Childhood Mortality Impact and Costs of Integrating Vitamin A Supplementation Into Immunization Campaigns

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A B S T R A C T

Country-specific activity and coverage data were used to estimate the childhood mortality impact (deaths averted) and costs of integrating vitamin A supplements into immunization campaigns conducted in 1998 and 1999.

More than 94 million doses of vitamin A were administered in 41 countries in 1998, helping to avert nearly 169 000 deaths. During 1999, delivery of more than 97 million doses in 50 countries helped avert an estimated 242 000 deaths.

The estimated incremental cost per death averted was US $72 (range: 36–142) in 1998 and US $64 (range: 32–126) in 1999. The estimated average total cost of providing supplementation per death averted was US $310 (range: 157–609) in 1998 and US $276 (range: 139–540) in 1999. Costs per death averted varied by campaign, depending on the number and proportion of the child population reached, number of doses received per child, and child mortality rates. (*Am J Public Health.* 2000;90: 1526–1529)

The World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) jointly recommend that vitamin A supplementation efforts be integrated into routine and supplemental immunization activities such as national and subnational immunization days in countries where vitamin A deficiency is a public health problem. Countries carrying out immunization days for polio eradication are encouraged to provide 1 age-appropriate oral high dose of vitamin A to all children aged 6 to 59 months during these activities.[1] In addition, countries are encouraged to add vitamin A supplementation to other targeted health initiatives and immunization campaigns, such as measles and tetanus toxoid vaccination campaigns and "mopping-up" operations for polio eradication, particularly when these initiatives are focused on difficult-to-reach populations in which vitamin A deficiency is a problem.

In the absence of improved dietary intake or fortification strategies, to maintain adequate vitamin A stores children 6 to 59 months of age need to receive vitamin A supplementation every 4 to 6 months. This might be accomplished during routine immunization services; other routine health services; multi-antigen campaigns in which vitamin A supplements are given concurrently with polio, DTP (diphtheria and tetanus toxoids and pertussis), measles, and tetanus vaccines; micronutrient days (national campaigns in which micronutrients such as iron, iodine, and vitamin A are delivered); or specific vitamin A campaigns.

Here we summarize results from vitamin A supplementation activities that were integrated into immunization campaigns during 1998 and 1999. We discuss the potential impact of such efforts on child mortality and the estimated costs associated with each death averted.

Methods

WHO continuously collects retrospective and prospective data from countries about immunization campaigns and vitamin A supplementation activities. Dates of activities, age group targeted, number of children targeted, number of children reached with vitamin A, and other information is integrated into a global database. For this commentary, information from this database was combined with United Nations Population Division mortality data.[2] The following equation was used to estimate the number of deaths averted (Z) as a result of the provision of vitamin A supplements:

$$Z=(y\times t\times m),$$

where y=deaths in the absence of vitamin A supplementation (United Nations Population Division mortality data), t=proportion of all targeted children reached, and m=assumed mortality reduction due to vitamin A supplementation.

Estimates were adjusted for variations in the age groups targeted by different countries during their campaigns. If 2 doses at least 4 months apart were delivered during a single calendar year, then the estimated all-cause mortality reduction (m) was estimated to be 23%, consistent with the results of a meta-analysis of 8 randomized controlled trials.[3,4] If only 1 dose was delivered during the year, or 1 dose was delivered nationally and a second subnationally, then mortality was assumed to be reduced by 11.5%. For the 2 countries where reported vitamin A coverage exceeded 100% (owing to underestimation of the size of the target population, misclassification of doses administered to children outside the target age group, or other reasons), a coverage figure of 100% was used.

The following calculations were made to estimate the costs (both incremental and average) per death averted:

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Note. The full tables containing country-specific data for vitamin A supplementation coverage levels, estimated deaths averted, and costs associated with provision of supplements can be found at: http://www.who.int/vaccines.

$$I=(v\times k\times d)/Z$$
$$A=(b\times k\times d)/Z,$$

where I=incremental cost per death averted above cost for polio immunization alone, A=average total cost per death averted for delivering vitamin A supplements alone, v=assumed incremental cost per child reached in addition to costs already incurred for polio vaccination (US $0.10), b=assumed average total cost per child reached for delivering vitamin A supplement alone (US $0.43), k=total number of children reached in a campaign, d=total number of doses administered (or campaigns held) during 1 year, and Z=estimated number of deaths averted with vitamin A supplementation.

For costing, the incremental cost (v) of US $0.10 per child reached with vitamin A was estimated on the basis of WHO experience and country-specific activity budgets, which included the provision of supplements with polio campaigns. The incremental cost comprised the cost of the capsule plus the costs of additional training, personnel, logistics, and supplies (tally forms, scissors, and containers). The average total cost of delivering vitamin A alone (b) was estimated to be US $0.43 per child on the basis of polio campaign cost data available from WHO (i.e., US $0.50 per child reached with polio vaccine during a campaign, of which US $0.09 is for oral polio vaccine; a dose of vitamin A was estimated to cost US $0.02). For countries where 2 doses of vitamin A were delivered in 1 year, both incremental and average total costs were doubled (i.e., d was equal to 2).

The assumed mortality reduction used in the impact estimates was varied for each country by a range of 2/3 to 4/3 to analyze the robustness of the assumption. This robustness was similar to that reported in randomized controlled trials in which, under a fixed-effects model, mortality reduction ranged from 29% to 16%.[3,4] The cost assumptions used here were also varied by 2/3 and 4/3. By combining the high range of mortality reduction with the low range of costs, and vice versa, we derived least and most conservative estimates of costs per death averted.

To estimate the clinical effectiveness of vitamin A supplements, we examined data from 2 countries, the Philippines and Vietnam, that had measured actual childhood mortality rates and vitamin A deficiency prevalence before and during vitamin A supplementation activities. Data from these countries were particularly useful for assessing the actual impact of vitamin A supplementation because these countries (1) integrated vitamin A supplements with national immunization days annually between 1993 and 1997 and followed them with micronutrient days 6 months later, (2) collected precise mortality data for the 5-year periods preceding and during supplementation, and (3) carried out population-based surveys to determine the prevalence of vitamin A deficiency after supplementation was initiated.

Results

Coverage

Vitamin A supplements were integrated into immunization campaigns that primarily targeted children aged 6 to 59 months in 41 countries with a vitamin A–deficiency problem in 1998 and in 50 such countries in 1999. More than 94 million doses were administered in 1998 and more than 97 million doses were administered in 1999, although some reached the same children in the same year because of a 2-dose strategy. In all, 31 (59%) of 53 campaigns in 1998 and 35 (54%) of 65 campaigns in 1999 achieved 80% coverage or better.

Following WHO and UNICEF recommendations, 10 countries in 1998 and 14 countries in 1999 used the following combinations of strategies to provide 2 doses of vitamin A to all or part of their targeted child populations:

1998

- Two national immunization days or health day campaigns (Nicaragua)
- National immunization day (Bangladesh, Ethiopia, Mauritania, Nepal, Zambia) or subnational immunization day (Vietnam) and a national vitamin A campaign
- National immunization day and a measles campaign (Sudan)
- Subnational immunization day and a measles campaign (Cambodia, Congo)

1999

- Two national immunization days or health day campaigns (Afghanistan, Bolivia, Ecuador, Nicaragua)
- Two subnational immunization days (Iran)
- National immunization day (Bangladesh, Ethiopia, Nepal, Niger, Sierra Leone) or subnational immunization day (India, Zambia) and a national or subnational vitamin A campaign
- National immunization day and a measles campaign (Angola, Eritrea)

Estimated Impact

An estimated 169 000 deaths in 1998 and 242 000 deaths in 1999 were averted. The incremental cost per death averted was US $72 (range: 36–142) in 1998 and US $64 (range: 32–126) in 1999. The average cost per death averted was US $310 (range: 157–609) in 1998 and 276 (range: 139–540) in 1999. Variations in the costs per death averted by country can be explained in part by the campaign strategy used (1 or 2 doses in a single year) and the number and proportion of the child population targeted and reached. Variations in child mortality rates between countries also accounted for some of the variations; incremental costs per death averted declined exponentially as child mortality rates increased (Figure 1).

Actual Impact

Childhood mortality rates declined in the Philippines between the periods 1988–1992 and 1993–1997 and in Vietnam between the periods 1987–1991 and 1992–1996 (Table 1). In the Philippines, infant mortality decreased by 5%, child mortality decreased by 47%, and mortality among children younger than 5 years decreased by 22%, while in Vietnam all 3 rates decreased by 30%.[5,6] Although many factors and interventions may have contributed to these declines, vitamin A supplementation was probably one of the most important contributors, particularly because this intervention reached a high proportion of the children who were targeted nationwide.

Cross-sectional surveys were conducted in 3 provinces (Quezon, Northern Samar, and Zambanga del Sur) in the Philippines in 1991 (before universal vitamin A supplementation) and in 1994 (Table 2).[7] The prevalence of night blindness and Bitot spots decreased by 73% and 55%, respectively. The prophylactic efficacy of vitamin A supplementation was estimated at 76%, 77%, and 94% for night blindness and 22%, 46%, and 93% for Bitot spots for coverage levels of less than 75%, 75% through 89%, and 90% or higher, respectively. These data suggest that the impact of vitamin A supplementation depended on reaching the low socioeconomic status groups at highest risk for vitamin A deficiency.

In Vietnam, the National Vitamin A Deficiency and Protein-Energy Malnutrition Prevalence Survey (carried out after the first round of vitamin A supplementation during national immunization days) concluded that the preschool population was xerophthalmia-free by WHO criteria (i.e., prevalence of night blindness <1.0%, of Bitot spots <0.5%, and of corneal xerosis or ulceration <0.05%) (Table 2).[8] A comparison of results from this survey with those of the National Blindness Survey conducted between 1985 and 1988 revealed that the prevalence of night blindness had declined from 0.37% to 0.05%, of Bitot spots from 0.16% to 0.045%, and of corneal scars from 0.12% to 0.048%. These findings suggest that the vitamin A supplementation program had an 86.8% to 90.3% effectiveness in preventing xerophthalmia.[8]

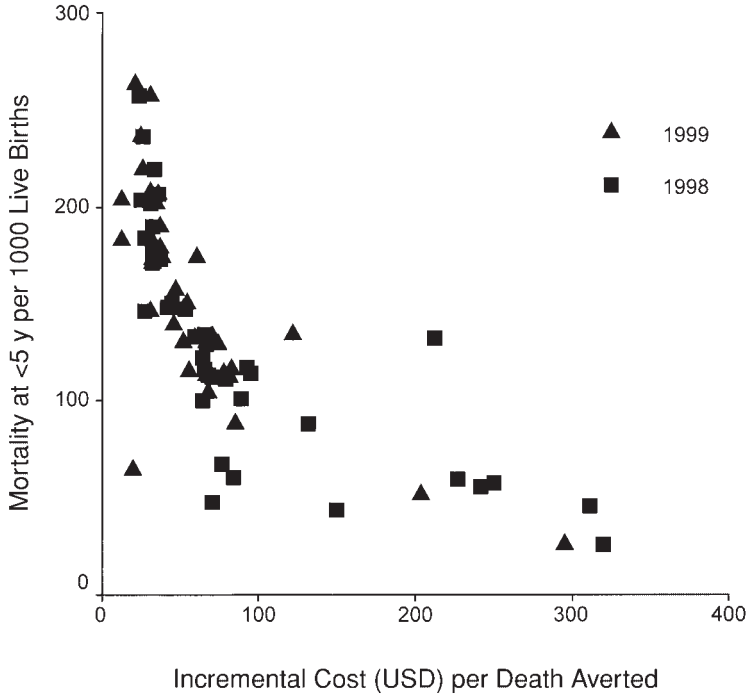

FIGURE 1—Estimated incremental cost per death averted and child mortality rate associated with vitamin A supplementation during immunization campaigns, 1998–1999.

TABLE 1—Actual Childhood Mortality[a] Before and During Administration of Vitamin A Supplements: Philippines[5] and Vietnam[6]

Country and Period	Infant Mortality	Child Mortality	Mortality Among Children Younger Than 5 Years
Philippines			
1988–1992	36.8	26.2	62.1
1993–1997	35.1	13.8	48.4
Vietnam			
1987–1991	40.0	14.0	53.5
1992–1996	28.2	9.8	37.7

[a]Rate per 1000 births.

TABLE 2—Vitamin A Coverage and Prevalence of Night Blindness and Bitot Spots Before and During Administration of Vitamin A Supplements: Philippines[7] and Vietnam[8]

Country and Period	Vitamin A Coverage, %	Prevalence of Night Blindness, %	Prevalence of Bitot Spots, %
Philippines			
1991	5.7	2.32	1.09
1994	80.4	0.63	0.49
Vietnam			
1985–1988	<5.0	0.37	0.16
1994	94.0	0.05	0.045

Discussion

The estimates of mortality impact and costs per death averted have limitations. First, the assumption that all-cause mortality would be reduced by 23% if 2 doses of vitamin A supplement were delivered was based on applying results from controlled clinical trials to uncontrolled country experiences for the purposes of this analysis. More specifically, country-specific factors that might modify the impact of vitamin A supplementation in each country were not accounted for. These factors included child mortality rate reductions, nutritional habits, measles and diarrhea burden and case management practices, and measles immunization coverage.

The use of country-reported data on percentage and number of children targeted and reached to estimate costs per death averted was also a limitation. The quality of these data vary owing to inaccuracies in census data, tallying of doses administered, and misclassification of children's ages, and this leads to underestimation or overestimation of the proportion of targeted children reached.

Nevertheless, estimates of the number of deaths averted as a result of vitamin A supplementation are probably conservative, for several reasons. First, when performing the calculations to derive the estimates, we followed 3 rules: (1) when countries conducted 2 national campaigns and reported different coverage levels, the lower figure was used in calculations; (2) if one dose was delivered nationally and a second dose subnationally, a mortality reduction of 11.5% was assumed and applied only to the information from the national campaign; and (3) if a country provided vitamin A supplements but did not provide data to WHO on the number or proportion of children targeted and reached, data for that country were not included in the calculations. The estimates are also conservative because they do not account for reductions in morbidity associated with vitamin A supplementation.[3,4,9–18]

While the mortality impact estimates do not account for vitamin A supplements delivered as part of routine health services (which could decrease the impact of supplements provided during campaigns), it is likely that this effect is limited. Only 26 of 118 countries with a vitamin A deficiency problem reported to WHO in 1999 that they had integrated vitamin A supplements into their routine immunization services. Of these, only 6 could provide data on the level of vitamin A coverage achieved. In 4 of these countries, coverage with 1 dose of vitamin A by 1 year of age was below 65%, while survey data for the other 2 countries suggest that the reported coverage estimates were substantially inflated.

Despite their limitations, the estimates presented here provide an order of magnitude concerning the child mortality impact and costs of vitamin A supplements integrated into immunization campaigns. Although the data are still preliminary, there is both country-specific and general evidence to suggest that provision of vitamin A supplements has saved thousands of children's lives in a short time. The estimated

23% reduction in all-cause child mortality was derived from a meta-analysis of 8 randomized controlled trials in developing countries, making vitamin A one of the most studied public health interventions.[3,4]

The incremental cost to incorporate vitamin A supplements into existing programs is relatively small and can be financed even in countries where vitamin A deficiency is a major public health problem. Successful uptake has been facilitated by a coordinated donor effort involving the Canadian International Development Agency, the Micronutrient Initiative, the US Agency for International Development, UNICEF, and WHO. Since 1997, through the Micronutrient Initiative, the government of Canada has donated more than 800 million vitamin A capsules to support vitamin A supplementation activities and has provided operational funding to both UNICEF and WHO.

Immunization campaigns have allowed a large number of children in countries with clinical and subclinical vitamin A deficiency to receive supplements of vitamin A. An increasing number of countries are providing vitamin A supplements as a part of their immunization campaigns and other health activities; both the number of countries and the total number of immunization campaigns in which vitamin A was provided have nearly doubled since 1997. These findings highlight the progress made and the enormous impact linking supplementation with immunization services has had on reducing vitamin A deficiency in a short time. Current efforts associated with polio eradication, the accelerated control of other vaccine-preventable diseases (e.g., measles), and sustainable outreach services all represent opportunities for providing vitamin A supplements.[18–22]

Although the integration of vitamin A supplementation into immunization campaigns has been successful, challenges remain. Most children still receive only a single dose of vitamin A each year. In countries with a vitamin A deficiency problem, children aged 6 to 59 months should receive vitamin A supplementation every 4 to 6 months (i.e., 2 to 3 times per year) for maximum impact. For children younger than 1 year, ideal opportunities to provide supplements include routine immunization contacts; for example, supplements could be provided to postpartum mothers with first immunization contact (BCG vaccine, diphtheria and tetanus toxoids and pertussis vaccine [DTP]) or directly to children with measles vaccination. Recommendations concerning vitamin A supplementation for infants younger than 6 months will be issued soon on the basis of new information about the safety and efficacy of supplementation for this age group. Vitamin A could feasibly be linked to the early immunization schedule for DTP, thereby defining an optimal schedule for maintaining adequate vitamin A status throughout the first year of life.

Regular contacts beyond the first year of life remain a challenge, but strategies that link every child health contact with screening for eligibility to receive vitamin A should be encouraged. For example, contacts related to integrated management of childhood illness, delayed immunization or booster doses, and growth monitoring are all effective means of providing vitamin A to older children, particularly when combined with ongoing immunization campaigns.

At a minimum, all countries with vitamin A deficiency problems are encouraged to follow the WHO/UNICEF recommendation of integrating vitamin A into their polio national immunization days while the opportunity exists.[19–22] □

Contributors

P. Ching, M. Birmingham, and T. Goodman planned the study and data analyses, and M. Birmingham and T. Goodman conducted the data analyses. All of the authors interpreted the results, contributed to the writing, and commented on previous versions of this paper.

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