the percentage reduction in mortality due to vitamin A, the proportion of preventable deaths occurring among malnourished children, and the sensitivity of weight classification, were varied at the same time to test the sensitivity of the model to multiple changes in assumptions.

Calculations for the original model and the sensitivity analysis were performed using standard computer spreadsheet software (Lotus 123). A detailed description of the model is available from the authors.

# Results

The results of the cost effectiveness analysis are shown in Table 2. They indicate that universal distribution of vitamin A to all pre-schoolers is the most effective method for preventing deaths and the most efficient in terms of cost per death averted. In absolute terms narrow targeting was the least expensive but would result in 11 318 fewer lives being saved than universal distribution. The universal approach would cost 12% more but result in a 327% increase in the number of deaths averted. While broad targeting had a lower cost per death averted than narrow targeting it appeared to be the least efficient

**Table 2.** First year costs and effects of different strategies for distributing high dose vitamin A capsules to pre-schoolers in the Philippines

	Universal distribution	Broad targeting	Narrow targeting <sup>b</sup>
Number of deaths averted	14 773	7178	3455
Total cost (in US dollars)	\$992 894	\$1 034 510	\$888 659
Average cost per death averted	\$67.2	\$144.1	\$257.2

to mildly, moderately & severely malnourished children
to moderately & severely malnourished children

alternative. It would cost more than the universal approach yet result in 7595 fewer deaths being prevented. These results indicate that universal distribution is the preferred strategy.

### Sensitivity analysis

Although the number of deaths averted and the costs varied during the sensitivity analysis, the overall conclusion about the most cost-effective strategy was robust. Universal distribution of vitamin A remained the most cost-effective strategy (see Table 3 which includes the range of values used in the sensitivity analysis). Even if it is assumed that all mortality preventable by vitamin A occurs among malnourished children, targeting is still inefficient because the intervention is inexpensive and the classification of children as malnourished is sufficiently inaccurate that some pre-schoolers who could obtain benefit from vitamin A would not receive the supplement. Assuming lower efficacy of supplementation as might be postulated for areas with a low prevalence of vitamin A deficiency also does not significantly change the cost-effectiveness of universal distribution relative to the targeted approaches. Over a wide range of assumed reductions in mortality resulting from vitamin A supplementation, the universal strategy remained the most cost-effective approach although the absolute cost per death averted changed substantially (Figure 1).

Assuming that only some of the children would have to be weighed during the mass campaigns because they had been weighed previously would also not alter the conclusion of the analysis nor would entirely excluding from the model the cost of weighing and classifying children. Other factors which were found to significantly reduce the advantage of universal distribution include more accurate classification of malnourished children and increased cost of vitamin A capsules, although the latter would have to increase 824% before a targeted approach would become more cost-effective.

Even changing a number of key assumptions at the same time did not alter the conclusion that universal distribution was the most efficient strategy. For example, assuming that vitamin A reduced mortality by only 5%, that all preventable deaths occurred among malnourished children, and that weight classification was perfectly sensitive, would not alter the decision to adopt the universal approach.

Generally as the fixed costs of a public health programme increase as a proportion of total cost, targeting becomes less efficient. Fixed costs accounted for approximately 40% of the total cost of each approach (Table 4). Reducing fixed costs such as training and public information (as might happen after the first year) did not substantially change the results of the analysis. The actual vitamin A capsules constituted 40% of the total average costs in the universal approach. Weighing and classifying children accounted for 44% of total costs of the broad targeting approach and 52% if the supplements were targeted narrowly. Even if the expense of weighing children was excluded, the cost per death averted using the broadly targeted approach would still be 19% higher than with universal distribution.

# Discussion

The decision about whether to target efficacious public health interventions to high risk groups or areas must be made on a case-by-case basis. However, in the situation examined here, targeting vitamin A supplements to individual children who are malnourished is both less effective and less efficient than universal distribution. This conclusion arises because vitamin A is very effective, relatively inexpensive to purchase and deliver universally, and because the cost of defining high risk groups is relatively costly and inaccurate.

All cost-effectiveness analyses are conducted with incomplete data and require estimates for certain

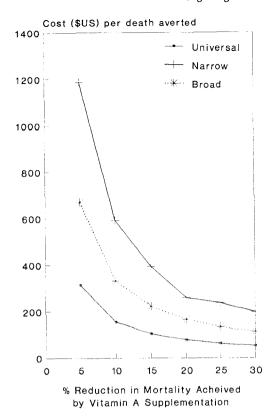
Table 3. Results of sensitivity analysis, effect of changes in assumptions on cost (in US\$) per death averted

Parameter modified	Value/estimate in orginal model	Tested value/ estimate	Universal distribution	Broad targeting	Narrow targeting	Ratio of broad/universal
none (original model)	_	_	67.21	144.12	257.20	2.14
% preventable deaths that occur among mild, moderate &	55%	100%	67.21	87.27	257.20	1.30
severely malourished		43 %	67.21	174.41	257.20	2.59
% preventable deaths that occur among moderate & severely	19%	24%	67.21	144.12	223.58	2.14
malnourished		12%	67.21	144.12	325.78	2.14
expected decrease in mortality due to vitamin A deficiency	23%	12%	129.40	276.97	493.43	2.14
		6%	261.24	557.11	988.83	2.13
mortality rate from vitamin A capsule toxicity	1/100 000	1/10 000	70.28	148.06	259.62	2.11
	17100 000	1/2000	88.19	168.54	270.98	1.91
mortality rate among children 6 to 59 months (per 1000 live births)	36	50	48.33	103.68	185.13	2.15
		20	121.45	260.02	463.34	2.14
sensitivity of weight classification done by midwives compared to 'expert'	80%	100%	67.21	117.41	221.10	1.75
	80%	60%	67.21	186.55	307.38	2.78
% children needing weighing during vaccination campaign (targeted approaches)	100%	0%	62.71	80.17	124.35	1.19
		50%	62.71	112.14	190.77	1.67
cost of vitamin A capsules and their distribution	\$0,029	\$0.084	121.59	177.24	268.82	1.46
	\$0.028	\$0.056	94.40	160.68	263.01	1.70

parameters. In this analysis information was lacking on the proportion of vitamin A preventable deaths occurring among malnourished children and the efficacy of vitamin A supplementation in the Philippines. (Obtaining efficacy data now would be impossible because any prospective study that assigned children to a placebo would be unethical.) Nonetheless, the conclusions were robust when subjected to sensitivity analysis and the difference between universal distribution and both broad and narrow targeting were large.

A possible compromise between targeting individuals and providing a service universally is to focus attention on high risk geographical areas. In the case of vitamin A this has usually meant concentrating on locations where xerophthalmia prevalence has been documented to be above 1.5%, a cut-off point established by WHO in 1982. 10 There are a number of issues that need to be addressed in using this geographical approach.

The first problem is how to establish the cut-off point. The WHO guidelines use xerophthalmia prevalence to 'diagnose' risk in a way analogous to a normal value in clinical medicine. Xerothphalmia prevalence above 1.5% requires vitamin A intervention programmes while no action is deemed necessary if the



**Figure 1.** Average cost (US dollars) per death averted according to assumed reduction in mortality achieved by vitamin A supplementation

prevalence is below 1.5%. The best way of defining a normal value in a clinical setting is the point at which therapy has been shown to do more good than harm.<sup>11</sup> For example, the normal value of diastolic blood pressure has been defined by the results of randomized trials showing improvements in outcomes by treatment of blood pressures of greater than 105 mm Hg and more recently, greater than 90 mm Hg. In the case of vitamin A, the recent evidence makes it clear that the prevalence of xerophthalmia which should provoke action is lower than 1.5%. The VAST study in Ghana on vitamin A and survival<sup>12</sup> demonstrated a 19% decrease in overall mortality as a result of supplementation in a population with a 0.7% xerophthalmia prevalence and relatively high consumption of vitamin A rich foods. A recent study from Brazil reported a 20% reduction in severe diarrhoea in an area with no xerophthalmia. 13 These results suggest that the most appropriate cut-off point

**Table 4.** Average cost per vitamin A preventable death in three supplementation strategies, and cost elements for distributing vitamin A capsules to pre-schoolers in the Philippines

	Universal distribution	Broad targeting <sup>a</sup>	Narrow targeting <sup>b</sup>		
Diagnosis of malnutrition	NA°	\$63.9 (44%)	\$132.8 (52%)		
Cost of vitamin A supplements	\$27.5 (41%)	\$16.6 (11%)	\$5.8 (2%)		
Fixed costs	\$26.9 (40%)	\$55.7 (39%)	\$115.8 (45%)		
Costs of administering vitamin A	\$12.8 (19%)	\$7.9 (6%)	\$2.8 (1%)		
Total average cost per death averted	\$67.2 (100%	\$144.1 (100%)	\$257.2 (100%)		

to mildly, moderately & severely malnourished children

not applicable

is zero, i.e. that significant effects of vitamin A supplementation will be found in populations with no xerophthalmia.

This conclusion is strengthened by two other findings. All of the published randomized trials specifically excluded any children with clinical signs of xerophthalmia from the study. Therefore, the striking declines in mortality rates that were observed occurred in children who had no clinically detectable evidence of vitamin A deficiency. Among the published studies there was also no relationship found between the prevalence of xerophthalmia in the study areas and the effectiveness of vitamin A supplements. Similar reductions in mortality were found in areas with 13% and 0.7% xerophthalmia prevalence.

Even if the cut-off rate is not zero, high risk populations are unlikely to be uniformly distributed throughout the country and national data will not identify these areas. This appears to have happened in the Philippines where a national survey concluded that xerophthalmia prevalence was low (0.7% for night blindness and 0.2% for Bitot's spots) but separate surveys in three different provinces found high rates of night blindness (range 1.6 to 4.4% and Bitot's spots (range 0.6 to 2.7%). <sup>14</sup> These provinces clearly

b to moderately & severely malnourished children

needed vitamin A intervention programmes regardless of the national results.

Managers of programmes that rely on geographical targeting would have to decide on the level of disaggregation needed. If provincial level data is required, in the Philippines this would mean carrying out 78 prevalence surveys and each one would have to be able to identify whether vitamin A deficiency was of public health significance. In order to distinguish a 1.5% xerophthalmia prevalence rate from 0.5% with 95% confidence (i.e. alpha = 0.05) and 80% power (i.e. 1-beta = 0.8) would require a sample size of 3495 children. Thus, for the 78 provinces in the Philippines, 272 610 children would have to be examined.

There have been recent efforts to elucidate new techniques for assessing vitamin A status such as the modified relative dose-response assay and the plasma retinol-binding protein response test. <sup>16</sup> Although these assays are of academic interest, it is not clear that they will be useful in the field. Unlike xerophthalmia prevalence, these new tests were not carried out in the areas where the randomized trials of vitamin A were conducted. Hence, without new prospective studies, which would probably be unethical, the cut-off points, or normal values, for these tests could not be rigorously established. The new diagnostic tests would also have to confront the issue of geographical disaggregation and how many children would need to be tested

The results of our analysis strongly suggests that targeting of vitamin A programmes is not an efficient use of health care resources. This should not be surprising. Other public health interventions, such as immunization, are applied universally regardless of the risk faced by the individual recipient. Thus, every developing country needs to ensure that all preschoolers receive the benefits of vitamin A. More generally, the use of cost-effectiveness analysis can help policy-makers decide whether it makes sense to target a public health intervention.

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# **Biographies**

Dr Bejamin Loevinsohn is a Canadian physician specializing in epidemiology and programme implementation. He obtained his medical training at McMaster University in Ontario and his public health training at Harvard University. He worked in Nicaragua and Sudan prior to coming to the Philippines. At the time of the

first national immunization day, he was a resident advisor to the Child Survival Program in the Philippine Department of Health. He is currently working as a health specialist for the Asian Development Bank where he has responsibility for health project design and implementation in Bangladesh, Cambodia and Laos, as well as health policy development for the Bank.

Dr Roland Sutter was born and raised in Switzerland. He went to the University of Zurich Medical School (MD, 1979) and Tulane University School of Public Health and Tropical Medicine (MPH&TM, 1981), worked from 1981 to 1987 with International Organization for Migration (IOM) in Thailand organizing preventive services, and since 1987 has been with the Centers for Disease Control and Prevention (CDC) where he is currently the Deputy Chief for Technical Affairs in the Polio Eradication Activity.

Dr Maria Otelia Costales is a public health physician who graduated from the University of the Philippines in 1979 and obtained her Masters degree in public health from the same university in 1988. She worked for the Philippine Department of Health from 1988 until 1995, first as a training officer and medical specialist and then as division chief in charge of the national EPI and ARI programs. From 1993 until 1995, Dr Costales was the officer in charge of the Maternal and Child Health Service and the National Immunization Day Program Manager. She is currently the country representative in the Philippines for AVSC International.

Correspondence: Dr Benjamin P Loevinsohn, Asian Development Bank, PO Box 789, Manila 0980, Philippines.