Maternal vitamin A:
Effects on mothers, effects on offspring

Vitamin A deficiency can compromise maternal health and survival and offset child development in poor societies.

In Gangetic South Asia, vitamin A deficiency contributes to maternal undernutrition during pregnancy and lactation. However, while known to exist, the need to estimate its extent, severity and health consequences, and the public health benefits of prevention, among mothers and children is an urgent research priority. Over the past two decades the Center for Human Nutrition of the Johns Hopkins Bloomberg School of Public Health (JHU) has been investigating this nutritional problem in rural South Asia, with support of the Bill and Melinda Gates Foundation and USAID, by conducting community intervention trials and epidemiological studies in its two large population research sites, in Nepal (Nepal Nutrition Intervention Project - Sarlahi, or NNIPS) and Bangladesh (The JiVitA Project). The goals of the research have been to inform and guide policies and programs for preventing vitamin A deficiency and its short and long term consequences among mothers and their offspring throughout the region.

Maternal night blindness
Along the southern rural plains of Nepal, in the district of Sarlahi, home to a quarter of a million people, JHU’s studies have revealed that 10-15% of pregnant women develop night blindness, a visual disturbance during twilight attributable to vitamin A deficiency. Women with night blindness are far more likely to have health problems than those with normal night time vision, reflected by a greater chance of being biochemically vitamin A-deficient, wasted, anemic and ill with infections during pregnancy. Night blind mothers face a higher risk of their infants dying in the first half of infancy than non-night blind gravida and a far higher risk of their own mortality, largely due to infection, for up to two years following pregnancy in comparison to pregnant women without the condition (Figure). This extended health risk exists even though the inability to see at night often resolves shortly after giving birth. That is, the health risk associated with this condition persists long after the clinical symptom disappears. Given that night blindness can be gleaned from a simple, standardized history, these findings in Nepal, which have been corroborated by studies in India and elsewhere, led the International Vitamin A Consultative Group to issue policy briefs during the past decade warning of its existence in pregnancy and offering methods and cutoffs for its assessment. The findings led the Demographic Health Surveys over the past decade to include a history of maternal night blindness in its core module that has generated country prevalence rates and formed the basis for the most recent World Health Organization estimates of there being nearly 10 million pregnant women at a given time with night blindness, among an estimated 19 million with physiologically significant vitamin A deficiency in low income countries.

Effects of maternal vitamin A supplementation
Nepal: A major question of the past 15 years has been whether maternal vitamin A supplementation could reduce health risks and improve maternal and infant survival?
A first trial carried out by JHU among ~22,000 pregnancies in Sarlahi District, Nepal, showed that weekly, maternal supplementation with vitamin A, either “preformed” or in the form of its plant precursor beta-carotene, given to meet recommended dietary levels before, during and following pregnancy, could reduced maternal mortality by ~44%, from 704 to 385 deaths per 100,000 pregnancies11 (Table). No overall impact was observed on infant mortality, except among babies born to mothers prone to night blindness, whose risk of death was markedly reduced by maternal vitamin A supplementation12. Longer term effects, however were apparent among offspring. Specifically, a ~10 year follow-up study supported by the Gates Foundation was the first to observe an increase in lung capacity among preadolescent children whose mothers received weekly vitamin A supplements versus placebo13, a finding predicted from decades of animal studies. Further, children born to vitamin A supplemented mothers exhibited a higher circulating level of natural antibodies, derived from cell lines that tend to mature in number in early infancy14, a finding also supported by experimental findings in animals. It is equally plausible that hearing loss could have been lowered, stemming from the vitamin’s role in regulating middle and inner ear development, but this has not yet been examined. Other health and development outcomes that have been assessed, including blood pressure, metabolic syndrome15 and cognition, have not been found to be affected at prepubescent ages.

Bangladesh: The mortality impact observed in Nepal spurred wider interest to extend the findings to other undernourished settings. At the turn of the millennium, JHU set up the JiVitA site in northern Bangladesh2 [see Brief No. 1] where a second, placebo-controlled trial (JiVitA-1) of weekly vitamin A or beta-carotene supplementation was conducted among 60,000 enrolled mothers. Neither a reduction in maternal or infant mortality was observed16. The lack of maternal mortality impact has been attributed to contextual differences17. In Bangladesh, the mortality rate of women related to pregnancy turned out to be far lower, ~30% that seen in Nepal (231 per 100,000) (Table), which was accompanied by a more varied and nutritious diet, a lower prevalence of vitamin A deficiency (~7% vs 19%) and a higher birth attendance rate. However, other health benefits are emerging, such as a recently reported 30-40% lower incidence of bacterial vaginosis among vitamin A or beta-carotene versus placebo supplemented mothers18, a finding that is consistent with a known role for vitamin A in maintaining the integrity of the epithelial linings of the cervix and vagina19. Bacterial vaginosis has been estimated to affect ~8% of all pregnant women and is a risk factor for preterm birth18. Analyses are underway to explore additional plausible effects of maternal supplementation. [A third trial, in Ghana, has also not observed a significant reduction in maternal mortality with weekly vitamin A supplementation, likely reflecting population differences in risks of vitamin A deficiency, maternal mortality and other risk factors17]. Findings from JiVitA-1 and the earlier NNIPS-2 trials continue to reveal new evidence on how maternal and early life micronutrient exposures, including vitamin A, can influence short and long term health and survival in the vast, population dense Gangetic flood plains of South Asia.

### Mortalities: Night Blind vs. Non-Night Blind Women

<table>
<thead>
<tr>
<th>Postpartum, wks</th>
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<th>Non-night blind</th>
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<tbody>
<tr>
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<tr>
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*Figure. Period-specific mortality rate per 100,000 pregnancies among night blind and non-night blind women in placebo group in the NNIPS-2 randomized maternal vitamin A or beta-carotene supplementation trial in Sarlahi, Nepal, 1994-97*2.
### References


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**JiVitA** is a project of the Center for Human Nutrition of Johns Hopkins University, spanning 19 unions of Gaibandha and Rangpur Districts in rural Northwestern Bangladesh. JiVitA has been conducting community trials, supported by epidemiologic, ethnographic, and laboratory research since 2000, to reveal the impact of public health interventions in order to guide nutrition and health programs and policies in Bangladesh and elsewhere in South Asia.
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