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Environmental Determinants of Early Childhood Development in Rural Kenya

By

Erin Michelle Milner

A dissertation submitted in partial satisfaction of the
requirements for the degree of
Doctor of Philosophy
in
Environmental Health Sciences
in the
Graduate Division
of the
University of California, Berkeley

Committee in charge:
Professor Robert C. Spear, Chair
Professor John R. Balmes
Professor Lia C.H. Fernald

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Environmental Determinants of Early Childhood Development in Rural Kenya

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By Erin Michelle Milner

Abstract

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Erin Michelle Milner

Doctor of Philosophy in Environmental Health Sciences
University of California, Berkeley
Professor Robert C. Spear, Chair

Environmental risk factors can play an important and immediate role in limiting early childhood development in low- and middle-income countries (LMICs). Forty-three percent of children under five years in LMICs are at risk of not meeting their developmental potential, with children in sub-Saharan Africa being at greatest risk. Children under age three years are particularly vulnerable due to their rapid brain development and sensitivity to nutrient effects on growth, cognition, and school attainment. Climate and weather shifts can also drive disease patterns, like the spread of malaria. Environmentally-driven food security, dietary patterns, and malaria are understudied in relation to early childhood development. However, these factors may be associated with developmental outcomes among children before the age of five years due to their hypothesized impacts on nutrition, brain growth, and overall health with lifelong and intergenerational implications.

Kenya has a large rural population facing challenges adapting to climate change and coping with food insecurity. While the country has a national early childhood development policy, much of the curriculum focuses on preschool-aged children and measures of early childhood development in Kenya are limited and vary by region, measure or domain assessed, and cultural differences. About one-quarter of Kenya's population is chronically food insecure and levels of stunting and underweight in rural areas, western Kenya, and around Lake Victoria are high. Malaria is also endemic in Kenya and a leading cause of child morbidity and mortality. Kenya therefore serves as an optimal place to study associations between food insecurity, children's fatty acid and fish intake, malaria, and early childhood development.

The association between three dimensions of food insecurity (timing, intensity, and duration) and three domains of early childhood development (gross motor, communication, and personal social) were examined. Longitudinal data were collected from 303 households (including 309 children under age two years at baseline) visited nine times over two years in a community around Lake Victoria in rural Kenya. Children in households experiencing more severe food insecurity three months prior (timing) had significantly lower gross motor, communication, and personal social developmental scores using lagged models controlling for current food insecurity. Children in households that experienced greater aggregate food insecurity over the past two years (intensity) had significantly lower gross motor, communication, and personal social developmental scores. Amount of time exposed to food insecurity (duration) was associated with lower gross motor, communication, and personal social developmental scores. All results were

attenuated with the addition of maternal education, household wealth, and child anthropometry to models.

Fatty acid and fish consumption among children around Lake Victoria in the same population in rural Kenya was evaluated in relation to gross motor, communication, and personal social development. The majority of fatty acids, including long-chain polyunsaturated fatty acids that are important for early childhood development, in this population's diets came from fish. Nile perch and dagaa were the most common fish species consumed. Lagged longitudinal analyses over a two year period show that greater amounts of fish consumed three months ago were associated with higher current gross motor, communication, and personal social developmental scores among children under 13.5 months, controlling for current fish consumption, child characteristics, and household demographics. Larger amounts of fatty acids (total omega 3 fatty acids, AA, EPA, and DHA) consumed three months ago were associated with higher current communication developmental scores, controlling for current fatty acid intake, child characteristics, and household demographics. Higher intake of EPA and AA three months ago was associated with greater current personal social developmental scores among children under 13.5 months. In this highly food insecure population, fishery resources can help mitigate nutrient deficiencies, especially of fatty acids, which can be particularly threatening during the complementary feeding stage. Fish may serve as a nutritional safety net where access to nutrient-dense foods is often limited. Findings provide evidence supporting the conservation of natural resources in LMICs and around Lake Victoria by enforcing resource use regulations and implementing market systems to benefit local communities and children's development.

The association between malaria and gross motor, communication, and personal social development was analyzed among 652 children 24 months of age in rural western Kenya. Eighteen percent of children had malaria and 20% of children were at risk for gross motor delay, 21% were at risk for communication delay, and 23% were at risk for personal social delay. Having a positive malaria test was significantly associated with increased odds of a child being at risk for gross motor, communication, and personal social delay adjusting for child characteristics, household demographics, study cluster, and intervention treatment arm. Mediation analyses suggest that anemia was a significant mediator in the pathway between malaria infection and being at risk for gross motor, communication, and personal social development delays. The proportions of the total effect of malaria on being at risk for developmental delay that is mediated by anemia across subscales was small (ranging from 9% of the effect on gross motor development to 16% of the effect on communication development mediated by anemia). Overall, malaria may be associated with short-term child development delays during a vulnerable period in early life. Therefore, preventative malaria measures and immediate treatment are imperative for children's optimal development, particularly in light of projections of continued high malaria transmission in Kenya and Africa.

Environmental Determinants of Early Childhood Development in Rural Kenya

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Dedication

This dissertation is dedicated to my father, Michael Vance Milner, whose stubborn love challenged me to be confident about my passionate convictions and whose spirit maintained a strong presence throughout my graduate career. Although he never wanted me to venture to Africa, he became my proudest fan for doing so. His curiosity and humor never faltered, and he has kept me going on this magic carpet ride.

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Chapter 1

Introduction and Background

1.1 Background

Forty-three percent of children under five years in low- and middle-income countries (LMICs) are at risk of not meeting their developmental potential (1). Children reach their developmental potential when they acquire developmental competencies for behavioral, socio-emotional, academic, and economic accomplishments (1). Child development is an interactive and accumulative process with an ordered progression of perceptual, motor, cognitive, language, socio-emotional, and self-regulation skills (2). Progression rates may vary as children acquire culture-specific skills (3). The acquisition of skills in middle childhood, adolescence, and adulthood builds on capacities established in early childhood with multigenerational effects (1).

Early Childhood Development Dynamics

Exposure to risk factors leads to developmental delays that may be evident in the first year of life and worsen during early childhood, continuing throughout life. Exposures in utero can affect fetal development and according to the Barker hypothesis, environmental conditions and maternal malnutrition during pregnancy can lead to persisting changes in the infant's body's function and structure with long-term health implications (4). Children under age three years are particularly vulnerable due to their rapid brain growth (1) while the period between conception and age two years (first 1,000 days) is sensitive to nutrient effects on child growth, cognition, and school attainment (5). Early childhood development programs and opportunities are often limited among children under three years prior to starting school. Adversities throughout early life can accumulate to delay development (6). Longitudinal follow-up studies assessing interventions early in life show beneficial effects on health biomarkers, adult wage earning (7,8), competence (e.g. general knowledge, educational attainment, and intelligence quotient) (9,10), social inhibition (10), depressive symptoms (10), and growth in the subsequent generation (11,12).

There are a variety of factors that influence the acquisition of competencies, including health, nutrition, security and safety, responsive caregiving, and early learning (1). Enabling household- and community-level environments are important for ensuring adequate development. The social, economic, political, cultural, and climatic context of a child's early life can lay the foundation for skill acquisition. Poverty, nutritional deficiencies, and low quality resources often coincide to threaten proper development (1). Low socioeconomic status in early childhood can lead to poor cognitive, academic, and behavioral performance and the effects of being raised in poverty can extend into adulthood (6,13). Environmental factors explain some socioeconomic-based differences in brain development and effects vary depending on the timing, dose, and duration of nutrient deficiencies (14).

Health and nutrition are particularly important factors contributing to children reaching their developmental potential (15). Disease prevention and treatment are critical for reducing nutrient losses, maximizing nutrient absorption, and for providing children with the opportunity to engage with their environment for optimum motor, communication, and socio-emotional development. Nutrition in terms of maintaining proper breastfeeding practices and consuming diverse diets with adequate macronutrients and micronutrients is imperative for growth and brain development. Food security can underlie access to adequate foods. Undernourished or frequently ill children are at high risk for developmental problems (1). Therefore, there are advantages to

integrating early childhood development with health and nutrition sector programming within government and non-governmental sectors.

Environmental Factors Related to Early Childhood Development

Early childhood development is complex and while risk factors such as poverty and stunting are well described, there is less evidence about the role of environmental factors. Recent and projected altered ecosystems and landscapes related to climate change threaten communities that rely on natural resources for food and income (16,17). The dependence of rural and vulnerable populations in LMICs on the environment for subsistence livelihoods such as agriculture and fishing practices creates concern about sustained food security and nutrition (18,19). Climate and weather shifts can also drive disease patterns, like the spread of malaria (20-22). Environmentally-driven food security, dietary patterns, and malaria are understudied in relation to early childhood development. However, these factors are potential predictors of developmental outcomes among children before the age of five years due to their hypothesized impacts on nutrition, brain growth, and overall health.

Environmental Risks and Early Childhood Development in Sub-Saharan Africa and Kenya

Sub-Saharan Africa has the highest percentage of children (60%) at risk for not reaching their developmental potential globally as it holds the largest burden of stunting and extreme poverty worldwide (1). Sixty-two percent of people in sub-Saharan Africa reside in rural areas (23). Much of this population is reliant on subsistence livelihoods, which are dependent on environmental conditions such as climate, seasons, land and soil quality, watersheds, and lake and ocean productivity (19,24). The region is also home to some of the highest rates of food insecurity and undernutrition (25), diverse climate change occurrences (19), and diseases like HIV (26) and malaria (27).

In Kenya in 2015, 74% of the population was rural (23) and about 10 million people (about one-quarter of its population) were food insecure (25). Households in Kenya face challenges in adapting to climate change (28) and coping with food insecurity (29). Rural areas and households in the Western and Nyanza provinces (study sites) have high rates of food insecurity (29). The prevalence of malaria and other acute infections in children, is also high in the Western and Nyanza provinces (29). The prevalence of stunted, underweight, and wasted children is higher in rural areas compared with urban areas in Kenya and highest among the poorest populations (29). The Western and Nyanza provinces have fairly high rates of stunting among children under five years (25% and 23%, respectively), which is a risk factor for poor development. Diets in rural areas and the Western and Nyanza provinces are also inadequate with low dietary diversity and low rates of recommended breastfeeding practices (29). Kenya is a malaria-endemic country with stable transmission around Lake Victoria in the western regions of Kenya throughout the year (29).

Kenya has a national early childhood development policy focusing on children up to eight years of age involving multiple sectors, including health, nutrition, education, social services, and water and sanitation (30). However, much of the early childhood development curriculum and focus throughout the country are on preschool-aged children. Measures of early childhood development in Kenya are limited and vary by region within the country, measure or domain assessed, and cultural differences.

1.2 Dissertation Overview

This dissertation assesses three key environmental factors that are hypothesized to be associated with early childhood development outcomes: food security, fish and fatty acid intake, and malaria. Rural Kenya serves as a promising location to study these dynamics due to its large rural subsistence-based population, its high degree of food insecurity, the importance of the Lake Victoria fishery to livelihoods and diets, and its high prevalence of malaria.

This dissertation is divided into five parts. The current chapter provides a brief framing and overview of the literature underlying the motivation for subsequent chapters. Three chapters follow assessing the relation between three environmental factors and early childhood development outcomes in rural Kenya. The fifth and final chapter includes conclusions tying together the implications of the dissertation findings.

The three specific aims of the dissertation research are:

1. To analyze the association between various dimensions of household food security and early childhood development using longitudinal data collected around Lake Victoria, Kenya over two years
2. To assess the importance of fish to early childhood development using longitudinal data collected over two years in a highly food insecure community around Lake Victoria, Kenya
3. To investigate the relation and pathway between malaria and early childhood development using blood tests collected in rural western Kenya.

1.3 Contributions of the Dissertation

This dissertation uses primary data collected in rural Kenya between 2012 and 2016 to provide a multifaceted in-depth assessment of three environmental determinants of early childhood development among children under age five years. The research aims to fill some of the gaps in understanding the food insecurity, natural resource-dependent dietary, and malarial disease drivers of developmental outcomes in vulnerable populations that have received less attention, yet are important given their pervasiveness. Expanding upon existing early childhood development literature with robust longitudinal studies (Chapters 2 and 3) and new areas of exploration (Chapter 4) may provide evidence to support targeted interventions enabling children to reach their fullest potential.

Chapter 2 presents the multidimensional associations between household food security and early childhood development outcomes where food insecurity is widespread and livelihoods are dependent on agriculture and fishing. Its rigorous methodology includes a robust longitudinal evaluation of the complexities of acute and chronic food insecurity in relation to gross motor, communication, and socio-emotional development.

Chapter 3 examines the importance of the quantity and quality of fish consumption to early childhood development in a highly food insecure population reliant on fishery resources. It reports on the quantity and types of fish consumed across seasons in light of fishery declines.

The contribution of fish to children's dietary quality in terms of fatty acids is also described. Finally, this chapter explores associations between children's fish intake and their gross motor, communication, and socio-emotional development over two years.

Chapter 4 assesses the relation between malaria and early childhood development in the context of a water, sanitation, hygiene, and nutrition integrated intervention as part of a randomized controlled trial where malaria is endemic. The chapter entails a thorough examination of malaria and the potential mediating effects of anemia on children's gross motor, communication, and socio-emotional development.

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Chapter 2

Multifaceted Dimensions of Household Food Insecurity Associated with Early Childhood Development

2.1 Introduction

Worldwide, one in nine people are food insecure, and most reside in low- and middle-income countries (LMICs) (1). Food security is when people have sustained physical, social, and economic access to sufficient, safe, and nutritious food that meets their dietary needs and food preferences (2). The African continent has the highest prevalence of food insecurity globally and it is the only region where the number of food insecure people has increased since 1990 (1). Sub-Saharan Africa also has the highest percentage of children at risk for developmental delays and a high burden of poor child development risk factors, including stunting and extreme poverty (3).

While one component of food security is nutritional adequacy, other components include food access, availability, utilization, and stability (4). These definitions of food security encompass more than current nutritional status, capturing vulnerability to future barriers to accessing appropriate and adequate food (5,6). Food security is affected by resource availability, environmental conditions, economics, politics, and social structures. There are many drivers of food accessibility, including seasonality, land availability and quality, water and irrigation techniques, agriculture inputs, livestock rearing resources, wild foods (animals, fish, plants) availability, climate, finances, markets, and subsidies or import/export regulations. Food insecurity can be chronic or transitory (4). Food security contributes to dietary intake and nutritional outcomes (e.g. BMI, stunting, wasting, underweight).

Household food insecurity resulting in the insufficient quantity and quality of food is of particular concern for children. Dietary deficiencies in early childhood emerging from food insecurity can limit physical growth and cognitive development during this critical period, even while controlling for socioeconomic status (7-9). Forty-three percent of children under age five years in LMICs are at risk of not meeting their developmental potential (10). About 17% of children under age five in LMICs are underweight and 13% are undernourished (1). Undernutrition and psychosocial stress during the first 1,000 days are often the cause of developmental deficits (11). Failure to meet development milestones has lifelong implications for later educational attainment, economic productivity, and chronic health, contributing to the cyclical intergenerational nature of poor nutrition and suboptimal development (10,12-14).

Associations between Food Insecurity and Child Development

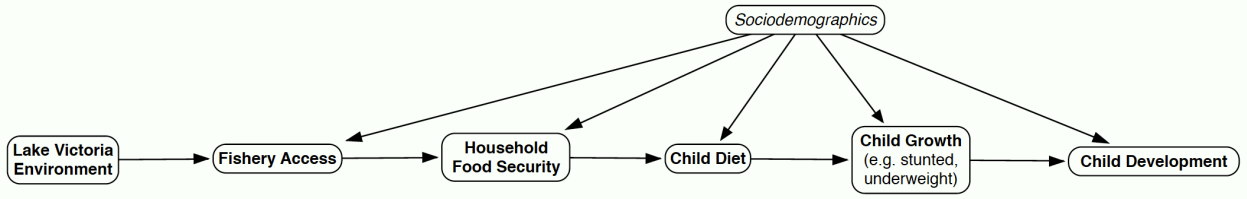
In a review of research on the association between household food insecurity and child intellectual, behavioral, and psycho-emotional development in the U.S., food insecurity was associated with suboptimal behavioral and intellectual outcomes independent of poverty status (15). In papers published since the review, similar findings of associations between household food insecurity and child development in high-income countries were documented. For example, one nationally representative U.S.-based study found significant cross-sectional associations between household food insecurity and mental disorders among children age 4 to 11 years, controlling for socioeconomic status (16). In a review of studies assessing relations between food insecurity and child health and behavior in Canada, food insecurity was associated with poor language comprehension, delays in socio-emotional, cognitive, and motor development, and higher levels of hyperactivity/inattention (17).

Studies in LMICs also show significant associations between food insecurity and child development outcomes, but there are few rigorous studies examining this question. One study in Bangladesh, for example, found household food security was associated with better language comprehension and expression after controlling for socioeconomic status (18); food insecurity was also associated with reduced quality of maternal-infant interactions in Bangladesh, which can affect children's development (19). In Uganda, food insecurity was associated with parental depression, which then was associated with poor school functioning and social and behavioral child outcomes (20).

Mechanisms Linking Food Insecurity and Child Development

Food insecurity is hypothesized to impact child development through pathways involving insufficient or inappropriate diet, leading to suboptimal growth thereby resulting in poor development (8). Undernutrition, illness, and psychosocial stress during the first 1,000 days are frequent causes of developmental deficits and represent a clear way in which food insecurity could be linked to child development outcomes (3). Food insecurity has been associated with poor physical growth, including stunting and underweight, in Colombia (21), Pakistan (22), Bangladesh (23), Nepal (24), Ethiopia (23), and pooled analyses across several LMICs (25,26) after socioeconomic status adjustments. Food insecurity adjusted for socioeconomic status has additionally been associated with infant feeding in Bangladesh (27).

Figure 1. Conceptual diagram of the relation between food security and child development in the context of the Lake Victoria fishery.



Several studies in LMICs have further found associations between stunting and poor developmental outcomes. A recent meta-analysis of 68 studies in 29 LMICs found significant cross-sectional and prospective associations between greater height-for-age Z-scores and better cognitive ability, earlier walking age, and higher motor scores (28). Most stunted children remain stunted as adults, which has long-term health implications (10). Moreover, a recent prospective cohort study in Jamaica found that the impact of stunting on development continues in the next generation of children (14).

Another relevant pathway connecting food security relates to caregiver stress and how that may influence responsive and nurturing caregiving, which can then affect child development (29). Maternal depression has been linked to psychological and developmental disturbances in infants and children in LMICs (30). Food insecurity is among the adversities undermining families' capacity to provide nurturing care (3) and is a risk factor for maternal depression in LMICs (31). In a recent review of relations between maternal mental health and early childhood outcomes in LMICs, food insecurity was found to be an important mechanism underlying adverse child mental health (32). After controlling for socioeconomic status, food insecurity was associated with caregiver psychosocial stress in Ethiopia (33) and parental depression in Uganda (20). In Jamaica, mothers' self-esteem was independently associated with the level of stimulation

provided to the child (34). In Bangladesh, maternal depression independently predicted infants' impaired motor development (35). Maternal depression can also negatively impact child growth, particularly in LMICs, which proceeds to impact developmental outcomes (36).

Differential Vulnerability

Effects of food insecurity on child development are likely to vary by age and stage of the child's development due to differential vulnerability across the life course. For example, children under three years are particularly vulnerable because of the sensitivity of early brain development and limited attention to early childhood development during this period (3). In a discussion of the timing and economic efficiency of early childhood development investments, Doyle et al. argue that antenatal and early childhood interventions may be most beneficial for developmental outcomes. In this article, socioeconomic gradients in socio-emotional functioning and cognitive skills were observed by age three years with evidence of the early emergence of the intergenerational transmission of socioeconomic inequalities related to cognitive, behavioral, and emotional development that may persist throughout life (37). Similarly, in a meta-analysis of child development interventions from 24 low-, middle-, and high-income countries outside of the U.S., interventions targeting infants and toddlers rather than older children had greater effects (38). Further, in a review of consequences of food insecurity, Hadley and Crooks cite several longitudinal studies in LMICs showing a dose response relationship between food insecurity and stunting and underweight (39). Due to this potential for increased vulnerability among younger children and the prospective relation between food insecurity and child nutrition, food insecurity in the recent past may be more strongly associated with developmental outcomes than current food insecurity. Similarly, extended periods of food insecurity may have worse effects on children's development due to increased risks for chronic undernutrition and caregiver stress over time.

Food Security and Nutrition in Kenya and the Lake Victoria Basin

About one-quarter of Kenya's population is chronically food insecure (1). Despite having natural resources available, many communities in Kenya and around Lake Victoria are unable to access them due to cost and the export industry (40,41); for these reasons, these regions experience high rates of food insecurity and child malnutrition. The prevalence of food insecurity in the Lake Victoria area is particularly high (42) with one study among island communities in Kenya reporting 60% of households being moderately or severely food insecure (40). In the 1950s, non-native fish species (exotic tilapia and Nile perch) were introduced into the lake (43), initially contributing to a productive fishing industry. However, this resulted in one of the largest mass extinctions in recent history as Nile perch outcompeted local cichlid species for food (44,45). Since the 1990s, the quantity of fish caught from Lake Victoria has been steadily declining (46). The increasing pressure put on the lake resulting from international and domestic demands for fish contributes to concerns about long-term food insecurity among communities in the area (47,48). Food insecurity in the Lake Victoria basin is complex and is at least partially determined by involvement in the fishery and a household's level of dependence on fish (40,46,47,49). As fish are continuing to be less available, malnutrition is also of growing concern as there is a high prevalence of stunting (23%) and underweight (7%) on the shores of Lake Victoria (42,50,51).

Contributions of this Research

Given the well-defined connections among malnutrition, caregiver stress, and developmental outcomes, further research is required to elucidate the extent to which food insecurity may contribute to these factors. Additional longitudinal research with multiple time points is important due to the sensitivity of timing of exposure to developmental risk factors, and potentially delayed or compounded effects of acute and chronic food insecurity. Nuances of food insecurity are important to quantify to address its complexity and accurately understand how it impacts child health. Robust measures of socioeconomic status also need to be aptly accounted for in analyses to disentangle effects of poverty and food insecurity on early childhood development.

Research assessing the link between food insecurity and child development is limited, particularly in LMICs where food insecurity is more prevalent. Much of the evidence is cross-sectional, focused on school-age children, and often limited by not appropriately accounting for socioeconomic status. Most studies also evaluate food security at one time point using one summary measure failing to account for seasonality and complexities of household food security (6). Moreover, child development outcomes are often assessed at one time point and frequently focus on one developmental domain.

Objectives

Three dimensions of food insecurity (timing, intensity, and duration) were assessed to comprehensively understand the relation between household food insecurity and three domains of child development (gross motor, communication, and personal social). Three hypotheses were tested: (1) greater food insecurity experienced by a household three months ago (*timing*) is associated with lower current child development scores, while controlling for current food insecurity, (2) more frequent food insecurity over the past two years (*intensity*) is associated with lower child development scores at the end of the two years, and (3) longer food insecurity over the past two years (*duration*) is associated with lower child development scores at the end of the two years.

2.2 Methods

Setting and Population

The study was conducted on Mfangano Island located within Homa Bay County in Nyanza Province, Kenya. Lying within Lake Victoria, Mfangano Island is 65 km^2 with a population of 21,000 (52). Broadly representative of much of the Lake Victoria region and island communities, the island's inhabitants are vulnerable to changes in the lake as fishery involvement for trade and subsistence is widespread (40). Mfangano Island is rural with no running water or paved roads, and limited electricity and health services.

Sample Selection

In July 2012, households were selected with stratified random sampling based on the regions of Mfangano Island. The selection criteria required that participants were household units with adult heads of household and their children consuming meals together. All participants had to be living on Mfangano Island and each household was required to have at least one child under the

age of two years in residence. The four regions bordering the lakeshore (North, South, East, and West) are defined by the Kenyan government, and two additional regions – a nearby island (Takawiri) and a community atop a small mountain at the center of the island (Sokolo) – were separately defined for sampling because of geographic diversity and hypothesized differences in livelihoods. Data were collected on a total of 303 households. The number of households selected from each region was proportional to its population. Six households had twins and both children were included in the study and analyses, yielding a total of 309 children. Five child deaths, including one twin, occurred during the study (2012 – 2015) and these participants were removed from analyses. Therefore, final results include 299 households and 304 children.

Study Design

Data were collected from December 2012 to April 2015 as part of a longitudinal panel study on fishing livelihoods, fish consumption, and child nutrition. Participants were located every three months over two years for a total of nine visits. Local enumerators conducted surveys in Dholuo, the regional language. Surveys and data collection tools were developed from validated measures and locally adapted.

Sociodemographics

Demographics, including household size (number of members) and maternal education (categorized into: none or some primary school and completed primary school or beyond), were assessed using standardized questionnaires administered three times every 12 months during the two-year study. An asset index was created from the first principal component of a principal components analysis (including assets such as housing composition, electricity, toilet facilities, and ownership of clock, radio, camera, computer, television, phone, refrigerator, land, livestock, solar lighting, and furniture). This approach has been shown to be a good proxy for household wealth and is correlated with consumption expenditures (53-55).

Anthropometry

Anthropometric measurements, including weight, length/height, and head circumference for each child were taken every three months (nine times in total) using standard techniques (56,57). Weight was measured using Seca digital scales (Seca 803 Digital Floor Scale; Seca Ltd., Chino, CA, USA). Length (children < 24 months) was measured using infantometers (Seca 417 Mobile Infantometer; Seca Ltd., Chino, CA, USA) and height (children > 24 months) was measured using stadiometers (Seca 213 Mobile Stadiometer; Seca Ltd., Chino, CA, USA). Standardized Z-scores for length/height-for-age (LAZ/HAZ) and weight-for-age (WAZ) were calculated to assess child growth according to WHO guidelines (57). Children were then classified as stunted (LAZ/HAZ < -2) or underweight (WAZ < -2).

Household Food Insecurity

The Household Food Insecurity Access Scale (HFIAS) was used to measure household food insecurity (58). The scale is widely utilized internationally and has been validated in several LMICs (59-63). The HFIAS has also been correlated with indicators of poverty and food consumption in various contexts (59,62-64). It includes nine questions about food access, quantity, and quality over the previous 30 days and was administered to households every three months (nine total household visits). Questions were scored from zero to three depending on whether the respondent experienced the described condition never (0 times), rarely (1-2 times),

sometimes (3-10 times), or often (>10 times). Food insecurity scores were calculated by summing each household's responses to the nine HFIAS questions at each time point and dividing scores by 10 for ease of interpretation. Scores at each time point range from 0 (least food insecure) to 2.7 (most food insecure, maximum possible value).

Three variables assessing different dimensions of household food insecurity were created using the HFIAS scores: timing, intensity, and duration. *Timing* values are the raw scores at each time point. The *intensity* of food insecurity was calculated as each household's cumulative score across all nine time points over the two-year study, ranging from 0 (least food insecure) to 24.3 (most food insecure, maximum possible value). The *duration* of food insecurity was quantified as the number of times (of the nine time points) throughout the two-year study that a household had a food insecurity score in the bottom quartile (most severely food insecure). The duration variable of food insecurity ranges from zero to nine times.

Child Development

Three domains of child development were assessed: gross motor, communication, and personal social. The corresponding subscales of the Ages and Stages Questionnaire: Inventory (ASQ:I) were used to measure each developmental outcome every six months for a total of five times (65). The ASQ:I is a newly modified version of the Ages and Stages Questionnaire (ASQ), which has been widely used for the developmental screening of children under five years of age (66-68) and has been used in LMICs (69). The questionnaires of the ASQ:I contain a series of age-specific items assessing the achievement of developmental milestones and tracking the child's progress. The five original subscales (Gross Motor, Communication, Personal Social, Fine Motor, and Problem Solving) were piloted to assess respondent bias, maternal accuracy in reporting children's abilities, cultural appropriateness, and feasibility, according to standard procedures (70). Gross Motor, Communication, and Personal Social responses were most accurate, valid, and feasible to administer in the field. The Gross Motor subscale evaluates body and muscle movement, including tasks like standing, walking, and balancing. The Communication subscale assesses language development and the use of words or sounds to express feelings. The Personal Social subscale reflects emotional responses and social interactions. Continuous scores for each subscale were calculated and converted to Z-scores at two-month age intervals to adjust for age. The ASQ:I was translated and adapted for this study by using local culturally appropriate items, examples, and tasks, but no substantial changes were made to the original questionnaires.

Statistical Analyses

All statistical analyses were conducted in Stata 14 (StataCorp, 2015). Three sets of linear multivariate analyses were undertaken to test each hypothesis corresponding to the three dimensions of food insecurity (Table 1). For the timing, intensity, and duration dimensions of food insecurity, three regression models were built for each child development subscale (Gross Motor, Communication, and Personal Social). The first model was comprised of child-level covariates, including child age in months and child gender. Time-invariant household-level baseline variables such as household size, assets, and maternal education were added to the second model. Child stunting and underweight status were added to the third model as variables hypothesized to lie along the pathway (and therefore alter associations) between household food insecurity and child development.

Table 1. Descriptions of variables used in statistical analyses.

Variable	Variable type	Definition	Measurement frequency
Gross Motor	Dependent	Continuous Z-scores, ASQ:I	5 times, every 6 months
Communication	Dependent	Continuous Z-scores, ASQ:I	5 times, every 6 months
Personal Social	Dependent	Continuous Z-scores, ASQ:I	5 times, every 6 months
Timing	Independent	Continuous, each time point, HFIAS	9 times, every 3 months
Intensity	Independent	Continuous, cumulative all time points, HFIAS	9 times, every 3 months
Duration	Independent	Count, number of times severely insecure, HFIAS	9 times, every 3 months
Child age	Covariate, Model 1	Continuous, months	Baseline
Child gender	Covariate, Model 1	Binary	Baseline
Household size	Covariate, Model 2	Binary	Baseline
Maternal education	Covariate, Model 2	Binary	Baseline
Asset index	Covariate, Model 2	Continuous, PCA	Baseline
Stunted	Covariate, Model 3	Height-for-age Z-scores < -2	9 times, every 3 months
Underweight	Covariate, Model 3	Weight-for-age Z-scores < -2	9 times, every 3 months

Missing time-invariant baseline sociodemographic (e.g. maternal education) data were replaced with values collected at subsequent time periods. The large number of data collection rounds enabled us to replace other missing values for variables that changed between time points with a participant's average across other time points with available data. These updates were necessary for less than 10% of cases for all variables.

Food Insecurity Timing: Generalized Estimating Equation Models

Longitudinal linear multivariate generalized estimating equation (GEE) models were used to quantify the association between food insecurity timing and child development subscales across time. Marginal GEE models were used to compute population-average effects allowing for longitudinal changes and robust standard errors (71). Correlated data (numerous visits per household or child) were accounted for using an exchangeable correlation structure (71). Other correlation structures (e.g. independent) produced similar results, but the exchangeable structure was chosen because there were multiple measurements on the same child and each child came from an independent household. This approach allowed us to examine the relation between food insecurity and child development outcomes within and across individuals. A lagged food insecurity variable was created to estimate the effect of household food insecurity three months ago on current gross motor, communication, and personal social Z-scores. Stunting and underweight status at each time point were included in the final model. All models include ASQ:I scores from four data collection rounds (6 month, 12 month, 18 month, and 24 month follow-up) and corresponding lagged food insecurity scores from three months prior to each round, while controlling for current household food insecurity scores.

Food Insecurity Intensity and Duration: Linear Regression Models

Linear multivariate regression models were employed to assess the association between food insecurity intensity and duration, and Gross Motor, Communication, and Personal Social subscales. Food insecurity intensity and duration are cumulative measures over the entire two-

year study and therefore these variables were examined in relation to child development subscale Z-scores at the final data collection round. Stunting and underweight status are defined in these analyses as the aggregate number of times a child was stunted or underweight during the past two years to capture nutritional status over the study period.

Ethics

The study was approved by the University of California, Berkeley Center for the Protection of Human Subjects and the Kenya Medical Research Institute Ethical Review Committee. Adult participants provided written consent for themselves and their children prior to enrollment.

2.3 Results

Sociodemographics and Child Growth

Mean household size was six and 52% of mothers had not completed primary school (Table 2). The mean age of children at baseline was 12 months, ranging from 1 to 26 months, and children were 24 to 51 months at the last follow-up visit. The prevalence of stunting was 15% among children under 12 months of age at baseline, peaked among children 18 to 23 months of age when it was 34%, and was lower among children over 36 months (25%). The underweight prevalence was generally low (3-11%), but greater among children 12 months of age and older at baseline. The underweight prevalence was larger among younger children in later follow-up visits (e.g. at 12 month follow-up 10% of children under age 24 months were underweight, at 24 month follow-up 8% of children under 36 months were underweight).

Table 2. Sociodemographic and anthropometric characteristics of study population.

	Mean ± SD or N (%) (n = 304)
Household size (number of people)[a]	6 ± 2
Asset index[a,b]	0.00 ± 1.66
Maternal education (highest level attained)[a]	
None or primary not completed	155 (52)
Completed primary or beyond	144 (48)
Child age at baseline (months)	12 ± 7
Child sex (male)	146 (48)
Stunted[c] at baseline	
< 12 months of age	24 (15)
≥ 12 months of age	40 (28)
Underweight[d] at baseline	
< 12 months of age	14 (9)
≥ 12 months of age	15 (11)
Stunted at 12 month follow-up	
< 24 months of age	50 (30)
≥ 24 months of age	43 (31)
Underweight at 12 month follow-up	
< 24 months of age	16 (10)
≥ 24 months of age	9 (6)
Stunted at 24 month follow-up	
< 36 months of age	42 (26)
≥ 36 months of age	36 (25)
Underweight at 24 month follow-up	
< 36 months of age	13 (8)
≥ 36 months of age	4 (3)

[a] n=299 households as five twins participated in the study. Baseline values as variables are time-invariant.
[b] Derived by use of principal components, includes housing construction (roof, floor), electricity, toilet, and ownership of clock, radio, camera, computer, television, phone, refrigerator, land, livestock, solar lighting, and furniture (bed, cabinet, sofa).
[c] Height-for-age Z-score < -2.
[d] Weight-for-age Z-score < -2.

Food Insecurity

Mean food insecurity scores (*timing*) did not substantially change across time points (ranging from 0.94 in Round 1 to 0.80 in Rounds 6, 7, and 8), although there was a wide range of scores (Table 3). Food insecurity scores within households did not greatly fluctuate over time as there was more variability in food insecurity scores between households. Food insecurity intensity over the two years was moderate (mean = 7.54 ± 2.98, range = 0 to 15.3). The majority of households (68%) experienced severe food insecurity less than three times (*duration*), but nearly one-quarter of households experienced severe food insecurity for at least one year (half of the study duration).

Table 3. Timing, intensity, and duration of household food insecurity over 24-month data collection period.

Food insecurity dimension (n = 304)		
Timing[a]	Mean ± SD	Range
Round 1[b]	0.94 ± 0.51	0, 2.7
Round 2	0.88 ± 0.46	0, 2.5
Round 3	0.81 ± 0.44	0, 2.3
Round 4	0.83 ± 0.40	0, 2.0
Round 5	0.83 ± 0.43	0, 2.2
Round 6	0.80 ± 0.45	0, 2.4
Round 7	0.80 ± 0.41	0, 2.2
Round 8	0.80 ± 0.44	0, 2.2
Round 9	0.84 ± 0.47	0, 2.7
Intensity[c]	Mean ± SD	Range
Cumulative 24 months	7.54 ± 2.98	0, 15.3
Duration[d]	N (%)	
Never	107 (35)	
1-2 times	101 (33)	
3-4 times	47 (15)	
5-6 times	28 (9)	
≥7 times	21 (7)	

[a] Scores range from 0-2.7 and are the sum of Household Food Insecurity Access Scale (HFIAS) question responses; higher scores are indicative of greater food insecurity.
[b] Rounds represent three-month data collection periods.
[c] Scores range from 0-24.3 and are the sum of scores at all nine data collection rounds spanning 24 months; higher scores are indicative of greater food insecurity.
[d] Number of times a household is severely food insecure (bottom 25th percentile of intensity food insecurity scores) during nine data collection rounds over 24 months.

Multivariate Analysis

Timing

The timing of food insecurity was significantly associated with child development subscale Z-scores (Table 4). Specifically, children in households that had experienced food insecurity three months prior had significantly lower gross motor (β -0.14; 95% CI -0.27, -0.0033), communication (β -0.16; 95% CI -0.30, -0.023), and personal social (β -0.20; 95% CI -0.33, -0.073) Z-scores, even when controlling for current food insecurity status and child demographics (Model 1). With the addition of the socioeconomic (Model 2) and anthropometric (Model 3) variables, the food insecurity timing variable from a previous time period was still significant for the Communication and Personal Social subscales; the coefficient did not remain significant for the Gross Motor subscale, however.

Maternal education and asset index scores were significantly associated with all three child development domains in all Models 2 and 3. Children whose mothers completed primary school or beyond and who lived in wealthier households had higher gross motor, communication, and personal social Z-scores. Stunting (β -0.29; 95% CI -0.42, -0.17) and underweight (β -0.42; 95% CI -0.69, -0.15) status were significant in gross motor analyses, highlighting the potential role of

child malnutrition on the causal pathway. Stunting was also significant in communication (β -0.27; 95% CI -0.42, -0.13) and personal social (β -0.26; 95% CI -0.38, -0.15) analyses, suggesting that linear growth retardation may contribute to some of the association between food insecurity timing and communication and personal social Z-scores.

Table 4. Association between child development Z-scores and food insecurity timing[a] over 24 months controlling for child characteristics (Model 1), household demographics (Model 2), and child nutritional status (Model 3).[b]

	Model 1[c] β (95% CI) (*n* = 304)	Model 2 [c,d] β (95% CI) (*n* = 304)	Model 3 [c,d] β (95% CI) (*n* = 304)
Gross Motor			
Food insecurity 3 months ago	-0.14 (-0.27, -0.0033)*	-0.10 (-0.24, 0.032)	-0.097 (-0.23, 0.036)
Food insecurity current	-0.083 (-0.21, 0.043)	-0.051 (-0.18, 0.075)	-0.050 (-0.18, 0.079)
Child sex (1=male)	-0.045 (-0.19, 0.10)	-0.033 (-0.18, 0.11)	-0.015 (-0.15, 0.12)
Maternal education (1=completed primary or beyond)		0.21 (0.069, 0.36)**	0.20 (0.065, 0.33)**
Asset index (standardized scores)		0.046 (-0.0045, 0.097)§	0.044 (-0.0039, 0.092)§
Stunted (1=HAZ < -2)			-0.29 (-0.42, -0.17)**
Underweight (1=WAZ < -2)			-0.42 (-0.69, -0.15)**
Communication			
Food insecurity 3 months ago	-0.16 (-0.30, -0.023)*	-0.12 (-0.27, 0.017)§	-0.12 (-0.26, 0.019)§
Food insecurity current	-0.052 (-0.19, 0.086)	-0.013 (-0.15, 0.12)	-0.0070 (-0.14, 0.13)
Child sex (1=male)	-0.19 (-0.35, -0.028)*	-0.18 (-0.34, -0.019)*	-0.17 (-0.32, -0.014)*
Maternal education (1=completed primary or beyond)		0.19 (0.030, 0.35)*	0.18 (0.024, 0.33)*
Asset index (standardized scores)		0.070 (0.012, 0.13)*	0.069 (0.012, 0.13)*
Stunted (1=HAZ < -2)			-0.27 (-0.42, -0.13)**
Underweight (1=WAZ < -2)			-0.10 (-0.31, 0.11)
Personal Social			
Food insecurity 3 months ago	-0.20 (-0.33, -0.073)**	-0.17 (-0.30, -0.036)*	-0.16 (-0.29, -0.031)*
Food insecurity current	-0.0049 (-0.15, 0.14)	0.028 (-0.11, 0.17)	0.032 (-0.11, 0.18)
Child sex (1=male)	-0.17 (-0.33, -0.18)*	-0.16 (-0.31, -0.011)*	-0.15 (-0.30, -0.0048)*
Maternal education (1=completed primary or beyond)		0.14 (-0.011, 0.30)§	0.13 (-0.018, 0.28)§
Asset index (standardized scores)		0.063 (0.0056, 0.12)*	0.062 (0.0060, 0.12)*
Stunted (1=HAZ < -2)			-0.27 (-0.38, -0.15)**
Underweight (1=WAZ < -2)			-0.16 (-0.38, 0.062)

[a] Linear scores at each time point.
[b] Generalized Estimating Equations models employed with four time points included at six month intervals.
[c] Controlled for child age.
[d] Controlled for household size.
** $p < 0.01$
* $p < 0.05$
§ $p < 0.1$

Intensity

Children in households that were more intensely food insecure (cumulative food insecurity score) over the past two years had significantly lower gross motor (β -0.047; 95% CI -0.077, -0.018), communication (β -0.042; 95% CI -0.076, -0.0073), and personal social (β -0.042; 95% CI -0.074, -0.010) Z-scores (Table 5, Model 1). These findings remained significant with the inclusion of socioeconomic covariates (Model 2) and anthropometric measures (Model 3) for the Gross Motor subscale, but not for the Communication or Personal Social subscale.

Maternal education was significantly associated with all child development subscales. Low maternal education accounted for some of the association between food insecurity intensity and lower developmental scores. Stunting was also consistently significant across child development domains (gross motor: β -0.077; 95% CI -0.10, -0.048; communication: β -0.053; 95% CI -0.086, -0.019; personal social: β -0.056; 95% CI -0.087, -0.024) showing how food insecurity intensity was negatively associated with performance on the Gross Motor, Communication, and Personal Social subscales through a potential pathway of linear growth retardation.

Table 5. Association between child development Z-scores and food insecurity intensity[a] over 24 months controlling for child characteristics (Model 1), household demographics (Model 2), and child nutritional status (Model 3).[b]

	Model 1[c] β (95% CI) (*n* = 304)	Model 2[c,d] β (95% CI) (*n* = 304)	Model 3[c,d] β (95% CI) (*n* = 304)
Gross Motor			
Food insecurity	-0.047 (-0.077, -0.018)**	-0.030 (-0.062, 0.0010)§	-0.028 (-0.058, 0.0019)§
Child gender (1=male)	-0.026 (-0.20, 0.15)	-0.017 (-0.19, 0.16)	0.010 (-0.15, 0.17)
Maternal education (1=completed primary or more)		0.24 (0.063, 0.42)**	0.20 (0.035, 0.37)*
Asset index (standardized scores)		0.042 (-0.014, 0.098)	0.037 (-0.016, 0.089)
Stunted[e]			-0.077 (-0.10, -0.048)**
Underweight[e]			-0.0044 (-0.055, 0.046)
Communication			
Food insecurity	-0.042 (-0.076, -0.0073)*	-0.025 (-0.062, 0.012)	-0.022 (-0.057, 0.014)
Child gender (1=male)	-0.24 (-0.44, -0.034)*	-0.23 (-0.43, -0.027)*	-0.21 (-0.40, -0.013)§
Maternal education (1=completed primary or more)		0.18 (-0.031, 0.39)§	0.15 (-0.055, 0.35)
Asset index (standardized scores)		0.056 (-0.0095, 0.12)§	0.051 (-0.012, 0.11)
Stunted[e]			-0.053 (-0.086, -0.019)**
Underweight[e]			-0.065 (-0.12, -0.0045)*
Personal Social			
Food insecurity	-0.042 (-0.074, -0.010)*	-0.023 (-0.057, 0.011)	-0.021 (-0.054, 0.012)
Child gender (1=male)	-0.24 (-0.43, -0.053)*	-0.23 (-0.42, -0.044)*	-0.21 (-0.39, -0.028)*
Maternal education (1=completed primary or more)		0.24 (0.050, 0.43)*	0.21 (0.027, 0.40)*
Asset index (standardized scores)		0.055 (-0.0047, 0.12)§	0.051 (-0.0072, 0.11)§
Stunted[e]			-0.056 (-0.087, -0.024)**
Underweight[e]			-0.00036 (-0.057, 0.056)

[a] Linear scores, sum of HFIAS scores at all nine data collection rounds over 24 months, defined as cumulative severity of food insecurity.

[b] Linear multivariate regression models assessing the association between food insecurity intensity and child development scores at the end of the two-year study.

[c] Controlled for child age.

[d] Controlled for household size.

[e] Count variables, number of times child was stunted (HAZ < -2) or underweight (WAZ < -2) over two-year study, range 0-9 times.

** $p < 0.01$

* $p < 0.05$

§ $p < 0.1$

Duration

The duration of food insecurity (number of times food insecure in previous two years) was also significantly associated with all three child development subscales (Table 6, Model 1). The longer a household experienced severe food insecurity over the past two years, the lower a

child's development Z-scores were. Specifically, findings were significant at the $p < 0.05$ level for gross motor Z-scores (β -0.050; 95% CI -0.087, -0.012) and were significant at the $p < 0.1$ level for communication (β -0.042; 95% CI -0.086, 0.0013) and personal social (β -0.037; 95% CI -0.077, 0.0039) Z-scores. Across all child development subscales, food insecurity duration coefficients decreased as maternal education, household assets, and child malnutrition contributed to some of the associations.

Maternal education and asset index scores were also significant when added to models, paralleling reductions in the significance of associations with food insecurity duration (Model 2). Stunting was significant in all subscale analyses (gross motor: β -0.077; 95% CI -0.11, -0.049; communication: β -0.053; 95% CI -0.087, -0.019; personal social: β -0.056; 95% CI -0.088, -0.024). Similar to food insecurity intensity findings, underweight status was also significant (β -0.064; 95% CI -0.12, -0.0033) in communication analyses.

Table 6. Association between child development Z-scores and food insecurity duration[a] over 24 months controlling for child characteristics (Model 1), household demographics (Model 2), and child nutritional status (Model 3).[b]

	Model 1[c] β (95% CI) (*n* = 304)	Model 2[c,d] β (95% CI) (*n* = 304)	Model 3[c,d] β (95% CI) (*n* = 304)
Gross Motor			
Food insecurity	-0.050 (-0.087, -0.012)**	-0.032 (-0.071, 0.0061)§	-0.029 (-0.066, 0.0075)
Child gender (1=male)	-0.025 (-0.20, 0.15)	-0.015 (-0.19, 0.16)	0.012 (-0.15, 0.18)
Maternal education (1=completed primary or more)		0.25 (0.077, 0.43)**	0.22 (0.048, 0.38)*
Asset index (standardized scores)		0.048 (-0.0065, 0.10)§	0.042 (-0.0090, 0.094)
Stunted[e]			-0.077 (-0.11, -0.049)**
Underweight[e]			-0.0028 (-0.053, 0.048)
Communication			
Food insecurity	-0.042 (-0.086, 0.0013)§	-0.025 (-0.070, 0.020)	-0.020 (-0.063, 0.024)
Child gender (1=male)	-0.24 (-0.44, -0.033)*	-0.23 (-0.43, -0.026)*	-0.21 (-0.40, -0.013)*
Maternal education (1=completed primary or more)		0.19 (-0.018, 0.40)§	0.16 (-0.042, 0.36)
Asset index (standardized scores)		0.061 (-0.0026, 0.12)§	0.056 (-0.0047, 0.12)§
Stunted[e]			-0.053 (-0.087, -0.019)**
Underweight[e]			-0.064 (-0.12, -0.0033)*
Personal Social			
Food insecurity	-0.037 (-0.077, 0.0039)§	-0.017 (-0.059, 0.025)	-0.015 (-0.055, 0.026)
Child gender (1=male)	-0.24 (-0.43, -0.053)*	-0.23 (-0.42, -0.044)*	-0.21 (-0.40, -0.029)*
Maternal education (1=completed primary or more)		0.26 (0.065, 0.45)**	0.23 (0.041, 0.41)*
Asset index (standardized scores)		0.062 (0.0036, 0.12)*	0.059 (0.00091, 0.12)§
Stunted[e]			-0.056 (-0.088, -0.024)**
Underweight[e]			0.00028 (-0.056, 0.057)

[a] Count variable, number of times a household is severely food insecure (bottom 25th percentile of intensity food insecurity scores) during nine data collection rounds over 24 months.

[b] Linear multivariate regression models assessing the association between food insecurity duration and child development scores at the end of the two-year study.

[c] Controlled for child age.

[d] Controlled for household size.

[e] Count variables, number of times child was stunted (HAZ < -2) or underweight (WAZ < -2) over two-year study, range 0-9 times.

** $p < 0.01$

* $p < 0.05$

§ $p < 0.1$

2.4 Discussion

The timing, intensity, and duration of household food insecurity were significantly associated with three domains of children's development (gross motor, communication, and personal social); these associations were often attenuated with the inclusion of household- and child-level variables. Food insecurity three months in the past (*timing*) was negatively associated with current child development subscale Z-scores. Children in households with more severe food insecurity (*intensity*) had lower gross motor, communication, and personal social Z-scores. More frequent household food insecurity (*duration*) was also associated with poorer child development. As expected, maternal education and household socioeconomic status as well as child malnutrition, measured through stunting and underweight, contributed broadly to associations between food insecurity and developmental outcomes.

Food insecurity timing is a measure of acute food insecurity while intensity and duration are indicators of chronic food insecurity. Although conceptually different, food insecurity intensity and duration are correlated ($R^2 = 0.85$) and show similar patterns of associations with child development scores. The larger coefficients in models assessing food insecurity timing suggest that recent experiences of food insecurity may be particularly important in proximate changes in child development scores. Critically, short-term food insecurity, measured through the timing variable, was significantly associated with child development independent of the association with child growth, suggesting that food insecurity may have immediate consequences for child development. Such outcomes may result from either or both restrictions on food access and consumption that may not yet be observable in anthropometric indicators as well as the psychosocial consequences that affect care for children and increase stress within food insecure households.

The present study has several strengths. The consistency in the direction, magnitude, and significance of effects across all dimensions of food insecurity and child development subscales contributes to the robustness of results. The longitudinal nature of the study allowed analyses to capture some of the complexity of household food insecurity. The nine measurements of food insecurity at three-month intervals spanning two years enabled analyses to account for seasonality and nuances in households' experiences of food insecurity over time and to assess anthropometric measurements and ASQ:I scores during children's critical period of growth and development. Assessing three dimensions of household food insecurity (timing, intensity, and duration) and multiple domains of child development also yields a more comprehensive understanding of the dynamics of acute and chronic food insecurity households encounter. Controlling for socioeconomic status provided further evidence of the importance of food insecurity beyond poverty. Finally, building models by systematically adding variables to analyses allowed for an extensive evaluation of how food insecurity can affect child development as well as the potential pathways of impact.

The study also has several limitations. Household food insecurity and child development are complex and this study is limited by the definitions and measures of each. The HFIAS primarily focuses on food insecurity access, failing to capture other aspects of food insecurity like food availability, utilization, nutrition, intrahousehold allocation, and feeding practices (72,73). This tool can be subject to bias in terms of recall and subjectivity as it inquires about participants'

perceptions. While demonstrations of ASQ:I items were facilitated, bias may also be present in the child development measures as the tool is based on caregiver report. This study only assessed three components of children's development and therefore interpretations are restricted to these domains. Other variables related to food insecurity and child development such as dietary intake, caregiver mental health, and elements of childcare were not included in these analyses, but may contribute to these relations. Moreover, while the study population is comparable to others reliant on natural resources and subsistence fishing and agriculture livelihoods, the generalizability of results may be confined by the isolation of the island. Causal interpretations cannot be made, but the longitudinal data collected at multiple time points allowed for rigorous analyses.

Household food insecurity in the study population was widespread and reflects similar findings of food insecurity in Kenya and Lake Victoria communities (1,42). The prevalence of underweight and stunted children in this study population were comparable to national, rural, and Nyanza Province values (42), suggesting these results may have broad analogs in communities experiencing similar rates of food insecurity and malnutrition. Results highlight that both acute and chronic household food insecurity are associated with a variety of domains of development in early childhood. The significant associations found between food insecurity and child development outcomes confirm past findings (74,18). Part of this association may occur through a pathway of chronic malnutrition, which is observed in previous studies in LMICs examining food insecurity and stunting among children under age five years (26). Linear growth retardation as a potential mechanism in these analyses is corroborated by research reporting stunting as a predictor of various developmental outcomes (3,11,75). These findings reinforce the need for integrated nutrition interventions (3,12,76) and nutrition-sensitive food security programs (77) to address chronic food insecurity.

These results are also important because food insecurity and poor child development are widespread throughout LMICs. The role of food insecurity in children's development in this study highlights the need to better understand and address this association. Findings regarding the timing of food insecurity suggest the immediacy of effects of food insecurity on child development and the potential for food insecurity metrics to be an early indicator of these poor outcomes. Rural households' food security is closely tied to their dependency on local natural resources, and increasing environmental changes in sensitive regions (i.e., freshwater fisheries) threatens sustained food security. Seasonal, climatic, and political threats to food insecurity thus have the potential to affect not only household food insecurity and nutrition, but may forebode short- and, ultimately, long-term effects on child development.

Future research can further examine the diverse, multidimensional pathways between household food insecurity and child development that lead to adverse outcomes. By assessing multiple dimensions of food insecurity, research can provide a more comprehensive understanding of its effects. The effects of food insecurity on child development can be better understood through assessments of additional domains of child development and evaluations of potential mediators on the pathway between these. Similar studies can also be replicated in other populations to ensure findings are generalizable. The particular role of parental care and child diet, and formal mediation analyses of indicators of child malnutrition (i.e., stunting) can help explain how food insecurity affects children's development. Expanded research can also inform targeted

interventions that can prevent and build resilience to food insecurity which may benefit children's developmental potential and have intergenerational effects. Interventions targeting the integrated food insecurity, malnutrition, and development risks that vulnerable children face early in life can reduce economic and health inequities (3,12,76).

2.5 Conclusion

These findings highlight the crucial need for policies and programs to address acute and chronic food insecurity. Study results provide evidence of poor developmental outcomes among young children in food insecure households. A more complete understanding of the consequences of food insecurity is critical and can be attained by analyzing its various dimensions in more comprehensive ways. Food insecurity may have short-term implications for child development and therefore preventing and building resilience to even temporary food insecurity is urgent. Acute and chronic household food insecurity may impact early childhood development through a pathway of linear growth retardation suggesting that sustainable integrated interventions could have multifaceted benefits. For the hundreds of millions of people in LMICs who are food insecure, improving food security is paramount for enabling vulnerable children to meet their full potential. In recognizing the compounding adverse effects of food insecurity and poor development across generations, food security research and interventions need to continue to be prioritized both for households in LMICs today and for their families in the future.

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Chapter 3

Fish Quantity and Quality Longitudinally Associated with Early Childhood Development

3.1 Introduction

As children in low- and middle-income countries (LMICs) start to wean in the first year of life, they are at increased risk of malnutrition as complementary foods are often inadequate to meet nutritional needs (1). In fact, the period from 6 to 24 months represents one of, if not the highest risk period, for linear growth retardation (1). Complementary foods are often inadequate to meet nutritional needs for babies and toddlers as they transition away from exclusive breastfeeding, and nutrition is compromised during this period by exposure to infectious agents in the environment (1). Fatty acid intake specifically and nutrition in general are most critical during pregnancy and the first two years of life as nutritional deficiencies during this period contribute to later childhood growth and cognitive performance delays with lifelong health implications (2-5). Forty-three percent of children under age five years in LMICs are at risk for not meeting their developmental potential (6). Suboptimal development in early life can have negative consequences for later school achievement, employment, and health (7-9) with intergenerational effects (10).

Fish for Polyunsaturated Fatty Acids

Fish and seafood are the best sources of polyunsaturated fatty acids (PUFAs), but increased consumption of these foods is not always affordable, sustainable, or feasible. Fish stocks globally are under pressure and marine fish are a better source of PUFAs than freshwater fish (11). Increasing fish consumption rather than intake of plant foods may be more efficient to increase fatty acid status (12). In many regions, fish are not only a source of high-quality food, but also income (13,14). Access to fish is complicated by pricing, gender, and export dynamics of this high-value food (14,15). Fish access for local consumption, especially in LMICs, may be restricted to certain fish, which are often lower in value. These issues underscore the importance of fish to the provision of sufficient PUFA intake, especially long-chain PUFAs that are most important for development (12).

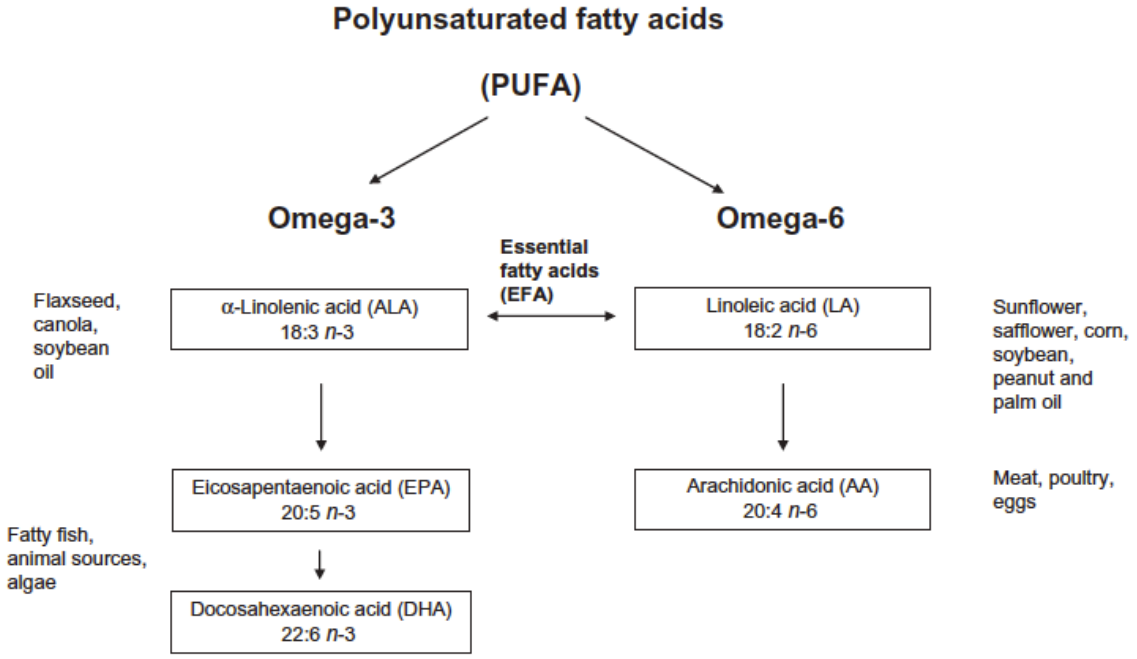
Fatty Acids Overview

Fat is composed of various fatty acids, including PUFAs, which play different functional and structural roles. Long-chain PUFAs (i.e., EPA, DHA, and AA) are especially important for infant and child brain development in addition to mental health, behavior, cognition, gene expression and regulation, intracellular communication, and long-term metabolic processes (16-18). There is no evidence of growth improvement following fatty acid supplementation in children older than two years demonstrating the importance of adequate intake in early life (12,19). PUFAs are essential fatty acids meaning they are not synthesized by the body and must be obtained from the diet. Key PUFAs include omega-3 fatty acids such as alpha-linolenic acid (ALA) and eicosapentaenoic acid (EPA), which are precursors to docosahexaenoic acid (DHA), and omega-6 PUFAs such as arachidonic acid (AA) and its precursor linoleic acid (LA) (Figure 1).

DHA and AA are the two most abundant long-chain PUFAs in the brain where they are critical for infant development (20,21). DHA is important for neurodevelopment, short-term memory, visual acuity, immune system function, automatic nervous system function, and metabolic pathways (20,22-24). EPA likely plays a more substantial role in immunological health in children (21,24). Low omega-3 PUFA intake in early life may have a negative effect on mental and motor development because the brain is growing at a rapid rate during this time (11). While

all PUFAs are important for growth and development, low ALA and/or high LA can result in reduced cognitive function and behavioral development. Even when diets are sufficient in ALA, high consumption of LA can lead to brain development impairments due to the inhibition of conversion of ALA to DHA (25). Moreover, conversion of short-chain PUFAs (e.g. ALA) into long-chain PUFAs (e.g. DHA) can be low particularly early in life (26-29). Therefore, it is important to ensure optimal levels of specific PUFAs are obtained and the direct intake of foods with DHA and AA can be a more efficient source of PUFAs compared with consumption of foods with shorter chain PUFAs.

Figure 1. Classification of polyunsaturated fatty acids (PUFAs) (12).



Omega-3 PUFA intake is particularly valuable for infants' and children's growth and development. Low omega-3 PUFA intake in early life may have a negative effect on mental and motor development because the brain is growing at a rapid rate during this time (11). A meta-analysis of RCTs assessing the impact of omega-3 supplementation for at least three months on cognition in infants, children, and adults in high-, middle-, and low-income countries found significant improvements in language, motor, and cognitive abilities among children under five years receiving supplements (19). Recently, RCTs with lipid-based nutrient supplement (LNS) (which contain PUFAs, including DHA) interventions designed to enhance maternal and infant nutritional status were undertaken to evaluate effects on infant growth and development. Studies show that provision of maternal and child LNS may affect walking at 12 months, but not motor, language, or socio-emotional development at 18 months in Ghana (30) and Malawi (31).

Specific PUFA recommendations are limited. There is less evidence informing omega-3 compared to omega-6 PUFAs guidelines (11). Recommendations that do exist suggest that infants and young children age 6 to 24 months have about 35% of energy from fat in their total food supply, 3.0% to 4.5% of energy from LA (omega-6), and 0.4% to 0.6% of energy from ALA (omega-3) (32). Recommendations for malnourished (i.e., moderately stunted or wasted)

children are higher: their diet should contain at least 4.5% of energy (or 5g/1000kcal) from LA and at least 0.5% of energy (or 0.85g/1000kcal) from ALA (33). There are no recommendations about guidelines for the intake of long-chain PUFAs like DHA.

PUFA Intake in LMICs

Fat intake in low-income countries may be low, but little information about fat composition and fatty acids of foods consumed in these regions is known (25). Per capita supply of fat and omega-3 fatty acids increases with increasing GDP (11). Information on fatty acid intake in low-income countries in early life is scarce (11,34). PUFA status is of concern in low-income countries where fat consumption may be minimal and common sources of fat may have low ALA and high LA content. Although fat requirements in children in LMICs are similar to those in high-income countries, there may be additional needs imposed by environmental stressors such as recurrent infections (34). Consequences of inadequate PUFA intake in low-income countries have received little attention, despite potential implications for child development in these regions (25). The immune benefits of PUFAs for children in low-income countries where diseases or persistent enteropathy are widespread could also be particularly important (35).

While breast milk is an important source of PUFAs globally, there are large variations among populations and poor breastfeeding practices can put children at risk for insufficient intake (36). Alongside breast milk, fish are the primary source of EPA and DHA for young children while AA comes from other animal foods. Sources of ALA and LA are largely plant oils, nuts, and seeds while some animal meats also have LA. Optimal amounts of these PUFA-rich foods are not available or accessible in many LMICs (11). A review including 13 LMICs reported that the main sources of PUFAs in these countries are cereals and vegetable oils, which have small amounts of long-chain PUFAs that are not beneficial for infant development. The authors additionally found that the omega-3 PUFA supply in these countries was low and below recommended levels in countries with the lowest GDP (11). Complementary foods in LMICs are typically cereal-based with low fat content (11). In populations with predominantly plant-based diets, infants and young children will typically have intake values of omega-3 PUFAs that are below recommendations, particularly if breastfeeding is stopped early or there is a lack of animal-source foods (11). PUFA status may also be threatened when energy or caloric deficiency takes place (37) suggesting that food insecure populations are vulnerable. However, research on PUFAs in food insecure environments is limited and further research is needed to determine whether PUFAs are neuroprotective for children from disadvantaged or low-income backgrounds (37).

Mechanisms Linking Fish Intake and Child Development in LMICs

In LMICs, poor dietary diversity, including limited access to animal-source foods such as fish leads to low PUFA intake limiting growth and brain development, thereby contributing to developmental deficits. In a review of 11 LMICs' Demographic and Health Surveys, lower dietary diversity was significantly associated with smaller height-for-age Z-scores as a main effect or in an interaction in all but one country (38). In a review of dietary practices throughout Kenya, children were found to have inadequate energy, fat, and micronutrient intakes with low animal-source food and fish consumption, even in lakeside and oceanside communities (39). In an RCT with schoolchildren in Kenya, children in intervention groups with animal-source foods

in feeding programs had higher subject test scores compared with children in the control group, adjusting for average energy intake and socioeconomic status (40).
Caregiver stress and mental health is another mechanism linking fish and, more specifically, PUFA intake with child development. Lack of access to food can negatively affect caregiver mental health (41), thereby undermining caregiver capacity to provide nurturing care to support proper development (6). A family's dependency on degrading natural resources such as fisheries can induce vulnerabilities and stress in surrounding communities (42), especially among heads of households or caregivers. As fish consumption and subsistence-based diets fluctuate seasonally in Kenya and throughout LMICs (43), corresponding caregiver stress or depression can contribute to developmental problems in infants and children (44).

Lake Victoria and Fish Consumption

Malnutrition around Lake Victoria is widespread and complex due to the lake's history of ecological alterations. Lake Victoria supports Africa's largest inland fishery and a population of 35 million people (45). In the Nyanza province of Kenya at the base of the Lake Victoria fishery, the lowest levels of meat and other non-fish protein food (e.g. beans) consumption in the country have been reported (46). In the same region, the prevalence of stunted and underweight children is high. The introduction of Nile perch and exotic tilapia in the 1950s (47) led to one of the greatest extinctions in recent history, contributing to the loss of over 300 native cichlid species (48,49). Since then, the ecology of Lake Victoria has been rapidly changing and fish populations have been declining (50). Nile perch and dagaa are Lake Victoria's two key commercial species. While Nile perch populations have been declining due to overfishing, local cichlid populations have slowly rebounded (51). Similarly, dagaa is growing in production paralleling decreases in Nile perch catch. Introduced tilapia are increasingly scarce due to fishing pressure. The implications of the environmental changes in the Lake Victoria basin for fatty acid intake and child nutrition and development may be substantial and timely.

Around Lake Victoria, fish are a key component of diets. They are likely the main dietary supply of fatty acids in the area. They are also a substantial source of calories, protein, and micronutrients while serving as a nutritional safety net for fishing households (14,52). However, malnutrition is high in areas inhabited by fishermen, including the Lake Victoria basin, largely because these communities eat small amounts of some of the fish they produce and have limited access to other sources of nutrients (53).

Contributions of this Research

There are research gaps in understanding complementary feeding practices, fatty acid status, and fish consumption among children in LMICs and around Lake Victoria. While the nutritional importance of fish is known, the nutritional benefits fish provide to populations in LMICs, food insecure populations, and populations around Lake Victoria have not been comprehensively described. Although fish are available to communities, fluctuations in fishery access, consumption patterns, and intra-household allocation dynamics are not well quantified. Studies also assess omega-3 fatty acids as a group or focus on one PUFA such as DHA. Assessing several important individual omega-3 and omega-6 fatty acids comprehensively is critical because of the conversion of short-chain PUFAs to long-chain PUFAs and the complexities of interactions between omega-3 and omega-6 fatty acids in the body, contributing to potentially varied effects on child development. The fatty acid content of different fish species varies,

demonstrating the importance of understanding the role of consumption of specific species to nutrition and development. Moreover, there is limited longitudinal research assessing child development outcomes in relation to fish consumption in LMICs and food insecure populations. Many studies only evaluate fish intake at one time point or in one year and do not distinguish by fish type. The seasonality of fishery access and food insecurity creates the need for robust longitudinal assessments.

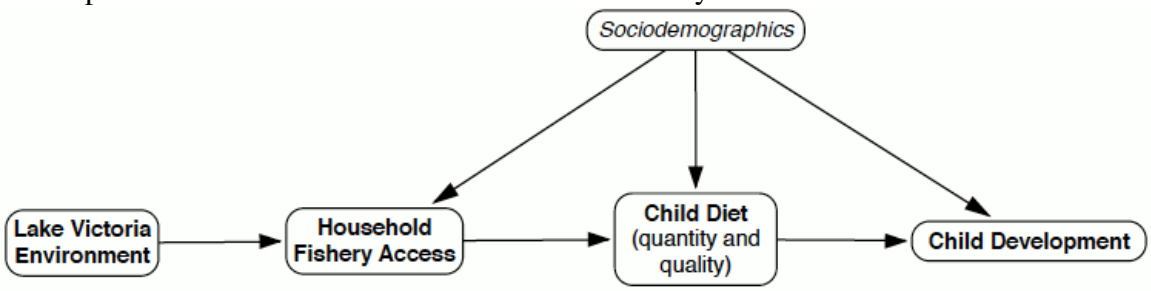
The main contribution of this study is to quantify the role of fish consumption in children's fatty acid status and development. Relating to this objective, we hypothesize that greater fish intake among children is associated with greater fatty acid consumption. In turn, we hypothesize that greater fatty acid intake is associated with better developmental outcomes. Another contribution of this research is to explore fatty acid intake from complementary foods. We hypothesize that fish are the main source of fatty acids from complementary foods and that fish intake will vary by season while fatty acid status will vary by fish species consumed. Overall, these dynamics are imperative to understand as an avenue through which fishery productivity changes could impact child development.

Objectives

This study aimed to assess the importance of fish and fatty acids to children around Lake Victoria (Figure 2). The objectives and related hypotheses of the research include:

1. Describe fatty acid intake (total omega-3 fatty acids, total omega-6 fatty acids, LA, AA, ALA, EPA, DHA) from complementary foods over two years
   Hypotheses:
   a) Short-chain PUFA and omega-6 fatty acid intake are greater among all children
   b) Fatty acid intake from complementary foods is greater among older children
2. Assess the types of fish consumed over two years and whether there are seasonal differences in fish type consumption
   Hypotheses:
   a) There are seasonal differences in fish type consumption
   b) The most consumed species are Nile perch and dagaa
3. Describe the contribution of fatty acid intake from fish to total fatty acid intake from complementary foods over two years
   Hypotheses:
   a) Long-chain PUFA (AA, EPA, and DHA) intake is greater among older children
   b) Total omega-3 fatty acid intake is greater among older children
4. Analyze associations between fish intake, fatty acid intake, and child development outcomes over two years
   Hypotheses:
   a) Greater amounts (grams) of fish consumed three months ago is associated with higher current gross motor, communication, and personal social child development Z-scores
   b) Greater total omega-3 fatty acid and long-chain PUFA (EPA, DHA, and AA) intake are associated with higher current gross motor, communication, and personal social child development Z-scores

Figure 2. Conceptual diagram of the relation between fishery resources, dietary intake, and child development in the context of the Lake Victoria fishery.



3.2 Methods

Setting and Population

The study was conducted on Mfangano Island located within Homa Bay County in Nyanza Province, Kenya. Lying within Lake Victoria, Mfangano Island is 65 km^2 with a population of 21,000 that is similar to lakeside communities in Kenya, Tanzania, and Uganda (54). Broadly representative of much of the region, the island's inhabitants are vulnerable to changes in the lake as fishery involvement for trade and subsistence is widespread (15). Mfangano Island is rural with no running water or paved roads, and limited electricity and health services. Food insecurity is pervasive with studies reporting 60% to 75% of households being moderately or severely food insecure (15,55).

Sample Selection

Households were selected with stratified random sampling based on the sub-locations of Mfangano Island in July 2012. The selection criteria required that participants were household units with adult heads of household and their children consuming meals together. All participants had to be living on Mfangano Island and each household was required to have one child under the age of two years in residence. The four sub-locations bordering the lakeshore (North, South, East, and West) are defined by the Kenyan government, and two additional sub-locations – a nearby island (Takawiri) and a community atop a small mountain at the center of the island (Sokolo) – were added for sampling because of geographic diversity and hypothesized differences in livelihoods. Data were collected on a total of 303 households. The number of households selected from each sub-location was proportional to its population. Six households had twins and both children were included in the study and analyses, yielding a total of 309 children. Five child deaths, including one twin, occurred during the study (2012 – 2015) and these participants were removed from analyses. Therefore, final results include 299 households and 304 children.

Study Design

Data were collected from December 2012 to April 2015 as part of a longitudinal panel study on fishing livelihoods, fish consumption, and child nutrition. Participants were located every three months over two years for a total of nine visits. Local enumerators conducted surveys in Dholuo, the regional language. Surveys and data collection tools were developed from validated measures and locally adapted.

Sociodemographics

Household demographics, including household size, asset ownership, and maternal education were assessed using standardized questionnaires administered three times every 12 months. Socioeconomic status was defined with an asset index created using the first principal component from a principal components analysis, which has been shown to produce a good proxy for household wealth and is correlated with consumption expenditures (56-58).

Anthropometry

Anthropometric measurements, including weight, length/height, and head circumference for each child were taken every three months (nine times in total) using standard techniques (59,60). Weight was measured using Seca digital scales (Seca 803 Digital Floor Scale; Seca Ltd., Chino, CA, USA). The length of children under 24 months of age was measured using infantometers (Seca 417 Mobile Infantometer; Seca Ltd., Chino, CA, USA) and the height of children over 24 months of age was measured using stadiometers (Seca 213 Mobile Stadiometer; Seca Ltd., Chino, CA, USA). Standardized Z-scores for length/height-for-age (LAZ/HAZ) and weight-for-age (WAZ) were calculated to assess child growth according to WHO guidelines (60). Children were then classified as stunted (LAZ/HAZ < -2) or underweight (WAZ < -2).

Dietary Intake

Dietary intake of the target child was assessed using a 24-hour recall questionnaire completed by the child's mother every three months (61). The 24-hour recall instrument included questions about all foods and beverages consumed over the past day, including portion size, cooking method, and ingredients. Questions asking about the frequency and duration of breastfeeding were included (61). Recipes of all meals consumed were recorded, including ingredients and their weights before cooking. The final weight of each food item after cooking was also recorded. Standardized utensils were used to weigh standard quantities of ingredients and food items. These utensils were demonstrated to participants during the 24-hour recall as consumption was reported in terms of these standard units. A dietary database was created with the nutrient composition of all foods reported (62-64). This dietary database disaggregated the ingredients in food items using the recipes and standard units, yielding nutrient information for each ingredient consumed. The caloric and fatty acid intake of all children was then calculated. Caloric intake was compared to international requirements (IOM and WHO) based on child age (65,66). Final dietary intake data represent complementary food consumption as breast milk intake was not quantitatively measured.

Children's fish consumption was assessed in the 24-hour recall questionnaire as well as with a supplementary survey administered to mothers every three months inquiring about their child's fish consumption in the previous three days. Detailed data about fish type, cooking method, frequency, and quantity consumed was collected. The dietary database aforementioned was used to calculate grams, calories, and fatty acids consumed from fish intake. Analyses focus on the four main types of fish in Lake Victoria that are also the most frequently consumed species: Nile perch, tilapia, dagaa, and cichlids. Nile perch and tilapia are larger fish and sizes consumed by the study population range between 100g and 1.5kg. Dagaa and cichlids are small, sardine-like species.

Child Development

Three domains of child development were assessed: gross motor, communication, and personal social. The corresponding subscales of the Ages and Stages Questionnaire: Inventory (ASQ:I) were used to measure each developmental outcome every six months for a total of five times (67). The ASQ:I is a modified version of the Ages and Stages Questionnaire (ASQ) (68), which is widely used for the developmental screening of children under five years of age (69-71), and has been used in LMICs (72). The questionnaires contain a series of age-specific items assessing the achievement of developmental milestones and tracking the child's progress. The five original subscales (Gross Motor, Communication, Personal Social, Fine Motor, and Problem Solving) were piloted to assess respondent bias, maternal accuracy in reporting children's abilities, cultural appropriateness, and feasibility, according to standard procedures (73). Gross Motor, Communication, and Personal Social responses were most accurate, valid, and feasible to administer in the field. The Gross Motor subscale evaluates body and muscle movement, including tasks like standing, walking, and balancing. The Communication subscale assesses language development and the use of words or sounds to express feelings. The Personal Social subscale reflects emotional responses and social interactions. The ASQ:I was translated and adapted for this study by using local culturally appropriate items, examples, and tasks, but no substantial changes were made to the original questionnaires. Continuous scores for each subscale were calculated and converted to Z-scores at two-month age intervals to adjust for age.

Statistical Analyses

All statistical analyses were conducted in Stata 14 (StataCorp, 2015). Three sets of analyses were undertaken to test hypotheses for each domain of child development. Longitudinal linear multivariate generalized estimating equation (GEE) models were used to separately quantify the longitudinal association between 1) the quantity of fish consumption and child development outcomes and 2) diet quality (fatty acid intake) and child development outcomes. Marginal GEE models were used as a standard method to compute population-average effects allowing for longitudinal changes with repeated measures and robust standard errors (74). Correlated data (numerous visits per household or child) were accounted for using an exchangeable correlation structure (74). Other correlation structures (e.g. independent) produced similar results, but the exchangeable structure was chosen because there were multiple measurements on the same child and each child came from an independent household. This approach allowed for examining the relation between fish consumption and child development outcomes across and within individuals. All models include ASQ:I scores from four data collection rounds (6 month, 12 month, 18 month, and 24 month follow-up) and corresponding lagged fish quantity and fatty acids values from three months prior to each round (Table 1). All models controlled for current fish quantity and fatty acid values, child characteristics (gender, age, and breastfeeding status), and household demographics (household size, maternal education, and assets).

Table 1. Descriptions of variables used in statistical analyses.

Variable	Variable type	Definition	Measurement frequency
Gross Motor	Dependent	Continuous Z-scores, ASQ:I	5 times, every 6 months
Communication	Dependent	Continuous Z-scores, ASQ:I	5 times, every 6 months
Personal Social	Dependent	Continuous Z-scores, ASQ:I	5 times, every 6 months
Fish consumption (quantity)	Independent	Binary	9 times, every 3 months
Fish consumption (quality)	Independent	Continuous, grams	9 times, every 3 months
Omega 3 intake	Independent	Continuous, grams	9 times, every 3 months
EPA intake	Independent	Continuous, grams	9 times, every 3 months
DHA intake	Independent	Continuous, grams	9 times, every 3 months
AA intake	Independent	Continuous, grams	9 times, every 3 months
Child age	Covariate	Continuous, months	Baseline
Child gender	Covariate	Binary	Baseline
Breastfeeding status	Covariate	Binary	9 times, every 3 months
Household size	Covariate	Binary	Baseline
Maternal education	Covariate	Binary	Baseline
Asset index	Covariate	Continuous, PCA	Baseline
Stunted	Covariate	Height-for-age Z-scores <-2	9 times, every 3 months
Underweight	Covariate	Weight-for-age Z-scores <-2	9 times, every 3 months

Lagged independent variables (quantity and quality) were created to estimate the association between fish consumption and fatty acid intake three months ago and current gross motor, communication, and personal social Z-scores. This lag was hypothesized to exist based on the time lapse between intake and the manifestation of developmental outcomes. The quantity of fish consumption and quality of dietary intake (assessed via fatty acid levels) were separately analyzed. Individual fatty acids were evaluated in separate models because values are collinear. Fatty acids that come from fish and are particularly important for development were analyzed in models. These include total omega 3 fatty acids, and long-chain AA, EPA, and DHA. Associations were assessed among all children and separately among younger and older children. Models were created for different age groups because at baseline this population was zero to two years old and dietary patterns among children in this age group often vary due to breastfeeding practices and the weaning process. Therefore, there are hypothesized differences in complementary food and fish intake as younger children consume more breast milk. The age cut-off used in analyses incorporating breastfeeding was 13.5 months, which is the mean age of breastfeeding children in this population.

Missing time-invariant baseline sociodemographic (e.g. maternal education) data were replaced with values collected at subsequent time periods. The large number of data collection rounds enabled us to replace other missing values for variables that changed between time points with a participant's average across other time points with available data. These updates were necessary for less than 10% of cases for all variables.

Ethics

The study was approved by the University of California, Berkeley Center for the Protection of Human Subjects and the Kenya Medical Research Institute Ethical Review Committee. Adult participants provided written consent for themselves and their children prior to enrollment.

3.3 Results

Sociodemographics and Child Nutrition

Mean household size was six and 52% of mothers had not completed primary school (Table 2). The mean age of children at baseline was 12 months, ranging from 1 to 26 months. Children were 24 to 51 months at the last follow-up visit. At baseline, 17% of children exclusively breastfed and consumed no complementary foods. The majority of these exclusively breastfed children were under age six months. The percent of children exclusively breastfeeding decreased with consecutive data collection periods. The percent of children breastfeeding was high at baseline (75%). As the cohort aged, the prevalence of breastfeeding decreased paralleling an increased intake of complementary foods. The underweight prevalence was greater among children 12 months of age and older at baseline (11%), but was low. The underweight prevalence was larger among younger children compared with older children in later follow-up visits (e.g. at 12 month follow-up 10% of children under age 24 months were underweight, at 24 month follow-up 8% of children under 36 months were underweight). The prevalence of stunting started to increase from 6 months of age when complimentary feeding was introduced (e.g. at baseline 28% of children 12 months of age or older were stunted), peaked among children 18 to 23 months of age, and decreased slightly among the oldest children (25% of children 36 months of age or older were stunted).

Table 2. Sociodemographic and anthropometric characteristics of study population.

	Mean ± SD or N (%) *n* = 304
Household size (number of people)[a]	6 ± 2
Asset index[a,b]	0.00 ± 1.66
Maternal education (highest level attained)[a]	
None or primary not completed	155 (52)
Completed primary or beyond	144 (48)
Child age at baseline (months)	12 ± 7
Child age at 12 month follow-up (months)	24 ± 7
Child age at 24 month follow-up (months)	36 ± 7
Child sex (male)	146 (48)
Exclusively breastfeeding at baseline	51 (17)
Breastfeeding status	
Baseline	228 (75)
12 month follow-up	91 (30)
24 month follow-up	4 (1)
Calories (kcal) from complementary foods	
Baseline	431 ± 338
12 month follow-up	729 ± 276
24 month follow-up	903 ± 304
Stunted[c] at baseline	
<12 months	24 (15)
≥12 months	40 (28)
Underweight[d] at baseline	
<12 months	14 (9)
≥12 months	15 (11)
Stunted at 12 month follow-up	
<24 months	50 (30)
≥24 months	43 (31)
Underweight at 12 month follow-up	
<24 months	16 (10)
≥24 months	9 (6)
Stunted at 24 month follow-up	
<36 months	42 (26)
≥36 months	36 (25)
Underweight at 24 month follow-up	
<36 months	13 (8)
≥36 months	4 (3)

[a] *n*=299 households as five twins participated in the study. Baseline values as variables are time-invariant.

[b] Derived by use of principal components, includes housing construction (roof, floor), electricity, toilet, and ownership of clock, radio, camera, computer, television, phone, refrigerator, land, livestock, solar lighting, and furniture (bed, cabinet, sofa).

[c] Height-for-age Z-score < -2.

[d] Weight-for-age Z-score < -2.

Dietary Intake

Caloric and Fatty Acid Intake

Caloric and fatty acid intake were greater among older children (Table 3) as many younger children were breastfeeding. Average caloric intake for each age group was lower than international (IOM and WHO) requirements, however, values are only from complementary foods. Similarly, total omega-6 fatty acid and LA intakes from complementary foods were lower than adequate intakes for all age groups. ALA, EPA, and DHA values met adequate intake values mandated by the IOM (ALA) (62) and WHO (EPA, DHA) (63). Among the omega-6 fatty acids, LA consumption was largest which is indicative of the population's plant-based diets. Omega-3 fatty acid intake was higher than omega-6 intake among children over 12 months of age (e.g. children 12 to 17 months old consumed 509mg of omega-3 fatty acids compared with 404mg of omega-6 fatty acids, children 36 months of age and older consumed 1099mg of omega-3 fatty acids compared with 727mg of omega-6 fatty acids).

Table 3. Child caloric and fatty acid intake from complementary foods by age from the entire two-year study (*n* = 304, 9 time points) [a]. (Mean ± SD followed by the median (interquartile range) for each age group)

Age (mos)	Calories (kcal)	Omega 3 (mg)	Omega 6 (mg)	LA (mg)	AA (mg)	ALA (mg)	EPA (mg)	DHA (mg)
<6	138 ± 201	42 ± 188	70 ± 147	57 ± 103	7 ± 40	15 ± 41	11 ± 66	14 ± 77
n=110	0 (0,222)	0 (0,10)	0 (0,79)	0 (0,75)	0 (0,0)	0 (0,9)	0 (0,0)	0 (0,0)
6-11	399 ± 238	249 ± 456	251 ± 252	167 ± 138	46 ± 88	57 ± 88	76 ± 144	101 ± 200
n=292	371 (239,522)	21 (6,341)	173 (84,331)	139 (74,222)	1 (0,58)	14 (4,78)	3 (0,99)	3 (0,128)
12-17	567 ± 245	509 ± 578	404 ± 296	238 ± 142	94 ± 116	111 ± 110	154 ± 190	212 ± 252
n=435	551 (401,685)	357 (32,812)	350 (188,548)	211 (142,305)	59 (1,122)	76 (25,157)	94 (3,194)	163 (3,398)
18-23	744 ± 303	755 ± 746	563 ± 366	332 ± 192	1345 ± 144	162 ± 139	219 ± 236	321 ± 335
n=559	695 (554,894)	573 (100,1068)	506 (291,748)	289 (199,413)	112 (4,223)	130 (57,232)	185 (6,367)	211 (7,415)
24-35	835 ± 284	941 ± 742	663 ± 356	389 ± 194	167 ± 147	193 ± 134	272 ± 264	409 ± 338
n=977	797, (647,995)	818 (408,1322)	607 (416,845)	356 (256,479)	120 (59,236)	161 (98,257)	188 (92,370)	402 (199,601)
≥36	896 ± 278	1099 ± 784	727 ± 364	438 ± 221	190 ± 146	212 ± 129	307 ± 273	494 ± 377
n=363	863 (721,1056)	1015 (555,1566)	668 (473,909)	400 (299,519)	171 (106,245)	192 (119,273)	279 (165,389)	411 (209,803)

[a] The total sample size across all time points is 2,736 (which amounts to 1 observation for all 304 children at each of the 9 time points). Some children may be in each age category twice since data was collected at three-month intervals.

Fish Intake

Dagaa and cichlid fish species contain the largest amount of calories per 100g (Table 4). Dagaa have the highest amounts of total omega-3 fatty acids (1910mg/100g) and long-chain PUFAs, including AA (295mg/100g), EPA (459mg/100g), and DHA (996mg/100g). Cichlids have high omega-6 (1590mg/100g) and LA (1380mg/100g) quantities. Nile perch and tilapia, which are similar in size, contain similar amounts of calories (Nile perch: 109kcal/100g, tilapia: 121kcal/100g) and total omega-3 (Nile perch: 1275mg/100g, tilapia: 1180mg/100g) and omega-6 fatty acids (Nile perch: 609mg/100g, tilapia: 573mg/100g). Nile perch fish also contain relatively high amounts of long-chain AA (278mg/100g) and EPA (455mg/100g).

Table 4. Caloric and fatty acid content of 100g of fish species most commonly consumed by the study population.

	Calories[a] (kcal)	Omega-3 (mg)	Omega-6 (mg)	LA (mg)	AA (mg)	ALA (mg)	EPA (mg)	DHA (mg)
Nile Perch[b]	109	1275	609	63	278	255	455	510
Tilapia[b]	121	1180	573	73	197	285	355	475
Dagaa[c]	285	1910	539	206	295	233	459	996
Cichlids[c]	285	1220	1590	1380	180	138	152	631

[a] Hotz et al., 2012 (62).
[b] All fatty acids from Masa et al., 2011 (75).
[c] All fatty acids from Fiorella et al., in review (76).

Fish consumption increased as children aged throughout the two-year study, and by 12 months, 75% of the children ate fish at least once during the previous three days (Table 5). Dagaa consumption was most frequent followed by Nile perch intake; although due to its larger size, Nile perch was consumed in the greatest quantity. Among the sizes of Nile perch consumed, smaller fish (<500g) were most commonly eaten.

Table 5. Child fish consumption in the previous three days by age during the entire two-year study (n = 304, 9 time points) [a].

Age (mos)	Ate fish N (%)	Total fish (g) Mean ± SD	Nile Perch (g) Mean ± SD	Tilapia (g) Mean ± SD	Dagaa (g) Mean ± SD	Cichlids (g) Mean ± SD	Other (g) Mean ± SD
<6 *n=110*	7 (6)	9 ± 44	6 ± 32	2 ± 17	0.5 ± 4	0 ± 0	0 ± 0
6-11 *n=292*	128 (44)	96 ± 133	77 ± 121	14 ± 50	5 ± 17	0 ± 0	0 ± 0
12-17 *n=435*	318 (75)	154 ± 139	124 ± 134	11 ± 44	17 ± 29	0.5 ± 4	1 ± 10
18-23 *n=559*	474 (88)	168 ± 125	124 ± 124	12 ± 47	28 ± 31	1 ± 7	2 ± 15
24-35 *n=977*	901 (95)	180 ± 120	127 ± 128	10 ± 43	37 ± 33	4 ± 15	2 ± 12
≥36 *n=363*	347 (96)	172 ± 112	114 ± 122	6 ± 31	43 ± 33	6 ± 16	2 ± 15

[a] The total sample size across all time points is 2,736 (which amounts to 1 observation for all 304 children at each of the 9 time points). Some children may be in each age category twice since data was collected at three-month intervals.

Fish consumption increased with time throughout the two-year study and by the second data collection visit (Round 2) the majority of children ate fish at least once during the previous three days (Table 6). Among the children who ate fish, dagaa consumption was most frequent followed by Nile perch intake; although due to its larger size, Nile perch was consumed in the greatest quantity. There are minor seasonal differences in Nile perch consumption. Nile perch intake was lowest during Rounds 1, 3, 7, and 9 and highest during Rounds 4 and 8. Dagaa consumption was greatest during the last year of the study with the last round having the most fish consumed. Tilapia, cichlid, and other fish were consumed in very small quantities and intake of these species did not vary seasonally.

Table 6. Child fish consumption in the previous three days by data collection round during the entire two-year study.

Round[a]	Ate fish N (%)	Total fish (g) Mean ± SD	Nile Perch (g) Mean ± SD	Tilapia (g) Mean ± SD	Dagaa (g) Mean ± SD	Cichlids (g) Mean ± SD	Other (g) Mean ± SD
1, *n=304*	148 (49)	98 ± 131	76 ± 114	8 ± 38	14 ± 27	0 ± 0	0 ± 0
2, *n=300*	207 (69)	139 ± 140	106 ± 133	11 ± 48	20 ± 29	0 ± 3	0 ± 6
3, *n=296*	216 (73)	134 ± 129	89 ± 115	21 ± 56	21 ± 30	2 ± 11	1 ± 11
4, *n=296*	247 (83)	199 ± 136	175 ± 136	8 ± 33	19 ± 30	1 ± 7	1 ± 12
5, *n=295*	249 (84)	152 ± 124	108 ± 116	13 ± 49	29 ± 31	2 ± 10	0 ± 6
6, *n=295*	275 (93)	170 ± 111	121 ± 119	9 ± 40	36 ± 34	2 ± 10	1 ± 12
7, *n=295*	271 (92)	150 ± 110	88 ± 111	10 ± 44	40 ± 32	4 ± 15	6 ± 26
8, *n=295*	285 (97)	225 ± 123	187 ± 136	9 ± 37	30 ± 30	4 ± 14	1 ± 9
9, *n=295*	277 (94)	141 ± 102	76 ± 104	5 ± 28	45 ± 34	8 ± 19	0 ± 6

[a] Rounds represent three-month intervals.

Table 7. Child caloric and fatty acid intake by age from fish during the previous 24 hours over the entire two-year study (*n* = 304, 9 time points)[a]. (Mean ± SD followed by percent of total caloric or fatty acid intake from fish)

Age (mos)	Calories (kcal)	Omega-3 (mg)	Omega-6 (mg)	LA (mg)	AA (mg)	ALA (mg)	EPA (mg)	DHA (mg)
<6	3 ± 17	33 ± 186	15 ± 187	2 ± 10	7 ± 40	6 ± 36	11 ± 65	14 ± 76
n=110	1	4	3	1	5	4	4	4
6-11	23 ± 50	228 ± 450	98 ± 190	15 ± 34	45 ± 88	42 ± 81	73 ± 144	98 ± 200
n=288	5	31	20	7	33	28	32	32
12-17	50 ± 63	466 ± 573	198 ± 255	35 ± 57	91 ± 116	83 ± 106	148 ± 188	205 ± 251
n=423	8	53	34	14	55	46	55	55
18-23	81 ± 88	714 ± 748	292 ± 321	60 ± 89	135 ± 145	122 ± 136	218 ± 237	321 ± 338
n=541	11	67	40	17	71	55	70	71
24-35	105 ± 89	892 ± 751	361 ± 328	85 ± 113	166 ± 149	147 ± 135	269 ± 266	407 ± 340
n=949	13	75	46	21	79	62	78	79
≥36	129 ± 102	1032 ± 780	407 ± 323	114 ± 144	187 ± 146	161 ± 130	301 ± 273	484 ± 372
n=360	14	80	49	23	83	66	83	83

[a]The total sample size across all time points is 2,736 (which amounts to 1 observation for all 304 children at each of the 9 time points). Some children may be in each age category twice since data was collected at three-month intervals.

The contribution of fish to caloric and fatty acid intake increased as children aged (Table 7). Fish were a main source of omega-3 fatty acids, AA, EPA, and DHA intake among children older than 12 months as over 50% of these fatty acids were from fish.

Associations Between Fish Quantity and Quality and Child Development

Fish Quantity and Child Development

Whether a child ate fish (β 0.22; 95% CI 0.064, 0.38; p 0.006) and the amount of fish the child consumed (β 0.012; 95% CI 0.00020, 0.0024; p 0.046) three months ago were significantly associated with current communication Z-scores among all children when controlling for current intake, child characteristics, and household demographics. Greater fish consumption three months ago among younger children (under age 13.5 months) was significantly associated with higher current gross motor (β 0.0071; 95% CI -0.0013, 0.015), communication (β 0.0077; 95% CI 0.0045, 0.010), and personal social (β 0.012; 95% CI 0.0069, 0.016) Z-scores, controlling for current fish consumption, child characteristics, and household demographics (Table 8). Associations between the amount of fish consumed three months ago and child development outcomes were not significant among older children (age 13.5 months and older).

Table 8. Association between current child development Z-scores and fish consumption three months ago over 24 months among children under 13.5 months, controlling for current fish consumption, child characteristics[a], and household demographics[b] (n = 100).

	β (95% CI)
Gross Motor	0.0071 (-0.0013, 0.015)§
Communication	0.0077 (0.0045, 0.010)**
Personal Social	0.012 (0.0069, 0.016)**

[a] Child gender, breastfeeding status

[b] Household size, maternal education, assets

** $p < 0.01$

* $p < 0.05$

§ $p < 0.1$

Fish Quality and Child Development

The amount of PUFAs most important for child development due to their contribution to brain growth and function (omega-3 fatty acids and long-chain EPA, DHA, and AA) consumed three months ago were significantly associated with current communication Z-scores among all children when controlling for current fatty acid intake, child characteristics, and household demographics: omega-3 (β 0.0077; 95% CI 0.00080, 0.015), EPA (β 0.024; 95% CI 0.0041, 0.044), DHA (β 0.015; 95% CI -0.00042, 0.030), and AA (β 0.041; 95% CI 0.0063, 0.076) (Table 9). When stratifying by age, greater quantities of EPA and AA consumed three months ago were significantly associated with higher current communication Z-scores among younger (EPA: β 0.13; 95% CI 0.0084, 0.27; AA: β 0.22; 95% CI 0.00091, 0.44) and older (EPA: β 0.018; 95% CI 0.00018, 0.036; AA: β 0.031; 95% CI 0.0015, 0.063) children. Larger EPA and AA intake three months ago was also significantly associated with greater current personal social Z-scores among younger children (EPA: β 0.25; 95% CI 0.060, 0.44; AA: β 0.40; 95% CI 0.077, 0.71).

Table 9. Association between current child development Z-scores and fatty acid consumption three months ago over 24 months among all children, children under 13.5 months, and children over 13.5 months, controlling for current fatty acid intake, child characteristics[a], and household demographics[b] (n = 304).

	All Children β (95% CI)	Young Children β (95% CI)	Older Children β (95% CI)
Gross Motor			
Omega-3 (g)	0.0019 (-0.0048, 0.0085)	0.014 (-0.036, 0.064)	0.0012 (-0.0051, 0.0075)
EPA (g)	0.0042 (-0.015, 0.023)	0.055 (-0.13, 0.24)	0.0016 (-0.016, 0.020)
DHA (g)	0.0041 (-0.011, 0.019)	0.027 (-0.077, 0.13)	0.0030 (-0.012, 0.017)
AA (g)	0.0049 (-0.028, 0.038)	0.088 (-0.20, 0.38)	0.00064 (-0.030, 0.032)
Communication			
Omega-3 (g)	0.0077 (0.00080, 0.015)*	0.037 (-0.0075, 0.081)	0.0058 (-0.00064, 0.012)§
EPA (g)	0.024 (0.0041, 0.044)*	0.13 (0.0084, 0.27)*	0.018 (0.00013, 0.036)§
DHA (g)	0.0015 (-0.00042, 0.030)§	0.075 (-0.036, 0.19)	0.012 (-0.0026, 0.026)
AA (g)	0.041 (0.0063, 0.076)*	0.22 (0.00091, 0.44)§	0.031 (0.0015, 0.063)§
Personal Social			
Omega-3 (g)	0.0066 (-0.0016, 0.015)	0.063 (-0.011, 0.14)§	0.0030 (-0.0044, 0.010)
EPA (g)	0.014 (-0.012, 0.040)	0.25 (0.060, 0.44)**	0.0032 (-0.020, 0.026)
DHA (g)	0.013 (-0.0050, 0.031)	0.12 (-0.056, 0.29)	0.0052 (-0.011, 0.022)
AA (g)	0.032 (-0.010, 0.074)	0.40 (0.077, 0.71)*	0.013 (-0.025, 0.050)

[a] Child gender, breastfeeding status

[b] Household size, maternal education, assets

** $p < 0.01$

* $p < 0.05$

§ $p < 0.1$

3.4 Discussion

Increased fish consumption was associated with better gross motor, communication, personal social development. The quantity of fish consumed was particularly important for younger children as greater fish consumption three months ago was significantly associated with better gross motor, communication, and personal social development in this group. Higher quality diets in terms of fatty acids was also associated with better developmental outcomes as larger intakes of fatty acids that are most important for development (total omega-3 fatty acids, EPA, DHA, and AA) were significantly associated with greater communication Z-scores. EPA and AA were especially critical for communication and personal development among younger children. Fish consumption and fatty acid intake among children in this population is high and increased with child age. The contribution of fish to diets in terms of total omega-3 fatty acids, AA, EPA, and DHA is substantial, especially among older children who are more dependent on complementary foods. Nile perch and dagaa fish were the most frequently consumed species and there were minor seasonal fluctuations in intake.

This study has a number of strengths. The longitudinal nature of the study allowed for a comprehensive assessment of dietary intake across seasons and as children went through their most critical stage of growth and development. The nine measurements of fish intake and diets at

three-month intervals spanning two years enabled analyses to account for nuances in children's experiences over time. Data collected about fish types consumed also informs fishery dynamics and drivers of fatty acid intake. Results are strengthened by the robust dietary measurements taken through the strategic collection of quantified local recipes and compilation of a dietary database incorporating the nutrient composition of local foods. Assessing the quantity of fish intake in addition to the quality of diets related to fish consumption yields a thorough understanding of the importance of the fishery to diets and health. Repeated ASQ:I assessments over two years produce meaningful findings. The multiple domains of child development examined further provide a more comprehensive analysis of the implications of children's fish consumption and fatty acid intake.

Child development and dietary intake, especially among children under age five years who are still breastfeeding, are complex and this study is limited by measures of each. Dietary data are based on caregiver recall and only represent intake over the previous day at each time point. Many fatty acid nutrient values in the dietary database came from the USDA as there are limited data available on the fatty acid content of foods consumed in LMICs and specifically in Kenya. Although complementary feeding practices in young children are important, dietary intake is challenging to accurately assess due to reliance on breast milk. The quantity and quality of breast milk consumed was not accounted for in analyses so a comprehensive picture of diets among breastfeeding children is difficult to obtain. Although demonstrations of ASQ:I items were administered, the tool is based on caregiver report so bias may also be present in the child development measures. Interpretations of results are restricted to the three domains of children's development assessed as other domains were not evaluated. Moreover, the generalizability of results may be limited by the isolation of the island despite the study population being comparable to others reliant on natural resources and subsistence fishing and agricultural livelihoods. The longitudinal data collected at multiple time points allowed for rigorous analyses, but causal interpretations cannot be made.

The prevalence of stunted and underweight children in this study population were comparable to national, rural, and Nyanza Province values (77), suggesting these results may be applicable to communities experiencing similar rates of malnutrition. The increase in caloric and fatty acid intake from complementary foods over the study duration was expected as children aged and were weaned off of breast milk. The higher omega-3 fatty acid intake compared with omega-6 fatty acids is not surprising given the communities' proximity to the fishery. EPA and AA levels are highest in Nile perch and dagaa. Therefore, it is reasonable that these fatty acids had strong associations with child development scores since these two fish species were most widely consumed.

Although younger children ate less fish and had lower fatty acid intakes from complementary foods, most were breastfeeding through their first year of life. Breast milk is one of the best sources of omega-3 fatty acids and breastfed infants are less likely to be at risk for insufficient intakes compared with those not breastfed (12). Breast milk fatty acid content in this population is high and higher than in most fish species consumed (76). Thus, it is likely that children who are breastfeeding and consuming some fish have high fatty acid intakes. Significant associations between fatty acids and developmental outcomes among younger children can be at least partially explained by breastfeeding and the presumably large amounts of fatty acids consumed

from breast milk as breastfeeding status was significant in most models. Moreover, after age two years there is no evidence of growth improvement following fatty acid supplementation demonstrating the importance of adequate intake early in life (12). Older children who are more dependent on complementary foods may also be at greater risk for developmental delays if diets are insufficient as PUFA status is unlikely to be protected during periods of energy deficiency (37). PUFA synthesis can also be affected by micronutrient deficiencies, which are common in LMICs particularly during the complementary feeding stage (25). This may be cause for fewer significant associations among older children in this population as caloric intake was lower than international recommendations suggesting diets were inadequate, especially among non-breastfeeding children or children consuming little breast milk. Older children in this study population also consumed more omega-6 fatty acids than younger children, which can have adverse effects on omega-3 fatty acid status (11).

The lack of significant associations between fatty acid intake and gross motor development may be because motor skills are often more strongly related to energy and macronutrient intake and growth. Some studies in LMICs have reported stunting to be a strong predictor of poor motor outcomes (78,79). Communication and personal social domains are complementary so the consistency in the strength and magnitude of associations with these outcomes is expected. Communication and language skills are precursors to socio-emotional development and this can explain why fatty acids associations are significant with communication Z-scores, but not personal social Z-scores among older children.

These findings shed light on the importance of fish to the nutrition and health of children around Lake Victoria and in similar lakeside communities during their most critical period of growth and development. In this population that is highly food insecure (15,55), fishery resources can help mitigate nutrient deficiencies, especially of fatty acids, which can be particularly threatening during the complementary feeding stage. When children stop exclusively breastfeeding and are most vulnerable to growth faltering and developmental delays, dietary supplementation of fatty acids, which can include fish consumption, is critical. The frequency of fish consumption and contribution of fish to diets in terms of fatty acids in this study provides further evidence of the value of the Lake Victoria fishery not only for income and food security, but also for health. Therefore, there are ramifications for declining fish populations and this study provides additional motivation for conserving the Lake Victoria fishery. Results have similar implications for comparable situations where communities in LMICs residing in close proximity to fisheries or natural resources (e.g. wild bushmeat) rely on vulnerable ecosystems for an accessible critical source of nutrition. Although consumption of small Nile perch is more affordable and accessible to local communities due to cost and demands of larger markets, catching these fish that have not reached reproductive age contributes to decreasing fish populations. This presents a paradox whereby the intake of the available fish that are critical for the health of vulnerable populations is also a contributing factor to fishery declines. Enforcement of catch regulations can be better implemented and market systems can be put in place to give local communities access to larger Nile perch. In light of the changing fishery and seasonal fluctuations, it may be important for households to also incorporate other sources of omega-3 fatty acids into their diets to decrease dependence on the vulnerable fishery resource and build resilience.

Further research is needed to elucidate the extent to which fishery resources impact children's development. Longitudinal studies assessing seasonal trends and exposure to other related risk factors for poor developmental outcomes will be useful to more comprehensively understand the role of diets and fish in children's development in food insecure populations. Reliable dietary databases need to be built and include nutrient compositions of local foods, including fatty acids. Additional research should also incorporate biological measures of fatty acid levels in the body to capture how dietary fatty acids are synthesized in the body given the complexities of omega-6 and omega-3 interactions and challenges in quantifying breast milk intake during complementary feeding. Other domains of child development can be evaluated to understand nuances and mechanisms in the pathway between diets and developmental outcomes.

3.5 Conclusion

This study informs the developmental benefits provided by fish to young children around Lake Victoria and in similar lakeside communities. Fish may serve as a nutritional safety net in food insecure populations, enabling children to consume omega-3 fatty acids through the increased quality of complementary foods and breast milk which are critical early in life yet often unavailable. These findings create further impetus to address some of the complexities of conserving natural resources in LMICs by enforcing resource use regulations and implementing market systems to benefit local residents. While the sustainability of ecosystems has been linked to nutrition, this research provides evidence of its importance for children's development. The accessibility of fish in susceptible communities can also help mitigate children's exposure to key risk factors for poor development such as poverty and stunting. Therefore, integrated policies and programs addressing the complexities of natural resource use and availability in vulnerable populations are paramount and may contribute to children meeting their developmental potential.

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Chapter 4

Association between Malaria Infection and Early Childhood Development Mediated by Anemia

4.1 Introduction

Malaria is a leading cause of morbidity (1) and mortality (2), particularly among children under five years of age (3). In 2015 more than two-thirds of malaria deaths were among children under five years (4). Ninety percent of all malaria deaths occurred in Africa in 2015 (4). Children under five years have a high risk of acquiring malaria and are more likely to experience severe adverse effects compared to children over five years (5,6). Children in this age group in the same populations are also at risk for developmental delays. Forty-three percent of children under five years of age in low- and middle-income countries (LMICs) are at risk of not meeting their developmental potential, with children in Africa being at greatest risk (7). There is growing evidence suggesting malaria is a risk factor for poor child development (8). However, there is an existing research gap in quantifying the risk of milder cases of malaria, understanding the pathway between malaria infection and poor child development, and evaluating the impact of malaria on younger children (under age five years). Better understanding the role of malaria in children's development is important because developmental delays during the first five years of life can have lifelong health implications.

Characteristics of the Association between Malaria and Child Development

Developmental deficits related to malaria are complex and varied. In a systematic review of the relation between *P. falciparum* infection and cognitive function, Kihara et al. report that specific parts of the brain may not always be impacted more than others by malaria as the effects can vary and be diffuse (9). Impairments are driven by severity of malaria, symptomology, and pre- and post-disease exposure (10). Therefore, malaria has been found to be significantly associated with a variety of impairments such as language (11,12), motor (13), memory (13-15), executive function (12), and attention (14-16) in prospective case-control studies of children in sub-Saharan Africa. Results vary, however, largely due to heterogeneity in the timing of malaria onset compared with outcome assessments, sample sizes, and measurements of risk factors, malaria infection, and child development outcomes (9,10). Moreover, most of these studies and existing research assesses cerebral or severe malaria and not acute or mild infections.

Malaria can affect child development through a variety of pathways. The path to cognitive impairment may result from many interacting biological and social risk factors (11). Such risk factors for cognitive impairment related to malaria include fetal exposure to malaria, repeated infections, seizures, coma duration, psychosis, impaired consciousness, hypoglycemia, hyperpyrexia/high fever, illness and inflammation, antimalarial medication, absence of schooling, malnutrition/poor nutritional intake, and low socioeconomic status (5,17). The functions that are impaired may depend on the stage of brain growth at which the infection is encountered, and impairment may not manifest until a child is older (5). *P. falciparum* affects neurocognitive performance in the short- and long-term (10).

Age at malaria infection is a critical factor influencing cognitive impairment (5,6) and the pathways between malaria and child development change with age (18). Moreover, Kihara et al.'s systematic review of the relation between *P. falciparum* infection and cognitive function in LMICs, found that recovery from neurocognitive impairment may be influenced by age as children were less likely to completely recover from infection compared with adults; although children in included studies range from 5 to 16 years of age (9). The majority of research focuses

on school-age children. In another review of the associations between malaria and cognitive development in children in LMICs, Fernando et al. concluded that cognitive abilities and school performance were impaired in children with malaria when compared with healthy controls (19). In Zambia, malaria parasite exposure in early childhood was associated with lower ability to cope with cognitive tasks and decreased socio-emotional development at preschool age (20). A longitudinal study of primary school students in Mali similarly found that higher malaria parasite loads were significantly associated with lower cognitive scores (21). Malaria infection was also associated with poor math and language school performance among children in Brazil (22) and Sri Lanka (23), however a wide age range (5 to 16 years) of children were included in these studies.

Although most data come from school-age children, malaria attacks are more common and severe in younger children and cognitive effects might be worse in children under five years of age (6,8). In cross-sectional studies in Zanzibar, Tanzania malaria was associated with lower motor activity among 5 to 19 month old children (24) and 10 to 14 month old children (18) controlling for socioeconomic status, and among crawlers after additionally controlling for length-for-age Z-scores, anemia status, and season (24). In the same setting, children age five to nine months with a higher incidence of malaria had lower language scores, were less active, took longer to walk unassisted, were carried more, and fussed more. In children age 10 to 14 months, higher incidence of malaria was associated with later onset of walking, which in turned predicted lower total motor activity and more time being carried (25).

In Uganda several longitudinal studies have shown associations between malaria infection and later development among children under five years. Two studies found that 12 months after having malaria, children had low cognitive ability, attention, memory (16), gross motor, fine motor, visual perception, and language scores (13); however, these studies only include children who had one cerebral malaria episode. Poorer cognitive performance at two or three years of age was also associated with more episodes of malarial illness in Uganda in an RCT of malarial prevention methods (26).

Limited research exists on asymptomatic or mild malaria and repeated attacks, which is important because mild and repeated infections are common in LMICs and may have stronger negative developmental effects. A single malaria infection may not itself lead to an impaired outcome, but may predispose the affected child to adverse effects following repeated exposure, especially when the child faces a variety of health risks (5). The studies that do assess asymptomatic malaria show mixed results. In a panel study in Mali, children with asymptomatic malaria had significantly lower school achievement test scores; however, authors concluded that asymptomatic malaria may have less effect on cognitive abilities than symptomatic malaria (21). Olney et al. also found higher incidences of malaria to have stronger associations with motor ability in younger children (10 to 14 months) (25). In a case-control study in Yemen comparing asymptomatic parasitemic with non-parasitemic primary school children, the parasitemic children performed worse than non-parasitemic children on fine motor tests. Yet, there was no difference in changes in cognitive test scores between those who became non-parasitemic two weeks later and those who remained parasitemic, and no association with cognitive outcomes (27).

Anemia Mechanism Linking Malaria and Child Development

Malaria may impact early childhood development through a pathway of anemia/low hemoglobin concentrations. Malaria can induce anemia because it leads to the maldistribution of iron and suppression of the production of red blood cells (28). In turn, iron-deficiency anemia is a major risk factor for developmental delays in children (7,8). Iron is important for growth (29) and can affect neurodevelopmental outcomes (30). Therefore, anemia may be an important mechanism in the relation between malaria and child development.

There is substantial research on the association between malaria and subsequent anemia/lower hemoglobin concentrations in sub-Saharan Africa, however study designs and the strength of effects vary. In Kenya, malaria was associated with lower hemoglobin concentrations among children 6 to 35 months (31) and one study attributed two-thirds of anemia cases among children under age five years to malaria infection (32). Malaria was also associated with increased odds of anemia among children under five years in cross-sectional assessments in Ethiopia (33) and Cote d'Ivoire (34). Similar cross-sectional associations were found between higher malaria parasite densities and lower hemoglobin concentrations among children age 5 to 19 months in Tanzania, and this study was more robust and nuanced as it included continuous measures of malaria parasite load and hemoglobin concentrations (18). While these studies include children under age five years who are at greater risk for adverse effects and biology suggests that malaria infection precedes malaria, they are cross-sectional so interpretations about the direction of the effects are limited.

The few robust and comprehensive RCTs or longitudinal studies in sub-Saharan Africa that have assessed the association between malaria and anemia/lower hemoglobin concentrations show consistent results. In Ghana, malaria infection was associated with later anemia among children age 6 to 108 months and during the rainy season malaria infection rates were higher and hemoglobin concentrations were lower (35). Capturing seasonal effects is important since malaria has seasonal cycles. In a longitudinal study in Kenya, children age 2 to 36 months with asymptomatic malaria had increased pathogenesis to anemia demonstrating how even mild infection could have adverse effects (36). Similarly, malaria explained the majority of anemia cases observed in Zambia among children under two years (37). These longitudinal studies provide evidence suggesting that malaria infection precedes anemia.

Although there is also evidence that iron deficiency can lead to poor child development, there is a research gap in assessing malaria, anemia, and child development. In an RCT of malarial prevention among children under three years in Uganda, anemia mediated the negative association between malarial illness and cognitive performance in all treatment arms (26). In Tanzania, hemoglobin concentrations played a significant role in the pathway between malaria and motor abilities among children as they started to walk (24). More studies longitudinally evaluating the pathways (including anemia) between mild and severe malaria infection and a variety of child development outcomes among children under five years are needed to elucidate causal mechanisms and account for seasonal and age-dependent nuances.

Malaria and Child Health in Kenya

Malaria is widespread throughout Kenya and a leading cause of morbidity and mortality in the country (38). About 74% of the Kenyan population is at risk for malaria and malaria accounts for

30% to 50% of all outpatient clinic or hospital visits (38). Malaria is estimated to cause 20% of all deaths in children under age five years in the country (38) and the disease is common in this vulnerable population of young children (39). The *P. falciparum* malaria parasite is predominant in East Africa and has more severe cerebral and adverse symptoms associated with it than other parasites like *P. vivax* (40). In western Kenya, malaria transmission is perennial with seasonal peaks in May to July and October to November (41). Malaria is endemic in western Kenya and the Western province has the highest prevalence of *P. falciparum* in the country (39).

The prevalence of other indicators of poor child health related to nutrition and child development is high. In 2011, the prevalence of anemia among children under five years in Kenya was 46% (42). Malaria has been found to underlie most deaths caused by anemia in many parts of Kenya (32,43,44). Nationally, 26% of children under age five years in Kenya are stunted, 11% are underweight, and 4% are wasted. In the Western province, 25% of children under age five years are stunted, 9% are underweight, and 2% are wasted (39). Information about early childhood development in Kenya is limited and most of the program and policy efforts in the country focus on preschool-age children despite the importance of development in younger years (45).

Contributions of this Research

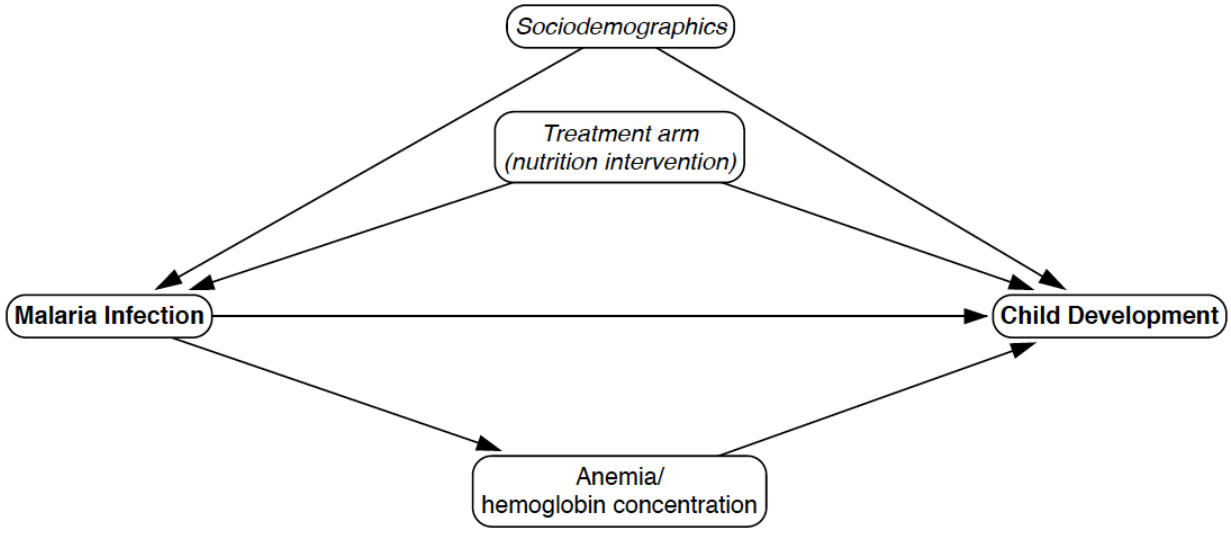
Thus far, studies are varied in their measures of cognitive impairment and in the time intervals between malaria infection and child development assessments. Hence, conclusions about the association between malaria and child development are challenging to draw. Most research has been done on children with cerebral or severe malaria while few studies look at mild or asymptomatic infections. The majority of studies focus on children above five years of age, despite the fact that younger children are at greater risk for getting malaria and for having more adverse reactions to disease onset. Further, assessments of the relations between malaria, anemia, and developmental outcomes are limited and inconsistent. Much of the research on the association between malaria and child development does not include measurements of anemia. Given the high prevalence of malaria and developmental delays among children under five years of age in LMICs and Africa, there is a need to better understand how malaria infection impacts early childhood development.

Objectives

This study aimed to understand the association between malaria and early childhood development (Figure 1). The objectives of the research are to:

1. Analyze associations between malaria infection and three child development outcomes
   Hypothesis: Malaria infection (binary) is associated increased odds of being at risk for gross motor, communication, and personal social developmental delays
2. Assess the role of anemia as a potential mediator in the pathway between malaria infection and child development outcomes
   Hypothesis: Anemia is a significant mediator along the pathway between malaria infection and being at risk for gross motor, communication, and personal social developmental delays

Figure 1. Conceptual diagram of relation between malaria infection and child development with anemia/hemoglobin concentrations as a mediator.



4.2 Methods

Setting and Population

The study was conducted in Bungoma and Kakamega counties in the Western province of Kenya. The region is rural and the majority of the population is subsistence farmers. These data come from the WASH Benefits trial which is a cluster-randomized controlled trial assessing the impact of water, sanitation, and hygiene (WASH) and nutrition interventions individually and combined on child health outcomes (46). The WASH Benefits trial took place from November 2012 to July 2016. Households were selected to participate in the trial using a census if they were in a rural community (defined as <25% of residents living in a rented home [most families in rural areas own homes compared with urban households in Kenya], <2 gas stations, and <10 shops in the area) and had limited access to water and sanitation (defined as communities where >80% of residents did not have access to piped water). Female participants were eligible for enrollment into the study if they were pregnant, if they or their partner owned their house, and if they were not planning to move within the next 12 months. The infant that was in utero during the village census was the target child.

Study Design

Households were visited at baseline and two follow-up periods, one and two years later. A subset of 1,500 children from four arms of the WASH Benefits trial (WASH, WASH and Nutrition, Nutrition, or Active Control) were invited to participate in a sub-study assessing environmental enteropathy and hemoglobin concentrations from biological samples. Children were selected based on the intervention arm they were enrolled in and their proximity to the laboratory since biological samples needed to be refrigerated in a timely manner. This sample size was calculated based on having the power to detect differences in environmental enteropathy biomarkers. In total, 1,437 children participated in the environmental sub-study.

Caregivers brought study children to a central location for sub-study data collection between August 2015 and April 2016. Blood samples for malaria and anemia diagnoses and health surveys were completed. All caregivers were asked for permission for their child to participate in blood sample collection and a separate consent was obtained. Permission for blood collection was obtained from 652 caregivers and therefore malaria and hemoglobin measurements only exist for this subset of children. An average of two to three months later, caregivers brought study children to a central location for main trial data collection including a child development assessment. Local enumerators conducted most surveys in Kiswahili, the regional language. Surveys and data collection tools were developed from validated measures and locally adapted.

Malaria and Anemia Data Collection

Venus blood samples were drawn from sub-study participant children in a central location within villages for biomarker analyses and drops of this blood or finger prick blood was used to assess malaria parasites and hemoglobin concentrations. Tests for *P. falciparum, P. vivax, P. ovale,* and *P. malariae* were conducted using rapid diagnostic kits (SD Bioline, Malaria Ag, P.f, P.f, P.v, Alere). The kits can detect parasite levels up to 28 days after infection. Axillary temperatures were taken for all children and if the malaria parasite test was positive and the child's temperature was 37.5 degrees Celsius or higher, he/she was referred to the nearest clinic for malaria treatment. Capillary blood samples were collected to measure hemoglobin concentrations using a Hemocue machine (Angelholm, Sweden). Anemia was defined as having a hemoglobin concentration below 11.0 g/dL (47). A medical history form was also completed with caregivers about the child's recent experiences with illness, prophylaxis, and treatment related to a variety of health conditions, including malaria. While 652 children provided blood samples, complications with capillary blood collection occurred with three children, so the number of children with hemoglobin concentration data was 649.

Sociodemographics

Household demographics, including asset ownership and maternal education, were assessed using standardized questionnaires administered at baseline. Socioeconomic status was defined with an asset index using baseline survey results for all sub-study participants. The asset index was created using the first principal component from a principal components analysis, which has been shown to produce a good proxy for household wealth and is correlated with consumption expenditures (48-50). Items included in the asset index were housing structure, electricity, and ownership of a radio, television, mobile phone, clock, bicycle, motorcycle, gas stove, and car. Maternal education was categorized into: incomplete primary school, completed primary school, and any secondary school.

Child Development

Three domains of child development were assessed: gross motor, communication, and personal social. The corresponding subscales of the Extended Ages and Stages Questionnaire (EASQ) were used to measure each developmental outcome among all WASH Benefits trial participants during the last data collection round. The EASQ is a modified version of the Ages and Stages Questionnaire (ASQ), which is widely used for the developmental screening of children under five years of age (51-53) and has been used in LMICs (54). The questionnaires contain a series of age-specific items assessing the achievement of developmental milestones and tracking the child's progress. The EASQ was piloted to assess respondent bias, maternal accuracy in

reporting children's abilities, cultural appropriateness, and feasibility according to standard procedures (30). The Gross Motor subscale evaluates body and muscle movement, including tasks like standing, walking, and balancing. The Communication subscale assesses language development and the use of words or sounds to express feelings. The Personal Social subscale reflects emotional responses and social interactions. The EASQ was translated and adapted for this study by using local culturally appropriate items, examples, and tasks, but no substantial changes were made to the original questionnaires. Continuous scores for each subscale were calculated and converted to age-adjusted Z-scores based on the control group within the larger WASH Benefits trial. Children were considered at risk for delay in this population if their Z-scores were below the 25th percentile of control group Z-scores for each domain. This method of defining being at risk for delay was used as a conservative strategy because there was no prior research informing a culturally appropriate clinical cut-off in this study population. Binary variables were used to incorporate a quantitative definition of poor development and to be consistent with analyses used in the main WASH Benefits publications.

Statistical Analyses

All statistical analyses were conducted in Stata 14 (StataCorp, 2015). Three sets of logistic multivariate analyses were undertaken to test the hypotheses corresponding to each child development outcome (gross motor, communication, and personal social). Two regression models were built for each child development outcome to assess the pathways between malaria and being at risk for gross motor, communication, and personal social delays. The first model included malaria infection and the child development outcomes. Anemia status was added to the second model. All models were adjusted for child characteristics (sex and age), household demographics (asset index and maternal education), study cluster, and whether the household received the nutrition intervention (Table 1). The other intervention arms were not included because they were not likely confounders.

The nutrition intervention entailed nutrition education and all children in the participating household receiving a lipid-based nutrient supplement with iron. Higher iron levels can increase malaria risk among children (55). However, iron supplementation can also increase hemoglobin concentrations in young children (56). Therefore, the interaction between malaria status and participation in the nutrition intervention was also analyzed in multivariate models to assess whether being in a nutrition treatment arm differentially affected malaria infection.

Table 1. Descriptions of variables used in statistical analyses.

Variable	Variable type	Definition	Collection timeline
Gross Motor	Dependent	Binary (at risk for delay), EASQ	Endline, months after malaria/anemia
Communication	Dependent	Binary (at risk for delay), EASQ	Endline, months after malaria/anemia
Personal Social	Dependent	Binary (at risk for delay), EASQ	Endline, months after malaria/anemia
Malaria infection	Independent	Binary, blood test results	Endline, months before EASQ
Anemia	Covariate/ potential mediator	Binary, hemoglobin concentration <11.0 g/dL	Endline, months before EASQ, same time as malaria
Child age	Covariate	Continuous, months	Endline, based on EASQ collection date
Child sex	Covariate	Binary	Endline
Maternal education	Covariate	Categorical (primary incomplete, primary complete, some secondary)	Baseline
Asset index	Covariate	Continuous, PCA	Baseline
Treatment arm	Covariate	Binary, participation in nutrition intervention	Baseline

Mediation analyses were then undertaken using the binary_mediation method in Stata (57) to assess whether anemia was a mediator along the pathway between malaria infection and being at risk for gross motor, communication, and personal social delays. Like the Sobel-Goodman test for continuous outcomes, the binary_mediation technique shows that mediation occurred if: 1) malaria was significantly associated with the mediator (anemia), 2) malaria was significantly associated with developmental delay in the absence of the mediator (anemia), 3) the mediator (anemia) was significantly associated with developmental delay, and 4) the effect of malaria on developmental delay shrank upon the addition of the mediator (anemia) to the model. The proportion of the total effect of malaria on being at risk for gross motor, communication, and personal social delay that is mediated by anemia was also calculated and reported.

Children with missing malaria, or child development assessments were removed from analyses. Fifty-seven children (9%) had missing data from one of these measurements and thus were not included in final analyses. The final sample size was therefore 592 children.

Ethics

The WASH Benefits trial is registered as a clinical trial with the U.S. National Institutes of Health (https://clinicaltrials.gov/ct2/show/NCT01704105). Ethical approval was obtained from the University of California, Berkeley Center for the Protection of Human Subjects and the Kenya Medical Research Institute Ethical Review Committee. Adult participants provided written consent for themselves and their children prior to enrollment.

4.3 Results

Sociodemographics and Child Health

Maternal education in this population was low as 53% of mothers did not complete primary school (Table 2). The mean age of children was 24 months, and 29% were stunted and 7% were underweight. The prevalence of anemia among children in this study was 31%. Eighteen percent of children had a positive malaria blood test suggesting that they were infected with a malaria parasite in the previous month. The majority of children (81%) were infected with *P. falciparum*. A similar percent of children were at risk (had Z-scores in the lowest quartile based on control group domain Z-scores) for gross motor (20%), communication (21%), and personal social (23%) delays in this population.

Table 2. Sociodemographic and child health characteristics of study population.

	Mean ± SD or N (%) (*n* = 592)
Asset index[a]	-0.094 ± 0.92
Maternal education	
Some primary, not completed	314 (53)
Completed primary	151 (26)
At least some secondary	127 (21)
Child age (months)	24 ± 2
Child sex (male)	285 (48)
Stunted (LAZ/HAZ < -2)	170 (29)
Underweight (WAZ < -2)	40 (7)
Anemic (Hb < 11.0 g/dL)	186 (31)
Positive malaria test	109 (18)
At risk for gross motor delay[b]	118 (20)
At risk for communication delay[b]	126 (21)
At risk for personal social delay[b]	139 (23)

[a] Derived by use of principal components, includes housing structure, electricity, and ownership of a radio, television, mobile phone, clock, bicycle, motorcycle, gas stove, and car.

[b] Children were considered at risk for delay if their Z-scores were below the 25th percentile of control group Z-scores for each domain.

Multivariate Associations

Having a positive malaria test was significantly associated with increased odds of a child being at risk for gross motor (OR 2.22; 95% CI 1.35, 3.64), communication (OR 1.92; 95% CI 1.19, 3.09), and personal social (OR 2.86; 95% CI 1.81, 4.55) delay adjusting for child characteristics, household demographics, study cluster, and participation in the nutrition treatment arm (Model 1, Table 3). The odds of a child being at risk for developmental delays across all subscales decreased with the addition of anemia (Model 2) to models, however still remained significant. The strength and significance of the associations were greater for personal social delays across Models 1 and 2. Anemia was only significant in personal social analyses. Interactions between malaria and participation in a nutrition intervention were not significant as treatment arm did not play a role in this association.

Table 3. Multivariate associations[a] between being at risk for developmental delays[b] and malaria infection (Model 1) with adjustments for anemia (Model 2) as a potential mediator (n = 592).

	Model 1 OR (95% CI)	Model 2 OR (95% CI)
Gross Motor		
Malaria (1=positive RDT)	2.22 (1.35, 3.64)**	2.03 (1.21, 3.42)**
Child age (months)	0.74 (0.65, 0.83)**	0.73 (0.65, 0.83)**
Treatment arm (1=nutrition)	0.71 (0.46, 1.09)	0.73 (0.47, 1.12)
Anemia (1=anemic[c])		1.30 (0.81, 2.08)
Communication		
Malaria (1=positive RDT)	1.92 (1.19, 3.09)**	1.73 (1.05, 2.86)*
Child age (months)	1.07 (0.95, 1.20)	1.07 (0.40, 0.91)*
Treatment arm (1=nutrition)	1.07 (0.71, 1.61)	1.11 (0.73, 1.67)
Anemia (1=anemic[c])		1.35 (0.87, 2.10)
Personal Social		
Malaria (1=positive RDT)	2.86 (1.81, 4.55)**	2.46 (1.52, 3.99)**
Child age (months)	0.82 (0.74, 0.92)**	0.82 (0.73, 0.91)**
Treatment arm (1=nutrition)	1.15 (0.77, 1.73)	1.22 (0.81, 1.83)
Anemia (1=anemic[c])		1.59 (1.03, 2.47)*

[a] Logistic regression models, additionally controlled for child sex, asset index, maternal education, and study cluster.
[b] Risk for developmental delay defined as having a Z-score below the 25th percentile control group Z-score.
[c] Hb < 11.0 g/dL.
** $p<0.01$
* $p<0.05$
§ $p<0.1$

Mediation

Anemia was a significant mediator in the pathway between malaria infection and being at risk for gross motor, communication, and personal social development delays (Table 4). Across all subscales, malaria was significantly associated with being anemic and developmental delays, anemia was significantly associated with developmental delays, and the effect of malaria on developmental delays shrank upon the addition of anemia to the models. The proportion of the total effect of malaria on risks for developmental delays that is mediated by anemia in this population was greatest with the Communication subscale (16%), however, all proportions were small (Table 5).

Table 4. Mediation analyses of anemia on pathway between malaria and being at risk for gross motor, communication, and personal social delay[a] (n = 592).

	Gross Motor[b] OR (95% CI)	Communication[b] OR (95% CI)	Personal Social[b] OR (95% CI)
Malaria[c] and anemia[d]	4.42 (2.86, 6.82)**	4.42 (2.86, 6.82)**	4.42 (2.86, 6.82)**
Malaria and child development (no anemia)	2.15 (1.35, 3.44)**	2.04 (1.28, 3.23)**	2.91 (1.87, 4.53)**
Anemia and child development	1.46 (0.96, 2.22)§	1.60 (1.06, 2.40)*	1.89 (1.28, 2.81)**
Malaria and child development (with anemia)	2.02 (1.23, 3.30)**	1.83 (1.13, 2.97)*	2.54 (1.60, 4.05)**

** $p<0.01$
* $p<0.05$
§ $p<0.1$
[a] Mediation analyses assessed using binary_mediation Stata technique. Table includes mediation test results of four regressions evaluating the association between: 1) malaria and anemia, 2) malaria and child development outcome (without anemia), 3) anemia and child development outcome, and 4) malaria and child development outcome (with anemia).
[b] Risk for developmental delay defined as having a Z-score below the 25th percentile control group Z-score.
[c] Binary, 1=positive RDT
[d] Binary, 1=anemic (Hb < 11.0 g/dL)

Table 5. Proportion of the total effect of malaria on being at risk for gross motor, communication, and personal social delay that is mediated by anemia (n = 592).

	Anemia
Gross motor	0.091
Communication	0.16
Personal social	0.14

4.4 Discussion

A positive malaria blood test was associated with increased odds of being at risk for gross motor, communication, and personal social delays, while controlling for a range of individual- and household-level variables. The odds of being at risk for personal social delays were greater than the odds of being at risk for delays in the other two domains. Across subscales, the addition of the potential mediator (anemia) to models led to smaller odds of being at risk for delays. Formal mediation analyses demonstrated that anemia was a mediator in the pathway between malaria infection and being at risk for developmental delays in all three domains. However, the proportion of the total effect mediated by anemia was small.

This study has several strengths. The use of blood tests to indicate the presence of malaria parasites provides a robust measure of infection. Including all cases of malaria rather than only severe or cerebral incidents is beneficial for understanding associations between milder forms of malaria that are more widespread and child development. Although the amount of time between the malaria blood test and the child development assessments varies, the time between measurements allows for a more accurate measure of the association between malaria and child development as there may be a lag between infection and the manifestation of measurable effects

on development. Incorporating multiple domains of child development yields a more comprehensive understanding of the implications of malaria infection. The use of a control group to calculate standardized child development scores enabled analyses to more accurately assess whether a child is at risk for delay in this population, giving more meaning to results. Building models by systematically adding a hypothesized mediator to analyses allowed for a more thorough assessment of the potential pathways of impact. Further mediation analyses strengthened findings and substantiated the role of anemia.

There are limitations to these analyses as the pathways between malaria and child development are complex and the study is cross-sectional. The blood tests detect parasites up to approximately one month after infection and do not yield parasite load. Thus, it is difficult to know when a child was infected and the severity of malaria, and therefore the extent to which infection could affect child development outcomes. Only one malaria diagnosis was collected and repeated infections, which may be common in this endemic area, could have greater effects on child development. Although there was time between the malaria diagnosis and child development assessment, there is only one measure of each and therefore causal implications cannot be drawn. Although there was a lag between malaria and child development measurements, malaria and anemia measurements were taken at the same time, further limiting the conclusions about the pathways of impact.

Given that 74% of the population of Kenya is living in a malaria endemic region (38), the prevalence of malaria (18%) in this population was lower than expected. Although studies show mixed results, these findings corroborate research that demonstrates an association between malaria infection and child development, particularly among children under age five years and who are not exclusively experiencing severe malaria. While few studies undertake formal mediation analyses, results are comparable to two assessments from Zanzibar, Tanzania looking at malaria, hemoglobin concentrations, and motor development among children under two years (18,24). Children with higher malaria parasite densities in Zanzibar had significantly lower hemoglobin concentrations (18). Malaria was directly and indirectly associated with motor abilities after controlling for anemia status in these two assessments (24).

This study's findings are important because they highlight how malaria may be associated with child development outcomes. The focus on children under five years of age adds to the literature as exposure to risk factors like malaria during this vulnerable time period is critical for development, yet understudied. Significant associations between malaria and gross motor, communication, and personal social domains in this young population emphasize the importance of preventing and treating malaria early in life. Patterns of malaria are likely to shift throughout Africa with climate change as certain geographies may be more impacted. Climate change coupled with human population density projections for the continent suggest that malaria transmission will remain high in the coming years (58,59), additionally highlighting the need to mitigate malaria infections. Finally, these results further inform the pathway of impact with the inclusion of robust mediation analyses demonstrating the role anemia may play. Understanding this pathway can provide further impetus for addressing malaria.

Future research can shed light on the pathways between malaria and child development. More longitudinal studies with repeated measures of malaria and child development outcomes can

inform causal relations in addition to the timing of effects. The assessment of additional domains of development can provide a more comprehensive understanding of the impacts of malaria. The role of less severe and repeated cases of malaria can also support the targeting of interventions to the largest number of children who are most susceptible to risks for delay. Longitudinal research assessing different hemoglobin concentrations and other mediators is important for better understanding the nuances of mechanisms of impact and when programs can be most effective.

4.5 Conclusion

This study provides evidence of how malaria may impact children's development. Malaria may be associated with short-term child development effects during a critical developmental period. These findings suggest that anemia may play a significant role in the pathway. The high prevalence of malaria and large percentage of children at risk for developmental delays in LMICs motivates the need for policies and programs to address some of the complexities of malaria infection. Preventative malaria measures and immediate treatment are imperative, particularly in light of projections of continued high malaria transmission in Africa. Overall, combating malaria may enable children to reach their full developmental potential, which can have lifelong and intergenerational benefits.

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Chapter 5

Summary and Conclusions

5.1 Summary

A large number of children in low- and middle-income countries (LMICs) are at risk of not meeting their developmental potential, which has lifelong and intergenerational implications. While stunting and poverty are established key risk factors for developmental delays, the role of environmental determinants is less clear and understudied. Households in LMICs are dependent on their environments for food, subsistence livelihoods such as agriculture, and drinking water. These communities are also susceptible to environmentally-driven diseases like malaria. Climate change, which is projected to continue to impact weather and landscapes throughout sub-Saharan Africa, also has the potential to influence food security, access to natural resources, and disease patterns.

Kenya is at the epicenter of many of these dynamics. A large proportion of its population is food insecure and dependent on subsistence agriculture and fishing for income and food. Rates of stunting and underweight, indicators of undernutrition, are high, particularly in rural areas. This presents a paradox since Kenya harbors one of the most productive parts of Lake Victoria, providing communities access to natural resources, including fish and water for farming. Moreover, although the country has a national child development policy, similar to many countries, activities focus on children who are preschool-age or above. The importance of optimal development before age three years creates impetus for policies and programs to target this younger population that is also at risk for adverse effects of malnutrition and infectious diseases. This dissertation aimed to better understand some of the environmental determinants of early childhood development to inform interventions and maximize vulnerable children's potential.

The second chapter comprehensively assessed the relation between household food insecurity and children's gross motor, communication, and socio-emotional development in a highly food insecure population around Lake Victoria in rural Kenya. Food insecurity is widespread in many LMICs, yet is seasonal and complex, and therefore critical to carefully measure. Acute and chronic food insecurity were associated with worse gross motor, communication, and socio-emotional development among children. Thus, there are immediate benefits to ameliorating even short-term food insecurity by improving the availability of and access to nutritious foods. Building resilience to sustained food insecurity and improving coping strategies can also benefit children's wellbeing.

The third chapter builds on the second one by evaluating the role of fish and fatty acids in children's diets in the same rural population around Lake Victoria in Kenya. Fish consumption among children was high, but declines in Nile perch have implications for continued intake of this commonly consumed species and therefore fatty acid levels. The amount of fish consumed and quality in terms of fatty acid content were associated with children's gross motor, communication, and socio-emotional development. Fish intake was particularly important for children as they were dependent on complementary foods. Hence, reducing overfishing, enforcing catch regulations, and creating market systems enabling local communities to have access to fish can allow children to reach their developmental potential. Interventions to diversify diets with other sources of fatty acids may also be critical so families are less reliant on threatened natural resources.

The fourth chapter looks at how malaria is associated with children's gross motor, communication, and socio-emotional development in an inland population in rural western Kenya. Malaria is endemic in both study populations and much of Kenya in addition to sub-Saharan Africa. Malaria adversely affects children under age five years who are also most susceptible to risks for developmental deficits due to their rapid brain growth and nutrient sensitivities. The significant association found between child malaria infection and risk for developmental delays creates further impetus to prevent and treat the disease. The role of anemia informs how impacts can occur and contributes to literature informing integrated interventions to improve nutrition and children's development.

5.2 Conclusions

The large number of children not meeting their developmental potential in LMICs needs to be addressed. Comprehensively understanding the factors putting children at risk for developmental delays is important for the implementation of effective interventions. Three key environmental determinants (food insecurity, fish and fatty acid intake, and malaria infection) may be associated with developmental deficits. Integrated policies and programs that provide households with sustained access to adequate amounts of quality foods to address acute and chronic food insecurity can benefit children's development. Specifically increasing the availability of long-chain polyunsaturated fatty acids in children's diets as they start to wean can improve developmental outcomes. This may involve conserving natural resources like wild foods such as fish or building the capacity of households dependent on subsistence agriculture and livestock practices to have continued access to nutrient-dense bioavailable foods. Improving nutrition in terms of anemia and stunting combined with malaria prevention and treatment among children under five years of age can also contribute to optimal development. As climate change may threaten food security and malaria incidence, adapting to changing environmental conditions is timely. Addressing environmental determinants of early childhood development can be pivotal for enabling vulnerable children to reach their full potential.