DISTRIBUTION AGREEMENT

Signature ___________________________________ Date______________

Michelle Deneen

A Community-Based Integrated Agriculture and Nutrition Program is Associated with Improved Vitamin A Status of Lactating Women but not their Infants in Western Kenya

By Michelle Deneen

Degree to be awarded: Master of Public Health

Global Epidemiology

Committee Approval:

Signature ____ Date_______________

Amy Webb Girard, PhD
Committee Chair
Assistant, Professor, Hubert Department of Global Health
Rollins School of Public Health, Emory University

Signature ____ Date_______________

Aryeh Stein, MPH, PhD
Committee Member
Professor, Hubert Department of Global Health and Department of Epidemiology
Rollins School of Public Health, Emory University

A Community-Based Integrated Agriculture and Nutrition Program is Associated with Improved Vitamin A Status of Lactating Women but not their Infants in Western Kenya

By Michelle Deneen

B.S., Pepperdine University, 2012

Thesis Committee Chair: Amy Webb Girard, PhD

An abstract of a thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements of the degree of Master of Public Health in Global Epidemiology
2015

A Community-Based Integrated Agriculture and Nutrition Program is Associated with Improved Vitamin A Status of Lactating Women but not their Infants in Western Kenya

ABSTRACT

By Michelle Deneen

Background. Vitamin A deficiency is a significant public health problem in Western Kenya. Agricultural household food production interventions using biofortified crops such as orange-fleshed sweet potato (OFSP) show potential for addressing vitamin A deficiency.
Objective. The objective of this study is to determine whether an integrated agriculture, antenatal care, and nutrition program is associated with maternal and infant retinol binding protein (RBP) and anemia at nine months postpartum.
Methods. This is a nested cohort study within a larger study in which 8 health facilities and their catchment areas were randomized to control or intervention. The intervention included nutrition education during antenatal care, nutrition training for community health workers, monthly women's clubs, and OFSP voucher distribution at antenatal care visits, redeemable at local vine farmers. Sociodemographic and biochemical data were collected from women at enrollment in early pregnancy and again from women and infants at four and nine months postpartum. Mixed modeling was used to test associations of program participation with low RBP (women <1.05 µmol/L, infants <0.83 µmol/L) and anemia at nine months, controlling for clustering by sublocation, baseline differences, and key sociodemographic factors.
Results. The odds of low RBP were decreased for intervention mothers compared to control mothers (OR=0.42, 95%CI: 0.19-0.95). Maternal anemia, infant low RBP, and infant anemia at nine months did not differ by intervention.
Conclusions: This integrative program improved the vitamin A status of women but not infants. Further research is needed to understand which aspects of the intervention contributed to improved maternal vitamin A status.

A Community-Based Integrated Agriculture and Nutrition Program is Associated with Improved Vitamin A Status of Lactating Women but not their Infants in Western Kenya

By Michelle Deneen

B.S., Pepperdine University, 2012

Thesis Committee Chair: Amy Webb Girard, PhD

A thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements of the degree of Master of Public Health in Global Epidemiology

2015

ACKNOWLEDGMENTS

The author would like to thank the COVA participants for their willingness to participate in the study, the Mama SASHA staff including the COVA staff, the International Potato Center (CIP), and the faculty of Rollins School of Public Health at Emory University, particularly the thesis chair, Dr. Amy Webb Girard and thesis committee member Dr. Aryeh Stein for their valuable guidance and mentorship in this project. The findings and conclusions in this thesis are those of the author and do not necessarily represent the views of the Mama SASHA project or Rollins School of Public Health. I greatly appreciate the contributions of Dr. Donald Cole, Dr. Jan Low, Dr. Carol Levin, Dr. Fredrick Grant, Mr. Okuku Haile Selassie and Mrs. Rose Wanjala, all of the Mama SASHA Project. Financial support for the author to travel to the Kenyan field office was received through the RSPH Global Field Experience program from the Anne E. and William A. Foege Global Health Fund and the Mama SASHA project.

TABLE OF CONTENTS

CHAPTER 1: INTRODUCTION

Maternal and child malnutrition is a major public health problem around the world, with the greatest burden in low-income countries. Maternal nutritional status during pregnancy as well as nutritional status in infancy and childhood can affect many health outcomes throughout the lifespan. Adequate nutrition early in life is crucial to development, and has long-term effects on many structures and functions in children.

Vitamin A deficiency specifically can cause vision loss and poor immune function, and the highest prevalence is in pregnant women and young children. The most common strategies for addressing vitamin A deficiency are supplementation and fortification, but those often do not reach, or are not sustainable in, rural and very poor communities where they are much needed [1]. Household food production and agriculture strategies may be a better alternative for meeting the needs of rural women and children [1-3]. However, most of the existing studies on household food production interventions are not methodologically rigorous, so it remains difficult to determine if these types of programs are truly effective at improving the nutritional status of women and children [1].

The data for this thesis comes from a sub-study of the larger Mama SASHA (Sweet potato Action for Security and Health in Africa) project in Western Kenya. The project's goal was to increase vitamin A knowledge in mothers to improve the vitamin A status in both the mothers and their infants. Facilities and their catchment areas (rather than individuals) were randomized to receive either standard of care or the intervention which involved three components: enhanced nutrition education and counseling during prenatal care visits, receiving vouchers for orange-fleshed sweet potato vines, and participation in monthly mother's clubs focused on nutrition. The Cohort Study of Vitamin A (COVA) study is a nested cohort study within the larger project. Mothers were recruited at their first antenatal care visit and were also studied in the final trimester of pregnancy, as well as four and nine month post-partum. At each visit, they completed a questionnaire, gave a blood sample, and had basic anthropometry measurements taken. At the four and nine month post-partum visits, mothers additionally gave breast milk samples, and infant blood samples and anthropometry were taken.

The objective of this thesis is to assess whether the intervention was associated with improved vitamin A status and anemia of mothers and their infants at 9 months postpartum. This thesis will additionally examine whether varying degree of program participation in Mama SASHA activities was associated with vitamin A and anemia status. In light of recent critiques of nutrition sensitive agricultural evaluations, analyses controlled for the clustered design of the study, significant differences at enrollment and potentially influential covariates. This thesis will be valuable in identifying potential integrated intervention opportunities to improve maternal and child nutrition in Kenya and other low-income countries.

CHAPTER 2: LITERATURE REVIEW

2.1 Burden and Physiologic Effects of Vitamin A Deficiency

Vitamin A deficiency is a major public health problem but is often forgotten in place of more obvious diseases such as malaria, tuberculosis, and HIV-AIDS. The Institute for Health Metrics and Evaluation estimate nearly 120,000 deaths worldwide, nearly 30,000 direct global DALYs (disability adjusted life years) and over 10 million indirect global DALYs are attributable to vitamin A deficiency annually, based on 2010 data [4]. This burden is disproportionately concentrated in low-income countries in Southeast Asia and Africa; 4-6% of Africa's total disease burden is due to vitamin A deficiency [5]. Kenya, like many other African countries, has a high burden of vitamin A deficiency. A nutrition intervention study in Kenyan school children in Embu district found that 22% of children had severe vitamin A deficiency and an additional 69% had moderate vitamin A deficiency at baseline (before their intervention) [6].

Micronutrient deficiencies, and vitamin A deficiency in particular, have adverse health consequences independent of other forms of undernutrition. Undernutrition commonly refers to underweight (≤2 standard deviations from median weight for age), stunting (≤2 standard deviations from median height for age), and wasting (≤2 standard deviations from median weight for height for age). While often accompanied by these forms of malnutrition, vitamin A deficiency alone causes many poor health outcomes. It can lead to vision problems including blindness, impaired growth and development, and poor immune function [7, 8]. One meta-analysis found that vitamin A supplementation in children under 5 was associated with a 24% decrease in all-cause mortality, as well as a decrease in mortality from diarrhea and incidence of measles [8]. The prevalence of vision problems was 70% lower in children receiving adequate vitamin A supplements than those who did not [8].

Pregnant and lactating women and their infants are at an especially high risk of vitamin A deficiency and the health problems resulting from this deficiency. Fetal and newborn vitamin A status is entirely dependent on maternal intake of vitamin A, so dietary recommendations for pregnant and lactating mothers are higher than for other women [9]. The effects of maternal vitamin A deficiency are long lasting; maternal vitamin A is essential to fetal kidney development, which may be associated with hypertension later in life [10, 11]. Adequate vitamin A in pregnancy may also be associated with decreased risk of low birth weight and small for gestational age [12, 13], though these associations are not seen in all studies [14]. Additionally, vitamin A deficiency is associated with anemia, or low hemoglobin, independent of iron status [15, 16] and supplementation has been shown to decrease anemia in pregnancy [14, 17]. The mechanisms by which vitamin A affects hemoglobin occurs is not clearly understood [16].

2.2 Dietary Sources of Vitamin A and Bioavailability

Vitamin A comes from the diet in multiple forms: as retinol, retinyl esters, or provitamin A-carotenoids [9]. Retinol is found in animal products, especially liver and liver oils, while carotenoids are found in yellow, orange, and green leafy vegetables [9]. Carotenoids, primarily beta carotene, are the most important source of vitamin A in contexts such as Kenya, where meat and other animal products are not major components of the diet. Carotenoids, however, must be converted to retinol in the body, so more must be consumed to provide the body with equivalent amounts of retinol [9]. Beta carotene conversion — the ability to convert beta carotene from foods and supplements into retinol — varies widely, from 3.6-28:1 by weight [18]. Many factors are associated with the varying bioavailability; the most important are food matrix (i.e. molecular make-up of the food), processing, and presence of fat, other carotenoids, and dietary fiber in the meal [19]. The varying bioconversion of beta carotene does not affect its safety as a source of vitamin A because conversion to vitamin A in the body decreases as the dose of beta carotene increases, reducing the likelihood of overdose [20, 21].

2.3 Factors Associated with Vitamin A Deficiency

Extensive and growing evidence indicate that many sociodemographic and economic factors are important determinants of malnutrition and vitamin A deficiency, in particular [22-30]. As with many adverse health outcomes, risk of vitamin A deficiency increases with lower socioeconomic status [22, 24, 26, 28]. Parental education [24] and family size [22] may also be independently associated with a higher risk of vitamin A deficiency. A cross-sectional study in rural communities in the Philippines found associations between low maternal education and employment and increased risk of vitamin A deficiency [27].

A study in Indonesia found that women whose families spent less of their food money on animal and plant-based foods and more on rice were at higher risk for vitamin A deficiency, indicating that vitamin A deficiency is more common in poorer women who can only afford grains [23]. Another study in Indonesia found that parental education, household earnings, and land ownership were significantly associated with serum retinol level [25]. In Malawi, lower maternal age and having no paid work were associated with higher levels of vitamin A deficiency [29].

Gender inequality and cultural beliefs surrounding pregnancy also impact women's micronutrient status. One example of this is in intra-household food allocation. Even if a household has an adequate supply of vitamin A rich foods, it is common in Kenya for women to have last priority for food allocation [31]. Additionally, cultural practices and norms may cause women to reduce overall food intake or intake of specific foods during pregnancy for fear of a big baby [32]. Some foods are also considered taboo during pregnancy based on superstitions [32].

2.4 Strategies for Addressing Vitamin A Deficiency

Myriad approaches exist to mitigate vitamin A and other micronutrient deficiencies, and research is ongoing to identify strengths and weaknesses of each approach within various and complex contexts. The most extensively researched strategies include supplementation, fortification, and agriculture. In considering these various strategies for scaled implementation, policy makers and programmers must consider a range of issues including intervention effectiveness, costs, feasibility of implementation, ability to reach and impact target populations, and cultural acceptability. The interplay of these issues means that no single intervention is likely to be successful for every population in every location. Rather, a combination of strategies targeted appropriately to different populations is required [33].

2.4.1 Supplementation

Micronutrient supplementation is the most commonly applied approach for mitigating micronutrient deficiencies among women of reproductive age and young children. Supplementation is very popular because specific nutrients can be delivered directly to the individual, bypassing difficult behavioral and socio-economic changes such as increasing dietary diversity or access to healthy foods. Supplementation with vitamin A is also highly efficacious. A meta-analysis on the preventive effects of vitamin A supplementation found that supplementation significantly reduced all-cause infant and child mortality as well as diarrhea-specific mortality with minimal side effects [34]. The results of a meta-analysis by Thorne-Lyman and Fawzi (2012) showed that vitamin A supplementation, largely in the form of its precursor beta-carotene, was also associated with a decreased risk of anemia during pregnancy [14]. Additionally, because multiple micronutrients can be supplemented at the same time without substantially impacting absorption [35], co-deficiencies can be easily addressed.

Supplementation, however, is not without challenges. Health workers often distribute multiple micronutrient supplements for pregnant women and young children during antenatal care visits or at the time of immunizations. This approach makes it easy to target pregnant women and children, but since poor women and children are generally less likely to receive antenatal care and routine immunizations, this method of distribution may not be equitable [36]. This potential for inequity highlights delivery logistics as the biggest downside to supplementation programs, despite their success at reducing mortality.

Intermittent (e.g. every six months) high-dose supplementation, rather than physiologic doses given much more frequently, is a common strategy to partially overcome the logistics barrier for many types of supplements, including vitamin A. However, no large studies show any benefit on mortality or vitamin A deficiency from this type of supplementation [37, 38].

2.4.2 Fortification

Fortification of staple foods can be very effective at reaching entire populations. The basic concept is to add micronutrients of interest, such as iron, folic acid, vitamin A or iodine to staple foods or condiments. The most commonly fortified foods include sugar, flour (wheat and maize), oil and salt. Many countries have successfully fortified oil, margarine, and sugar with vitamin A, and it could potentially be added to cereal flours and meals as well [39]. One significant challenge with fortification in low-income countries, however, is the lack of a staple that is both widely consumed and amenable to fortification. A second limitation is the decentralized nature of staple grain processing in low-income contexts. In countries with many small flour mills, for example, it is difficult to implement and monitor fortification programs [39]. Finally, many of the poorest and most rural people do not consume substantial amounts of processed staples, preventing the benefits of fortification from reaching those with the greatest need [40]. For infants in particular, population level fortification often provides an insufficient quantity of micronutrients per gram of fortified staple as the fortificant level is set for adult needs. Specially fortified infant staple grains are often prohibitively expensive for low income households. Home-based fortification with micronutrient powders for children under two – the addition of a small sachet of lipid encapsulated micronutrients to child porridges – is considered a more effective strategy for reaching this particular population but this method has many of the same issues as supplementation in distributing the powders [41] and in reaching rural populations.

2.4.3 Agricultural Interventions

Agricultural interventions, especially in the form of household food production, are another approach used to combat low dietary diversity and resulting micronutrient deficiencies. Several reviews examined the effects of agricultural interventions on maternal and child nutrition. Berti (2004), found that while these strategies consistently increase food production, nutritional improvements require additional inputs, namely nutrition education and marketing and gender inclusivity [2]. A later review by Girard (2012) confirmed the importance of education and gender considerations, but also noted that evidence for the effects of agriculture interventions on micronutrient intake and status is growing in quantity and quality [1]. Agricultural interventions are generally promising in terms of sustainability, but the necessity to adapt programs to each context and their susceptibility to seasonality and drought [42] are potential weaknesses.

In recent years, biofortification has been increasingly promoted as a viable approach to addressing micronutrient deficiencies through agriculture. Biofortification consists of intentionally breeding crops to be richer in micronutrients. The general concept is that biofortified seeds are a very cost-effective solution, since seeds only need to be distributed at one point in time, after which they are self-sustaining [43]. While dietary diversification of foods naturally rich in nutrients would be ideal, biofortification provides a potential alternative in poverty-stricken areas where improving dietary diversification with existing locally available crops is extremely difficult [44]. The initial research and development money required is one obstacle to biofortification [43].

Orange-fleshed sweet potato (OFSP) is biofortified to be high in beta carotene and energy, with potential utility in countries where consumption of sweet potato as a staple food is high, such as Kenya. The traditional white and yellow sweet potato varieties in Kenya are very low in beta carotene compared to OFSP [45]. Even after boiling, OFSP retains a high level of bioavailable vitamin A [46, 47]. Most other vitamin A rich foods are expensive or unavailable in poor, rural areas, making OFSP an especially promising tool to address vitamin A deficiency in Western Kenya [48]. OFSP grows well in east Africa and is a culturally acceptable substitute for other varieties of sweet potato, so distributing vines and creating demand remain the biggest challenges [45, 48].

Hotz et al. (2012), implemented a program in rural Mozambique using OFSP and an integrated agricultural, demand creation, and marketing program [49]. The intervention was successful both at increasing the proportion of sweet potatoes consumed that were OFSP and overall vitamin A intake [49]. A similar agriculture program by the same group in Uganda was also successful at achieving these two outcomes, as well as increasing serum retinol levels in children [50]. In a different integrated nutrition and agriculture intervention in Mozambique, the program increased household production of OFSP and significantly increased vitamin A intakes and serum retinol levels in young children [51].

2.5 The Mama SASHA Project

The Mama SASHA (Sweet potato Action for Security and Health in Africa) Project was a 5-year integrated nutrition, agriculture and health proof of concept project that utilized OFSP to combat vitamin A deficiencies in Western Kenya. Western Kenya is largely rural and poor, and has the highest prevalence of vitamin A deficiency in the country [52]. The project targeted pregnant and lactating women with enhanced nutrition education and health services and agricultural support in the form of vouchers OFSP planting materials delivered via community and facility based platforms.

The community-based intervention had four components:

1. Health workers were trained in antenatal nutrition topics, especially related to vitamin A and OFSP. They provided education to women at antenatal care visits.
2. Community health workers were trained in the same topics and facilitated linkages of women to antenatal care and led pregnant mothers clubs.
3. Women's clubs met monthly in each community with pregnant women and new mothers to discuss health and nutrition topics.
4. Women received vouchers for OFSP vines at antenatal care visits, which were redeemable at locally established vine multipliers (i.e. specially trained farmers) as part of the project.

The control facilities received standard of care and health education at antenatal care visits as mandated by the Kenyan government. There were no women’s clubs or OFSP activities in the control communities.

The data for this thesis comes from a nested sub-study of the larger Mama SASHA project, called the Cohort Study of Vitamin A (COVA) study. COVA is a nested cohort study within the larger intervention study. The study recruited mothers during their first prenatal care visit and followed-up with visits in the final trimester of pregnancy, as well as four and nine month post-partum. At each visit, women completed a questionnaire, gave a blood sample, and had basic anthropometry measurements taken. At the four and nine month post-partum visits, mothers additionally gave breast milk samples, and infant blood samples and anthropometry were taken.

CHAPTER 3: MANUSCRIPT

3.1 Title

A Community-Based Integrated Agriculture and Nutrition Program is Associated with Improved Vitamin A Status of Lactating Women but not their Infants in Western Kenya

3.2 Contribution of the Student

The student, Michelle Deneen, formulated the research question, developed analysis plan, conducted all analysis, and did all writing of the thesis with advisement from the faculty committee members.

3.3 Abstract

Background. Vitamin A deficiency is a significant public health problem in Western Kenya. Agricultural household food production interventions using biofortified crops such as orange-fleshed sweet potato (OFSP) show potential for addressing vitamin A deficiency.

Objective. The objective of this study is to determine whether an integrated agriculture, antenatal care, and nutrition program is associated with maternal and infant retinol binding protein (RBP) and anemia at nine months postpartum.

Methods. This is a nested cohort study within a larger study in which 8 health facilities and their catchment areas were randomized to control or intervention. The intervention included nutrition education during antenatal care, nutrition training for community health workers, monthly women's clubs, and OFSP voucher distribution at antenatal care visits, redeemable at local vine farmers. Sociodemographic and biochemical data were collected from women at enrollment in early pregnancy and again from women and infants at four and nine months postpartum. Mixed modeling was used to test associations of program participation with low RBP (women <1.05 μmol/L, infants <0.83 μmol/L) and anemia at nine months, controlling for clustering by sublocation, baseline differences, and key sociodemographic factors.

Results. The odds of low RBP were decreased for intervention mothers compared to control mothers (OR=0.42, 95%CI: 0.19-0.95). Maternal anemia, infant low RBP, and infant anemia at nine months did not differ by intervention.

Conclusions: This integrative program improved the vitamin A status of women but not infants. Further research is needed to understand which aspects of the intervention contributed to improved maternal vitamin A status.

3.4 Background

The Institute for Health Metrics and Evaluation estimate nearly 120,000 deaths worldwide, nearly 30,000 direct global DALYs (disability adjusted life years) and over 10 million indirect global DALYs are attributable to vitamin A deficiency annually [4]. This burden is disproportionately concentrated in low-income countries in Southeast Asia and Africa; 4-6% of Africa's total disease burden is due to vitamin A deficiency [5]. Kenya, like many other African countries, has a high burden of vitamin A deficiency. A nutrition intervention study in Kenyan school children in Embu district found that 22% of children had severe vitamin A deficiency and an additional 69% had moderate vitamin A deficiency at baseline (before their intervention) [6].

Vitamin A deficiency can cause vision loss and poor immune function, and the highest prevalence is in pregnant women and young children. The most common strategies for addressing vitamin A deficiency are supplementation and fortification, but those often do not reach, or are not sustainable in, rural and very poor communities where they are much needed [1]. Household food production and agriculture strategies may be a better alternative for meeting the needs of rural women and children [1-3]. However, most of the existing studies on household food production interventions are not methodologically rigorous, so it remains difficult to determine if these types of programs are truly effective at improving the nutritional status of women and children [1].

Orange-fleshed sweet potato (OFSP) is biofortified, via traditional plant breeding strategies, to be high in beta carotene, with potential utility as a vitamin A strategy in countries where consumption of sweet potato as a staple food is high, such as Kenya. The traditional white and yellow sweet potato varieties in Kenya are very low in beta carotene compared to OFSP [45]. Even after boiling, OFSP retains a high level of bioavailable vitamin A [46, 47]. Most other vitamin A rich foods are expensive or unavailable in poor, rural areas, making OFSP an especially promising tool to address vitamin A deficiency in Western Kenya [48]. OFSP grows well in east Africa and is a culturally acceptable substitute for other varieties of sweet potato, so the biggest challenges remaining are distributing vines and creating demand [45, 48].

This analysis will assess an integrated agriculture, nutrition and antenatal care program promoting production and consumption of OFSP by pregnant and breastfeeding women and their infants 6 months and older. The objective is to assess whether the intervention was associated with improved vitamin A status and anemia of mothers and their infants at 9 months postpartum. This analysis will additionally examine whether varying degree of program participation in Mama SASHA activities was associated with vitamin A and anemia status. In light of recent critiques of nutrition sensitive agricultural evaluations, analyses controlled for the clustered design of the study, significant differences at enrollment and potentially influential covariates. This analysis will be valuable in identifying potential integrated intervention opportunities to improve maternal and child nutrition in Kenya and other low-income countries.

3.5 Methods

3.5.1 Overview

The Mama SASHA (Sweet potato Action for Security and Health in Africa) Project was a 5-year integrated nutrition, agriculture and health proof of concept project that utilized OFSP to combat vitamin A deficiencies in Western Kenya. The project targeted pregnant and lactating women with enhanced nutrition education and health services and agricultural support in the form of vouchers OFSP planting materials delivered via community and facility based platforms. Eight facilities and their catchment areas in Bungoma and Busia counties Western Kenya were purposively selected based on size-related variables (number of service providers, antenatal clinics (ANC) attendance numbers, and population served), coverage with community health workers (CHW) linked to APHIA II[1], and location criteria. Four facilities and their catchment areas were then randomized to receive the intervention, and four were randomized to be a control. Contamination of two control sites and their catchment areas with OFSP activities led to the selection of two additional facilities in Bungoma County to serve as replacement controls for the Cohort Study of Vitamin A (COVA).

3.5.2 Study Population and Recruitment

COVA, which ran from November 2012 to July 2014, was a cohort study nested within the larger Mama SASHA project designed to measure impacts of the intervention on women and infant's vitamin A status and elucidate potential pathways of impact. The study recruited 505 women at their first prenatal care visit (control=255, intervention=250) from participating facilities. Inclusion criteria were being 17-40 years

---

[1] A USAID-funded health systems strengthening project, implemented by PATH

of age, in early/mid pregnancy (10-24 weeks), planning to breastfeed, and planning to live in their current village until 10 months postpartum. Exclusion criteria were previous involvement with Mama SASHA during earlier pregnancy, living in an intervention village but visiting a control facility, or living in a control village but visiting an intervention facility. The women completed an extensive questionnaire and had blood samples taken at the initial visit and at three subsequent visits in late pregnancy, at 4 months postpartum and at 9 months postpartum for purposes of quantifying food security, diet patterns, program participation, micronutrient status, anthropometry, and anemia. Women additionally gave breast milk samples at 4 and 9 months postpartum to assess breast milk retinol concentrations. Women were excluded from further follow up if they had multiple births or gave birth very preterm (<36 weeks) or to a child with very low birth weight (<1500grams). At the postpartum visits, dietary information and blood samples were collected from the infants for determining intakes of vitamin A rich foods and micronutrient and anemia status.

3.5.3 Intervention and Control

The community-based intervention had four components:

5. Health workers were trained in antenatal nutrition topics, especially related to vitamin A and OFSP. They provided education to women at antenatal care visits.
6. Community health workers were trained in the same topics and facilitated linkages of women to antenatal care and led pregnant mothers clubs.
7. Women's clubs met monthly in each community with pregnant women and new mothers to discuss health and nutrition topics.

8. Women received vouchers for OFSP vines at antenatal care visits, which were redeemable at locally established vine multipliers (i.e. specially trained farmers) as part of the project.

The control facilities received standard of care and health education at antenatal care visits as mandated by the Kenyan government and implemented by the APHIA II program. There were no women's clubs or OFSP activities in the control communities.

3.5.4 Collection of Biochemical Data

Approximately 500 μL of capillary blood were collected by finger prick from mothers and by heel prick from infants. Hemoglobin was quantified from capillary samples collected from a finger or heel prick using a Hemocue Hemoglobin Analyzer [53]. Quantification used the third drop of blood after wiping away the first two drops. Hemocue devices were calibrated each morning using standardized techniques. For the detection of Vitamin A deficiency, retinol binding protein [RBP] was measured with a sensitive and inexpensive Sandwich ELISA technique [54, 55]. This method also simultaneously measured C-reactive protein (CRP) and alpha-1-acid glycoprotein (AGP) as indicators for acute and chronic infection as well as the iron status indicators, ferritin and transferrin receptor. Using CRP and AGP, RBP levels were corrected for inflammation using the Thurnham correction factor method [56].

Hemoglobin levels were adjusted for altitude. A Garmin GPS device measured elevations of health facilities and villages in the field, and elevations were compared to Google Earth data to confirm. All elevations were above 1000m and below 2000m above sea level. Based on WHO guidelines, the adjustment for this elevation range is subtraction of 0.5g/dl [57].

3.5.5 Variable Specification

The data for this analysis was taken from the enrollment and nine-month postpartum visits. All women were asked about participation in Mama SASHA activities at each COVA visit. Women from control communities were asked these same questions to monitor potential contamination. Program participation for the intervention group was classified as full participation or partial/no participation. Full participation (n=83) included any women who received OFSP vouchers, redeemed the vouchers, and attended the women's clubs at any time. Partial/no participation (n=109) included women who were in an intervention community but did not report participating in all three of these components at some point. Because all intervention women in the COVA study received antenatal care, they were exposed to the enhanced nutrition counseling that included information about OFSP and vitamin A. Additionally, Mama SASHA intervention communities received community based activities including field days that promoted OFSP. As such, women in COVA who did not participate in women's clubs or voucher redemption are not equivalent to controls and are thus considered a unique participation group from the controls.

A wealth index was created from the COVA enrollment data. All assets and household characteristic variables with heterogeneity useful for distinguishing the relatively rich from the relatively poor were included. Each asset or household characteristic had a minimum value of 0 and a maximum value of 1. Summing the values of asset and household characteristic variables created the normally distributed wealth index. Wealth index scores were on a scale of 0-20 and were further divided into quartiles.

Food insecurity at enrollment and at nine months was assessed using FAO's Household Food Insecurity Access Scale (HFIAS) [58]. The scores were used to determine the Household Food Insecurity Access Prevalence Category (HFIAP) [58]. Household Dietary Diversity scores at enrollment and at nine months were determined using 2010 FAO Guidelines [59]. Maternal and Household Dietary Diversity was calculated using food frequency questionnaires from the COVA survey and 2010 FAO Dietary Diversity categories [59]. A weighted maternal dietary diversity score (food consumption score) was calculated using FANTA guidelines [60]. Maternal education level was categorized into either primary or post primary.

The most common months of major OFSP harvest are November through March. For the purpose of modeling, the month of the 9-month postpartum visit was classified as during major OFSP harvest or not during major OFSP harvest.

Anemia status was determined based on altitude-adjusted hemoglobin levels and using cutoffs specified by WHO for non-pregnant women and children 6-59 months of age [57]. For logistic regression, anemia was dichotomized into anemic and not anemic. RBP was considered "low" if serum concentration was less than 1.05 μmol/L for women [61], and less than 0.83 μmol/L for infants [62].

3.5.6 Data Analysis

Differences between intervention and control were tested using t-tests for normally distributed continuous variables, Wilcoxon Mann-Whitney for non-normally distributed variables, and chi-squared tests for categorical variables. Mantel-Haenzel chi-squared tests were used to test differences in categorical variables when cell counts were low.

Differences by participation levels (including control as a level) were analyzed using ANOVA tests for normally distributed continuous variables. Kruskal-Wallis tests were used for non-normally distributed continuous variables. Chi-squared tests were again used for categorical variables, and Mantel-Haenzel chi-squared tests were used when cell counts were low.

Mixed logistic regression (using SAS's PROC GLIMMIX) with a random intercept and with sublocation as a random effect were used to examine associations between intervention assignment and low serum levels of RBP and anemia status in both mothers and infants. A similar modelling approach was used to examine associations between level of program participation and low serum levels of RBP and anemia status in these groups. Sublocations (n=22), which are between districts and villages in size, were used in analysis of clustering to allow for more degrees of freedom than facility clusters (n=4 per intervention group), but with more participants per group than in each village. The number of participants per sublocation was between 2 and 67 (median=11.5, IQR: 6-38.5). Covariates considered in the modeling process for maternal outcomes were wealth index quartile at enrollment, household food insecurity prevalence category at nine months, maternal education at enrollment, maternal mid-upper arm circumference at enrollment (due to baseline difference), household dietary diversity category at enrollment (due to baseline difference), RBP or altitude-adjusted hemoglobin at baseline respective to the outcome in the model, and season of the 9-month postpartum visit (major OFSP harvest season or not). Covariates considered in models of infant outcomes were maternal wealth index quartile at enrollment, household food insecurity prevalence category at nine months, maternal education at enrollment, season of the 9-month postpartum visit (OFSP harvest season or not), age in weeks at the 9-month postpartum visit, infant sex, and reported receipt of a vitamin A supplement since birth. Household food security was not anticipated to be affected by this intervention, so it is not on the causal pathway, but food security impacts a family's ability to obtain the healthiest foods. The interaction terms of each of these variables with participation were also considered, but none were significant.

The final set of covariates to be used in each model was determined by using the hierarchical backward elimination approach to achieve the least biased, most precise and most parsimonious model (21). Table 1 shows which covariates were included in all final models and their sample sizes. Collinearity was examined between all covariates in each model using condition indices and VDPs. Age in weeks could not be evaluated for significance in the infant models due to multicollinearity issues. All data analysis was completed in SAS version 9.4 (Cary, NC).

3.5.7 Ethics

The study protocol was reviewed and approved by the Institutional Review Board of Emory University, Atlanta, GA, USA and the Ethical Review Committee of the Kenya Medical Research Institute (KEMRI). All participants provided written informed consent prior to data collection.

3.6 Results

Between enrollment in early pregnancy and 9 months postpartum, 122 women and 121 infants were lost to follow-up (Figure 1). The primary reasons for loss to follow-up were early delivery (n=48), relocation (n=43) and refusal to continue participating (n=25). Compared to mothers initially enrolled who were lost to follow-up, the mothers retained to nine-months postpartum did not differ significantly on any characteristics at enrollment (Appendix Table A1).

Table 2 shows sociodemographic and biologic variables for the 384 women not lost to follow-up, at enrollment during early pregnancy. At enrollment, intervention mothers had significantly less diverse household diets and smaller mid-upper arm circumference. The prevalence of low RBP (13.9% overall) and any anemia (31.1% overall) did not differ significantly by group at enrollment.

Table 3 shows outcomes of interest for all women at nine months postpartum as well as infant characteristics at nine months. Intervention mothers were significantly less food secure than controls at nine months, though more intervention women and infants had consumed OFSP in previous seven days. Though maternal mid-upper arm circumference was still significantly smaller in intervention mothers, the prevalence of low RBP in intervention mothers was lower than control mothers (7.5% and 13.7%, respectively); this difference was borderline statistically significant (p=0.051). Infant hemoglobin level was significantly higher in less than full participation infants compared to controls but no statistically significant differences were observed by intervention assignment nor were differences seen in prevalence of low RBP by intervention assignment or by participation level in infants.

In regression analysis, mothers in intervention communities had significantly lower odds of low RBP (OR: 0.42 and 95% CI: 0.19-0.95; Table 4) following adjustment for clustering, differences at baseline and other potentially influential covariates. Neither intervention assignment nor level of participation was associated odds of maternal anemia (Table 4). Neither intervention assignment nor level of participation was associated with odds of low RBP or anemia among infants (Table 4).

3.7 Discussion

The prevalence of marginal vitamin A deficiency, as measured by infection adjusted RBP <0.83 µmol/L, was relatively high (25.4%) in this population of nine month old infants in a rural area of Western Kenya, though lower than the observed prevalence in an earlier intervention using OFSP in Uganda [50] and in an earlier study in Kenya [6]. The maternal prevalence of marginal vitamin A deficiency at nine months postpartum (10.7%), measured as RBP <1.05 µmol/L, was much lower than in infants and was similar to that found in the Uganda study [50]. The prevalence of maternal anemia overall (31.1% during pregnancy and 27.2% at nine months postpartum) were similar to what Alusala et al. found in Western Kenya [63]. The prevalence of infant anemia, at 69.2%, was much higher than maternal anemia consistent with other studies in Kenya [64, 65].

Overall, our findings show that an integrated approach to OFSP delivery is promising for improving vitamin A status of lactating women in a region where sweet potato is a staple food. The improvement in vitamin A status among women is consistent with other intervention studies using OFSP [49, 50]. It is less clear if the integrated approach can improve vitamin A status of infants or the anemia status of women and infants. The degree of participation did not appear to differentially affect odds of marginal vitamin A deficiency. Interestingly, the prevalence of low RBP among women in intervention communities who participated fully in program activities was similar to those with minimal participation, though this may have been the result of reduced power to detect differences due to stratification. These results may suggest a similar phenomenon as was seen in the OFSP study in rural Uganda; increasing program intensity resulted in diminishing returns, meaning that as the number and intensity of activities increased, the relative benefit of each additional activity decreased [50]. This is very important for considering cost effectiveness of future similar programs.

The intervention was not associated with infant vitamin A status. In the Uganda study, the intervention significantly improved serum retinol in children ages 3-5 years old who were exposed to the OFSP intervention for 2 years. The differences in age and duration of exposure may explain the inconsistent findings. At nine months of age, most Kenyan infants have, ideally, only been eating complimentary foods for a couple of months. It is plausible that the OFSP intervention will have a greater effect as these children age, as their intakes of OFSP increase and vitamin A stores accumulate. A subsample of this study population participated in a 24-hour dietary recall and the intervention was significantly associated with increased beta carotene and vitamin A IU intakes in both women and children [66]. This indicates that the intervention is likely improving consumption of vitamin A rich foods like OFSP, but it has not yet translated into higher concentrations of serum RBP or hemoglobin. Breast milk analysis is ongoing for this study, and may help elucidate whether increased intakes and RBP levels in intervention mothers correspond to levels of carotenoids in the breast milk.

The intervention was not associated with infant or maternal anemia at 9 months. This is not entirely unexpected as the program did not aim to shift iron intakes or other factors that may contribute to anemia such as malaria. Though mechanisms have not been entirely elucidated, vitamin A is hypothesized to impact anemia through its ability to mobilize iron from red blood cells for incorporation into hemoglobin. Thus to see an effect of OFSP on anemia may require an increase in iron intakes or higher iron stores than occurred in this project [67, 68]. Maternal report of the child receiving vitamin A supplements since birth was not significantly associated with infant low RBP or anemia. This survey question did not address how often or how recently the child had taken the supplement, only whether they had ever received one since birth. The Kenyan government administers high-dose vitamin A supplements every six months, as well at the time of oral polio vaccine administration. Consequently, it is very likely that these 9-month-old infants last received the supplements about 3 months prior; we would expect that the effects of vitamin A supplementation on RBP would likely be diminished by the 9 month follow up.

We hypothesized that increasing levels of program participation would result in a greater association with low RBP and anemia in our population. We observed that increasing participation did not have a substantial impact on the outcomes. This could be due to the fact that the primary differentiating component between less than full participation and full participation women was attendance at mother's clubs. If the mother's clubs were not themselves the effective component of the intervention, the associations by participation levels as specified would be the same for all intervention mothers and infants. In order to maintain stability and power in the models, participation level could not be broken down further into smaller subgroups. The crudeness of the participation categorization could have contributed to the smaller association with low RBP in full participation women than in partial participation women. It could also be that the randomization of only eight facilities and their catchment areas did not adequately control for some other confounding factor that differed among facilities.

The strengths of this study include that it was longitudinal and randomized by facility catchment area. Extensive data was collected from mothers and infants at each visit. Additionally, the biochemical indicators (RBP and hemoglobin) set this study apart from many that look only at reported intake of vitamin A. This is important because the biochemical measurements can give insight into actual absorption of adequate quantities of vitamin A. Furthermore, analyses took into account clustering by facility catchment area (i.e. sublocation), differences at baseline and other potentially influential covariates; the limited application of these analytical considerations was recently cited as a major limitation in the evidence base for nutrition sensitive agriculture [69]. As such, this research fills a critical gap in the evidence.

This study was not without limitations. The biggest concern is sample size, which became particularly problematic when doing multivariate modeling. The study was initially powered to detect differences in serum RBP if 400 women were successfully followed-up; more women than anticipated were lost to follow up between enrollment in early pregnancy and nine months postpartum (n=505 at enrollment and n=383 mothers/384 infants at nine months postpartum). Fortunately, those lost to follow-up did not collectively differ from those who were followed up, based on baseline characteristics from enrollment in early pregnancy. The only difference approaching significance was that the women lost to follow-up had a lower prevalence of RBP <1.05 μmol/L than those who were followed up (7.4% and 13.9%, respectively, p=0.057). The women were not informed of their RBP status since samples had to be sent out for testing, so it is unlikely that it directly affected their follow-up with the study. It would be expected to see greater improvements from the intervention in a population with a higher prevalence of low

RBP, so had women lost to follow-up stayed in the study, the observed effect size may have been smaller. One control mother sent her infant for the final visit with someone else, which allowed us to obtain biochemical data on the infant, but not the most recent sociodemographic variables that were used as covariates in the modeling stage, nor the mother's biochemical data. Another limitation resulting from sample size is that it limits our ability to detect confounding by covariates due to the same power issue that prevents us from detecting association by level of participation.

Few successful interventions currently exist for improving maternal vitamin A status before and between pregnancies; high dose supplementation is avoided for fear of teratogenicity. The intervention evaluated in this analysis shows potential for meeting the vitamin A needs of this high risk population in a safe and effective way. Future research should evaluate the effectiveness of antenatal care, nutrition education, and agricultural integration for the reduction of vitamin A deficiency in other contexts and regions, as this integration appears to have potential as an effective and sustainable way to address vitamin A deficiency. More research is also needed on the possible pathways by which this intervention is acting and possible reasons why increased intakes of beta carotene and vitamin A IU have not translated to improved RBP concentrations in infants or anemia status in both mothers and infants.

3.8 References

1. Girard, A. W., Self, J. L., McAuliffe, C., & Olude, O. (2012). The effects of household food production strategies on the health and nutrition outcomes of women and young children: a systematic review. *Paediatr Perinat Epidemiol, 26 Suppl 1*, 205-222. doi: 10.1111/j.1365-3016.2012.01282.x
2. Berti, P. R., Krasevec, J., & FitzGerald, S. (2004). A review of the effectiveness of agriculture interventions in improving nutrition outcomes. *Public Health Nutr, 7*(5), 599-609. doi: 10.1079/phn2003595
3. Underwood, B. A. (2000). Overcoming micronutrient deficiencies in developing countries: is there a role for agriculture? *Food & Nutrition Bulletin, 21*(4), 356-360.
4. Institute for Health Metrics and Evaluation (IHME). *GBD Database.* Retrieved February 28, 2015, from http://www.healthdata.org/search-gbd-data?s=vitamin a deficiency deaths
5. World Health Organization: The World Health Report: 2002: Reducing the risks, promoting healthy life. (2002).
6. Siekmann, J. H., Allen, L. H., Bwibo, N. O., Demment, M. W., Murphy, S. P., & Neumann, C. G. (2003). Kenyan school children have multiple micronutrient deficiencies, but increased plasma vitamin B-12 is the only detectable micronutrient response to meat or milk supplementation. *The Journal of nutrition, 133*(11), 3972S-3980S.
7. Organization, W. H. (2009). Global prevalence of vitamin A deficiency in populations at risk 1995-2005: WHO global database on vitamin A deficiency.
8. Mayo-Wilson, E., Imdad, A., Herzer, K., Yakoob, M. Y., & Bhutta, Z. A. (2011). Vitamin A supplements for preventing mortality, illness, and blindness in children aged under 5: systematic review and meta-analysis. *Bmj, 343*.
9. Berti, C., Biesalski, H., Gärtner, R., Lapillonne, A., Pietrzik, K., Poston, L., . . . Cetin, I. (2011). Micronutrients in pregnancy: current knowledge and unresolved questions. *Clinical nutrition, 30*(6), 689-701.
10. Bhat, P. V., & Manolescu, D.-C. (2008). Role of vitamin A in determining nephron mass and possible relationship to hypertension. *The Journal of nutrition, 138*(8), 1407-1410.
11. El-Khashab, E. K., Hamdy, A. M., Maher, K. M., Fouad, M. A., & Abbas, G. Z. (2013). Effect of maternal vitamin A deficiency during pregnancy on neonatal kidney size. *Journal of perinatal medicine, 41*(2), 199-203.
12. Ramakrishnan, U., Manjrekar, R., Rivera, J., Gonzáles-Cossío, T., & Martorell, R. (1999). Micronutrients and pregnancy outcome: a review of the literature. *Nutrition Research, 19*(1), 103-159.
13. Ramakrishnan, U. (2004). Nutrition and low birth weight: from research to practice. *The American journal of clinical nutrition, 79*(1), 17-21.
14. Thorne-Lyman, A. L., & Fawzi, W. W. (2012). Vitamin A and carotenoids during pregnancy and maternal, neonatal and infant health outcomes: a systematic review and meta-analysis. *Paediatr Perinat Epidemiol, 26 Suppl 1*, 36-54. doi: 10.1111/j.1365-3016.2012.01284.x

15. Sales, M. C., de Azevedo Paiva, A., de Queiroz, D., Costa, R. A. F., da Cunha, M. A. L., & Pedraza, D. F. (2013). Nutritional status of iron in children from 6 to 59 months of age and its relation to vitamin A deficiency. *Nutr Hosp, 28*(3), 734-740.
16. Semba, R. D., & Bloem, M. W. (2002). The anemia of vitamin A deficiency: epidemiology and pathogenesis. *European journal of clinical nutrition, 56*(4), 271-281. doi: 10.1038/sj.ejcn.1601320
17. Fawzi, W. W., Chalmers, T. C., Herrera, M. G., & Mosteller, F. (1993). Vitamin A supplementation and child mortality: a meta-analysis. *Jama, 269*(7), 898-903.
18. Tang, G. (2010). Bioconversion of dietary provitamin A carotenoids to vitamin A in humans. *The American journal of clinical nutrition, 91*(5), 1468S-1473S.
19. Grune, T., Lietz, G., Palou, A., Ross, A. C., Stahl, W., Tang, G., . . . Biesalski, H. K. (2010). β-Carotene is an important vitamin A source for humans. *The Journal of nutrition, 140*(12), 2268S-2285S.
20. Haskell, M. J. (2012). The challenge to reach nutritional adequacy for vitamin A: beta-carotene bioavailability and conversion--evidence in humans. *Am J Clin Nutr, 96*(5), 1193s-1203s. doi: 10.3945/ajcn.112.034850
21. Novotny, J. A., Harrison, D. J., Pawlosky, R., Flanagan, V. P., Harrison, E. H., & Kurilich, A. C. (2010). Beta-carotene conversion to vitamin A decreases as the dietary dose increases in humans. *J Nutr, 140*(5), 915-918. doi: 10.3945/jn.109.116947
22. Ahmed, F., Mohiduzzaman, M., Barua, S., Shaheen, N., Margetts, B., & Jackson, A. (1992). Effect of family size and income on the biochemical indices of urban school children of Bangladesh. *European journal of clinical nutrition, 46*(7), 465-473.
23. Campbell, A. A., Thorne-Lyman, A., Sun, K., de Pee, S., Kraemer, K., Moench-Pfanner, R., . . . Semba, R. D. (2009). Indonesian women of childbearing age are at greater risk of clinical vitamin A deficiency in families that spend more on rice and less on fruits/vegetables and animal-based foods. *Nutrition Research, 29*(2), 75-81.
24. Khatry, S. K., West, K. P., Katz, J., LeClerq, S. C., Pradhan, E. K., Wu, L. S.-F., . . . Pokhrel, R. P. (1995). Epidemiology of xerophthalmia in Nepal: a pattern of household poverty, childhood illness, and mortality. *Archives of ophthalmology, 113*(4), 425-429.
25. Kjolhede, C. L., Stallings, R. Y., Dibley, M. J., Sadjimin, T., Dawiesah, S., & Padmawati, S. (1995). Serum retinol levels among preschool children in Central Java: demographic and socioeconomic determinants. *International Journal of Epidemiology, 24*(2), 399-403.
26. Mele, L., West, K. P., Pandji, A., Nendrawati, H., Tilden, R., & Tarwotjo, I. (1991). Nutritional and household risk factors for xerophthalmia in Aceh, Indonesia: a case-control study. The Aceh Study Group. *The American journal of clinical nutrition, 53*(6), 1460-1465.
27. Rosen, D., Sloan, N., Del Rosario, A., & De la Paz, T. (1994). Risk factors for vitamin A deficiency in rural areas of the Philippines. *J Trop Pediatr, 40*(2), 82-87.

28. West Jr, K. P., & Darnton-Hill, I. (2008). Vitamin A deficiency *Nutrition and health in developing countries* (pp. 377-433): Springer.
29. Patel, K., Bentley, M., Flax, V., Shahab-Ferdows, S., Allen, L., Chasela, C., . . . van der Horst, C. (2013). Prevalence of Vitamin A Deficiency and Associations with Socioeconomic Status in Lactating HIV-infected Malawian Mothers. *The FASEB Journal, 27*(1_MeetingAbstracts), 619.618.
30. Rohner, F., Woodruff, B. A., Aaron, G. J., Yakes, E. A., Lebanan, M. A. O., Rayco-Solon, P., & Saniel, O. P. (2013). Infant and young child feeding practices in urban Philippines and their associations with stunting, anemia, and deficiencies of iron and vitamin A. *Food & Nutrition Bulletin, 34*(Supplement 1), 17S-34S.
31. Hyder, A. A., Maman, S., Nyoni, J. E., Khasiani, S. A., Teoh, N., Premji, Z., & Sohani, S. (2007). The pervasive triad of food security, gender inequity and women's health: exploratory research from sub-Saharan Africa. *African Health Sciences, 5*(4), 328-334.
32. *Fact Sheet No.23, Harmful Traditional Practices Affecting the Health of Women and Children*. (1994). Paper presented at the United Nations Regional Seminar on Traditional Practices Affecting the Health of Women and Children, Colombo, Sri Lanka.
33. Bhutta, Z. A., Das, J. K., Rizvi, A., Gaffey, M. F., Walker, N., Horton, S., . . . Black, R. E. (2013). Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? *Lancet, 382*(9890), 452-477. doi: 10.1016/s0140-6736(13)60996-4
34. Imdad, A., Yakoob, M. Y., Sudfeld, C., Haider, B. A., Black, R. E., & Bhutta, Z. A. (2011). Impact of vitamin A supplementation on infant and childhood mortality. *BMC Public Health, 11*(Suppl 3), S20.
35. Rivera, J. A., Hotz, C., González-Cossío, T., Neufeld, L., & García-Guerra, A. (2003). The effect of micronutrient deficiencies on child growth: a review of results from community-based supplementation trials. *The Journal of nutrition, 133*(11), 4010S-4020S.
36. Victora, C. G., Barros, F. C., Assunção, M. C., Restrepo-Méndez, M. C., Matijasevich, A., & Martorell, R. (2012). Scaling up maternal nutrition programs to improve birth outcomes: A review of implementation issues. *Food & Nutrition Bulletin, 33*(2), 6-26.
37. Mason, J., Greiner, T., Shrimpton, R., Sanders, D., & Yukich, J. (2014). Vitamin A policies need rethinking. *International Journal of Epidemiology*, dyu194.
38. Mason, J. B., Ramirez, M. A., Fernandez, C. M., Pedro, R., Lloren, T., Saldanha, L., . . . Eisele, T. (2011). Effects on vitamin A deficiency in children of periodic high-dose supplements and of fortified oil promotion in a deficient area of the Philippines. *International Journal for Vitamin and Nutrition Research, 81*(5), 295-305.
39. Dary, O., & Mora, J. O. (2002). Food fortification to reduce vitamin A deficiency: International Vitamin A Consultative Group recommendations. *The Journal of nutrition, 132*(9), 2927S-2933S.
40. Imhoff-Kunsch, B., Flores, R., Dary, O., & Martorell, R. (2007). Wheat flour fortification is unlikely to benefit the neediest in Guatemala. *The Journal of nutrition, 137*(4), 1017-1022.

41. De‐Regil, L. M., Suchdev, P. S., Vist, G. E., Walleser, S., & Peña‐Rosas, J. P. (2013). Home fortification of foods with multiple micronutrient powders for health and nutrition in children under two years of age (Review). *Evidence‐Based Child Health: A Cochrane Review Journal, 8*(1), 112-201.
42. Underwood, B. A. (2000). Dietary approaches to the control of vitamin A deficiency: An introduction and overview. *Food & Nutrition Bulletin, 21*(2), 117-123.
43. Bouis, H. E., Hotz, C., McClafferty, B., Meenakshi, J. V., & Pfeiffer, W. H. (2011). Biofortification: a new tool to reduce micronutrient malnutrition. *Food Nutr Bull, 32*(1 Suppl), S31-40.
44. Mayer, J. E., Pfeiffer, W. H., & Beyer, P. (2008). Biofortified crops to alleviate micronutrient malnutrition. *Current opinion in plant biology, 11*(2), 166-170.
45. Tumwegamire, S., Kapinga, R., Zhang, D., Crissman, C., & Agili, S. (2005). Opportunities for promoting orange-fleshed sweetpotato as a mechanism for combat vitamin-A deficiency in Sub-Saharan Africa. *African Crop Science Journal, 12*(3), 241-252.
46. Kidmose, U., Christensen, L. P., Agili, S. M., & Thilsted, S. H. (2007). Effect of home preparation practices on the content of provitamin A carotenoids in coloured sweet potato varieties (Ipomoea batatas Lam.) from Kenya. *Innovative Food Science & Emerging Technologies, 8*(3), 399-406.
47. Vimala, B., Nambisan, B., & Hariprakash, B. (2011). Retention of carotenoids in orange-fleshed sweet potato during processing. *Journal of food science and technology, 48*(4), 520-524.
48. Low, J., Walker, T., & Hijmans, R. (2001). *The potential impact of orange-fleshed sweet potatoes on vitamin A intake in Sub-Saharan Africa.* Paper presented at the A paper presented at a regional workshop on food based approaches to human nutritional deficiencies.
49. Hotz, C., Loechl, C., de Brauw, A., Eozenou, P., Gilligan, D., Moursi, M., . . . Meenakshi, J. V. (2012). A large-scale intervention to introduce orange sweet potato in rural Mozambique increases vitamin A intakes among children and women. *Br J Nutr, 108*(1), 163-176. doi: 10.1017/s0007114511005174
50. Hotz, C., Loechl, C., Lubowa, A., Tumwine, J. K., Ndeezi, G., Nandutu Masawi, A., . . . Gilligan, D. O. (2012). Introduction of beta-carotene-rich orange sweet potato in rural Uganda resulted in increased vitamin A intakes among children and women and improved vitamin A status among children. *J Nutr, 142*(10), 1871-1880. doi: 10.3945/jn.111.151829
51. Low, J. W., Arimond, M., Osman, N., Cunguara, B., Zano, F., & Tschirley, D. (2007). A food-based approach introducing orange-fleshed sweet potatoes increased vitamin A intake and serum retinol concentrations in young children in rural Mozambique. *J Nutr, 137*(5), 1320-1327.
52. WHO. (2006). *Vitamin and Mineral Nutrition Information System: World Health Organization Global Database on Vitamin A Deficiency: Kenya.*
53. Trumbo, P., Yates, A. A., Schlicker, S., & Poos, M. (2001). Dietary reference intakes: vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. *Journal of the American Dietetic Association, 101*(3), 294-301.

54. Erhardt, J. G. (2011). Measurement of the Vitamin A and Iron Status in Blood Samples. http://www.nutrisurvey.net/blood_samples.
55. Erhardt, J. G., Estes, J. E., Pfeiffer, C. M., Biesalski, H. K., & Craft, N. E. (2004). Combined measurement of ferritin, soluble transferrin receptor, retinol binding protein, and C-reactive protein by an inexpensive, sensitive, and simple sandwich enzyme-linked immunosorbent assay technique. *J Nutr, 134*(11), 3127-3132. doi: 134/11/3127 [pii]
56. Thurnham, D. I., & McCabe, G. P. (2012). Influence of infection and inflammation on biomarkers of nutritional status with an emphasis on vitamin A and iron. *Report: Priorities in the assessment of vitamin A and iron status in populations: 15–17 September 2010*.
57. WHO. (2011). *Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity*. Geneva, World Health Organization: Vitamin and Mineral Information System (WHO/NMH/NHD/MNM/11.1).
58. Coates, J., Swindale, A., & Bilinsky, P. (2007). Household Food Insecurity Access Scale (HFIAS) for measurement of food access: indicator guide. *Washington, DC: Food and Nutrition Technical Assistance Project, Academy for Educational Development*.
59. Kennedy, G., Ballard, T., & Dop, M. C. (2011). *Guidelines for measuring household and individual dietary diversity*: Food and Agriculture Organization of the United Nations.
60. WFP. (2008). *Food Consumption Analysis: Calculation and use of the food consumption score in food security analysis*.
61. Baeten, J. M., Richardson, B. A., Bankson, D. D., Wener, M. H., Kreiss, J. K., Lavreys, L., . . . McClelland, R. S. (2004). Use of serum retinol-binding protein for prediction of vitamin A deficiency: effects of HIV-1 infection, protein malnutrition, and the acute phase response. *The American journal of clinical nutrition, 79*(2), 218-225.
62. Engle-Stone, R., Haskell, M. J., Ndjebayi, A. O., Nankap, M., Erhardt, J. G., Gimou, M.-M., & Brown, K. H. (2011). Plasma retinol-binding protein predicts plasma retinol concentration in both infected and uninfected Cameroonian women and children. *The Journal of nutrition, 141*(12), 2233-2241.
63. Alusala, D., Estambale, B., Magnussen, P., Friis, H., Luoba, A., & Mwaniki, D. (2008). Predictors of serum ferritin and haemoglobin during pregnancy, in a malaria-endemic area of Western Kenya. *Annals of tropical medicine and parasitology, 102*(4), 297-308.
64. van Eijk, A. M., Ayisi, J. G., Ter Kuile, F. O., Misore, A. O., Otieno, J. A., Kolczak, M. S., . . . Nahlen, B. L. (2002). Malaria and human immunodeficiency virus infection as risk factors for anemia in infants in Kisumu, Western Kenya. *The American journal of tropical medicine and hygiene, 67*(1), 44-53.
65. Crawley, J. (2004). Reducing the burden of anemia in infants and young children in malaria-endemic countries of Africa: from evidence to action. *The American journal of tropical medicine and hygiene, 71*(2 suppl), 25-34.
66. Webb Girard, A., Deneen, M. L., A; , Okuku, H., Cole, D., Levin, C., Low, J., & Grant, F. (2015). *An integrated agriculture, health and nutrition program increased vitamin A intakes among mothers and their infants in Western Kenya:*

Findings from the Mama SASHA Cohort Study of Vitamin A (COVA) . Paper presented at the Experimental Biology, Boston.

67. Allen, L. H. (2002). Iron supplements: scientific issues concerning efficacy and implications for research and programs. *The Journal of nutrition, 132*(4), 813S-819S.
68. Semba, R., & Bloem, M. (2002). The anemia of vitamin A deficiency: epidemiology and pathogenesis. *European journal of clinical nutrition, 56*(4), 271-281.
69. Ruel, M. T., Alderman, H., Maternal, & Group, C. N. S. (2013). Nutrition-sensitive interventions and programmes: how can they help to accelerate progress in improving maternal and child nutrition? *The lancet, 382*(9891), 536-551.
70. Brody, C. M., Bellows, N., Campbell, M., & Potts, M. (2013). The impact of vouchers on the use and quality of health care in developing countries: a systematic review. *Glob Public Health, 8*(4), 363-388. doi: 10.1080/17441692.2012.759254
71. Freeman, M., Quick, R., Abbott, D., Ogutu, P., & Rheingans, R. (2009). Increasing equity of access to point-of-use water treatment products through social marketing and entrepreneurship: a case study in western Kenya. *Journal of water and health, 7*(3), 527-534.
72. Kenya, P. R., Gatiti, S., Muthami, L. N., Agwanda, R., Mwenesi, H. A., Katsivo, M. N., . . . van Andel, F. G. (1990). Oral rehydration therapy and social marketing in rural Kenya. *Social Science & Medicine, 31*(9), 979-987. doi: http://dx.doi.org/10.1016/0277-9536(90)90107-4

3.9 Tables and Figures

Table 1: Summary of models used in final analysis.

Outcome of Interest[a]	Crude Sample Size[b]	Final Model Sample Size[c]	Covariates in Model
Maternal Low RBP	383	376	Maternal education, RBP concentration at enrollment, season of 9-month visit
Infant Low RBP	384	350	Wealth Index Quartile, maternal education, season of 9-month visit, receipt of vitamin A supplements
Maternal Anemia	383	378	Maternal education, Household Dietary Diversity Category at enrollment, season of 9-month visit, household food security category, altitude-adjusted hemoglobin at enrollment
Infant Anemia	384	352	Wealth Index Quartile, maternal education, season of 9-month visit, receipt of vitamin A supplements

[a] For all models, exposure is participation level classified as intervention full participation, intervention partial/no participation, and control. Covariates included in all models were maternal education, wealth index quartile, and food security category as fixed effects and village and health facility as random effects. SAS's PROC GLIMMIX was used for all modeling.

[b] Crude sample size is based on all participants who have any data for the 9-month postpartum visit.

[c] Final model sample size is based on participants who have data for all covariates.

Figure 1. Loss-to-follow-up diagram detailing the reasons for exclusion or loss to follow-up from enrollment in early pregnancy to the final visit at 9 months postpartum. Some women missed visit 2 but came back for visit 3, which explains the fluctuating sample size seen here.

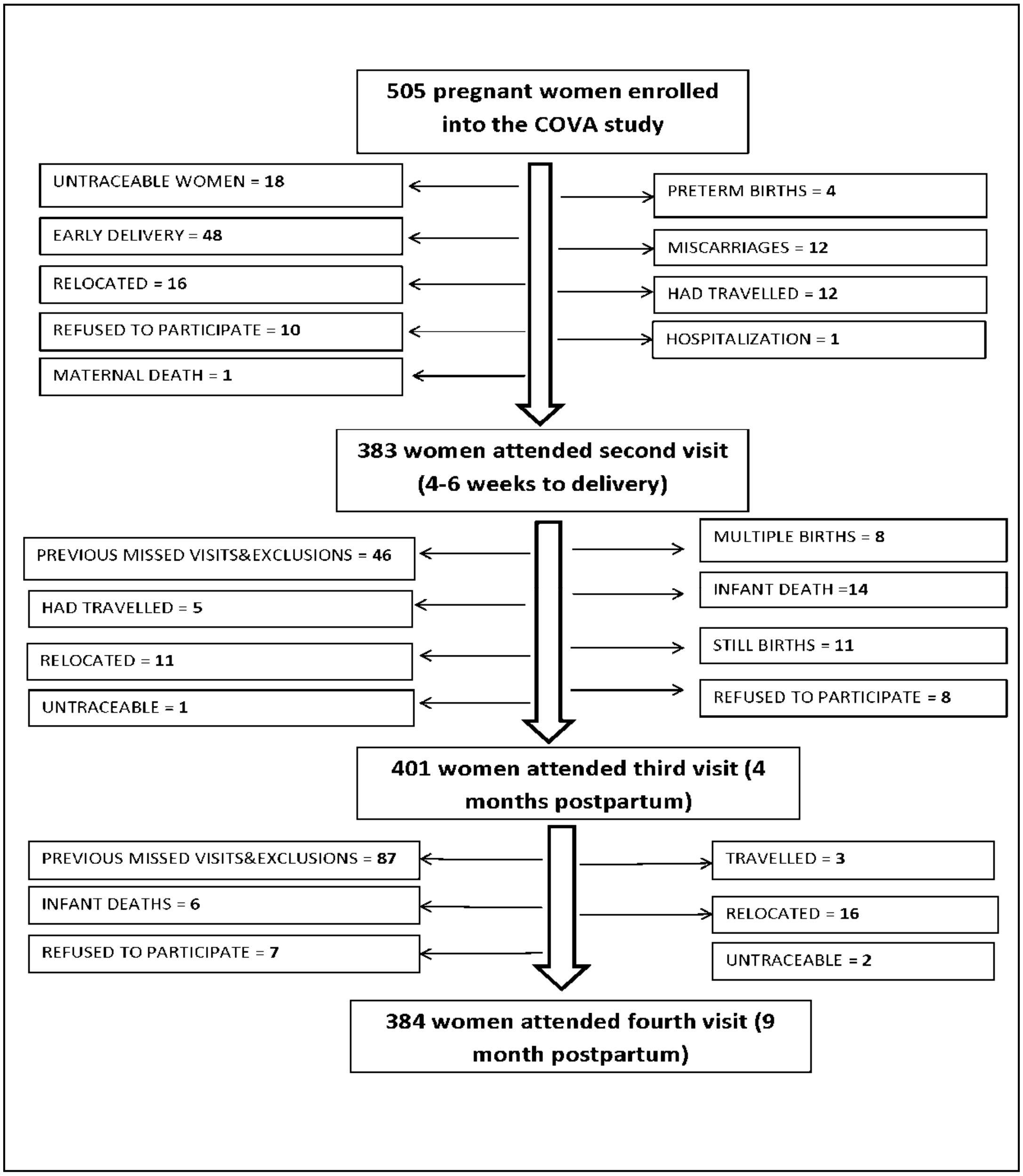

Table 2: Baseline statistics from enrollment in early pregnancy for the 383 COVA mothers included in these analyses by program participation level.

						Intervention by Participation Level		
	N	**Overall** (N=383) Mean±SD or n (%)	**Control** (N=191) Mean±SD or n (%)	**All Intervention** (N=192) Mean±SD or n (%)	p-value[a]	**Less than full participation** (N=109) Mean±SD or n (%)	**Full participation** (N=83) Mean±SD or n (%)	p-value[b]
Sociodemographic Characteristics at Enrollment in Early Pregnancy								
Wealth Index	381	8.6±1.8	8.6±1.7	8.6±1.9	0.734	8.7±2.0	8.3±1.8	0.229
Maternal Education Level	383				0.255			0.519
Primary		118 (30.8%)	64 (33.3%)	54 (28.1%)		31 (28.4%)	23 (27.7%)	
Post-Primary		265 (69.2%)	127 (66.5%)	138 (71.9%)		78 (71.6%)	60 (72.3%)	
Maternal Food Consumption Score	383	71.5±17.1	71.3±17.0	71.6±17.2	0.865	72.5±16.7	72.2±14.6	
Household Dietary Diversity Category	383				<0.001			0.004
Low		26 (6.8%)	7 (3.7%)	19 (9.9%)		13 (11.9%)	6 (7.2%)	
Medium		184 (48.0%)	78 (40.8%)	106 (55.2%)		65 (59.6%)	41 (49.4%)	
High		173 (45.2%)	106 (55.5%)	67 (34.9%)		31 (28.4%)	36 (43.4%)	
Household Food Security Category	379				0.207			0.267
Food secure		120 (31.7%)	62 (32.8%)	58 (30.5%)		33 (30.3%)	25 (30.9%)	
Mildly insecure		87 (23.0%)	45 (23.8%)	42 (22.1%)		25 (22.9%)	17 (21.0%)	
Moderately insecure		85 (22.4%)	34 (18.0%)	51 (26.8%)		25 (22.9%)	26 (32.1%)	
Severely insecure		87 (23.0%)	48 (25.4%)	39 (20.%)		26 (23.9%)	13 (16.1%)	
Biological Measures at Enrollment in Early Pregnancy								
Maternal Hemoglobin (g/dL), altitude adjusted	383	11.4±1.5	11.4±1.6	11.5±1.5	0.584	11.4±1.6	11.6±1.3	

						Intervention by Participation Level		
	N	**Overall** (N=383) Mean±SD or n (%)	**Control** (N=191) Mean±SD or n (%)	**All Intervention** (N=192) Mean±SD or n (%)	p-value[a]	**Less than full participation** (N=109) Mean±SD or n (%)	**Full participation** (N=83) Mean±SD or n (%)	p-value[b]
Maternal Anemia[c]	383				0.362			0.304
Not Anemic		264 (68.9%)	131 (68.6%)	133 (69.3%)		76 (69.7%)	57 (68.7%)	
Mild Anemia		64 (16.7%)	27 (14.1%)	37 (19.3%)		18 (16.5%)	19 (22.9%)	
Moderate Anemia		52 (13.6%)	31 (16.2%)	21 (10.9%)		14 (12.8%)	7 (8.4%)	
Severe Anemia		3 (0.8%)	2 (1.1%)	1 (0.5%)		1 (0.9%)	0 (0.0%)	
Maternal Retinol Binding Protein corrected[d], µmol/L	382	1.4±0.4	1.6±0.5	1.4±0.4	0.530	1.4±0.3	1.5±0.4	0.530
Maternal Low Retinol Binding Protein corrected[e]	382	53 (13.9%)	30 (15.7%)	23 (12.0%)	0.300	13 (11.9%)	10 (12.2%)	0.584
Maternal Upper Arm Circumference (cm)	383	26.1±3.1	27.0±3.4	25.3±2.5	<0.001	25.0±2.4	25.6±2.6	<0.001

[a] p-values from two sample t-tests comparing all intervention to control mothers

[b] p-values comparing intervention by participation level to controls, using Mantel Haenzel chi squared or ANOVA as appropriate.

[c] Anemia was classified according to WHO cutoffs for pregnant women: non anemia ≥11.0g/dL, mild anemia 10.0-10.9g/dL, moderate anemia 7.0-9.9g/dL, severe anemia <7.0g/dL[57].

[d] Corrected for inflammation using CRP and AGP levels

[e] Low is defined as <1.05 µmol/L

Table 3: Statistics at 9-months postpartum for 384 mother-infant dyads by program participation level.

						Intervention by Participation Level		
	n	**Overall** (N=384) Mean±SD or n(%)	**Control** (N=192) Mean±SD or n(%)	**All Intervention** (N=192) Mean±SD or n (%)	p-value[a]	**Less than full participation** (N=109) **Mean±SD or n (%)**	**Full participation** (N=83) Mean±SD or n (%)	p-value[b]
Sociodemographic Characteristics at 9 Months Postpartum								
Maternal Food Consumption Score	382	73.1±14.8	73.7±14.2	72.6±15.3	0.473	72.9±15.8	72.2±14.6	0.740
Household Dietary Diversity Category	382				0.637			0.633
Low		10 (2.6%)	5 (2.6%)	5 (2.6%)		4 (3.7%)	1 (1.2%)	
Medium		166 (43.5%)	78 (41.1%)	88 (45.8%)		50 (45.9%)	38 (45.8%)	
High		206 (53.9%)	107 (56.3%)	99 (51.6%)		55 (50.5%)	44 (53.0%)	
Household Food Security Category	382				0.002			0.034
Food secure		158 (41.4%)	90 (47.4%)	68 (35.4%)		33 (30.3%)	35 (42.2%)	
Mildly insecure		76 (19.9%)	41 (21.6%)	35 (18.2%)		24 (22.0%)	11 (13.3%)	
Moderately insecure		87 (22.8%)	36 (19.0%)	51 (26.6%)		31 (28.4%)	20 (24.1%)	
Severely insecure		61 (16.0%)	23 (12.1%)	38 (19.8%)		21 (19.3%)	17 (20.5%)	
Maternal Consumption of OFSP in last 7 days	382	49 (12.8%)	0 (0.0%)	49 (25.5%)	<0.001	28 (25.7%)	21 (25.3%	<0.001
Infant Consumption of OFSP in last 7 days	384	86 (22.4%)	0 (0.0%)	86 (44.8%)	<0.001	35 (32.1%)	51 (61.5%)	<0.001
Infant age (weeks)	371	35.7±1.5	35.6±1.3	35.9±1.7	0.046	36.2±2.0	35.6±1.0	0.004
Infant sex (% Female)	371	174 (46.9%)	84 (44.7%)	90 (49.2%)	0.445	50 (49.5%)	40 (48.8%)	0.683
Biological Measures at 9 months								
Maternal Hemoglobin Level, altitude adjusted g/dL	378	12.7±1.6	12.6±1.7	12.8±1.5	0.343	12.9±1.6	12.7±1.4	0.476
Maternal Anemia[c]	378				0.5			0.366
Not Anemic		275 (72.8%)	139 (73.2%)	136 (72.3%)		79 (75.2%)	57 (68.7%)	
Mild Anemia		61 (16.1%)	25 (13.2%)	36 (19.2%)		17 (16.2%)	19 (22.9%)	

						Intervention by Participation Level		
	n	**Overall** (N=384) Mean±SD or n(%)	**Control** (N=192) Mean±SD or n(%)	**All Intervention** (N=192) Mean±SD or n (%)	p-value[a]	**Less than full participation** (N=109) **Mean±SD or n (%)**	**Full participation** (N=83) Mean±SD or n (%)	p-value[b]
Moderate Anemia		39 (10.3%)	24 (12.6%)	15 (8.0%)		8 (7.6%)	7 (8.4%)	
Severe Anemia		3 (0.8%)	2 (1.1%)	1 (0.5%)		1 (1.0%)	0 (0.0%)	
Maternal Retinol Binding Protein corrected[d], µmol/L	377	1.7±0.5	1.6±0.5	1.7±0.5	0.243	1.7±0.5	1.7±0.6	0.480
Maternal Low Retinol Binding Protein corrected[e]	377	40 (10.6%)	26 (13.7%)	14 (7.5%)	0.051	6 (5.8%)	8 (9.6%)	0.103
Maternal Upper Arm Circumference (cm)	380	25.6±3.6	26.3±3.7	25.0±3.4	0.002	24.7±3.8	25.3±2.9	0.008
Infant Birth Weight (kg)	363	3.4±0.9	3.3±0.8	3.4±0.9	0.723	3.5±1.2	3.3±0.5	0.265
Infant Hemoglobin Level, altitude adjusted, g/dL	377	10.6±5.7	10.1±1.4	11.2±8.0	0.08	11.9±10.5	10.2±1.3	0.030
Infant Anemia[f]	377				0.314			0.639
Not Anemic		116 (30.8%)	56 (29.5%)	60 (32.1%)		37 (35.2%)	23 (28.1%)	
Mild Anemia		125 (33.2%)	62 (32.6%)	63 (33.7%)		35 (33.3%)	28 (34.2%)	
Moderate Anemia		127 (33.7%)	65 (34.2%)	62 (33.2%)		32 (30.5%)	30 (36.6%)	
Severe Anemia		9 (2.4%)	7 (3.7%)	2 (1.1%)		1 (1.0%)	1 (1.1%)	
Infant Retinol Binding Protein corrected[d], µmol/L	374	1.7±1.5	1.8±1.5	1.7±1.4	0.677	1.8±1.5	1.6±1.4	0.622
Infant Low Retinol Binding Protein corrected[e]	374	95 (25.4%)	48 (25.4%)	47 (25.4%)	0.999	26 (25.2%)	21 (25.6%)	0.998

[a] p-value comparing all intervention dyads to controls using two-sample t-tests.

[b] p-value comparing control to intervention by participation level, using ANOVA or Mantel Haenzel chi squared appropriate.

[c] Anemia was classified according to WHO cutoffs for non-pregnant women: non anemia ≥12.0g/dL, mild anemia 11.0-11.9g/dL, moderate anemia 8.0-10.9g/dL, severe anemia <8.0g/dL [57].

[d] Corrected for inflammation using CRP and AGP levels

[e] Low is defined as <1.05 µmol/L

[f] Anemia was classified according to WHO cutoffs for children 6-59 months: non anemia ≥11.0g/dL, mild anemia 10.0-10.9g/dL, moderate anemia 7.0-9.9g/dL, severe anemia <7.0g/dL [57].

Table 4. Odds ratios and 95% CI for low retinol binding protein[a] and anemia[b] in 378 mothers and 352 infants included in models at 9 months post-partum.

Variable	**Low RBP[a] OR (95% CI)**	**Anemia[b] OR (95% CI)**
Mothers[c]		
By intervention assignment		
Control (n= 190)	Reference	Reference
All intervention (n= 188)	0.42 (0.19-0.95)[d]	1.12 (0.58, 2.18)
By participation level		
Control (n=190)	Reference	Reference
Intervention, not full participation (n=105)	0.30 (0.10-0.86)[d]	0.86 (0.40-1.84)
Intervention, full participation (n=83)	0.60 (0.23-1.59)	1.55 (0.71-3.37)
Infants[e]		
By intervention assignment		
Control (n=178)	Reference	Reference
All intervention (n=174)	1.00 (0.59-1.70)	1.04 (0.65-1.68)
By participation level		
Control (n=178)	Reference	Reference
Intervention, not full participation (n=98)	1.01 (0.55-1.87)	0.99 (0.57-1.73)
Intervention, full participation (n=76)	0.99 (0.51-1.94)	1.13 (0.61-2.08)

[a] Low retinol binding protein is defined as<1.05 μmol/L for mothers and as <0.83 μmol/L for infants

[a] Anemia for women was defined according to WHO cutoffs for non-pregnant women using altitude-adjusted hemoglobin levels: non anemia ≥12.0g/dL, anemia <12.0g/dL [57]. For infants, anemia was defined according to WHO cutoffs for children 6-59 months: non anemia ≥11.0g/dL, anemia <11.0g/dL [57].

[c] Maternal low RBP ORs were estimated using mixed model with participation level as exposure, low RBP as outcome, with sublocation as random effect. Covariates included in the model are maternal education level, season of 9-month visit, and serum RBP concentration at baseline. Maternal anemia ORs estimated using mixed model with participation level as exposure, anemia as outcome, with sublocation as random effect. Covariates in model are household food security category at nine months, maternal education level, household dietary diversity category at enrollment, season of 9-month visit, and altitude-adjusted hemoglobin level at baseline.

[d] 95% confidence interval does not include 1

[e] Infant ORs estimated using mixed models with participation level as exposure, low RBP or anemia as outcome, with sublocation as random effect. Covariates in model are maternal education level, wealth index quartile at enrollment, season of 9-month visit, and receipt of vitamin A supplements.

CHAPTER 4: RECOMMENDATIONS AND CONCLUSIONS

4.1 Summary of Key Findings

Vitamin A deficiency and anemia are significant public health concerns for pregnant and lactating women and their infants both globally and in this rural area of Western Kenya. The Mama SASHA (Sweet potato Action for Security and Health in Africa) program integrated agriculture, nutrition education, and antenatal care to promote orange-fleshed sweet potato (OFSP) as a strategy to improve vitamin A status among this high risk population. When evaluated using a community based, cluster randomized longitudinal design, this approach was associated with a significantly decreased odds of low retinol binding protein (RBP) (<1.05 µmol/L) among mothers followed from early/mid pregnancy through 9 months postpartum when clustering and covariates were taken into account. Significant associations were not observed for maternal anemia, low RBP in infants, and infant anemia at nine months postpartum. Increasing degree of program participation was not associated with any of the outcomes. This may indicate that the community intervention impacted the community as a whole equally or that some components of participation of were especially effective, mitigating the effectiveness of full individual participation.

A lack of effect on infant vitamin A and anemia status is not consistent with previous studies using OFSP as a vehicle for delivering vitamin A [49-51]. This inconsistency could be due to the timing of the intervention and measurements because most infants would only have been eating complimentary foods for a few months by the time the nine-month measurements were taken. Given that a subsample from this study who participated in a 24-hour dietary recall showed significantly increased intakes of beta carotene and vitamin A IU for intervention mothers and infants, there is potential that this intervention may impact the infants as they get older [66].

4.2 Public Health Implications and Recommendations

4.2.1 Future Research

This study was limited by total sample size (n=384 at 9-months postpartum) as well as the number of clusters (8 facilities and catchment areas cluster analyzed, 22 sublocations used for cluster analysis). As with overall sample size, this small number of clusters limits statistical power to detect significant associations. Larger longitudinal studies are needed in Western Kenya as well as other contexts in order to determine whether all the components of the Mama SASHA program are effective, or if some could be scaled-back or eliminated without losing benefit to achieve improved effectiveness, sustainability and cost-effectiveness. Future cluster-randomized trials should increase the number of clusters to increase power. Future research should continue to evaluate the effectiveness of antenatal care, nutrition education, and agricultural integration for the reduction of vitamin A deficiency in other contexts and regions, as this integration appears to have some potential as an effective and sustainable way to address vitamin A deficiency. More research is also needed on the possible pathways by which this intervention is acting and possible reasons why increased intakes of beta carotene and vitamin A IU [66] have not translated to blood concentrations, particularly in infants, before future programs invest the large amount of resources required for such integrated approaches. The analysis of breast milk collected in this study is ongoing, which may elucidate the pathway between maternal RBP levels and infant RBP levels.

4.2.2 Programs

At this time, there is evidence that this integrated agriculture and nutrition education intervention is effective at improving maternal RBP, but not for infants or for reducing anemia. Few successful interventions currently exist for improving maternal vitamin A status before and between pregnancies; high dose supplementation is avoided for fear of teratogenicity. This OFSP-focused intervention shows potential for meeting the vitamin A needs of this high risk population in a safe and effective way. Future research should evaluate the effectiveness of antenatal care, nutrition education, and agricultural integration for the reduction of vitamin A deficiency in other contexts and regions, as this integration appears to have potential as an effective and sustainable way to address vitamin A deficiency.

Future nutrition programs should consider integrating antenatal care and agriculture to promote vitamin A consumption, especially including OFSP production and consumption, but only after additional research is done, as suggested above. Antenatal care is a convenient setting for vitamin A nutrition education, promoting vitamin A consumption, and delivering vouchers for nutrition services because pregnant women and infants are the highest risk populations for vitamin A deficiency and antenatal care visits are a pre-existing point of contact with pregnant women. A potential problem with this approach is that poor women and children are generally less likely to receive antenatal care, so this method of programming may not be equitable [36]. A recent systematic review, however, found that vouchers are effective at reaching target populations and increasing healthcare utilization [70]. Thus, vouchers, such as were used in Mama SASHA to delivery OFSP planting material, may incentivize both earlier antenatal care visits and more frequent visits, counteracting the potential inequity of programing using antenatal care [70]. Perhaps another approach, such as social marketing, could equally reach pregnant and lactating women, without taking valuable time during antenatal visits. Social marketing has been effectively used in Kenya to increase equitable utilization of point-of-use water treatment [71] and use of oral rehydration salts [72].

Integrative programs including agriculture have the potential to increase dietary diversity long-term [2]. As such, these integrative programs are more sustainable than vitamin A interventions such as supplementation, which rely on continuous input of resources from external groups. If OFSP is successfully promoted as a substitute for white and yellow sweet potatoes, which are consumed in high quantities but are low in vitamin A, the resources required will decrease over time, as OFSP becomes the sociocultural norm. In an extremely competitive funding environment for global health initiatives, sustainability and cost-effectiveness are among the most important factors to consider in program design. OFSP programs focused on pregnant women should be considered for feasibility and effectiveness in other contexts where sweet potato consumption is high.

4.2.3 Policies

Since intakes of vitamin A and maternal RBP were associated with the intervention, the Ministry of Health of Kenya should work with the Ministry of Agriculture to create policies that ensure OFSP vines and other seeds of vitamin A rich foods are available, accessible, and affordable, particularly in regions where vitamin A deficiency is highest and that OFSP is actively supported by the agricultural sector where conditions are conducive and promoted by health sector where sweet potatoes are a common staple. Policies such as these promote sustainable and equitable improvements in the vitamin A status of the most vulnerable populations in the country.

APPENDIX: Supplementary Analysis

Table A1: Loss to follow-up analysis from enrollment in early pregnancy to 9-month postpartum visit.

		Overall (N=505)	**Lost to Follow-Up** (N=122)	**Followed-Up** (N=383)	
	N	Mean±SD or n (%)	Mean±SD or n (%)	Mean±SD or n (%)	p-value[a]
Sociodemographic Characteristics at Enrollment in Early Pregnancy					
Wealth Index	503	8.5±1.8	8.4±1.7	8.6±1.8	0.093
Maternal Education Level	505				0.657
Primary		153 (30.3%)	35 (28.7%)	118 (30.8%)	
Post-Primary		352 (69.7%)	87 (71.3%)	265 (69.2%)	
Maternal Food Consumption Score	505	70.7±17.6	68.4±19.0	71.5±17.1	0.279
Household Dietary Diversity Category	505				0.262
Low		39 (7.7%)	13 (10.7%)	26 (6.8%)	
Medium		235 (46.5%)	51 (41.8%)	184 (48.0%)	
High		231 (45.7%)	58 (47.5%)	173 (45.2%)	
Household Food Security Category	501				0.307
Food secure		164 (32.7%)	44 (36.1%)	120 (31.7%)	
Mildly insecure		115 (23.0%)	28 (23.0%)	87 (23.0%)	
Moderately insecure		103 (20.6%)	18 (14.8%)	85 (22.4%)	
Severely insecure		119 (23.8%)	32 (26.2%)	87 (23.0%)	
Maternal Consumption of OFSP in last 7 days	505	22 (4.4%)	6 (4.9%)	16 (4.2%)	0.946
Biological Measures at Enrollment in Early Pregnancy					
Hemoglobin Level, altitude adjusted g/dL	505	11.5±1.5	11.6±1.4	11.4±1.5	0.279
Anemia[b]	505				0.968
Not Anemic		346 (68.5%)	82 (67.2%)	264 (68.9%)	
Mild Anemia		88 (17.4%)	24 (19.7%)	64 (16.7%)	
Moderate Anemia		68 (13.5%)	16 (13.1%)	52 (13.6%)	
Severe Anemia		3 (0.6%)	0 (0.0%)	3 (0.8%)	
Retinol Binding Protein corrected[c], µmol/L	504	1.4±0.4	1.5±0.4	1.4±0.4	0.269

Low Retinol Binding Protein corrected[d]	504	62 (12.3%)	9 (7.4%)	53 (13.9%)	0.057

[a] p-values determined using two-sample t-tests comparing lost to follow-up to followed-up mothers.

[b] Anemia was classified according to WHO cutoffs for pregnant women: non anemia ≥11.0g/dL, mild anemia 10.0-10.9g/dL, moderate anemia 7.0-9.9g/dL, severe anemia <7.0g/dL [57].

[c] Corrected for inflammation using CRP and AGP levels

[d] Low is defined as <1.05 µmol/L

[e] Statistically significant at α=0.05