TECHNICAL BRIEF

Vitamin A Deficiency: Counting the Cost in Women's Lives

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INTRODUCTION

Over half a million women around the world die each year from conditions related to pregnancy and childbirth (1). The vast majority of these deaths occur in Asia and Africa, areas where prenatal care and delivery services are lacking and a woman's nutritional status is often compromised. Sadly, the majority of women die from conditions that are preventable and could be addressed with proper maternal health programs, improved nutrition status, and better access to prenatal care and delivery systems.

PURPOSE OF BRIEF

This brief examines how vitamin A deficiency may influence maternal mortality in various regions of the world. Current estimates suggest that somewhere between 13.3–22 percent (72,618–104,000) of maternal deaths could be prevented if vitamin A deficiency were completely eliminated (2;3). This could be accomplished by scaling-up programs for improving women's vitamin A status in countries in Asia and Africa where maternal vitamin A deficiency is most prevalent and maternal mortality rates are high.

Two recent projects have estimated the number of maternal deaths attributable to vitamin A deficiency. These come from: 1) a situation analysis of micronutrient deficiencies conducted by the Academy for Educational Development for the Global Alliance for Improved Nutrition (GAIN) using the PROFILES software package (referred to as the PROFILES project) (3) and 2) the Comparative Risk Factor Assessment Project, which was initiated by the World Health Organization and used a standardized methodology to measure the global burden of disease due to more than 20 preventable risk factors (referred to as the CRA project) (2). This brief compares the methods these two projects used to estimate the number of maternal deaths due to vitamin A deficiency.

DEFINING MATERNAL MORTALITY

There are several definitions of maternal mortality in widespread use. The Tenth Revision of the International Classification of Disease (ICD-10) divides maternal deaths into various categories according to the timing and underlying cause of death. For the purpose of this brief a maternal death due to vitamin A deficiency will follow the ICD-10 definition for a 'pregnancy-related death', that is *the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the cause of death* (1).

VITAMIN A DEFICIENCY AND PREGNANCY-RELATED DEATHS

There is biological evidence suggesting that vitamin A deficiency may increase mortality by increasing women's risk of pregnancy-related infections and other conditions that can lead to death (4). Empirical evidence from a single randomized placebo-controlled field trial that included ~20,000 pregnant women living an area of southern Nepal where vitamin A deficiency is prevalent also suggests that interventions which improve women's vitamin A status can reduce maternal mortality. A substantial reduction (40 percent) in pregnancy-related mortality was observed among the women who received vitamin A or beta-carotene supplements on a weekly basis before, during, and after pregnancy (5). The study also showed that pregnant women who became night blind, a well-known sign of vitamin A deficiency, were several times more likely to die in the first six weeks after delivery than those who did not (6).

Additional field trials are currently underway in Bangladesh and Ghana to investigate the health benefits of improving vitamin A status during pregnancy and determine if the results observed in Nepal can be replicated in other settings. In Bangladesh, women are receiving a weekly dose of vitamin A, beta-carotene, or a placebo from early pregnancy through delivery and three months postpartum, while women in Ghana are receiving a weekly dose of vitamin A or a placebo. Results from these two trials are expected in 2007 (Bangladesh) and in 2008 (Ghana).

PROFILES AND THE CRA PROJECTS

Table 1 provides a side-by-side comparison of the methods, assumptions, and sources of data used by the PROFILES and CRA projects. The PROFILES project analyzed data from a subset of 65 countries, mainly located in Asia and Africa where maternal vitamin A deficiency is most prevalent. The PROFILES project attributed 13.3 percent (n = 72,618) of the maternal deaths in those countries to vitamin A deficiency. The CRA project included 191 countries and attributed 21–22 percent (n = 109,000) of all maternal deaths, to vitamin A deficiency. These estimates are generally consistent with each other. However, it is worth examining the calculations in greater detail to determine how future estimates of vitamin A deficiency and maternal mortality may be affected by the use of different assumptions.

Both projects used a similar analytical approach to estimate the number and proportion of maternal deaths attributable to vitamin A deficiency. The four basic steps followed by both projects include:

Background data were collected for each one of the selected countries (or sub-regions) of interest. The PROFILES project estimated the prevalence of vitamin A deficiency among pregnant women (PrevVAD), the annual number of live births, and the maternal mortality ratio for individual countries. The CRA project estimated the prevalence of vitamin A deficiency among pregnant women (PrevVAD), the annual number of live births, and the total number of maternal deaths due to all causes for 14 different sub-regions of the world.

The relative risk of death (RR) among 'vitamin A deficient' pregnant women was estimated from the published results of the intervention trial in Nepal. The relative risk of death measured how much more likely pregnant women with either night blindness (PROFILES project) or low serum retinol concentrations (CRA project) were to die over a fixed period of time compared to pregnant women without those conditions.

The population attributable fraction (PAF) was calculated as PAF = [PrevVAD*(RR-1)]/[PrevVAD*(RR-1)+1], which represents the proportion of maternal deaths due to vitamin A deficiency. The total number of maternal deaths from all causes was multiplied by the PAF to arrive at the number of maternal deaths attributable to vitamin A deficiency for each country (or sub-region) of interest.

Finally, these results were totaled across the countries (or sub-regions) to generate a grand total number of maternal deaths attributable to vitamin A deficiency. The overall proportion of deaths attributable to vitamin A (for either the group of 65 or 191 countries) was then calculated by dividing the total number of maternal deaths attributable to vitamin A deficiency by the total number of maternal deaths from all-cause mortality.

KEY DIFFERENCES

Although the two projects used a similar analytical approach, the final results were affected by the use of slightly different assumptions and sources of data (see Table 1). The factors that had the greatest impact are mentioned here. First, the projects included different countries in their analysis (65 vs. 191). The PROFILES project concentrated on estimating the burden of disease for a group of high-risk countries located primarily in Asia and Africa, while the CRA project calculated the burden of disease due to vitamin A deficiency for the entire world. Second, each project defined 'vitamin A deficiency' differently (night blindness vs. low serum retinol concentrations among pregnant women) and used different sources of information to estimate prevalence rates. The prevalence of night blindness was 5.4 percent (PROFILES), while the prevalence of low serum retinol concentrations was slightly higher at 5.6 percent (CRA). Finally, the projects used different estimates for the relative risk of death that were consistent with the way each project defined vitamin A deficiency (RR=3.85 for night blindness (PROFILES) vs. RR=4.51 for low serum retinol concentrations (CRA), see Table 1).

Figure 1 illustrates how the estimated proportion of maternal deaths due to vitamin A deficiency would changes if different assumptions are used. Results were calculated for vitamin A deficiency prevalence rates ranging from 2.5–15 percent and a relative risk of death ranging from 1.5–10. This example shows how applying different relative risk estimates from the ongoing field trials in Bangladesh and Ghana could affect estimates of the burden of disease due to vitamin A deficiency in settings where vitamin A deficiency prevalence rates vary.

IMPLICATIONS FOR NUTRITION POLICY AND PROGRAMS

This brief presents two sets of quantitative estimates for the contribution of vitamin A deficiency to maternal mortality. These calculations suggest that a substantial number of maternal deaths in Asia and Africa could be prevented, just by eliminating vitamin A deficiency among women of reproductive age.

In reality, micronutrient deficiencies rarely occur in isolation. An overview of global data shows high prevalence rates of individual micronutrient deficiencies in many of the same countries. Thus, many women may suffer from multiple micronutrient deficiencies at the same time. Some of these nutrients affect closely related biological systems. For example, both vitamin A and zinc play important roles in maintaining aspects of immune function (7) and both vitamin A and iron affect hemoglobin metabolism (8).

However, relatively little data is available to quantify the joint distribution of multiple micronutrient deficiencies. To date, no published studies have estimated the impact that multiple deficiencies have on specific health outcomes, including maternal mortality. Another group working on iron deficiency as a risk factor for the CRA project measured the global burden of disease due to iron deficiency anemia and attributed 115,000 maternal deaths to this particular risk factor (9). Theoretically, the potential number of maternal deaths saved by reducing vitamin A deficiency (n=109,000) and iron deficiency anemia (n=115,000) can be counted separately. In reality, the total number of lives saved by implementing a comprehensive set of intervention programs would probably be slightly less than the sum of these two figures suggests. Programs that succeed in reducing both vitamin A deficiency and iron deficiency anemia will almost certainly save some women who were at high risk of mortality from both of these conditions, but will also benefit all of the women by reducing other adverse health outcomes that are independently associated with each one of these nutrition-related conditions.

In summary, current estimates suggest that eliminating vitamin A deficiency could prevent somewhere close to 100,000 maternal deaths each year. While these estimates are uncertain in some respects, they should continue to stimulate important discussions about the role that micronutrient deficiency control programs have in improving health outcomes for millions of women around the world and inspire decision-makers to consider launching vitamin A deficiency control programs for women of reproductive age.

Table 1. Comparison of the methodology, assumptions, and data sources used to quantify the number of maternal deaths attributable to vitamin A deficiency

Variables	**PROFILES Projection**	**CRA Project**
Number of countries	A) 65 countries listed in Annex 1 of the Profiles Projection (3)	K) 191 member states of the World Health Organization, classified into the 14 epidemiological sub-regions defined in the The world health report 2002 (10)
Level of analysis	B) Calculations done at the individual country level, then summed to obtain a total estimate for the group of 65 countries	L) Calculations done at the sub-regional level, then summed or averaged, as needed, across the 14 sub-regions to obtain a global estimate
Definition of vitamin A deficiency	C) Night blindness among pregnant women	M) Low serum retinol concentrations (< 0.70 mol/L)
Prevalence of vitamin A deficiency among pregnant women	D) 5.4 percent (n=5,276,382); based on Tables on the global burden of vitamin A deficiency (11) and updated Demographic and Health Survey datasets	N) Global estimate = 6.8 percent prevalence (n=7,257,000 cases); the prevalence of low serum retinol concentrations listed for 98 countries in West 2002 (12) was combined with an assigned prevalence of zero for the remaining 93 countries
Annual number of live births	E) 97,722,000; based on the World Population Prospects online database (13)	Not needed for the CRA project
Maternal mortality ratio	F) 560	Not needed for the CRA project
Total number of pregnant women	Not needed for the PROFILES projection	O) Global estimate = 107,413,000; defined as the annual number of live births listed in The state of the world's children 2001 (14)

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Variables	PROFILES Projection	CRA Project
Relative risk (RR) of death among vitamin A deficient pregnant women vs. non-vitamin A deficient pregnant women	G) RR=3.85 Estimate based on the relative risk of death (RR = 0.26) among Nepali women in the placebo group who did not develop night blindness during pregnancy vs. those who did (6). This translates into a relative risk of death for night-blind pregnant women of 1/0.26=3.85.	P) RR=4.51 Estimate based on the protective effect of vitamin A or beta-carotene vs. placebo supplementation against death among pregnant Nepali women through 6 weeks postpartum (RR=0.60), adjusted for a 19 percent prevalence of low serum retinol concentrations in the population (5); see text and Table 4.4 in Rice et al for a detailed description of the steps used in the adjustment process (2)
Total number of maternal deaths per year	H) 547,080; calculated by multiplying the number of births in a given year (Bt) [from step E] * the maternal mortality ratio (MMR) [from step F]	Q) 509,000; based on data annex tables produced by the Global Burden of Disease Study 2000 (15) to support the CRA project (2)
Percentage of maternal deaths attributable to vitamin A deficiency	I) 13.3 percent; calculated by dividing the total number of deaths due to vitamin A deficiency [from step H] by total number of maternal deaths [from step J]	R) 21 percent (15–29 year old women), 22 percent (30–44 year old women); calculated by dividing the total number of maternal deaths due to vitamin A deficiency in each age group [from step S] by the total number of maternal deaths in each age group for each of the 14 sub-regions separately; the global PAF for each age group was calculated as a weighted average based on the number of deaths in each region
Number of maternal deaths attributable to vitamin A deficiency	J) 72,618 (3); deaths related to night blindness (Dnb) were calculated as a function of the number of births in a given year (Bt), the maternal mortality ratio (MMR) and the population attributable fraction of deaths associated with night blindness (PAFnb): DnB = Bt*MMR*PAFnb for each country separately, then summed across the 65 countries	S) 104,000 (based on data annex tables produced for the Global Burden of Disease Study 2000) (15) to support the CRA project (2); deaths related to low serum retinol concentrations (Dsr) were calculated as a function of the number of maternal deaths (Dgbd) and the population attributable fraction of deaths associated with low serum retinol concentrations (PAFsr): Dsr = Dbgd * PAFsr for each of the 14 sub-regions separately, then summed across sub-regions

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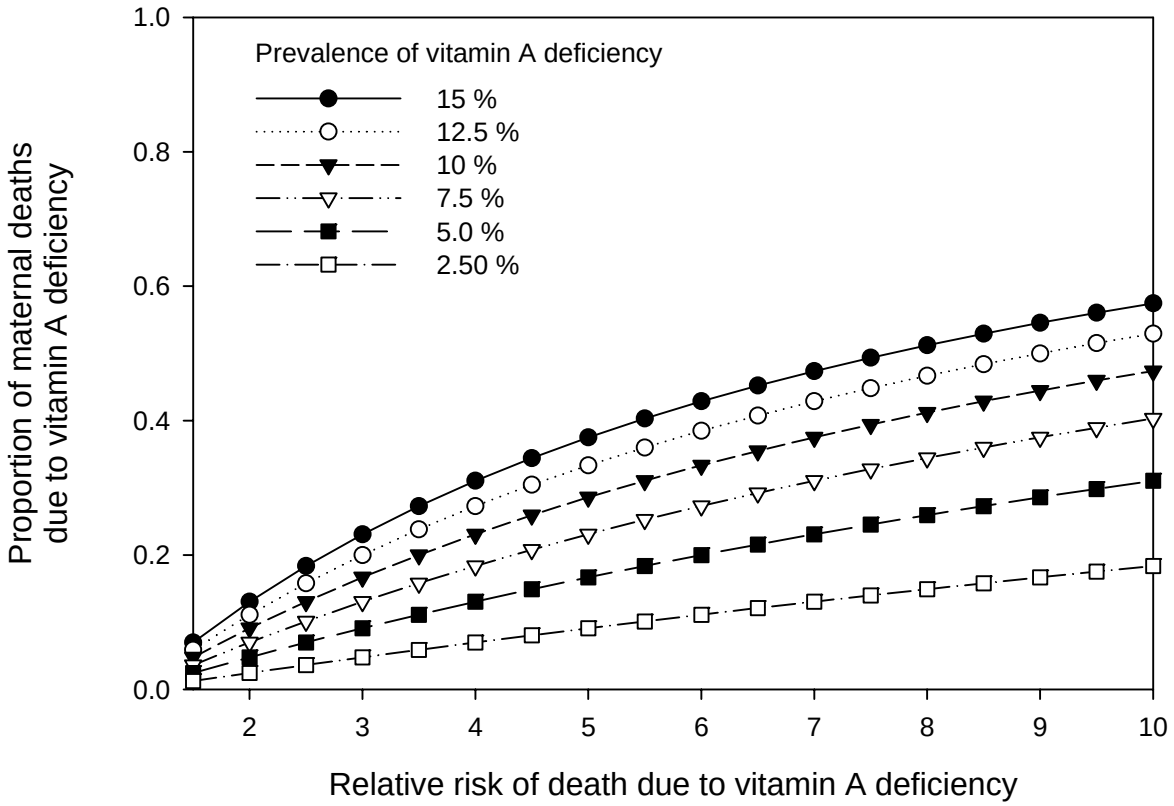

Figure 1. Estimated proportion of maternal deaths due to vitamin A deficiency assuming different relative risks of death and different prevalence rates of vitamin A deficiency

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