UNDERSTANDING INTERGENERATIONAL MALUTRITION IN RURAL BANGLADESH: A SYSTEMS APPROACH

by

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A dissertation submitted to Johns Hopkins University in conformity with the requirements for the degree of Doctor of Philosophy

Baltimore, Maryland

January 12, 2015

Abstract

Background: Determinants of malnutrition across the lifecycle are complex. Beyond host characteristics and behavioral choices, the immediate environment and broader societal context remains a challenge to measure. The JiVitA-1 trial in rural northwest Bangladesh reveals intergenerational spatial patterns of malnutrition, based on mid-upper arm circumference (MUAC), that converge with age from early life onward, suggesting possible contextual influences. This dissertation explores these spatial patterns, and investigates interactions among biological, socioeconomic and contextual factors on trajectories of nutritional status from birth to adulthood in this typical rural South Asian population.

Methods: Spatial analysis with multiple-linear regression was used to assess independent and synergistic effects of individual, household and community factors, added sequentially, on MUAC among mother-infant dyads. Explanatory improvements and spatial correlation accounted for by characteristics at each level was considered.

Results: Multilevel regression models explained 13.2%, 14.5%, and 11.7% of variabilty in MUAC of infants at birth and six months and expectant mothers, respectively. Most variability in MUAC was explained by individual and household-level variables. Community influences accounted for 0.3%, 0.4%, and 0.7% of the variability in MUAC at the two infant ages and among women, respecitvely. Infant growth between birth and six months was guided by initial size ($r^2 = 0.33$), and modified further by household and community socioeconomic-status (SES) and maternal nutritional status. The full multilevel model accounted for 40% of the variance in growth rate, 1% of which was attributed to community context. Including individual- and household-level variables provided modest reductions in residual spatial autocorrelation of MUAC, compared to reductions associated with contextual factors. Promising contextual variables included neighborhood economic structure, maternal education, elevation, population density, and travel-time to markets. Many contextual variables were correlated, indicating that those living in wealthier neighborhoods enjoy healthier environments, which may reinforce benefits of greater household and neighborhood SES.

Conclusions: A systems science approach revealed multi-level and age-specific influences on infant and maternal nutritional status in this rural Bangladesh setting. Contextual variables explained differences in MUAC and reduced residual spatial autocorrelation more than individual and household variables combined. Correlations between contextual variables also indicated economically-driven population sorting in this typical rural setting.

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Acknowledgements

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Chapter 1 Introduction

1.1 Rationale

In 2010, approximately 7.6 million children worldwide never lived to see their fifth birthday [1], and nearly all of these deaths occurred in developing countries [2–4]. Poor nutritional status, defined as the lack of and/or faulty utilization of energy and nutrients required to meet metabolic needs, is a leading cause of under-five ("child") mortality. Each year, 53% of children deaths (approximately 5.6 million) are either directly or indirectly attributable to undernutrition [5–8]. Malnutrition is also a major cause of under-five morbidity in the developing world, as 33% (144 million) of global disability-adjusted life years (DALYs) in these regions are estimated to be a direct result of nutrition-related causes, which often coexist [9].

Children born to poorer families and malnourished mothers start life at a marked disadvantage, which continues impact health trajectories throughout life. As infants, they are more likely to be small for gestational age, low birthweight (LBW), and have smaller anthropometric measurements through infancy [10–19]. The nutritional status and diet of new mothers continues to impact child growth as nutrients are shared via breastmilk [14,15,20,21]. Poor growth in early childhood, especially in the first two years, can lead to irreversible damage and reduced human capital [22–28]. Malnutrition in infancy is associated with increased risk of alcohol and drug use, elevated blood pressure [29–34], insulin resistance [31], stroke [35], and metabolic syndrome [36], as well as reduced mental development [27,37,38], future academic performance [28,39], fertility [39], and ultimately adult economic productivity [26]. Furthermore, the offspring of women who were malnourished as young children themselves experience higher risk of poor fetal growth[30] and of being LBW [22]. Therefore, early childhood nutritional status can act as a multi-factorial indicator for future health, productivity, and intergenerational success.

A child's health can also be influenced by the socio-economic status of their parents. Children born to poorer families experience poorer health in childhood and reduced productivity and health as adults [40–42]. This effect may be exacerbated with prolonged poverty [19]. Additionally, children born to uneducated mothers tend to have reduced anthropometry [43] and are less likely to go to school [44], which is related to future economic productivity. Since malnutrition is so closely tied with poverty, and both malnutrition and poverty can be intergenerational, their combined effects further entrench offspring in desperate circumstance.

Emanuel (1986) defined intergenerational influences as "conditions, exposures, and environments experienced by one generation that relate to the health, growth and development of the next generation." These influences may become more pronounced when generations share similar circumstance. Substantial improvements in linear growth have been observed with change in circumstance related to child adoption, family migration, or swift national socio-economic development [18]. Children born to mothers who were malnourished as children can experience nearly normal growth when "profound improvements in health, nutrition and the environment take place before conception" [18]. Healthy growth in the first two years of life is particularly important. It is in this period where growth faltering is most pronounced [45–47], and recovery is increasingly difficult if improvements are not made [48]. If children are to break from the shackles of intergenerational malnutrition, it is imperative that we gain a better systemic understanding of the factors which influence this phenomenon, to better design effective interventions.

The current nutritional literature is replete with studies exploring the impact of individual and household factors, while largely ignoring contextual influences beyond the home. This narrow perspective of health and nutritional status fails to consider the hierarchical amalgamation of causality. Several studies have noted that individuals of similar nutritional status are more likely to reside in close proximity to one another, even after controlling for relevant individual variables [49–52]. Nevertheless, the effects resulting in "clustering" remain unclear. Fenn et al. (2007), Balk et al. (2005), and Morris (2000) suggest that this phenomenon simply results from individuals with similar individual and household characteristics clustering together [53,54]. Alternatively, some authors attribute this phenomenon to contextual influences from the environment [55–57], such as land use, topography, climate, and road access; or from neighbors [58–61], such as urbanicity, community-level educational attainment, social participation, and community employment.

The current body of evidence suggests that individual nutritional status is a consequence of more than just individual or household factors. Rather, it is also a product of interactions between individual circumstance, local context, and intergenerational influences. A more complex analytical approach may be appropriate for the study of individual health and nutritional status. Systems biology, or systeomics, is a novel approach to understanding causes and effects in complex biological systems through integration of discovery and hypothesis-driven science [62,63]. The objective of discovery science is to uncover all of the elements in a system, while hypothesis-driven science aims to generate hypotheses and test them experimentally. These techniques are only recently being used in epidemiology [64], mostly in the study of obesity [65,66]. Approaching individual nutritional status as a system requires identification of the system's multilevel elements and uncovering the network and relative direction of effects.

Two primary hurdles have hindered the incorporation of spatially explicit effects from the environment and community in the analysis of nutritional status: sample size requirements and spatial data availability. Environmental and community effects are often much smaller in magnitude than those applied at the individual or household scale and, thus, require substantially larger samples. In addition, the availability and quality of spatial data from the developing world is currently lacking, despite the fact that in recent years, spatial data from developed countries has become far more available.

In light of these common obstacles, data collected from a cohort study conducted in northwest Bangladesh provides a rare opportunity to detect and evaluate the role of spatial effects in determining nutritional status. This large study population resides within a contiguous geographic area, and the dataset includes a rigorously collected set of geospatial data on the population and the context in which they live (see Figure 5 & Figure 6). Observations from this study have provided intriguing evidence for intergenerational malnutrition as an ecologic phenomenon. Across this 435 square kilometer research site, a spatial trend in the anthropometry among expectant women was observed, with healthier women in the west, near the national highway, and thinner women in the east, near a frequently flood-prone river. This pattern mirrored a previously known gradient of socioeconomic status[67]. This pattern was, however, not manifested in the anthropometry of newborns, seemingly protected from the nutritional status of their mothers; however, by roughly six months, infant anthropometry mirrored that of their mothers relative to the respective means of that population. Thus, over the course of the first six months of life, near random spatial distribution of birth anthropometry rapidly take on the spatially distinctive character seen among adult women (see Figure 14). The objective of this doctoral research is to consider the spatial patterning of this intergenerational trend and investigate the interactions of biological, socio-economic, and contextual forces at several levels to determine the underlying effects leading to the observed spatial patterning.

The analyses implemented in this dissertation are loosely based on the constructs of systems biology, by considering nutritional status and growth trajectories as a cumulative result from effects and interactions at multiple scales. As global initiatives “pluck the lowest hanging fruits” to reduce malnutrition and mortality, particularly in mothers and children, we must improve our understanding to find more creative ways to achieve progress in breaking the cycle of intergenerational malnutrition. Identifying the degree to which characteristics of the individual, location, and context influence nutritional status in early life might unlock potential strategies to disrupt this cycle. Historically, public health interventions with the greatest impact have involved making changes to components of the environment or context around individuals to effect changes in health outcomes at the individual level.

1.1 Organization of the dissertation and study objectives

The objective of this dissertation is to investigate the manner in which individual nutritional status is influenced by one's location, as described by the characteristics of neighbors and environmental context, as two broad categories that enhance the individual-centered model of nutritional status. This thesis research project was designed to identify characteristics of community context which influence nutritional status and to evaluate their relative contributions and interactions after accounting for salient individual and household effects established in the literature. Age-specific effects at the individual, household, and contextual levels will be explored at three key time-points: in expectant mothers, newborns, and infants at six months. This analysis also considers how nutritional status at each time-point relates to the others.

This dissertation is organized into seven chapters. Chapter One provides the rationale behind this thesis research project and the study objectives. The available literature regarding the importance, epidemiology, assessment, and determinants of nutritional status, as well as influential frameworks and analytical hurdles directing research progress and understanding is reviewed in Chapter Two. Chapter Three discusses the data from the JiVitA project primarily used through this doctoral research. The specific research aims of this doctoral thesis are addressed in Chapter Four with a population of expectant mothers; in Chapter Five with populations of newborns and infants at roughly six months of age; and in Chapter Six with the growth trajectories of infants in their first six months of life. Each chapter introduces relevant background literature and motivation, describes study methodologies, presents and interprets findings, and discusses potential intervention implications. Chapter Seven synthesizes the findings, conclusions, and intervention implications drawn from this thesis research. Recommendations for further examination will also be provided.

The following are the specific aims for Chapters Four, Five and Six:

1. Identify and evaluate individual, household, and community level determinants of maternal nutritional status, infant nutritional status at birth and six months, and infant growth trajectory in the first six months of life;
2. Explore the relative contributions of and interplay between individual, household, and community-level determinants of maternal nutritional status, infant nutritional status at birth and six months, and infant growth trajectories in the first six months of life;
3. Describe the extent to which factors at each level account for spatial correlation between observations of maternal nutritional status, infant nutritional status at birth and six months, and infant growth trajectories in the first six months of life.

Chapter 2 Literature Review

2.1 Introduction

This section provides background from the current literature drawing from the nutritional research followed by specific methods which may help elucidated the multilevel web of causality and spatial nature of undernutrition. Nutritional topics addressed include assessment methods, direct causes, relevant analytical frameworks, and determinants of nutritional status. The section covering determinants of nutritional status will discuss the individual, household, and contextual-level factors impacting individual nutritional status. Methodological topics discussed include spatial clustering and correlation as they relate to nutritional status, as well as how systems biology may help provide a novel analytical approach to understand nutritional outcomes.

2.2 Assessment of nutritional status

Nutritional status is often assessed using anthropometry, which is the measurement of human dimensions or proportion of dimensions, often in conjunction with age. Anthropometric measurements are typically related to a standardized well-nourished reference population, expressed as a Z score. The standardized Z score facilitates cross-population comparisons and adjusts for differences in age and sex. Anthropometric measurements can include weight, height, head, chest and mid-upper arm circumference, body mass index, triceps and subscapular skin folds, and others, usually adjusted for by age and/or sex. Birthweight, determined by a combination of intrauterine growth and gestational age at birth, acts as a cross-sectional multifactorial indicator of public health, which encompasses long-term maternal nutrition, health, occupational stress, and obstetric healthcare.

Anthropometric measurements each have their strengths and weaknesses. Many are highly correlated with each other and other physiologic conditions. Chest circumference, head circumference, and mid-upper arm circumference (MUAC) in newborns have been significantly correlated with each other [68] and with birthweight [13,68–71]. At birth, cut-offs for MUAC and chest circumference provide simple, reliable, and highly correlated (r ≈ 0.81 - 0.87) field proxy indication of low-birthweight [68,69,71] and neonatal mortality [13,69] in emergency settings. MUAC at birth has also been reported as a valid estimate of gestational age (r = .961) [70]. Weight and height provide better estimates of lean mass versus fat mass [31]. Fat mass is better estimated with skin fold measurements, while MUAC predicts both lean and fat mass equally [31,72–74]. MUAC-for-age and growth velocity are reported to be sensitive to short-term changes in nutritional status [75,76].

The primary outcome of interest in these analyses is mid-upper arm circumference (MUAC). MUAC was chosen over other anthropometric measurements for its ease of field administration and its relation to physiologic processes [73,77]. As noted above, MUAC is highly correlated with other anthropometric measurements [13,69,71,78], has demonstrated sensitivity to short term changes in nutrition [75,78–84], predicts lean and fat mass equally well [31], and has been used to indicate episodes of growth faltering [85]. Furthermore, maternal MUAC has been previously associated with infant MUAC [84] and birthweight [12,13,16,17].

2.3 Direct causes of malnutrition

Direct causes of malnutrition are infection, insufficient dietary intake, or a combination of the two. A deleterious synergism exists between infection and undernutrition, each multiplicatively exacerbating the other. Infectious disease are chiefly responsible for mortality related to nutritional deficiency. When malnourished, mortality risk from infectious and chronic disease, as well as all-cause mortality, is elevated [8,86]. From recent estimates of global child mortality, approximately 64% is attributable to infectious causes [1], and roughly 53% are either directly or indirectly attributable to undernutrition [5–8,87,88]. Both acute and chronic infections impact nutritional status and linear growth, either through a systemic response or through sustained morbidity [89].

Infections influence nutritional status through decreased food intake and nutrient absorption, direct nutrient loss, increased metabolic need or catabolic loss, and potentially impaired nutrient transport to target tissues [89]. Being malnourished can also increase susceptibility to infection through decreased immune function. Poor nutritional status leads to reduced production and/or attenuated functional ability of all cellular components of the immune system [90].

2.3.1.Infection

Gastro-intestinal and respiratory infections are primarily linked with nutritional deficiencies. Malnutrition associated with recurrent and severe cases of diarrhea impairs weight and height gains and can reduce “catch-up” growth, permanently effecting future stature [25]. Francis (2012) reported similar results associated with helminth infections [91]. The link between gastro-intestinal infection and undernutrition has been observed by many [5,7,8,25,48,85,90–99].

Unlike diarrheal disease, respiratory infection is more a symptom and less a cause of malnutrition. Children deficient in vitamin A [100], iron and zinc [101], and others micronutrients [102] experience elevated incidence of respiratory infection. In addition to malnutrition, increased risk of respiratory infection is also associated with poor indoor air quality [103,104] and crowding [105].

2.3.2.Dietary Intake

In addition to infection, a diet lacking in sufficient protein, energy, and micronutrients is a dominant cause of malnutrition. Differences in nutritional status are largely attributable to differences in dietary intake [48,55,84,99,106–111]. Maternal diets balanced in protein and energy correspond with demonstrated improvements in fetal growth[109] and birthweight [84], and a decrease in stunting risk [110,112]. Protein energy malnutrition (PEM) is particularly problematic in Asia, which experiences the highest prevalence of stunting [112]. For young children, the quantity and quality of breastmilk as well as complimentary feeding practices are directly related with child nutritional status which will be discussed later in detail. A diet poor in animal food products, which are rich with protein and micronutrients, is a risk factor for stunting.

2.3.3. Micronutrient Malnutrition

Micronutrient deficiency is another factor related to nutritional status and related morbidity and mortality. While this is not a focus of this doctoral research, it will be discussed here briefly. Reduced anthropometric growth has been primarily associated with deficiencies in Vitamin A [82,83,113–115], Zinc [116–120], Iodine [80], and Iron [99,121–123]. In 2004, Vitamin A, Zinc, Iron, and Iodine, deficiencies were respectively attributable to 6.5%, 4.4%, 0.2%, and 0.03% of deaths and 5.3%, 3.8%, 0.5%, and 0.6% of DALYs globally [108]. The disease burden is considerably larger for vitamin A and Zinc than for Iron and Iodine, indicating their relative biological importance. Other micronutrients have been reported to impact fetal and infant growth and include Vitamins B [124–126], C [125], D [81,127–130], E [115], Folate [131], Calcium [132], Copper [133], and Selenium [133]. These and others have been suggested, in a 2007 joint statement by the WHO, WFP and UNICEF, for multi-micronutrient (MM) supplementation [134]. MM supplementation has been reported to increase birth anthropometry [79,135] and growth in infants and children [79]. South Asia and sub-Saharan Africa experience especially high prevalence of MM deficiencies [108,116,120,124].

2.4 Analytical Framework

While infection and dietary intake are fairly well-established direct causes of individual nutritional status and mortality, there is some disagreement regarding the pathways by which distal forces, such as neighborhood and environment, are asserted on nutrition. The oft-cited 1990 UNICEF causal framework (Figure 1) begins to peel back these layers, including more distal multisectoral influences [136]. This framework was left flexible, intending to generate relevant research questions and acknowledged multi-level causes originating in regional circumstance. Mosley and Chen (1984) proposed a “proximate determinants framework” (Figure 2), suggesting that the distal influence of socioeconomic status dictates child survival through mediators at the individual, household, and community level [137]. Both of these seminal frameworks approach individual health holistically, recognizing the intricate web of direct, mediated, and modified multi-level effects. Moreover, they both consider nutritional status and mortality along the same spectrum indicating individual health. The association between nutritional status and increased risk of mortality has been noted by many [106,137,138] ; however this pattern of mortality risk is based on survivors and does not account for censored cohort members who did not survive long enough for their measurements to be included.

A blend of these frameworks was created (Figure 3) incorporating biologic causes from the child and mother, and interdependent causes occurring between community members. The cyclical intergenerational consequences have been highlighted as the long-term consequence of undernutrition feedback for later generations, as poor maternal nutritional status, and reduced economic productivity and social status. This conceptual framework will motivate our review of the proximate determinates of nutritional status.

2.5 Determinants of nutritional status

The investigation of various proximate determinants of nutritional status has resulted in a substantial body of literature, with some of the determinants more fully explored than others. The salient findings from this literature informed the variable selection used in this thesis and will be reviewed here. Determinants will be grouped as individual, household, and community effects following the recommendations of Mosley and Chen (1984) and UNICEF (1990).

2.5.1.Individual

Given the close bond between mother and child, particularly during neonatal and infant periods, determinants at the individual level may include characteristics of both the mother and child. They are, however, subject to different biological processes, each applying both independent and interdependent effects.

2.5.1.1. Child

Individual characteristics of infants are substantial predictors of early childhood growth trajectories. Growth in early life is affected primarily by an infant's parity, gender, age, and anthropometry at birth. Increased parity decreases low birthweight risk[12,139], while birth order has been associated with reduced anthropometry later in childhood [140,141]. Fetal development and gestational age at birth are directly related to anthropometry at birth and highly predictive of future longitudinal growth [12,70,142–144].

Some previous work has entertained possible ethnic differences that could explain differences in nutritional trajectories in early life. For example, several studies describe a "thin-fat" phenotype in South Asian infants, referring to babies which are smaller, but have adiposity comparable to children from developed countries. These findings indicate that genetic factors may be related to differences in anthropometry [20,29,31,145–147]. However, this assertion has been refuted by several seminal studies that better control for differences in socio-economic and environmental conditions [148–150].

2.5.1.2. Mother

Determinants of maternal nutritional status at the individual level operate through biological, behavioral, or productivity pathways. Biological factors such as age have been explored in numerous studies [77,151–153] which suggest that the association between maternal nutritional status and age changes throughout life, notably around ages 19 and 40. Birth anthropometry is also influenced by maternal age, potentially due to changes in physiology, maternal anthropometry, and fertility. Elevated risk of low birthweight has been associated with adolescent [17,154] as well as older mothers[16,17,21], indicating a non-linear relationship.

Biological Pathways

Mothers act as a biological conduit by which many external factors must pass before influencing the child. This is particularly true in-utero, and continues through childhood, weakening with time after birth. Fetal development, birthweight, and infant growth are closely connected to maternal nutritional status. During gestation, nutrients available through the placenta, depending upon the mother's metabolic and endocrine status, are partition nutrients to storage, use, and circulation. Uterine blood flow and the availability of circulating proteins are determined by the cardiovascular adaptations to pregnancy, such as increased blood plasma volume [155]. Such associations are supported by a 1994 study of adolescent mothers who were still growing themselves and experienced elevated risk of lower birth weight even when maternal weight gain during pregnancy had appeared sufficient. This finding was attributed to the reservation of nutrient stores for continued adolescent development rather than for fetal growth [154]. In post-adolescent women, however, maternal anthropometry and increases associated with pregnancy are consistently strong predictors of infant birthweight and birth MUAC [10–17,31,156]. Thame et al. (2004) found maternal weight gain in pregnancy to be associated with placental volume and rate of intrauterine growth [10]. Maternal nutritional status and diet continue to impact growth through infancy and into childhood [14,15,20,21,59].

Behavioral Pathways

Behaviors are linked to local traditions, norms, and attitudes and have been associated with nutritional status. Improved hygiene behaviors such as hand-washing have demonstrated reductions in disease [97,98,123,157–159] and are often accompanied with improvements in nutritional status [5,7,85,91–93,96,108,160]. Hygiene interventions are frequently paired with improvements in sanitation and drinking water, which will be discussed in the household section. Religious affiliation may similarly impact maternal anthropometry through behaviors such as food preparation, diet restrictions, and fasting. Several studies have found significant anthropometric differences between religious groups [161,162], and compared to Muslims [151,152,163].

Mothers' infant feeding behaviors have significant implications for infant morbidity, mortality, and growth trajectory. Inadequate breastfeeding is linked to approximately 1.4 million deaths and 44 million DALYs (10%) in children under five years of age [124]. The WHO and UNICEF recommend breastfeeding, initiated as early as possible, exclusively until 4-6 months (depending upon maternal nutritional status), and up to two years, paired with nutritional and hygienic locally-available weaning foods thereafter [164,165]. Longer duration of exclusive breast feeding between birth and six months of age has been associated with decreased risk of diarrhea [166–170] and sick visits [171], which directly relate to child nutritional status [89] and increased infant growth [149,166,168,172]. Early introduction of complementary foods (< 3 months) while breastfeeding was associated with higher risk of respiratory infection and decreased anthropometry at 3, 6 and 9 months of age [169]. The volume and composition of breast milk is minimally affected by maternal nutritional status, unless it is severe [124]. However, several studies have noted associations between maternal deficiency of select micronutrients and decreased concentrations of such micronutrients in breast milk [124,173]. Appropriate hygiene, such as hand-washing, is also important in this period to prevent episodes of diarrhea [174].

Productivity Pathways

Individuals' economic productivity may be related to their skills, health, and/or time [137]. Skills are typically measured by educational attainment and/or occupation, both of which are closely linked with economic productivity and, ultimately, health. A complex association between educational attainment and nutritional status has been observed in that, as education increases, the likelihood of being under- *and* overweight decreases [153,175,176]. Furthermore, highly educated mothers tend to have healthier and better nourished infants [4,17,21,50,144,174,177–183]. The effect of maternal education on child growth may not be consistent at all ages: Sahn et al. (1997) found maternal education to have a greater positive influence on child growth at younger ages (< 2 years) [179].

Concomitant with maternal education, maternal autonomy, as measured by access to money and decision making, is also positively correlated with infant nutriture [178,184]. A mother's ability to work outside the home for income, for example, can improve household income, increase skills, and strengthen female autonomy; however, the time working may limit the time allotted for other health-promoting behaviors, such as food preparation and child care. Depending on her employment, mothers may also be exposed to occupational hazards, such as agro-chemicals and pesticides, which have been shown to increase the risk of preterm birth, small-for gestational age, and perinatal mortality [185,186]. Given the importance of maternal nutritional status in regards to the health of their children, surprisingly very little research has focused on the effects that impact the nutritional status of mothers.

2.5.2.Household

Beyond characteristics of individuals, one of the most important factors related to child nutritional status is household economic status. The effects of household economic status are systemic, influencing diet, food security, maternal and paternal nutritional status, water, sanitation, hygiene, environmental health, educational attainment, and healthcare access. Increases in economic status have been associated with improvements in nutritional status [11,21,59,78,108,179,187–191], growth [31,148] and birthweight [16,17] , and decreased risk of infection [192]. Economic status is an underlying condition that is difficult to measure directly; however, several indicators have been used successfully, such as asset-based indices [81,177,193–197], wealth/affluence[198–200], and deprivation/poverty[201–203]. These indicators can either be measured absolutely or interdependently, relative to peers. Interdependent economic measures will be discussed in a later section.

Health effects associated with socioeconomic status (SES) are typically mediated through hazardous exposures (e.g., poor sanitation/water quality or agricultural soil) or limited access to resources (e.g., cook stove or healthy food). Under this premise, economic status, as it relates to health effects, can be conceptualized as an latent variable indicated by ownership or utility of types of assets [204]. Asset-based estimates of SES are commonly used in the developing world context [81,177,193–197] and have been associated with other indicators of health and wealth, such as school attendance, improved welfare, improved health, and protection from flooding [182,196,197,204–207]. Proximate determinants at the household level include various assets and characteristics of the household closely associated with wealth. Household characteristics that impact the health and nutrition of its members include the type of roof, type of floor, method of sanitation [94,97,157,159,208,209], availability of drinking water [209,210], availability of electricity, indoor air quality [85,209], cooking fuel/location [104,139,177,209,211], number of rooms [54,108,192,209,212] , and the number of people living in the household [108,163,209]. Ownership of modes of transportation improves access to medical facilities, markets for goods and food, and employment, which in turn can improve health status. Assets such as radios, televisions, and other sources of information can provide households with knowledge of nutrition, hygiene, and other healthy behaviors. Other assets such as soap, cleaning supplies, a wash basin [174], and bed nets are preventative assets that may impact health status. These assets and characteristics are closely linked with economic status and are often elements of an index that may help measure latent living conditions [81,177,193–197,204].

2.5.3.Context

Aspects of the community that act as proximate determinants of health and nutritional status, suggested by Mosley and Chen (1984), include the ecological setting, the political economy, the health system, and degree of urbanicity. These aspects are associated with the wealth and potential productivity of a community. The ecological setting consists of climate seasonality (temperature and precipitation patterns), soil, and elevation. Seasonal changes in precipitation and temperature can assert direct effects on health through changes in disease transmission as well as indirect effects through agricultural production and other economic activity. Flooding, for example, may impact disease transmission and result in loss of assets and earnings. Seasonal fluctuations in diarrhea incidence and pathogen prevalence in conjunction with increases in precipitation and/or changes in temperature have been observed in several studies [213–222]. Drought and average daily rainfall have also been associated with child growth [55], malnutrition [57] , and mortality [223]. There is general consensus regarding seasonal differences in food intake and nutritional status [55,75,224–226].

Agricultural production, which impacts food security, quality, and price, is dictated by seasonal variations in climate and soil type. Length of growing season and farming system, for example, have been related to global variation in mortality rates [223]. Variables related to soil fertility have demonstrated associations with underweight status [56,57,227,228]. Furthermore, health may be impacted by soil-transmitted parasites. Elevation has also been reported to have an effect on anthropometry [15,49,55]. This association with health status may be a result of several pathways, such as exposure to flooding [90,229–231] or malaria [55,223]. Iannotti (2009) reported that infants of mothers who previously resided in high-altitude regions had significantly larger chest circumference and greater length compared to mothers who did not [15]. Increased relief has also been observed to negatively affect infant anthropometry. This may be due to the remoteness of these regions or the strenuous lifestyles required [55].

The political economy includes characteristics of the public institutions associated with the production of goods, physical infrastructure, and political institutions. Health determinants related to political economy include access to public goods such as infrastructure (railroads, roads, electricity, communications, water, and sewage), and institutions such as production organization, schools, health centers, law enforcement, public administration, and popular associations such as labor unions, cooperatives, and political parties [137]. Leventhal et al. (2000) specifically cites institutional resources and social organization/collective efficacy as important influences on child development [232]. Health status improvements have been observed with increased access to markets[233–235] and public goods such as schools, health services [21,23,60,99,195,232,236–239], electricity [139,236], paved roads [57,210,240], and piped water [57,60,94,229,236,241]. Several community interventions have demonstrated that improvements in water and sanitation facilities decrease incidence of diarrheal disease [94,209,213,242–244] and improve nutritional status [94,95].

The health system is composed of institutional actions, such as disease-control measures for prevention, healthcare subsidies for treatment and public information/education, and motivation for both prevention and treatment. These proximate determinants of health predominantly stem from public policy. Since the data used in this thesis were not from a multi-site study and since public policies should, in theory, be similar across the study site, these variables will not be included in this analysis.

2.5.3.1. Rural-Urban Effects

Differences in nutritional status between rural and urban populations have been reported by many [91,94,180,181,192,245,246]. These differences may be a cumulative result of the previously discussed community components. Several studies found that the rural-urban nutritional gradient would disappear after accounting for differences in individual economic status [245,246]. Others have found differences in sanitation or rates of infection to be chiefly responsible after accounting for economic status and other confounders [91,94,177,192]. Urban centers may provide better health and education services as well as economic activity and consumer goods. Distance from urban centers may act as an indicator of isolation from public goods and services, which has been associated with child nutritional status [99] and mortality [223]. The effect of isolation may be mediated by increased food insecurity in remote areas [107]. In addition to decreased access to public infrastructure and services, distance from urban centers may also be associated with decreased population density. Often the distinction of urban versus rural context is made based on differences in population density. A relation between increasing population density and increasing infection transmission rates [193,247] and increased risk of stunting [59] have been suggested by others. Distance to institutional resources, however, may not best describe access. For example, in a study of growth and nutritional status in Bolivian tribal children, access to education was better measured by the number of teachers in a village instead of by distance [99].

2.5.3.2. Neighbor Effects

An element not included or discussed in the Mosley and Chen framework is the potential contextual effects from other community members. The research interest in these types of effects is increasing as studies observe notable and significant interdependent contextual effects. This may be due to synergy related to the concentration of particular characteristics, or social interactions, support, and cohesion. Community economic structure has demonstrated an independent association with child nutritional status [21,177,180,190,191,248], birth outcomes [180,249–252], and mortality [253]. The effect of community economic status on nutrition has also shown interactions with race/ethnicity [181,248,251,252]. Interdependent economic measures account for the structured difference between individuals' economic status. Inequality estimated by the Gini Coefficient, for example, is a measure of disparity of resource distribution among a population; details of its calculation can be found elsewhere [254]. Using the Gini coefficient, inequality has been associated with greater food poverty [235] and stunting[190]. Relative measures of income, initially proposed by Duesenberry [255], and deprivation, as proposed by Deaton [256] , have been suggested as alternate interdependent measures accounting for individual status. Relative deprivation has helped explain differences in nutritional intake in children living in China [257], intrauterine growth restriction in the US [19] , and anthropometry of British children [258].

Average neighborhood education, though lesser studied, has also emerged in the research as a strong predictor of nutritional status [58,141,176].

These individual-community interactions may be related to elements of social capital such as trust, reciprocity, and social cohesion, which are reported to substantially affect health [200,232,259], child outcomes [4], and birthweight [248,251,260]. Stress from lack of community social order, control, and collective efficacy has been associated with negative mental and physical health outcomes [200,232,259–262]. Others have also observed interactions between individual and area-level characteristics influencing child nutrition [21,49,110,250]. Peer support has demonstrated positive effects on maternal and child health [11,232,248,263], and community instability and disorder has negative effects [232,248,260].

2.6 Spatial Autocorrelation

Linear regression techniques, which are often used in epidemiological analyses, have four basic assumptions: a linear relationship, normality, equal variance, and independence of errors. Statistical errors are the difference between observed values and the unobservable true function value. The differences between observed values and an estimated function values are called residuals. Residuals differ from statistical errors in that residuals are deviations between a sample of observed values and those estimated from a function, which may not be complete or correct. Therefore, residuals are comprised of two components: random/statistical error and bias. Bias reflects systematic errors such as missing variables/confounders or correlation between observations which were not accounted for by the estimated function.

Correlation between observations, which changes with differences in time and/or space, is called autocorrelation. The presence of autocorrelation creates an information paradox that simultaneously reduces and increases available information. When observations are highly correlated, less information is provided, reducing the effective sample size compared with observations that are truly independent [264–268]. Assuming independences, when autocorrelation exists, may yield inaccurate coefficients, standard errors, and significance statistics, which could lead to incorrect inference. On the other hand, spatial autocorrelation between observations may provide additional information contained in the structure of model residuals. Residual error is often seen as a nuisance parameter, with mean zero, among independent observations in linear regression, or treated with study design or mixed modeling techniques. To simply control for autocorrelation potentially ignores informative shrouded in the residuals which may illuminate other key effects.

Analysis of the spatial distribution of health and disease has long been a tool of surveillance and hypothesis-generation since the early part of the 18th century [269–271]. Early maps, such as John Snow's spatial mapping of cholera cases around the Broad-street pump, indicated an understanding of the spatially heterogeneous distribution of disease, often implicating environmental origins. Spatial heterogeneity or "clustering" of similar observations is often indicative of spatial autocorrelation. With recent technological and methodological advances, epidemiological research increasingly includes the use of spatial autocorrelation to illuminate broader causal frameworks in many health-related fields such as substance abuse [272,273], infectious disease [215,216,274–277], risk and mortality estimation [278–281], and nutrition [282–284]. For the purposes of this review, discussion will focus on research pertaining to maternal and child nutrition and related mortality.

Globally, the majority of cases of malnutrition and related mortality are clustered within Africa and Asia, more specifically within sub-Saharan Africa and South Asia [4]. Black et al. [3] reports that over 50% of the world's deaths of children under-five years are concentrated in six countries. These figures are reviewed, again, in a later analysis which indicates that "within those six countries, 55.9% of their deaths are concentrated within 10.0% of the land area, holding 34.4% of the combined population" [285]. Geographic clustering in mortality and nutritional status has been observed by many others [3,49–52,55–57,60,61,160,223,240,285]. Nevertheless, the underlying mechanisms resulting in spatial patterning remain unclear.

Fenn et al. (2007), Balk et al. (2005), and Morris (2000) suggest that this phenomenon is simply a result of individuals with similar individual and household characteristics clustering together [53,54,56]. Alternatively, some authors attribute this phenomenon to characteristics of the environment [55–57], such as land use, topography, climate, and road access; or to the influence of others in the community [58–61], such as urbanicity, community-level educational attainment, social participation, and community employment. These exogenous effects have largely been ignored in the nutritional literature. Previous research has favored reductionist methodologies which focus on individuals and households instead of attempting to understand the greater context.

Individuals with similar characteristics often do reside within close proximity. This effect is referred to as *population sorting,* which is driven by economic and social processes [286]. If individual and household characteristics alone were driving observed spatial variation, simply accounting for their independent effects should remove observable spatial clustering. This, however, is not the case [223,260].

Population sorting frequently marginalizes the most economically disadvantaged households into the least desirable locales, which are often associated with elevated environmental risks. Studies have observed that those of lower SES residing closer to polluting facilities [287] have greater difficulty relocating from regions prone to natural hazards [288], and have a modified acute effect from exposure to black smoke pollution [289]. Several analyses have considered area-based environmental health hazard exposure from multiple dimensions such as air pollution, climate, industrial facilities, UV radiation, and green space, as they related to proximate household economic status. These analyses have found multiple environment deprivation to be associated with economic status in the UK[290,291] and New Zealand[292]. On the other hand, populations of higher socio-economic status are drawn to areas with improved infrastructure and green-space [293,294].

Proximate determinates of nutritional status, such as infectious disease and available nutrients, may also vary across space. Transmission of many infectious agents is often tied to environmental exposure or interpersonal contact. Clustering of diseases such as pneumonia [105,295–297], SARS [298], diarrheal disease [299–303], cholera[274], chryptosporidiosis [275], malaria [299,304], West Nile virus [305] , and “fever” [302,303] have been observed, potentially indicating exogenous factors. When infection was a result of a vector such as a mosquito, clustering was attributable to factors favorable to the vector [299,304,305]. Spatial variability in helminth infection is largely related to geographic factors such as temperature, elevation, and distance to large water bodies [306].

Differences in dietary intake can help explain geographic/spatial variation in nutritional status. Mueller and Smith (1999) found healthier child growth in regions of Papua New Guinea that subsisted on cassava and sweet potato as staples, compared with those subsisting on banana, sago, and taro. This difference in diet accounted for between 25% and 50% of the geographical variation in growth [55].Spatial variation in micronutrient status has also been observed [282,307–309]. These variations have been associated with geographic factors such as surface temperature [282], vegetation indices [282], elevation [282], and sunlight [309]. Spatial variation of malnutrition and parasitic infections are also reported as substantial contributing to micronutrient deficiency [307,308]. Several studies have associated spatial heterogeneity of soil type/composition with the nutrient density in agricultural crops [310–312] , even in 1000 meter sampling grids. Soil micronutrient composition may have a significant effect on rural populations practicing subsistence agriculture.

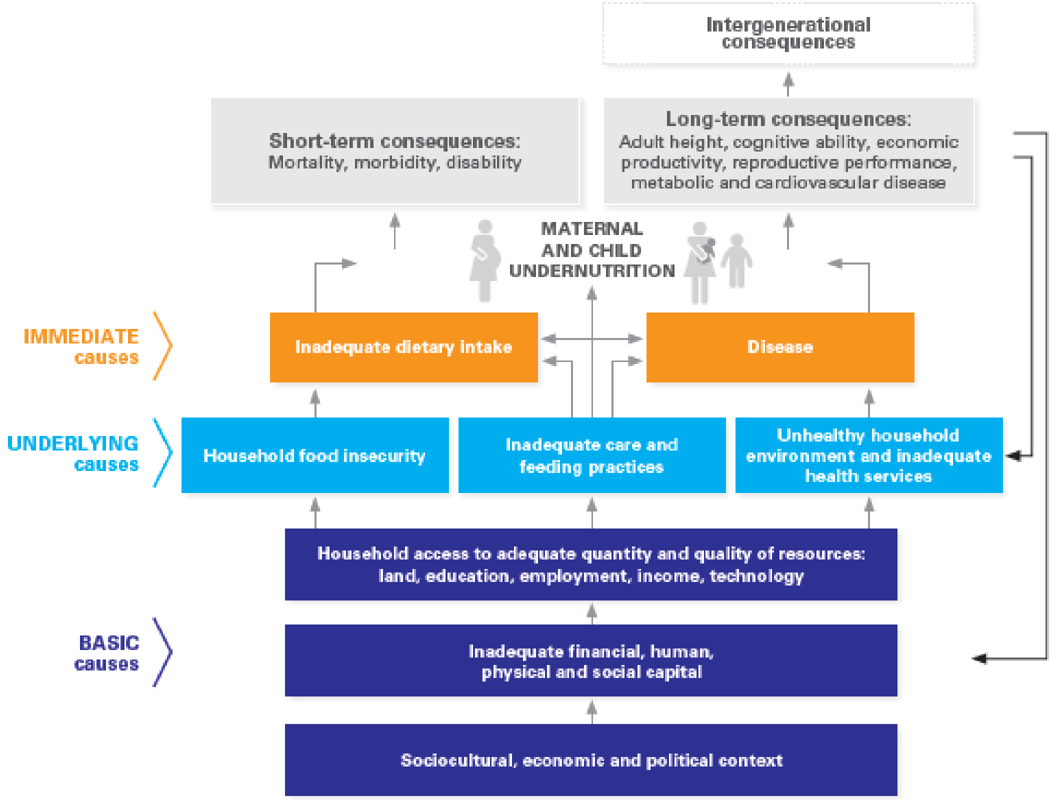
2.7 Systems biology and ecology

As suggested by Mosley and Chen (1984), UNICEF (1990) and many others [56,191,223,285,313] , and corroborated by the literature discussed, a holistic approach is appropriate if we are to untangle the web of causality determining individual health status. Conventional epidemiological methods typically focus on the health of individuals, while tending to overlook the health of the individual's circumstance or context, which may be the ultimate cause. This is to say: the Titanic sank because it had a hole in it, not because it hit an iceberg. Biology and ecology may provide the field of epidemiology with some methodological perspective. Biology tends to look inward, treating cells as the basic units of life, which interact with each other and create tissues, which comprise organs, many of which create an organism; each level contributing to the health of the organism. Ecology tends to look outward, treating organisms as the basic units, wherein similar organisms create populations of species, which interact with other species of plants and animals, all of which comprise ecosystems; each part determining the health of the ecosystem. Epidemiology has tended to focus on characteristics of the individual and, perhaps, household, while often treating effects of the greater context as a nuisance instead of a source of influence.

Systems biology, or systeomics, is a novel approach to understanding complex biological systems and genetics through integration of discovery and hypothesis-driven science [62,63]. The objective of discovery science is to uncover all of the elements in a system, while hypothesis-driven science aims to generate hypotheses and test them experimentally. The systems science process of component identification and hypothesis testing is depicted in Figure 4, taken from Sauer et al. (2007) [63]. These techniques are only recently being used in epidemiology [64], mostly in the study of obesity (see Figure 5) [65,66,314]. Ideker et al. (2001) outlines several important features of biological information which are applicable in epidemiological research: "(1) it operates on multiple hierarchical levels of organization; (2) it is processed in complex networks; (3) these information networks are typically robust, such that many single perturbations will not greatly affect them;(4) there are key nodes in the network where perturbations may have profound effects; these offer powerful targets for understanding and manipulation of the system" [62]. Understanding the full system of effects is useful for decision support services and policy planning – to observe the upstream and downstream ramifications when just one part of the system is modified or perturbed.

Approaching individual nutritional status as a system requires identifying the system's elements and uncovering the network and relative direction of effects. Since much of the previous literature has predominantly focused on individual and household unidirectional effects, much of the system is unknown. Epidemiological research should give considerable attention to understanding these interrelated effects, given the close ties between disease, nutrition, and health status. A more comprehensive understanding could provide more creative and potentially more effective interventions, improving the health of populations instead of focusing on individuals.

2.8 Figures



The black arrows show that the consequences of undernutrition can feed back to the underlying and basic causes of undernutrition, perpetuating the cycle of undernutrition, poverty and inequities.

Source: Adapted from UNICEF, 1990.

Figure 1: The UNICEF conceptual framework

This conceptual framework was taken from the UNICEF 2013 report titled *IMPROVING CHILD NUTRITION: The achievable imperative for global progress* [315], and was adapted from the 1990 conceptual framework published in the *UNICEF POLICY REVIEW* [136]. This figure depicts the multi-level and cyclical causation of maternal and child undernutrition, however fails to consider interdependent effects, biological causes or incorporate how population density may related to available resources and disease transmission.

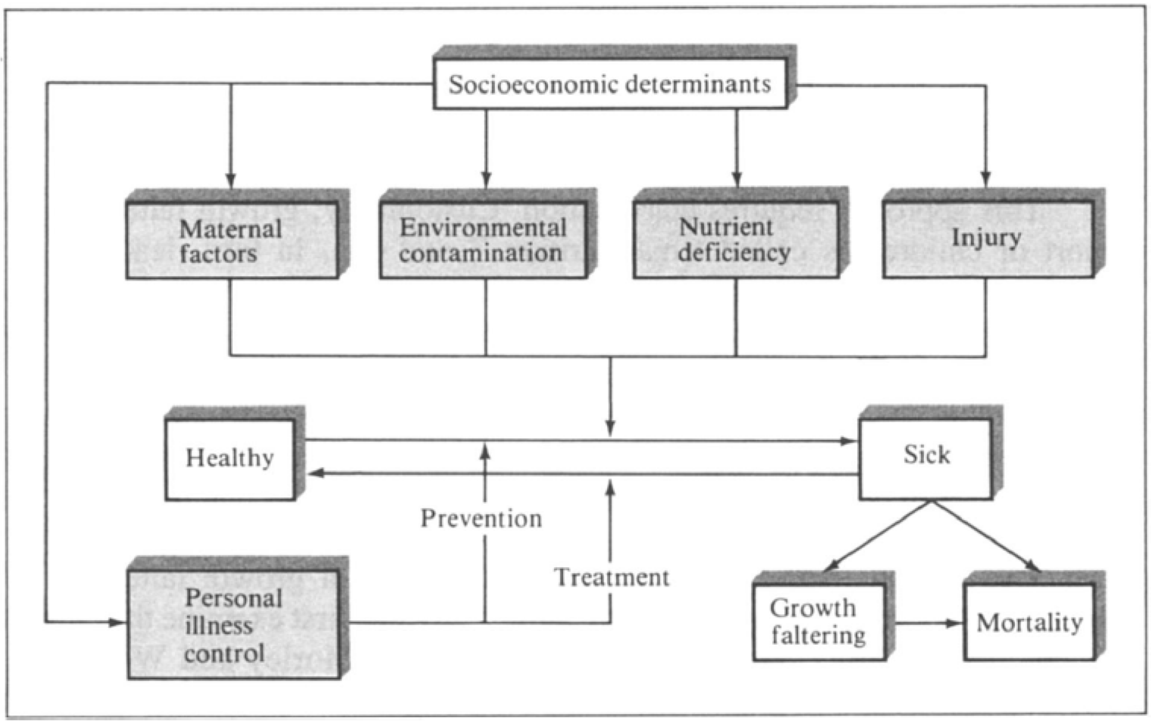


Figure 2: The Mosley and Chen Proximate Determinants Framework

This figure depicts the framework proposed by Mosley and Chen (1984) [137] , which shows how these five groups of "proximate determinants" operate on the health dynamics of a population. They include factors of personal illness control, which accounts for both rates of illness (through prevention) and rates of recovery (through treatment).This model does not provide definition of effects from higher levels of context and interdependent neighbors.

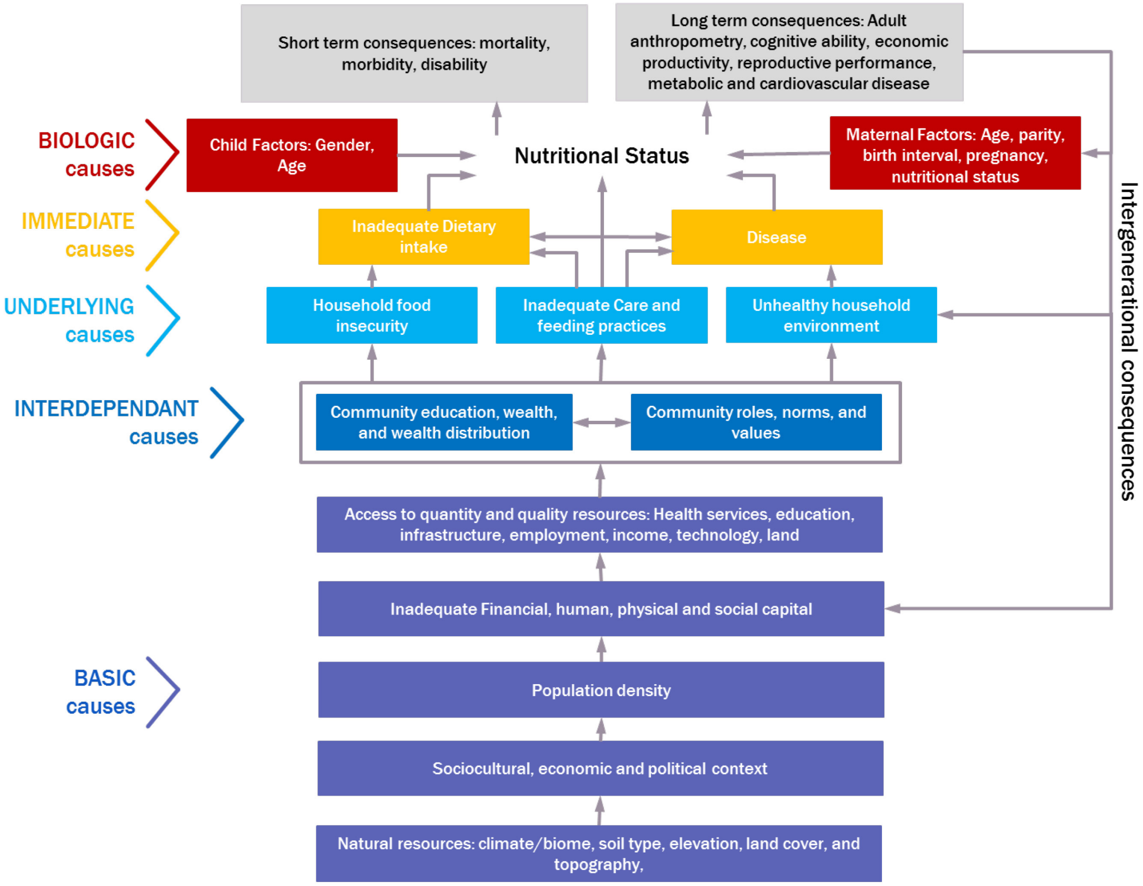
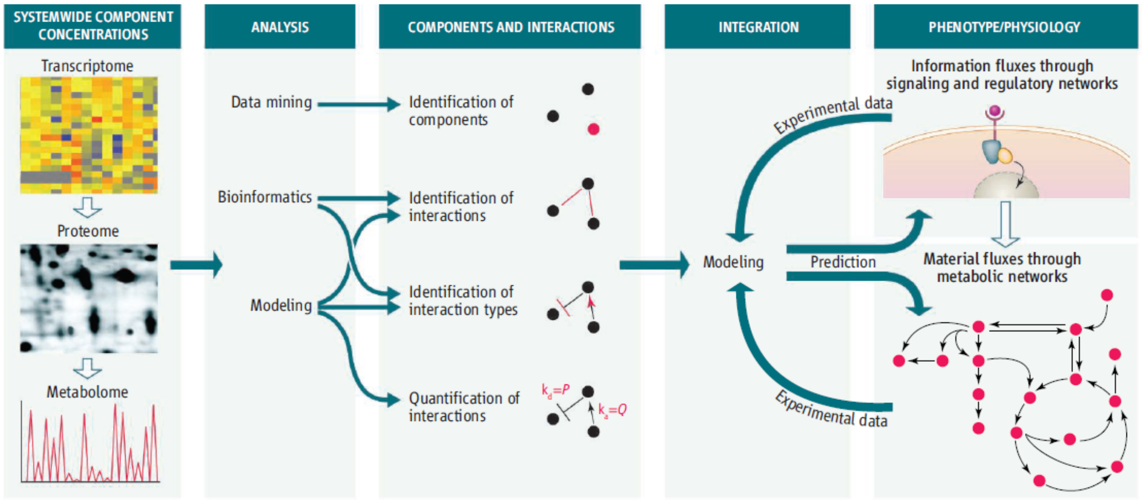


Figure 3: Proposed Conceptual Framework

This figure depicts a conceptual framework derived from both the UNICEF framework and that proposed by Mosley and Chen (1984), adapted to suit the analytic approach being undertaken in this dissertation. This framework includes biologic and multilevel causes of nutritional status as well as intergenerational feedback effects.



A systems roadmap. The comprehensive component concentrations reported by Ishii *et al.* provide input data for inferring component interactions using computational methods. The challenge for computational modeling methods yet to be developed is to predict the functional network state from the concentrations and to infer the information processing network that controls the functional state.

Figure 4: A systems roadmap from Sauer et al., Science, 2007

This figure depicts the iterative processes of systems science.

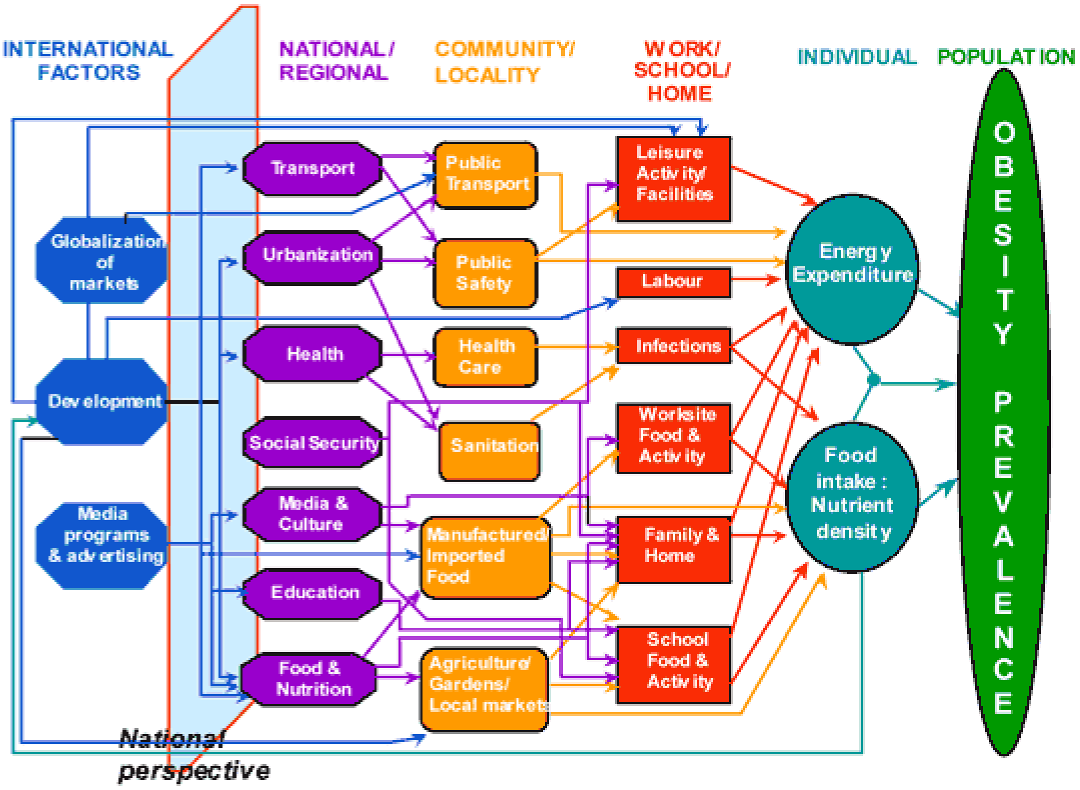


Figure 5: Levels of determinants and sectors of society implicated in the complex systems of obesity from Huang et al., Preventing Chronic Disease, 2009

This figure depicts the complex and hierarchical system of influences leading to obesity in individuals.

Chapter 3 The JiVitA dataset

Data used for this analysis were collected as part of the JiVitA trial which has been described in great detail elsewhere [67,316]. In brief, the study site is a contiguous rural area of approximately 435 sq. km located in northwest rural Bangladesh (Figure 5). The site was selected to reflect vital, health, and nutritional risks of the rural Bangladeshi population [67]. It encompasses 19 rural unions within the Gaibandha and Rangpur Districts. The study area was divided into 596 sub-areas, called "sectors," for the purposes of labor management and treatment randomization, each containing approximately 250 households. The site is situated to the west of the Jamuna river and experiences considerable seasonal flooding. The site is also characterized by its remoteness and agrarian nature and is similar in context to many areas of south Asia.

The study population is a sample from a prospective cohort that was enrolled in a double-masked, cluster-randomized, dual-intervention, placebo-controlled trial conducted by the JiVitA project. The primary goal of the study was to establish the efficacy of weekly vitamin A (VA) or beta-carotene supplementation in early pregnancy through 3-mo post-partum in reducing pregnancy-related, all-cause mortality in women. Secondary aims included impacts on fetal loss, infant (< 3 mo) mortality, maternal obstetric and infectious morbidity, infant infectious morbidity, maternal and infant micronutrient status, fetal and infant growth and prematurity, gross external birth defects, and infant growth to six months of age.

The study identified women eligible to participate in the supplementation trial beginning in July 2001. Eligible women were of reproductive age (13-44 years), married, not sterilized or menopausal, living with their husbands who were not sterilized, and consenting to be enlisted into a 5-weekly, home-based, pregnancy surveillance system. Women currently pregnant or post-partum and lactationally amenorrheic were placed on a "waiting list" for future eligibility once menstruation resumed. Eligible women in the surveillance system who were detected as being pregnant were enrolled between August 2001 and October 2006. At enrollment, household and maternal data regarding socio-economic status, pregnancy history, recent morbidity, diet, anthropometry, alcohol and tobacco use, and household logistics were collected.

Study randomization was performed at the cluster/sector level, and participants were allocated to one of three study groups: placebo, VA (7000 µg retinol equivalents or 23,300 IU VA palmitate), or beta-carotene (42 mg all-trans beta-carotene). Vital status was assessed at weekly supplementation visits from 9 weeks gestation for mothers and from birth for infants, until 12 weeks post-partum and monthly thereafter. Data regarding breast and complementary feeding, vaccination, antenatal and post-partum care, maternal and infant morbidity and infant anthropometry were assessed at roughly three and six months post-partum. Gestational age was estimated using the interval between the dates of birth and the mother's last menstrual period. Since nutritional status was one of the primary outcomes of interest, anthropometry was meticulously measured in triplicate. Of the roughly 125,257 women eligible to participate in the trial, approximately 59,666 were detected as pregnant and enrolled. Data were subsequently collected from 42,185 infants with additional measurements from a subset of 18,157 as newborns (see Figure 7: Study population flow chart).

For the purposes of identification, enrollment, and tracking of study participants, the JiVitA Geographic Information System was established as a method of rural addressing. The system includes 236,681 landmarks, 149,402 of which are households, study and political boundaries, local roads and paths, and hydrologic features (Figure 6). Many of these data were digitized and merged from 1:3960-scale cadastral maps produced by the British Survey of India in the 1930s. The system was maintained and updated throughout the JiVitA – 1 study period. The details of the JiVitA Geographic Information System can be found elsewhere[317].

3.1 Figures

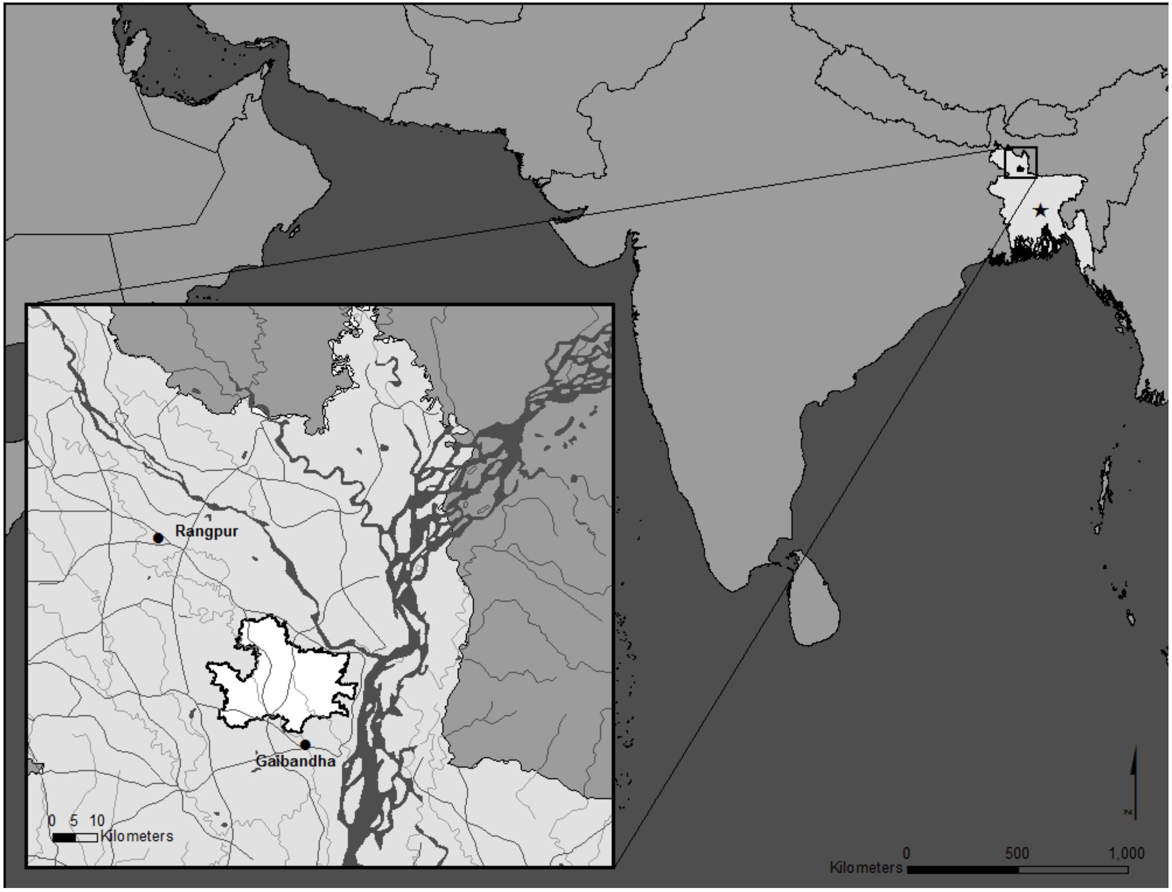


Figure 6: JiVitA study site reference map

Reference image depicts the approximately 435 sq. km JiVitA study site which is located in the Gaibandha and Rangpur districts, west of the convergence of the Teesta and Jamuna Rivers in Northwest Bangladesh.

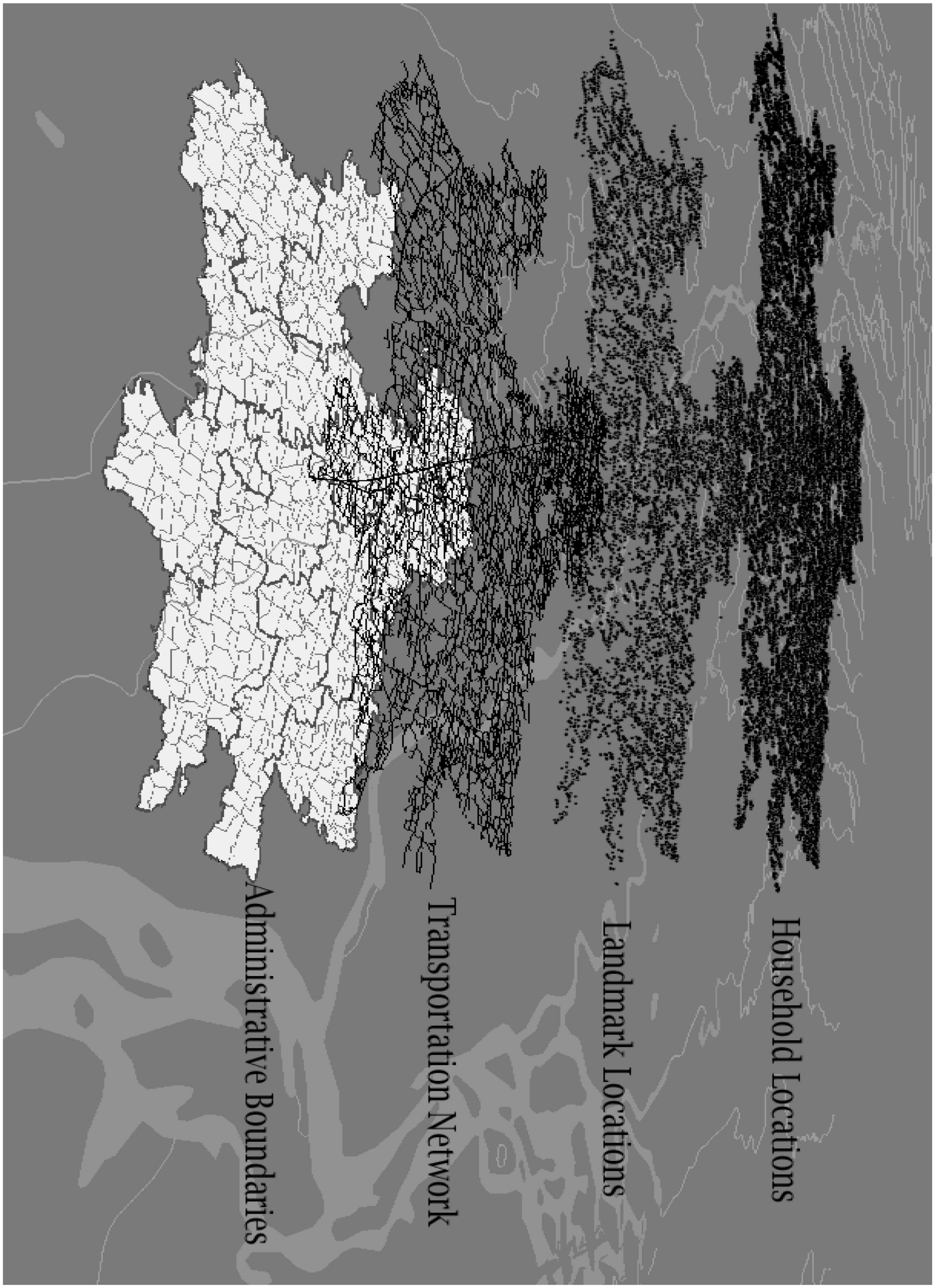


Figure 7: JiVitA Geographic Information System

Image depicts some of the geographic data created as part of the JiVitA study

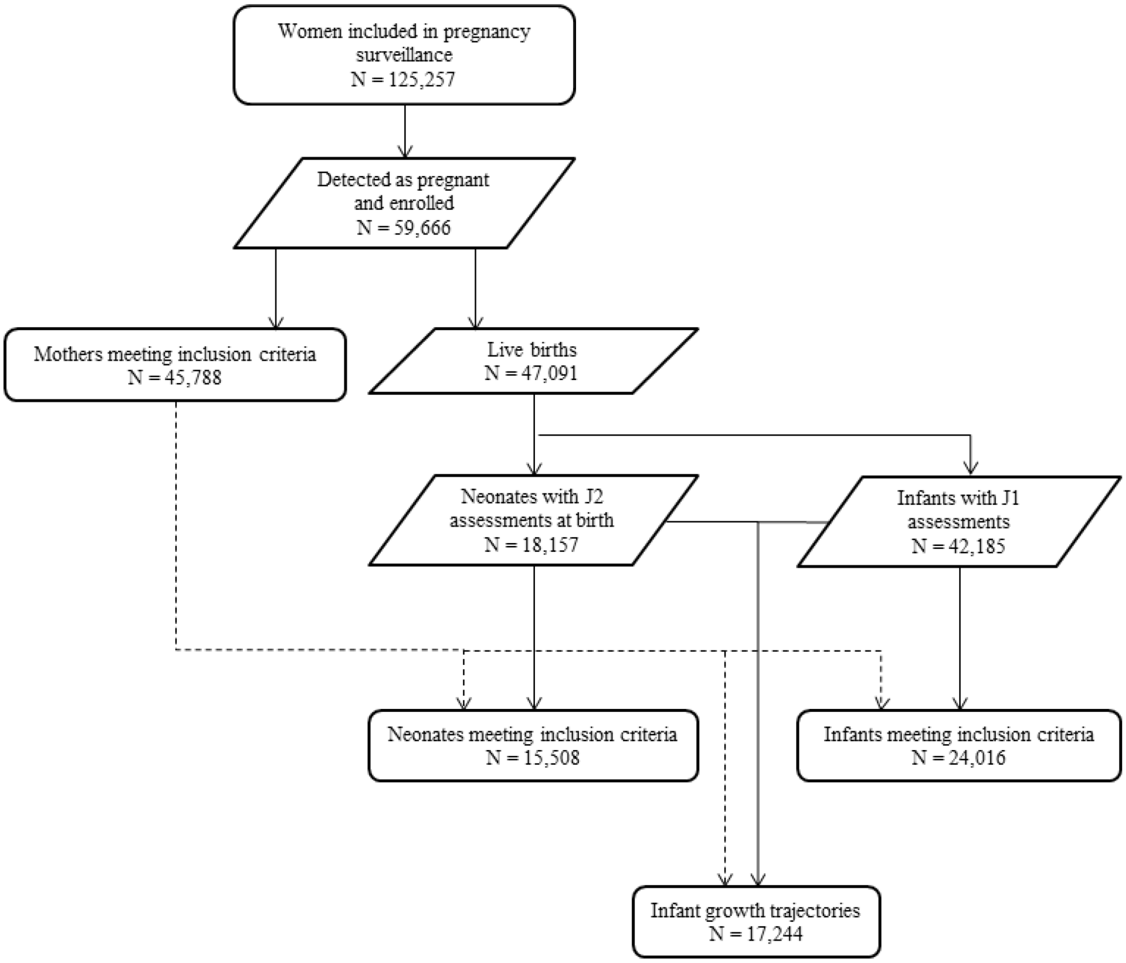


Figure 8: Study population flow chart

This flow chart describes the creation of the study populations for each of the three analyses conducted as part of this dissertation.

Chapter 4 Exploring nutritional status of expectant mothers in northwest Bangladesh: A systems approach

4.1 Abstract

Maternal nutritional status has substantial importance for a healthy pregnancy and thriving children, however, surprisingly very little research has focused on the effects that impact the nutriture of mothers. Furthermore, many have noted nutritional status to cluster spatially for which the causes are uncertain. This analysis explores the determinants of maternal nutritional status at the individual, household and contextual level and attempts to explain observed spatial patterning. Data were obtained from the JiVitA-1 vitamin A supplementation trial in northwest Bangladesh. Determinants were grouped by level and added sequentially to a linear regression model after adjusting for seasonal, secular and spatial error effects. Residual spatial correlation from each sequential model was observed with correlograms and interpolated maps. Determinants at the individual, household and contextual level accounted for 7.7%, 3.0%, and 1.0% of the variance, respectively. The full model accounted for a total of 11.6% of the variance. Contextual variables accounted for substantially more spatial correlation than individual or household variables. The strongest determinants were measures of SES such as maternal education, household economic status, the average and distribution of neighborhood wealth and average neighborhood maternal education. Other promising contextual variables include population density, elevation, and travel-time to permanent bazaar and paved road. The findings from this analysis support previous research suggesting the relevance of location and community for understanding the system of influences on individual health outcomes. Contextual variables were interrelated with one another as well as with variables at other levels, providing independent and modified associations. Public health programing should encompass multilevel interventions targeting not only at-risk individuals, but also at-risk communities.

4.1 Introduction

Maternal nutritional status has substantial importance for a healthy pregnancy and thriving children. Maternal anthropometry before and during pregnancy is correlated with the anthropometry of their children at birth and beyond [10–17,31,156]. Malnutrition during pregnancy can also impact offspring later in life through increased risk of hypertension [30], lung cancer [318] and insulin resistance [319]. The nutritional status and diet of new mothers continue to impact child growth as nutrients are shared via breastmilk [14,15,20,21]. These effects in infancy can lead to irreversible damage and reduced human capital later in life [22–28]. In addition to the consequences for the child, maternal malnutrition can also put the mother's life at risk: decreased nutritional status in mothers at delivery is attributable for at least 20% of maternal mortality, based on a 2008 estimate[124]. Given the importance of maternal nutritional status in regards to the health of their children, surprisingly very little research has focused on the effects that impact the nutritional status of mothers.

The current body of nutritional literature has primarily centered around the impact of individual and household factors, while generally overlooking the community context. This narrow perspective of health and nutritional status fails to consider the hierarchical amalgamation of causality motivating our analysis and depicted in the conceptual framework presented in Figure 3. Several studies have noted that individuals of similar nutritional status are more likely to reside in close proximity to one another, even after controlling for relevant individual variables [49–52]. Nevertheless, the effects which result in "clustering" remain unclear. Fenn et al. (2007) and Morris (2000) suggest that this phenomenon is simply a result of individuals with similar individual and household characteristics clustering together [53,54]. Alternatively, some authors attribute this phenomenon to characteristics of the environment [55–57], such as land use, topography, climate, and road access; or to the influence of others in the community [58–61], such as urbanicity, community-level educational attainment, social participation, and community employment. These findings, when taken together, complement our framework and should be considered fully. There have been relatively few studies that include community effects, which are predominantly explored in childhood.

Two primary hurdles have hindered the incorporation of spatially explicit effects from the environment and community in the analysis of nutritional status: sample size requirements and spatial data availability. Environmental and community effects are often much smaller in magnitude than those applied at the individual or household scale and, thus, require substantially larger samples. In addition, the availability and quality of spatial data from the developing world is currently lacking, despite the fact that in recent years, spatial data from developed countries has become far more available.

In light of these common obstacles, data collected from a cohort study conducted in northwest Bangladesh provides a rare opportunity to detect and evaluate the role of spatial effects in determining maternal health, as indicated by nutritional status. The large study population resides within a contiguous study area, and the data includes a rigorously collected geospatial information system. The incorporation of spatial analysis with multiple linear regression techniques allows for an assessment of the independent as well as synergistic effects of factors at the individual, household, and community levels. For this analysis, community characteristics will include spatially explicit effects of location, relative to community assets and the characteristics of neighbors. Findings from this analysis may improve understanding of the complex effects contributing to maternal malnutrition, and could inform intervention efforts taking a multi-level approach to address at-risk populations.

4.2 Subjects and Methods

4.2.1.Study Population and Data

Data used for this analysis were collected as part of the JiVitA trial. The study population has been described in great detail elsewhere [67]. In brief, the study site is a contiguous rural area of approximately 435 sq km located in northwest rural Bangladesh (Figure 5) situated to the west of the Jamuna river. The site is characterized by its remoteness and agrarian nature and was selected to reflect vital, health, and nutritional risks of many rural south Asian populations [67]. For the purposes of identification, enrollment, and tracking of study participants, the JiVitA Geographic Information System was established as a method of rural addressing (Figure 6). The details of the JiVitA Geographic Information System can be found elsewhere[317].

4.2.2.Sample Selection

The JiVitA study identified women eligible to participate in the supplementation trial beginning in July 2001. Eligible women were of reproductive age (13-44 years), married, not sterilized or menopausal, living with their husbands who were not sterilized, and consenting to be enlisted into a 5-weekly, home-based, pregnancy surveillance system. Women currently pregnant or post-partum and lactationally amenorrheic were placed on a “waiting list” for future eligibility once menstruation resumed. Eligible women in the surveillance system who were detected as being pregnant were enrolled between August 2001 and October 2006. At enrollment, household and maternal data regarding socio-economic status, pregnancy history, recent morbidity, diet, anthropometry, alcohol and tobacco use, and household logistics were collected. Since nutritional status was one of the primary outcomes of interest, anthropometry was meticulously measured. Of the roughly 125,257 women eligible to participate in the trial, approximately 59,666 were detected as pregnant and subsequently enrolled.

4.2.3. Dependent Variable

The primary outcome of interest is mid-upper arm circumference (MUAC) among mothers at nine weeks gestation (assumed to be nearly equivalent to pre-pregnancy nutritional status). MUAC will be treated as a continuous variable. MUAC measurements were performed in triplicate by JiVitA field staff trained and standardized in anthropometry and then averaged. MUAC, as stated in Chapter 2, was chosen over other anthropometric measurements for its ease of field administration, its relation to physiologic processes [73,77], and demonstrated sensitivity to short term changes in nutrition [75,78–84]. Maternal MUAC is also associated with infant MUAC [84] and birthweight [12,13,16,17]. Maternal MUAC was not standardized to the international reference population, because this analysis is restricted to those residing within the study area.

4.2.4. Independent Variables

For this analysis of maternal nutritional status, effects were considered at the individual, household and community levels. Variables of interest were identified through an extensive literature review and discussed in greater detail in Chapter 2. Individual variables previously associated with adult nutritional status and included in this analysis were maternal age[77,151–153], years of education[153,175,176], hygiene behavior[5,7,85,91–93,96,108,160], employment[178,184], and religion[161,162] [151,152,163]. Hygiene behavior includes washing hands before eating and after defecation. Household variables noted in the literature and included are presence of improved sanitation facilities[94,97,157,159,208,209], ownership of non-laundry soap[5,7,85,91–93,96,108,157,160], household size[108,163,209], crowding[54,108,192,209,212], and an assets-index of household living standards[81,177,193–197,204]. Since there are fewer studies which that have examined community variables, with conflicting results, several community variables were considered for inclusion in the regression analysis. Community variables discussed in the literature and considered were the neighborhood average household economic status[21,177,180,190,191,248], neighborhood economic inequality[21,235], neighborhood average educational attainment[58,141,176], population density[59,193,247], elevation[15,49,55], travel time to market/bazaar[233–235], travel time to a paved road[57,210,240], travel time to a healthcare service provider (HSP) [21,23,60,99,195,232,236–239], and the proportion of neighbors who had unimproved sanitation facilities, own a bar of soap not for cloths washing, and who wash their hands after defecation/before eating[5,7,85,91–93,96,108,157,160].

4.2.5.Data Analysis

Statistical analysis was conducted using R Statistical Software (Version 3.0.2)[320]. MUAC measurements will be standardized and centered at mean zero so within study population comparisons could be made. Exploratory data analysis (EDA) was conducted to evaluate data distribution and potential collinearity and confirm regression assumptions. A variogram was created from observed MUAC data to observe the degree of spatial dependence with distance and to determine the diameter of individuals' "neighborhood." A variogram is a function describing spatial dependence through the variance of difference between pairs of observed values, in regards to distance between the pairs. Neighborhood was defined as the distance when increase in variance observed in the variogram becomes negligible in conjunction with field knowledge.

Linear Regression techniques were employed to evaluate statistical associations. To explore possible mediation and confounding, simple linear regression was use to provide variable coefficients for comparison against coefficients in multivariate linear regression models. Five multivariate models were estimated and are described below:

Model 1: Control Model – The Control Model adjusted for seasonality and secular effects. Model 1 included a variable indicated if the mother was enrolled the week after Ramadan, and dummy variables for the twelve months in a year and for each year mothers were enrolled into the study (2001 – 2006). Given the period of fasting which occurs during Ramadan, there were expected decreases in nutritional status. Significant seasonal variations were also expected, as the region of the study area experiences substantial seasonal changes in precipitation and temperature and associated growing seasons and, therefore, changes in labor and income. There were also numerous NGOs operating in the area, with much work in the region striving to improve various aspects of maternal and child health during the period this study was underway; therefore, a secular improvement in health was expected. These background temporal changes were controlled for.

Model 2: Mother Model – In addition to the Control Model variables, the Mother Model included characteristics of the mother including her age, education, hygiene behavior, religion, and employment status. The effect of maternal age was assumed to be non-linear based on the previously discussed literature, with changes in growth velocity at ages 19 and 40. These changes were confirmed through EDA and incorporated using linear-spline coefficients. The association between educational attainment and maternal MUAC, in this analysis, was assumed to be linear and was confirmed in EDA. Hygiene behavior, such as washing hands with soap before eating and after defecation, was adjusted for, using binary indicator variables.

Model 3: Household Model – This model built upon the Mother Model by including proximate characteristics of the household. Variables included presence of unimproved sanitation, ownership of a bar of soap not used for laundry, the number of household members alone and adjusted by the number of rooms (crowding), and a living standards index (LSI), a measure of household assets. Binary variables were used to indicate presence of unimproved sanitation and bar soap ownership. The effect of household size and crowding was assumed to be linear and confirmed using EDA. The assets-based living standards index (LSI) is a proxy for economic status, which is consistently related to nutritional status [108,153,175,321]. The use of an assets-based index is a well-recognized method to approximate the underlying household economic status in developing settings [81,177,193–197,204]. The LSI used in this analysis was created by Gunsteinsson et al.

(2010) using principal component analysis (PCA), which is regularly used in this application [196].

Model 4: Community Model – The Community Model added characteristics of the household location and the characteristics of the proximal neighbors to the Household Model. Variables included the neighborhood average LSI, neighborhood economic inequality (GINI), neighborhood average education, population density, elevation, and the travel times to the nearest paved road and bazaar. Neighborhood was defined the variogram calculated for spatial autocorrelation of maternal MUAC and field knowledge. Neighbors were households who were also enrolled in the study and within the "neighborhood" of a given household. Estimates were calculated based on the neighbors of a given household with the values of the given household removed. Estimates were made in this manner for all study households to calculate average LSI, neighborhood GINI coefficient (based on LSI), and average education.

Population density was calculated for the study area using a kernel smoothed intensity function from the household locations which were weighted by household size and with values extracted for each household location. This data is not derived from a 100% population sample, so will act as the best proxy for true population density. Household elevation values were estimated from Shuttle Radar Topography Mission (SRTM) data [322]. In this analysis, travel-time estimates were calculated from a road network with attributes noting road quality. Travel velocities were based on those chosen by Entwisle et al. (1997)[323] and by Tanasescu et al. (2002)[324] for regions of similar context. Average velocities chosen were 40 mph for paved national highway, 20 mph on paved and 10 mph on non-paved roads, 5 mph on gravel paths, and an assumed walking speed of 2 mph for all non-road/path areas. Velocities were then converted to meters/second. Map surfaces were calculated with cumulative increasing travel time from a destination of interest (bazaar, paved road, etc.). Household travel times were extracted from the map surface based on household location.

Model 5: Spatial Error Correction – This model re-estimated the Community Model using spatial regression techniques. Given the potential spatial auto-correlation of the outcome and parameter variables, Model 5 adjusted coefficient confidence intervals to account for the reduced effective sample size. The Lagrange multiplier diagnostics for spatial dependence was used to determine if a spatial errors model or a spatial lag model was more appropriate to adjust for the residual spatial dependence resulting from the compete community model.

To observe how characteristics from each level account for spatial correlation, correlograms were created from the residuals of each sequential model. Correlograms were chosen over semi-variograms, which are generally more common in spatial statistics, to retain a common scale of reference (-1:1) so clear comparisons could be made. Correlograms, semi-variograms and covariograms all essentially have similar calculations and are used to evaluate spatial auto-correlation.

4.3 Results

A total of 59,854 expectant mothers completed the pregnancy enrollment form; however, due to duplicate locations and missing and incomplete data, 14,066 women were excluded from this analysis (see Figure 7: Study population flow chart). Expectant mothers were required to have complete and unique location data within the designated study boundary at the time of enrollment, as well as complete anthropometric assessment. Inclusion in the analysis also required complete covariate information. Analysis was conducted using the remaining 45,788 participants after exclusions were made. There were no statistical differences in anthropometry between expectant mothers with complete or missing data. Mothers had a mean MUAC of 22.79 cm, 23 years of age, and 3.592 years of education and about 16% are paid to work. The area was, by a vast majority, Muslim (92%). Distribution information can be found in Table 1 for all variables considered.

After inspection of the variogram (Figure 8 & Figure 9) for maternal MUAC and discussions with field staff, two neighborhood radii were selected: 200 meters and 2000 meters. Neighborhood variables were created for both radii and tested. Given the sample size (N= 45788), most pair-wise variable correlations were significant regardless of the magnitude of the correlation. Several variables are worth noting for potential collinearity. Living Standards Index (LSI), for example, had substantial and significant positive correlations with maternal education, household size, hygiene behavior, and improved sanitation and negatively correlated with crowding. The correlations between LSI and neighborhood variables were stronger for those at 200 meters compared to those at 2000 meters. Population density had notable collinearity with measures of education, wealth, inequality, and, unsurprisingly, isolation.

Table 2 presents the simple linear regression results. The simple linear regressions provided univariate estimates for the associations between MUAC and relevant variables. Taken generally, SES, sanitation and hygiene variables at all levels provided notable bivariate associations. Several community variables had promising associations. The proportion of neighbors who own bars of non-laundry soap, hand-wash before eating and after defecation, and have improved sanitary facilities as well as elevation had significant positive associations with maternal MUAC. Increasing population density and flood risk had significant negative bivariate associations. Mother and household variables tended to provide more explanatory ability and were chosen to be included over several promising community variables in cases when issues of multi-collinearity were presented. Variables such as neighborhood proportion without improved sanitation, and neighborhood proportion that wash their hands after defecation, for example, were collinear with several other individual and exogenous variables and, while they demonstrated favorable associations with the outcome, were removed from the multiple linear regression analysis to maintain statistical stability. The results from the multiple linear regression analysis are displayed in Table 3 and described below.

Model 1 - Control: To account for the substantial seasonal weather and flooding differences in the study area, monthly dummy variables were included. Seasonal dummy variables provided substantial reductions in AIC over more basic Sine/Cosine adjustment. The only months to provide significant coefficients were February–April, which were in the positive direction. The year dummy variables were all significant and increasing in magnitude with time. The indicator variable for measurements made the week after Ramadan was also significant and negative.

Model 2 - Mother: Addition of the Mother variables increased the significance and magnitude of the monthly control variables and decreased the significance and magnitude of the year control variables, particularly the 2002 and 2003 dummy variables, which lost significance at a .05 level. Maternal age was modeled using a linear spline to adjust for the non-linear effects of age. All maternal age spline coefficients were significant and indicated increasing MUAC until age 18 when the rate of increase decreased until approximately age 40 when MUAC begins to decrease with age. Maternal educational attainment had a linear increasing relationship with maternal MUAC. Maternal hygiene behaviors, measured by washing hands after defecation and before eating, were both found to be positively associated with maternal MUAC. Those mothers who reported as Muslim had significantly lower MUAC compared to those who did not report as Muslim.

Model 3 – Household: Addition of the household variables further increased the monthly and decreased the yearly control variables’ magnitude and significance. Household variables also increased the magnitude and significance of maternal age, but decreased the effects of maternal education and hygiene behavior. Unimproved sanitation, housing size, and crowding generally reduced maternal MUAC, while owning a bar of soap and having greater living standards (LSI) increased MUAC. LSI demonstrated the greatest effect on maternal MUAC.

Model 4 – Community Model – The Community model added characteristics of the household location and the characteristics of the proximal neighbors to Model 3. Community variables did not have any notable impact on the control variables beyond that of the household and maternal variables. There were also subtle reductions in the maternal and household effects, with the exception of small increases in the coefficients for mothers who washed their hands with soap after defecation and those who owned a bar of soap.

Variables calculated for a 200-meter neighborhood provided greater explanatory ability than those calculated for the 2000 meter neighborhood, with the exception of the neighborhood GINI coefficient. Since the range of the observed local GINI coefficients ranged from 34.09 to 34.34, it was mean-centered to make regression intercepts more interpretable. Maternal MUAC had a positive and significant association with increasing average neighborhood educational attainment with no notable change to the individual-level maternal education variable. Population density demonstrated a non-linear association with maternal MUAC. Decreases in maternal MUAC were observed with increasing population density until approximately 650 people per sq. km when maternal MUAC began to increase. Elevation had a positive and significant association with maternal MUAC. Arm circumferences appeared to decrease with increasing distance to bazaars and decrease with increasing distance from a paved road. Average neighborhood LSI had a minor, non-significant effect; however, when treated as an effect modifier, the interaction term was significant and positive.

Model 5 – Community Spatial Regression Model - Results from the Lagrange multiplier diagnostics for spatial dependence indicated a spatial errors regression model would better adjust for the residual spatial dependence found in our complete community model compared to a spatial lag model based on their significance values, $< 2.2 * 10^{-16}$ versus 0.0104 respectively. Coefficient values and significance levels for control, mother, and household variables experienced very little change after adjusting for residual spatial dependence. Coefficient values for the community variables experienced very little change; however, the significance values experienced some reductions. Coefficients for elevation and travel time to bazaar became non-significant at an alpha level of 0.05.

4.3.1.Residual Spatial Correlation

Residual spatial correlation for each model was observed using correlograms. Figure 10 illustrates the change of residual spatial correlation with the addition of variables at each level in this population of expectant mothers. The observed outcomes and residuals from the control model exhibit similar patterns of spatial correlation. Characteristics of the mother and household provided notable decreases in spatial correlation. Community variables, by and large, provided the greatest reduction of spatial correlation.

4.4 Discussion

The findings from this analysis support previous research suggesting the relevance of location and community for understanding the system of influences on individual health outcomes. Contextual variables were correlated with one another as well as with variables at other levels, providing independent and modified associations. Spatial dependence can be treated as a statistical nuisance, and adjusted for using spatial errors regression. However, this method discards spatial information and does not provide any insight into the complicated causal pathways leading to malnutrition. Community variables, while elucidating a greater system of influences on individual nutritional status, also notably reduced spatial correlation between residuals.

One of our key findings involves the synergy that exists between household SES and the average SES of the surrounding neighborhood. The mother and household level effects behaved as expected, consistent with current literature. Household socio-economic status (SES), as measured by the LSI, explained much of the variation in mothers' MUAC, however, its influence was modified by the neighborhood context. Individuals of a given household SES will, on average, not only have better nutritional status when living in neighborhoods with higher average SES, but also appreciate greater increases in nutritional status with each incremental increase in household SES. For example, the wealthiest mother had an estimated MUAC which was 2.27 cm greater than the poorest mother were they to reside in the same neighborhood. However, were the wealthiest mother to live in the wealthiest neighborhood, she would have a MUAC which was 5.48 cm greater than the poorest mother residing in the poorest neighborhood, on average. These findings provide further evidence indicating the importance of the neighborhood SES structure to explain individual nutritional differences.

In addition, this analysis demonstrates the importance of addressing economic inequality, such that, as neighborhood inequality decreases, maternal MUAC improves. Neighborhood inequality was the strongest community variable and one of the strongest variables overall, with those mothers living in neighborhoods with the greatest economic inequality measuring 0.5 cm thinner MUAC than those in the most equal, on average. In similar analyses exploring the deleterious effects of greater inequality, associations with greater food poverty [235], higher risk of stunting[190], and higher preventable and immediate death rates [325] were reported. Greater local inequality may impact health through reduced quality of infrastructure and public resources, or potentially through increased psychological stress, and weaker social ties and interpersonal support systems [326].

The neighborhood GINI coefficient performed better when neighborhoods were defined as 2000-meter compared to a smaller 200-meter neighborhood. The GINI coefficient is a measure of dispersion and may require a larger sample to create the needed variation to detect differences. Larrea and Kawachi (2005) and Reinbold (2011) also found the GINI coefficient to be more informative with calculations from larger areas [21,190].

Educational attainment, at both the individual and neighborhood levels, was also associated with improved nutritional status. While controlling for all other variables, mothers could enjoy nearly identical nutritional improvements, were they, or their neighborhood average, to improve educational attainment by one year. The nutritional benefits of greater maternal education at the individual and neighborhood level may be more directly mediated by improved nutritional knowledge [23,108]. Interventions in rural areas, which improve nutritional knowledge, in even a small number of individuals, have been shown to benefit the overall neighborhood nutritional status as information disseminates through the community [327]. The benefits of increasing average community knowledge is appreciably larger than that of an individual in isolation[327], and may follow social contact networks [328].

This analysis also considered nutritional effects associated with isolation from infrastructure and resources, such as the nearest bazaar, paved road or health service provider. Our findings indicate that, after controlling for relevant confounders, mothers who spend more time traveling to the nearest permanent bazaar had smaller MUAC than those residing closer, which was anticipated. This finding builds on the sparse and inconsistent body of prior nutritional research exploring the effect of isolation from food markets[234,329–332]. The conflicting reports appear to largely fall between developed and developing contexts. Previous work in the region by Ahmad et al. (2005) found that pregnant Bangladeshi women had lower dietary diversity if they lived greater than 0.5 km from a local bazaar[234], which could help explain the differences observed.

Of particular interests was the positive association between travel time to a paved road and nutritional status that was observed in both the simple and multivariate regression models. This finding diverges from those in the literature and may indicate other factors at play in this association. For example, the region has not eliminated lead-based fuel. Lead exposure has been shown to hinder growth in adolescence and children[333–335], which can lead to reduced adult anthropometry. Distance from road was also correlated with several other confounding variables that could be more directly related to maternal nutriture.

Establishing a relationship between the outcome and distance to a health service provider was difficult due to complexities in the health system. For example, an analysis by Sikder et al. (2011) noted many expectant women in this study area would turn to village doctors and other non-certified providers as "first-line providers" of which data were not available. Furthermore, certified basic care was available within a close proximity nearly anywhere in the study area. More sophisticated care required substantial travel for many residing in the study area; however, this was less associated with nutritional status in the study area, particularly after accounting for isolation from other resources such as bazaars and paved roads.

Population density also demonstrated an interesting association with nutritional status. Average MUAC was positively associated with population density until population density reached approximately 300 people/sq km, at which point the association became negative, as MUAC decreased particularly sharply from 450-650 people/sq. km. It then decreased less sharply from 650+ people/sq km in an unadjusted association. After adjusting for other model parameters, MUAC displayed a steady decrease to approximately 650 people /sq. km at which point MUAC increased sharply. This may be an indication of the 'Urban' effect affiliated with access to infrastructure or resources. As Bulk (2004) noted, approximately 650 people/sq. km may be a relevant cut-off to designate urban areas in the developing world, as opposed 1000 people/sq. km, which is conventionally used in developed countries . Differences in nutritional status between rural and urban populations have been reported by many [91,94,180,181,192,245,246]. Rural-urban differences in child nutritional status may be related to differences in occupation, behaviors, income, social collectiveness, isolation, or a combination of these. Several studies found the rural-urban nutritional gradient would disappear after accounting for differences in individual economic status [245,246].

Secular and seasonal variables responded as variables were added at each level. Decreases in significance of yearly dummy variables and increases in significance of monthly dummy variables may be related to the adjustment for secular changes in asset ownership and education which experienced increases during the course of the study. Other variables considered for secular changes included household size, crowding, and age when pregnancy was detected, none of which had any notable observed changes during the course of the study. After adjusting for factors of the mother, household, and community, the magnitude of significant seasonal protective effects, in the early part of the year (February – April) and summer (July and August), and negative effects in December, increased. These effects may be related to local agricultural systems, annual economic oscillations, seasonal climate, and/or potentially flooding.

Several variables were omitted completely from the multivariate linear regression. The source of drinking water, which is often included in analyses of this type, was not included as nearly the entire study population (99.51%) received water from a tube well/irrigation pump. Variables related to public infrastructure, such as electricity, piped water, and sewer, were omitted, as these amenities were not provided publicly in the region. Any existing infrastructure improvements had been purchased at the household level, and were thus incorporated in the LSI.

Due to issues of collinearity with stronger individual- and household-level variables, many community-level variables were dropped from the multiple regression models to maintain statistical stability and improve AIC. The proportion of neighborhood households without improved sanitation, for example, exhibited a strong negative bivariate relation with maternal MUAC, yet was also highly collinear with measures of wealth, education, and unimproved sanitation at the household-level and was therefore omitted from the Community model. Similar issues were related to data on the proportion of neighbors who washed their hands after defecation. After adjusting for confounders, these associations either reversed direction or became non-linear.

The collinear relationships between community-level variables also help describe the multifactorial conditions of neighborhood wealth. Wealthier neighborhoods had higher maternal educational attainment, were more economically homogenous, were closer to health service providers, permanent bazaars, and paved roads, and were in areas of higher elevation and reduced flood risk. People in wealthier neighborhoods were more likely to own a non-laundry bar of soap, have improved sanitary facilities, and wash their hands before eating and after defecating. Those living in wealthier neighborhoods typically enjoy holistically healthier environments which may reinforce the benefits of greater household and neighborhood SES. The findings of this analysis suggest a systems approach would be appropriate in nutritional and health status analyses. Furthermore, our analysis adds to the literature on maternal nutritional status by demonstrating the importance of various spatially explicit variables.

4.4.1.Limitations

This analysis could have been limited in several ways. First, the variables examined in our analysis represent a sample of the most salient variables indicated in the literature, and thus do not include all known and unknown effects at each level. As a result, the proportion of the variance accounted for by each level is only a result of the respective variable samples. Nevertheless, data collected as part of the JiVitA trial was comprehensive given available literature and compared to similar studies in developing settings at the time of this analysis. While this exploration has provided valuable insight into the associations between individual- and community-level SES and maternal nutritional status, the establishment of a causal pathway would be facilitated by a more exhaustive set of data. As examples of information missing from the present analysis, neighborhood economic structure may be indicative of local elements of social capital such as trust, reciprocity, and social cohesion, which are reported to substantially affect individual health [200,232,259]. Lack of social order in communities has been associated with negative mental and physical health outcomes [200,232,259–262]. Furthermore, peer support has demonstrated positive effects on maternal and child health [11,232,248,263]. Qualitative research in these areas could potentially help elucidate the causal pathways between neighborhood economic structure and individual health outcomes in developing settings.

Second, the location information collected for this study is limited to the household location and does not account for full daily environmental exposure from places of employment, relatives'/friends' residences, and commutes. Some studies have suggested that GPS tracking of individual daily movement patterns provides greater precision in estimating environmental exposures [336,337]. Additional research should consider individuals' geospatial, familial and social networks as they pertain to child wellness, as this approach may help to tease out these systemic causal pathways.

4.4.2. Intervention Implications

This analysis confirms that, in addition to characteristics of the individual and household, maternal nutritional status is influenced by attributes of the community context. A systems approach to nutritional research improves our comprehensive understanding of individual outcomes while also explaining the factors that lead to clustering. Our results demonstrate how neighborhood wealth modifies the effects of household SES on nutritional status as well as the multifactorial health benefits of living in wealthier communities. These findings suggest interventions should not only target individuals and households with elevated nutritional risk, but also features of the communities where they live.

While improving average neighborhood SES may not be directly in the scope of many health interventions, the health-related characteristics of wealthier neighborhoods might be. Our findings suggest that improving neighborhood maternal education, hygiene behaviors, sanitary facilities, transportation infrastructure, and decrease exposure to environmental hazards such as flooding, could potentially improve the nutritional status of expectant mothers as well as others. Programs intending to improve the nutritional status of “at risk” mothers should take a holistic, or systemic, approach by providing individual, environmental and structural modifications. The urban planning concept of intergenerational communities, for example, engages individuals, neighborhoods, and political bodies to meet the resource needs of both the young and the old through community organization and municipal land use policies [338]. Intergenerational community programs may promote mentoring, tutoring, education, and physical fitness. Furthermore, educational interventions which take a greater community focus may, directly and indirectly, improve the health of expecting and new mothers as well as other community members due to knowledge shared through social networks[327,328]. Multi-level interventions hold great promise for improving overall community health behaviors and nutritional status; however, additional research is needed to better understand the ecologic mechanisms which apply varying influence on maternal nutritional status in developing settings. Interventions of this type may, however, be more challenging to measure in terms of impact and coverage compared to having discrete outcomes, which are preferred in program evaluation and budgeting.

4.5 Conclusion

This analysis demonstrated the analytical merits of treating maternal nutrition from a more comprehensive ecological framework by identifying several ways in which the attributes of the community influence maternal anthropometry and help to explain observed spatial patterning of individuals with similar nutritional status. These findings may be generalized to most of rural southern Asia, and possibly, more broadly to other developing contexts. Future studies, particularly in developing settings, should collect data ecologically, including attributes of location, community/neighbors, and infrastructure, in addition to the canon of routine individual and household factors. These attributes help evaluate and account for systemic effects and spatially dependent observations. Considering the multi-level causality of health outcomes can elucidate greater understanding and generate more creative, and potentially more effective, intervention initiatives.

4.6 Tables

Table 1: Descriptive Statistics of the JiVitA -1 population of expectant women between 2001 and 2007

Mother variables	**Mean**	**SE**
Maternal MUAC (cm)	22.79	2.02
Maternal age (years)	23.17	6.59
Education (years)	3.59	5.41
Mother paid for work (%)	15.85%	
Non-Muslim (%)	7.90%	
Week after Ramadan (%)	6.75%	
Handwashing before eating (%)	14.65%	
Handwashing after defecation (%)	41.26%	
Household variables		
Unimproved sanitation (%)	57.63%	
Crowding	3.20	1.27
Household size	4.49	2.08
Own non-laundry barsoap (%)	80.19%	
LSI*	-0.01	1.00
Context variables		
Average LSI*†	-0.04	0.35
Gini Coef‡§	0.00	0.05
Average Education†	3.42	1.24
Pop. Density (100pp/sq. km)	5.47	1.30
Elevation (m)	25.47	1.88
Travel Time to Bazaar (hr)	2.34	1.36
Travel Time to Paved Rd. (hr)	3.80	2.88
Own barsoap ¶†	0.41	0.13
Without improved sanitation ¶†	0.58	0.18
Handwash before eating ¶†	0.15	0.11
Handwash after defecation ¶†	0.41	0.13
Weeks of observed flooding	4.30	7.40

Characteristics of the JiVitA-1 population of 47,753 expectant mothers and their respective households and communities

* Living Standards Index

† Includes neighbors within a 200 meter radius

‡ Includes neighbors within a 2000 meter radius

§ Mean Centered

¶ Proportion

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Table 2: Simple linear regression coefficients estimating scaled and mean centered maternal MUAC

Mother variables	**Est.**	**SE**	**t-value**	**R²**
Maternal age (years)	0.0080674	0.0007341	10.99	0.003
Education (years)	0.050896	0.001139	44.69	0.042
Mother paid for work	21.06%	0.012886	16.341	0.006
Non-Muslim	11.00%	0.017159	6.412	0.001
Week after Ramadan	-15.12%	0.017621	-8.582	0.002
Handwashing before eating	20.12%	0.012576	15.998	0.006
Handwashing after defecation	23.18%	0.009284	24.97	0.013
Household variables				
Unimproved sanitation	-42.56%	0.009219	-46.17	0.044
Crowding	-0.078275	0.003716	-21.07	0.010
Household size	0.035734	0.002216	16.13	0.006
Own non-laundry barsoap	31.51%	0.01166	27.01	0.016
LSI*	0.282401	0.004483	62.995	0.080
Context variables				
Average LSI*†	0.45077	0.0131	34.418	0.025
Gini Coef‡§	-4.180769	0.193767	-21.58	0.010
Average Education†	0.11786	0.00372	31.68	0.021
Pop. Density (100pp/sqkm)	-0.048347	3.57E-03	-13.55	0.004
Elevation (m)	0.02788	0.00247	11.29	0.003
Travel Time to Bazzar (hr)	0.0114	6.88E-03	-4.903	0.000
Travel Time to Paved Rd. (hr)	-0.03375	3.27E-03	3.487	0.001
Own barsoap ¶†	0.64538	0.03898	16.56	0.006
Without improved sanitation ¶†	-0.71479	0.02594	-27.56	0.016
Handwash before eating ¶†	0.33816	0.043515	5.633	0.002
Handwash after defecation ¶†	0.24511	0.03449	9.804	0.001
Weeks of observed flooding	-0.002525	0.000624	-4.047	0.000

Coefficient values are changes in standard deviation in scaled and centered MUAC from the JiVitA-1 population of 47,753 expectant women

* Living Standards Index

† Includes neighbors within a 200 meter radius

‡ Includes neighbors within a 2000 meter radius

§ Mean Centered

¶ Proportion

Table 3: Multivariate regression coefficients estimating scaled and mean centered maternal MUAC

	Mother Model			Mother + Household Model			Mother + Household + Context Model		
n = 45788	**Est.**	**SE**	**t-value**	**Est.**	**SE**	**t-value**	**Est.**	**SE**	**t-value**
Intercept	-0.99	0.08	-12.48	-0.66	0.08	-8.14	-0.85	0.11	-7.62
Mother variables									
Maternal age (years)	0.03	0.00	6.74	0.03	0.00	7.39	0.03	0.00	7.20
(age > 19 years)	-0.01	0.00	-2.39	-0.02	0.00	-3.24	-0.02	0.00	-3.18
(age > 40 years)	-0.09	0.02	-4.96	-0.09	0.02	-5.38	-0.09	0.02	-5.20
Education (years)	0.05	0.00	43.21	0.02	0.00	12.74	0.02	0.00	10.59
Handwashing after defecation	0.10	0.01	10.17	0.03	0.01	3.26	0.04	0.01	3.86
Handwashing before eating	0.03	0.01	2.55	0.01	0.01	1.01	0.01	0.01	0.85
Mother paid for work	0.07	0.01	5.73	0.07	0.01	5.58	0.05	0.01	4.18
Non-Muslim	0.10	0.02	5.77	0.08	0.02	4.82	0.05	0.02	3.26
Household variables									
Unimproved sanitation				-0.03	0.01	-2.21	-0.02	0.01	-1.86
Crowding				0.04	0.01	3.36	0.05	0.01	3.85
Household size				-0.03	0.00	-9.18	-0.02	0.00	-7.96
Own non-laundry barsoap				-0.02	0.00	-4.00	-0.02	0.00	-3.48
LSI				0.23	0.01	26.61	0.21	0.01	23.80
Community variables									
Average LSI*†							0.04	0.02	1.72
Gini Coef‡§							-1.00	0.12	-8.19
Average Education †							0.02	0.01	4.05
Pop. Density (100pp/sq. km)							-0.02	0.00	-3.55
(>650pp/sq. km)							0.09	0.02	5.23
Elevation (m)							0.01	0.00	2.59
Travel Time to Bazzar (hr)							-0.01	0.00	-2.67
Travel Time to Paved Rd. (hr)							0.01	0.00	5.54
LSI x Average LSI*							0.07	0.01	5.90
R^2	**0.07707**			**0.109**			**0.1159**		
AIC	**126425.9**			**124816.5**			**124464.7**		

Seasonal and secular effects have been adjusted for in all models; coefficient values are changes in standard deviation in scaled and centered MUAC from the JiVitA-1 population of 47,753 expectant women

* Living Standards Index

† includes neighbors within a 200 meter radius

‡ includes neighbors within a 2000 meter radius

§ Mean Centered

4.7 Figures

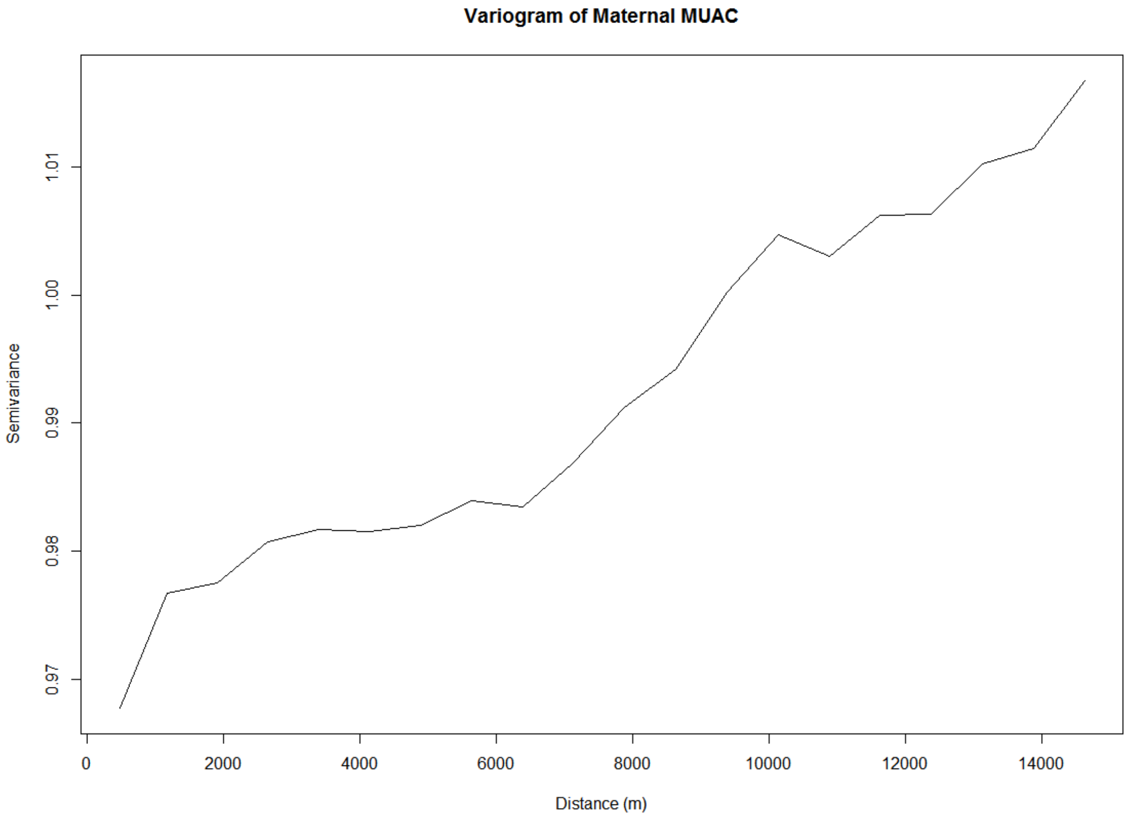

Figure 9: Variogram of Maternal MUAC

This figure depicts the change in semivariance, on the y-axis, between observations of maternal MUAC with increasing distance, in meters, on the x-axis. Semivariance was calculated for distances between zero and 15,000 meters divided into 20 bins.

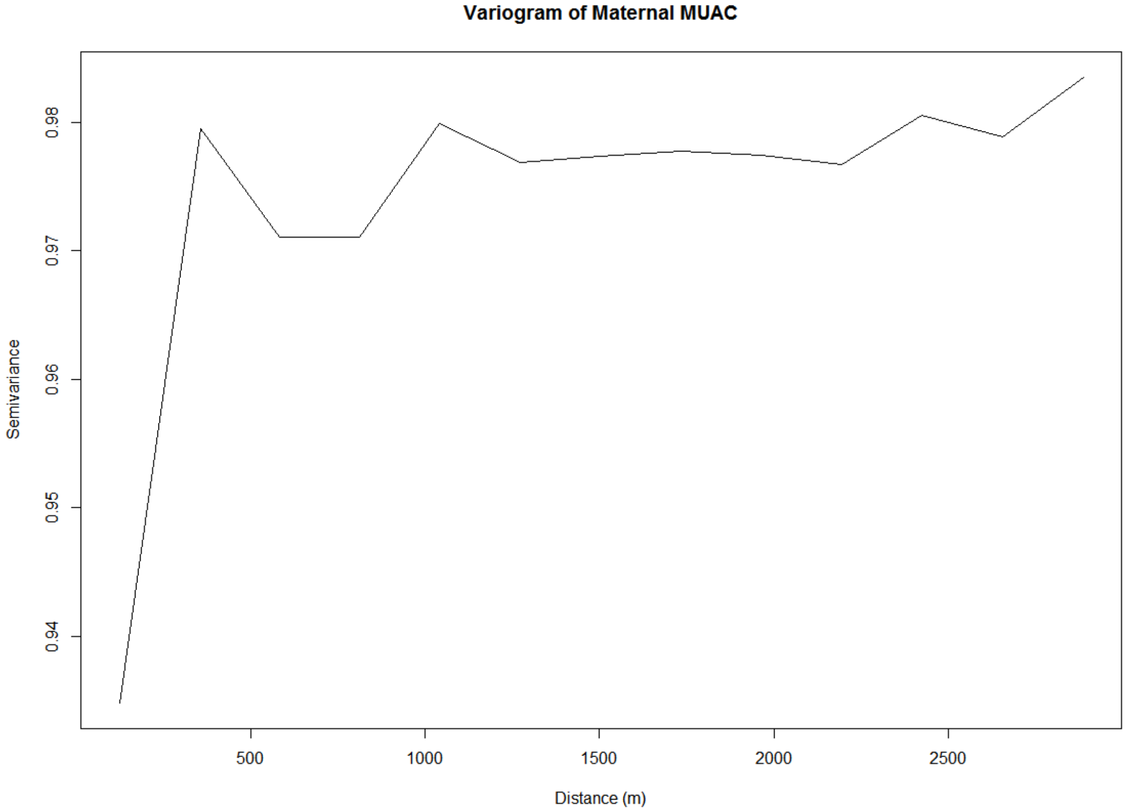

Figure 10: Variogram of Maternal MUAC

This figure depicts the change in semivariance, on the y-axis, between observations of maternal MUAC with increasing distance, in meters, on the x-axis. Semivariance was calculated for distances between zero and 3,000 meters divided into 13 bins.

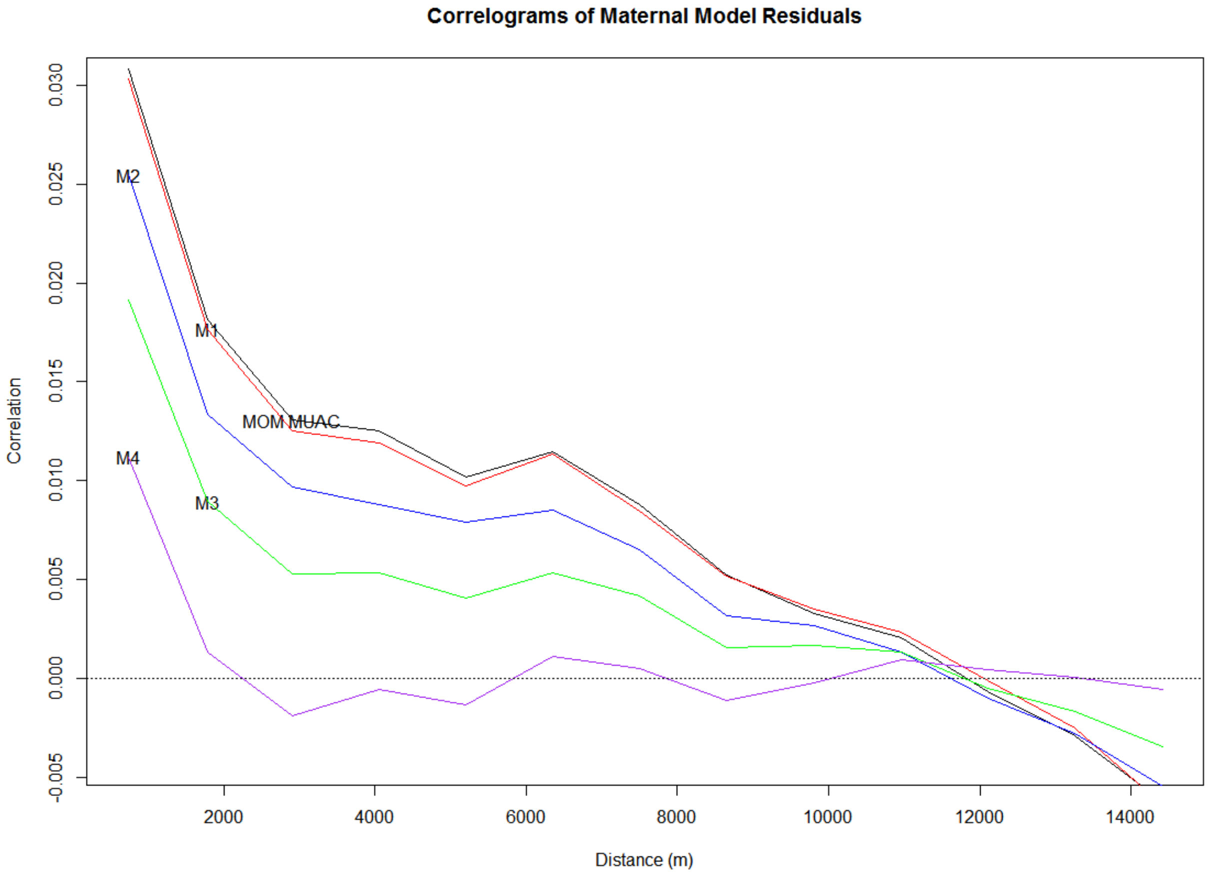

Figure 11: Correlograms of maternal MUAC and explanatory model residuals

Depicts spatial correlation between observations and explanatory models in the mothers; MOM MUAC (black) = Unadjusted Maternal MUAC; M1(red) = Control Model; M2 (blue) = Mother Model; M3 (green) = Household Model; M4 (purple) = Community Model. The dashed line indicates the point of zero correlation. Correlation is on the y-axis and distance, in meters, is on the x-axis.

Chapter 5 Understanding Age-specific Effects on Nutritional Status in Early Infancy: A Systems Approach

5.1 Abstract

Poor nutritional status in infancy can lead to premature mortality and reduced productivity later in life. Children of similar nutritional status have been known to cluster spatially, indicating potential contextual effects. Little research has explored contextual influences, after accounting for determinants of the individual and household, and particularly how these influences may change in the first few months of life. This analysis investigates how the influence of individual, household and contextual determinants change with regard to infant nutritional status at birth compared to those aged six months. This analysis also intends to explore how determinants at each level account for residual spatial correlation. With data from the JiVitA-1&2 trials in northwest Bangladesh, determinants were grouped by level then added sequentially to a linear regression model accounting for seasonal, secular and spatial error effects. Residual spatial correlation from each sequential model was observed with correlograms and interpolated maps. Determinants of infant nutritional status at the child, mother, household and contextual levels accounted for 8.5%, 4.0%, 0.5% and .3% of the respective variance at birth, and 7.6%, 5.7%, 0.8%, and 0.4% at roughly six months. The full models accounted for a total of 13.2% and 14.5% of the variance at birth and six months respectively. Contextual variables accounted for substantially more spatial correlation than individual or household variables in both groups, however, there was limited spatial correlation in the group of newborns. The strongest determinants were related to socioeconomic status (SES) such as maternal education, household economic status, the average and distribution of neighborhood wealth and average neighborhood maternal education. SES variables such as maternal education and household economic status applied a nearly constant effect in both groups, while the effect of those associated with disease transmission, such as soap ownership and household size increased with age. The findings from this analysis suggest the increasing nutritional influence of location and community with age as well as accounting for

spatial clustering. Many of the nutritional differences in both age groups were explained by characteristics of the child and the mother. Public health programing needs to target healthy mothers and pregnancies to give children a healthy starting point as well as role of the environment and community as it becomes increasingly important with age.

5.1 Introduction

Poor nutritional status in infancy can lead to irreversible damage later in life and reduced human capital [22–28]. Inadequate nutrition in early childhood hinders mental and motor development [27,37,38], which may negatively affect future academic performance and intelligence [28,39], adult economic productivity [26], and future health status[29–36,143].

The body of research exploring factors related to malnutrition has focused primarily on the individual and household levels, while tending to neglect the community context. This overemphasis on individual characteristics has failed to acknowledge nutritional status as a systemic condition that results, in large part, from community influences. Several studies have identified spatial heterogeneity, or clustering, of malnutrition[49,50], in that, those who have similar nutritional status tend to live in close proximity to one other. Spatial clustering may indicate shared influence between observations, associated with their relative location; and decreased effective sample size resulting from spatial dependence. Understanding the origins of spatial clustering provides an opportunity to have a greater understanding of the etiologies and determinants of malnutrition. Some authors have attempted to explore this phenomenon, suggesting that nutritional status of young children may be influenced by environmental factors [55–57] such as land use, climate, topography, and road access, as well as contextual effects [58–61] such as urbanicity, population density, community-level education, social participation, community employment, and access to health facilities.

There is a paucity of studies that have considered how location-specific influences may change during the first few months of life as infants develop and have greater interaction with their surroundings. It is in this period that growth faltering is most pronounced, [45–47] and recovery is increasingly difficult if improvements are not made [48]. Several factors have impeded the analyses of community characteristics like these. Spatially explicit data, such as elevation, individual locations, agricultural variables, and distance to resources, are often of poor quality or non-existent. It may also be challenging to merge these data with individual data. Furthermore, community effects are often weaker than those at the individual or household levels, and thus require larger sample sizes to detect significant differences.

In this analysis, the relative contributions of and interplay between determinants of child nutritional status at the individual, household, and community levels are explored, drawing from the conceptual framework detailed in Figure 3. Our primary objectives were to assess (1) how these determinants and their health impacts change between the early neonatal period and roughly six months of age, and (2) the extent to which contextual factors at the community level account for spatial correlation between observations.

5.2 Methods

5.2.1.Study Population and Data

Data used for this analysis were collected as part of the JiVitA trial, a prospective cohort, enrolled in a double-masked, cluster-randomized, dual-intervention, placebo-controlled trial conducted by the JiVitA project. The study population has been described in great detail elsewhere [67]. Eligible expectant women were enrolled between August 2001 and October 2006. At enrollment, household and maternal data regarding socio-economic status, pregnancy history, recent morbidity, diet, anthropometry, alcohol and tobacco use, and household logistics were collected. Data regarding breast and complementary feeding, vaccination, antenatal and post-partum care, maternal and infant morbidity and infant anthropometry were assessed at roughly three and six months post-partum. Gestational age was estimated using the interval between the dates of birth and the mother's last menstrual period. Since nutritional status was one of the primary outcomes of interest, anthropometry was meticulously measured in triplicate.

Of the roughly 125,257 women eligible to participate in the trial, approximately 59,666 were detected as pregnant and subsequently enrolled. Data were collected from 42,185 infants with measurements from a subset of 18,157 as newborns. For the purposes of identification, enrollment, and tracking of study participants, the JiVitA Geographic Information System was established in 2003 as a method of population enumeration. The system includes 236,681landmarks, 149,402 of which are households, study and political boundaries, local roads and paths, and hydrologic features. Many of these data were digitized and merged from 1:3960-scale cadastral maps produced by the British Survey of India in the 1930s. The system was maintained and updated throughout the JiVitA – 1 study period. The details of the JiVitA Geographic Information System can be found elsewhere [317].

5.2.2.Dependent Variable

The primary outcome of interest for this analysis is mid-upper arm circumference (MUAC) among infants at birth and mid-infancy. Mid-infancy is defined as roughly six months of age (between 150 and 210 days since birth). MUAC is treated as a continuous variable. As was discussed in detail in Chapter 2 and Chapter 3, MUAC measurements were performed in triplicate by JiVitA field staff trained and standardized in anthropometry and the mean was used. MUAC was chosen over other anthropometric measurements for its ease of field administration and its relation to physiologic processes [73,77] and demonstrated sensitivity to short term changes in nutrition [75,78–84]. Infant MUAC has been suggested as a strong proxy for birthweight [13,68–71,78,339,340] and gestational age[70,339].

5.2.3. Independent Variables

The last several decades have generated an extensive body of knowledge related to the determinants of nutritional status in early childhood. For this analysis of nutritional status in infancy, effects at the child, mother, household and community level will be considered, both at birth and mid-infancy. The salient findings from this literature, previously discussed in Chapter 2, aided in the variable selection for this analysis and will be briefly reviewed here. Child variables associated with nutritional status and included will be parity[12,139–141], gestational age[12,70,142–144], gender[72,148,149,341], and in the case of mid-infancy, age in days since birth[72,148,149,341]. Mother variables included will be age in years[16,17,21,154], MUAC[10–17,31,156], years of schooling[4,17,21,50,144,174,177–183], still breastfeeding the infant at the time of measurement[149,166,168,172], hand washing with soap after defecation and before eating[5,7,85,91–93,96,108,160], employment status[178,184] and being Muslim[151,152,163]. Household variables which will be included are having unimproved sanitation[94,97,157,159,208,209], non-laundry bar of soap, number of household members[108,163,209], and an asset-based living standards index (LSI) [81,177,193–197,204]. Community aspects included are the average LSI[21,177,180,190,191,248], local Gini coefficient[21,235], average years of education for mothers[58,141,176], population density[59,193,247], elevation[15,49,55], and travel time to the nearest permanent bazaar[233–235] and paved road[57,210,240]. Criteria for inclusion require observations to have unique locations within the study boundary and complete variable information at each analytical level. Additionally, for the mid-infancy population, only infants for which anthropometric measurements were made between 150 and 210 days from birth were included.

5.2.4. Data Analysis

The samples at birth and mid-infancy will be treated as two cross-sectional population analyses. MUAC measurements will be standardized and centered at mean zero for each sample so equivalent comparisons can be made. Statistical analysis was accomplished using R Statistical Software. Exploratory data analysis was conducted to evaluate data distribution and potential collinearity and confirm regression assumptions.

To evaluate statistical associations, linear regression techniques were employed. Coefficients from both simple and multivariate regressions were compared to determine possible mediation and confounding. Effects at each level were added sequentially to observe associated explanatory gains. Six multivariate models were developed, each building upon the prior, and are described below.

Model 1: Control Model – The Control Model adjusted for seasonality and secular effects. Model 1 includes dummy variables for each of the twelve months in a year and for each year data were collected (2001 – 2006). The study area experiences substantial seasonal changes in precipitation, temperature and associated growing seasons, which is tied to labor and income. Significant seasonal variations are expected. There were also numerous NGOs and government programs operating in the region working to improve various aspects of maternal and child health during the period this study was underway; therefore, a secular improvement in health was expected. The dummy variables contained in this control model will attempt to control for these background temporal changes.

Model 2: Child Model – Building on the control model variables, Model 2 includes characteristics of the child. These variables are parity, gestational age, and gender. Age, in days since birth, was added for the mid-infancy population to adjust for differences in growth. Parity and gestational age were assumed to have linear associations with MUAC at both time-points. A binary indicator variable for gender was also included.

Model 3: Mother Model – In addition to the control and child variables, characteristics of the mother and her infant care behaviors were included in the mother model. These characteristics are age, education, breastfeeding, hygiene behavior, employment status and religion. Age and education were treated as continuous variables. A binary variable was used to indicate if the child was still breastfed at the time of the anthropometry measurement. Hygiene behavior was indicated with binary variables for hand washing after defecation and before eating. Binary variables were also used indicate if a mother was non-Muslim or received money for her work.

Model 4: Household Model – Model 4 built upon the Mother Model by including proximate characteristics of the household. Variables included presence of unimproved sanitation, ownership of a bar of soap not used for laundry, the number of household members and a living standards index (LSI), a measure of household assets. Binary variables were used to indicate presence of unimproved sanitation and bar soap ownership. The effect of household size was assumed to be linear and confirmed using EDA. The assets-based living standards index (LSI) is a proxy for economic status. which is consistently related to nutritional status [108,153,175,321]. The use of an assets-based index is a well-recognized method to approximate the underlying household economic status in developing settings [81,177,193–197,204]. The LSI used in this analysis was created by Gunsteinsson (2010) using principal component analysis (PCA) [196].

Model 5: Community Model – Model 5 built upon the household model by adding characteristics of household location and characteristics of proximal neighbors. Added variables are the neighborhood average LSI, local economic inequality (Gini coefficient), neighborhood average years of maternal education, population density, elevation and the travel times to the nearest paved road, and bazaar. Neighborhood was defined as 200 meters for all variables except for the local Gini coefficient estimates, which was defined as 2000 meters. These distances were established from a previous study of maternal nutritional status (cite paper 1), through analysis of spatial auto-correlation and field knowledge. The values were calculated for a given household location from the values of other enrolled mothers within either 200 or 2000 meters, excluding the values from the given household.

Population density was calculated for the study area using a kernel smoothed intensity function from household locations weighted by household. These data are not derived from a 100% population sample, so will act as the best proxy for true neighborhood values and population density. Household elevation values were estimated from Shuttle Radar Topography Mission (SRTM) data[322]. In this analysis, travel time estimates were calculated from a road network and accounting for road quality. Travel velocities were based on those chosen by Entwisle et al. (1997)[323] and by Tanasescu et al. (2002)[324] in regions with similar context. Average velocities chosen were 40 mph for paved national highway, 20 mph on paved and 10 mph on non-paved roads, 5 mph on gravel paths, and an assumed walking speed of 2 mph for all non-road/path areas. Velocities were then converted to meters/second. Map surfaces were calculated with cumulative increasing travel time from a destination of interest (bazaar, paved road, etc.). Household travel times were extracted from the map surface based on household location.

Model 6: Spatial Error Correction – This model re-estimated the Community Model using spatial regression techniques. Given the potential spatial auto-correlation of the outcome and parameter variables, Model 6 adjusted coefficient confidence intervals to account for the reduced effective sample size. The Lagrange multiplier diagnostics for spatial dependence was used to determine if a spatial errors model or a spatial lag model was more appropriate to adjust for the residual spatial dependence resulting from the compete exogenous model.

To observe how characteristics from each level account for spatial correlation, correlograms were created from the residuals of each sequential model at both time-points. Correlograms were chosen over semi-variograms, which are generally more common in spatial statistics, to retain a common scale of reference (-1:1) so clear comparisons could be made. Correlograms, semi-variograms and covariograms all essentially have similar calculations and evaluate spatial auto-correlation.

5.3 Results

5.3.1.Early Neonatal Period

Anthropometric measurements were taken as soon as possible after birth (median: 18 hours of age [IQR: 9-36 hours])[316]. Of the 17,116 live infants born to consenting mothers, only 15,508 met analysis inclusion criteria (see Figure 7: Study population flow chart). Infants had a mean MUAC of 9.47 cm, 51% were male. Infants were born at 38 weeks gestation, on average. This was the first birth for 44.8% of mothers. Mothers, on average, were about 21 years of age, had a MUAC of 23 cm and 4 years of education. They tended to be Muslim (91.7%), unemployed (77.6%), breastfeed their infant after birth (69%), and wash their hands with soap after defecation (55%), but tended not to wash hands with soap before eating (76%). The majority of households had a non-laundry bar of soap (84%), and roughly half of the households didn't have improved sanitation. The average household had four members (IQR: 3-5). The study site had an average local Gini coefficient (based on household LSI) of 34 which coincides well with the World Bank 2005 national estimate of 33.2 [342]. The average elevation for the study site was 25 meters (range: 18-32 meters) above sea-level and population density of 547 people per square kilometer (range: 104-857ppl/sqkm). Household members must travel, on average, 2.4 hours to the nearest permanent bazaar and 3.8 hours to the nearest paved road. Distribution information for the early-neonatal variables can be found in Table 4.

5.3.2.Mid-Infancy Period

Of the 47,091 live infants for which data were collected, only data from 24,016 infants were included for analysis (see Figure 7: Study population flow chart). Anthropometry was assessed at approximately 6 months (median: 171 days after birth [IQR: 168 – 177 days]). Infants in this sample, on average, had a MUAC of 13 cm and were born at 38 weeks gestation, half of which were male (50.2%). This was the first birth for the majority of mothers (39%). Mothers, on average, were 22 years old, had a MUAC of 22.84 cm, and 3.8 years of schooling. Most women were still breastfeeding their infant (99%), were Muslim (91.6%), unemployed (82%), and didn't wash their hands with soap before eating (81%) or after defecation (51%). Households typically had four members (IQR:3-5), owned a non-laundry bar of soap (82%), and didn't have improved sanitation (56%). The community characteristics for this sample (Gini coefficients, elevation, population density and travel times) were identical to those of the neonatal sample. Variable distribution information for the mid-infancy sample can be found in Table 4.

5.3.3. Collinearity

Collinearity was tested using a correlation matrix for the variables of interest. Given the sample size, nearly all Pearson's correlations were significant ($\alpha < 0.05$). Several collinear relations may exist and values were nearly identical for both samples. LSI, for example, had notable positive correlations with maternal education ($R = 0.61$), neighborhood average LSI ($R = 0.38$) and education ($R = 0.30$), household size ($R = 0.5$), improved sanitation ($R = 0.6$), non-laundry bar of soap ($R= 0.37$) and other hygiene related variables. LSI was negatively correlated with parity ($R = -0.25$). All variables associated with isolation (travel times and population density) had weaker, but consistently negative correlations with LSI, education, and elevation. Maternal age was positively correlated with parity and employment, and negatively correlated with education, LSI, and other variables associated with economic status.

5.3.4. Exploratory Data Analysis

To confirm regression assumptions, variable data distributions and associations were evaluated. For variables which were considered continuous, many had generally normal distribution and near-linear associations. Maternal age and parity were two notable exceptions. Maternal age was observed to have a non-linear association with child MUAC. Average child MUAC appeared to increase until, approximately, the maternal age of 21, when average child MUAC would begin to decrease. This non-linear association was observable in both age groups and adjusted for as a linear spline with a knot at the maternal age of 21in the regression models for both groups. The effect of parity appeared to have the greatest effect between nulliparous and primiparous women in the neonatal group, while the association was clearly linear and negative in the mid-infancy group. The parity distributions were also right skewed. Log-linear transformation was considered for parity and other slightly skewed variables, however, did not substantially change associations in the simple or multivariate regression models and would make interpretation more abstruse.

5.3.5.Regressions

Table 5 presents the simple linear regression results. The simple linear regressions provided univariate estimates for the associations between MUAC and relevant variables at the two age periods. Maternal age, having un-improved sanitation, hand washing after defecation, LSI, and both individual and neighborhood maternal education variables all had univariate coefficients which were similar at the two age periods. Gestational age, household size, religion and longer travel time to a permanent bazaar were associated with larger effects in the early neonatal period than in the mid-infancy period. Variables which had larger effects in mid-infancy were being breastfed, parity, gender, maternal nutritional status, maternal employment, hand washing before eating, owning non-laundry soap, neighborhood average LSI, local inequality (Gini), elevation and population density.

Table 6 displays the results for the multivariate regression analysis. As additional variables were added to the multivariate model many of the variable coefficients experienced some decrease in magnitude and significance compared to the simple regression estimates. This is related to possible mediation and confounding from other variables. Figure 11 displays increases in the proportion of variance accounted for with the addition of each level of variables.

Seasonality and secular trends explained a greater proportion of the variance, based on R^2, in the early neonatal period (1.33%), compared to mid-infancy (0.38%). With the addition of descriptive model variables, seasonal effects became more pronounced in the early months of the year for the early neonatal period (February – June) and in mid-infancy (February – March). Annual control variables provided some puzzling results. In the early neonatal period, the influence of 2005 became increasingly negative and significant, while the positive influence of 2006 decreased and lost significance with the addition of descriptive variables. There are only seven neonatal observations which occurred in 2007. This small sample could explain the consistent and significant coefficient. In the mid-infancy period, the annual dummy coefficients became increasingly negative and significant as descriptive variables were added to the model.

The addition of child-level variables provided significant explanatory improvements over the control variables, slightly more-so in mid-infancy compared to the early-neonatal period(R^2 increased by 5.4% in neonates vs. 6.2% in mid-infants). The effect of gender became greater with the addition of other child characteristics compared to the simple regression. Gender coefficients did not change much with the addition of variables at other levels. Gender has a more substantial impact on child MUAC in mid-infancy compared to the early-neonatal period. Results from the full community model indicate the female arm circumference is approximately 0.44 standard deviations (SD) thinner than that of males in mid-infancy compared to the early-neonatal period when female MUAC is only 0.06 SD thinner than males. Coefficients for gestational age in both groups decreased slightly from the simple regression and after adding other child and mother-level variables, but were not affected when household or community variables were added. The effect of gestational age also remained highly significant in all regression models, although, less pronounced in mid-infancy. Parity became positive and significant in the early neonatal period and remained negative and significant for mid-infancy once added to the multivariate model compared to the simple regression. The parity effect increased in the neonatal and decreased in the mid-infancy periods with the addition of maternal variables, but didn't change after adding household or community variables. Results also indicate child MUAC increases by approximately 0.07 SD per month of age in the mid-infancy sample.

Characteristics of the mother also provide considerable explanatory power for both age groups, however, slightly more so in mid-infancy (R^2 increased by 4.7% in neonates vs. 6.6% in mid-infants). Maternal age had similar effects in the simple and multivariate regressions in both age groups. Child MUAC in both groups tended to increase by 0.03 SD with each year of maternal age, until mothers were 21, when child MUAC would begin to decrease by 0.004 SD per year of maternal age. The coefficients for maternal education decreased from the simple regression estimates in the multivariate model for both age groups, however, remained relatively constant and highly significant when other variable levels were added. With each additional year of maternal education was associated with 0.018 SD and 0.011 SD greater MUAC in the early-neonatal and mid-infancy periods, respectively. The effect of breastfeeding experienced subtle decreases in the multivariate estimates for both age groups compared those from the simple regressions; however, the effects did not change and remained highly significant when household and community variables were added. Infants, who were still breast fed at the time of assessment, had MUAC measurements which were 0.11 SD and 1.06 SD larger than those who were not in the early neonatal and mid-infancy period, respectively, based on the full model. The hand washing variables appeared to be confounded by other maternal factors, such as education, and became non-significant in the multivariate models. The effect of maternal employment became significant and increased in magnitude in the early neonatal period, but decreased in magnitude and lost significance in the mid-infancy period, compared to the simple regression estimates. The coefficients for being non-Muslim slightly decrease in magnitude when included in the multivariate models, compared to the simple regression estimates, and continue to decrease with the addition of household and community-level variables. The children of non-Muslim mothers had an average MUAC which was 0.14 SD larger in the early-neonatal period and 0.08 in mid-infancy compared to their Muslim counterparts.

The addition of household-level variables provided modest explanatory increases for both age groups, with slightly higher gains in mid-infancy as compared to the early neonatal period (R^2 increased by 0.6% in neonates vs. 0.8% in mid-infants). The effect of LSI had a subtle decrease in magnitude from the simple regression estimate, when added to the multivariate model; however changed very little when community-level variables were added. LSI applied a comparable effect, increasing MUAC by about 0.1 SD in both age groups with each unit integer increase in LSI. The coefficient for household size changed sign to become negative for both age groups, once added to the multivariate model, and was only significant in mid-infancy. With each additional household member, child MUAC would decrease by 0.02 SD in mid-infancy. This change in sign was associated with the addition of LSI indicating confounding. The effect of non-laundry bar soap also only remained significant in the mid-infancy period once adjusting for other variables of interest. Coefficients for both household size and bar soap decreased in magnitude for both age groups, compared with the univariate estimates. Having unimproved sanitary facilities no longer applied a significant influence after accounting for other variables, such as LSI and maternal education, which confound the association.

The inclusion of community-level variables produced some minor explanatory improvements in both groups (R^2 increased by 0.3% in neonates vs. 0.5% in mid-infants).The coefficients for neighborhood economic and education variables decreased slightly after adjusting for other levels of descriptive variables however provided the most stable community effects in both age groups. The community economic structure appeared to have a stronger influence in mid-infancy, while maternal education in the community was more important in the early neonatal period. MUAC in mid-infancy had a significant positive association with neighborhood average LSI and significant negative association with increasing local inequality (Gini). The effect of neighborhood average maternal education was positive and significant for early neonates. The interaction coefficient for LSI and neighborhood average LSI was only significant for the early neonatal group.

The observations in this analysis occur within close proximity of each other and contain some spatial auto-correlation which required adjustment. The Lagrange multiplier diagnostics for spatial dependence indicated a spatial errors model was more appropriate compared to a spatial lag model. Spatial error adjustment resulted in negligible changes to control, child, mother and household coefficients and significant values. Many community variables, including population density, elevation, and travel time became non-significant. Estimates for neighborhood average LSI remained unchanged and strongly significant, but only in mid-infancy. The effects of local inequality, in mid-infancy, and neighborhood average maternal education, in the neonatal period, decreased in magnitude and significance, but remained significant at an alpha level of 0.05.

5.3.6. Residual Spatial Correlation

Residual spatial correlation for each model at both time-points was observed using correlograms. Figure 12 and Figure 13 illustrates the change of residual spatial correlation with the addition of variables at each level and after adjusting for spatially correlated errors in the early neonatal and mid-infancy periods, respectively. Observations in mid-infancy are noticeably more correlated than those made near birth. The observed outcomes and residuals from the control model exhibit similar spatial correlation in both age groups. Child-level variables slightly increase spatial correlation in the neonate group, and only slight reduction at mid-infancy. Mother variables provide notable decreases in spatial correlation for both groups. Household variables, when added to the models, did not reduce spatial correlation in the neonatal group, however had observable decrease in the mid-infancy group. Community variables, by and large, provided the greatest reduction of spatial correlation in both groups. The residual spatial correlation from the spatial error models disappeared, as expected, in both groups.

5.4 Discussion

These findings suggest that child and mother variables have a much stronger effect on MUAC during the first six months of life, compared to household and community variables. Seasonality and secular trends had more influence in the early-neonatal period than in mid-infancy. Household- and community-level variables played a greater role in explaining differences in nutritional status in mid-infancy than in the early neonatal period. Infants displayed greater spatial dependence with age. Spatial dependence, as a statistical nuisance, can be adjusted for using spatial errors regression; however, this method does not provide any insight into the complicated causal pathways leading to malnutrition. Community variables, while elucidating a greater system of influences on individual nutritional status, also notably reduced spatial correlation between residuals.

Generally, the individual- and household-level variables behaved as expected based on the body of nutrition literature. The effects of LSI and maternal age were nearly constant between the age groups. Many variables demonstrated significant importance in both age groups; however, the magnitude differed between the age groups indicating either diminishing or enhancing influence with time. Increases in parity, for example, are associated with larger MUAC in neonates, however, smaller MUAC later in infancy. This change in effect may be related to parity acting as birth-order in mid-infancy which others have also associated with decreased nutritional status [140,141]. The effect of gestational age is significant in both age groups; however, the magnitude diminishes in mid-infancy. This change is expected and most likely a result of early catch-up growth in premature infants [343–345].

The role of religion, particularly Islam, in explaining differences in child anthropometry has been noted in several studies [163,183,346]. Islamic doctrine has strong recommendations on diet, the practice of consumption and times of fast and feast which may impact the nutriture of a mother and developing fetus. Muslim children are typically not required to fast until they reach puberty. These practices may explain the greater religion effect in newborns which wanes by mid-infancy.

Employment status may indicate increased maternal autonomy[347–350], which has been associated with improved child health status [50,141,178,184]. This positive effect was not apparent in this analysis in either age group after adjusting for other descriptive variables. Maternal employment status was, however, associated with decreased MUAC in the early neonatal period which could be related to occupational hazards[351] or less time spent at home with the child[137].

The effects of biological variables, such as maternal MUAC, breastfeeding, gender and maternal age, while significant in both age groups, were enhanced in the mid-infancy period. These findings corroborate the reams of studies resounding the importance of maternal nutriture and breastfeeding to improve infant growth trajectories and breaking intergenerational malnutrition.

Household size and owning non-laundry soap were only significant in mid-infancy which may be related to infectious transmission in the local environment to which infants are increasingly exposed with age. The negative effect of increasing household size could also be related to increasing division of resources or crowding. These findings demonstrate the dynamic process which occurs early in life as infants increasingly interact and are exposed to the household environment and ultimately influence nutriture.

Maternal education and household economic status (LSI) are strongly inter-related; however the manner in which they influence child nutritional status is complex. The results from our analysis indicate the influences change over the course of the first few months of life. Maternal education was more important in the early neonatal period, compared to mid-infancy; an effect which became more pronounced at the community level. The community economic structure, while only slightly modified the household effect for newborns, explained much of the difference in mid-infancy nutriture. Similar age-specific effects were found in a population of young children in Maputo, Mozambique. The study reported maternal education having a greater influence on child anthropometry in the first two years of life compared to household economic status which applies a greater influence after a child's second birthday [179]. These observed community effects may be related to the exchange of knowledge and resources between neighbors, as indicated by the variable, and/or aspects of the neighborhoods which wealthier, better educated households tend to reside.

Increasing community average SES was closely related greater equality and community maternal education, all of which may apply multifactorial neighborhood health effects. They were positively correlated with other health related community variables such as proportion of neighbors practicing hand-washing behaviors, having improved sanitation facilities, and owning non-laundry soap as well as elevation, population density, and shorter travel times to closest bazaar and paved road. Living in a wealthier neighborhood not only indicated having wealthier neighbors, but also living in a healthier environment. Many community-level variables were considered and dropped in this analysis in favor of greater model stability, as they exhibited collinearity with significantly stronger variables.

Other variables which are regularly included in similar studies, such as source of, and distance to drinking water, piped sewer, and presence of electricity, were also explored but excluded from the analysis. Nearly 100% of the samples receive their drinking water from wells which are nearly ubiquitous. Furthermore, these and other similar variables were also included in the creation of the LSI.

Seasonality coefficients, while not a focus of this analysis, provided some interesting results. Patterning of monthly coefficients exhibited two notable "seasons": a long season from February through July, and a short season from September through November. These seasons had very different effects, on average, for the early neonatal compared to the mid-infancy group. The long season had a beneficial effect for those in the early neonatal period and a detrimental effect for those in mid-infancy and vis-versa for the short season. These anthropometric patterns may be associated with the Aman (November -mid-December) rice harvest and the smaller Aus (June-August) and Boro (April-May) harvests and related nutritional and economic response experienced by the mother. Household liquid capital could fluctuate with these harvests, creating this seasonal pattern in infant nutriture or maternal nutriture during gestation. Unfortunately, data were not collected for changes in household liquid income. This temporal pattern in anthropometry, and relation to the fetal development cycle, is quite involved. Further investigation would be required to tease out any clear relationship or causality.

5.4.1.Limitations

The analysis could have been limited by the following. First, anthropometric data for this analysis were only collected at two time points in the first months of life. Some observations were also dropped because anthropometric measurements were not made within the mid-infancy window (150 – 210 days). A longer observation period with more regular measurement points could have provided more robust results regarding the effect of the community with increasing age.

Second, the variables examined in our analysis represent a sample of the most salient variables indicated in the literature, and thus do not include all known and unknown effects at each level. As a result, the proportion of the variance accounted for by each level is only a result of the respective variable samples. Nevertheless, data collected as part of the JiVitA trial was comprehensive given available literature and compared to similar studies in developing settings at the time the trial was conducted. While this analysis has provided valuable insight into the associations between individual and community level SES and child nutritional status, the establishment of a causal pathway would be facilitated by a more exhaustive analysis.

Third, the location information collected for this analysis is limited to the household location and does not account for full daily environmental exposure from places of employment, relatives'/friends' residences, and commutes. Some studies have suggested that GPS tracking of individual daily movement patterns provides greater precision in estimating environmental exposures [336,337]. Additional research should consider individuals' geospatial, familial and social networks as they pertain to child wellness, as this approach may help to tease out these systemic causal pathways.

5.4.2. Implications for nutritional interventions

This analysis confirms that, in addition to characteristics of the child and mother, attributes of the household and community provide modest, yet notable, influence to child nutriture, which appears to increase with infant age. In particular, community variables afford insight into the system of effects leading to malnourishment while also largely reducing residual spatial correlation. Several individual features, such as maternal anthropometry, maternal age, breastfeeding, and child gender, also appear to have increasing effect with age during infancy. These findings demonstrate the systemic and changing influences of individual, household and community characteristics throughout the first six months of life. Interventions targeting characteristics with increasing effect with age may provide exponentially beneficial effects for childhood nutritional status.

Through increased understanding of the complex system of influences resulting in maternal and child undernutrition, public health programming can further corroborate current initiatives for continued progress. Interventions intending to promote healthy child growth, which only target individuals, disregard the increasing influence of the environment and community with age. Interventions need to take an ecological approach, combining the successes of individual programs with structural and environmental components. Structural components include laws, policies and standard operational procedures [352]. Environmental components include living conditions, resources, social pressure, and opportunities available to individuals [352].

While initiatives to radically improve economic circumstance are often challenging and long-term in scope, energy could be spent to improve the factors, often tied with economic circumstance, which exist in the health pathway. In the case of this analysis, efforts to promote better education, hygiene and sanitation throughout communities, which were correlated with wealthier neighborhoods, may produce similar health improvements as improving wealth itself and be, perhaps, a little less arduous. As examples, environmental/structural approach could stigmatize poor hand-washing behavior, promote family planning around seasonal nutritional fluctuations associated with harvests, or encourage the transmission of healthy information at a societal scale.

5.5 Conclusion

These findings are generalizable for most of rural southern Asia, and potentially, more broadly in other developing contexts. This analysis has demonstrated the analytical merits of treating infant nutrition from a more comprehensive ecological framework and elastically through time. Future studies should collect data holistically, including attributes of location, community/neighbors, and infrastructure, in addition to the canon of routine individual and household factors. Considering multi-level causality of health outcomes can elucidate greater understanding and generate more creative, and potentially more effective, intervention initiatives.

5.6 Tables

Table 4: Descriptive Statistics of the JiVitA -1 population of Infants as newborns and rough six months of age assessed between 2001 and 2007

	Newborns		**Infants**	
N	15508		24016	
Child	**Mean**	**SD**	**Mean**	**SD**
MUAC (cm)	9.47	1.08	13.03	1.05
Parity	1.13	1.40	1.28	1.50
Gestational Age (weeks)	37.82	2.88	37.67	2.95
Sex (% Female)	49.33%		49.82%	
Age (Days)			173.8	9.66
Mother				
Age (Years)	21.84	5.74	22.06	5.72
MUAC (cm)	23.01	2.01	22.84	2.00
Education (Years)	4.14	4.03	3.78	4.04
Breastfed (%)	68.81%		99.32%	
Wash hands after Defecation (%)	54.99%		48.84%	
Wash hands before eating (%)	24.20%		18.95%	
Paid for work (%)	22.42%		17.56%	
Non-Muslim (%)	8.26%		8.34%	
Household				
Unimproved sanitation (%)	49.27%		55.87%	
Barsoap ownership (%)	84.20%		82.09%	
Household size	4.33	2.07	4.3	2.02
LSI	0.14	1.00	0.01	0.99
Community				
Average LSI (200m)	-0.03	0.35	-0.04	0.35
GINI (2000m)	34.18	0.05	34.18	0.05
Average Education (Years)	3.44	1.24	3.43	1.24
Population Density (100 ppl/sqkm)	5.47	1.29	5.48	1.28
Elevation (m)	25.46	1.89	25.47	1.88
Travel time to bazaar (Hours)	2.36	1.37	2.34	1.35
Travel time to paved road (Hours)	3.81	2.87	3.82	2.90

Characteristics of the JiVitA-1 population of newborns and infants at six months and their respective mothers, households and communities

Table 5: Simple linear regression results

	Newborns				**Infants**			
N	15508				24016			
Child	**Coef.**	**SE**	**t-value**	**R²**	**Coef.**	**SE**	**t-value**	**R²**
Parity	0.00	0.01	-0.81	0.000	-0.06	0.00	-13.39	0.007
Gestational Age (weeks)	0.08	0.00	30.36	0.056	0.03	0.00	12.73	0.007
Female	-0.05	0.02	-2.99	0.001	-0.43	0.01	-34.21	0.046
Age (Days)					0.00	0.00	4.11	0.001
Mother								
Age	0.04	0.00	8.65	0.005	0.03	0.00	8.99	0.005
Age > 21	-0.05	0.01	-7.87		-0.05	0.00	-10.48	
MUAC	0.08	0.00	20.71	0.027	0.11	0.00	34.70	0.048
Education	0.04	0.00	20.22	0.026	0.04	0.00	24.35	0.024
Breastfed	0.17	0.02	9.93	0.006	0.93	0.08	11.93	0.006
Wash hands after Defecation	0.09	0.02	5.61	0.002	0.09	0.01	6.92	0.002
Wash hands before eating	0.03	0.02	1.49	0.000	0.06	0.02	3.63	0.001
Paid for work	-0.02	0.02	-1.02	0.000	0.05	0.02	3.07	0.000
Non-Muslim	0.21	0.03	7.40	0.003	0.19	0.02	7.99	0.003
Household								
Unimproved sanitation	-0.22	0.02	-14.23	0.013	-0.25	0.01	-19.69	0.016
Barsoap ownership	0.16	0.02	7.43	0.003	0.26	0.02	15.47	0.010
Household size	0.04	0.00	10.49	0.007	0.01	0.00	4.05	0.001
LSI*	0.18	0.01	23.20	0.033	0.18	0.01	27.65	0.031
Context								
Average LSI*†	0.30	0.02	13.29	0.011	0.38	0.02	20.69	0.017
GINI Coef‡§	-1.06	0.17	-6.41	0.003	-2.23	0.13	-16.71	0.011
Average Education†	0.09	0.01	14.57	0.013	0.09	0.01	18.37	0.014
Pop. Density (100 ppl/sq. km)	-0.03	0.01	-5.16	0.002	-0.04	0.00	-8.81	0.003
Elevation (m)	0.01	0.00	2.02	0.000	0.02	0.00	6.21	0.002
Travel time to bazaar (Hr)	-0.03	0.01	-4.39	0.001	-0.02	0.00	-3.51	0.000
Travel time to paved road (Hr)	0.00	0.00	-0.54	0.000	0.00	0.00	-1.14	0.000

Coefficient values are changes in standard deviation in scaled and centered MUAC from the respective study populations of newborns and infants

* Living Standards Index

† Includes neighbors within a 200 meter radius

‡ Includes neighbors within a 2000 meter radius

§ Mean Centered

Table 6: Multivariate regression coefficients estimating scaled and mean centered newborn and infant MUAC

	Child Model						Mother Model						Household Model						Context Model					
	Newborn			Infant			Newborn			Infant			Newborn			Infant			Newborn			Infant		
	Est.	SE	t value	Est.	SE	t value	Est.	SE	t value	Est.	SE	t value	Est.	SE	t value	Est.	SE	t value	Est.	SE	t value	Est.	SE	t value
(Intercept)	**-3.469**	**0.104**	**-33.40**	**-2.250**	**0.161**	**-13.97**	**-5.212**	**0.146**	**-35.65**	**-4.836**	**0.179**	**-27.07**	**-5.006**	**0.152**	**-32.84**	**-4.527**	**0.181**	**-25.03**	0.14	6.681	0.02	**-4.46**	**0.207**	**-21.53**
Child Variables																								
Breastfed	**0.176**	**0.016**	**10.82**	**1.149**	**0.071**	**16.10**	**0.143**	**0.016**	**8.92**	**1.156**	**0.070**	**16.48**	**0.138**	**0.016**	**8.63**	**1.183**	**0.070**	**16.94**	**0.13**	**0.016**	**8.03**	**1.18**	**0.070**	**16.90**
Parity	**0.012**	**0.004**	**2.68**	**-0.062**	**0.004**	**-14.81**	**0.043**	**0.009**	**4.86**	**-0.046**	**0.007**	**-7.02**	**0.047**	**0.009**	**5.23**	**-0.033**	**0.007**	**-4.93**	**0.05**	**0.009**	**5.22**	**-0.03**	**0.007**	**-4.82**
Gestational Age	**0.088**	**0.003**	**33.62**	**0.031**	**0.002**	**14.91**	**0.081**	**0.003**	**31.20**	**0.023**	**0.002**	**11.36**	**0.080**	**0.003**	**31.14**	**0.023**	**0.002**	**11.28**	**0.08**	**0.003**	**30.89**	**0.02**	**0.002**	**10.91**
Female	**-0.071**	**0.015**	**-4.75**	**-0.438**	**0.012**	**-36.39**	**-0.067**	**0.015**	**-4.51**	**-0.435**	**0.012**	**-37.20**	**-0.066**	**0.015**	**-4.50**	**-0.435**	**0.012**	**-37.36**	**-0.07**	**0.015**	**-4.44**	**-0.43**	**0.012**	**-37.41**
Age (Days)				**0.002**	**0.001**	**3.07**	NA			**0.002**	**0.001**	**3.13**	NA			**0.002**	**0.001**	**3.20**	NA			**0.00**	**0.001**	**3.60**
Mother Variables																								
Age							**0.028**	**0.005**	**6.19**	**0.035**	**0.004**	**9.58**	**0.029**	**0.005**	**6.37**	**0.034**	**0.004**	**9.16**	**0.03**	**0.005**	**6.10**	**0.03**	**0.004**	**9.28**
Age Linear Spline (21)							**-0.028**	**0.006**	**-5.09**	**-0.037**	**0.004**	**-8.15**	**-0.032**	**0.006**	**-5.70**	**-0.038**	**0.004**	**-8.38**	**-0.03**	**0.006**	**-5.48**	**-0.04**	**0.004**	**-8.54**
MUAC							**0.058**	**0.004**	**15.23**	**0.093**	**0.003**	**30.52**	**0.052**	**0.004**	**13.53**	**0.085**	**0.003**	**27.68**	**0.05**	**0.004**	**13.12**	**0.08**	**0.003**	**26.76**
Educational Atainment							**0.036**	**0.002**	**16.92**	**0.027**	**0.002**	**16.18**	**0.022**	**0.002**	**8.98**	**0.012**	**0.002**	**5.96**	**0.02**	**0.003**	**7.64**	**0.01**	**0.002**	**5.61**
Handwash after defecation							**0.036**	**0.015**	**2.35**	0.019	0.012	1.57	**0.013**	**0.015**	**0.85**	-0.012	0.012	-0.93	0.01	0.015	0.94	0.00	0.012	-0.13
Handwash before eating							-0.032	0.018	-1.79	0.003	0.016	0.16	**-0.036**	**0.018**	**-2.04**	-0.006	0.016	-0.38	**-0.04**	**0.018**	**-2.21**	0.00	0.016	-0.32
Mother paid for work							**-0.073**	**0.018**	**-3.99**	0.029	0.016	1.79	**-0.069**	**0.018**	**-3.79**	0.025	0.016	1.56	**-0.07**	**0.018**	**-3.94**	0.00	0.016	0.31
Non-Muslim							**0.163**	**0.027**	**6.06**	**0.089**	**0.021**	**4.24**	**0.154**	**0.027**	**5.72**	**0.084**	**0.021**	**3.98**	**0.15**	**0.027**	**5.54**	**0.07**	**0.021**	**3.18**
Household Variables																								
Unimproved Sanitation													0.004	0.019	0.21	-0.028	0.016	-1.75	0.00	0.019	-0.03	-0.02	0.016	-0.96
Bar soap ownership													-0.002	0.022	-0.10	**0.064**	**0.017**	**3.84**	0.01	0.022	0.27	**0.06**	**0.017**	**3.45**
Household size													-0.001	0.004	-0.18	**-0.019**	**0.003**	**-5.62**	0.00	0.004	0.07	**-0.02**	**0.003**	**-4.57**
LSI*													**0.098**	**0.013**	**7.48**	**0.114**	**0.011**	**10.77**	**0.09**	**0.014**	**7.01**	**0.10**	**0.011**	**9.08**
Exogenous Variables																								
Average LSI*†																			**-0.09**	**0.036**	**-2.53**	**0.09**	**0.028**	**3.10**
GINI Coef‡§																			-0.14	0.196	-0.72	**-1.17**	**0.155**	**-7.55**
Average Education†																			**0.04**	**0.010**	**3.69**	0.00	0.008	0.02
Pop. Density (100pp/sqkm)																			**-0.0186**	**0.007**	**-2.50**	-0.0054	0.006	-0.91
Elevation																			**-0.01**	**0.004**	**-2.36**	0.00	0.003	-0.05
Travel time to bazaar (hr)																			**-0.0222**	**0.006**	**-3.83**	-0.0043	0.005	-0.93
Travel time to paved road (hr)																			0.0006	0.003	0.19	-0.0029	0.002	-1.25
LSI x Average LSI*																			**0.07**	**0.018**	**3.56**	-0.01	0.015	-0.97
R²	**0.0845**			**0.0757**			**0.1244**			**0.1326**			**0.1295**			**0.1407**			**0.1321**			**0.1451**		
AIC	**45977.0**			**71212.9**			**44856.1**			**69105.9**			**44756.5**			**68746.8**			**44599.5**			**68542.8**		

Seasonal and secular effects have been adjusted for in all models; coefficient values are changes in standard deviation in scaled and centered MUAC from the respective study populations of newborns and infants. Bold values indicate p-value <0.05

* Living Standards Index

† Includes neighbors within a 200 meter radius

‡ Includes neighbors within a 2000 meter radius

§ Mean Centered

5.7 Figures

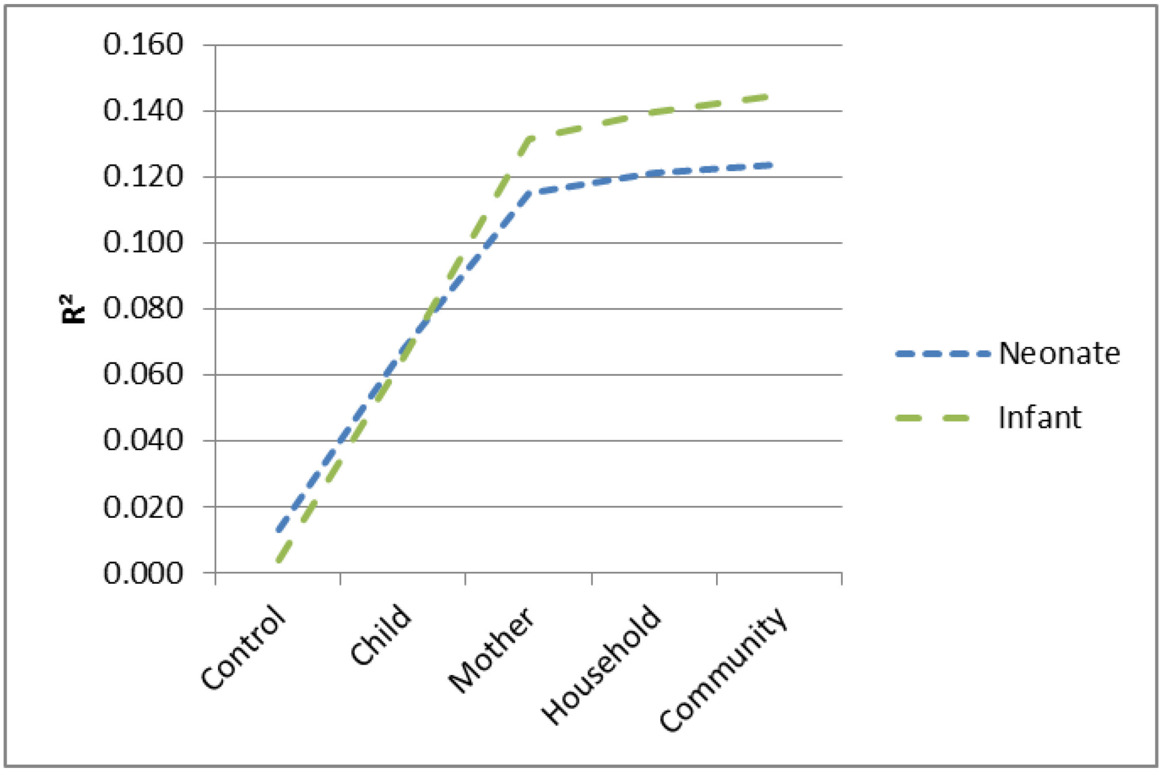

Figure 12: Variance accounted for with addition of each level of variables

This graph depicts, on the y-axis, the variance accounted for (R^2) with the addition of each level of variables on the x-axis. Note a greater proportion of variance is accounted for by mother, household and community variables in the infant group, compared to the neonate group.

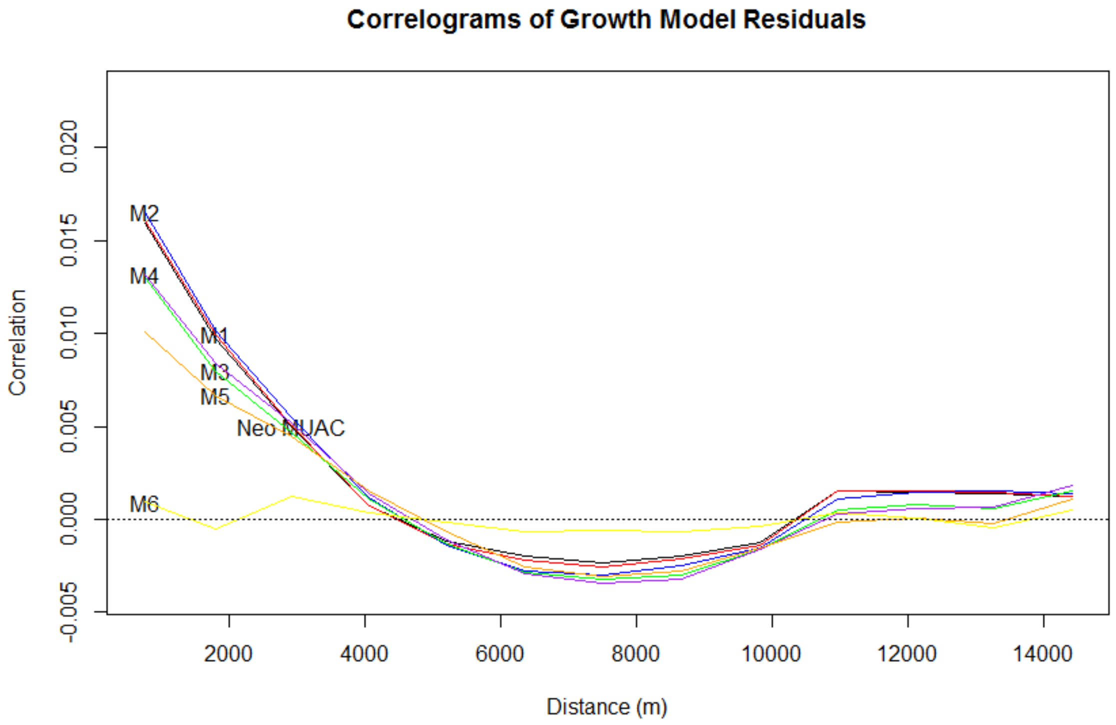

Figure 13: Correlograms for growth model residuals in the neonatal group

Correlograms depicting spatial correlation between observations and explanatory models in the newborn group. Neo MUAC (black) = Unadjusted Neonatal MUAC; M1(red) = Control Model; M2 (blue) = Child Model; M3 (green) = Mother Model; M4 (purple) = Household Model; M5 (orange) = Community Model; M6 (yellow) = Spatial Errors Community Model. The dashed line indicates the point of zero correlation. Correlation is on the y-axis and distance, in meters, is on the x-axis.

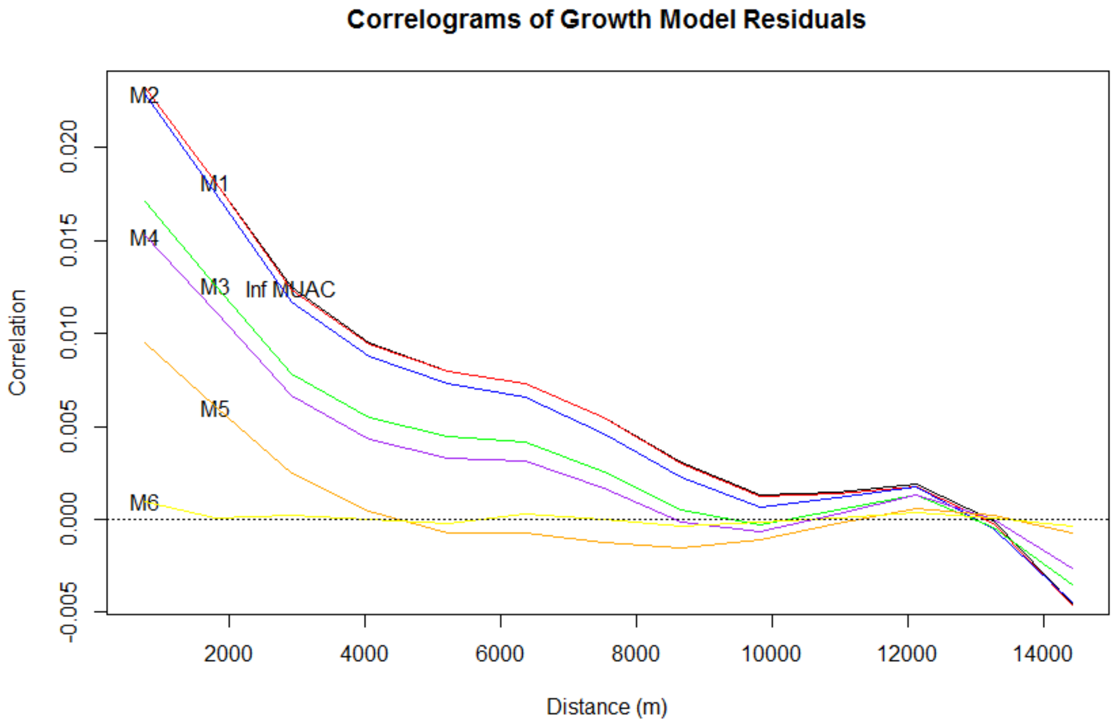

Figure 14: Correlograms for growth model residuals in the mid-infancy group

Correlograms depicting spatial correlation between observations and explanatory models in the mid-infancy group. Inf MUAC (black) = Unadjusted Infant MUAC; M1(red) = Control Model; M2 (blue) = Child Model; M3 (green) = Mother Model; M4 (purple) = Household Model; M5 (orange) = Community Model; M6 (yellow) = Spatial Errors Community Model. The dashed line indicates the point of zero correlation. Correlation is on the y-axis and distance, in meters, is on the x-axis.

Chapter 6 Ending intergenerational malnutrition: A systems approach to explain heterogeneity in infant growth trajectories

6.1 Abstract

The effects of poor growth early in life can resonate well into adulthood. The body of nutritional literature has noted those of similar nutritional status to cluster spatially, indicating possible contextual influences. Previous research investigating differences in growth trajectories has primarily focused on characteristics of the pregnancy, the mother, and the child at birth, while predominantly ignoring context. This analysis considers the role of context in determining differences in growth trajectories, and accounting for spatial correlation, after adjusting for relevant characteristics of the child, mother and household. Using data from the JiVitA-1&2 trials in northwest Bangladesh, determinants were grouped by level then added sequentially to a linear regression model accounting for seasonal, secular and spatial error effects. Residual spatial correlation from each sequential model was observed with correlograms and interpolated maps. Determinants of infant growth at the child, mother, household and contextual levels explained 35.9%, 2.1%, 0.8% and 1.3% of the respective variance. Contextual variables accounted for more spatial correlation than any other group of variables and explained more of the variance than household-level variables. MUAC at birth alone attributed 32.7% of the variance. Determinants related to socioeconomic status (SES), such as maternal education, household economic status, the average and distribution of neighborhood wealth and average neighborhood maternal education also provided notable influence. The findings from this analysis suggest, after accounting for child and mother-level covariates, context better explains differences in growth trajectories than household characteristics and modifies effects at lower levels. Public health programing needs to target adolescent girls, mothers and pregnancies as early as possible to give children a healthy starting point as well as role of the environment and community as they modify child and mother effects.

6.1 Introduction

Children born to poorer families and malnourished mothers start life at a marked disadvantage, which continues to reverberate throughout life. Those born to malnourished mothers are more likely to be small for gestational age, low birth weight, and have smaller anthropometric measurements through infancy [10–19]. Poor growth in early childhood, especially in the first two years, can lead to irreversible damage and reduced human capital [22–28]. Nutritional status in infancy is associated with mental development [27,37,38], future academic performance [28,39], alcohol and drug use, fertility [39], blood pressure [29–34], insulin resistance [31], risk of stroke [35], metabolic syndrome [36] and ultimately adult economic productivity [26]. Therefore, early childhood nutritional status can act as a multi-factorial indicator for future health and productivity.

A child's health can also be influenced by the socio-economic status of their parents. Children born to poorer families experience poorer health in childhood and reduced productivity and health as adults [40–42]. This effect may be exacerbated with prolonged poverty [19]. Additionally, children born to uneducated mothers tend to have reduced anthropometry [43] and are less likely to go to school [44], which is related future economic productivity. Since malnutrition is so closely tied with poverty, and both malnutrition and poverty can be intergenerational, these effects further entrench offspring into desperate circumstance.

Generally speaking, individual nutritional status is determined through two primary pathways: biology and socio-economy. Biological factors include age, gender, parental anthropometry, fetal development[12,70,142–144], anthropometry at birth[22], infection [5,7,85,89,91,92,96,160], among others. Socio-economic factors are considered to be one of the basic causes of ill health and poor nutritional status in individuals, as mediated through hazardous exposures (e.g., suboptimal sanitation, drinking water quality, hygiene) as well as limited access to health-promoting resources (e.g., high-quality food, healthcare, electricity, health insurance) [136,137]. A household's economic status is closely linked to education, each enhancing the other, and higher academic attainment is associated with greater earning potential and greater economic standing. Education is also related to knowledge of healthy behaviors[23,108]. These pathways substantially influence health in both adults and their children, and have been explored at length during the past several decades of research. While such explanatory models have provided considerable implications for intergenerational malnutrition, they have not accounted for all of the differences in individual nutritional status.

Several authors have reported spatial patterning, or clustering, of malnourished populations [3,49–52,56,57,60,160,223,240,285]. This phenomenon suggests that malnutrition may be subject to contextual influences. Others have considered this issue, reporting external influences from agricultural factors [56,57,227,228], elevation [15,49,55], rural-urban differences [91,94,180,181,192,245,246], distance from urban centers [99], population density [59], community economic structure [21,177,180,190,191,248], average neighborhood educational attainment [43,58,141,176], individual-community interactions[21,49,110,250], community stability [232,248,260], and increased access to public goods such as schools, health services [21,23,60,99,195,232,236–239], electricity [139,236], paved roads [57,210,240], and piped water [57,60,94,229,236,241]. Until recently, spatially explicit data, such as that which was used in these types of studies, has been difficult to acquire in conjunction with study time, scale and location. Data sources were often not available, of poor quality, or did not match the study period or geographic scale. Most of the analyses referenced above required data from many external sources, potentially impacting validity, as opposed to being collected holistically as part of a comprehensive dataset.

Much of the nutrition literature has focused on individual and household determinants and has failed to consider how contextual factors, discussed previously, may be transmitted between generations and, ultimately, impact longitudinal growth trajectories in infancy. Emanuel (1986) defined intergenerational influences as “conditions, exposures, and environments experienced by one generation that relate to the health, growth and development of the next generation." These influences may become more pronounced when generations share similar circumstance. Substantial improvements in linear growth have been observed with change in circumstance related to child adoption, family migration, or swift national socio-economic development [18]. Children born to mothers who were malnourished as children can experience nearly normal growth when "profound improvements in health, nutrition and the environment take place before conception" [18]. Healthy growth in the first two years of life is particularly important. It is in this period which growth faltering is most pronounced [45–47] and recovery is increasingly difficult if improvements are not made [48]. If children are to break from the shackles of intergenerational malnutrition, it is imperative that we gain a better understanding of the system of influences so as to design interventions to be as effective as possible.

The current body of evidence upholds the premise that individual nutritional status is a consequence of more than just individual or household factors. Rather, it is a product of an interaction between individual circumstance, local context and intergenerational influences. A more complex analytical approach may be appropriate for the analysis of individual health and nutritional status. Systems biology, or systeomics, is an approach typically used in genetics research to observe complex interactions between the causes and effects in biological systems [63]. In the case of nutritional epidemiology, using this type of approach, individuals may be considered as cells, their households and families as tissue, and their neighborhoods as organs, such that individuals are interconnected to the system as a whole, applying positive, negative, and interactive effects.

The present analysis explores infant growth trajectories as an ecological product resulting from an interaction of biological, socio-economic and contextual forces. Data from a comprehensive cohort study in north-west Bangladesh has provided intriguing evidence for intergenerational malnutrition as an ecologic phenomenon. From these data, a spatial trend is observed in anthropometry of expectant mothers across the study area, with healthier women in the west and thinner women in the east. This pattern was not well manifested in the anthropometry of their newborns, seemingly protected from the status of their mothers; however, by roughly six months, infant anthropometry mirrored that of their mothers relative to the respective means. Thus, over the course of the first six months of life, the near random distribution of birth anthropometry rapidly take on the spatially distinctive character of their mothers (see Figure 14). The objective of this analysis is to consider the spatial patterning of this intergenerational trend and investigate the interactions of biological, socio-economic, and contextual forces at several levels to determine the underlying effects leading to the observed spatial patterning. The analysis implemented in this analysis is loosely based on the constructs of systems biology.

6.2 Subjects and Methods

6.2.1.Study Population and Data

Data used for this analysis were collected as part of a sample from a prospective mother-infant dyad cohort that was enrolled in a double-masked, cluster-randomized, dual-intervention, placebo-controlled trial conducted by the JiVitA project. The study population has been described in detail elsewhere [67]. In brief, the study site is a contiguous rural flood prone area of approximately 435 sq km located to the west of the Jamuna river, in northwest Bangladesh (Figure 5). The site was selected to reflect vital, health, and nutritional risks of the rural Bangladeshi population [67]. The site is also characterized by its remoteness and agrarian nature and is similar in context to many areas of south Asia.

Of the 125,257 women eligible to participate in the trial, 59,666 were detected as pregnant and subsequently enrolled between August 2001 and October 2006. From those enrolled, data were collected for 42,185 of their infants, 18,157 of these infants had additional measurements as newborns. Since nutritional status was one of the primary outcomes of interest, anthropometry was meticulously measured in triplicate.

For the purposes of identification, enrollment, and tracking of study participants, the JiVitA Geographic Information System was established as a method of rural addressing (Figure 6). The system includes 236,681 landmarks, 149,402 of which are households, study and political boundaries, local roads and paths, and hydrologic features. The system was maintained and updated throughout the JiVitA – 1 study period (2001-2007). The details of the JiVitA Geographic Information System can be found elsewhere [317].

6.2.2. Variables of interest

The primary outcome of interest is the average daily change in mid-upper arm circumference (MUAC) among children at birth and mid-infancy (between 5-7 months since birth). Change in MUAC was treated as a continuous variable. Values were mean centered and scaled based on the sample distribution such that the primary outcome was standard deviation from mean zero. This adjustment was meant to provide outcome values relative to the study population. MUAC measurements were performed by JiVitA field staff trained and standardized in anthropometry. Triplicate measurements were taken for precision and then averaged. As discussed in Chapter 2, MUAC was chosen over other anthropometric measurements for its ease of field administration and its relation to physiologic processes [73,77]. MUAC is highly correlated with other anthropometric measurements [13,69,71,78], has demonstrated sensitivity to short term changes in nutrition [75,78–84], predicts lean and fat mass equally well [31] and has been used to indicate episodes of growth faltering [85].

To explore the manner in which the observed spatial patterning relates to interacting biological, socioeconomic, and contextual forces, this analysis will consider effects at several levels which were discussed in Chapter 2. Biological forces will include child gender and MUAC at birth, and maternal MUAC, age and breastfeeding behavior. Anthropometry at birth is closely related to maternal anthropometry and both are associated with fetal development/gestational age at birth, maternal age, and socioeconomic status. Socioeconomic forces will include maternal education and a household living standards index. Contextual forces considered are the neighborhood average LSI and maternal educational attainment, local inequality (Gini), population density, elevation, and travel time to the nearest bazaar and paved road.

6.2.3.Data Analysis

Statistical analysis was accomplished using R Statistical Software (Version 3.1.1)[353]. Exploratory data analysis (EDA) was conducted to evaluate data distribution and potential collinearity and confirm regression assumptions. Neighborhood was defined through both field knowledge and observation of spatial dependence in outcome measurements, using a correlogram. Correlograms were used to compare spatial auto-correlation between observation locations for all variables of interest. Correlograms were chosen over semi-variograms, which are generally more common in spatial statistics, to retain a common scale of reference (-1:1) so clear comparisons could be made. Correlograms, semi-variograms and covariograms all essentially have similar calculations and evaluate spatial auto-correlation.

To evaluate statistical associations, linear regression techniques were employed. Coefficients from both simple and multivariate regressions were compared to determine possible mediation and confounding. Dummy variables for month and year of birth were added to all multivariate regressions to adjust for seasonality and secular trends. Effects at each level were added sequentially to observe associated explanatory gains. Five multivariate models were estimated and are described below.

Model 1: Child Model – The child model adjusts for child gender and MUAC at birth. Gestational age and parity were not included since they are closely related with anthropometry at birth. These variables adjust for the primary biological pathways at the child level which are associated with growth rate.

Model 2: Mother Model – The mother model adjust for maternal age and MUAC. This model builds on the child model by adjusting for variables of primary biological influence on child growth rate. Maternal MUAC also partially mediates the effects of maternal socioeconomic status.

Model 3: Socioeconomic Model – The socioeconomic model adjusts for maternal education and household living standards. This model builds on the mother model, which accounts for biological factors associated with child growth at the child and mother level, and adds variables associated with circumstance which may influence child growth either directly or indirectly.

Model 4: Context Model – The context model builds on the socioeconomic model and explores the effects applied from an individual's location and community. Variables considered are elevation, population density, travel time to the nearest permanent bazaar and paved road, neighborhood economic structure (average living standards and local Gini coefficient), and neighborhood average maternal education.

Model 5: Context Model with Interactions – Interactions between individual socioeconomic variables and context variables were also considered. Contextual variables and interactions were then selected based on variable coefficient significance and improvements to overall model fit.

Residual spatial auto-correlation from each model was evaluated using correlograms. Model residuals were also exported from R and imported into ArcGIS 10.2.2 where they were interpolated using ordinary kriging and mapped for visual inspection.

6.3 Results

Data were available from 59,854 expectant mothers, and 47,091 children, however, only a subset of 18,157 had measurements as newborns which were made as close to birth as possible (median:

18 hours of age [IQR: 9-36 hours])[316]. After exclusions, data from 17,244 children were included (see Figure 7: Study population flow chart). Table 7 depicts the dependent and independent variable distributions. The children, on average, had a MUAC of 9.46cm at birth and 13.00cm in mid-infancy, and gained 0.02 cm in MUAC per day in between. They were born at a median of 38 weeks gestation and roughly half (48.33%) were female. They were born to generally uneducated and malnourished mothers (mean MUAC: 22.97) with nearly half falling below the 23cm cut-off for “low MUAC” [354]. The study population was reasonably isolate, most needing to travel over two hours to the nearest permanent bazaar and three hours to the nearest paved road. Distribution of resources was fairly equitable (mean Gini: 34.18) and comparable to the World Bank’s 2005 national estimate of 33.2[342].

6.3.1.Neighborhood Determination

After considering observed spatial dependence and field knowledge, neighborhood was defined as those living within 200m and 2000m. Both radii were evaluated for context variable calculations. With the exception of the local Gini calculation, variables were more influential when calculated with the 200m radius. The local Gini variable was more influential when neighbors within the 2000m radius were included, most likely related to Gini being an estimate of dispersion.

6.3.2.Collinearity

Potential collinearity between variables of interest was assessed with pair-wise Pearson’s correlation calculations. Due to the sample size, most of the correlation coefficients were significant, regardless of magnitude. Early Neonatal MUAC was correlated with gestational age (R = 0.22), maternal MUAC (R = 0.17), LSI (R = 0.19), maternal education (R = 0.16) and the neighborhood averages for LSI (R = 0.11) and maternal education (R= 0 .11). These variables were also closely correlated to each other. Maternal education was closely associated with LSI both at the individual (R = 0.60) and neighborhood (R = 0.76) level. Context variables were also correlated with each other with R values generally ranging between +/- 0.1 to +/- 0.53.

6.3.3.Regression Analysis

Table 8 displays the results of the simple linear regressions. Generally, much of the difference in growth rate was explained through biological variables at the child-level. MUAC at birth was negatively associated with child growth rate and accounted for the greatest portion of variance ($R^2 = 0.327$). Female gender and gestational age were also negatively associated with growth rate and accounted for 2.6% and 1.3% of the respective variance. Biological variables at the mother-level demonstrated non-linear associations with child growth. Infant growth rate was positively associated with maternal age and maternal MUAC until 21 years of age and 26cm, respectively, when the slope of association would change. This non-linear association was observed graphically and statistical for both maternal variables. Addition of the mother-level biological variables improved the fit, based on R^2, of the child-model from 0.359 to 0.38 and decreased AIC by 865.94. Interestingly, the socioeconomic variables were non-significant in the simple linear regressions, however, became significant ($p < 0.0001$) after adjusting for the biological variables at the child and mother level. Maternal educational attainment and household living standards are both positively associated with child MUAC growth rate. The addition of socioeconomic variables provided modest improvements in model fit, increasing R^2 from 0.38 to 0.39 and decreased AIC by 220.04 from the mother-model.

The model fit improvements associated with the contextual variables were comparable to those of the household variables, increasing R^2 from 0.39 to 0.40. Contextual and interaction variables decreased AIC by 390.87, which is nearly twice the reduction found when household variables were added to the model. Economic inequality (Gini) was one of the strongest contextual variables. Many of the economic context variables exhibited convoluted non-linear associations with residuals from the previously discussed more basic models. Exploratory data analysis suggested these observed non-linear associations may be the result of variable interaction. Many significant interactions were found, however, interactions between MUAC at birth and LSI and between gestational age and average neighborhood LSI were conceptually plausible and provided the greatest improvements in model fit. These interactions depicted an interesting phenomenon. The growth of infants who were born early and/or smaller, to wealthier households was notably faster than their poorer counterparts, while infants who were born later in gestation and/or larger to wealthier households grew more slowly than those of poorer circumstance. Elevation was significant and positively associated with anthropometric growth when added to the household model, however, became non-significant when economic context variables were added and was excluded from the full model. Population density was significant and positively associated with growth, even after adjusting for other relevant context variables. Results from the multivariate regression analysis can be seen in Table 9.

6.3.4.Spatial Correlation

Spatial auto-correlation of the variables of interest was explored using correlograms. Figure 15 displays correlograms for our study population of mothers and their children at birth and roughly six months of age. The correlation between early neonates appears to be present and similar to mothers at closer distances (<2000m), however, disappears quickly at approximately 4000m. Correlation between infants within closer proximity (<2000m) was much higher than early neonates and mothers, however, weakened rapidly and remained until roughly 8000m. The correlation between mothers was lower than infants, but similar to neonates in close proximity (<2000m) and waned slowly with distance until about 12000m. The correlograms created for select explanatory variables can be seen in Figure 16 - Figure 18. Correlograms indicated some spatial auto-correlation of LSI and maternal education between observations. The biological effects of maternal age, gestational age and child gender occurred nearly randomly across space, as expected. This was further corroborated when these variables were included into regression models and residual auto-correlation was observed. After adjusting for these biological effects at the child level, model residual spatial correlation increased. Addition of mother and SES variables only slightly decreased residual spatial correlation. Context variables, however, provided substantial decreases in correlated residuals. Local inequality (Gini) accounted for considerably more of the residual spatial correlation than any other explanatory variable. Reductions in residual spatial correlation accounted for by each multivariate regression can be seen in Figure 19 and Figure 20.

6.4 Discussion

The findings from this analysis have provided supporting evidence for the relevance of location and community in determining infant health and nutritional status. Biological factors of the mother and child were important in explaining differences in infant growth trajectories. Infants enjoy protective effects from higher economic status both at the household and community levels, which interact with characteristics of newborns resulting in differing growth trajectories. Birth size, gestational age, and infant gender were generally dispersed randomly across the study site. After accounting for these variables, model residuals became substantially more spatially correlated. Community economic structure, inequality, in particular, was primarily responsible spatial clustering observed in this analysis. This analysis also reveals population sorting; a more pervasive societal issue which marginalizes economically disadvantaged households into locations with greater environmental hazards, in our seemingly homogenous rural developing setting.

The predominant effect determining anthropometric growth in this population of infants was anthropometry at birth. Infants with the greatest MUAC as newborns grew at a rate that was roughly six standard deviations slower than those born with the smallest MUAC. This effect is most likely related to catch-up growth which has been observed in several other studies [355,356]. MUAC in the first few days of life alone accounted for approximately 32% of the variance in infant MUAC growth. Child-model residuals demonstrated strikingly more spatial correlation than were observed in infant growth alone. This suggests much of the spatial randomness in MUAC growth was accounted for by characteristics of the child and some of the unadjusted effects have spatial structure.

Maternal variables, such as MUAC and age, were also important in explaining growth-rate differences. The associations of maternal MUAC and age with change in infant arm-circumference were found to be non-linear. The association between maternal MUAC and infant growth was continuous, positive and significant. There was a noticeable change in association for mothers with MUAC greater than 26 cm, when the rate of increase lessened, but remained positive. The depreciated benefit after 26cm provides evidence supporting this as a cutoff for healthy maternal MUAC as suggested by others[316,357–359], since an optimum maternal MUAC has not been adequately explored[354]. The association between maternal age and infant growth was positive with a peak at the maternal age of 21, where, thereafter, the association was negative. Within the study population, maternal age ranged from 9 to 48. Holding all else constant, infants born to 21 year-old mothers grew approximately 0.2 standard deviations faster than their counterparts born to the oldest and youngest mothers. This may suggest a peak of female reproductive health at approximately 21 years of age, similar to the findings of Ketterlinus (1990) related to risk of LBW[360]. Valero De Bernabé (2004) also noted this parabolic association with low birthweight [361]. This could represent a peak of physiological and/or psychological maturity as well as necessary reproductive competence. Mother and SES variables improved overall model fit, however only minor decreases in residual spatial auto-correlation.

Context variables provided similar improvements to overall model fit and reduced residual spatial auto-correlation considerably. Local inequality was particularly important in explaining the spatial patterning of growth-rate differences across the study area. The average change in MUAC of infants living in the most economically equal neighborhoods was 0.4 standard deviations larger than those living in the least economically equal neighborhoods, holding all other variables constant. This finding is particularly interesting in that data for local variation in economic inequality is rarely available or explored. The local Gini variable performed better with the 2000m radius than the 200m radius used for other contextual variables. Others have also found inequality (Gini) to be less sensitive with smaller spatial resolution [21,190]. In similar analyses, greater inequality was associate with higher rates of stunting[21,190], greater food poverty [235], and higher preventable and immediate death rates [325].

Neighborhood average maternal educational attainment and average LSI were also important contextual variables associated with approximately 0.24 and 0.12 standard deviations of growth rate difference, respectively, across the study population. Similar studies have also found community average maternal education[141] and SES[191] to independently influence child health as well as modify the effects of individual and household characteristics. These studies suggested the importance of basic community resources as determinants of child health.

While household SES was a dominant determinant of child health in this analysis, community economic structure modified individual circumstance considerably. On average, the nutritional status of children born to poorer households living in wealthier neighborhoods often surpassed wealthier households residing in poorer neighborhoods (see Figure 21). This was particularly apparent when infants were stratified by birth anthropometry (see Figure 22). Neighborhood economic structure appeared to 'sort' individual growth better than household circumstance alone after adjusting for birth size. The observed synergy between individual and neighborhood circumstance could be homophily, a network-level effect of similarity of social contacts – as proposed by Centola (2011). Unhealthy individuals who interact with healthy individuals, are more likely to adopt similar healthy behaviors, however, unhealthy individuals interacting in a network of similar unhealthy individuals are the least likely to adopt healthy behaviors [328]. Those residing in wealthier neighborhoods may also have access to more shared resources, improved public provisions and have greater neighbor support and social cohesion.

During the model building process, it became clear there was notable collinearity between the contextual variables. Wealthier households tended to reside near other wealthy households, creating wealthier neighborhoods. Those wealthier neighborhoods tended to be at higher elevation with lower risk of flooding, closer to paved roads and regular bazaars and with somewhat greater population density. Neighborhoods with greater average wealth also tended to have less inequality and greater average maternal educational attainment. Aspects such as elevation and proximity to paved roads may be related to household income generation. Brown (2003), in an analysis conducted in Nepal reported that households located closer to primary roads had smaller land holdings, greater access to agrochemicals and greater access to income through off-farm employment; more remote households had larger landholdings and were more reliant on subsistence agriculture. Authors reported land use was largely related to household elevation and suggested inequality in landholdings largely translated into economic inequality[294]. Brouwer et al. (2007) conducted in Bangladesh reported that households with lower income and less access to productive natural assets (i.e. landholdings) experienced increased risk of flooding. In addition, this analysis observed greater disparity in income and asset distribution at the community level in areas with greater flood risk [207].

Our analysis and others have found economically vulnerable populations are disproportionally exposed to hazardous environmental conditions and experience greater health risks. Poorer households are often marginalized into communities which experience elevated environmental risks. Studies have observed those of lower SES residing closer to polluting facilities [287], have greater difficulty relocating from regions prone to natural hazards [288], and have a modified acute effect from exposure to black smoke pollution [289]. Several analyses have considered area-based environmental health hazard exposure from multiple dimensions such as air pollution, climate, industrial facilities, UV radiation, and green space, as they related to proximate household economic status. These analyses have found multiple environment deprivation to be associated with economic status in the UK[290,291] and New Zealand[292].

6.4.1.Limitations

This analysis could have been limited by the following. First, this analysis only considered anthropometric measurements made at two time-points during infancy. Furthermore, measurements were attempted at precise time intervals (i.e. 0, 3 and 6 months), however, for multitude of reasons, and they occurred earlier or later than the intended time point. These findings could have been more robust had this study had a longer observation period and data been collected at precise time points.

Second, since data collection only occurred at one study location and many of the effects are context specific, our inferences may not be generalizable elsewhere. Similar analyses would need to be reproduced in different developing locales for global inferences to be made. The study population was however, representative of rural developing southern Asia and inferences may be applicable in similar settings.

Third, the association between infant growth and neighborhood circumstance provides suggestive evidence for multi-level health influences, however, doesn't elucidate causal pathways. Future research should investigate how characteristics of the community assert forces on individual health. These effects may be related to shared resources and knowledge, circulating values and norms, social capital and support, collective efficacy and organization, or social and familial contact networks. Additionally, previous work has suggested the period of poverty (permanent vs. contemporaneous) was related to greater risk of restricted inter-uterine growth[19]. Data detailing the tenure of poverty exposure were not available for this study and could have provided greater explanation for differences in infant growth.

6.4.2. Intervention Implications

The findings of this analysis suggest intervention efforts intending to break intergenerational malnutrition should focus on improving maternal nutritional status, increasing maternal education at the individual and neighborhood level and creating healthier environments. These recommendations complement those of Underwood (2002) to interrupt the intergenerational consequences of malnutrition. They suggest intervention efforts should focus on adolescent girls, pregnant women and lactating women and their children up to 2 years, with particular focus on women in the pre-conception period [362]. The nutritional status of soon-to-be mothers, as it is related to the initial size and gestational age of infants, which is closely related to growth rate, could provide the greatest impact for future generations. The nutritional benefits of greater maternal education at the individual and neighborhood level may be more directly impacted through improved nutritional knowledge [23,108]. Interventions in rural areas, which improve nutritional knowledge, in even a small number of individuals, increase the over-all neighborhood nutritional benefit as information disseminates through the community [327]. The benefits of increasing average community knowledge is appreciably larger than that of an individual in isolation[327], and may follow social contact networks [328]. Substantial changes in context have also observed improved linear growth in children[18], however, these changes were associated with child adoption, family migration or large-scale societal economic development. These types of interventions are, to say, less-than ideal. Interventions could, instead, focus on aspects of what makes healthier environments which promote healthy child growth. Such aspects could include improved societal nutritional knowledge, hygiene practices, social cohesion and support as well as collective efficacy, or public provisions and infrastructure.

6.5 Conclusion

In conclusion, differences in growth trajectories, after accounting for birth size, gestational age and infant gender, are determined through differences in biological features of the mother as well as household and community socioeconomic circumstance. Interventions should focus on the health and education of mothers, household economic status and community circumstance in efforts to improve infant growth trajectories and break the chains of intergenerational malnutrition in developing settings.

This analysis also demonstrated the research advantages of taking a more holistic systems biology approach to understanding differences in nutritional status. Individual factors had significant interactions with household- and community-level characteristics which helped explain differences in infant growth trajectories. Community context played a significant role in sorting infant anthropometry, more-so than individual-level SES. Future research should consider a systems approach to improve understanding of the ecologic causal pathways surrounding intergenerational undernutrition.

6.6 Tables

Table 7: Descriptive statistics of the JiVitA-1 population of infants assessed between 2001 and 2007

	Mean	**SD**
Child		
MUAC Growth Rate	0.02	0.01
Gestational Age (weeks)	37.86	2.84
Early Neonatal MUAC (cm)	9.46	1.08
Mid-Infancy MUAC (cm)	13.00	1.04
Female (%)	49.59%	
Mother		
MUAC (cm)	22.97	2.00
Age (years)	21.89	5.86
Breastfed at 6 months (%)	99.27%	
Socioeconomic		
Household LSI	0.17	1.01
Maternal Education	4.27	4.04
Context		
Average LSI*†	-0.02	0.36
Average Maternal Education†	3.46	1.24
Gini Coefficient‡§	0.01	0.05
Pop. Density (100ppl/sq. km)	5.49	1.31
Elevation (m)	25.45	1.88

* Living Standards Index

† Includes neighbors within a 200 meter radius

‡ Includes neighbors within a 2000 meter radius

§ Mean Centered

Table 8: Simple linear regression results

	Coef.	SE	t value	R²
Child				
Newborn MUAC (scaled)	-0.58	0.006621	-87.833	0.327
Gestational Age (weeks)	-0.04	0.002799	-14.65	0.013
Female	-0.32	0.01566	-20.46	0.026
Mother				
MUAC (cm)	0.01	0.00396	3.274	0.001
Age (years)	0.00	0.00136	-3.252	0.001
Breastfed	0.52	0.09932	5.235	0.002
Socioeconomic				
Household LSI*	0.00	0.007838	0.289	0.000
Maternal Education	0.00	0.001966	-0.37	0.000
Context				
Average LSI*†	0.05	0.024072	2.029	0.000
Average Maternal Education†	0.00	0.006858	0.705	0.000
Gini Coefficient‡§	-1.14	1.79E-01	-6.331	0.003
Pop. Den. (100ppl/sq. km)	-0.01	0.006592	-1.062	0.000
Elevation (m)	0.01	0.004483	2.061	0.000

Coefficient values are changes in standard deviation in scaled and centered MUAC from the JiVitA-1 population of 17,244 infants

* Living Standards Index

† Includes neighbors within a 200 meter radius

‡ Includes neighbors within a 2000 meter radius

§ Mean Centered

Table 9: Multivariate regression results

	Model 1: Child			Model 2: Mother			Model 3: SES			Model 4: Context			Model 5: Context + Interactions		
Variables	**Est.**	**SE**	**t value**	**Est.**	**SE**	**t value**	**Est.**	**SE**	**t value**	**Est.**	**SE**	**t value**	**Est.**	**SE**	**t value**
Intercept	-0.269	0.09	-2.91	-2.619	0.16	-16.06	-2.616	0.16	-16.13	-2.607	0.19	-13.87	-2.552	0.19	-13.62
Child															
Gestational Age (weeks)	0.012	0.00	5.25	0.009	0.00	3.79	0.008	0.00	3.50	0.008	0.00	3.35	0.006	0.00	2.49
Newborn MUAC ‖	-0.597	0.01	-88.98	-0.620	0.01	-92.19	-0.634	0.01	-93.91	-0.639	0.01	-94.65	-0.512	0.01	-87.08
Female	-0.354	0.01	-27.72	-0.356	0.01	-28.25	-0.354	0.01	-28.27	-0.351	0.01	-28.13	-0.352	0.01	-28.31
Mother															
MUAC (cm)				0.069	0.00	16.95	0.062	0.00	15.20	0.058	0.00	14.27	0.058	0.00	14.22
MUAC: > 26 (cm)				-0.002	0.00	-2.12	-0.004	0.00	-3.38	-0.003	0.00	-3.12	-0.003	0.00	-2.46
Age (years)				0.012	0.00	3.19	0.016	0.00	4.40	0.016	0.00	4.20	0.017	0.00	4.49
Age: > 21 (years)				-0.022	0.00	-4.68	-0.023	0.00	-5.00	-0.022	0.00	-4.73	-0.023	0.00	-5.01
Breastfed at six months				0.737	0.07	9.94	0.794	0.07	10.76	0.793	0.07	10.81	0.794	0.07	10.87
Socioeconomic															
Household LSI*							0.064	0.01	8.19	0.059	0.01	7.17	0.291	0.01	7.67
Maternal Education							0.011	0.00	5.45	0.009	0.00	4.29	0.010	0.00	4.94
Context															
Average LSI*†										-0.005	0.03	-0.17	1.282	0.24	5.29
Average Maternal Education†										0.020	0.01	2.42	0.019	0.01	2.32
Mean Centered Local Gini Coefficient (w/in 2000m)										-1.660	0.16	-10.11	-1.640	0.16	-10.03
Pop. Den. (100ppl/sq. km)										0.011	0.01	1.98	0.012	0.01	2.16
Elevation (m)										0.000	0.00	-0.12	0.000	0.00	0.01
Newborn MUAC x LSI*													-0.062	0.01	-10.67
Average LSI† x Gestational Age													-0.034	0.01	-5.31
R^2	**0.359**			**0.3802**			**0.3883**			**0.395**			**0.4008**		
AIC	**37998.75**			**37132.81**			**36912.77**			**36673.41**			**36521.9**		

Coefficient values are changes in standard deviation in scaled and centered MUAC from the JiVitA-1 population of 17,244 infants

* Living Standards Index

† Includes neighbors within a 200 meter radius

‡ Includes neighbors within a 2000 meter radius

§ Mean Centered

‖ Standard deviation

6.7 Figures

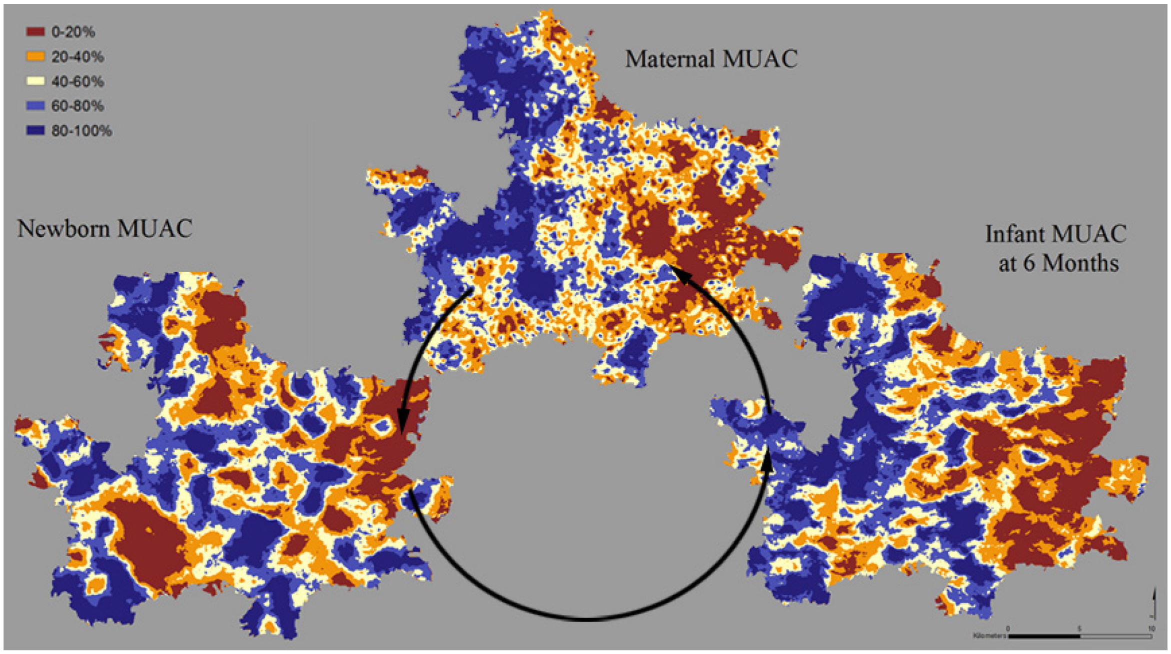

Figure 15: Intergenerational spatial patterning across the JiVitA study site

This figure depicts the spatial patterning in mid-upper arm circumference (MUAC) observed by quintile across the JiVitA study site for mothers and their children as newborns and at approximately six months of life. Dark blue/brown indicates the largest/thinnest MUAC. Note the relative homogeneity of MUAC distribution at birth, turning into a near-mirror image of maternal MUAC gradient by 6 months of life.

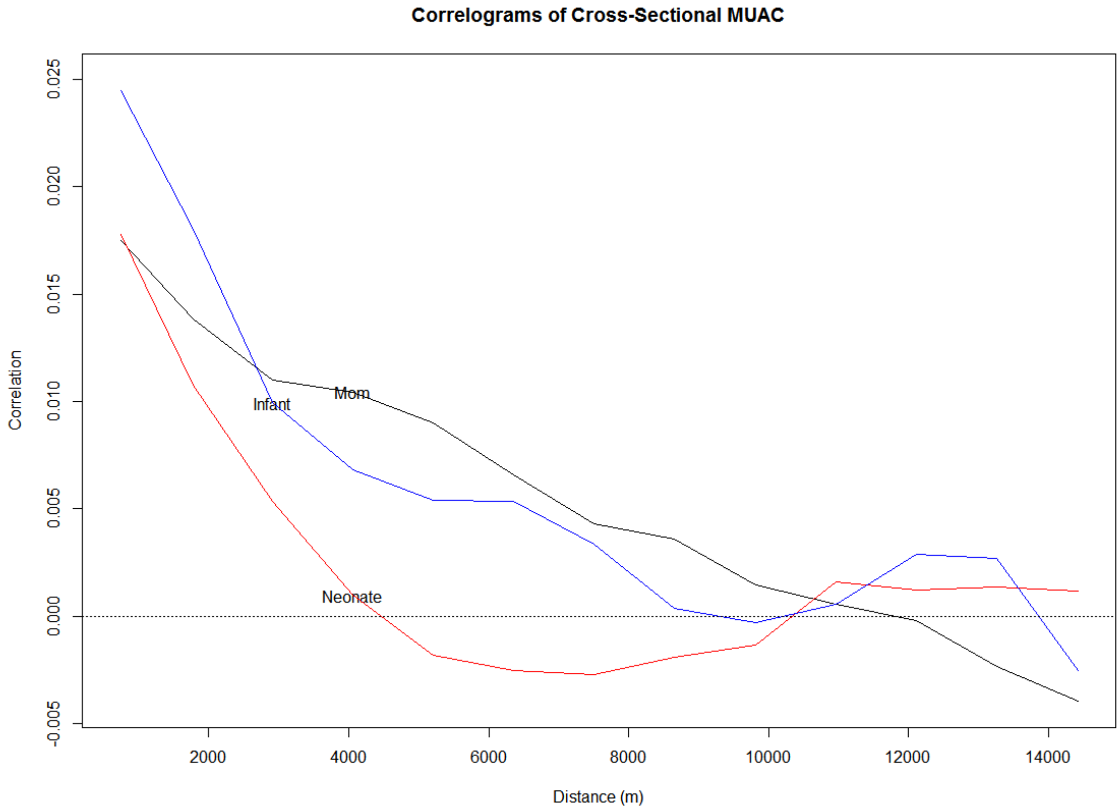

Figure 16: Correlograms of Mid-upper Arm Circumference

Correlograms depicting spatial correlation between observations in population of mothers, newborns and infants at six months. Mom (black) = Unadjusted Maternal MUAC; Neonate (red) = Unadjusted Newborn MUAC; Infant (blue) = Unadjusted Infant MUAC at about six months. The dashed line indicates the point of zero correlation. Correlation is on the y-axis and distance, in meters, is on the x-axis. Note quick reduction of correlation with distance in the neonatal/newborn group compared to the more sustained trends in mothers and infants at roughly six months

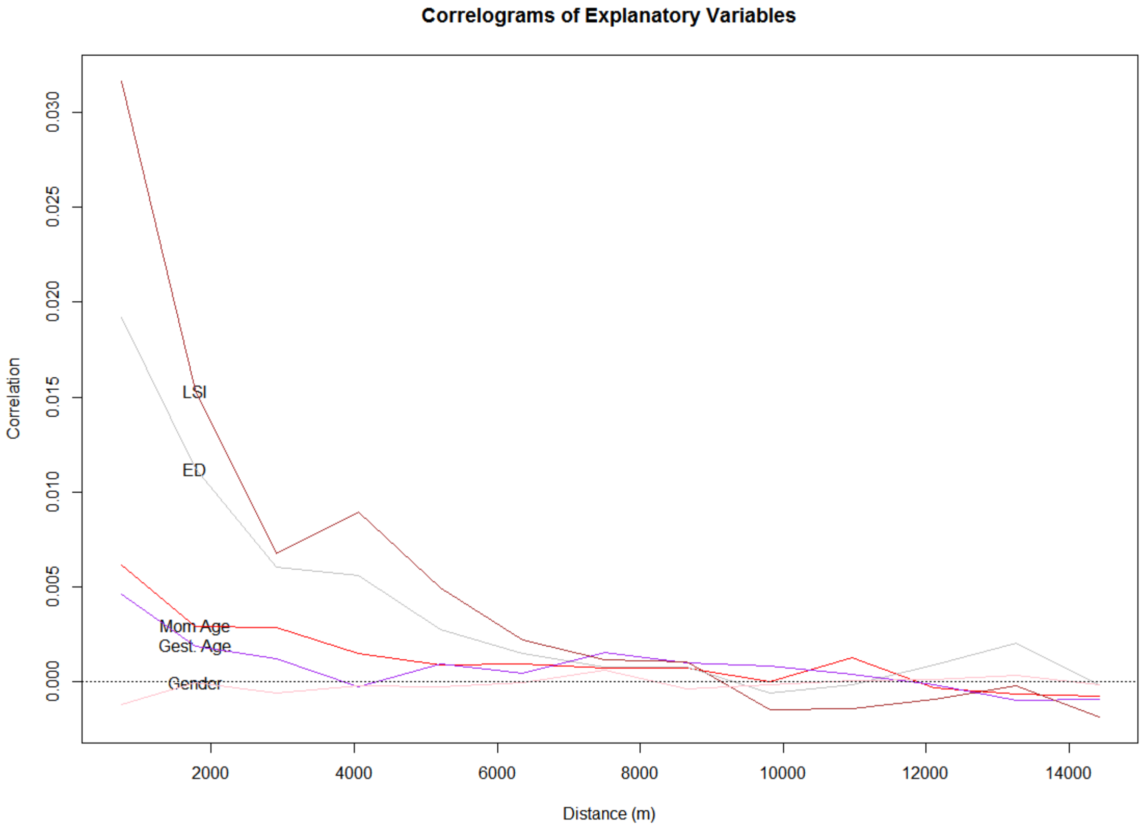

Figure 17: Correlograms of select explanatory variables

Correlograms depicting spatial correlation between observations' selected explanatory variables. LSI (maroon) = Household Living Standards Index; ED (gray) = Maternal educational attainment; Mom Age(red) = Maternal age; Gender (purple) = Child gender. The dashed line indicates the point of zero correlation. Correlation is on the y-axis and distance, in meters, is on the x-axis. This figure shows the relative scale of difference in the spatial correlation found in select variables. Note the spatial correlation of education and LSI compared to the randomness found in the spatial distribution of maternal age, gestational age and gender.

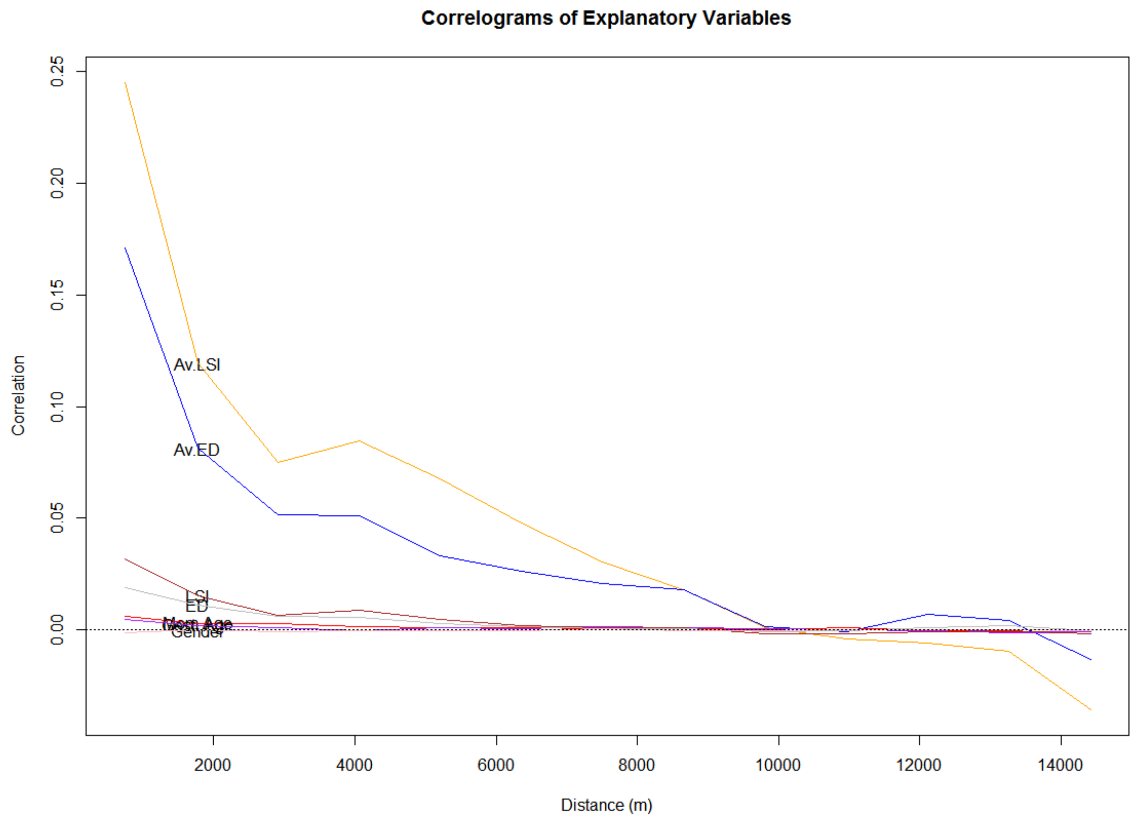

Figure 18: Correlograms of select explanatory variables

Correlograms depicting spatial correlation between observations' selected explanatory variables. Av. LSI (Gold) = Neighborhood (200 m) average Living Standards Index; Av. ED (blue) = Neighborhood (200 m) average maternal educational attainment; LSI (maroon) = Household Living Standards Index; ED (gray) = Maternal educational attainment; Mom Age (red) = Maternal age; Gender (purple) = Child gender. The dashed line indicates the point of zero correlation. Correlation is on the y-axis and distance, in meters, is on the x-axis. This figure shows the relative scale of difference in the spatial correlation found in select variables and how contextual variables are far more correlated than those at the individual and household levels.

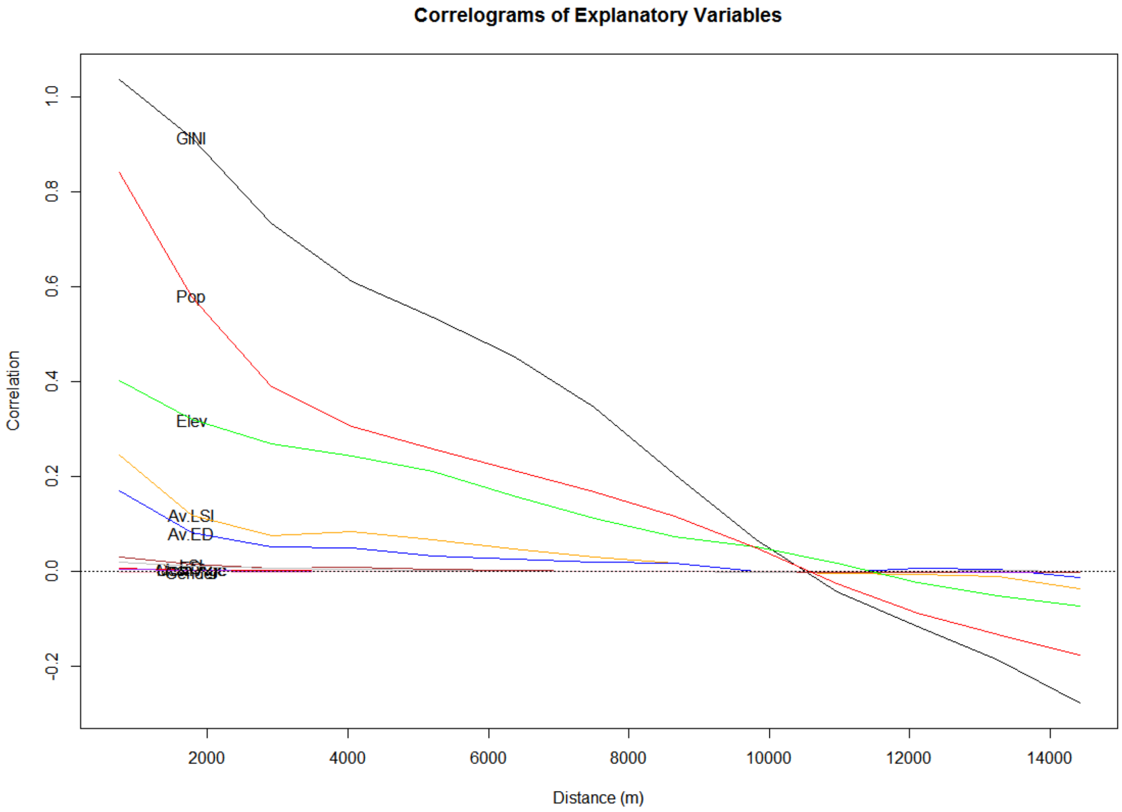

Figure 19: Correlograms of select explanatory variables

Correlograms depicting spatial correlation between observations' selected explanatory variables. GINI (black) = Local (2 km) inequality measured by the Gini coefficient; Pop (red) = Population density; Elev (green) = Household elevation; Av. LSI (Gold) = Neighborhood (200 m) average Living Standards Index; Av. ED (blue) = Neighborhood (200 m) average maternal educational attainment; LSI (maroon) = Household Living Standards Index; ED (gray) = Maternal educational attainment; Mom Age(red) = Maternal age; Gender (purple) = Child gender. The dashed line indicates the point of zero correlation. Correlation is on the y-axis and distance, in meters, is on the x-axis. This figure shows the relative scale of difference in the spatial correlation found in select variables and how contextual variables are far more correlated than those at the individual and household levels.

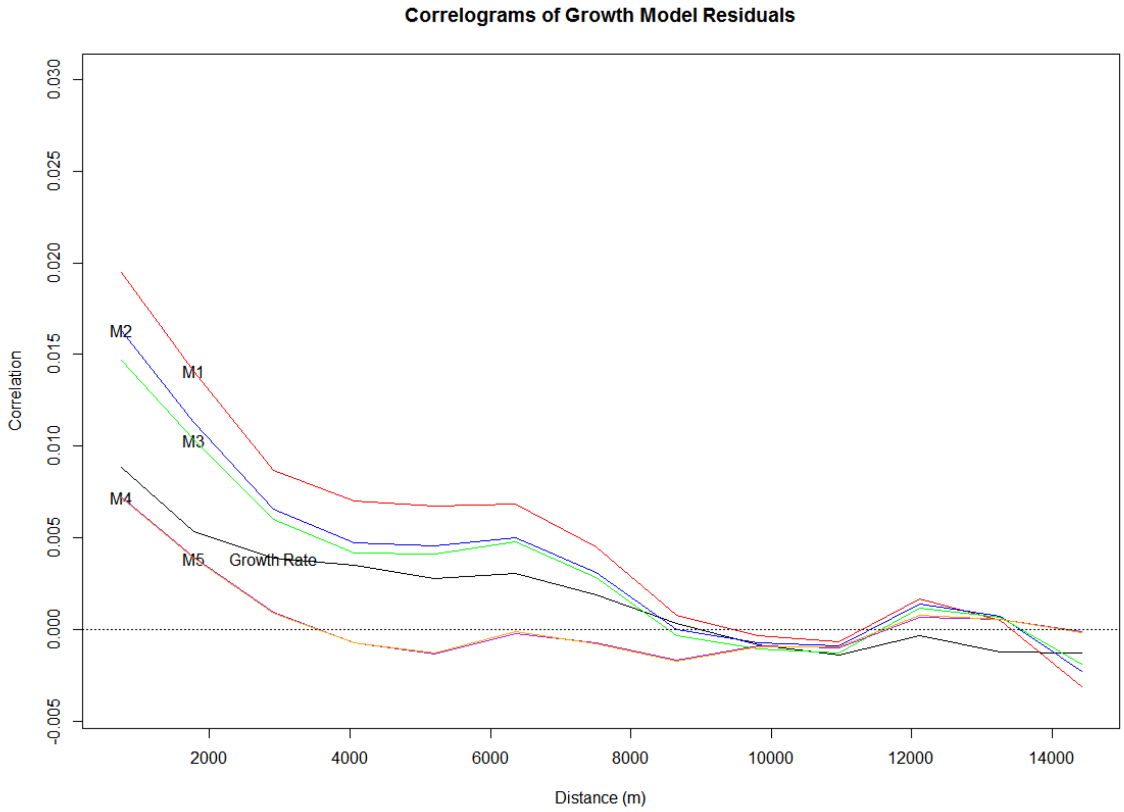

Figure 20: Correlograms of residual spatial auto-correlation from regression models

Correlograms depicting spatial correlation between observations and explanatory models in the mid-infancy group. Growth Rate (black) = Unadjusted change in infant MUAC between birth and roughly six months of age; M1(red) = Child Model; M2 (blue) = Mother Model; M3 (green) = Socioeconomic Model; M4 (orange) = Community Model; M5 (yellow) = Community Model with interactions. The dashed line indicates the point of zero correlation. Correlation is on the y-axis and distance, in meters, is on the x-axis. Note how inclusion of individual-level variables removes spatial randomness and increases correlation in M1, M2, and M3, and context level variables account for much of the observed spatial correlation.

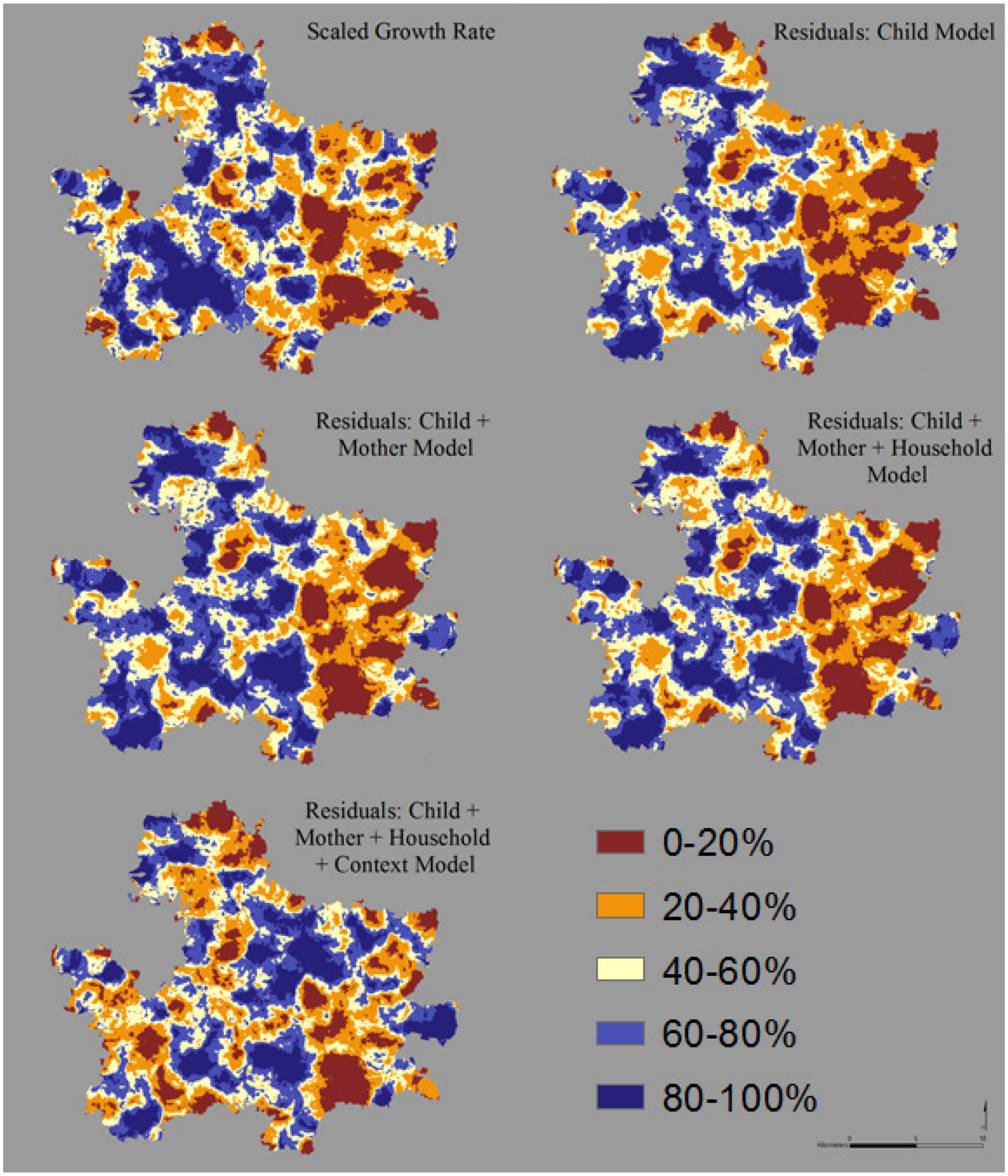

Figure 21: Spatial trends in growth model residuals with addition of variable levels

This figure depicts the change in spatial trends of residual values after accounting for variables at the child, mother, household, and contextual levels. Note, concomitant with Figure 19, the spatial patterning in growth rates becomes more pronounced with the addition of child variables, then is reduced with the addition of mother and household variables, and nearly disappears after adding contextual variables.

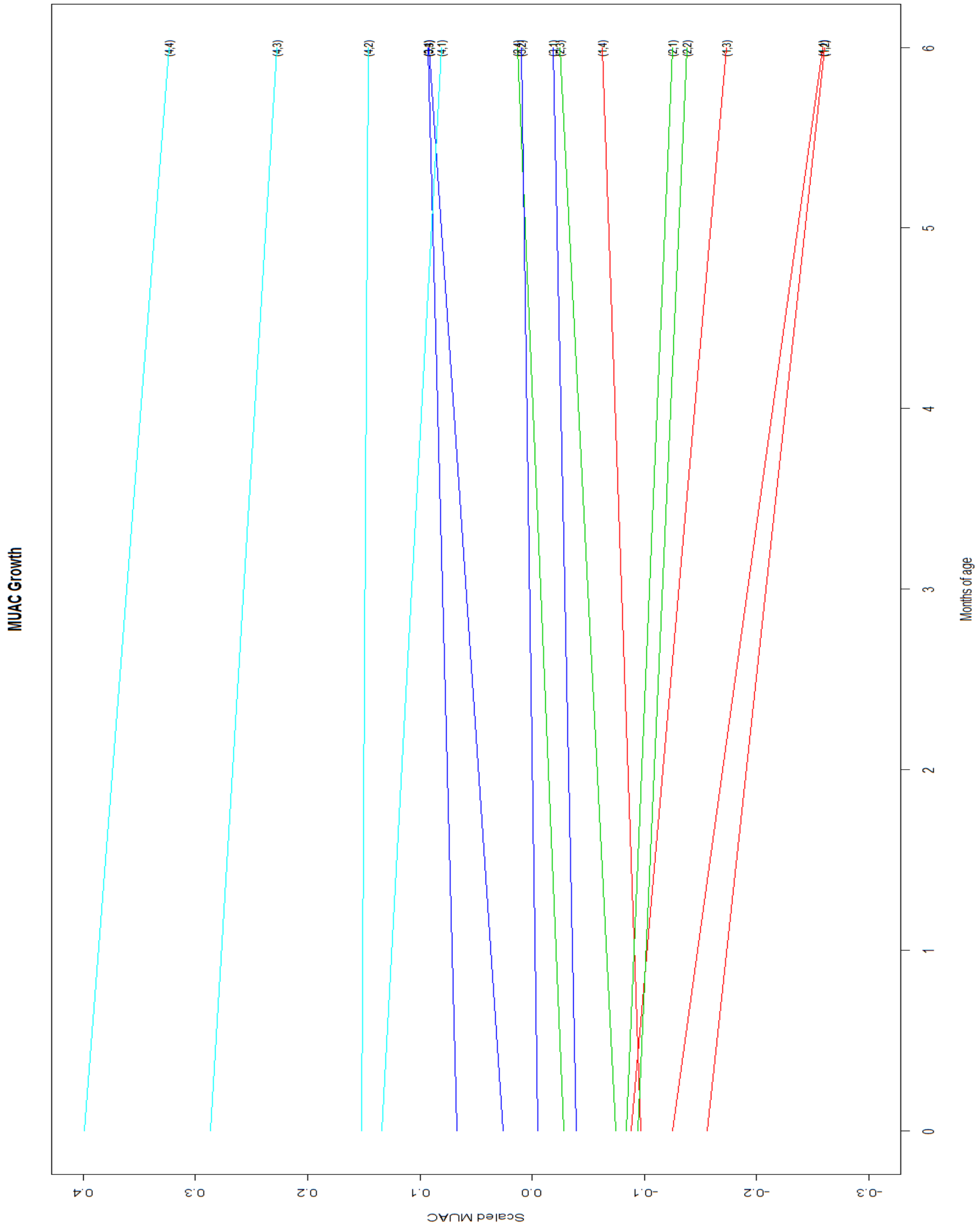

Figure 22: Mean change in child MUAC between birth and six months subset by quantile household LSI and neighborhood average LSI

Colored by individual LSI (highest:lowest, LSI = Light blue, dark blue, green, red). Numbers in parentheses are highest:lowest, 4:1 (Individual LSI, Neighborhood average LSI). Note how, generally, the nutritional status of those in each individual economic strata is modified by the neighborhood economic status, with those living in the wealthiest neighborhood doing far better than their economic peers residing in poorer neighborhoods.

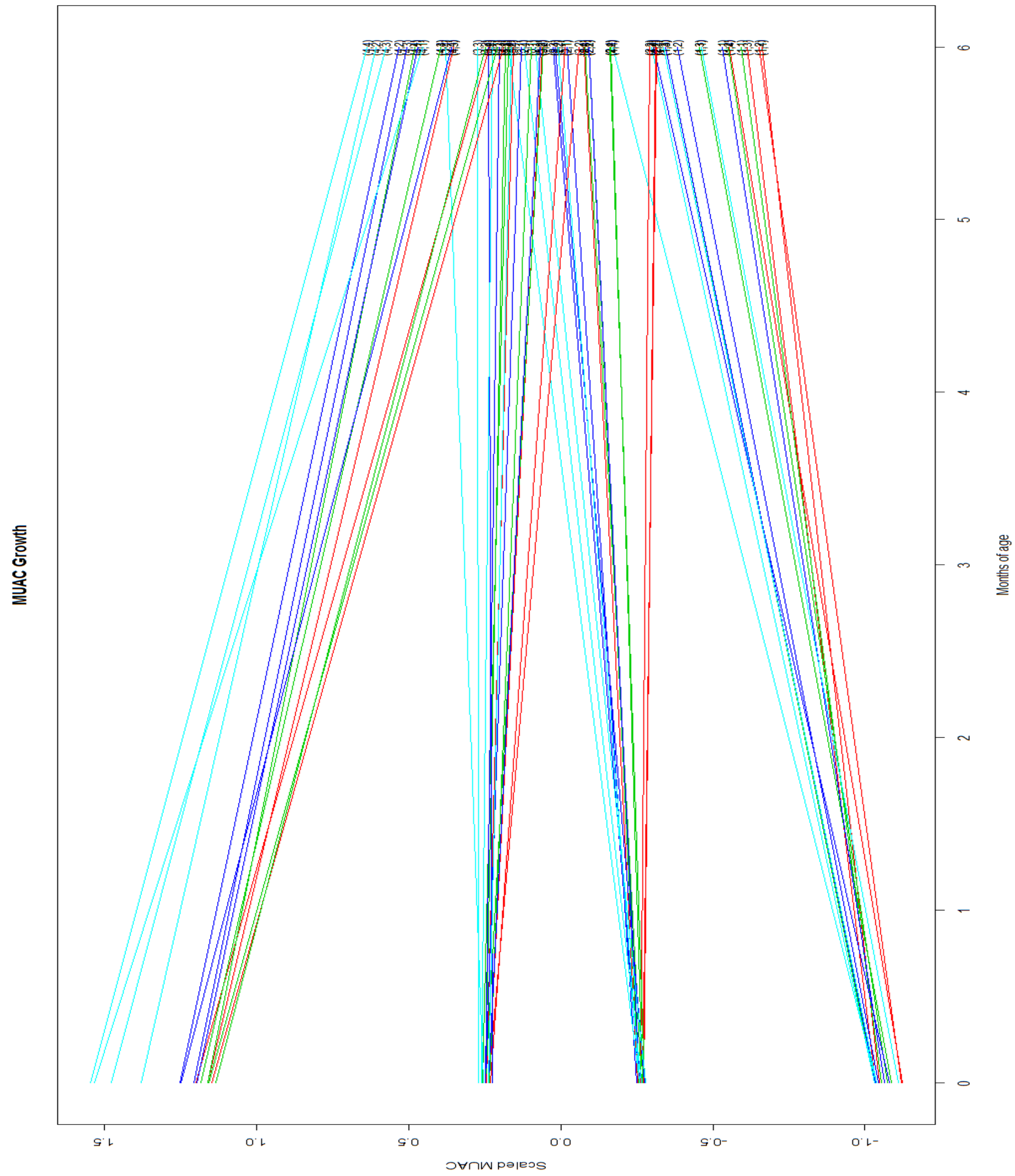

Figure 23: Mean change in child MUAC between birth and six months subset by birth MUAC, household LSI and neighborhood average LSI quantiles

Colored by individual LSI (highest:lowest LSI = Light blue, dark blue, green, red). Numbers in parentheses are highest:lowest, 4:1 (Birth MUAC, Neighborhood average LSI). Note how, generally, the nutritional status of those in each individual economic strata is modified by the neighborhood economic status, even after stratifying by birth size, with those living in the wealthiest neighborhood doing far better than their economic peers residing in poorer neighborhoods.

Chapter 7 Conclusions

The objective of this doctoral research was to investigate the manner in which individual nutritional status is influences by one's location, as it pertains to community members and context, as well as inter-generational forces. This analysis identified characteristics of community context which influenced nutritional status and evaluated their relative contributions and interactions after accounting for salient individual and household effects established in the literature. Age-specific effects at the individual, household and contextual levels were explored at three key time-points: expectant mothers, newborns and infants at six months. This analysis also considered how nutritional status at each time point related to one another and ultimately determine anthropometric growth trajectories early in life. Furthermore, this research assessed spatial correlation between observed dependent and independent variables of interest and described how attributes at various levels contribute to spatial patterning. A holistic systems science approach was employed to achieve the research objectives of this dissertation which demonstrated statistical and explanatory benefits.

7.1 Summary of results

To break the cycle of intergenerational malnutrition we need to focus on the health and nutritional status of women prior to conception. In our population of expectant mothers the median MUAC was 22.6cm, and for 50%, their MUAC was <22cm, a cutoff conventionally used to identify wasting in adult women [77,354]. Others, however, have suggested higher cutoffs to determine pregnant women at risk for LBW, SGA and neonatal morbidity [17,363,364]. Karim et al. (1997) found the odds of pregnant Bangladeshi women with MUAC under 23cm to be five times greater than those with greater MUAC[17]. Using a cutoff of 23.5 cm, Lechtig (1988) reported odds of LBW to be eight times higher in undernourished pregnant Brazilian women. This was apparent in our analysis as nearly 50% of the newborn population was below the 9 cm cutoff associated with

LBW[13,68,69,71]. At six months, roughly 50% were below 1 SD and 25% were below 2 SD the WHO MUAC-for-age reference mean. Nearly 5% would be identified as have severe acute malnutrition having MUAC below 11.5 cm, based on the WHO and UNICEF 2009 guidelines.

Initial MUAC was a chief determinant of growth trajectories as it explained about 33% of the variation. Infant MUAC increased, on average, by about 0.64 ± 0.21cm per month. Differences in growth trajectories, after accounting for birth size, gestational age and infant gender, were determined through differences in biological features of the mother as well as household and community socioeconomic circumstance. Similarly, Klemm (2002) noted initial anthropometry accounted 40-60% of growth variation until infants were six months of age, however, only accounted for 4-22% between six and eleven months of age[365].

When the age-groups were explored cross-sectionally, individual characteristics account for the greatest proportion of the variance accounted for by our models which included variables at all levels. However, the proportion of variance accounted for by household and community variables increased from newborns, to infants, and then, substantially, in mothers (see Figure 23). This could indicate a longitudinal trend of increasing nutritional influence from the environment. Seasonality had a greater influence in newborns and mothers than in infants.

Since the outcomes were centered and scaled, coefficients are interpreted as differences in population standard deviations for one unit change in a given independent variable. Therefore, effect comparisons can be made between our three age-group populations and age-specific effects can be observed. For example, with a one unit increase in household LSI, the MUAC of a given newborn is, on average, 0.09 SD larger, however, the increase is 0.1 SD and 0.21 SD for infants and mothers. These estimates indicate mothers stand to gain a much greater nutritional benefit with a single unit increase in household LSI than infants or newborns. Maternal educational, on the other hand, has a fairly constant effect with newborns, infants and mothers increasing MUAC by 0.020, 0.011, and 0.016 SD per additional year attained. Maternal education, while generally being a strong variable at both the individual and contextual levels in all three analyses, was particularly important for newborn nutritional status. Coefficient values can be seen for select individual and household characteristics in Figure 24 and for contextual characteristics in Figure 25. Variables associated with infectious agents, such as unimproved sanitation, household size, and hand-washing tending to have a greater effect in infants and mothers.

Variables which only applied to the infant groups also demonstrated age-specific effects (see Figure 26). The effect of breastfeeding, gender, and maternal nutritional status were notably larger in mid-infancy, than at birth. Maternal age had a nearly constant effect. Parity had an inverse effect as it was beneficial at birth and detrimental later in infancy, this could, however, be related to birth-order and the shared resources and infections associated with having siblings. Conversely, the effect of gestational age diminished with age. Factors like gestational age, which are associated with birth size, may account for less variation in anthropometry later in childhood.

This dissertation demonstrated the research advantages of taking a more holistic systems biology approach to understanding differences in nutritional status. Individual factors had significant interactions with household- and community-level characteristics which helped explain differences in infant growth trajectories. Neighborhood average SES played a significant role in sorting infant anthropometry between birth and six months, more-so than individual-level SES. Figure 27 displays the average changes in infant MUAC between birth and six months subset by individual LSI quantile and neighborhood average LSI quantile. Infants of higher individual wealth tend to be born larger and stay larger than their poorer counterparts. This association is, however, modified by neighborhood average LSI. Infants born to less wealthy households still enjoy the benefits of residing in wealthier neighborhoods, in some cases, surpassing the average growth of infants from wealthier households residing in poorer neighborhoods.

Even though much of the literature cites SES to be one of the more promising determinants of nutritional status, when this association was explored, stratifying infants by individual and community level LSI *and* maternal MUAC, alarming results were found. Children born to healthier mothers (light blue) tended to maintain their relative healthier nutritional status compared to children born to mothers with smaller MUAC. The stratified growth trajectories of infants tended to maintain similar nutritional ranking relative to their peers, however their average slopes were diverging, modified by both community and household wealth (see Figure 28 & Figure 29).

Local inequality was a major contextual contributor to nutritional status in all three analyses. It explained significant differences in maternal MUAC, infant MUAC at six months of age, and MUAC growth trajectories. Local inequality accounted for substantial residual spatial correlation in our regression analyses. In our exploratory stratified analysis, local inequality modified the associations between infant growth trajectories and maternal MUAC (Figure 30), household LSI (Figure 31), neighborhood average LSI (Figure 32). Differences in nutritional status associated with local GINI coefficients were scale dependent, responded to inequality calculated over a greater spatial area, which others have also found [21,190]. Previous research also found inequality to be associate with higher rates of stunting[21,190], greater food poverty [235], and higher preventable and immediate death rates [325].

In addition to the contextual variables previously discussed, many exogenous effects were considered, which were not included in the full regression analyses, due to multi-collinearity with stronger variables. These contextual correlations did, however, help describe the multifactorial conditions accompanying neighborhood wealth. Wealthier neighborhoods had higher maternal educational attainment, were more economically homogenous, were closer to health service providers, permanent bazaars, and paved roads, and were in areas of higher elevation and reduced flood risk. People in wealthier neighborhoods were more likely to own a non-laundry bar of soap, have improved sanitary facilities, and wash their hands before eating and after defecating. Those living in wealthier neighborhoods typically enjoy holistically healthier environments which may reinforce the benefits of greater household and neighborhood SES.

7.2 Intervention Implications

The findings from this thesis research suggest intervention efforts intending to break intergenerational malnutrition should focus on improving maternal nutritional status, increasing maternal education at the individual and neighborhood level and creating healthier environments. These recommendations complement those of Underwood (2002) to interrupt the intergenerational consequences of malnutrition. They suggest intervention efforts should focus on adolescent girls, pregnant women and lactating women and their children up to 2 years, with particular focus on women in the pre-conception period [362]. These recommendations have also been made by several others [18,45–47,366].

Interventions improving nutritional status of soon-to-be mothers, which is related to the birth size, gestational age at birth, and ultimately to infant growth rate, could provide the greatest impact for future generations. Strategies should include interventions at multiple levels. Individual-level interventions, such as food and micronutrient supplementation, would be complimented by nutrition education classes, family planning services, and prenatal care provided at the community level and regional/national-level interventions such as radio, television and other mass-media educational campaign or custom information exchanged through mobile phones.

Infants born to poor households residing in poorer neighborhoods with greater economic inequality were observed to have lower nutritional status than similarly poor households in wealthier more economically equal neighborhoods. Intervention strategies targeting ‘at risk’ individuals, residing in ‘at risk’ neighborhoods, could be a more effective strategy than targeting individuals or geographic regions alone. Storeygard et al. (2008) reported, globally, half of all infant deaths occur in 2.5% of the world’s populated land area where 29.3% of the global population resides. Intervention efforts focusing in the regions with the greatest mortality density could provide the benefit of heath resources to the greatest number in need with limited administrative costs. Fenn et al. 2007 considered geographically targeted intervention coverage. Authors concluded nutritional status is primarily determined by individual and household characteristics, compared to community context; however, given the hurdles of blanket coverage, also suggested resource allocation to high risk regions to selected high risk individuals as a possible cost-effective strategy.

Reliable health data from civil registration are only available from 38 countries over the past decade, most of which are developed [2], and only account for about 3% of global deaths in children [1,367]. This leaves the majority of child deaths as statistical estimates [1,2,367]. Mortality data are rarely available at subnational levels, making geographic targeting of health interventions more difficult. Public and private investments in public health should make timely location-based health surveillance and tracking data collection a central priority.

The growth of available and ubiquitous mobile technology may provide viable health surveillance and tracking solutions. Mobile phone ownership grew from 1 billion in 2000 to nearly 6 billion in 2012 [368]. In 2010, approximately 77% of mobile phones were in developing countries, increasing from 22% in 2000 [368]. Mobile technology has made location-specific data collection far more accessible and affordable. Furthermore, the internet has become a critical medium for the acquisition, dissemination and transmission of information. Analysis of internet queries and social media exchanges have provided promising low-cost surveillance tools for timely and location specific (based on IP address) disease surveillance [369]. Health workers can use mobile technology in the field to collect mortality and morbidity information which can be spatially referenced.

7.3 Limitations

This doctoral research could have been limited in the following ways. First, the variables examined in our analysis represent a sample of the most salient variables indicated in the literature, and thus do not include all known and unknown effects at each level. As a result, the proportion of the variance accounted for by each level is only a result of the respective variable samples. Contextual variables such as land use, soil type, climate, local polluting facilities, indoor and outdoor air quality, seasonal fluctuations in liquid income as well as others discussed in Chapter 2 have been associated with nutritional and health status, however were not included in these analyses. In many cases data were not extant, readily available or reliable. Intermittent climate data were acquired from a weather station located in Rangpur, a city located about 80 km to the north of the study area, however, no clear associations were found either directly, or when combined with flood data collected by the JiVitA project team. Dietary intake was also cited as a direct determinate of nutritional status. Unfortunately these data were not available. Information was collected regarding mothers' dietary diversity with a focus on foods containing vitamin A, which was the focus of the JiVitA-1 supplementation trial. Multiple techniques were attempted to include dietary diversity as a proxy for intake, however, no model improvements were observed. Additionally, pervious work has suggested the period of poverty (permanent vs. contemporaneous) was related to greater risk of restricted inter-uterine growth[19]. Data detailing the tenure of poverty exposure were not available for this analysis and could have provided greater explanation for differences in infant growth.

Second, this analysis only considered anthropometric measurements made at two time-points during infancy. Measurements were attempted at precise time intervals (i.e. 0, 3 and 6 months), however, for multitude of reasons, and they occurred earlier or later than the intended time point. Some observations were dropped because anthropometric measurements were not made within the mid-infancy window (5 – 7 months). Age differences at mid-infancy were adjusted for based on estimated days since birth. Furthermore, data were only collected at birth for a subset of the greater study cohort, limiting longitudinal hypotheses. This is a particular limitation given the importance of birth anthropometry as it relates to growth, future anthropometry and morbidity. These findings could have been more robust had this study had a longer observation period and complete data been collected precisely at all time-points.

7.4 Generalizability of results

Since data collection only occurred at one study location and many of the effects are context specific, our inferences may not be generalizable elsewhere. This analysis would need to be reproduced in different developing locales with diverse economic and environmental context characteristics for global inferences to be made. The site and population selected for the JiVitA-1 trial was, however, intended to be representative of rural southern Asia[67], therefore the validity of our inferences could be applicable in the region. Estimates are based on outcomes which were scaled to the study population and may not be transportable to other developing populations. Similar to many systems sciences in genetics, which attempt to completely sequence the genetic architecture of a specific species and establish all related biological pathways, our findings advance the understanding of similar human systems, however the magnitude and types of effects may differ between systems.

7.5 Recommendations for future research

This thesis research has validated the analytical benefits of a systems science approach to broaden the understanding of nutritional status. Nutritional status was affected by characteristics from multiple levels and observed these effects to change with age. This research also demonstrated the contributions of specific variables resulting in spatial patterning of nutritional status in mothers, newborns, infants and infant growth in the first six months of life. Based on the findings and methodologies of this dissertation, additional research could take several directions. Studies could continue to identify new multilevel ecological effects in this population, test the effects found in this research in a new locale, or delve deeper into the promising variables identified in this population to establish causality. There were several contextual variables which were not able to tested in these analyses due to data availability. Future research in this area explore more environmental characteristics associate with agriculture, soil type, land use, aspects of ground water, weather and climate, exposure to types of pollution, exposure to animal waste, and outdoor and indoor air quality. Social and economic variables which could also be considered are seasonal fluctuations of liquid income and exchange of funds, goods and services.

This research established associations between individual nutritional status and neighborhood economic structure, but did not establish the causal pathway. For example, neighborhood economic structure may be indicative of local elements of social capital such as trust, reciprocity, and social cohesion, which are reported to substantially affect individual health [200,232,259]. Lack of social order in communities has been associated with negative mental and physical health outcomes [200,232,259–262]. Furthermore, peer support has demonstrated positive effects on maternal and child health [11,232,248,263]. Qualitative research in these areas could potentially help elucidate the causal pathways between neighborhood economic structure and individual health outcomes in developing settings.

There was also additional information available from the JiVitA-1 dataset. Anthropometric measurements were made when infants were roughly three months of age. The three-month measurements were not in this research since the greatest change observed in the exploratory data analysis was between birth and six months of age. This time-point could help test the consistency and gradient of age-specific multilevel effects explored in this dissertation.

Future research could also consider changes in household context to test the temporality of the association and provide experimental evidence inferring causality. Data from the JiVitA-1 study indicate, of the 59,854 pregnant women enrolled in the study, 173 of them had moved by the time their child was born, and 230 had moved by the time their child was 6 months old. Comparisons could be made between these households and others which did not move but were in comparable neighborhood context. Given the size of the total dataset, these few households did not provide any notable differences, however, they were not considered at length.

The location information collected for this study is limited to the household location and does not account for full daily environmental exposure from places of employment, relatives'/friends' residences, and commutes. Some studies have suggested that GPS tracking of individual daily movement patterns provides greater precision in estimating environmental exposures [336,337]. Additional research should consider individuals' geospatial, familial and social networks as they pertain to child wellness, as this approach may help to tease out these systemic causal pathways and better ascertain contextual exposures.

Another consideration for future research which was not fully explored in this dissertation is different methods for calculating neighborhood social characteristics, such as average educational attainment and LSI, among others. Neighborhood calculations made in this dissertation were simple averages of neighbor values falling within the 200 m or 2000 m ranges. Future research may consider testing effect differences between this method and one which incorporates spatially weighted averages, weighting neighbors residing closer with greater influence.

Future research may also evaluate spatial variation of variable specific effects employing geospatially weight regression techniques. These techniques estimate regression coefficients spatially from nearby values allowing the effects and associated significance figures to vary over the surface of data. These methodologies are useful in determining effects that are context specific, however, are lesser used since they do not provide global effect estimates which are more accepted in the literature.

7.6 Figures

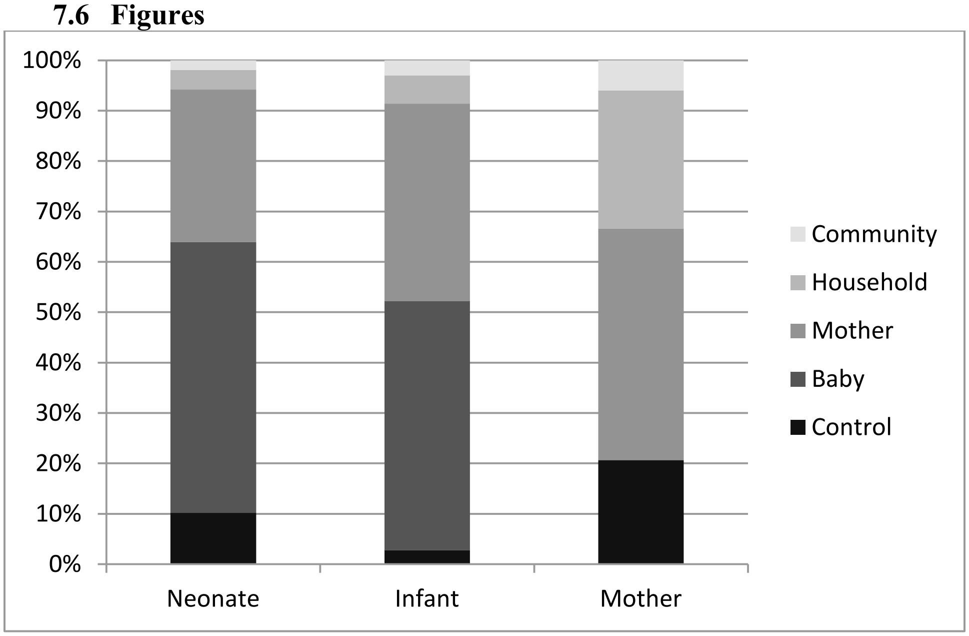

Figure 24: The proportion of total R^2 accounted for by each level of variables

This figure depicts that the proportion of R^2 accounted for by each level of variables from each respective full model. Note the proportion of variance accounted for by community and household variables increases with age between the three groups.

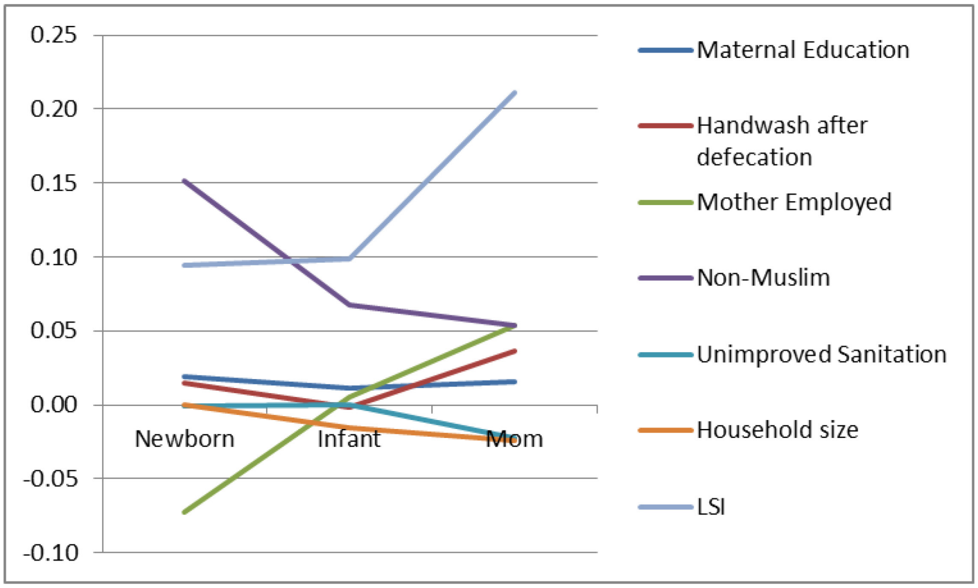

Figure 25: Change in select coefficient values between each age group

On the y-axis are units of standard deviation and age groups are indicated on the x-axis. This figure depicts the change in coefficient values between the three age groups.

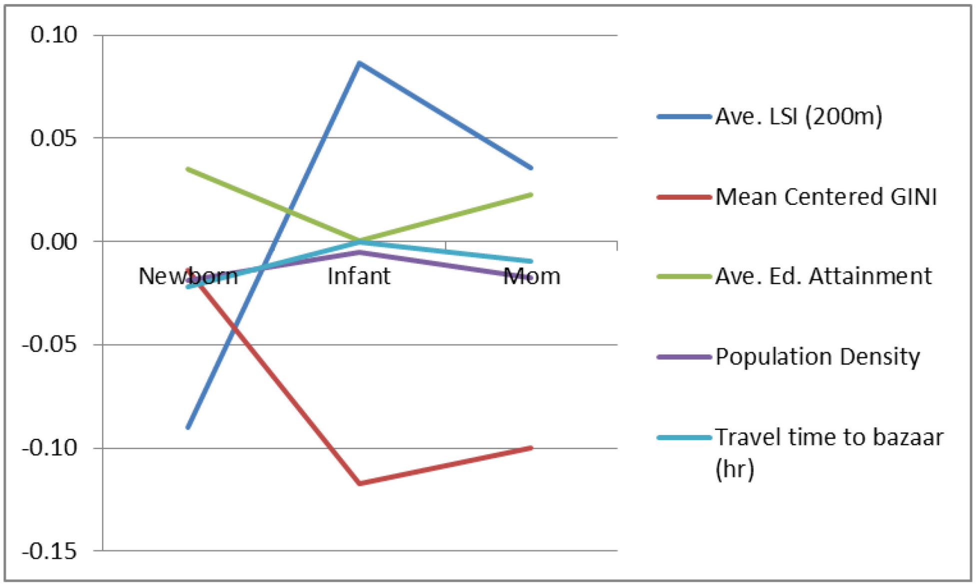

Figure 26: Change in select context variable coefficient values between each age group

On the y-axis are units of standard deviation and age groups are indicated on the x-axis. This figure depicts the change in coefficient values between the three age groups. Note the possible carry-over context effect between mother and newborn.

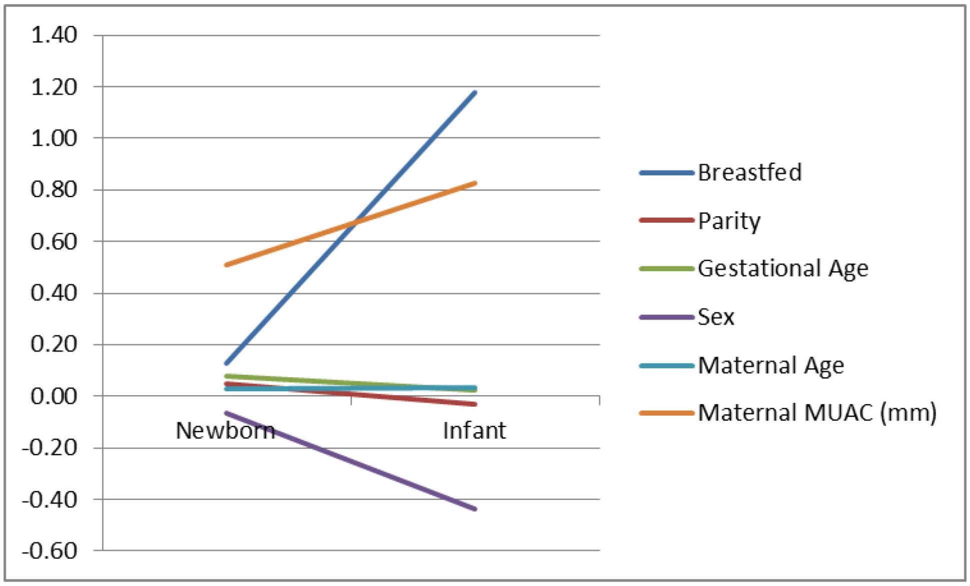

Figure 27: Change in select coefficient values between the newborn and mid-infancy age groups

On the y-axis are units of standard deviation and age groups are indicated on the x-axis. This figure depicts the change in coefficient values between birth and mid-infancy. Note the increasing influence with age of breastfeeding, maternal nutritional status, and child gender.

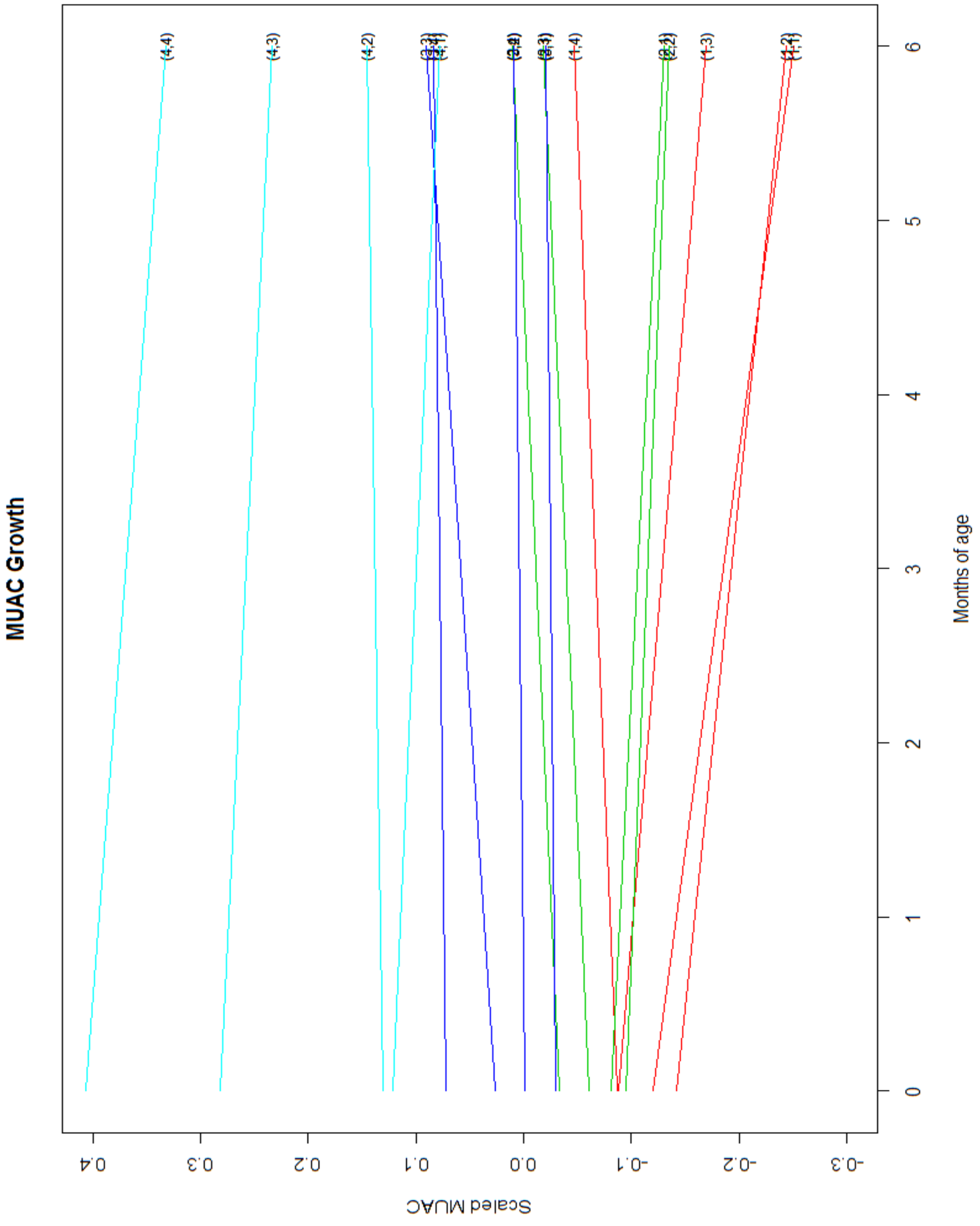

Figure 28: Mean change in child scaled MUAC between birth and six months subset by quantile household LSI and neighborhood average LSI

Colored by individual LSI (highest:lowest → Light blue, dark blue, green, red). Numbers in parentheses are highest:lowest, 4:1 (Individual LSI, Neighborhood average LSI). Note how, generally, the nutritional status of those in each individual economic strata is modified by the neighborhood economic status with those living in the wealthiest neighborhood doing far better than their economic peers residing in poorer neighborhoods.

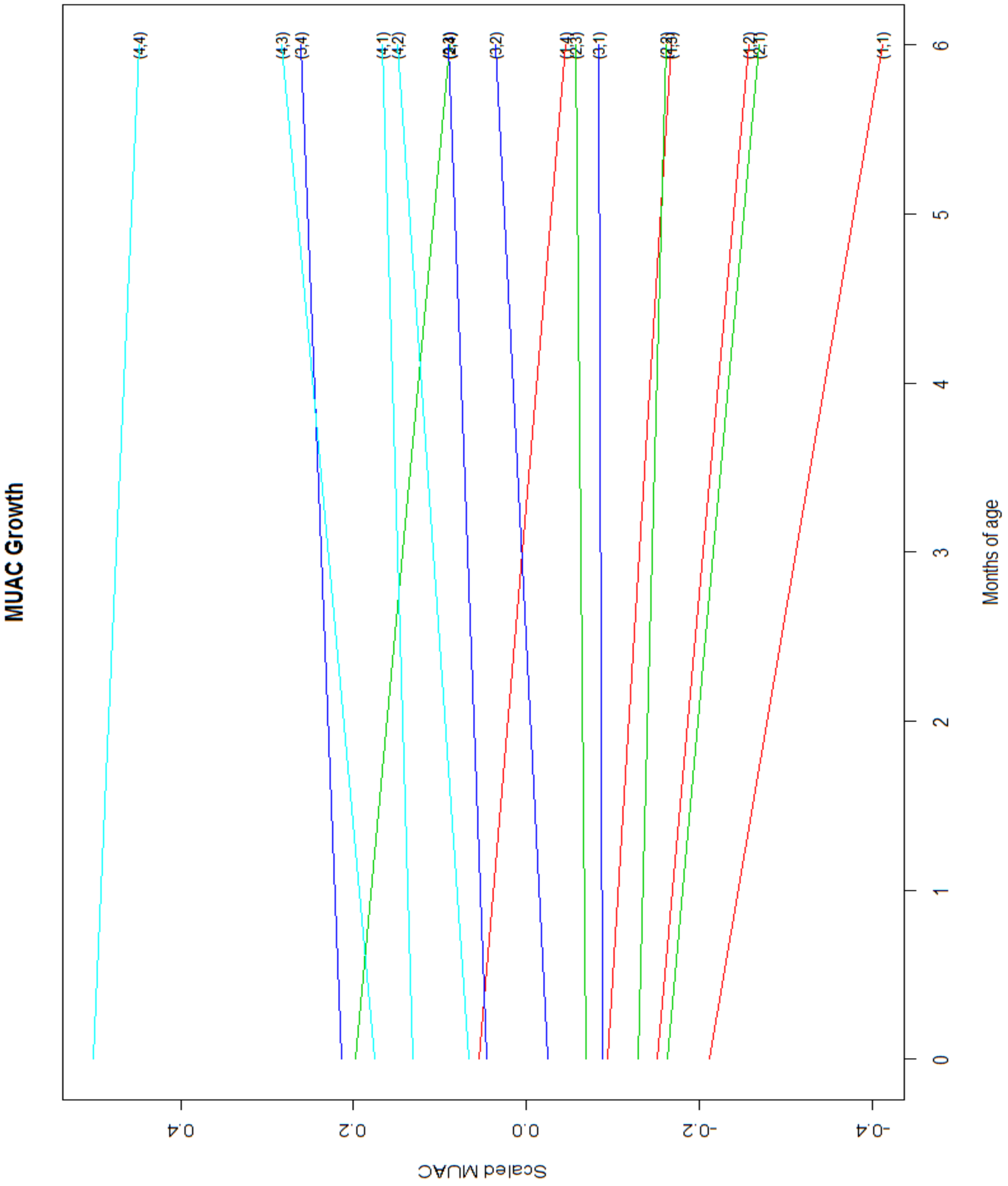

Figure 29: Mean change in child scaled MUAC between birth and six months subset by maternal MUAC and household LSI quantiles

Colored by Maternal MUAC (highest:lowest → Light blue, dark blue, green, red). Numbers in parentheses are highest:lowest, 4:1, (Maternal MUAC, Household LSI). Note how, generally, infant nutritional status is stratified by both maternal MUAC and Household economic status, with infants from healthier mothers and wealthier households increasing in nutritional status, compared to those with less favorable circumstance.

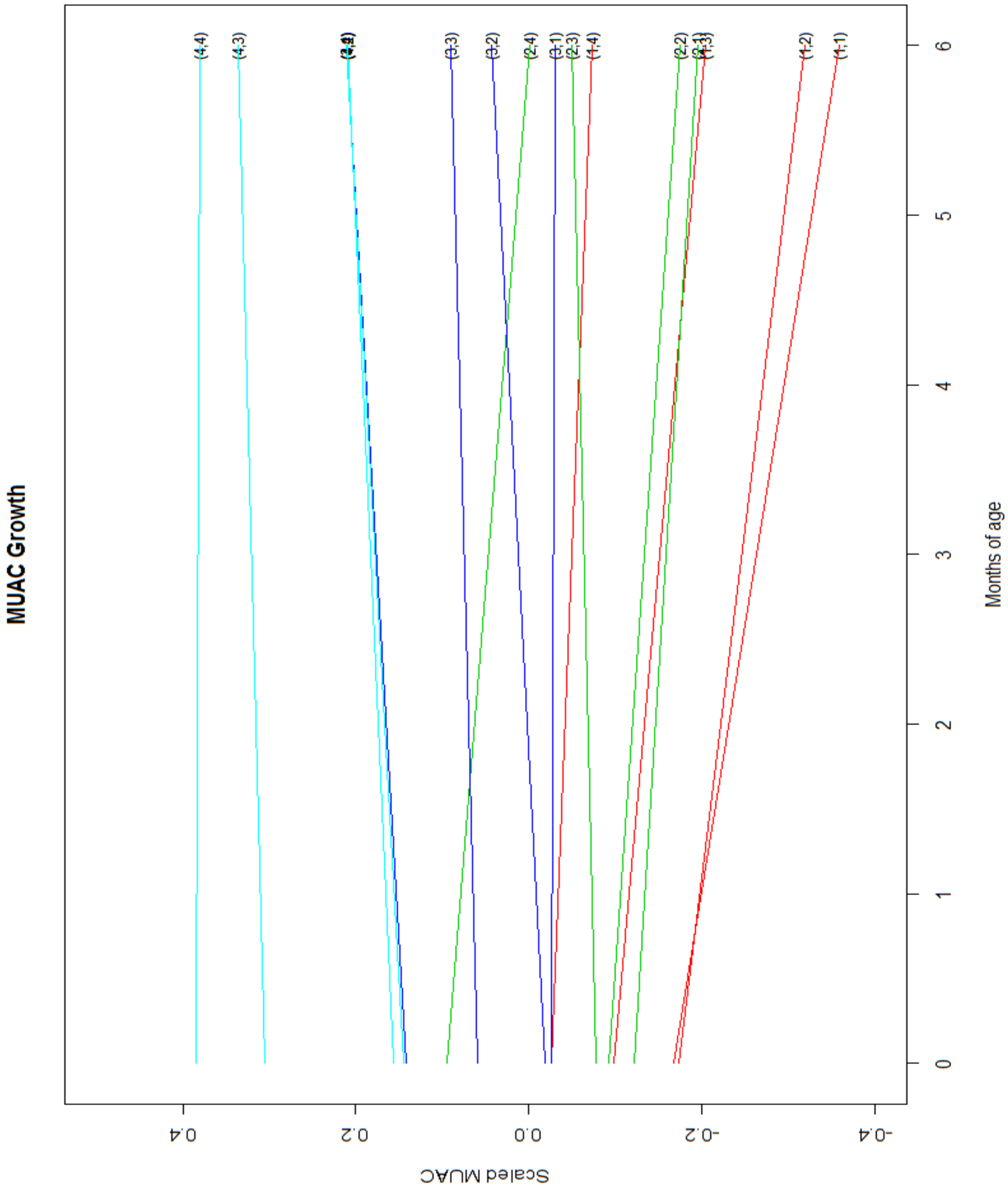

Figure 30: Mean change in child scaled MUAC between birth and six months subset by maternal MUAC and neighborhood average LSI quantiles

Colored by Maternal MUAC (highest:lowest → Light blue, dark blue, green, red). Numbers in parentheses are highest:lowest, 4:1, (Maternal MUAC, Neighborhood average LSI). Note how, generally, infant nutritional status is stratified by both maternal health and neighborhood wealth.

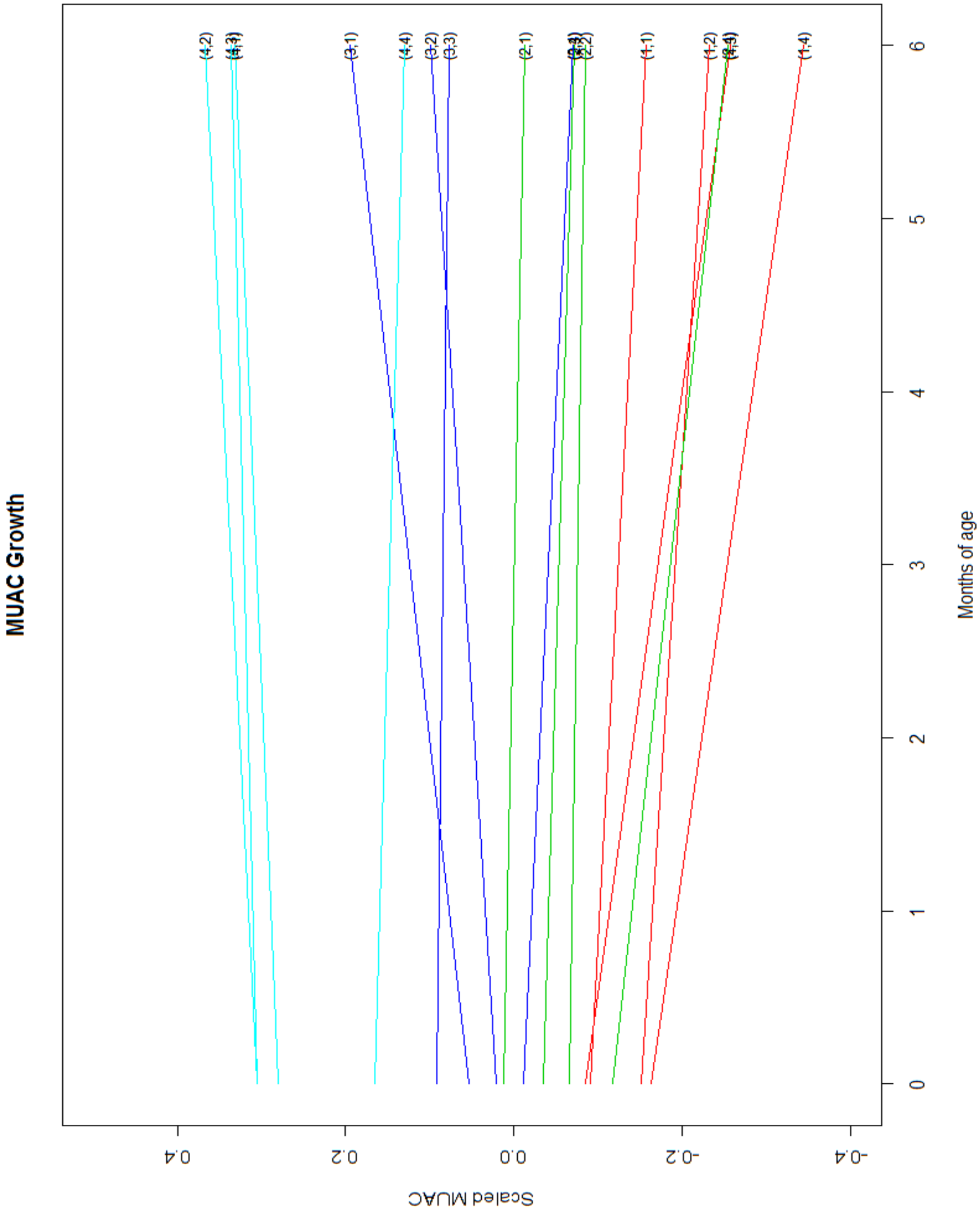

Figure 31: Mean change in child scaled MUAC between birth and six months subset by maternal MUAC and local Gini quantiles

Colored by Maternal MUAC (highest:lowest → Light blue, dark blue, green, red). Numbers in parentheses are highest:lowest, 4:1, (Maternal MUAC, Local Gini). Note how, generally, the nutritional status of those in each maternal MUAC strata is modified by neighborhood economic inequality, with the nutritional status of those living in greater neighborhood equity (1) increasing and diverging from their peers residing in neighborhoods with greater inequality (4).

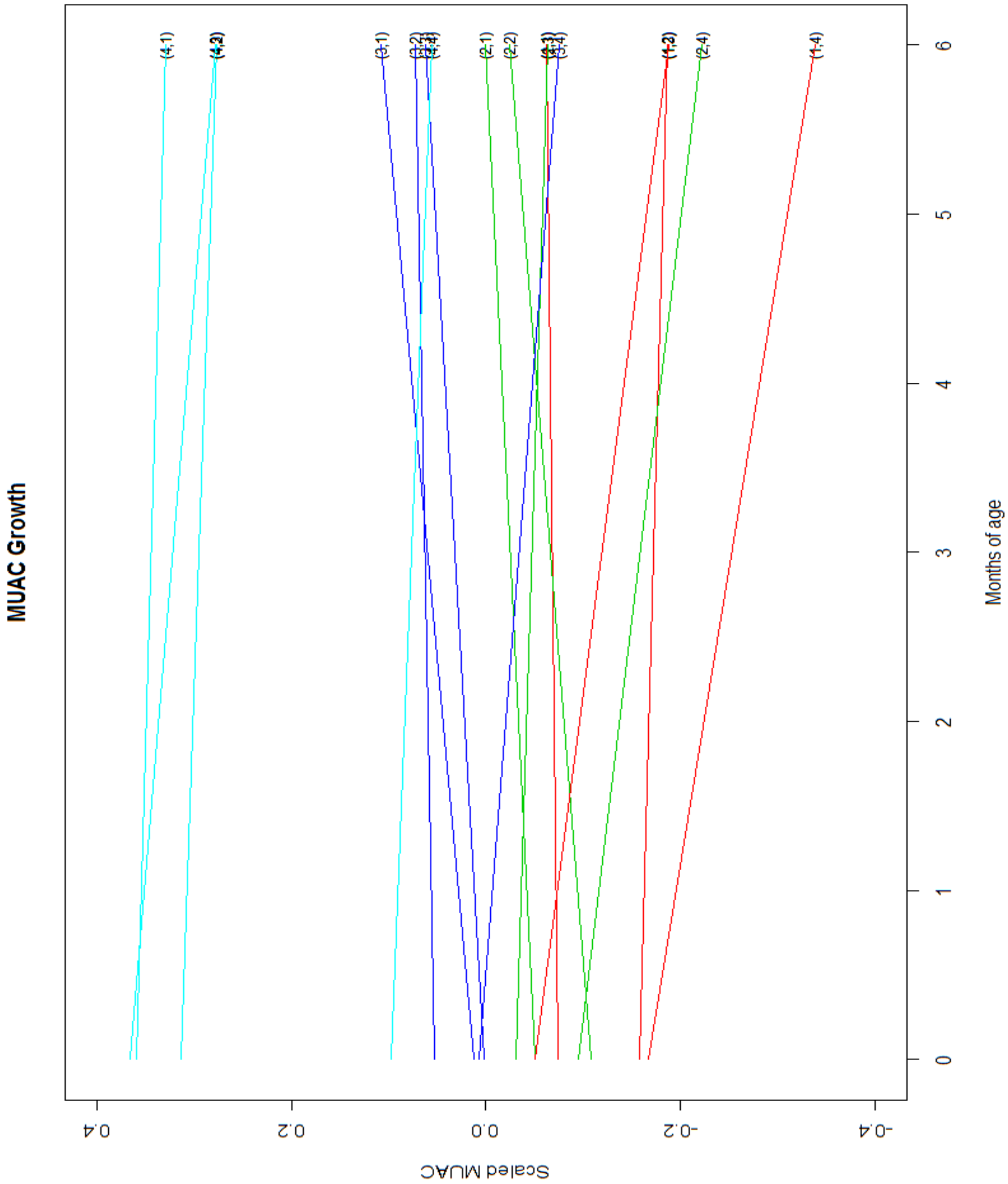

Figure 32: Mean change in child scaled MUAC between birth and six months subset by individual LSI and local Gini quantiles

Colored by individual LSI (highest:lowest → Light blue, dark blue, green, red). Numbers in parentheses are highest:lowest, 4:1, (Individual LSI, Local GINI). Note how, generally, the nutritional status of those in each individual economic strata is modified by the neighborhood economic inequality, with those living in relative equal neighborhoods improve far better than their economic peers residing in neighborhoods with greater inequality.

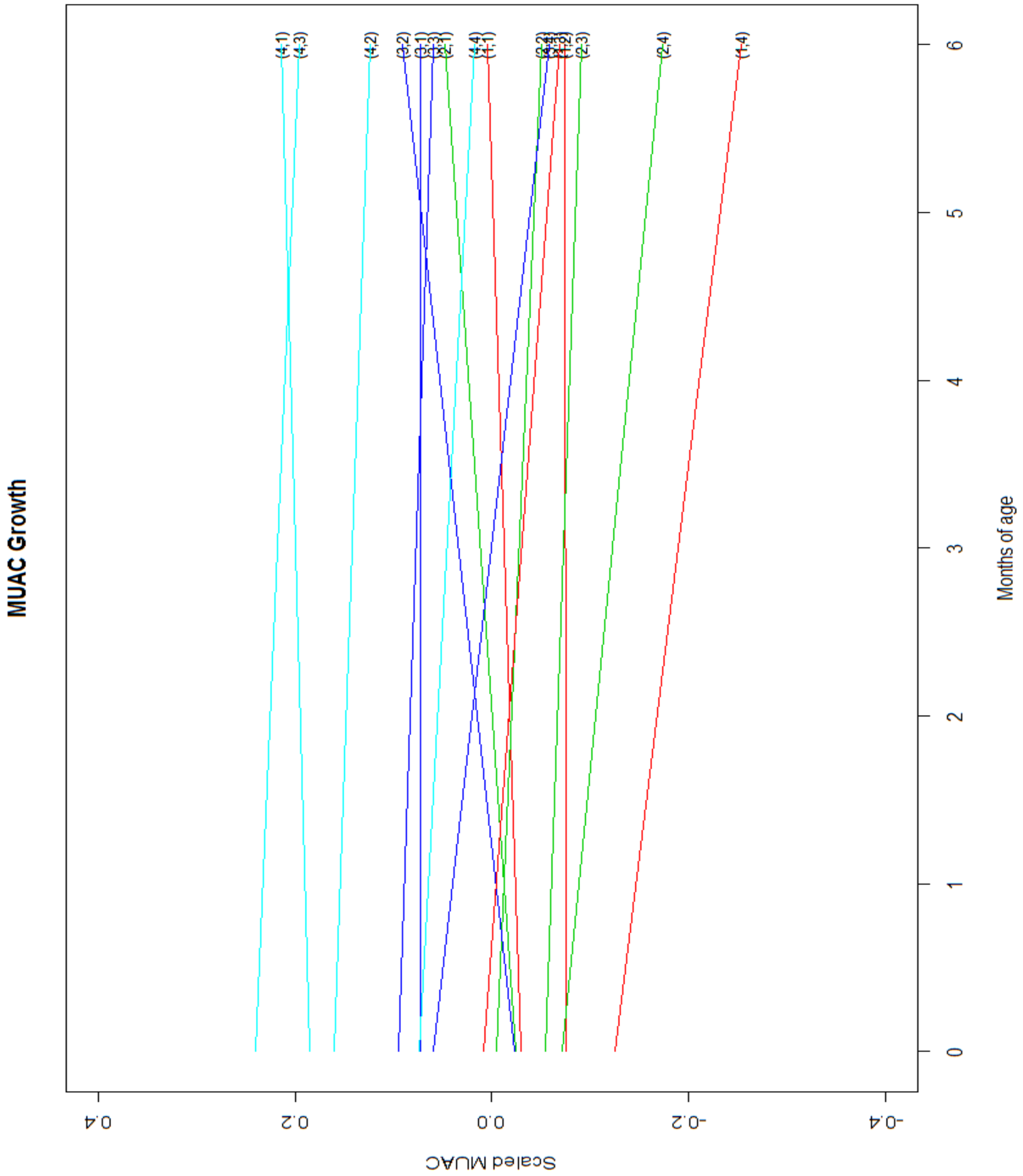

Figure 33: Mean change in child scaled MUAC between birth and six months subset by neighborhood average LSI and local Gini quantiles

Colored by neighborhood average LSI (highest:lowest → Light blue, dark blue, green, red). Numbers in parentheses are highest:lowest, 4:1, (Neighborhood average LSI, Local GINI). Note how, generally, the nutritional status of those in each neighborhood economic strata is modified by neighborhood economic inequality, with those living in neighborhoods with relatively less inequality grow more rapidly than their economic peers residing in neighborhoods with greater inequality.

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Curriculum Vitae

EDUCATION

Johns Hopkins Bloomberg School of Public Health

Ph.D. Department of International Health: Global Disease Epidemiology and Control Division, 2015
Thesis: Understanding Intergenerational Malnutrition in Rural Bangladesh: A Systems Approach

M.H.S. Department of Environmental Health Sciences, 2009
Thesis: Methods of Sustainable Landuse in Agriculture and Forestry
Graduate research with Dr. Keith West and Dr. Alain Labrique, 2011-2015
Graduate research with Dr. William Pan, 2008-2011

University of Maryland, College Park
M.A. Geography, 2007
Thesis: Owner Occupancy and the Social and Physical Environment in Baltimore City
Advisors: Dr. Martha Geores (UMD); Dr. Debra Furr-Holden (JHSPH)

University of Maryland, Baltimore County
B.S. Geography, 2005
B.A. Visual Arts, 2005
Minors: Political Science and Art History
Certificate: Geographic Information Systems

PROFESSIONAL RESEARCH

Johns Hopkins School of Public Health: Department of International Health, Baltimore, Maryland
Geospatial Data Specialist, 2011-2012

- Prepared a full report evaluating the methods of spatial data collection and analysis used as part of the JiVitA project including future recommendations
- Assisted in the hiring, training, and management of field staff tasked with spatial data collection
- Compiled spatial data from multiple sources to augment geospatial information systems including generating detailed field map books used to located enrolled participants in the field and creating a real-time system of spatial data collection using mobile devices and cloud-based storage

National Institute on Drug Abuse, Baltimore, Maryland
IRTA Pre-Doctoral Fellow, 2009-2013

- Constructed methodologies, which include spatial interpolation models, spatial odds-ratios, time-series and principal component analysis, and "fuzzy-matching," to estimate effects of factors related to the built environment on psychological stress and substance abuse, ascertaining exposure from GPS tracking and GIS data
- Derived and validated a novel approach to clean raw GPS tracking data in public health applications
- Conducted spatial analysis and statistics, data acquisition, primary and secondary data analysis, literature review and writing of scientific papers as part of the Clinical Pharmacology and Therapeutics Research Branch

Johns Hopkins School of Public Health: Department of International Health, Baltimore, Maryland
Senior Research Assistant, 2008-2011

- Created and managed multi-level databases, Access survey forms, graphs, charts, maps and other figures as part of the Population-environment Dynamics Influencing Malaria Risk in the Peruvian Amazon project
- Incorporated ecological fragmentation estimators, multivariate logistic regression and spatial auto-correlation models to investigate the relationship between prevalence of anopheles darlingi larva and land use, land cover and other ecological aspects

- Co-taught a training and educational program for study investigators in Addis-Ababa, Ethiopia as part of the Health and Wealth Survey conducted by the Gates Institute

RK&K Engineers, Baltimore, Maryland
Environmental and GIS Planner, 2007

- Prepared estimates for environmental impact statements used to inform infrastructure engineering design decisions
- Produced a workflow model using ArcGIS and Python scripts which reduced the time required for environmental impact estimates from approximately three days to nearly 10 minutes.
- Used remotely sensed data to determine impervious surface change in Maryland's critical areas of estuary and prepared documentation informing State government officials about the rate of Chesapeake Bay shoreline development.

Mayor's Office in the City of Baltimore/CitiStat, Baltimore, Maryland
Senior Resource/Spatial Analyst, 2005-2007

- Developed an agent-based model to approximate student walking routes to schools from which the results were used to determine crossing guard placement, student enrollment and for safe city bike routes
- Integrated network databases with a mapping interface to geographically link citizen complaints and city personnel responsibility for the Department of Solid Waste and the Office of Code Enforcement
- Updated spatial data typology and verified resource allocation for the Department of Elections and Baltimore City Schools

Pacific Institute for Research and Evaluation/Johns Hopkins, Calverton/Baltimore, Maryland
Research Consultant, 2005-2009

- Directed the spatial aspects of project research methods used in the conception of a community environmental health evaluation investigating the influence of social and physical environments on behavior
- Served as the primary spatial analyst and technician for the research group, spatially referencing survey data, generated maps and statistically modeling survey observations
- Prepared materials for several lectures, conferences and presentations. The main study aims were focused on the influence social and physical environments have on behavior.

Parks and People Foundation Urban Grant, Baltimore, Maryland
Principle Investigator, 2004-2005

- Wrote the funded research grant to investigate the association between street lighting and street crime (property and violent crimes) in Baltimore, Maryland and resulting scientific report.
- Gathered spatial data of street lighting and vegetative conditions along streets and public thoroughfares and requisitioned crime and planementric data from the City of Baltimore
- Generated three-dimensional mathematical models of crime 'risk' and street lighting incorporating shadows from street vegetation and other aspects of the built environment across the study site

PUBLICATIONS

Epstein D, Tyburski M, **Craig IM**, Phillips KA, Jobes M, Vahabzadeh M, Mezghanni M, Lin J, Furr-Holden CDM, Preston KL. Real-time tracking of neighborhood surroundings and mood in urban drug misusers: Application of a new method to study behavior in its geographical context. Drug and Alcohol Dependence. (2014) 134: 22-29. PMID: 24332365

Craig IM, Labrique A, Epstein D, Preston K. Methods for GPS Point Validity Discrimination in a Participant Health Tracking Application. (In Progress)

Craig IM, Sikder S, Labrique A, Wakil MA, West K, Christian P. Methods in geospatial analyses of route-based distance to health facilities in northwest rural Bangladesh. (In Progress)

Craig IM, Sundaram M, Labrique A, Siddique AB. Geographic characteristics and trends of early newborn feeding behaviors in rural Bangladesh. (In Progress)

Ren S, Agarwal S, **Craig IM**, Larsen-Cooper E, Labrique A. Supplying the demand: Evaluating marketing strategies and other variables on the utilization of an mHealth pilot in rural Malawi. (In Progress)

Craig IM, Labrique A, West K. Understanding differences in nutritional status of expectant mothers in northwest Bangladesh: A systems approach. (In Progress)

Craig IM, Labrique A, West K. Understanding Age-specific Effects on Nutritional Status in Early Infancy: A Systems Approach. (In Progress)

Craig IM, Labrique A, West K. Ending intergenerational malnutrition: A systems approach to explain infant growth trajectories. (In Progress)

Craig IM, Geores M, Furr-Holden D, Smart M. Owner occupancy and neighborhood social and physical disorder in Baltimore City: An application of the NIfETy assessment method. (In Progress)

Smart M, Whitaker D, **Craig IM,** Alexandre P, Furr-Holden D. Substance Use and Misuse: Geographic Barriers to Treatment on Demand in Baltimore City. (Under Review, *Journal of Urban Health*)

CONFERENCE PAPERS, PRESENTATIONS AND CONTRIBUTIONS

Craig IM. A spatially relevant systems approach to understanding intergenerational malnutrition in rural Bangladesh. Poster Presentation: Discovering the World Through GIS; November 2014; Baltimore, MD.

Epstein DH, Preston KL. NPR Staff. In Baltimore, Mapping the World of Addiction. All Things Considered. http://www.npr.org/2011/11/20/142554574/in-baltimore-mapping-the-world-of-addiction; November 2011.

Preston KL, Esptein DH. **Craig IM**, Vahabzabeh M. Lin JL, Phillips K. Real-time methods to quantify exposure to psychosocial stress. Poster Presentation: European Behavioural Pharmacology Society; August 28, 2011; Amsterdam.

Craig IM. Mapping addiction [interview/profile on Geographical Momentary Assessment], Australia's Dateline television newsmagazine, aired August 2011.

Craig IM. Tracking drug users with GPS [interview on Geographical Momentary Assessment], Radio New Zealand's This Way Up science program, aired July 16, 2011.

Craig IM. On the trail of addiction [interview on Geographical Momentary Assessment], Urbanite Baltimore, published March 1, 2011.

Furr-Holden CDM, Pokorni J, **Craig IM,** Ballard B, Smart M. Environmental Strategies for Alcohol Prevention. Poster presented at the 29th Annual Scientific Meeting of the Research Society on Alcoholism; June 2006; Baltimore, MD.

Furr-Holden CDM, Pokorni J, **Craig IM**, Ballard B, Smart M. Environmental Strategies for Drug Prevention. Poster presented at the 67th Annual Scientific Meeting of the College for Problem on Drug Dependence; June 24-28, 2006; Scottsdale, AZ.

Furr-Holden CDM, Pokorni JP, **Craig IM,** Ballard WC, Smart MJ, Campbell KD. Environmental Strategies for Violence, Alcohol, Tobacco, and Other Drug Prevention. Poster presented at 14th Annual Meeting of the Society for Prevention Research; May, 2006; SanAntonio, TX.

Furr-Holden CDM, Pokorni JP, **Craig IM,** Ballard WC, Smart MJ, Campbell KD. Environmental Strategies for Violence, Alcohol, Tobacco, and Other Drug Prevention. Presentation at the Annual American Association of Geographers Meeting; March, 2006; Chicago, IL.

Craig IM, Ellis E. Vegetation Conflicts with Lighting as an Aid to Crime. Paper presented at: Parks and People Foundation and Baltimore City Public Works Planning Conference; January 20, 2005; Baltimore, MD.

AWARDS AND HONORS

2010	Invitation and Scholarship to attend the Advanced Spatial Analysis workshop in Geographically Weighted Regression at UC Santa Barbara, California
2007	Community Representative, Pigtown Safety Group, Baltimore, Maryland
2005-2006	Graduate Teaching Assistantship, Dept. of Geography, University of Maryland
2005	Socrates Program, Leicestershire, England
2004	Park's and People Foundation Research Grant, Baltimore, Maryland
2004	Dean's List, University of Maryland, Baltimore County
2004	Academic Honors, University of Maryland, Baltimore County
2004	Article of the Week, The Retriever Weekly, University of Maryland, Baltimore County
2003	Most Promising New Writer Award, The Retriever Weekly, University of Maryland, Baltimore County
2003	Academic Honors, University of Maryland, Baltimore County

TEACHING EXPERIENCE

Johns Hopkins
Lecture on the Use of Geographic Information Systems in Public Policy Research

University of Maryland, College Park

GEOG 170	Maps and Map Use
GEOG 211	Geography of Environmental Systems Laboratory
GEOG 373	Geographic Information Systems
GEOG 473	Geographic Information Systems and Spatial Analysis

University of Maryland, Baltimore County

GEOG 280	Map Use and Cartographic Principles
GEOG 386	Introduction to Geographic Information Systems
GEOG 486	Advanced Applications of Geographic Information Systems
PHED 249	Advanced Sailing

MEMBERSHIP AND PROFESSIONAL SOCIETIES

GTU - Geographic National Honor Society
American Public Health Association - Member

COMMUNITY

Sailing Instructor, Downtown Sailing Center, Baltimore (2013-Present)
Volunteer, Bikemore, Baltimore (2012-present)

Planning Committee Chairperson, Upper Fells Point Improvement Association, Baltimore (2010-present)
Skier Safety Patroller, Copper Mountain, Colorado (2007-2008)
Ski Coach, Special Olympics, Vail, Colorado (2007-2008)
Community Representative, Pigtown Safety Group (2006-2007)
Member, Citizens of Pigtown (COP), Pigtown, Baltimore, Maryland (2004-2007)
Volunteer, Pigtown Main Streets Association(2005-2007)
Volunteer Trail Maintainer, Gunpowder State Park, Whitehall, Maryland, (2001-2007)