ASSESSMENT OF MATERNAL AND INFANT OUTCOMES OF MODERATELY MALNOURISHED PREGNANT ADOLESCENTS IN MALAWI

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ABSTRACT

Assessment of Maternal and Infant Outcomes of Moderately Malnourished Pregnant Adolescents in Malawi

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Background: Adolescent childbearing and maternal malnutrition are common in low- and middle-income countries and are associated with increased risk for poor maternal and infant outcomes. Adolescent pregnancy compounded with moderate malnutrition exacerbates outcomes common to both individually. Supplementary foods may be a way to improve outcomes in malnourished adolescent pregnant women.

Objective: To retrospectively assess maternal and infant outcomes in moderately malnourished pregnant young adolescents (16-17 YO), older adolescents (18-19 YO), and adults (≥20 YO) in response to one of three nutritional interventions and in a pooled treatment group analysis, and to assess differences in infant outcomes by infant gender.

Methods: Height, weight, MUAC, and FH were measured in pregnant women with MUAC >20.6 cm and < 23.0 cm at baseline (N=1828) every 2 weeks over the course of enrollment while receiving either: 1) macro- and micronutrient fortified, peanut-based, ready-to-use supplementary food (RUSF), 2) corn-soy blended flour with a prenatal multiple micronutrient supplement (CSB-UNIMMAP), or 3) corn-soy blended flour with iron and folic acid (CSB-IFA). Each provided approximately double the RDA of most micronutrients, 900 kcal/day and 33-36 g/day protein. Postpartum maternal and infant measurements were taken at delivery, and after 6 and 12 weeks. Maternal age at enrollment variable was transformed from a continuous variable into a categorical variable; young adolescent (16-17 YO), older adolescent (18-19 YO), and adults (≥20 YO). General linear models with normal errors were used to compare: 1. Adolescent maternal and infant outcomes by intervention, 2. Adolescent maternal and infant outcomes by maternal age within each intervention group, 3. Maternal and infant outcomes in a pooled treatment analysis by maternal age, 4. Interaction effects between maternal age and intervention, 5. Infant outcomes by infant gender. If differences between groups were detected, they were tested using the Tukey HSD test (response) or the likelihood ratio-based odds ratios (categorical). Odds ratios were measured using effects likelihood ratio tests via logistic regression. Response variables included in the analyses were BMI and fundal height at enrollment.

Results: There were 297 young adolescents, 582 older adolescents, and 949 adults enrolled. Adolescents enrolled in the study at a younger gestational age than the adult mothers. Upon enrollment, BMI was greater and FH was smaller in the adolescent mothers than adults. At delivery, adolescent mothers had gained less weight on treatment, delivered with a lower final MUAC and FH, had increased odds of delivering extremely prematurely, and the greatest odds for delivering before recovery from malnutrition (MUAC ≥23.0 cm). Infants of young adolescent mothers were inferior anthropometrically to infants of the older mothers and had greatest odds of being underweight and stunted through 12 weeks of age. Young adolescents had the greatest odds for delivering LBW infants compared to the adults. Catch up growth was

observed in the infants of older adolescents by 12 weeks of age; however, no catch up was observed for the infants of young adolescents. No one intervention was more helpful than another in determining maternal and infant outcomes of the adolescent mothers, and male infants had greater odds of being underweight and stunted at 6 and 12 weeks of age.

Conclusions: Although adolescents did not appear to have characteristics of more severe clinical malnutrition, such as lower BMI, lower maternal height, and increased rates of HIV at baseline, maternal and infant outcomes were worse for the adolescent mothers compared to the older, more mature mothers. Adolescents gained less weight during pregnancy and delivered smaller infants that were unable to catch up linearly and with weight gain. Pregnant adolescents, particularly young adolescents, are a high-risk population and public health efforts should be made to delay the age of first pregnancy.

Keywords: Malnutrition, pregnancy, adolescent, supplementary foods, stunted.

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ABBREVIATIONS

AFA	Arm fat area
AMA	Arm muscle area
ANOVA	Analysis of variance
BMI	Body mass index
CSB+	Fortified corn soy blend
cm	Centimeter(s)
HCFA	Head circumference for age
HIV	Human immunodeficiency virus
HFIAS	Household Food Insecurity Access Scale
HSD	Honest significant difference
FH	Fundal height
g	Gram(s)
GWG	Gestational weight gain
IOM	Institute of Medicine
IFA	Iron and folic acid supplement
IUGR	Intrauterine growth restriction
kcal	Kilocalorie(s)
kg	Kilogram(s)
LAZ	Length for age Z score
LBW	Low birth weight
LSM	Least square mean
MMR	Maternal mortality ratio
MUAC	Mid-upper arm circumference
RDA	Recommended dietary allowance
RUSF	Ready-to-use supplementary food
SES	Socioeconomic score
SGA	Small for gestational age
TFR	Total fertility ratio
WAZ	Weight for age Z score
WHO	World Health Organization
WLZ	Weight for length Z score
YO	Years old

CHAPTER 1: INTRODUCTION

Maternal malnutrition is a global concern that affects many mothers, infants and children. Pregnant women and infants, in general, are among the most nutritionally vulnerable groups due to their physiologically higher nutrient requirements (Lartey et al., 2008). Maternal malnutrition refers to poor nutrition prior to conception, during pregnancy, and throughout lactation and is a particularly large issue in low- and middle-income countries where consumption of nutrient-poor foods is commonplace. It is an important contributor to maternal morbidity and mortality, and poor birth and infant outcomes and is associated with numerous short- and long-term consequences for both mother and infant (Ahmed et al., 2012). The environmental and economic conditions of sub-Saharan Africa result in high levels of food insecurity, poverty, heavy physical workloads, and frequent and short reproductive cycles, which together increases the risk of maternal malnutrition (Lartey et al., 2008).

Sub-Saharan Africa is the youngest region in the world, with 44% of its population aged below 15 years, making adolescent pregnancy a prevalent and relevant issue in this region (Mombo-Ngoma et al., 2016). About 16 million girls aged 15-19 years give birth every year, in addition to about 1 million girls less than 15 years old (WHO, 2014). Adolescent girls are an especially vulnerable group due to their rapid growth and development (Ahmed et al., 2012). The compounded nutrient demands from pregnancy during adolescence put pregnant adolescents at an increased risk for nutritional depletion, poor health outcomes for the mother, in addition to growth faltering for the offspring (Ahmed et al., 2012; Mombo-Ngoma et al., 2016). Many studies link adolescent pregnancy with higher risks of adverse pregnancy outcomes such as low birth weight (LBW), preterm delivery, stunting, and perinatal and maternal death compared to adult pregnant women; young adolescents (<15 years old) experience the greatest risk

(Ganchimen et al., 2013; Fall et al., 2015). Additionally, complications associated with adolescent pregnancy are made worse when the mother is depleted nutritionally prior to conception (Ahmed et al., 2012). Adolescent pregnancy compounded with moderate malnutrition further increases poor maternal and infant outcomes beyond that of either issue alone (Ahmed et al., 2012).

Recommendations regarding the type and quantity of nutrients required for undernourished pregnant adolescents remain unclear (Lassi et al., 2017). Current recommendations for malnourished pregnant women is supplementation throughout pregnancy with fortified corn-soy blend (CSB) flour in addition to a micronutrient supplement with iron and folic acid (IFA) (Annan et al., 2014; Manary et al., 2017). However, with consistently high rates of infant and maternal mortality seen throughout sub-Saharan Africa, new treatment methods need to be considered, such as lipid-based ready-to-use-supplementary food (RUSF) which has shown to alleviate malnutrition in children (Bhutta et al., 2008).

Despite advances in medicine worldwide, complications during pregnancy and childbirth are the second leading cause of death for girls ages 15-19 (WHO, 2014). Infants born to these mothers face substantially higher risks of dying than those born to women ages 20-24 and pregnant adolescents have a 50% higher risk for stillbirth and infant death compared to mothers ages 20-29 years (WHO, Adolescent Pregnancy, 2014). Additionally, the adolescent population is expected to increase dramatically by 2030, with a 93% increase expected in Malawi specifically (Loaiza & Liang, 2013). Further research is needed to gain an understanding of the nutrient requirements needed throughout adolescent pregnancy to assist in providing these women with a sufficient diet that supports optimal maternal and fetal health and development to mitigate the adverse pregnancy outcomes associated with adolescent pregnancy.

This analysis of adolescent data from the *Mamachiponde* study in Malawi seeks to determine whether or not three interventions are able to improve the nutritional status of moderately malnourished adolescent pregnant women ages 15-19 years old, and to determine if maternal and infant outcomes differ by age in this population.

CHAPTER 2: REVIEW OF LITERATURE

MATERNAL MALNUTRITION

Maternal nutritional status is an important predictor of maternal health, fetal growth, birth outcomes, and infant growth in low- and middle- income countries (Wrottesley et al., 2016). Consequences of maternal malnutrition lead to numerous short- and long-term implications for both the mother and infant (Lartey et al., 2008). **Figure 2.1** summarizes the nutritional factors that commonly result in maternal malnutrition in the African setting and the associated consequences on mother and infant.

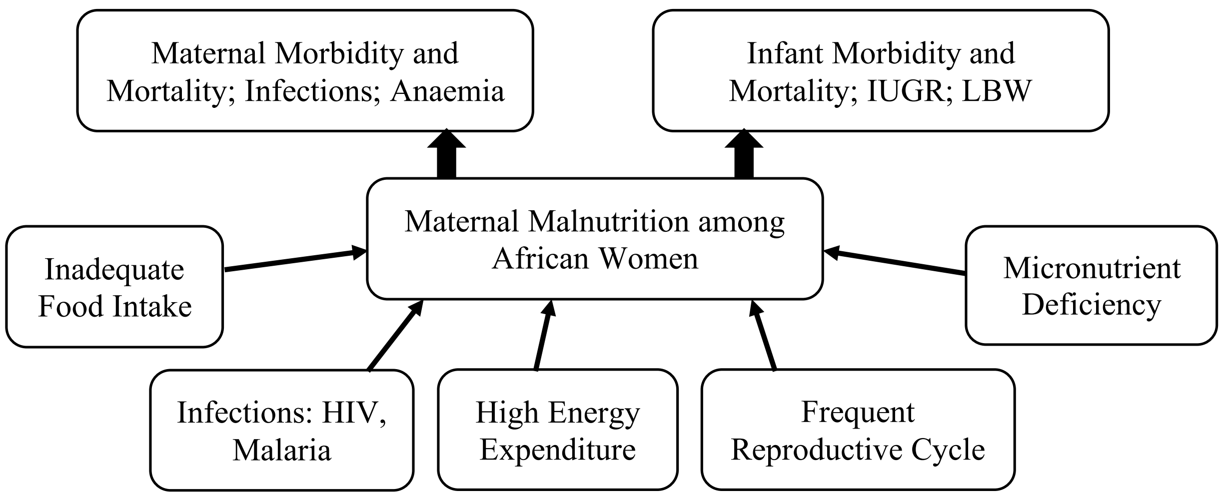


Figure 2.1 Causes of maternal malnutrition and its effect on maternal and infant health. (Adapted from Lartey et al., 2008)

The cause of maternal malnutrition is multifactorial and results from the interplay of a variety of nutritional, behavioral, sociodemographic, and environmental factors (Black et al., 2008) (**Figure 2.2**).

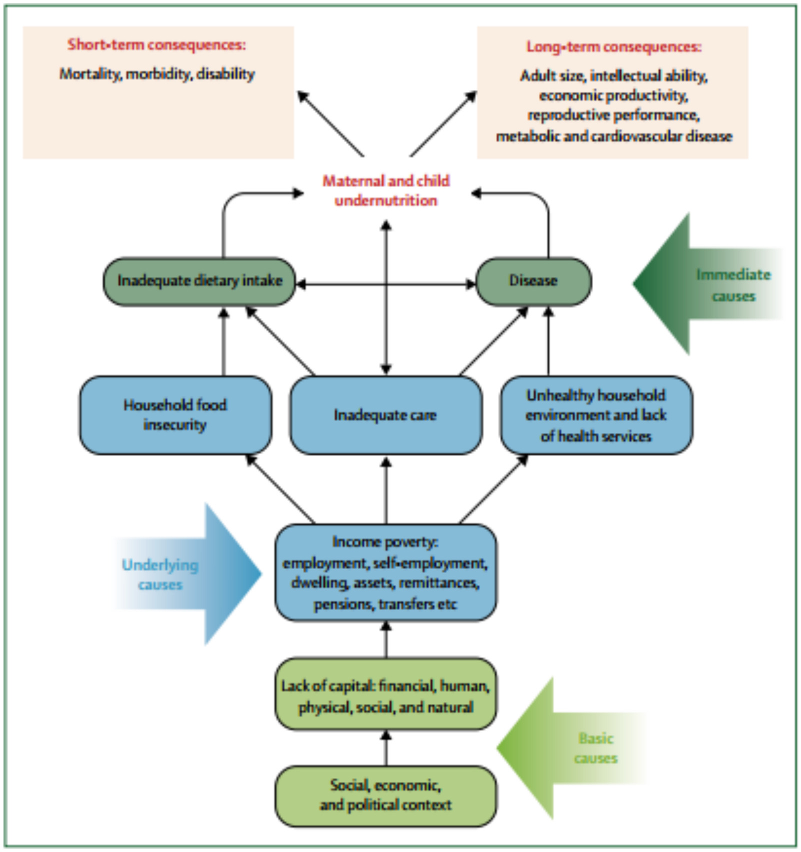


Figure 2.2 Diagram of the relationship between the basic, underlying, and immediate causes of maternal and child undernutrition and its short- and long-term consequences (Adapted from Black et al., 2008)

Maternal Consequences

Consequences of maternal malnutrition have detrimental implications to mother, offspring, and society as a whole. Maternal malnutrition can increase a mother's risk of nutrient deficiencies, short stature, low BMI, anemia, and maternal mortality (Black et al., 2008; Ahmed et al., 2012; Christian et al., 2015). Short stature and iron deficiency anemia both increase the risk of maternal mortality at delivery, and together they account for greater than 20% of maternal mortality worldwide (Black et al., 2008). Additionally, short stature of a mother in conjunction with poor maternal nutritional stores is associated with an increased risk of intrauterine growth restriction (IUGR), small for gestational age (SGA), preterm birth, and low birth weight (LBW)

(Black et al., 2008; Kozuki et al, 2015; Bisai, 2010), all of which may impose negative consequences on the infant. Specifically, maternal short stature <145 cm was most strongly associated with increased risk for poor outcomes compared to taller mothers (Kozuki et al, 2015). In a study using adolescent pregnant women in India, Bisai found short mothers (height ≤145 cm) to have a 2.74 and 9.0-fold greater risk of delivering a LBW baby than the average (146-155 cm) and tall (>155 cm) pregnant women (Bisai, 2010). Additionally, in a different study using women from Thailand, Toh-adam et al. found short stature <145 cm to be an independent risk factor for cephalopelvic disproportion, a condition in which the fetus' head or body is too large to fit through the mother's pelvis (Toh-adam et al, 2012; American Pregnancy Association, 2015). According to Kozuki et al., approximately 6.5 million SGA and/or preterm births in low- and middle-income countries are associated with short maternal stature (Kozuki et al, 2015).

Women living in sub-Saharan Africa, particularly those who are in the lowest wealth quintile and living in rural areas, are prone to having high rates of fertility and childbirth. Short pregnancies and frequent childbirth increases the burden of malnutrition by causing a woman's tissues to become depleted of essential nutrients with inadequate nutrition recovery prior to delivery (Ahmed et al., 2012). **Figure 2.3** highlights this vicious cycle and the intergenerational transfer of malnutrition that is frequently seen in low- and middle-income countries. LBW infants, and stunted children, adolescents, and adults can all result from this cycle, which can ultimately lead to pregnancy complications in the subsequent generation (Ahmed et al., 2012). These women who conceive while undernourished are less likely to improve their nutritional status during pregnancy, perpetuating this cycle of malnutrition (Ahmed et al., 2012).

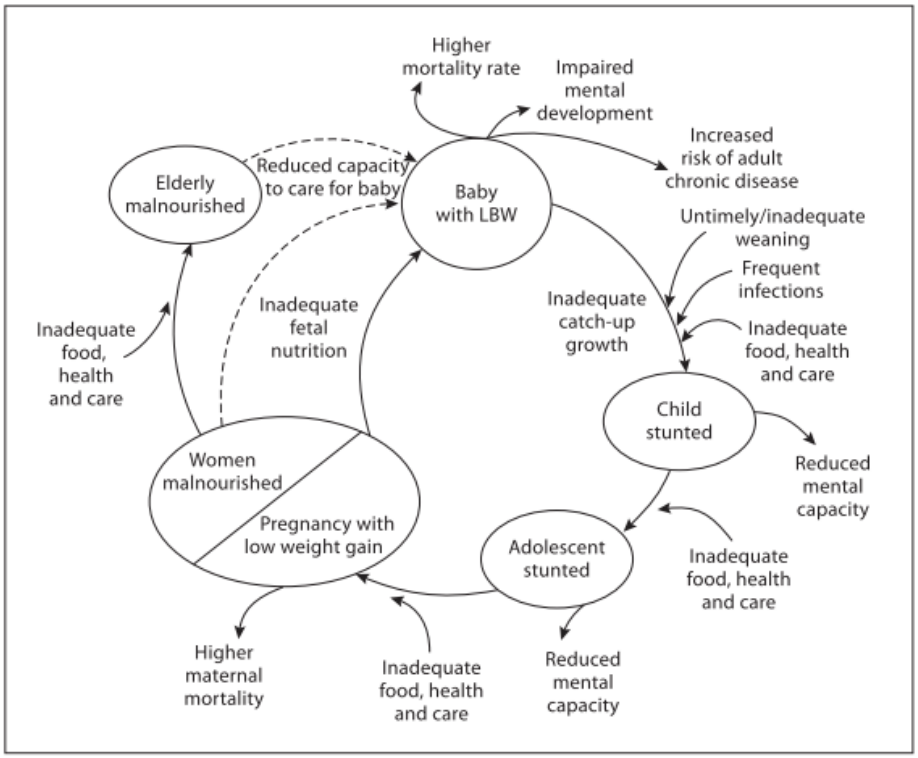


Figure 2.3 Nutrition through the life cycle, showing effects of LBW on child growth and development through adulthood. (Adapted From Ahmed et al., 2012)

Severe maternal malnutrition in pregnancy that continues into lactation in the postpartum period can also lead to changes in breast milk volume and composition (Black et al., 2008). The nutrient profile of breast milk is sensitive to maternal nutritional status and intake of particular micronutrients, especially Vitamin A, causing infants to be at an increased risk of depletion when maternal deficiency exists (Black et al., 2008).

Infant Consequences

Maternal malnutrition can have detrimental nutritional, physical, mental, and health effects on infants and children that often persist throughout adulthood. Infant and child undernutrition commonly begins in utero, and is a major underlying cause of child mortality in

about half of all deaths of children less than 5 years of age (Black et al., 2013). Additionally, undernutrition in sub-Saharan Africa accounts for one third of all undernourished children worldwide (UN, Millennium Development Goals Report, 2015). The first 1,000 days is the time from conception through year two (0-23 months) in a child's life and is a time of critical developmental and nutritional importance in which rapid physical and mental development occurs (Sullivan et al., 2016). During this time, the brain dominates the body's metabolism and specific nutrients are required in key amounts (Sullivan et al., 2016). Maternal malnutrition and poor diet directly influence the nutrients provided to the fetus in utero and have lasting effects on the child's life (Sullivan et al., 2016). Specifically, direct structural damage to the brain can occur as a result of malnutrition in utero, leading to impaired motor development and behavior (Victoria et al., 2008). Additional influences that limit fetal nutrient supply are preterm birth and placental insufficiency, which leads to reduced delivery of nutrients and oxygen to the fetus (Victoria et al., 2008). Poor birth outcomes that have been linked to maternal undernutrition include LBW, premature birth, neonatal mortality, stunting, wasting, and subsequent child malnutrition (Ahmed et al., 2012; Mombo-Ngoma et al., 2016; Papathakis et al., 2016).

Low Birth Weight

A LBW infant is defined as a neonate born at term (37 weeks of gestation) with a birth weight <2,500 g (Ahmed et al., 2012). LBW is a leading cause of prenatal and neonatal mortality, and it is more likely to occur in a developing country than an industrialized country (Black et al., 2008). Causes of LBW are multifactorial, however, the primary cause of LBW is preterm birth with the second cause being IUGR (Ngwira et al., 2015; Wrottesley, et al., 2016). IUGR and LBW together greatly limit infant and child growth and development, increase

vulnerability to disease and undernutrition, limit the ability to learn, and lead to less productive adults overall (Ahmed et al., 2012). Additional factors contributing to the development of LBW include low maternal education, young maternal age, marital status, low gestational weight gain (GWG), and parity, in addition to other environmental, demographic, and reproductive variables (Ngwira et al., 2015).

Birth weight is correlated with many socioeconomic, nutritional, and health factors. A recent study in Malawi identified that child birth order, maternal weight, height, and education, and family wealth were all significant predictors of infant birth weight (Ngwira et al., 2015). As education and wealth increased, they found the percentage of LBW infants in Malawi decreased (Ngwira et al., 2015). Additionally, a review of African studies by Wrottesley, et al. revealed that BMI during pregnancy was positively associated with birth weight (Wrottesley, et al., 2016). A recent study in Ethiopia found that a mid-upper arm circumference (MUAC) less than 23 cm, not attending antenatal care, and time (40-79 minutes) to walk to health facility were strong predictors of LBW (Assefa et al., 2012). Poor diet as a result of lower income and financial status, in addition to poor dietary literacy and limited access to prenatal care, may be explanations behind the high rates of LBW in less educated mothers (Muula et al., 2011).

Premature Birth

Preterm birth is defined as a birth occurring less than 37 weeks gestation, and is estimated to occur in more than 1 in 10 infants, or 15 million total infants every year (WHO, 2016). Premature birth is the leading cause of death among children under 5 years of age, and was responsible for approximately 1 million deaths in 2015 (WHO, 2016). Rates of premature birth are on the rise, and the survival rate for these infants varies considerably depending on its

location of birth (WHO, 2016). Preterm infants in low-income settings are disproportionately at risk for death and morbidity compared to those in high-income countries (WHO, 2016). Prematurity is categorized as moderate to late preterm (32 to <37 weeks gestation) and extremely preterm (<28 weeks gestation), with about 85% of premature deliveries occurring after 31 weeks (Platt, 2014). Common causes of preterm birth include maternal undernutrition, multiple pregnancies and infections and chronic conditions such as diabetes and high blood pressure, however it can also occur spontaneously with no apparent risk factors (WHO, 2016; Platt, 2014).

Preterm birth leads to numerous short- and long-term consequences for the infant (Platt, 2014). They are at a significantly higher risk for child undernutrition, infectious and non-infectious respiratory problems, readmittance to the hospital, necrotizing enterocolitis, retinopathy and other conditions of the eyes, hearing impairment, cognitive impairment, attention and activity disorders, and neurodevelopmental disability, the most common being cerebral palsy (Kozuki et al, 2015; Platt, 2014). A study conducted in rural Bangladesh sought to describe the burden and risk factors associated with preterm birth (Shah et al. 2014). Results of the study showed that maternal factors associated with an increased risk for preterm birth included socioeconomic status, with poorer women being at the most risk, poor nutritional status as indicated by a low MUAC, and antenatal iron intake, all of which are sources of concern in low- and middle-income countries (Shah et al, 2014).

Stunting

Stunting is the most prevalent form of undernutrition (Levels and Trends in Child Malnutrition, 2017). Although recent decreases in childhood stunting have taken place in Asia, rates in Africa have remained static, around 40% (de Onis et al., 2010). It is an irreversible

condition that is defined as a height-for-age more than two standard deviations below the median of the WHO Growth Standards and indicates poor linear growth (WHO, 2010). The development of a stunted infant and child typically begins in utero and commonly results in a stunted adult (Dewey & Begum, 2011). The main causes of stunting include chronic malnutrition as a result of repeat infection, poor feeding practices and inadequate diet, IUGR and preterm birth. Stunting, or linear growth, is considered to be a good anthropometric measure for monitoring the long-term impact on nutritional deficiency (Sullivan et al. 2016; Lartey et al., 2015; Dewey & Begum, 2011; Danaei et al., 2016).

There are a number of long-term consequences that result from stunting. It is a direct cause of short adult height and suboptimal physical function later in life which impacts economic productivity (Dewey & Begum, 2011, Mangani et al., 2015). Stunting is a key indicator of the underlying processes that lead to poor growth and additional adverse outcomes (Dewey & Begum, 2011). Specifically, childhood stunting has been associated with increased risk for morbidity and mortality, poor cognition and educational performance throughout childhood and into adulthood (de Onis et al., 2013; Mangani et al., 2015). Additionally, the limited longitudinal growth that occurs in stunting has been shown to be directly linked with growth through adulthood. It is estimated that stunting can reduce a country’s gross domestic product by as much as 3% (BMJ, 2015). Adair et al. (2007) found that a 1 cm increase in birth length was associated with a 1 cm increase in adult height in a sample of individuals from the Philippines, providing evidence for the positive relationship between infant length and adult height.

Highlighting the significance of the intergenerational transfer of malnutrition (**Figure 2.3**), adult mothers who were stunted as children are at an increased risk for restricted uterine blood flow, and limited growth of their uterus, placenta, and fetus, which can lead to IUGR in

their pregnancy (Dewey & Begum, 2011). This IUGR can lead to LBW, in addition to fetal distress, fetal death, delayed neurological and intellectual development, and a deficit in adult height (Dewey & Begum, 2011). This cycle of malnutrition and stunting is continuous, leading to many generations of stunted individuals.

Diagnosis of Maternal Malnutrition

Currently, there is no agreement on which anthropometric measurement methods are most appropriate to detect, monitor, and treat mild, moderate, or severe undernutrition in pregnancy (Papathakis et al., 2016). There are a number of different anthropometric measures that can be used in a low-income setting, including mid-upper arm circumference (MUAC), body mass index (BMI), and gestational weight gain (GWG).

Mid-Upper Arm Circumference

MUAC is an indicator of lean and fat mass with a lower measurement indicating low lean muscle mass and/or loss of subcutaneous fat (Papathakis et al., 2016). MUAC is a commonly used measure due to its many advantages in any setting, and even more so in rural, low-resource settings. It is simple, relatively inexpensive, and requires minimal equipment and calculations (Tang et al., 2013). Additionally, MUAC remains relatively unchanged over the course of pregnancy for adult women (Ververs et al., 2013). Many studies have found a correlation between MUAC and BMI in adult populations, however there are no globally recognized standard MUAC cutoffs to classify moderate or severe malnutrition in pregnant adolescents and adults (Tang et al., 2013; Papathakis et al., 2016). Suggested cutoffs vary by country and range from 21 cm to 23 cm (The Sphere Project, Appendix 4). According to The Sphere Project, a

MUAC of <20.7 cm indicates severe risk of fetal growth retardation, and a MUAC of <23 cm indicates a moderate risk (The Sphere Project, Appendix 4). A review by Ververs et al. revealed that most adverse pregnancy outcomes were associated with a MUAC <22 and <23 cm, and came to the conclusion that using <23 cm in an African setting is ideal for including most pregnant women at risk of LBW (Ververs et al., 2013).

Numerous studies have shown that there is a significantly higher risk of poor birth outcomes in those with low MUAC compared to a higher measure (Tang et al., 2013). Ververs et al. concluded that MUAC can be used as a reliable indicator of risk of LBW. Additionally, a low MUAC value has linked to disproportionate intrauterine growth, preterm birth/labor, birth asphyxiation, and SGA (Kalanda et al, 2006; Sebayang et al, 2012; Lee et al, 2009).

Body Mass Index

Pre-pregnancy BMI, a simple anthropometric measure of body fat and lean tissue based on an individual's height and weight, reflects pre-pregnancy maternal nutritional status and can be used to assess health in women (Papathakis et al., 2016). A lower BMI indicates possible wasting of fat and lean tissue (Ververs et al., 2013). Children born to underweight mother's (pre-pregnancy BMI <18.5 kg/m^2) have a greater risk of being stunted, wasted or underweight than infants born to mothers who are normal weight (pre-pregnancy BMI 18.5-24.9 kg/m^2) (Demographic and Health Survey (DHS), 2015-16). In a study of 2670 pregnant women, pre-pregnancy BMI was found to be positively associated with birth weight (Frederick et al., 2007). The researchers found that lean women with pre-pregnancy BMI of <19.8 km/m^2 had a 51% higher risk of delivering a LBW infant compared to the control group having a BMI of 19.8-20.6 kg/m^2 (Frederick et al., 2007). Although pre-pregnancy BMI has been shown to have a

relationship with birth outcomes, especially LBW, many women in developing countries do not know their pre-pregnancy weight, and typically do not seek out medical care until their second trimester (Papathakis et al., 2016). No cut off points exist that can be used for each specific trimester in an African setting (Ververs et al., 2013).

Gestational Weight Gain

GWG is the change in a mother's weight, including growth of the mother, fetus, and placental mass, throughout the physiologic state of pregnancy (Papathakis et al., 2016). Currently, the Institute of Medicine (IOM) recommends that women who are underweight (BMI <18.5 kg/m^2) gain 0.5 - 0.6 kg per week in the second and third trimesters, ultimately resulting in a 12.7 - 18.1 kg total pregnancy weight gain (IOM, 2009). GWG within the IOM guidelines has been shown to result in a reduction in risk of delivery of a LBW infant (Frederick et al., 2007). Research shows that there is a strong association between GWG and birth weight (Abubakari, Kynast-Wolf & Jahn, 2015). Ludwig & Currie, using birth weight data from the United States, found that every additional kilogram gained in pregnancy was associated with a 7.35 g increase in birth weight, and that the GWG observed in the women had the ability to affect birth weight by about 200 g (Ludwig & Currie, 2010).

Fundal Height; Arm Muscle Area; Arm Fat Area

Additional indicators of malnutrition include fundal height (FH), arm muscle area (AMA), arm fat area (AFA). Fundal height is defined as the distance between the pubic symphysis and the highest point of the uterine fundus (Tabrizi et al., 2012). It is a practical measurement used to monitor and screen for gestational age of the pregnancy or SGA, IUGR,

and LBW, especially in settings where ultrasound is not available and date of last mensural period is commonly unknown, such as in Malawi (Rhondo, Filho, & Valverde, 2003; Morse et al, 2009; Mongelli & Gardosi, 2004). In healthy mothers, FH often matches the gestational age of the fetus in weeks; as an example, if a healthy mother is 28 weeks into her pregnancy, her FH should be about 28 cm (Antenatal Care Module: 10, The Open University).

AMA and AFA are indicators of total arm muscle and fat mass during pregnancy and can be easily calculated by using other arm anthropometric measures. AMA is derived from two measurements, MUAC and triceps skinfold (TSF), while AFA is derived from MUAC and AMA (Thomas et al., 2012).

PREGNANCY IN ADOLESCENCE

Adolescence is the second most critical period of growth after infancy (Hanson et al., 2015). Adolescent pregnancy is defined by the World Health Organization (WHO) as a pregnancy in which the mother gives birth before the age of 20 years old (WHO, 2004). Roughly 11% of births worldwide are to adolescent women, ages 15-19 years old, with about 95% of these births occurring in low- and middle-income countries, and specifically in sub-Saharan Africa (WHO, 2014; Hanson et al., 2015). Adolescent fertility is roughly three times higher in low- and middle-income countries than in high-income countries (Black et al., 2013). From 2010 to 2030 the number of adolescent girls ages 10-17 in sub-Saharan Africa is expected to increase from 75 million to 113 million, further increasing the risk of adolescent pregnancy (**Figure 2.4**) (Loaiza & Liang, 2013).

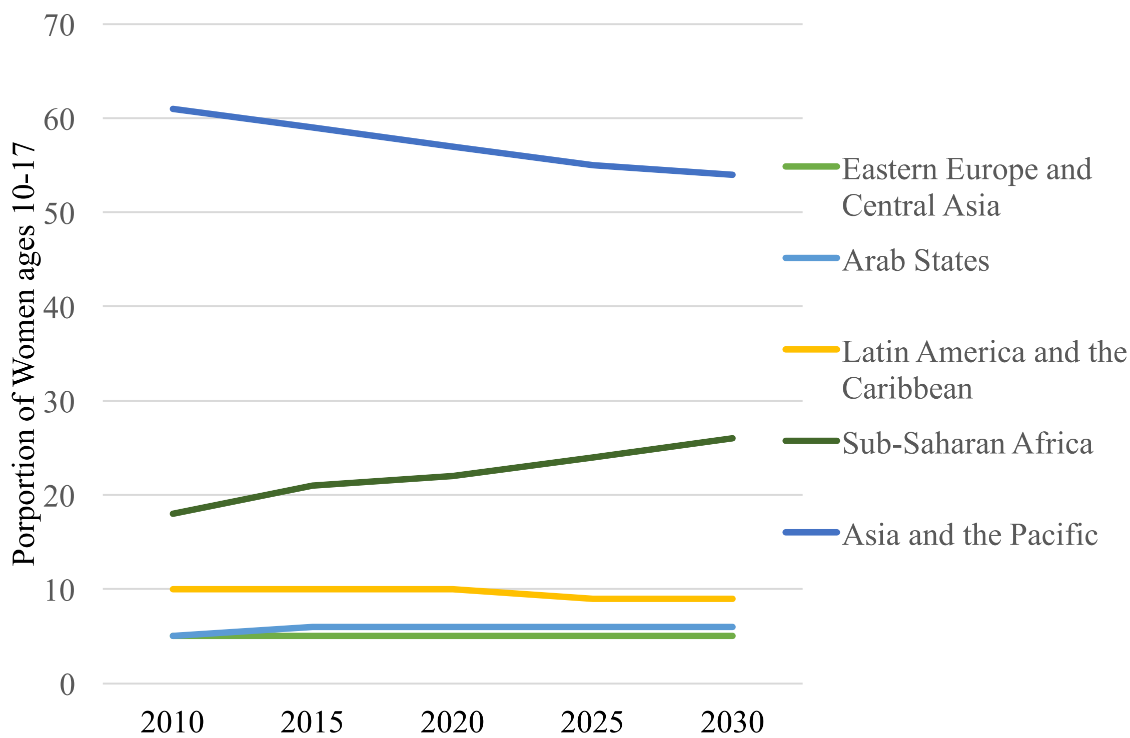


Figure 2.4 Proportion of women population aged 10-17 years, by United Nations Population Fund (UNFPA) regions. (Adapted from: Loaiza & Liang, Adolescent Pregnancy: A Review of Evidence, 2013)

Alone, adolescent pregnancy is associated with many poor maternal and infant outcomes that result from the competition for nutrients between mother and fetus (Hanson et al., 2015). However, adolescent pregnancy, compounded with malnutrition exacerbates outcomes common to both risks individually. The risk of maternal mortality is two times higher in adolescents' ages 15-19 compared with women in their twenties (Hanson et al., 2015). Adolescent mothers and their offspring pay a large health, social, and economic cost for early childbearing (Karra & Lee, 2012).

Factors Contributing to Adolescent Pregnancy

Various factors, such as socioeconomic status (SES), education, geographic location, and cultural and biological factors, are interrelated and greatly influence rates of adolescent pregnancy worldwide (**Figure 2.5**).

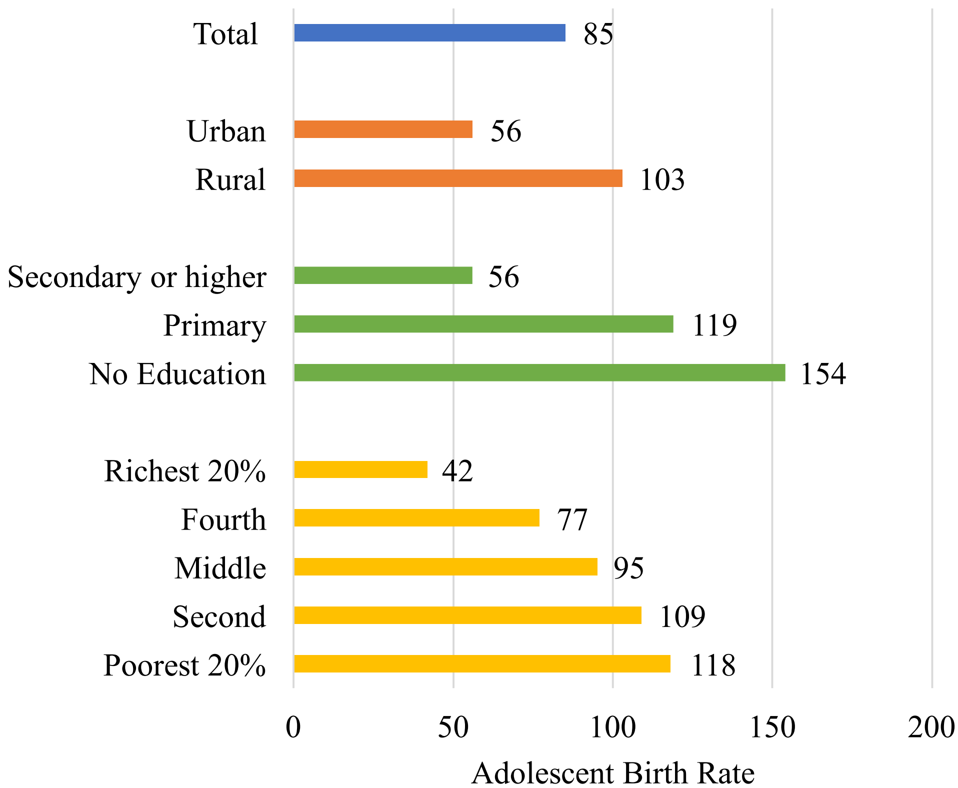


Figure 2.5 Adolescent birth rate (the average number of live births per 1,000 women aged 15 to 19) by United Nations Population Fund (UNFPA) background characteristics; Figure based on data for 79 countries, representing over 80% of the populations of these regions (Adapted from: Loaiza & Liang, Adolescent Pregnancy: A Review of Evidence, 2013)

A study examining SES and cultural factors associated with adolescent pregnancy in East Africa revealed that adolescent mothers were more likely to be poor, have received little to no education, and are less likely to be married, a factor that may come with additional stigma and social isolation (Neal et al., 2015). Additional studies conducted in Africa have found that a

lower SES, being raised without parents, especially their mother, and poor performance in school put adolescent girls at an increased risk for early pregnancy and childbirth (Christofides et al., 2014; Branson et al, 2016). A possible explanation for higher rates of adolescent pregnancy among girls of lower SES is that they may perceive pregnancy as a way to secure their financial and social future if the father of their child has an established family and if he is able to provide economic support (Christofides et al., 2014; Kaufman et al, 2001). Conversely, girls who come from families of higher SES may have a fear of disappointing their families by becoming pregnant and ruining their educational and social status (Christofides et al., 2014; Kaufman et al, 2001).

Education and geographic location have also been found to be strong predictors of adolescent pregnancy. Adolescent pregnancy is most common in adolescents with the least amount of education and in those who live in rural areas (Loaiza & Liang, 2013). In a study conducted in South Africa, researchers found that 74.1% of the pregnant adolescents involved in the study became pregnant due to lack of knowledge and 55% became pregnant due to a lack of understanding of the related risks of pregnancy (Mchunu et al., 2012). Additionally, 71.2% of the females reported not understanding how pregnancy happens or did not think about the possible risks involved in engaging in unprotected sexual intercourse (Mchunu et al., 2012). Alternately, a study in Cape Town found that students who are successful in school are exposed to their older peers at an earlier age, increasing the risk of earlier sexual experiences and possibly pregnancy (Lam et al, 2009).

Adolescents who reach menarche at an earlier age are more likely to have an early pregnancy since the girl is exposed to a longer period in adolescence in which she is able to conceive (Branson et al, 2015). The environment in which the adolescent grows up is also

pertinent to her risk for pregnancy. Social environments in which open communication regarding sexual intercourse is limited, or where relationship power is poorly balanced between men and women are associated with increased risk for adolescent pregnancy (Branson et al, 2015).

Studies on adolescent pregnancy have also revealed that pregnancy is sometimes intentional for a variety of reasons. Some adolescents have been shown to become pregnant with the intention of continuing their relationship or to persuade their partner to marry them (Kaphagawani & Kalipeni, 2016). Other adolescents become pregnant to prove their fertility, as a way to secure status and acceptance as a woman in society (Kaphagawani & Kalipeni, 2016; Jewkes et al., 2001).

Nutrient Needs

There is limited data on the precise nutrient needs of adolescents in pregnancy (Marangoni, et al., 2016). Current nutritional recommendations for pregnant adolescents are similar to those made for adult pregnant women. In general, weight gain and protein intake, in addition to most vitamin and mineral recommendations are the same (DRI, 1997). Although no amount has been specified in the literature, adolescents are generally recommended to gain more weight than adult mothers to improve their odds of delivering an infant of similar size (Rasmussen, Yaktine, & IOM, 2009). However, despite their similar recommendations overall, adolescents are at an increased risk for inadequate nutrition during pregnancy compared with adult women, primarily due to their higher calorie needs to support their own growth, as well as that of the fetus (Story & Hermanson, 2000; Marangoni, et al., 2016). Calorie recommendations according to the Dietary Reference Intakes (DRI) for all pregnant women, in general, are an

additional 340 kcal/d in the second trimester, and an additional 542 kcal/d in the third trimester (IOM, 2006). These amounts can vary significantly between individuals based on a variety of factors, such as physical activity levels. Adolescents who are very active, such as those living in Malawi, are likely to have increased calorie needs. However, even if pregnant adolescents are able to gain sufficient weight by consuming adequate energy intakes in pregnancy, their bodies improperly mobilize fat storage throughout pregnancy, creating a "nutritional competition" and limiting fetal growth (Scholl et al, 1994).

Calcium and phosphorus recommendations in particular are higher for pregnant adolescents. Calcium has a recommended dietary allowance (RDA) of 1300 mg/d for pregnant adolescents (≤18 years of age), compared to pregnant adults (19-50 years of age) who have an RDA of 1000 mg/d (DRI, 1997). Phosphorus requirements are nearly double for pregnant adolescents; they need 1250 mg/d compared to pregnant adults needing only 700 mg/d (DRI, 1997). An additional nutrient of concern is iron. Since iron deficiency is one of the most common nutritional deficiencies worldwide among both pregnant and non-pregnant adolescent girls across all socioeconomic groups, it is essential for this nutrient to be targeted in nutritional interventions to increase levels of consumption (Story & Hermanson, 2000).

Stratification of maternal age

In studies on adolescent pregnancy and its associated outcomes, maternal age is commonly classified into multiple groups. This classification is most commonly seen as young adolescents, older adolescents, and adults, with age ranges varying slightly in each category. It is appropriate to age stratify for two important reasons: 1) certain ages are more closely related physiologically to each other than others, and 2) it allows research findings to narrow in on a

particular age range that may be most at risk. Adolescents younger than 16 years of age have been shown to be at an increased risk of adverse pregnancy outcomes and have been categorized separately from older adolescents in previous studies (Chen et al., 2006; Momno-Ngoma et al, 2016; Althabe et al, 2015). Female pelvic structure is known to reach adequate maturity to support optimal pregnancy two years after the start of menses, at which point the pelvis height and diameter matures (Kaplanoglu et al, 2015). Adolescents who conceive less than 2 years after menarche, considered pregnancy at a low gynecological age, or at 16 years of age at conception or delivery have been shown to be at an increased risk for adverse outcomes (Gibbs et al., 2012; Conde-Agudelo et al, 2005). Since, menarche tends to occur later in girls with limited nutritional intake and in those who live in poor environmental conditions, such in Malawi, it is assumed by researchers that most adolescent mothers aged 16-17 years would have a low gynecological age, making it inappropriate to categorize them with older adolescents (Ganchimen et al, 2013).

Maternal Consequences

Adolescent pregnancy imposes a variety of consequences on the adolescent mother, child, and her family which impart detrimental effects on society as a whole (Kaphagawani & Kalipeni, 2016).

Health and Anthropometrics

Early childbearing is correlated with maternal mortality and contributes to the cycle of ill-health and poverty (WHO, 2014). Research varies as to the degree to which adolescent childbearing increases the risk of maternal mortality, however studies are consistent in reporting that adolescent maternal mortality is greater than that of adult women in their 20s (Nove et al,

2014; WHO, 2009). According to the WHO, adolescents less than 16 years of age have a maternal mortality risk two times that of women in their 20s (WHO, 2009). In a recent analysis using data from 144 countries and territories which sought to understand the current risks of maternal mortality in adolescent mothers, Nove et al. found that 82% of the world's adolescent maternal mortality occurs in sub-Saharan Africa and Asia (Nove et al, 2014). Pregnant adolescents aged 15-19 years in Africa are at an 12% greater risk of maternal mortality than pregnant women aged 20-24 years (Nove et al, 2014). Comparatively, pregnant adolescents aged 15-19 years worldwide are at a 37% greater risk of maternal mortality than their adult counterparts aged 20-24 (Nove et al, 2014). **Figure 2.6** shows the age-specific mortality ratios by region; results highlight the extraordinarily high rates of maternal mortality found throughout Africa at every age category.

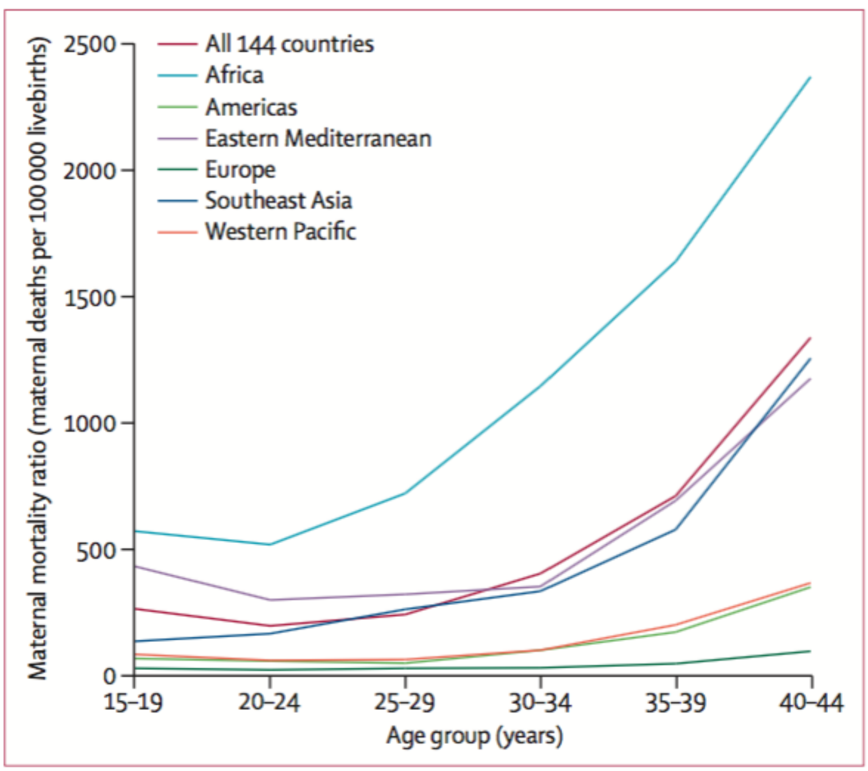


Figure 2.6 Age-specific maternal mortality ratios, by region. (Adapted from: Nove et al, 2014.)

Adolescence is a time of immense growth and development for females, during which about 50% of adult body weight and 15% of final adult height is obtained. In addition to important changes in body shape and composition, pregnancy in adolescence greatly increases health risks and compromises the growth and developmental capacity of both mother and fetus (Rah et al, 2008). The cause of limited growth in adolescent pregnancy is believed to be a competition for nutrients between the adolescent mother and her fetus, a process known as 'nutrient partitioning" (Johnson & Moore, 2015). Another explanation as to the limited growth of mother and fetus during adolescent pregnancy is that optimal fetal development is compromised in girls of low gynecological maturity to ensure a safe delivery for the mother (Johnson & Moore, 2015). In low- and middle- income countries adolescent mothers have an increased likelihood to also be physically immature because of stunted growth as a result of undernutrition (Fall et al, 2015). Some additional health complications that arise at an increased rate in adolescent mothers include anemia, HIV, and obstructed labor and pregnancy-induced hypertension, both of which increase risk for maternal mortality.

Obstructed labor is more prevalent in adolescent pregnant women due to the incomplete development of their bodies (WHO, 2009). The female pelvic structures reaches adequate maturation to support pregnancy at about 2 years after menses, at which point pelvic height and diameter have matured (Kaplanoglu et al, 2015; Gibbs et al, 2012). Emergency obstetric care, a health care service limited in rural areas of developing countries, is needed to treat obstructed labor to prevent uterine rupture and prevent the risk of maternal and infant mortality (WHO, 2009). Additionally, adolescent mothers that are able to survive obstructed labor are at risk of prolonged labor which can cause an obstetric fistula (WHO, 2009). Under normal circumstances

this can be rectified with surgery, however many women in Africa have limited access to treatment, leaving them with a condition leading to incontinence, and various side effects such as psychological issues and social isolation (WHO, 2009).

Adolescent mothers have an increased risk of anemia compared to adult pregnant women. In a study conducted in Thailand, the risk of anemia increased with decreasing maternal age (Thaithea & Thato, 2011). Anemia in pregnancy has been found to be associated with increased rates of maternal and perinatal mortality, premature delivery, LBW, and other various other adverse pregnancy outcomes (Thaithea & Thato, 2011). Its cause is typically not related specifically to the age of the pregnant woman, but rather to nutritional deficiency, especially that of iron and folic acid, and malaria and intestinal parasites common in developing countries (WHO, 2004).

Studies show that HIV infection incidence is greater in all pregnant women compared to lactating, non-pregnant, and non-lactating women, and this risk of infection is even greater in adolescent pregnant women (Gray et al, 2005; Christofides et al, 2014). Research by Gray et al. conducted in Uganda supports this by showing that pregnant women (HIV incidence 2.3 per 100 person years) are at a significantly higher risk of HIV infection acquisition compared to nonpregnant and nonlactating women (HIV incidence 1.1 per 100 person years) even after controlling for appropriate sociodemographic and behavioral factors (Gray et al, 2005). The research also shows that adolescent pregnant women ages 15-19 years have a risk ratio of HIV relative to nonpregnant/nonlactating women of 2.82 (1.23-6.42) compared to a risk ratio of 1.66 (0.94-2.94) and 1.46 (0.46-4.60) in women 20-29 and women >30, respectively (Gray et al, 2005). Additional research in South Africa support this data, showing that young adolescents 15 years of age or younger are 3 times more likely to acquire HIV (Christofides et al, 2014).

Possible explanations behind these findings are biological and behavioral in nature. Gray et al. speculates that hormonal changes in pregnancy may increase a woman's susceptibility to HIV infection by stimulating changes in the genital tract mucosa or the immune system (Gray et al, 2005). Christofides et al. highlights the possibility that early adolescent women with an increased risk for HIV infection also participate in more risky behavior than older adolescents, such as having more sexual partners and having experienced more physical and sexual violence (Christofides et al, 2014).

Anthropometrics and body composition measures of adolescents have also been shown to be negatively affected by pregnancy. A study by Rah et al. (2008) in rural Bangladesh revealed that pregnancy and lactation in adolescents, particularly those of low gynecological age, halted linear growth whereas the annual growth rate of nonpregnant/nonlactating women remained at 0.35 +/- 0.85 cm/yr (mean +/- SD). The researchers estimate that the adolescent pregnant women lose approximately 0.6-2.7 cm of attained height. Pregnant and lactating adolescent girls suffered from weight loss (0.76 +/- 2.51 kg), reduction in BMI (0.34 +/- 1.12 kg/m^2), and depletion of fat (MUAC loss) and lean body mass (AMA loss). Since weight and BMI of pregnant adolescents serves as a reflection of maternal energy stores, loss of these indicate depletion of maternal energy reserves, limiting the likelihood for a successful pregnancy (Rah et al, 2008). Additionally, short stature in a mother is associated with adverse birth outcomes. Kozuki et al. (2015) found there to be significant associations between short maternal stature and SGA and preterm birth in women from low- and middle-income countries.

Socioeconomic

Adolescent pregnancy and childbirth has been linked with poor educational achievement, poverty, and unemployment in the mothers, all of which have lifelong consequences on the well-being of mother and child (WHO, Adolescent Pregnancy, 2007). Adolescent mothers tend to have a lower SES, less education, and less stable partnerships than adult mothers (Fall et al, 2015).

Education is severely affected once an adolescent girl becomes pregnant. Often times, pregnant adolescents are forced to drop out of school because of the embarrassment and physical demands required of pregnancy. Research from South Africa showed that only about one third of adolescent girls return to school following childbirth, with young adolescent mothers (having their first child at 17 years or younger) being even less likely to return (Willan, 2013). In another South African study adolescent mothers were found to be 20% less likely to be enrolled in school and 25% more likely to drop out of school when compared to their peers, and also were two-thirds of a grade behind their nonpregnant peers (Ardington, 2012). Some adolescents do return to school, however their academic performance commonly suffers. Many adolescent mothers in school shift from performing well academically to becoming an average student; while others put very little effort into their school work as a result of the time and physical requirements of motherhood (Willan, 2013). Ultimately, the ability of an adolescent mother to return to school largely depends on her familial and social supports, and their capacity and willingness to help the girl with childcare and financial assistance (Willan, 2013). Limited educational attainment in adolescence is associated with a reduced ability to accumulate useful skills that are relevant to the job market and essential for being independent and productive in society (UNFPA, 2012).

Infant Consequences

Children born to adolescent mothers are at in increased risk for numerous health risks, including preterm birth, intrauterine growth restriction, infant mortality, and child undernutrition, which result from a variety of behavioral, social, and biological factors (Fall et al. 2015). Many adolescent mothers are unprepared and unable to manage the stresses and time commitment required of caring for an infant. Biological, psychosocial, and behavioral immaturity of the mother and inability to face pregnancy, childbirth and childcare increases the infant's risk for poor health outcomes (Zabin & Kiragu, 1998). Though research shows that the children of adolescent mothers are at an increased risk overall, the effect of young maternal age on child health and well-being differs across different social groups due to inequalities that exist in each (Geronimus, 1996).

Health

Risks for adverse perinatal outcomes increase with decreasing maternal age (Ganchimen et al., 2013). Frequent adverse health effects in this population include preterm delivery, LBW, SGA, stunting, and increased rates of neonatal and infant mortality, with offspring born to adolescent mothers being 2 times as likely to be stillborn or dye in the first month of life compared to adult mothers in their 20s (Chen et al, 2006; WHO, 2014).

Rates of LBW and preterm birth are frequent adverse side-effects of early childbearing (Ganchimen et al., 2013; Sagili et al., 2011; Fall et al., 2015; Althabe et al., 2015). Fall et al. (2015) determined that adolescent mothers had a 20-30% increased risk of LBW and preterm birth compared to mothers ages 20-24 years using data pooled data from five low- and middle-income countries. Multiple studies have also shown that very young maternal age, defined

slightly differently in each study, is more strongly associated with detrimental outcomes than older adolescents and adults (Mombo-Ngoma et al., 2016; Chen et al, 2006). A recent observational study revealed that very young maternal age (≤16 years) was most highly correlated with highest risk for delivery of a LBW infant and preterm birth, compared to adult mothers 20-30 years old (Mombo-Ngoma et al., 2016). The competition for nutrients between mother and fetus is the common explanation for the elevated rates of LBW that result from adolescent pregnancy (Ganchimen et al., 2013). The cause of preterm delivery in this population has been linked with the low gynaecological maturity of adolescents (Ganchimen et al., 2013).

Stunting is another relevant health effect of adolescent pregnancy. Fall et al. found that children of adolescent mothers had a 30-40% increased risk of stunting at two years of age (Fall et al, 2015).

Education and Cognition

Educational performance is stunted in children of adolescent mothers. Fall et al. (2015) found that children of adolescent mothers have a 30-40% increased risk of failure for her child to complete secondary school compared to adult mothers. Additionally, children of young adolescent mothers (17 years and younger) have lower levels of school readiness, lower math and reading scores, lower language, communication, and social skills, and lower physical and emotional well-being at the start of kindergarten compared to children of older mothers (SCAA, 2008). Additionally, these children are 50% more likely to repeat a grade, are less likely to complete high school, and have lower performance on standardized tests than children of adult mothers (Schuyler Center for Analysis and Advocacy (SCAA), 2008).

Cognition has also been shown to be lower in the offspring of adolescent mothers. In a study by Khatun et al. (2017), the offspring of adolescent mothers had an attenuated IQ lower by -1.4 points on average at 21 years of age, than offspring of mothers older than 20 years, solidifying the evidence that cognitive impairment is an adverse outcome for the offspring of adolescent pregnancy. This reduced IQ, compounded with the reduced likelihood for educational achievement may exacerbate the challenges faced by children of adolescent mothers, adding to the intergenerational transfer of psychosocial, health, and socioeconomic disadvantage seen in this population (Khatun et al, 2017).

Socioeconomic

Children of adolescent mothers are at a heightened risk for growing up in poverty and to continue to live within a lower SES into adulthood (SCCA, 2008). Data pulled from the US National Campaign to Prevent Teen and Unplanned Pregnancy show that children are who were born to an adolescent mother, whose parents were unmarried at the time of birth, and whose mother did not receive a high school diploma or GED are 9 times more likely to grow up in poverty compared to children who had none of these factors (SCCA, 2008). These children are also more likely to be unemployed and to become adolescent parents themselves (SCAA, 2008).

MALAWI DEMOGRAPHICS

Maternal Health

Malawi is a low-income country in sub-Saharan Africa with a population of 18.09 million and an economy that is largely agriculture-based (**Figure 2.7**) (The World Bank, 2016; Cords & Rickards, 2015). A large portion of the population is made up of youths and young adults, with

21.4% of the population falling between the ages of 15 and 19 (DHS, 2015-16). As of 2010, 50.7% of the population of Malawi lived below the national poverty line, with the majority living in rural areas in which more than 90% relied on rain-fed subsistence farming for survival (The World Bank, 2010b; Osgood et al., 2008).

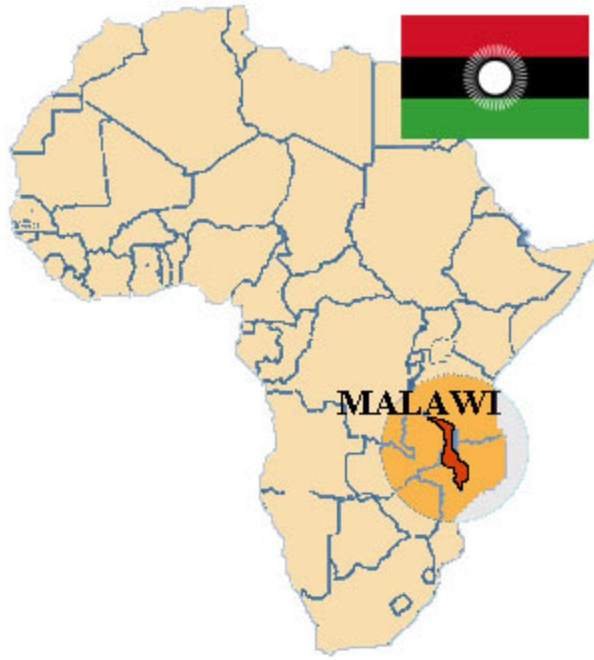


Figure 2.7 Map of Africa, highlighting Malawi. (Adapted from: http://malawiorphancareproject.org/about-malawi/)

Maternal Mortality Ratio

The maternal mortality ratio (MMR), defined as "the death of a woman while pregnant or within 42 days of pregnancy termination," is one of the highest worldwide, at 634 maternal deaths in every 100,000 live births, and accounts for 16% of all deaths to women ages 15-49 (Colbourn et al., 2013; The World Bank, 2015a; DHS 2015-16). The main causes of maternal mortality in Malawi include haemorrhage, infection and sepsis, hypertensive disorders, complications of unsafe abortion, iron-deficiency and malaria caused anaemia, and obstructed or prolonged labor (Titilayo, Palamuleni & Omisakin, 2016).

Fertility

Although the total fertility ratio (TFR) is going down with time in Malawi, the TFR is currently at 4.4 children per woman (DHS, 2015-16). Women living in rural areas have a higher TFR on average compared to those living in urban areas, and those in the lowest wealth quintile have on average 2.8 more children than women in the highest wealth quintile (DHS 2015-16) (**Figure 2.8**, **Figure 2.9**). The high TFR coupled with limited use and access to contraception, increases the burden of malnutrition by causing a woman's tissues to become depleted of essential nutrients as she continues on a vicious cycle of too many closely spaced pregnancies, preventing her body from recovering nutritionally (Ahmed et al., 2012).

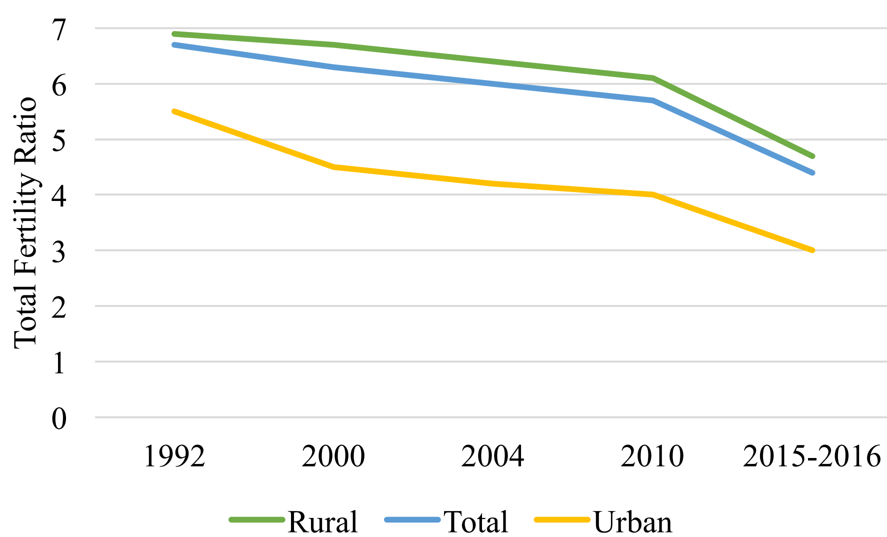


Figure 2.8 Trends in fertility by residence in Malawi defined by Total Fertility Ratio (TFR) (average number of children per woman) (Adapted from: Demographic and Health Survey (DHS) 2015-16 Malawi)

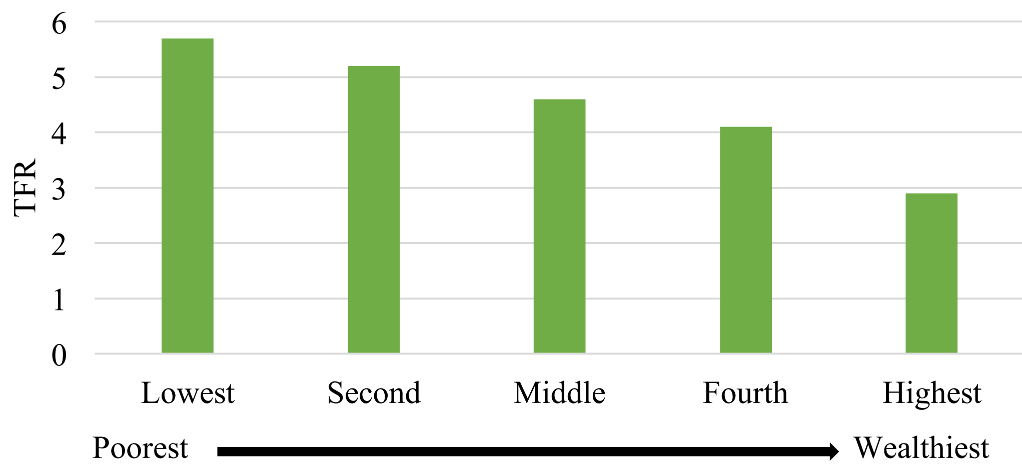


Figure 2.9 Fertility by household wealth in Malawi defined as Total Fertility Ratio (TFR) (average number of children per woman) (Adapted from: Demographic and Health Survey (DHS) 2015-16 Malawi)

BMI

Maternal BMI is a concern in Malawi. Women who are underweight, defined as having a BMI less than 18.5 kg/m^2, prior to conception and at the beginning of pregnancy have diminished energy stores and are likely deficient in important nutrients essential for maternal health, growth, and fetal and infant development (Hanson et al., 2015). In Malawi, 7% of women age 15-49 are classified as being underweight, with adolescent girls (15-19 years) representing the majority of this underweight group (DHS, 2015-16). Underweight BMI, in pregnancy is associated with LBW, shorter gestational length, preterm birth, IUGR, and smaller head circumference (Hanson et al., 2015). Underweight BMI compounded with the additional strain of pregnancy in adolescence, puts both the mother and fetus at a greater risk than that of an adult woman.

Malaria

Malaria is a major health concern for Malawians. In 2015, the incidence of malaria in Malawi was 188.8 per 1,000 people at risk in the country, with every Malawian resident living in a region of high malaria transmission, defined as greater than one case per 1,000 residents (The World Bank, 2015g; Mathanga et al., 2012). The disease is endemic and stable in Malawi, however there is significant seasonal variation, determined largely by the annual rainy season which typically begins in November/December and lasts through March/April in most regions of the country (Mathanga et al., 2012).

Recent efforts have been made to alleviate rates of malaria in the country, specifically targeting two vulnerable groups, pregnant women and infants (Mathanga et al., 2012). Malaria in pregnant women can cause health issues in pregnancy that have detrimental consequences on the offspring, and these consequences are often made worse by the compounding effect of malnutrition in the mother. Malaria in pregnancy can lead to an increased risk of LBW and maternal anemia (Cates et al., 2017; Feng et al., 2010).

Though not able to completely eliminate the disease, there has been success in significantly reducing its prevalence and thereby decreasing the prevalence of maternal anemia and LBW in Malawi (Feng et al., 2010). Malaria prevalence in pregnant women was recorded from 1997-2006 in a hospital in southern Malawi; results showed that the prevalence of peripheral parasitemia and placental malaria dropped from 23.5% and 25.2% to 5.0% and 6.8%, respectively (Mathanga et al., 2012).

Helminths

Helminth infection is another health concern for individuals living in Malawi, particularly in pregnant women, in which infection can lead to detrimental health effects to both mother and infant. Helminth infection in pregnancy has been shown to influence maternal anemia, the maternal immune system, and susceptibility of offspring to future helminth infection (Mpairwe, Tweyongyere, & Elliott, 2014; DHS, 2015-2016). The prevalence of infection varies across the country depending on two factors: the distribution of hosts and schistosome parasites in bodies of water and the behavioral patterns of humans (Makaula et al., 2014).

HIV

The prevalence of HIV infection in men and women ages 15-24 were 1.8% and 4.5%, respectively, in 2016 (The World Bank, 2015e & 2015f). HIV disproportionately affects women throughout all age groups across Malawi (DHS 2015-16; Ramlal et al., 2015). Approximately 60% of adults in Malawi living with HIV are female (Ramlal et al., 2015). HIV, coupled with poor nutritional status frequently leads to maternal malnutrition due to the wasting that commonly occurs with the disease (Lartey et al., 2008; Mehta et al., 2008). Additionally, poor nutrition either as a result of HIV-induced wasting or weight loss, or as a preexisting condition, is likely to increase the risk of mother-to-child transmission of HIV (Villamor et al., 2005).

Research from Malawi shows that pregnant women have an increased risk for acquisition of HIV compared to all non-pregnant women. Taha et al. reported a 2.19-fold higher rate of HIV incidence in pregnancy compared to the postpartum period (Taha et al, 1998).

Current Supplemental Nutrition Standard of Care

In Malawi it is recommended for adults with malnutrition to receive a fortified corn-soy blend (CSB) flour as supplementation (Annan et al., 2014). CSB+ is one of the main fortified blended foods used in moderate acute malnutrition management (Annan et al., 2014). It is usually mixed with water and cooked as porridge. In addition to CSB+, an iron and folic acid supplement (IFA) is commonly provided to pregnant women in their second and third trimesters through antenatal clinics in areas with high rates of iron deficiency (Manary et al., 2017). However, despite having a standard of care supporting food supplementation of moderately malnourished pregnant women, it is commonly not provided.

Ready-to-use supplementary foods (RUSF), on the other hand, were created to provide a nutrient- and energy-dense alternative to the conventional supplements available, such as enriched corn blends (Steenkamp et al., 2015). RUSFs have a low water content, decreasing the risk for microbial contamination. They also require no refrigeration, preparation, or cooking, making them ideal and practical for use in low- and middle-income countries where clean water and safe storage conditions are lacking (Steenkamp et al., 2015).

Health Care Services in Malawi

Health care services are an important component throughout pregnancy, during childbirth, and after delivery to ensure the wellbeing, health, and survival of mother and infant (DHS, 2015-16). Although almost all (95%) women ages 15-49 received antenatal care from a skilled provider at least once during their pregnancy, only half had at least four visits, the recommendation set forth by the WHO (DHS 2015-16). Use of a skilled healthcare provider for antenatal care increases with higher maternal education, is higher in urban areas than in rural,

and is slightly more common in wealthier women (DHS 2015-16). Institutional deliveries and delivery by a skilled provider are highly correlated with education status of the mother (DHS 2015-16). Institutional deliveries, those that occur in a health facility, have increased by 65% over the past 24 years, and home deliveries have decreased by 84% (DHS 2015-16). During delivery specifically, 90% of births are delivered by a skilled provider, such as a doctor, clinical officer, medical assistant, nurse or midwife (DHS 2015-16).

With a large portion of maternal and neonatal deaths occurring within the first 24 hours after delivery, postnatal care is critical to minimize complications, treat any issues that may arise during delivery, and provide nutrition and health information (DHS 2015-16). The Malawi Ministry of Health recommendation on health checks is that all women who deliver in a health facility should receive a health check within the first 24 hours post-delivery, and all women who deliver outside of a facility should be referred to a health facility within 12 hours post-delivery (DHS 2015-16). However, regardless of this recommendation, only half of all mothers ever received this postnatal check (DHS 2015-16).

Adolescent Pregnancy

Adolescent pregnancy is common throughout Malawi, with 29% of women ages 15-19 having begun childbearing (DHS 2015-16). As of 2015, the adolescent fertility rate in Malawi is 135 births per 1,000 women ages 15-19, 37% higher than the average adolescent fertility rate of Sub Saharan Africa (101 births per 1,000 women), and 206% higher than the average adolescent fertility rate worldwide (44.1 births per 1,000 women) (The World Bank, 2015h). The majority of adolescent pregnant women in Malawi live in rural areas, are 19 years of age, and are classified as being in the lowest wealth quintile (DHS 2015-16) (**Figure 2.10**).

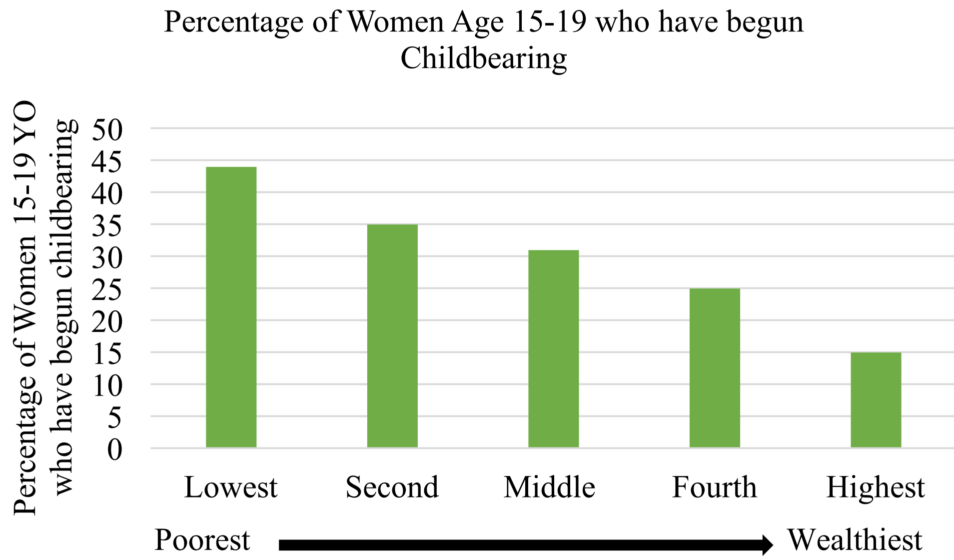


Figure 2.10 Graphical representation of adolescent pregnancy by household wealth in Malawi (Adapted from: Demographic and Health Survey (DHS) 2015-16 Malawi)

Compared to other countries in southern Africa, Malawi ranks third (35%) after Mozambique (42%) and Madagascar (36%) in terms of percent of women aged 20-24 that had a live birth before the age of 18 (Loaiza & Liang, 2013).

Adolescent pregnancy in Malawi contributes to its high child mortality and poor maternal health in Malawi. By age, perinatal mortality rates in Malawi are highest among mothers who are younger than age 20 (45 deaths per 1,000 live births) (DHS, 2015-16). A vicious cycle of intergenerational poverty exists in Malawi in which adolescents drop out of school earlier than their male counterparts, marry at a young age, become sexually active, fail use contraception, are exposed to sexually transmitted diseases, and become pregnant in their adolescent years, significantly limiting their ability to participate in school and their ability to provide adequate care to their children (World Bank Group, Policy Brief: Malawi, 2016).

Adolescent Contraceptive Use

Contraceptive use among adolescents in Malawi is relatively low, with 33.7% of sexually active, unmarried women ages 15-19 using any method of contraception, and 38.1% of married women ages 15-19 using any method of contraception (DHS, 2015-16). A study in Malawi found that adolescents are less likely to use contraception than older women and are more likely to use contraception more intermittently (Munthali & Chimbiri, 2003). Therefore, adolescents are at risk of pregnancy due to their limited use of contraception. Many reasons exist for non-contraceptive use in Malawi; these include limited availability of contraceptives, religious and cultural beliefs, poor quality of services including the negative attitudes of service providers and the presence of adults at clinics, the inability to negotiate contraceptive use with sexual partners, and the fear of side effects, stigma associated with contraceptive use, and general misconceptions (Kaphagawani & Kalipeni, 2016; Chonzi, 2000). One study in Malawi revealed that 57% of adolescent girls opted to risk pregnancy rather than asking their partner to use a condom (Kaphagawani & Kalipeni, 2016). Another revealed that only 6% of adolescents use condoms, increasing their risk of pregnancy and HIV infection (Allan Guttmacher Institute, 2005).

Knowledge of Reproductive and Sexual Health

Adolescents lack a general understanding of reproductive and sexual health, and the majority of information received by adolescents on this topic come from a variety of sources (Kaphagawani & Kalipeni, 2016). Sources of information include friends, peers, schools, health facilities, youth clubs, and radio, with friends/peers being the most important source and counselors coming in second (Kaphagawani & Kalipeni, 2016; Maluwa-Banda & Lunguzi, 2002). Communication regarding reproductive and sexual health is limited within families,

causing adolescent girls to seek out information from other, less reliable sources. Additionally, male partners may provide misleading information as a way to manipulate girls to engage in sexual interactions (Kaphagawani & Kalipeni, 2016; Jewkes et al., 2001).

Malnutrition

Research highlights the risk for inadequate nutrition during adolescent pregnancy worldwide (Brown, J. B., et al., 2014 & Marangoni, et al., 2016). Kalanda et al. (2006) showed this to be true in Malawi, specifically. Adolescent pregnant Malawian women ages 12-19 were noticeably more undernourished, as defined by either a maternal height less than 155 cm, weight less than 50 kg, MUAC less than 23 cm, or a BMI less than 18.5 kg/m^2, when compared to adult pregnant women (Kalanda et al, 2006). **Table 2.1** shows that all adolescent anthropometric measures were significantly less on average than those of adults at first attendance at the antenatal clinic while **Table 2.2** indicates that significantly more adolescents were underweight and had a lower MUAC than the older mothers.

Table 2.1 Anthropometry of adolescent (12-19 YO) compared with adult (>19 YO) pregnant women at first attendance to antenatal clinics in Malawi

Anthropometric measure	Adolescent (12-19 YO) Mean ± SD	Adult (>19 YO) Mean ± SD	*p* value
Mean weight (kg)*	49.5 ± 5.0	51.8 ± 6.4	<0.01
Mean height (cm) +	156 ± 6.1	157 ± 5.6	0.01
Mean MUAC (cm)+	24.1 ± 2.0	25.3 ± 2.1	<0.01
BMI (kg/m^2)*	20.4 ± 1.8	21.0 ± 2.3	0.001

*First attendance at or before 18 weeks gestation.
+First attendance at any gestation age.
BMI, body mass index; MUAC, mid-upper arm circumference
(Adapted from: Kalanda et al, 2006)

Table 2.2 Proportion of undernourished and illiterate adolescent (12-19 YO) and adult (>19 YO) pregnant Malawian women.

Anthropometric measure	Adolescent (12-19 YO)	Adult (>19 YO)	*p* value	Odds ratio (95% CI)
Weight <50 kg (%)*	53.4	37.3	0.01	1.9 (1.4, 2.7)
Height <50 cm (%)+	11.6	8.2	0.23	1.5 (0.8, 2.5)
MUAC <23 cm (%)+	25.8	10.5	0.01	3.0 (1.9, 4.6)
BMI <18 kg/m^2 (%)*	17.9	12.7	0.06	1.6 (1.0, 2.6)
Illiterate (%)	77.9	75.1	0.48	1.2 (0.8, 1.7)

*First attendance at or before 18 weeks gestation.
+First attendance at any gestation age.
MUAC, mid-upper arm circumference; BMI, body mass index
(Adapted from: Kalanda et al, 2006)

Infant Health

Mortality; Preterm Birth; Low Birth Weight

Though rates of survival for children through the 5th birthday have improved in Malawi, annual rates of premature birth, newborn death, and LBW are still high (UNICEF, 2017; World Bank, 2010a). Preterm birth is the primary contributor to neonatal mortality, defined as the death of an infant in their first 28 days of life (0-27 days) (WHO, 2016) (**Figure 2.11**). According to the WHO in 2016, Malawi was determined to have the highest rate of preterm birth per 100 live births, standing at 18.1 per 100 live births (WHO, 2016).

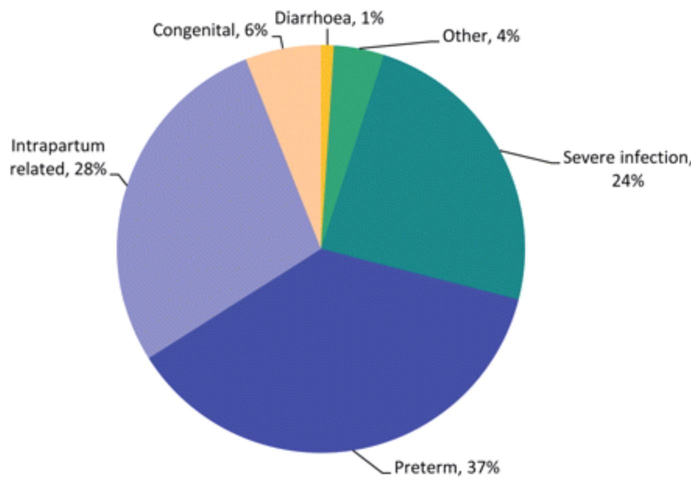


Figure 2.11 Malawi-specific neonatal mortality (defined as infant death in the first 28 days of life) estimates around year 2010 (Adapted from: Zimba et al, 2012)

In Malawi, 28,300 newborns die or are stillborn every year (UNICEF, 2017). Rates of neonatal, infant, and child mortality are 24%, 28%, and 35% higher, respectively, in Malawi compared to rates worldwide (**Table 2.3**) (The World Bank, 2016b-d, respectively).

Table 2.3 Rates per 1,000 live births of neonatal, infant and child mortality in Malawi, Sub-Saharan Africa, and Worldwide

Rate	Definition	Malawi	Sub-Saharan Africa	Worldwide
Neonatal Mortality Rate	Death within first 28 days of life	23.1	27.7	18.6
Infant Mortality Rate	Death within first year of life	39	53	30.5
Child Mortality Rate	Death within first 5 years of life	55	78	40.8

Data from: World Bank, 2016b-d

LBW is also common in Malawi; in 2010, 14% of births resulted in LBW infants contributing to the high rates of offspring mortality (The World Bank, 2010a).

Stunting

As of 2014, the prevalence of stunting was 42.4 per 1,000 live births in Malawi (The World Bank, 2014). Although there has been a 33% decrease in the prevalence of stunting in Malawi over the past 24 years, 37% of children under 5 are still considered stunted according to the most recent Malawi Demographic and Health Survey 2015-16 (DHS, 2015-16). Stunting in Malawi is found more frequently in children living in rural areas, children born to less educated mothers, and children living in the lowest wealth quintile (DHS, 2015-16).

SUMMARY STATEMENT

Maternal malnutrition and adolescent pregnancy are global concerns that negatively affect maternal health, fetal growth, birth outcomes, and infant growth. Individually, maternal malnutrition and adolescent pregnancy both lead to numerous short- and long term consequences on mother and child, including an increased risk for maternal mortality and morbidity, preterm delivery, delivery of a LBW infant, and stunting. In the absence of malnutrition, adolescent mothers and their offspring pay a large health, social and economic cost for early childbearing (Karra & Lee, 2012). However, the compounded effects of malnutrition in adolescent pregnancy exacerbate the associated adverse outcomes to a degree that is higher than what is commonly seen in each individually.

CHAPTER 3: MATERIALS AND METHODS

Objective

The main objective of this research was twofold: 1) to determine if the effects of treatment on adolescent mothers in the *Mamachiponde* study differed between the three treatment groups and 2) to determine if there were differences in maternal and infant outcomes between young adolescents (16-17 YO), older adolescents (18-19 YO), and adults (≥20 YO) in a pooled treatment group analysis. Differences in anthropometric outcomes were also assessed in infants by gender.

Participants

This research ('Adolescent substudy') is a substudy of a larger assessor-blinded randomized controlled clinical trial that assessed the effectiveness of the Malawian standard of care in treatment of moderate malnutrition in pregnancy against two other nutrition interventions.

Pregnant women with moderate malnutrition were recruited into the *Mamachiponde* study between March 2014 and December 2015 from 15 antenatal clinics in southern Malawi. The antenatal clinics were located in the health districts of Blantyre, Chikhwawa, Mulanje, and Zomba.

Inclusion criteria into the *Mamachiponde* study included:

- Moderate malnutrition as indicated by a MUAC ≥ 20.6 cm to ≤ 23.0 cm
- ≥ 16 years old
- Hemoglobin ≥ 70 g/L
- Fundal Height <35 cm
- Willingness to attend the antenatal clinic every two weeks during pregnancy

- Plans to remain in the area for delivery and until 3 months postpartum
- Provision of written and verbal consent

Exclusion criteria into the *Mamachiponde* study included:

- Severe malnutrition as indicated by a MUAC <20.6
- Pregnancy complications such as gestational diabetes, preeclampsia, hypertension
- Severe anemia as indicated by a blood hemoglobin <7.0 g/L
- Participation in any other nutrition study or supplemental feeding program
- <16 years old

Inclusion criteria for Adolescent substudy:

- Same as listed above for *Mamachiponde* study

Exclusion criteria for Adolescent substudy:

- Same as listed above for *Mamachiponde* study

The *Mamachiponde* study was registered in ClinicalTrials.gov NCT02120599 and was approved by the Institutional Review Boards of Washington University in St. Louis, California Polytechnic State University, San Luis Obispo, and the University of Malawi College of Medicine. All women gave verbal and written informed consent to be in the study for themselves and their infants.

Randomization and Blinding

Subjects were randomized in blocks of 60 to receive a micronutrient-fortified ready-to-use-supplementary food (RUSF), fortified corn soy blended flour (CSB+) with a multiple micronutrient supplement (UNIMMAP), or CSB+ with iron and folic acid (IFA) supplements using a random number generator which prospectively assigned participant identification

numbers to a study group labeled A, B, or C. Women selected a sealed blank envelope containing a study number that was linked to the randomly assigned treatment. While the data entry and analysis teams were blinded to the treatment received by each participant, the clinic teams and the study subjects were not blinded due to the fact that the treatments were visually distinct from each other. To maintain blinding of the clinic research team, at study entry the study nurse responsible for dispensing the food would look up each participant's identification number, select the appropriately assigned food, and would place it into an opaque bucket. The study nurses and drivers were the only study personnel who knew which treatment group each participant was placed in. It was essential for the study nurses to be aware of treatment assignment in order to give each mother the correct instructions for how to prepare and/or take the foods and supplements. Enrollment and measurement information were completed in the clinic, separate from treatment distribution. The study driver was also responsible for distributing the appropriate study food to each woman and would do so as a final step before leaving clinic by using her identification number to determine her assigned treatment. The driver would place it in an opaque bucket to prevent the rest of the research team and all other present mothers from seeing which treatment she was receiving. Data entry and analysis was completed completely blinded to intervention group.

Study Design

Mamachiponde was designed to determine the effectiveness of the treatment foods on the recovery of moderate malnutrition in pregnancy and in the improvement of maternal and infant outcomes, compared to the standard of care. Standard of care in Malawi is CSB+ with IFA supplements. All treatment foods and supplements were provided in a 14 day supply.

Study Foods

Two interventions, RUSF and CSB+ with UNIMMAP, were compared to CSB+ with IFA. CSB+ was a "super cereal" composed of "CSB with sugar" (World Food Program, 2014). Full nutrient profiles for each treatment are provided in **Appendix A**.

1. **RUSF**: This treatment provided 920 kcal/day, 36 g protein, and about 200% of the Recommended Dietary Allowance (RDA) for most micronutrients required in pregnancy. The energy content of RUSF was designed to provide the 360-450 kcals required during the second and third trimesters of pregnancy, as well as an additional 450-550 kcals to support recovery from moderate malnutrition. Since RUSF was formulated with the appropriate micronutrients, women receiving this treatment did not receive any additional supplements. RUSF was administered as ten 250 g bottles with a daily portion of 175 g.
2. **CSB+ with UNIMMAP**: This treatment included 893 kcal/day, 33 g protein, and provided women with >100% of the RDA for almost all micronutrients. CSB+ with UNIMMAP included 5 kg of CSB+ flour plus a standard antenatal micronutrient (UNIMMAP) supplement containing 15 micronutrients. The daily portion was 235 g/d.
3. **CSB+ with IFA**: This group served as the control; it is the standard of care for treatment of moderate and severe malnutrition during pregnancy in Malawi. CSB+ with IFA included 5 kg of CSB+ bimonthly (the same CSB+ was provided to the CSB+ with UNIMMAP group) with daily iron (60 mg) and folic acid (400 mcg) (IFA) supplements.

Participation and Data Collection

Baseline Data

Upon enrollment into *Mamachiponde*, the participant was interviewed and demographic and health information collected and recorded by trained study staff. Adolescents were defined as all women ≤ 19 years of age, based on WHO criteria (WHO, 2014). The Household Food Insecurity Access Scale survey was completed to identify level of household food insecurity (Coates, Swindale & Bilinsky, 2007). Women were identified as being food secure, or mild, moderately, or severely food insecure based on answers given to nine questions defined by Food and Nutrition Technical Assistance (FANTA III) guidelines (Coates et al, 2007).

Socioeconomic score (SES) was created using a ranking system with higher SES scores indicating a better socioeconomic status. The sum of the following variables were used to create SES with the ranking of their responses: roof type (Metal = 1; Thatch = 0), water source (Tap = 2; Borehole = 1; River/Stream/Well = 0), animals in house (Pig = 3; Goat = 2; Chicken = 1; Guinea Fowl = 0), number of radios (2 = 2; 1 = 1; 0 = 0), number of bicycles (2 or 3 = 2; 1 = 1; 0 = 0), electricity (Yes = 1; No = 0), and number of people who sleep in the same room (0, 1 , or 2 = 2; 3 = 1; ≥ 4 = 0).

Maternal dietary diversity was quantified using the Reciprocal Simpson’s Diversity Index (RSDI-10). RSDI-10 is based on a 10-food group classification; values may range between 1 and 10 with larger values indicating more diversity. The relative abundance of each food consumed from each food group determines the RSDI-10 output.

HIV status was recorded for all participants who had available test results, and for women who had not yet been tested, a rapid test was used to establish HIV status after routine counseling by the clinic voluntary counseling and testing counselors was complete.

Maternal Outcomes

Weight, height, MUAC, fundal height (FH) of each participant was measured by a study team member at bi-monthly antenatal clinic visits from enrollment to delivery. Weight was measured using a Seca 803 Precision for Health scale (Hamburg, Germany) and height was measured using a Seca stadiometer (Birmingham, UK). MUAC was measured two times to the nearest tenth of a centimeter on the left arm with a flexible measuring tape (TALC, Herts, UK) according to standard procedures. If measurements differed by more than 1 mm, a third measurement was made, and the two closest measurements were recorded and averaged for analysis. FH was measured in the supine position with a non-elastic tape, measured to the nearest 0.5 cm (Andersson & Bergstrom, 1995). A certified Malawian nurse trainer trained all Malawian nurses to measure FH with measurements made being inter-reliable to within 1.0 cm.

Maternal weight gain less than 454 g/week was used as an indicator of inadequate weight gain during pregnancy. Final fundal height <28 cm was used as an indicator of extreme premature delivery. Changes in MUAC and hemoglobin were defined as the average difference between the measurements at enrollment and terminal measurements for each woman before delivery. Maternal stature <145 cm was considered short stature.

Enrolled women returned to clinic every 2 weeks for anthropometric measurements (weight and MUAC) and health checks (blood pressure, interim illness questions, FH measurement), and to receive their two-week supply of treatment food and supplements. A woman "graduated" from the study when she reached a MUAC of ≥23.1 cm for two consecutive visits. After this two-week period, the treatment food was no longer provided, however iron and folic acid (IFA) supplements were continued for the remainder of her pregnancy. After

graduation, mothers were asked to visit clinic every 4 weeks to be assessed for relapse into malnutrition (MUAC < 23.0 cm). If MUAC dropped below 23.0 cm, mothers went back onto their assigned treatment food/supplements.

Infant outcomes

Infant anthropometric measures were collected at birth by a trained birth anthropometric team within 24-48 hours of delivery. The anthropometric team had regular communication with all woman expected to deliver within the upcoming two-week period. The team visited the infant within a few hours of being notified of delivery; at this time anthropometric measures were taken and recorded. Infant recumbent length was measured (Seca 417 length board, Hamburg, Germany) in triplicate to the nearest millimeter and averaged for analysis. Birth weight was measured in duplicate (Adam Equipment digital scale, MTB20, CT, USA) to the nearest 10 g and averaged for analysis. If the two measurements differed by more than 10 g, a third was taken and the two closest weights were averaged and used. Head circumference was measured (Seca head circumference measuring band 212, Hamburg, Germany) to the nearest millimeter in duplicate and averaged. Inter-observer variance was minimized as best as possible by periodic inter-observer comparison and standardized training and technique. Infant anthropometric measures of weight, length, MUAC, and head circumference, were also recorded at 6 and 12 weeks postpartum. At the 12 week visit, infant hemoglobin was also measured. Maternal weight and MUAC were recorded at 6 and 12 weeks postpartum.

Low birth weight was defined as having a birth weight <2.5 kg. Infant underweight was defined as a weight-for-age (WFA) Z-score of <-2, stunting as a length-for-age (LFA) Z-score of <-2, wasted as a weight-for-length (WFL) Z-score of <-2, small head circumference as a head

circumference-for-age (HCFA) Z-score of <-2. Severely underweight, stunted, wasted, and small head circumference was defined as having a WFA, LFA, WFL, and HCFA Z-score <-3, respectively.

Statistical Analysis Methods

Data were analyzed using JMP Pro software (Version12.1.0, SAS Institute, Cary, NC, USA). The World Health Organization (WHO) R macro (WHO Anthro (version 3.2.2, January 2011; http://www.who.int/childgrowth/software/en/) was used to calculate the anthropometric z-scores.

All baseline characteristic data was attained by using intention-to-treat analysis, which included 1,828 moderately malnourished pregnant women. Baseline characteristics and differences were tested using one-way analysis of variance (ANOVA) for continuous variables and chi-squared test for categorical variables. Connecting letters plots were created using Tukey-Kramer honest significance difference (HSD) tests for pairwise comparisons and categorical responses.

All maternal and infant outcome analysis was performed using an eligible outcome dataset with a sample size of 1755 moderately malnourished pregnant women. The eligible outcome dataset streamlined analysis by removing all women who were excluded or lost to follow up prior to collection of maternal and infant measures. Specifically, the eligible outcome dataset excluded 73 participants. Women for whom newborn outcomes were not collected were considered to have defaulted and were not included in the outcome analyses (n=5). Additionally, all mothers who were lost to follow up, defined as missing three consecutive clinic visits, during treatment (n=38) and who lacked infant data (n=10) were not included. Lastly, mothers who

gave birth to multiples (n=20), either twins or triplets, were not included in the maternal and infant outcome analyses. Only singleton pregnancies were included in the maternal and infant outcome comparisons.

Maternal age at enrollment variable was transformed from a continuous variable into a new categorical variable; young adolescent (16-17 YO), older adolescent, (18-19 YO), and adults (≥20 YO). Enrollment BMI and fundal height at enrollment were identified as response variables, and were controlled for in all maternal and infant outcome analyses.

General linear models with normal errors were used to compare: 1. Adolescent maternal and infant outcomes by intervention, 2. Adolescent maternal and infant outcomes by maternal age within each intervention group, 3. Maternal and infant outcomes in a pooled treatment analysis by maternal age. If differences between groups were detected, they were tested using Tukey HSD test (continuous variables) or likelihood ratio-based odds ratios (categorical variables). Odds ratios were measured using likelihood ratio tests via logistic regression. Interactions between maternal age and intervention were also eliminated using a general linear model with normal errors to determine if the association between the maternal and infant outcomes and maternal age differed by treatment group.

A general linear model was also used to compare infant outcomes by infant gender to determine if male or female infants are anthropometrically different through 12 weeks of age. An additional response variable included in the infant gender analyses was maternal age.

Least squares (LS) means are reported with standard error (SE) for all continuous variables and adjusted proportions (%) are reported with standard error (SE) for categorical variables for all outcome analyses.

Mean infant length, weight, and head circumferences were plotted on growth charts to determine percentile classifications of the infants.

CHAPTER 4: RESULTS

BASELINE CHARATERISTICS

The age range of the 1828 participants was 16 to 45 years with the median age being 20 years of age (**Figure 4.1**). Adolescents were defined as any pregnant participant <20 years of age, with young adolescents being 16-17 years old and older adolescents being 18-19 years old**.**

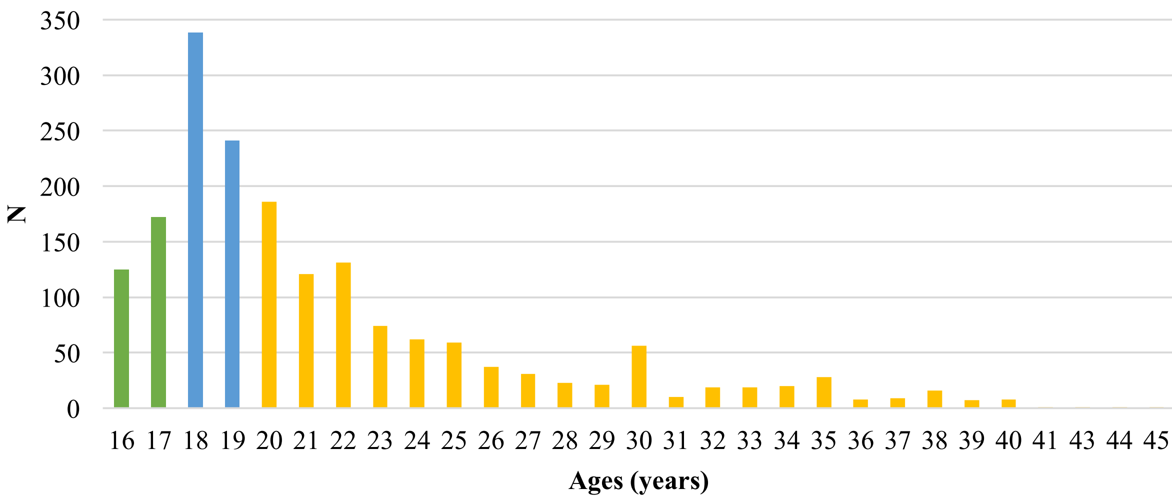


Figure 4.1 Age distribution of Mamachiponde participants
[1]N=1828
[2]Green bars represent young adolescents (16-17 YO), blue bars represent older adolescents (18-19 YO) and yellow bars represent adults (≥20 YO).

The average age of all adolescent participants was 17.8 years. For about 84% of adolescent mothers, this was their first pregnancy (**Table 4.1**). Anthropometric measures were similar across intervention groups at enrollment compared to the two other groups with the only difference of a mean fundal height of 1 cm less in the RUSF group (p=0.042). Though it did not reach significance, at enrollment adolescents in the CSB+ with UNIMMAP intervention group had a BMI 0.2 kg/m^2 greater than the two other intervention groups (p=0.0858). Overall, at enrollment BMI averaged 19.9 kg/m^2, with about 17% of adolescents being categorized as underweight (BMI <18.6 kg/m^2). Average enrollment MUAC for all adolescent participants was

22.2 cm and the average TSF was 9.7 mm. The mean adolescent height across all intervention groups was 154 cm, with about 55% if the adolescents being categorized as having short stature (height <155 cm). Most adolescents did not have very short stature, defined as a height <145 cm, which has been shown to be associated with adverse maternal and infant outcomes. Estimated weeks gestation at enrollment was approximately 24 weeks with 1.2 and 0.8 weeks less in the RUSF group compared to the CSB+ with UNIMMAP and CSB+ with IFA, respectively, however this did not reach significance ($p=0.0594$).

In general, the majority of adolescent mothers did not have HIV but were anemic at enrollment. Hemoglobin at enrollment averaged 9.9 g/L across intervention groups, with approximately 78% of adolescents categorized as being anemic at enrollment, defined as a hemoglobin <11g/L. About 21% of adolescent mothers reported illness in the previous 2 months prior to study enrollment.

Household food insecurity was high among adolescent mothers, with about 68% categorized as severely food insecure and about 23% categorized as moderately food insecure. Roughly 5% were food secure. Dietary diversity, quantified with the Reciprocal Simpson's Diversity Index, takes into account the types of food groups consumed in addition to the quantity of food consumed in each food group. Dietary diversity was 0.2 less in the CSB+ with UNIMMAP intervention adolescent group compared to the RUSF and CSB+ with IFA, however this did not reach significance ($p=0.0597$). Socioeconomic score (SES), a score created using a ranking system taking into account 7 different household variables, was similar among all adolescent treatment groups. The majority of adolescent mothers, about 72.5%, utilized a borehole as their clean water source, while about 11% used a tap. Educational level ranged from no schooling (about 5%) to tertiary school (0.3%), with the most common educational level

being 4-6 years (about 41%), followed by 7-8 years of education (about 32%). Adolescents most commonly lived in households with an average of 2.4 adults, with about 82% of the adolescent mothers sharing a household with their infant's father.

Table 4.1 Baseline nutritional and demographic characteristics at enrollment of adolescent women (<20 YO), by treatment group

Baseline Characteristic	RUSF n= 298	CSB+ with UNIMMAP n= 296	CSB+ with IFA n=282	P^2
Age, y	17.8 ± 1.0	17.8 ± 1.0	17.8 ± 1.0	0.7807
First pregnancy	253 (84.9)	250 (84.5)	233 (82.6)	0.7322
Number of Previous Pregnancies	0.2 ± 0.5	0.2 ± 0.4	0.2 ± 0.4	0.9430
BMI, kg/m^2	19.8 ± 1.4	20.0 ± 1.3	19.8 ± 1.2	0.0858
Underweight (BMI <18.6 kg/m^2)	60 (20.3)	43 (14.5)	46 (16.3)	0.1577
MUAC, cm	22.2 ± 0.6	22.3 ± 0.6	22.2 ± 0.6	0.3443
Height, cm	154.2 ± 5.5	153.7 ± 5.9	154.3 ± 5.5	0.3528
Short Stature (Height <155cm)[3]	162 (54.8)	169 (57.1)	148 (52.5)	0.5374
Very Short Stature (Height <145 cm)[3]	14 (4.7)	19 (6.4)	11 (3.9)	0.3695
Triceps Skinfold, mm	9.7 ± 2.2	9.8 ± 2.2	9.7 ± 2.2	0.7252
Estimated weeks gestation at enrollment	23.4 ± 6.1	24.6 ± 6.2	24.2 ±6.2	0.0594
Fundal Height, cm	21.4 ± 5.7[a]	22.4 ± 5.1[a]	22.4 ± 5.2[a]	0.0424
HIV-infected	5 (1.7)	7 (2.4)	4 (1.4)	0.678
Anemic at enrollment (Hgb <11g/L)	224 (75.4)	224 (75.7)	225 (79.8)	0.3791
Hemoglobin, g/L	10.0±1.6	9.9±1.4	9.8±1.4	0.1561
Mother's report of any illness in previous 2 months	65 (21.8)	67 (22.6)	62 (22.0)	0.9682
Household food insecurity[4]				
Secure	13 (4.4)	12 (4.1)	16 (5.7)	
Mild	12 (4.0)	15 (5.1)	14 (5.0)	
Moderate	64 (21.5)	65 (22.0)	70 (24.8)	
Severe	209 (70.1)	204 (68.9)	182 (64.5)	0.8234
Dietary Diversity[5]	4.6 ± 1.1	4.4 ± 1.1	4.6 ± 1.1	0.0597
SES (Socioeconomic Score)[6]	4.3 ± 1.5	4.3 ± 1.5	4.4 ± 1.7	0.9253
Clean water source used				
Borehole	217 (72.8)	219 (74.0)	199 (70.6)	0.6469
Tap	33 (11.1)	29 (9.8)	33 (11.7)	0.7533
Education				
None	17 (5.7)	18 (6.1)	10 (3.6)	
1-3 years	34 (11.4)	32 (10.9)	36 (12.8)	
4-6 years	121 (40.6)	121 (41.0)	115 (40.8)	0.9427
7-8 years	93 (31.2)	95 (32.2)	89 (31.6)	
Secondary	32 (10.7)	28 (0.5)	32 (11.4)	
Tertiary	1 (0.3)	1 (0.3)	0 (0.0)	
Adults in Household	2.4±1.0	2.3±0.8	2.4±0.9	0.1331
Mother Lives with infant's Father	248 (83.5)	241 (81.4)	231 (81.9)	0.7865

N=876

[1]Values expressed as unadjusted mean ± SD or *n* (%)

[2] *P* values calculated using one-way ANOVA (continuous measures) and Chi-square (categorical measures)

[3]Stature <145cm is an indicator of obstetric risk; Stature <155 is an indicator of SGA (small for gestational age)

[4]The Household Food Insecurity Access Scale (HFIAS) survey was used to categorize participants in level of household food insecurity based on answers given to nine questions

[5]Dietary diversity scores can range from 1 to 10, with larger values indicating more diversity

[6]SES was created using a ranking system; higher SES scores indicate better socioeconomic status

Analysis of pooled treatment groups stratified by age into young adolescents (16-17 YO), older adolescents (18-19 YO), and adults (≥20 YO) revealed no statistical differences between younger and older adolescents for almost all characteristics, but with both adolescent groups being statistically different from the adult mothers (**Table 4.2**). The average age of the adult mothers was 25 years, making the adults 8.4 and 6.6 years older, on average, compared to the younger and older adolescent mothers, respectively. The majority of adolescents were primigravid, compared to the adult mothers with almost 90% having been pregnant at least once previously (p=<0.0001). Adult mothers had, on average, 2.25 and 2.0 more previous pregnancies than young adolescent mothers and older adolescent mothers, respectively (p=<0.0001).

Young adolescent mothers on average, enrolled 0.4 weeks earlier than older adolescents, and about 1.1 weeks earlier than adult mothers (p=0.0216). Anthropometric measures of BMI and TSF were higher in young adolescent mothers compared to adult mothers; young adolescent mothers enrolled with a BMI of 0.4 kg/m^2 higher and a TSF 1 mm larger than the adult mothers (p=<0.0001, p=<0.0001, respectively). Fundal height was 1.1 cm larger in adult mothers at enrollment compared to young adolescent mothers (p=0.0004). On average, adolescent mothers were 0.5 kg heavier at enrollment, compared to the adult mothers (p=0.0147). MUAC, height, and rates of short stature did not statistically differ by maternal age (p=0.0846, p=0.1923, p=0.3336, respectively). MUAC averaged 22.3 cm across age groups, with the average height being about 154 cm. Roughly 23.8% of participants were categorized as being very short stature (height <145 cm), an indicator of obstetric risk.

Rates of HIV infection were significantly higher in adult mothers at enrollment compared to both younger and older adolescents (p=<0.0001). Rates of anemia (Hgb <11 g/L) at

enrollment were 18% and 16% higher in the younger adolescent and older adolescent groups, respectively, compared to the adult mothers (p=<0.0001). Hemoglobin was 0.4 g/L higher in the adults compared to both adolescent groups (p=<0.0001). Interestingly, rates of reported of illness in the 2 months prior to enrollment were 36% higher in the young adolescents compared to the older adolescents (p=0.0421).

Education differed across the three age groups; educational level ranged from no schooling to tertiary school (p=<0.0001). Rates of having no formal education were about 202% higher in adult mothers compared to both younger and older adolescents. Rates of having 7+ years of education were 27% and 40% higher for the younger and older adolescents, respectively, compared to the adult mothers. Household food insecurity, dietary diversity, and clean water source used did not statistically differ by maternal age stratification. The majority of women from all age groups were severely food insecure, with <5% on average being food secure. The majority of mothers utilized a borehole as their clean water source. Dietary diversity averaged 4.5 on a scale of 1-10, across age groups. Adolescent mothers were more likely to share a household with more adults than mature mothers, and were less likely to live with the infant's father (p=<0.0001, p=<0.0001, respectively).

Table 4.2 Baseline nutritional and demographic characteristics at enrollment, stratified by age

Characteristic	16-17 YO n= 297	18-19 YO n= 579	≥20 YO n=949	P^2
Age, y	16.6 ± 0.5[a]	18.4 ± 0.5[b]	25.0 ± 5.3[c]	<0.0001
First pregnancy	281 (94.6)[a]	455(78.6)[b]	117 (12.3)[c]	<0.0001
Number of Previous Pregnancies	0.05 ± 0.1[a]	0.3 ± 0.1[a]	2.3 ± 0.0[b]	<0.0001
BMI, kg/m^2	19.9 ± 1.3[a]	19.8 ± 1.3[a]	19.5 ± 1.4[b]	<0.0001
Underweight (BMI <18.6 kg/m^2)	47 (15.9)[a]	102 (17.6)[a]	227 (24.0)[b]	0.0009
MUAC, cm	22.2 ± 0.6	22.3 ± 0.6	22.3 ± 0.6	0.0846
Weight	47.0 ± 0.2	47.2 ± 0.2	46.6 ± 0.1	0.0147
Height, cm	153.7 ± 5.2	154.3 ± 5.8	154.3 ± 5.7	0.1923
Short Stature (Height <155cm)[3]	173 (58.3)	309 (53.3)	531 (56.1)	0.3336
Very Short Stature (Height <145 cm)[3]	10 (3.37)	34 (5.86)	42 (4.44)	0.2145
Triceps Skinfold, mm	9.9 ± 2.1[a]	9.7 ± 2.2[a]	8.9 ±2.3[b]	<0.0001
Estimated weeks gestation at enrollment	23.8 ± 6.2[a]	24.2 ± 6.2[a,b]	24.9 ±0.2[b]	0.0216
Fundal Height, cm	21.7 ± 5.3[a]	22.3 ± 5.3[a]	23.0± 5.6[b]	0.0004
HIV Infected	5 (1.7)[a]	11 (1.9)[a]	178 (18.8)[b]	<0.0001
Hemoglobin, g/L	9.9 ± 1.4[a]	9.9 ± 1.4[a]	10.3 ± 1.5[b]	<0.0001
Anemic at enrollment (Hgb <11 g/L)	231 (77.8)[a]	445 (76.6)[a]	623 (65.8)[b]	<0.0001
Mother's report of any illness in previous 2 months	75 (25.3) [a]	119 (20.6) [a,b]	176 (18.6) [b]	0.0421
Household food insecurity[4]				
Secure	11 (3.7)	30 (5.2)	46 (4.9)	
Mild	15 (5.1)	28 (4.8)	34 (3.6)	
Moderate	62 (20.9)	137 (23.7)	171 (18.0)	
Severe	209 (70.4)	387 (66.5)	697 (73.5)	0.0962
Dietary Diversity[5]	4.5 ± 1.1	4.5 ± 1.1	4.6 ±1.2	0.7733
SES (Socioeconomic Score)[6]	4.4 ± 1.6[a]	4.3 ± 1.6[a]	3.9 ± 1.8[b]	<0.0001
Clean water source used				
Borehole	209 (70.4)	426 (73.5)	657 (69.2)	0.1908
Tap	41 (13.8)	54 (9.3)	115 (12.1)	0.1007
Education				
None	17 (5.7)	28 (4.8)	151 (15.9)	
1-3 years	32 (10.8)	70 (12.1)	181 (19.1)	
4-6 years	130 (43.8)	228 (39.4)	314 (33.1)	<0.0001
7-8 years	93 (31.3)	184 (31.8)	176 (18.6)	
Secondary	25 (8.4)	67 (11.6)	119 (12.6)	
Tertiary	0 (0.0)	2 (0.4)	7 (0.7)	
Adults in Household	2.4 ± 0.9[a]	2.4 ± 0.9[a]	2.2 ± 0.7[b]	<0.0001
Mother Lives with infant's Father	232 (78.1)[a]	488 (84.3)[b]	842 (88.7)[c]	<0.0001

N=1828

[1]Values expressed as unadjusted mean ± SD or *n* (%)
[2] *P* values calculated using one-way ANOVA (continuous measures) and Chi-square (categorical measures)
[3]Stature <145cm is an indicator of obstetric risk; Stature <155 is an indicator of SGA (small for gestational age)
[4]The Household Food Insecurity Access Scale (HFIAS) survey was used to categorize participants in level of household food insecurity based on answers given to nine questions
[5]Dietary diversity scores can range from 1 to 10, with larger values indicating more diversity
[6]SES was created using a ranking system; higher SES scores indicate better socioeconomic status

MATERNAL OUTCOMES

Maternal Adolescent Outcomes by Intervention

Adolescent maternal outcomes were not statistically different across intervention groups after controlling response variables BMI and FH at enrollment. Weight gain from enrollment to delivery averaged 2.9 kg, with 93% of adolescents gaining less than 454 g/week (**Table 4.3**). Although not significant, adolescents in the RUSF group were on treatment slightly longer and received more rations of supplementary food (p=0.2842, p=0.2842, respectively). Overall, adolescents were on treatment for 9.6 weeks on average, and received about 4.8 rations of supplementary food. Adolescent MUAC at delivery was about 22.1 cm, approximately 0.20 cm less than the average MUAC at their enrollment. Mean final FH was 30.4 cm. Rates of delivery with a final FH less than 28 cm, an indicator of extreme premature delivery, was highest in the CSB+ with UNIMMAP group, however this was not significant (p=0.2041). Hemoglobin levels averaged 11.2 g/L across all intervention groups. Positive values for change in hemoglobin indicate that hemoglobin increased from enrollment to delivery on average for adolescents in all intervention groups, however, adolescents in the CSB+ with IFA experienced the greatest increase (p=0.0354). The CSB+ with IFA group increased their hemoglobin by 0.4 g/L more than the RUSF group.

Although significance was not met, adolescents in the CSB+ with UNIMMAP group gained less weight on treatment, experienced a greater decrease in MUAC on treatment, had the smallest final FH, and had the highest rates of premature delivery compared to the other two intervention groups.

Rates of miscarriage and stillbirth did not statistically differ by intervention group; on average, about 1% of infants were lost by miscarriage and stillbirth from adolescent pregnancies. Approximately 9.5% of adolescents were lost to follow up during treatment.

Table 4.3 Adolescent maternal outcomes, by treatment group

Outcome	RUSF n=282	CSB+ with UNIMMAP n=291	CSB+ with IFA n=274	*P*[3]
Weight gain from enrollment to final measurement[4], kg	2.89 (0.11)	2.82 (0.11)	2.98 (0.12)	0.6370
Weight gain[4,5] <454 g/week	93.6% (1.5)	90.9% (1.7)	93.4% (1.5)	0.3048
Time on Treatment, weeks[6]	10.0 (0.3)	9.3 (0.3)	9.6 (0.4)	0.2842
Rations of Supplementary Food Received[6]	5.0 (0.2)	4.6 (0.2)	4.8 (0.2)	0.2842
Final MUAC, cm	22.1 (0.1)	22.0 (0.1)	22.1 (0.1)	0.7322
Change in MUAC from Enrollment to Delivery	-0.19 (0.05)	-0.23 (0.05)	-0.19 (0.05)	0.8105
Final Fundal Height, cm	30.4 (0.18)	30.2 (0.17)	30.5 (0.18)	0.4910
Final Fundal Height <28 cm	8.9% (1.7)	10.6% (1.8)	6% (0.5)	0.2041
Hemoglobin, g/L	11.1 (0.1)	11.3 (0.1)	11.3 (0.1)	0.1106
Change in Hemoglobin from Enrollment to Delivery	1.1 (0.1)[a]	1.4 (0.1)[a,b]	1.5 (0.1)[b]	0.0354
Lost Pregnancy Type[7]				
Miscarriage	1% (0.00)	0.6% (0.00)	1.1% (0.00)	0.7064
Stillbirth	0.9% (0.00)	2.1% (0.00)	0.3% (0.00)	0.0924
Maternal Antenatal Lost to Follow up[7]	10.2% (1.8)	7.9% (1.6)	10.3% (1.8)	0.5009

N=847

[1]Adjusted for BMI and Fundal Height at enrollment
[2]Values expressed as least square means (LSM) (SE) for quantitative measures and adjusted proportions, % (SE) for categorical measures
[3]*P* values from Intervention in Effects test
[4]Weight gain analysis includes only women on treatment for at least 14 days who had singleton births and were not lost to follow-up
[5]Weight gain <454 g/week indicates inadequate weekly weight gain
[6]Unadjusted mean (SE)
[7]N=876

Adolescent maternal outcomes remained similar after analysis of maternal age within each intervention group (**Table 4.4**), highlighting that no treatment was able to affect either adolescent group more than the other. Overall, young adolescents had poorer maternal outcomes compared to the older adolescents, however significance was not met. The young adolescents in the CSB+ with UNIMMAP group gained the least amount of weight on treatment and had the highest rate of preterm delivery. Young adolescents in the RUSF group had a slightly higher rate

of inadequate weekly weight gain and the largest decrease in MUAC across treatment (significance not met).

Additionally, assessment of the effect of intervention on maternal outcomes in younger adolescents and older adolescent individually showed that no intervention was better able to improve outcomes among either adolescent age group (data not shown). In other words, maternal outcomes were similar among younger adolescents and older adolescents across each treatment group.

Table 4.4 Adolescent maternal outcomes in each intervention group, by maternal age

	RUSF n=282			CSB+ with UNIMMAP n=291			CSB+ with IFA n=274		
Outcome	16-17 YO n=97	18-19 YO n=186	*P*[3]	16-17 YO n=94	18-19 YO n=197	*P*[3]	16-17 YO n=96	18-19 YO n=180	*P*[3]
Weight gain from enrollment to final measurement[4], kg	3.10 (0.2)	3.06 (0.1)	0.8658	2.6 (0.2)	2.7 (0.1)	0.5972	3.1 (0.2)	2.9 (0.1)	0.5290
Weight gain[4.5] <454 g/week	94% (2.4)	93.5% (1.8)	0.8281	93.2% (2.6)	89.5% (2.2)	0.2452	92.5% (2.7)	93.8% (1.8)	0.6517
Final MUAC, cm	21.9 (0.1)	22.1 (0.1)	0.0824	22.0 (0.1)	22.1 (0.1)	0.8468	22.0 (0.1)	22.1 (0.1)	0.0773
Change in MUAC	-0.31 (0.1)	-0.14 (0.1)	0.1512	-0.25 (0.1)	-0.22 (0.1)	0.7651	-0.19 (0.1)	-0.18 (0.1)	0.9504
Final Fundal Height, cm	30.1 (0.3)	30.4 (0.2)	0.6005	30.0 (0.3)	30.4 (0.2)	0.1890	30.7 (0.3)	30.5 (0.2)	0.5864
Final Fundal Height <28 cm[3]	9.2% (2.9)	7.4% (1.9)	0.6370	15.5% (3.7)	8.2% (2.0)	0.1047	8.0% (2.8)	4.4% (1.5)	0.2837
Hemoglobin, g/L	10.9 (0.2)	11.1 (0.1)	0.5667	11.3 (0.2)	11.4 (0.1)	0.8943	11.1 (0.2)	11.4 (0.1)	0.1140
Change in Hemoglobin	1.12 (0.2)	1.03 (0.1)	0.7018	1.17 (0.2)	1.48 (0.1)	0.1593	1.49 (0.2)	1.51 (0.1)	0.9412
Lost Pregnancy Type[6]									
Miscarriage	1.7% (1.3)	0.7% (0.6)	0.4247	0.0% (0.0)	0.0% (0.0)	0.4118	2.0% (1.4)	1.1% (0.8)	0.5621
Stillbirth	1.0% (1)	1.0% (0.7)	0.9604	1.4% (1.2)	1.9% (1.0)	0.6765	0.0% (0.0)	0.4% (0.5)	0.3239
Maternal Antenatal Lost to Follow up[6]	8.1% (2.8)	11.1% (2.3)	0.4063	7.3% (2.7)	8.4% (2.0)	0.7344	8.1% (2.8)	11.1% (2.3)	0.4063

N=847
[1]Adjusted for BMI at enrollment and Fundal Height at Enrollment
[2]Values expressed as least square mean, mean (SE) for quantitative measures and adjusted proportions, % (SE) for categorical measures
[3]*P* values from Maternal Age in Effects test
[4]Weight gain analysis includes only women on treatment for at least 14 days; 103 women with only one visit who had singleton births and were not lost to follow-up were excluded from this analysis.
[5]Weight gain <454 g/week indicates inadequate weekly weight gain
[6]N=876

Rates of adolescent recovery and delivery before recovery were similar across intervention groups (**Table 4.5**). The majority of adolescents did not recover from moderate malnutrition before delivery (MUAC >23.0 cm). About 12.5% of adolescent mothers recovered during treatment and remained recovered through their delivery. Less than 5% of adolescent mothers recovered from moderate malnutrition during treatment with a subsequent relapse before delivery.

Table 4.5 Rates of recovery in adolescents, by treatment group

	RUSF		CSB+ with UNIMMAP		CSB+ with IFA		
Outcome	*n*	% (SE)	*n*	% (SE)	*n*	% (SE)	P^2
Delivered before Recovery[3]	187	67.8% (2.8)	200	70.2% (2.7)	186	68.3% (2.8)	0.8140
Recovered MUAC before Delivery without Relapse[4]	42	13% (2.0)	45	12.5% (1.9)	38	12.1% (2.0)	0.9474
Recovered MUAC before Delivery with Relapse	16	3.6% (1.1)	9	2.3% (0.9)	18	5.1% (1.3)	0.1379

[1]Adjusted for BMI and Fundal Height at enrollment
[2] *P* values for Intervention (Effect likelihood ratio test)
[3]Recovery defined as MUAC >23.0 cm
[4]Relapse defined as MUAC falling within ≥ 20.6 cm to ≤ 23.0 cm

Even after adjusting for maternal age, rates of recovery and delivery did not statistically differ across the interventions (**Table 4.6**). This highlights that there is no evidence that treatment with any intervention affects rates of recovery and delivery before recovery differently in the younger and older adolescent mothers. Overall, rates were consistent with those found in Table 4.5. Younger adolescent mothers were more likely to deliver their infant before recovering from moderate malnutrition than the older adolescents in the RUSF and CSB+ with IFA groups, however significance was not found. Young adolescents in the CSB+ with UNIMMAP group had the highest rates of recovery from malnutrition without relapse (significance not found). Adolescents, both younger and older, in the CSB+ with IFA group had the highest rates of recovery from moderate malnutrition with a subsequent relapse before delivery compared to all other adolescents (significance not found).

Table 4.6 Rates of recovery in adolescents in each treatment group, by maternal age

Outcome	RUSF				
	16-17 YO		18-19 YO		
	n	% (SE)	*n*	% (SE)	P^2
Delivered before Recovery[3]	68	71.4 (4.6)	119	64.1 (3.5)	0.2197
Recovered MUAC before Delivery without Relapse[4]	14	13.0 (3.4)	28	14.6 (2.6)	0.7137
Recovered MUAC before Delivery with Relapse	7	4.6 (2.1)	9	3.0 (1.3)	0.4051
	CSB+ with UNIMMAP				
	16-17 YO		18-19 YO		
	n	% (SE)	*n*	% (SE)	P^2
Delivered before Recovery[3]	63	69.4 (4.8)	137	69.9 (3.3)	0.9390
Recovered MUAC before Delivery without Relapse[4]	19	16.1 (3.8)	26	10.9 (2.2)	0.2010
Recovered MUAC before Delivery with Relapse	3	2.2 (1.5)	6	2.4 (1.1)	0.9189
	CSB+ with IFA				
	16-17 YO		18-19 YO		
	n	% (SE)	*n*	% (SE)	P^2
Delivered before Recovery[3]	67	75.1 (4.4)	119	68.3 (3.5)	0.2565
Recovered MUAC before Delivery without Relapse[4]	11	7.4 (2.7)	27	12.1 (2.4)	0.1903
Recovered MUAC before Delivery with Relapse	7	5.0 (2.2)	11	5.0 (1.6)	0.9988

[1]Adjusted for BMI and Fundal Height at enrollment
[2] *P* values for Intervention (Effect likelihood ratio test)
[3]Recovery defined as MUAC >23.0 cm
[4]Relapse defined as MUAC falling within ≥ 20.6 cm to ≤ 23.0 cm

Maternal Outcomes by Maternal Age

Age stratification of pooled participants revealed that maternal age played a role in determining many maternal outcomes (**Table 4.7**). Young adolescent mothers were on treatment for 1 week longer, on average, and received 0.6 more rations of supplementary food compared to the adult mothers (p=0.0161, p=0.0161, respectively). Older adolescents were on treatment for a similar amount of time and received a similar amount of rations compared to the younger adolescents and adults. Younger and older adolescents were statistically similar for weight gain

on treatment, final MUAC, change in MUAC from enrollment to delivery, final fundal height, and rates of final fundal height <28cm, but both were statistically different from the adult mothers. Adult mothers gained about 15% more weight than both the younger and older adolescent mothers during treatment (p=<0.0001), and more than 90% of all participants, regardless of age, experienced inadequate weekly weight gain (weight gain <454 g/week) (p=0.0882). Although adult mothers gained more weight on treatment, rates of inadequate weekly weight gain were highest for the adults, however significance was not found. While the change in MUAC from enrollment to delivery for the adult mothers was approximately 0.0 cm, indicating that MUAC remained the same while on treatment, the MUAC of younger and older adolescents decreased by about 0.2 cm as treatment progressed (p=<0.0001). Consistent with this, the final MUAC of young and older adolescents was 0.4 cm and 0.3 cm smaller than the final MUAC of adult mothers, respectively (p=<0.0001). Final fundal height of adult mothers was about 0.6 cm larger than that of the younger and older adolescent mothers (p=0.0003). Rates of final fundal height <28 cm, an indicator of extreme premature delivery, were 175% higher in young adolescents compared to the adult mothers (p=0.0012). Hemoglobin at delivery was about 11.3 g/L across all age groups (p=0.1773). Hemoglobin increased by 0.4 g/L and 0.3 g/L more in the older adolescent mothers and younger adolescents, respectively, than the hemoglobin in adult mothers during treatment (p=0.0006).

Rates of miscarriage and stillbirth were under 1% for all age categories (0.4569, p=0.7242, respectively). Rates of maternal loss to follow up were highest for older adolescents, with adult mothers having the lowest rates (p=0.0114).

Table 4.7 Maternal outcomes, stratified by maternal age

Outcome	16-17 YO n=287	18-19 YO n=563	≥20 YO n=905	P^3
Weight gain from enrollment to final measurement[4], kg	2.80 (0.11)[a]	2.77 (0.08)[a]	3.22 (0.06)[b]	<0.0001
Weight gain[4,5] <454g/week	93.1% (1.5)	92.3% (1.1)	94.7% (0.7)	0.0882
Time on Treatment, week[6]	9.9 (0.3)[a]	9.4 (0.2)[a,b]	8.9 (0.2)[b]	0.0161
Rations of Supplementary Food Received[6]	5.0 (0.2)[a]	4.7 (0.1)[a,b]	4.4 (0.1)[b]	0.0161
Final MUAC, cm	21.94 (0.06)[a]	22.08 (0.04)[a]	22.36 (0.03)[b]	<0.0001
Change in MUAC	-0.23 (0.05)[a]	-0.18 (0.04)[a]	-0.00 (0.03)[b]	<0.0001
Final Fundal Height, cm	30.23 (0.17)[a]	30.49 (0.12)[a]	30.98 (0.10)[b]	0.0003
Final Fundal Height <28 cm	11% (1.8)[a]	7.2% (1.1)[a]	4.2% (0.7)[b]	0.0012
Hemoglobin, g/L	11.18 (0.10)	11.33 (0.07)	11.39 (0.06)	0.1773
Change in Hemoglobin	1.31 (0.11)[a,b]	1.38 (0.08)[a]	1.02 (0.06)[b]	0.0006
Lost Pregnancy Type[7]				
Miscarriage	1.2% (0.06)	0.9% (0.00)	0.6% (0.00)	0.4569
Stillbirth	0.8% (0.01)	0.2% (0.00)	0.8% (0.00)	0.7242
Maternal Antenatal Lost to Follow up[7]	7.8% (1.6)[a,b]	10.6% (1.3)[a]	6.3% (0.01)[b]	0.0114

N=1755

[1]Adjusted for BMI and Fundal Height at enrollment
[2]Values expressed as least square means (LSM) (SE) for quantitative measures and adjusted proportions, % (SE) for categorical measures
[3]*P* values from Maternal Age in Effects test
[4]Weight gain analysis includes only women on treatment for at least 14 days who had singleton births and were not lost to follow-up
[5]Weight gain <454 g/week indicates inadequate weekly weight gain
[6]Unadjusted mean (SE)
[7]N=1828

The odds of delivering with a fundal height less than 28 cm, an indicator of extreme premature delivery, were 2.84 and 1.79 times greater for the younger and older adolescents, respectively, compared to the adult mothers (p=0.0004, p=0.0261, respectively) (**Table 4.8**). The odds of delivering extremely premature were not statistically different between younger and older adolescent mothers (p=0.1003).

Table 4.8 Odds of extreme premature delivery, stratified by maternal age

Age / Reference Age	Odds Ratio (95% CI)[2]	*P*
16-17 YO / ≥20 YO	2.84 (1.61-4.99)	0.0004
18-19 YO/ ≥20 YO	1.79 (1.07-2.99)	0.0261
16-17 YO / 18-19 YO	1.59 (0.91-2.75)	0.1003

N: 16-17 YO=287; 18-19 YO=563; ≥20 YO=905

[1]Extreme premature delivery indicated by Final Fundal Height <28 cm

[2]Tests and confidence intervals on odds ratios are likelihood ratio based

Younger and older adolescent mothers delivered their infants before recovery from moderate malnutrition (MUAC >23.0 cm) about 20% more often than adult mothers (**Table 4.9**). Specifically, the odds of delivering before recovery were 1.89 and 1.54 greater for the younger and older adolescents, respectively, compared to the adult mothers (p=0.0275, p=0.0043, respectively) (**Table 4.10**). Rates of recovering from moderate malnutrition during treatment and remaining recovered through delivery were highest for the adult mothers; rates were about 43% higher in the adults compared the younger and older adolescents (p=0.0069). Analysis of odds ratios revealed that the odds of recovering from moderate malnutrition during treatment without subsequent relapse were 1.51 and 1.53 greater for the adult mothers compared to the young adolescents and older adolescents, respectively (p=0.0275, p=0.0043, respectively). Rates of recovery from malnutrition with subsequent relapse before delivery were less than 5% for all age categories (p=0.2573), and no age group had greater odds.

Table 4.9 Rates of recovery in adolescents and adult mothers, stratified by maternal age

	16-17 YO		18-19 YO		≥20 YO		
Outcome	*n*	% (SE)	*n*	% (SE)	*n*	% (SE)	*P*[2]
Delivered before Recovery[3]	198	74.5 (2.6)[a]	375	70.4 (1.9)[a]	566	60.7 (0.6)[b]	<0.0001
Recovered MUAC before Delivery without Relapse[4]	44	12.8 (2.0)[a]	81	12.7 (1.4)[a]	163	18.2 (1.3)[b]	0.0069
Recovered MUAC before Delivery with Relapse	17	3.7 (1.1)	26	3.2 (0.7)	53	4.7 (0.7)	0.2573

[1]Adjusted for BMI and Fundal Height at enrollment
[2] *P* values for Intervention (Effect likelihood ratio test)
[3]Recovery defined as MUAC >23.0 cm
[4]Relapse defined as MUAC falling within ≥ 20.6 cm to ≤ 23.0 cm

Table 4.10 Odds of recovery, stratified by maternal age

Outcome	Age / Reference Age	Odds Ratio (95% CI)[2]	*P*
Delivered before Recovery[3]	16-17 YO / ≥20 YO	1.89 (1.40-2.57)	<0.0001
	18-19 YO / ≥20 YO	1.54 (1.22-1.95)	0.0003
	16-17 YO / 18-19 YO	1.23 (0.90-1.69)	0.2014
Recovered MUAC before Delivery without Relapse[4]	≥20 YO / 16-17 YO	1.51 (1.05-2.22)	0.0275
	≥20 YO / 18-19 YO	1.53 (1.14-2.08)	0.0043
	16-17 YO / 18-19 YO	1.02 (0.67-1.52)	0.9348
Recovered MUAC before Delivery with Relapse	≥20 YO / 16-17 YO	1.27 (0.72-2.33)	0.4133
	≥20 YO / 18-19 YO	1.50 (0.92-2.49)	0.1050
	16-17 YO / 18-19 YO	1.18 (0.61-2.22)	0.6185

N: 16-17 YO=287; 18-19 YO=563; ≥20 YO=905
[1]Adjusted for BMI and Fundal Height at enrollment
[2]Tests and confidence intervals on odds ratios are likelihood ratio based
[3]Recovery defined as MUAC >23.0 cm
[4]Relapse defined as MUAC falling within ≥ 20.6 cm to ≤ 23.0 cm

Interaction Effects

Analysis of the interaction effect between intervention and maternal age on maternal outcomes revealed that the relationship between maternal age and all maternal outcomes of interest do not statistically differ by intervention (data not shown). The effect of intervention on

maternal outcomes was also not indicated in the data; the only exception was final fundal height <28 cm (p=0.0455).

INFANT OUTCOMES

Anthropometric Outcomes of Infants of Adolescent Mothers by Intervention Group

Amongst all infants of adolescents, there were no differences in infant length, weight, MUAC, or head circumference measurements by treatment group at birth, 6 weeks, and 12 weeks (**Table 4.11**). Over the 12-week period, infants of older mothers consistently had greater anthropometric measures. At birth, infants were approximately 46.7 cm in length, weighed about 2.6 kg, and had a MUAC of 9.4 cm and a head circumference of 34.1 cm. At 6 weeks, infants were about 53.4 cm in length, weighed about 4.3 kg, and had a MUAC of 11.8 cm and a head circumference of about 38.0 cm. At 12 weeks, infants were about 58 cm in length, weighed about 5.5 kg, and had a MUAC of 13.1 cm and a head circumference of 40.3 cm. Rates of low birth weight were highest for the infants born to the adolescents in the CSB+ with UNIMMAP groups, however significance was not found (p=0.2759). Overall, rates of low birth weight for all infants was about 34%.

Table 4.11 Infant length, weight, MUAC, and head circumference at birth of adolescent mothers, 6 weeks, and 12 weeks, by treatment group

	RUSF		CSB+ with UNIMMAP		CSB+ with IFA		
Outcome	*n*	LSM (SE)	*n*	LSM (SE)	*n*	LSM (SE)	P^2
Birth							
Length, cm	226	46.7 (0.2)	223	46.7 (0.2)	229	46.8 (0.2)	0.8714
Weight, kg	232	2.7 (0.0)	233	2.6 (0.0)	239	2.6 (0.0)	0.4684
Weight <2.5 kg[3]	115	31.2 (0.0)	154	38 (0.0)	123	32.9 (0.0)	0.2759
MUAC, cm	225	9.4 (0.1)	222	9.3 (0.1)	229	9.4 (0.01)	0.6194
Head circumference, cm	224	34.2 (0.1)	219	34.0 (0.1)	227	34.2 (0.1)	0.4145
6 weeks							
Length, cm	227	53.4 (0.2)	218	53.2 (0.2)	228	53.6 (0.2)	0.1515
Weight, kg	227	4.3 (0.0)	218	4.2 (0.0)	228	4.4 (0.0)	0.1557
MUAC, cm	227	11.8 (0.1)	218	11.7 (0.1)	228	11.9 (0.1)	0.2359
Head circumference, cm	227	38.0 (0.1)	217	37.8 (0.1)	227	38.0 (0.1)	0.3493
12 weeks							
Length, cm	200	57.9 (0.2)	206	57.9 (0.2)	208	58.2 (0.2)	0.5078
Weight, kg	200	5.5 (0.1)	206	5.5 (0.1)	208	5.6 (0.1)	0.6987
MUAC, cm	200	13.0 (0.1)	206	13.1 (0.1)	208	13.1 (0.1)	0.8592
Head circumference, cm	200	40.4 (0.1)	205	40.2 (0.1)	208	40.3 (0.1)	0.3172

[1]Adjusted for BMI at enrollment, Fundal Height at Enrollment
[2]*P* values for Intervention (Effects test)
[3]Low birth weight defined as birth weight <2.5 kg; % (SE)

Anthropometric measures of infants born to adolescent mothers, remained similar for most measures when stratified by maternal age within each intervention group (**Table 4.12**). In the RUSF group, no differences in anthropometrics were seen at birth, however, significant differences were seen in weight at 6 weeks, and length and weight at 12 weeks. Infant weight at 6 weeks was almost 200 g greater in the infants of older adolescents compared to the infants of younger adolescents (p=0.0321). Compared with measurements at 12 weeks of age revealed that the infants of older adolescents were nearly 1 cm longer and weighed 200 g heavier than infants of the younger adolescents in the RUSF group (p=0.0142, p=0.0454, respectively).

Infant anthropometric measures for the CSB+ with UNIMMAP intervention group did not statistically differ between infants of younger and older adolescents; measurements were consistent with Table 4.11.

In the CSB+ with IFA intervention group, the infants of older adolescents were 0.7 cm longer than infants of the younger adolescents at birth (p=0.0183), however this difference in length was no longer present at 6 and 12 weeks. All other measurements were consistent with the findings in Table 4.11.

Assessment of the effect of intervention on infant length, weight, MUAC, and head circumference in younger adolescents and older adolescent individually, results showed that no intervention was better able to improve outcomes among either adolescent age group (data not shown). In other words, infant outcomes were similar among the infants of younger adolescents and older adolescents across treatment groups.

Table 4.12 Infant anthropometric measures from adolescent mothers in each treatment group, by maternal age

	RUSF			CSB+ with UNIMMAP			CSB+ with IFA		
	LSM (SE)			LSM (SE)			LSM (SE)		
Outcome	16-17 YO n=97	18-19 YO n=186	P^2	16-17 YO n=94	18-19 YO n=197	P^2	16-17 YO n=96	18-19 YO n=180	P^2
Birth									
Length, cm	46.2 (0.3)	46.8 (0.2)	0.0541	46.6 (0.3)	46.8 (0.2)	0.5738	46.3 (0.2)	47.0 (0.2)	0.0183
Weight, kg	2.6 (0.1)	2.7 (0.0)	0.1709	2.6 (0.1)	2.6 (0.0)	0.7000	2.6 (0.0)	2.6 (0.0)	0.6145
Weight <2.5 kg[3]	36.7 (0.0)	29.5 (0.0)	0.2753	40.9 (0.1)	36.0 (0.0)	0.4728	32.3 (0.0)	32.1 (0.0)	0.9782
MUAC, cm	9.3 (0.1)	9.5 (0.1)	0.2329	9.26 (0.1)	9.40 (0.1)	0.2563	9.3 (0.1)	9.4 (0.1)	0.6532
Head circumference, cm	34.0 (0.2)	34.2 (0.1)	0.2296	33.9 (0.2)	34.1 (0.1)	0.3296	34.3 (0.2)	34.1 (0.1)	0.2593
6 weeks									
Length, cm	53.0 (0.3)	53.6 (0.2)	0.0917	52.8 (0.3)	53.4 (0.2)	0.1543	53.4 (0.3)	53.8 (0.2)	0.3257
Weight, kg	4.19 (0.1)	4.37 (0.1)	0.0321	4.2 (0.1)	4.3 (0.1)	0.2182	4.3 (0.1)	4.4 (0.1)	0.5427
MUAC, cm	11.7 (0.1)	11.8 (0.1)	0.3944	11.6 (0.1)	11.8 (0.1)	0.2734	11.8 (0.1)	11.9 (0.1)	0.4162
Head circumference, cm	37.8 (0.2)	38.1 (0.1)	0.1153	37.6 (0.2)	37.9 (0.1)	0.1562	38.0 (0.2)	37.9 (0.1)	0.6682
12 weeks									
Length, cm	57.3 (0.3)	58.2 (0.2)	0.0142	57.5 (0.3)	58.1 (0.2)	0.1396	57.9 (0.3)	58.3 (0.2)	0.2810
Weight, kg	5.4 (0.1)	5.6 (0.1)	0.0454	5.4 (0.1)	5.6 (0.1)	0.0743	5.5 (0.1)	5.6 (0.1)	0.1561
MUAC, cm	12.9 (0.1)	13.1 (0.1)	0.2683	13.0 (0.1)	13.1 (0.1)	0.6083	13.0 (0.1)	13.1 (0.1)	0.4866
Head circumference, cm	40.2 (0.2)	40.5 (0.2)	0.2207	39.9 (0.2)	40.3 (0.1)	0.0644	40.1 (0.2)	40.3 (0.1)	0.2859

[1]Adjusted for BMI at enrollment, Fundal Height at Enrollment
[2]*P* values for Maternal Age (Effects test)
[3]Low birth weight defined as birth weight <2.5 kg; % (SE)

Amongst all infants of adolescents, there were no differences in infant Z scores at birth, 6 weeks, and 12 weeks by treatment group (**Table 4.13**). WFL Z score at birth was almost 0.2 less in the RUSF group compared to the CSB+ with UNIMMAP and CSB+ with IFA, however significance was not met (p=0.0680). From birth to 12 weeks of age, a gradual increase in infant Z scores was seen as age increased showing some “catch up” weight gain but not linear growth. At birth, WFA, LFA, WFL, and HCFA Z scores averaged -1.50, -0.60, -0.59, and 0.04, respectively. At 6 weeks of age, WFA, LFA, WFL, and HCFA Z scores averaged -1.03, -1.38, 0.33, and 0.05, respectively. At 12 weeks of age, WFA, LFA, WFL, and HCFA Z scores of all infants of adolescent mothers averaged -0.91, -1.33, 0.3, and 0.21, respectively.

Rates of underweight, stunting, wasting, and small head circumference in the infants did not statistically differ by intervention group among the adolescents. Rates of stunting at 6 weeks of age were highest in the CSB+ with UNIMMAP group, however significance was not met (p=0.0605).

Table 4.13 Infant anthropometric measures of adolescent mothers, by treatment group

Outcome	RUSF		CSB+ with UNIMMAP		CSB+ with IFA		
Birth	*n*	LSM (SE)	*n*	LSM (SE)	*n*	LSM (SE)	P^3
Weight-for-Age (WFA), Z-score	232	-1.43 (0.06)	230	-1.52 (0.06)	238	-1.52 (0.06)	0.4930
Length-for-Age (LFA), Z-score	226	-1.51 (0.08)	220	-1.48 (0.08)	228	-1.46 (0.08)	0.9077
Weight-for-Length (WFL), Z-score[4]	188	-0.47 (0.07)	179	-0.68 (0.07)	193	-0.62 (0.07)	0.0680
Head Circumference-for-Age (HCFA), Z-score	224	0.03 (0.09)	217	-0.14 (0.09)	226	0.00 (0.09)	0.3683
	n	% (SE)	*n*	% (SE)	*n*	% (SE)	P^3
Underweight, WFA < -2	229	24.6 (2.6)	224	29.3 (2.7)	230	23.6 (2.6)	0.3340
Stunted, LFA < -2	226	28.8 (2.7)	220	31.0 (2.7)	228	28.3 (2.7)	0.8013
Wasted, WFL < -2	188	3.5 (1.1)	179	6.7 (1.5)	193	7.8 (1.6)	0.1326
Head Circumference Small, HCFA < -2	224	7.0 (1.5)	217	4.5 (1.2)	226	3.9 (1.2)	0.2771
6 weeks	*n*	LSM (SE)	*n*	LSM (SE)	*n*	LSM (SE)	P^3
Weight-for-Age (WFA), Z-score	202	-0.98 (0.08)	191	-1.16 (0.08)	203	-0.95 (0.08)	0.1076
Length-for-Age (LFA), Z-score	202	-1.36 (0.09)	191	-1.50 (0.09)	203	-1.28 (0.09)	0.1954
Weight-for-Length (WFL), Z-score[4]	201	0.37 (0.07)	188	0.26 (0.07)	201	0.35 (0.07)	0.5155
Head Circumference-for-Age (HCFA), Z-score	202	0.13 (0.09)	190	-0.08 (0.09)	202	0.10 (0.09)	0.1729
	n	% (SE)	*n*	% (SE)	*n*	% (SE)	P^3
Underweight, WFA < -2	202	11.7 (1.9)	191	17.8 (2.2)	203	11.0 (1.9)	0.1033
Stunted, LFA < -2	202	24.0 (2.5)	191	31.1 (2.7)	203	21.0 (2.5)	0.0605
Wasted, WFL < -2	201	1.2 (0.6)	188	2.0 (0.8)	201	0.9 (0.6)	0.6716
Head Circumference Small, HCFA < -2	202	3.3 (1.1)	190	5.1 (1.3)	202	2.5 (0.9)	0.3770
12 weeks	*n*	LSM (SE)	*n*	LSM (SE)	*n*	LSM (SE)	P^3
Weight-for-Age (WFA), Z-score	193	-0.84 (0.08)	190	-0.97 (0.08)	192	-0.91 (0.08)	0.4734
Length-for-Age (LFA), Z-score	193	-1.30 (0.08)	190	-1.40 (0.09)	192	-1.29 (0.08)	0.5602
Weight-for-Length (WFL), Z-score[4]	193	0.35 (0.07)	190	0.31 (0.07)	192	0.24 (0.07)	0.5383
Head Circumference-for-Age (HCFA), Z-score	193	0.36 (0.09)	189	0.07 (0.09)	192	0.20 (0.09)	0.0810
	n	% (SE)	*n*	% (SE)	*n*	% (SE)	P^3
Underweight, WFA < -2	193	13.5 (2.0)	190	12.6 (1.9)	192	12.7 (2.0)	0.9653
Stunted, LFA < -2	193	23.9 (2.5)	190	27.2 (2.6)	192	23.6 (2.6)	0.6772
Wasted, WFL < -2	193	0.4 (0.4)	190	0.8 (0.5)	192	1.7 (0.8)	0.2627
Head Circumference Small, HCFA < -2	193	2.4 (0.9)	189	2.1 (0.8)	192	2.9 (1.0)	0.8640

N=847

[1]Values expressed as least square mean (LSM) (SE) for quantitative measures and adjusted proportions, % (SE) for categorical measures
[2]Adjusted for BMI and Fundal Height at enrollment
[3]*P* values for Intervention (Effects Test)
[4]188 infants were excluded from WFL z-score because they were too short (<45.00 cm)

Analysis of anthropometric measures of infants of adolescent mothers in each treatment group stratified by maternal age showed that in general, no treatment yielded better infant anthropometric outcomes in either adolescent age category (**Table 4.14**). Differences observed between the infants of younger and older adolescent mothers were largely inconsistent overall. At birth, LFA Z score was significantly smaller in the infants of young adolescent mothers, and WFL Z score was significantly smaller in the infants of older adolescent mothers within the CSB+ with IFA group (p=0.0145, p=0.0132, respectively). However, despite these differences at birth, no LFA and WFL Z scores differences were observed at 6 and 12 weeks within this intervention group. At 12 weeks, rates of wasting were significantly higher in the infants of younger adolescents compared to the adults (p=0.0279).

The infants of adolescents in the RUSF groups showed no statistical differences in anthropometric outcomes between younger and older adolescent mothers at birth and 6 weeks. However, at 12 weeks, WFA and LFA Z scores were significantly smaller in the infants of younger adolescents by -0.34 and -0.38, respectively (p=0.0192, p=0.0155, respectively). These Z scores translated to significantly higher rates of underweight and stunting for infants of young adolescent mothers at 12 weeks of age in the RUSF group. Rates of underweight and stunting were 125% and 101% higher infants of in the young adolescents compared to the infants of older adolescents receiving RUSF.

Infants of adolescents in the CSB+ with UNIMMAP group showed no anthropometric differences at birth and 6 weeks of age. However, at 12 weeks, LFA and HCFA Z scores were

significantly smaller in the infants of young adolescents compared to the infants of older adolescent mothers (p=0.0256, p=0.0074, respectively). These differences in LFA and HCFA did not translate to increased rates of stunting and small head circumference.

Assessment of the effect of intervention on Z scores in infants of younger adolescents and older adolescents individually, found no evidence that any intervention was better able to improve Z scores or rates of underweight, stunting, wasting or small head circumference among infants of either adolescent age group (data not shown). In other words, infant outcomes were not statistically different among younger adolescents and older adolescents across treatment groups.

Table 4.14 Infant anthropometric measures of adolescent mothers in each treatment group, by maternal age

Outcome	RUSF			CSB+ with UNIMMAP			CSB+ with IFA		
	16-17 YO n=97	18-19 YO n=186		16-17 YO n=94	18-19 YO n=197		16-17 YO n=96	18-19 YO n=180	
Birth	LSM (SE)		P^3	LSM (SE)		P^3	LSM (SE)		P^3
Weight-for-Age (WFA), z-score	-1.56 (0.11)	-1.38 (0.08)	0.2125	-1.55 (0.12)	-1.49 (0.08)	0.7109	-1.55 (0.1)	-1.49 (0.07)	0.5905
Length-for-Age (LFA), z-score	-1.73 (0.14)	-1.42 (0.10)	0.0641	-1.55 (0.14)	-1.44 (0.10)	0.5211	-1.70 (0.13)	-1.31 (0.10)	0.0145
Weight-for-Length (WFL), z-score[4]	-0.56 (0.11)	-0.45 (0.08)	0.3909	-0.68 (0.12)	-0.66 (0.08)	0.8700	-0.37 (0.12)	-0.75 (0.09)	0.0132
Head Circumference-for-Age (HCFA), z-score	-0.14 (0.16)	0.07 (0.11)	0.2883	-0.25 (0.15)	-0.05 (0.11)	0.2686	0.12 (0.13)	-0.06 (0.10)	0.2843
	% (SE)		P^3	% (SE)		P^3	% (SE)		P^3
Underweight, WFA < -2	31.0 (4.7)	21.3 (3.0)	0.1164	32.2 (4.8)	27.1 (3.2)	0.4335	23.9 (4.4)	22.2 (3.1)	0.7625
Stunted, LFA < -2	36.7 (4.9)	25.0 (3.2)	0.0766	34.1 (4.9)	29.3 (3.2)	0.4699	31.8 (4.8)	24.9 (3.2)	0.2712
Wasted, WFL < -2	3.1 (1.8)	3.9 (1.4)	0.7695	6.1 (2.5)	6.5 (1.8)	0.9144	6.0 (2.4)	8.0 (2.0)	0.5876
Head Circumference Small, HCFA < -2	10.5 (3.1)	5.4 (1.7)	0.1725	6.7 (2.6)	3.3 (1.3)	0.2598	4.6 (2.1)	2.5 (1.2)	0.3591
6 weeks	LSM (SE)		P^3	LSM (SE)		P^3	LSM (SE)		P^3
Weight-for-Age (WFA), z-score	-1.14 (0.12)	-0.92 (0.08)	0.1278	-1.39 (0.15)	-1.03 (0.11)	0.0508	-0.93 (0.12)	-0.96 (0.09)	0.8619
Length-for-Age (LFA), z-score	-1.47 (0.13)	-1.32 (0.10)	0.3544	-1.68 (0.17)	-1.39 (0.12)	0.1603	-1.32 (0.14)	-1.25 (0.10)	0.7017
Weight-for-Length (WFL), z-score[4]	0.30 (0.12)	0.40 (0.09)	0.4774	0.09 (0.12)	0.38 (0.09)	0.0639	0.42 (0.11)	0.29 (0.08)	0.3534
Head Circumference-for-Age (HCFA), z-score	0.02 (0.15)	0.17 (0.11)	0.4184	-0.25 (0.15)	0.03 (0.11)	0.1338	0.24 (0.14)	0.03 (0.10)	0.2312
	% (SE)		P^3	% (SE)		P^3	% (SE)		P^3
Underweight, WFA < -2	10.8 (3.2)	10.8 (2.3)	0.9967	21.3 (4.2)	15.6 (2.6)	0.3270	11.7 (3.3)	10.6 (2.3)	0.8083
Stunted, LFA < -2	25.9 (4.4)	23.1 (3.1)	0.6720	34.5 (4.9)	29.4 (3.2)	0.4822	23.7 (4.3)	18.2 (2.9)	0.3645
Wasted, WFL < -2	1.2% (1.5)	1.2 (0.8)	0.9723	4.6 (2.2)	0.8 (0.6)	0.0927	1.1 (1.1)	0.7 (0.6)	0.7480
Head Circumference Small, HCFA < -2	4.2% (2.0)	2.7 (1.8)	0.5613	7.8 (2.8)	3.0 (1.2)	0.1266	2.5 (1.6)	2.2 (1.1)	0.8738
12 weeks	LSM (SE)		P^3	LSM (SE)		P^3	LSM (SE)		P^3
Weight-for-Age (WFA), z-score	-1.06 (0.11)	-0.72 (0.09)	0.0192	-1.19 (0.14)	-0.86 (0.09)	0.0556	-1.00 (0.14)	-0.88 (0.10)	0.4914
Length-for-Age (LFA), z-score	-1.54 (0.12)	-1.16 (0.10)	0.0155	-1.70 (0.16)	-1.27 (0.11)	0.0256	-1.40 (0.15)	-1.23 (0.11)	0.3679
Weight-for-Length (WFL), z-score[4]	0.36 (0.11)	0.35 (0.09)	0.9741	0.37 (0.13)	0.30 (0.09)	0.6543	0.25 (0.14)	0.22 (0.10)	0.8560
Head Circumference-for-Age (HCFA), z-score	0.17 (0.17)	0.46 (0.13)	0.1742	-0.24 (0.14)	0.23 (0.10)	0.0074	0.06 (0.14)	0.27 (0.10)	0.2443
	% (SE)		P^3	% (SE)		P^3	% (SE)		P^3
Underweight, WFA < -2	18.2 (3.9)	8.1 (2.0)	0.0368	17.4 (3.9)	10.2 (2.2)	0.1812	12.0 (3.3)	13.4 (2.5)	0.7820
Stunted, LFA < -2	34.2 (4.8)	17.0 (2.8)	0.0075	36.2 (5.0)	23.2 (3.0)	0.0699	20.9 (4.1)	24.3 (3.2)	0.5984
Wasted, WFL < -2	0 (0.0)	0 (0.0)	0.4050	1.7 (1.3)	0.8 (0.6)	0.5617	4.4 (2.1)	0.5 (0.5)	0.0279
Head Circumference Small, HCFA < -2	2.3 (1.5)	1.9 (1.0)	0.8119	4.3 (2.1)	0.5 (0.5)	0.0507	5.0 (2.2)	1.4 (0.9)	0.1305

N=847

[1]Values expressed as least square mean (LSM) (SE) for quantitative measures and adjusted proportions (SE) for categorical measures
[2]Adjusted for BMI at enrollment and Fundal Height at enrollment
[3]*P* values for Age Stratified (Effects Test for quantitative measures and Effects Likelihood Ratio Test for categorical measures)
[4]188 infants were excluded from WFL z-score because they were too short (<45.00 cm)

Infant Anthropometric Outcomes by Maternal Age

Length

At birth and 6 weeks, infants of young adolescent mothers were about 1 cm shorter than the infants of adult mothers, with the infants of older adolescents falling at about the midpoint between the two (p=<0.0001, p=<0.0001, respectively) (**Figure 4.2**). From week 6 to week 12, the infants of older adolescents were able to catch up with the infants of the adult mothers, however the infants of young adolescents remained significantly shorter, at 0.6 cm and 0.9 cm behind infants of older adolescents and adults at 12 weeks, respectively (p=<0.0001). Figure 4.2 highlights this catching up of the infants of the older adolescent mothers to the infants of adult mothers.

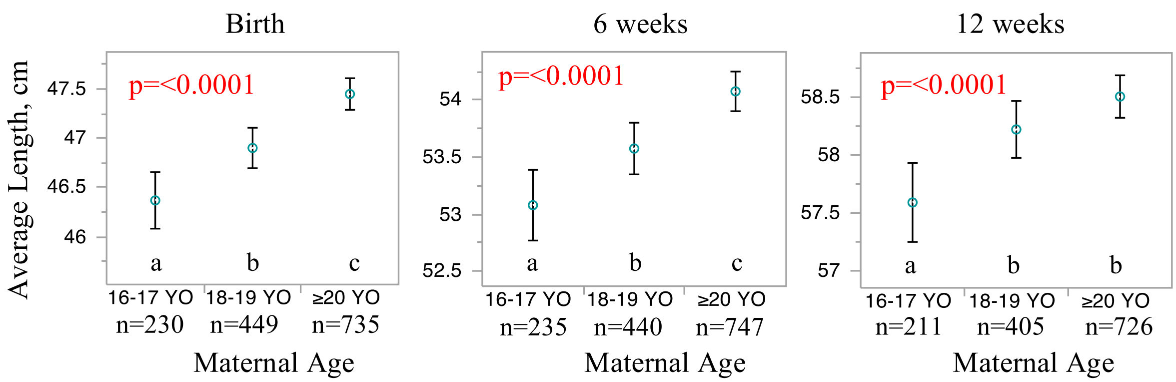
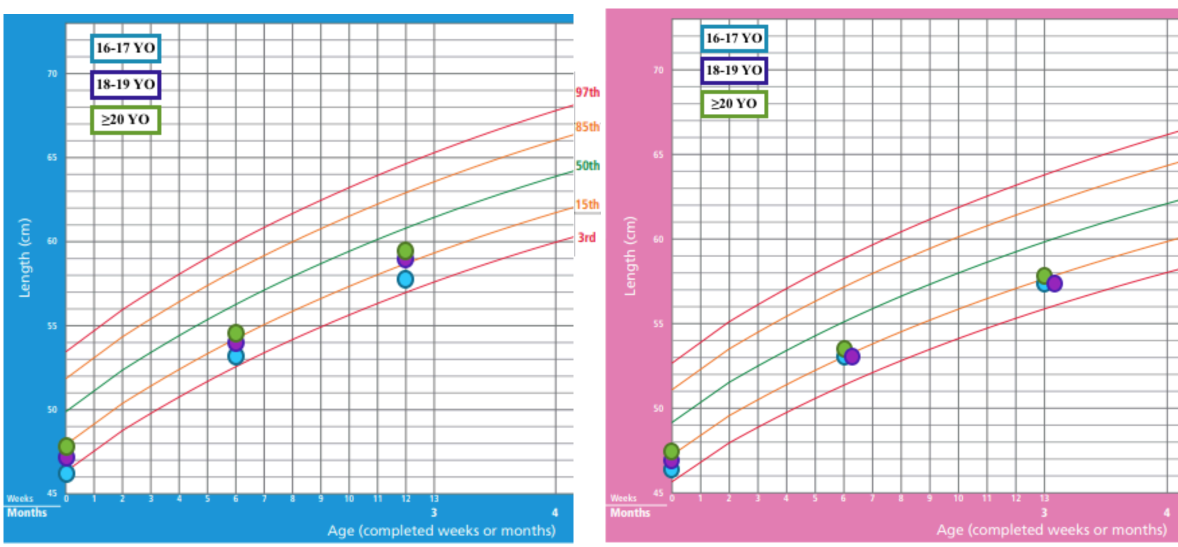


Figure 4.2 Average infant length, stratified by maternal age
[1]Values expressed as LSM; error bar indicates SE
[2]Adjusted for BMI and Fundal Height at enrollment
[3] *P* values for Age Stratified (Effects test)
[4]Tukey HSD test for significant differences

Least square mean length at birth, 6 weeks, and 12 weeks was assessed between male and female infants of young adolescents, older adolescents, and adult mothers. Mean male and female infant length was then plotted on the WHO growth charts to determine LFA percentiles of the infants at all three time points. Results revealed that male infants consistently followed the same pattern; infants of young adolescents were at the smallest percentile, infants of older

adolescents were at a greater percentile, and infants of adults were at the highest percentile at birth, 6 weeks, and 12 weeks of age (**Figure 4.3**). This pattern was also apparent at birth for the female infants. Conversely, the pattern was not observed at 6 and 12 weeks of age for the female infants; female infants of younger and older adolescent mothers at these ages had similar least square means, with the infants of adult mothers having the largest mean length.

While the WHO LFA percentiles were similar for all female infants regardless of maternal age, the percentiles for male infants ranged from about the 3rd percentile to about the 33rd percentile from birth to 12 weeks of age depending on the age of the mother.

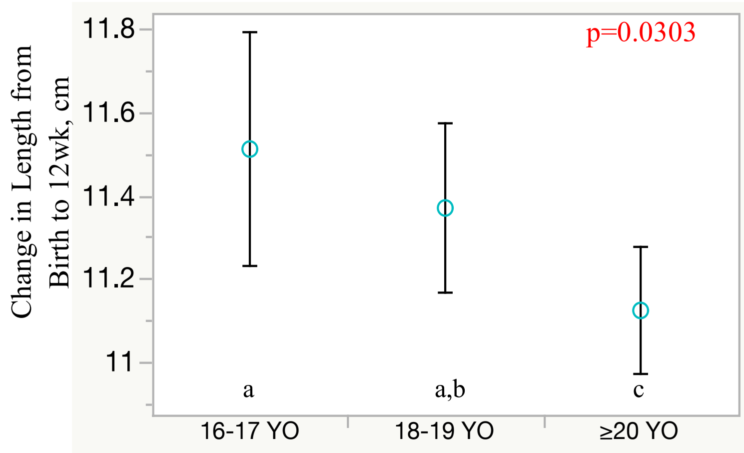


N at birth: 16-17 YO=109; 18-19 YO=211; ≥20 YO=353
N at 6 weeks: 16-17 YO=109; 18-19 YO=205; ≥20 YO=343
N at 12 weeks: 16-17 YO=101; 18-19 YO=189; ≥20 YO=333

N at birth: 16-17 YO=120; 18-19 YO=235; ≥20 YO=371
N at 6 weeks: 16-17 YO=125; 18-19 YO=229; ≥20 YO=392
N at 12 weeks: 16-17 YO=109; 18-19 YO=209; ≥20 YO=380

Figure 4.3 Mean length-for-age (LFA) percentiles for male and female infants of young adolescents, older adolescents, and adults
[1]Charts from: http://www.who.int/childgrowth/standards/en/

Assessment of change in length from birth to 12 weeks of age indicated that infants of young adolescent mothers gained the most length in 12 weeks compared to the infants of older adolescent and adult mothers (**Figure 4.4**). Infants of younger adolescents increased their length 0.14 cm and 0.39 cm more than the infants of older adolescents and adult mothers, respectively (p=0.0303).



n=184 n=351 n=632

Maternal Age

Figure 4. 4 Change in infant length from birth to 12 weeks, stratified by maternal age

[1]Values expressed as LSM; error bars represent SE
[2]Adjusted for BMI and Fundal Height at enrollment
[3] *P* values for Maternal Age (Effects test)
[4]Tukey honest significance test for significant differences

Weight

Weight at birth was similar among infants of young and older adolescents, but significantly less than infants of adult mothers by 200 g and 100 g, respectively (p=<0.0001) (**Figure 4.5**). By 6 weeks of age, the average infant weight from each age category differed from each other by 100 g, with the infants of young adolescent mothers having the lowest weight (p=<0.0001). By 12 weeks, the weight of the infants of older adolescents increased, putting them at the same average weight as infants of adult mothers (p=0.0008). The average weight of the infants of younger adolescents was 200 g less at 12 weeks of age. Figure 4.5 highlights the catch up growth seen in the infants of older adolescents at 12 weeks.

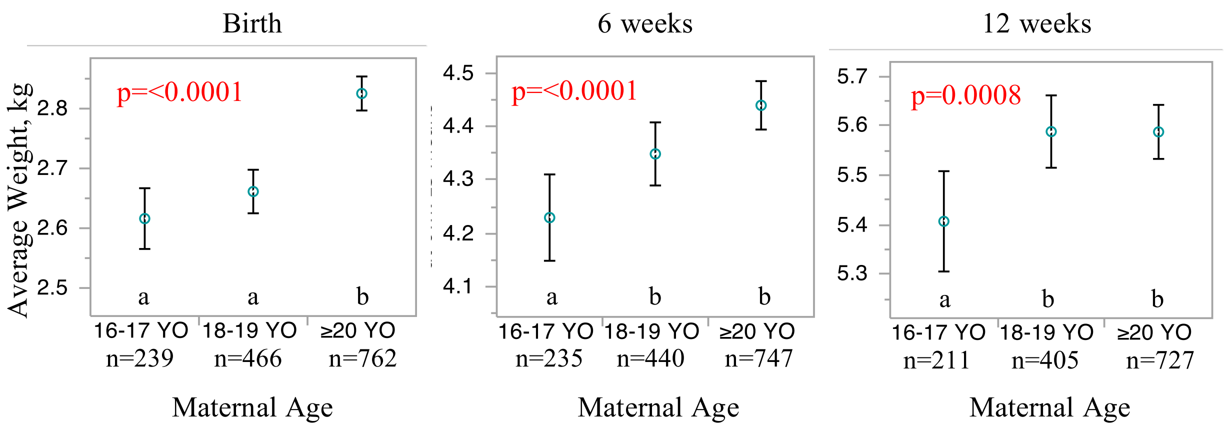


Figure 4.5 Average infant weight, stratified by maternal age
[1]Values expressed as LSM; error bar indicates SE
[2]Adjusted for BMI and Fundal Height at enrollment
[3] *P* values for Maternal Age (Effects test)
[4]Tukey honest significance test for significant differences

Rates of low birth weight (LBW), defined as having a birth weight less than 2.5 kg, were greater in infants of younger and older adolescent mothers compared to infants of adult mothers (p=<0.0001). On average, about 35% of infants born to adolescents (ages 16-19 years old) were low birth weight. The rate for LBW in the adolescent mothers was about 78% greater than the rate of LBW seen in the adult mothers.

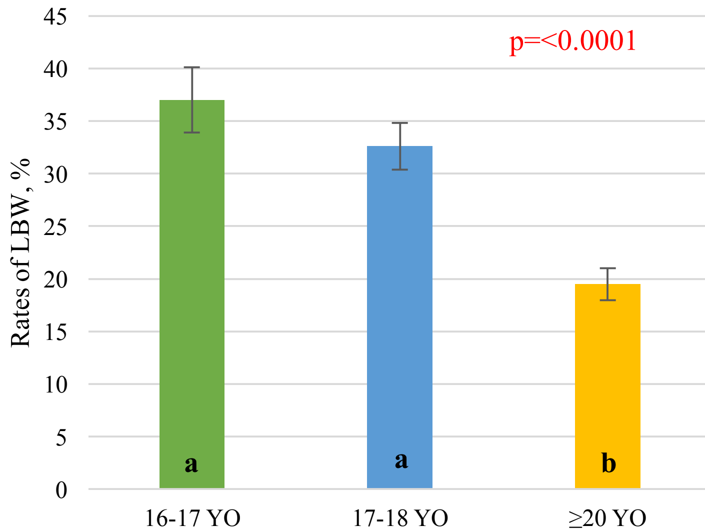


Figure 4.6 Rates of low birth weight (LBW), stratified by maternal age

N: 16-17 YO=287; 18-19 YO=563; ≥20 YO=905
[1]Values expressed as adjusted proportions, error bars represent SE
[2]Adjusted for BMI and Fundal Height at enrollment
[3]Tukey honest significance test for significant differences
[4]*P* value for Maternal Age (Effects test)
[5]Low birth weight defined as birth weight <2.5 kg

Odds for delivery of a LBW infant were significantly greater in the younger and older adolescent mothers compared to adults (**Table 4.15**). The odds of delivery of a LBW infant were 2.43 and 2.00 times greater for the infants of younger and older adolescent mothers, respectively, compared to the adult mothers (p=<0.0001, p=<0.0001). No difference in odds for delivery of a LBW infant were seen between the infants of younger and older adolescent mothers (p=0.2466).

Table 4.15 Odds of low birth weight (LBW), stratified by maternal age

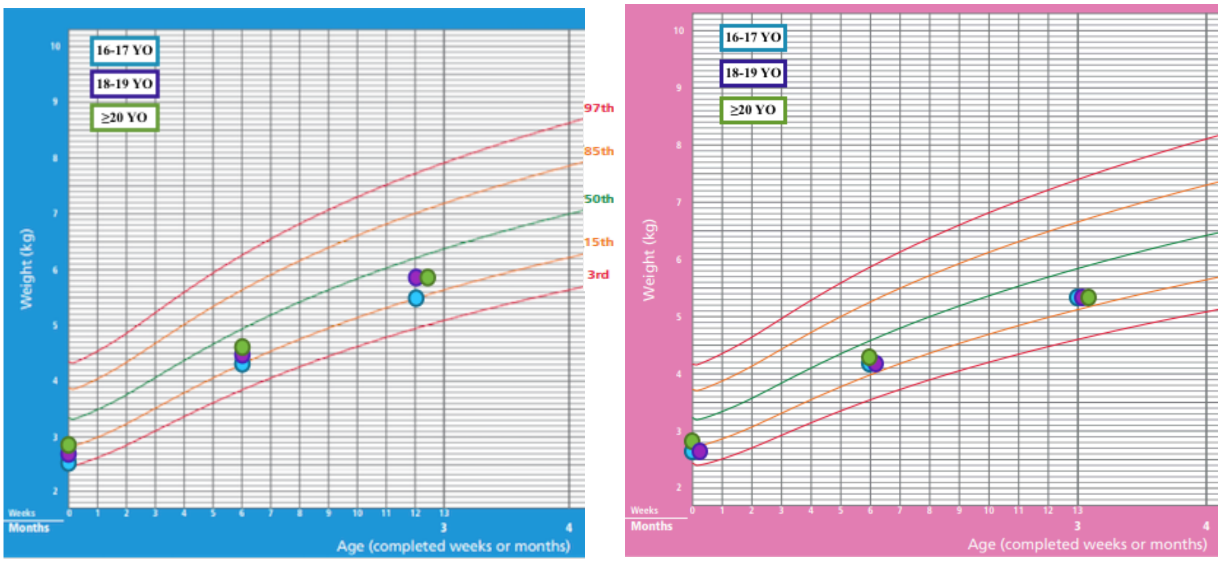
Age / Reference Age	Odds Ratio (95% CI)[1]	*P*
16-17 YO / ≥20 YO	2.43 (1.75-3.36)	<0.0001
18-19 YO/ ≥20 YO	2.00 (1.53-2.62)	<0.0001
16-17 YO / 18-19 YO	1.21 (0.87-1.63)	0.2466

N: 16-17 YO=287; 18-19 YO=563; ≥20 YO=905
[1]Tests and confidence intervals on odds ratios are likelihood ratio based
[2]Low birth weight (LBW) defined as birth weight <2.5 kg

Least square mean weight at birth, 6 weeks, and 12 weeks was assessed between male and female infants of young adolescents, older adolescents, and adult mothers. Mean male and

female infant weight was then plotted on the WHO growth charts to determine WFA percentiles of the infants at all three time points. Results revealed that male infants consistently followed a similar pattern at birth and 6 weeks of age; infants of young adolescents were at the smallest percentile, infants of older adolescents were at a greater percentile, and infants of adults were at the highest percentile (**Figure 4.7**). However, this pattern was not observed at 12 weeks of age in the male infants; at this age, the least square mean lengths of the infants of the older adolescents and adults appear similar and larger than the infants of the younger adolescents. This pattern was also not observed for the female infants; female infants of younger and older adolescent mothers had similar least square means at birth and 6 weeks, with the infants of adult mothers having the largest mean weight. By 12 weeks of age, the mean weight of all female infants were similar, at just above the 15th percentile for WFA.

While the WHO LFA percentiles were similar for all female infants regardless of maternal age, the percentiles for male infants ranged from about the 3rd percentile to about the 40th percentile from birth to 12 weeks of age depending on the maternal age.



N at birth: 16-17 YO=114; 18-19 YO=220; ≥20 YO=365
N at 6 weeks: 16-17 YO=109; 18-19 YO=205; ≥20 YO=343
N at 12 weeks: 16-17 YO=101; 18-19 YO=189; ≥20 YO=334

N at birth: 16-17 YO=124; 18-19 YO=243; ≥20 YO=386
N at 6 weeks: 16-17 YO=125; 18-19 YO=229; ≥20 YO=392
N at 12 weeks: 16-17 YO=109; 18-19 YO=209; ≥20 YO=380

Figure 4.7 Weight-for-age percentile of all maternal age groups
[1]Charts from: http://www.who.int/childgrowth/standards/en/

Infants of older adolescents showed the largest increase in weight gain from birth to 12 weeks (p=0.0016) (**Figure 4.8**); the infants of older adolescent mothers gained 10 and 14 g more than those of the infants of younger adolescents and adult mothers, respectively. This large increase in weight seen in the older adolescents is consistent with the catch up growth seen at week 12 in Figure 4.5.

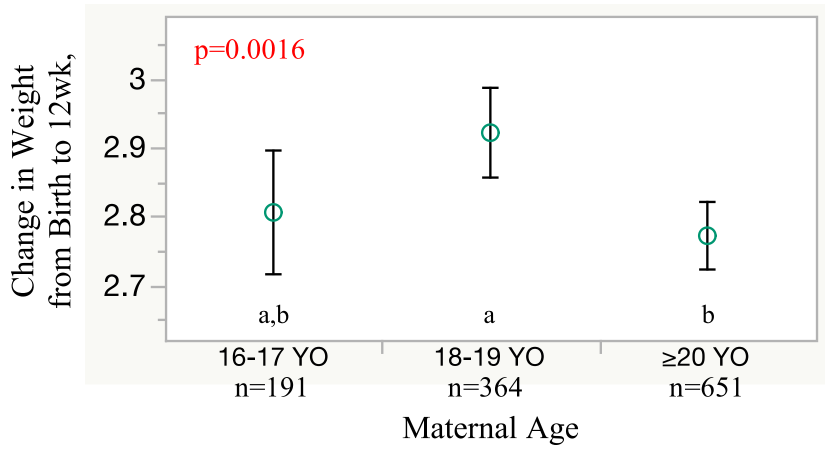


Figure 4.8 Change in infant weight from birth to 12 weeks, stratified by maternal age
[1]Values expressed as LSM; error bars represent SE
[2]Adjusted for BMI and Fundal Height at enrollment
[3] *P* values for Maternal Age (Effects test)
[4]Tukey honest significance test for significant differences

MUAC

Mean MUAC at birth for infants of adult mothers was 0.4 cm and 0.3 cm greater than the MUACs of infants of younger and older adolescent mothers, respectively (p=<0.0001) (**Figure 4.9**). By 6 weeks of age, the MUAC of infants of older adolescent mothers had "caught up" to the MUAC of infants of adult mothers, however the mean MUAC of infants of young adolescents remained 0.2 cm behind the infants of adult mother (p=0.0025). Unlike weight and length at 12 weeks, results show that infants from all age groups had similar MUAC at 12 weeks of age (p=0.3193).

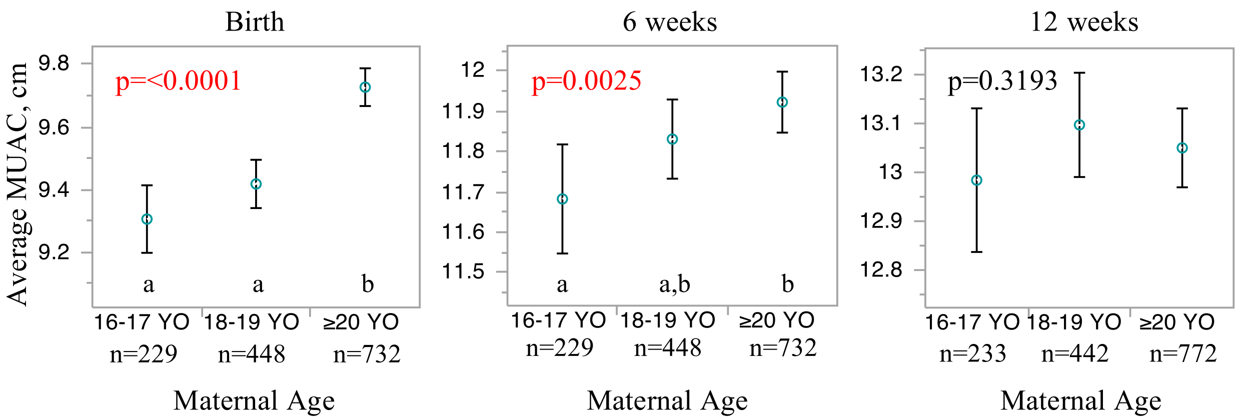


Figure 4.9 Average infant MUAC, stratified by maternal age
[1]Values expressed as LSM; error bar indicates SE
[2]Adjusted for BMI and Fundal Height at enrollment
[3] *P* values for Maternal Age (Effects test)
[4]Tukey honest significance test for significant differences

Infants of younger and older adolescents showed the largest increase in MUAC from birth to 12 weeks of age (p=<0.0001) (**Figure 4.10**); the infants of adolescent mothers increased their MUAC by 0.37 cm more, on average, than the infants of adult mothers.

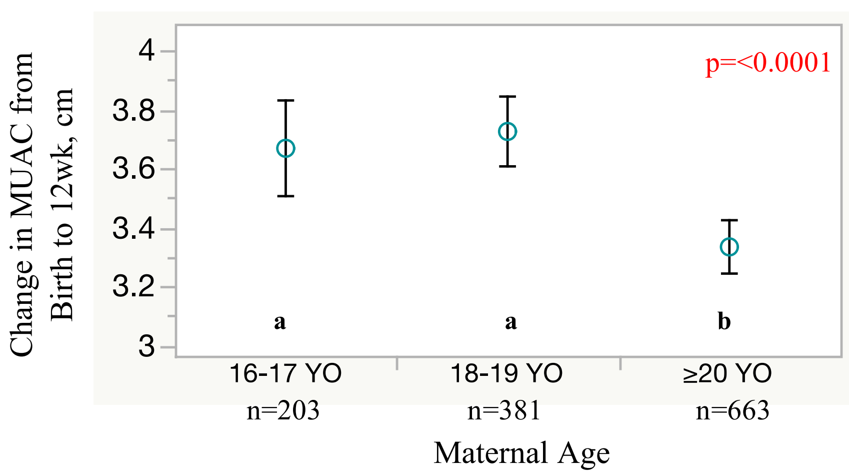


Figure 4.10 Change in infant Mid-Upper Arm Circumference (MUAC) from birth to 12 weeks, stratified by maternal age
[1]Values expressed as LSM; error bars represent SE
[2]Adjusted for BMI at enrollment, Fundal Height at enrollment
[3] *P* values for Maternal Age (Effects test)
[4]Tukey honest significance test for significant differences

Head Circumference

Analysis of mean infant head circumferences by maternal age showed that infants of older adolescents were statistically similar to both those of young adolescents and adults at birth and 6 weeks of age, however the relationship changed at 12 weeks, when the infants of older adolescents "caught up" to the infants of adult mothers (**Figure 4.11**). Figure 4.11 highlights the catch up growth of the older adolescents. Consistently from birth to 12 weeks of age, infants of younger adolescents had an average head circumference that was 0.3 cm smaller than the infants of adult women.

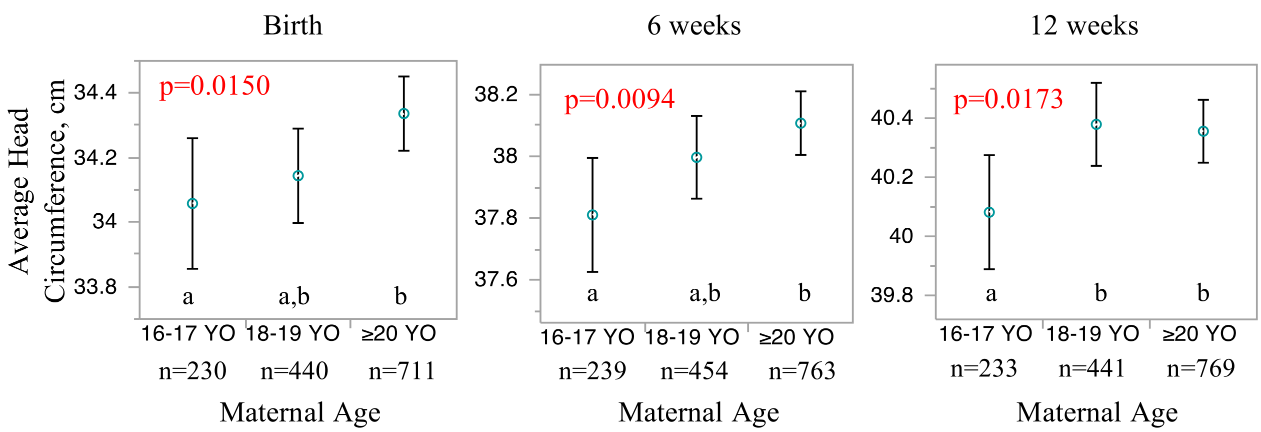
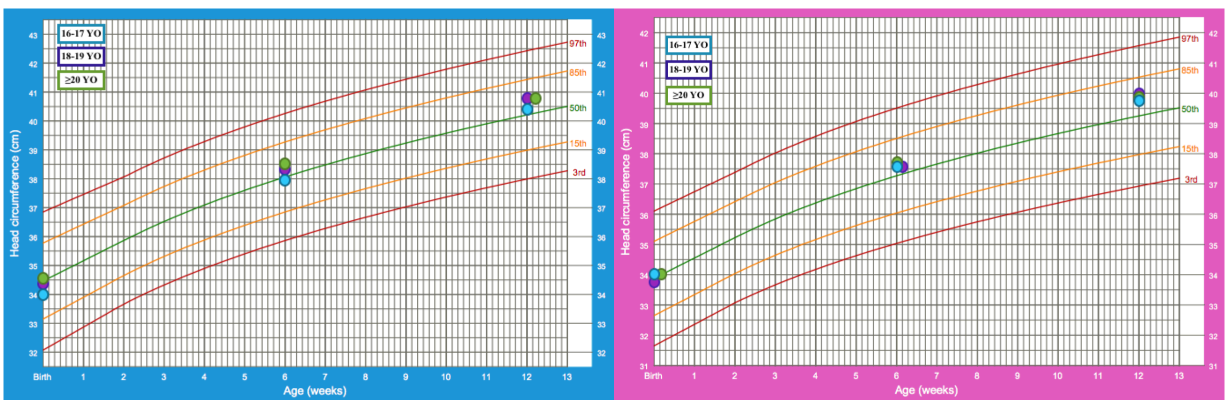


Figure 4.11 Average infant head circumference, stratified by maternal age
[1]Values expressed as LSM; error bar indicates SE
[2]Adjusted for BMI and Fundal Height at enrollment
[3] *P* values for Maternal Age (Effects test)
[4]Tukey honest significance test for significant differences

Least square mean head circumference at birth, 6 weeks, and 12 weeks was assessed between male and female infants of young adolescents, older adolescents, and adult mothers. Mean male and female infant weight was then plotted on the WHO growth charts to determine HCFA percentiles of the infants at all three time points. Results revealed that male infants consistently followed a similar pattern at birth and 6 weeks of age; infants of young adolescents were at the smallest percentile, infants of older adolescents were at a greater percentile, and

infants of adults were at the highest percentile (**Figure 4.12**). However, this pattern was not observed at 12 weeks of age in the male infants; at this age, the least square mean lengths of the infants of the older adolescents and adults appear similar and larger than the infants of the younger adolescents. This pattern was also not observed for the female infants; female infants of older adolescents had the smallest mean head circumference at birth, with all female infants falling at similar HCFA percentiles at birth, 6 weeks, and 12 weeks of age. Female infant HCFA percentiles ranged from about the 50th to the 66th percentiles, and the HCFA percentiles for the male infants ranged from about the 33rd percentile to the 66th percentile depending on maternal age.



N at birth: 16-17 YO=109; 18-19 YO=207; ≥20 YO=341
N at 6 weeks: 16-17 YO=110; 18-19 YO=214; ≥20 YO=352
N at 12 weeks: 16-17 YO=110; 18-19 YO=204; ≥20 YO=357

N at birth: 16-17 YO=120; 18-19 YO=231; ≥20 YO=362
N at 6 weeks: 16-17 YO=128; 18-19 YO=234; ≥20 YO=400
N at 12 weeks: 16-17 YO=122; 18-19 YO=230; ≥20 YO=400

Figure 4.12 Head circumference-for-age percentile of all maternal age groups
[1]Charts from: http://www.who.int/childgrowth/standards/en/

Infants of older adolescents experienced the greatest gain in head circumference from birth through 12 weeks of age, consistent with the catch up observed in Figure 4.11 (p=0.0355). Older adolescents gained 0.17 cm and 0.22 cm more in head circumference than the infants of younger adolescents and adults, respectively.

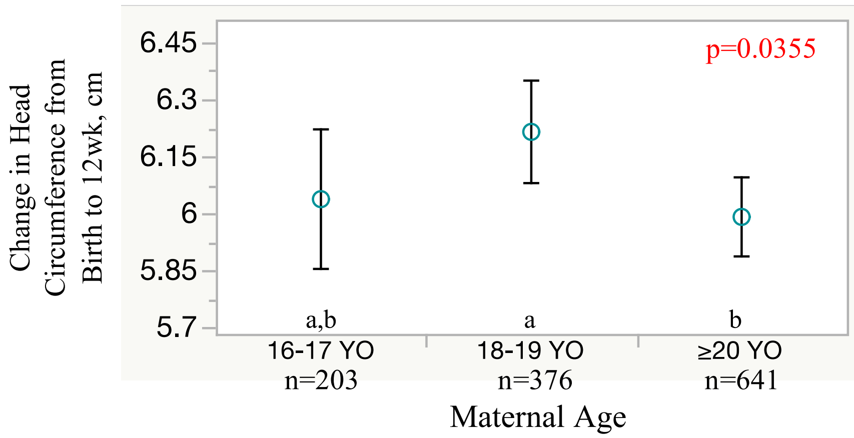


Figure 4.13 Change in infant length from birth to 12 weeks, stratified by maternal age
[1]Values expressed as LSM; error bars represent SE
[2]Adjusted for BMI at enrollment, Fundal Height at enrollment
[3] *P* values for Maternal Age (Effects test)
[4]Tukey honest significance test for significant differences

Interaction Effects of treatment

Analysis of infant length, weight, MUAC, and head circumference against intervention, after controlling for maternal age and BMI and FH at enrollment, revealed intervention to have no statistically significant effect on infant anthropometric measures at birth, 6 weeks, and 12 weeks of age (data not shown). The only exception was for low birth weight (weight<2.5 kg) (p=0.0171), indicating that the relationship between maternal age and low birth weight differed by treatment group. The interaction between intervention and maternal age also yielded non-significant results indicating that the relationship between maternal age and infant length, weight, MUAC and head circumference at birth, 6 weeks, and 12 weeks did not statistically differ by treatment.

Infant Death by Treatment Group

After adjustment for BMI and fundal height at enrollment, rates of infant death did not statistically differ by treatment group or by maternal age (data not shown). Similar to all other

outcomes measures, no significant interaction was seen for intervention and age stratification, indicating that the relationship between maternal age and rates of infant death did not statistically differ by intervention.

Z Scores

Weight-for-Age (WFA) Z score

Analysis of infant WFA Z scores against maternal age showed that WFA Z scores differed at all three time points across the three age groups (**Figure 4.14**). At birth and 6 weeks, WFA Z scores were similar between infants of younger and older adolescents with both being significantly smaller than the WFA Z scores of infants of adult mothers. On average, infants of adolescent mothers (ages 16-19 years old) had WFA Z scores 0.45 and 0.33 lower than the infants of adult mothers at birth and 6 weeks, respectively ($p=<0.0001$, $p=<0.0001$, respectively). At 12 weeks of age, the WFA Z score of the infants of older adolescent mothers was "caught up" to the WFA Z score of the infants of adult mothers. WFA Z score of the infants of young adolescents was about 0.30 lower than the average Z score of the infants of older adolescents and adults ($p=0.0010$).

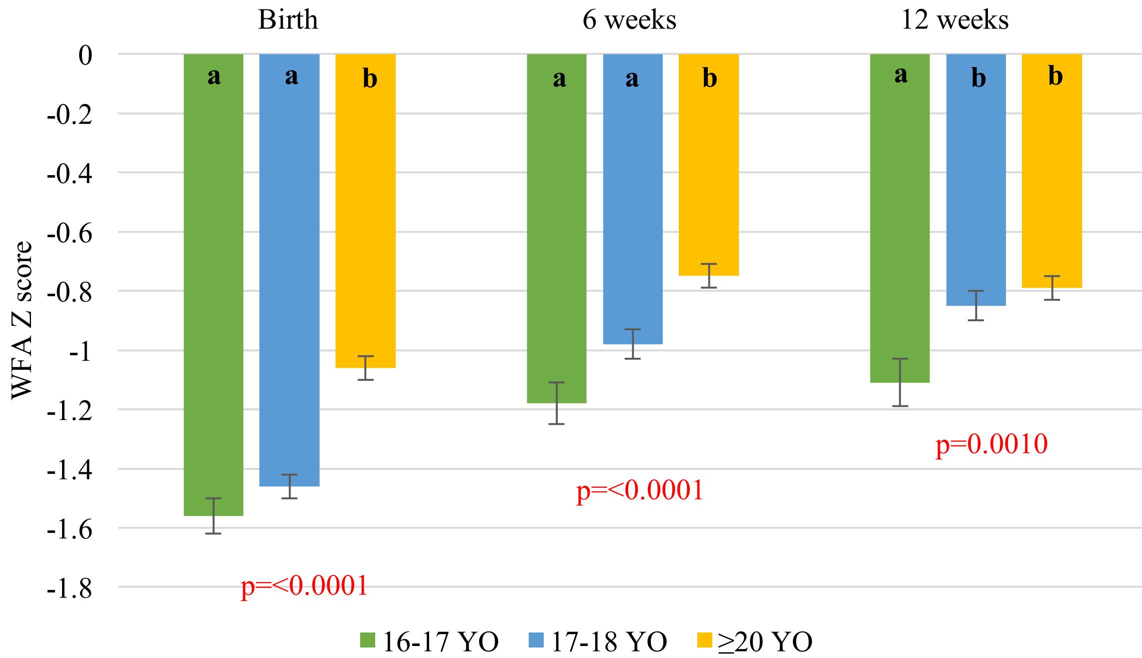


Figure 4.14 Infant WFA Z scores at birth, 6 weeks and 12 weeks, stratified by maternal age

Abbreviations: WFA, weight-for-age
N at birth: 16-17 YO=238; 18-19 YO=463; ≥20 YO=751
N at 6 weeks: 16-17 YO=206; 18-19 YO=392; ≥20 YO=668
N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=676
[1]Values expressed as least square mean; error bars represent standard error
[2]Adjusted for BMI at enrollment and Fundal Height at enrollment
[3] *P* values for Maternal Age (Effects Likelihood Ratio Test)

Underweight

Rates of underweight were significantly higher in the infants of young adolescent mothers compared to the infants of adults across all time points (**Figure 4.15**). Rates of underweight in the infants of older adolescents were similar to those of the infants of young adolescents at all times points. At birth and 6 weeks, the rate of underweight in the infants of young adolescents was 131% and 67% greater, respectively, than the rate of underweight seen in the infants of adult mothers (p=<0.0001). At 12 weeks, the rate of underweight in infants of older adolescent mothers was reduced enough to make them statistically similar to the rate found

in the infants of adult mothers (p=0.0208). At 12 weeks, the rate of underweight in the infants of the young adolescents was 80% greater than the adults.

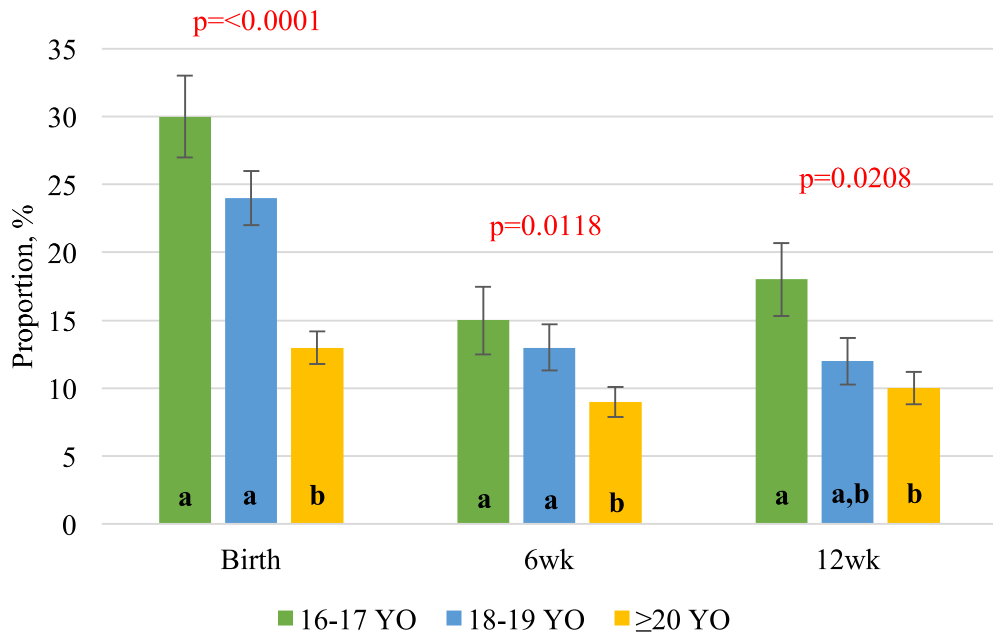


Figure 4.15 Proportions of underweight at birth, 6 weeks, and 12 weeks, stratified by maternal age

N at birth: 16-17 YO=238; 18-19 YO=463; ≥20 YO=751
N at 6 weeks: 16-17 YO=206; 18-19 YO=392; ≥20 YO=668
N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=676
[1]Values expressed as adjusted proportions; error bars represent standard error
[2]Adjusted for BMI and Fundal Height at enrollment
[3]*P* values for Maternal Age (Effects test)
[4]Underweight indicated by a WFA Z score <-2

The odds of delivering an underweight infant were 2.79 and 2.10 times greater for the younger and older adolescent mothers, respectively, compared to the adult mothers (p=<0.0001, p=<0.0001) (**Table 4.16**). Similarly, the odds of having an underweight infant at 6 weeks of age were 1.92 and 1.60 times greater for the younger and older adolescent mothers, respectively, compared to the adult mothers (p=0.0093, p=0.0242). The younger adolescents also had 1.98 times greater odds of having an underweight infant at 12 weeks compared to adult mothers (p=0.0054). All other odds ratios for underweight were nonsignificant.

Table 4.16 Odds of underweight at birth, 6 weeks, and 12 weeks, stratified by maternal age

	Age / Reference Age	Odds Ratio (95% CI)[2]	*P*
Birth	16-17 YO / ≥20 YO	2.79 (1.95-4.0)	<0.0001
	18-19 YO / ≥20 YO	2.10 (1.55-2.85)	<0.0001
	16-17 YO / 18-19 YO	1.33 (0.93-1.89)	0.1156
6 weeks	16-17 YO / ≥20 YO	1.92 (1.18-3.07)	0.0093
	18-19 YO / ≥20 YO	1.60 (0.16-2.38)	0.0242
	16-17 YO / 18-19 YO	1.20 (0.73-1.94)	0.4608
12 weeks	16-17 YO / ≥20 YO	1.98 (1.23-3.16)	0.0054
	18-19 YO / ≥20 YO	1.24 (0.81-1.86)	0.3149
	16-17 YO / 18-19 YO	1.60 (0.97-2.64)	0.0658

N at birth: 16-17 YO=238; 18-19 YO=463; ≥20 YO=751
N at 6 weeks: 16-17 YO=206; 18-19 YO=392; ≥20 YO=668
N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=676
[1]Underweight indicated by a WFA Z score <-2
[2]Tests and confidence intervals on odds ratios are likelihood ratio based

Severely Underweight

Rates of severely underweight were consistently higher in the infants of young adolescent mothers compared to infants of older adolescents and adults across all time points (**Figure 4.16**). At birth, rates severely underweight were similar between younger and older adolescent mothers; on average, rates of severely underweight were 173% higher in the adolescents compared to the adult mothers (p=0.0006). At 6 weeks of age, the rate of severely underweight in the older adolescents was statistically similar to that of infants of adult mother, with both having rates of severely underweight about 150% lower than rates found in the young adolescent mothers. Rates of severely underweight remained high in the infants of young adolescents at 12 weeks, however this did not reach significance (p=0.0549).

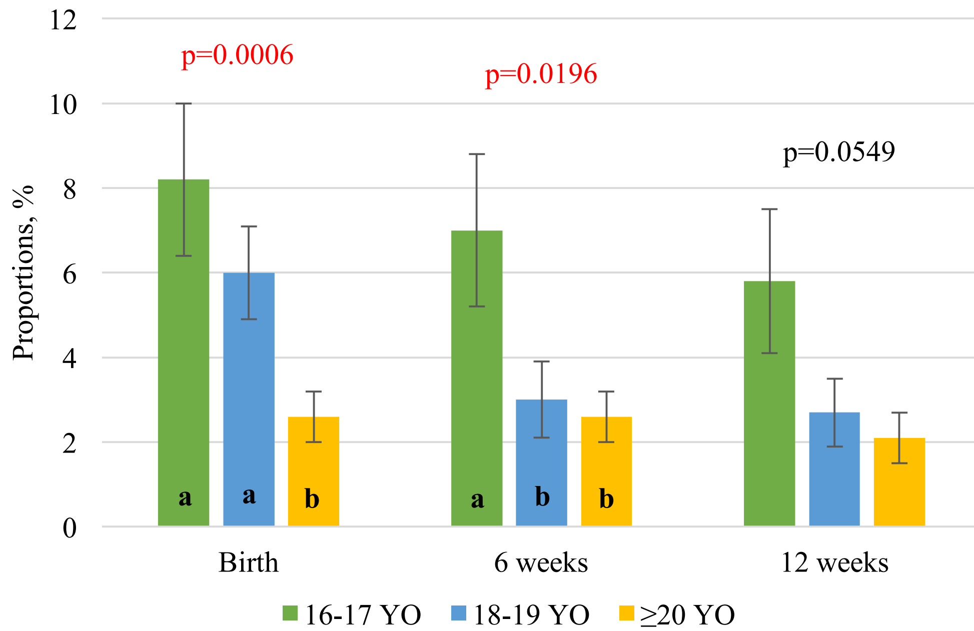


Figure 4.16 Proportions of severely underweight at birth, 6 weeks, and 12 weeks, stratified by maternal age

N at birth: 16-17 YO=238; 18-19 YO=463; ≥20 YO=751
N at 6 weeks: 16-17 YO=206; 18-19 YO=392; ≥20 YO=668
N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=676
[1]Values expressed as adjusted proportions; error bars represent standard error
[2]Adjusted for BMI and Fundal Height at enrollment
[3]*P* values for Maternal Age (Effects test)
[4]Underweight indicated by a WFA Z score <-3

Odds of having a severely underweight infant were highest for the young adolescent mothers at all three time points (**Table 4.17**). Specifically, odds of having a severely underweight infant at birth, 6 weeks, and 12 weeks of age were 3.31, 2.81, and 2.84 times greater, respectively, for the younger adolescent mothers compared to adult mothers (p=0.0004, p=0.0065, p=0.0168, respectively). Additionally, at 6 weeks, young adolescent mothers had 2.45 greater odds of having a severely underweight infant compared to the older adolescent mothers (p=0.0247). At birth, older adolescents mother also had significantly greater odds of having a severely underweight infant compared to the adult mothers.

Table 4.17 Odds of severely underweight at birth, 6 weeks, and 12 weeks, stratified by maternal age

	Age / Reference Age	Odds Ratio (95% CI)[2]	*P*
Birth	16-17 YO / ≥20 YO	3.31 (1.72-6.39)	0.0004
	18-19 YO / ≥20 YO	2.37 (1.31-4.34)	0.0042
	16-17 YO / 18-19 YO	1.40 (0.76-2.53)	0.2765
6 weeks	16-17 YO / ≥20 YO	2.81 (1.35-5.82)	0.0065
	18-19 YO / ≥20 YO	1.49 (0.53-2.42)	0.7172
	16-17 YO / 18-19 YO	2.45 (1.12-5.45)	0.0247
12 weeks	16-17 YO / ≥20 YO	2.84 (1.22-6.46)	0.0168
	18-19 YO / ≥20 YO	1.28 (0.54-2.90)	0.5644
	16-17 YO / 18-19 YO	2.22 (0.92-5.43)	0.0763

N at birth: 16-17 YO=238; 18-19 YO=463; ≥20 YO=751
N at 6 weeks: 16-17 YO=206; 18-19 YO=392; ≥20 YO=668
N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=676
[1]Severely underweight indicated by a WFA Z score <-3
[2]Tests and confidence intervals on odds ratios are likelihood ratio based

Length-for-Age (LFA) Z score

Analysis of infant LFA Z scores against maternal age stratification showed that LFA Z scores differed across age groups at birth, 6 weeks, and 12 weeks of age (**Figure 4.17**). At birth and 12 weeks of age, all mean infant LFA Z scores in each age category were statistically different from each other, with Z scores of infants being lowest in the infants of young adolescents, greater in the infants of older adolescents and greatest in the infants of adult mothers. Across all time points, infants of young adolescent mothers had about a 0.5 lower mean Z score compared to the adult mothers. By 12 weeks of age, infants of older adolescents LFA Z scores were able to catch-up to the infants of the more mature mothers.

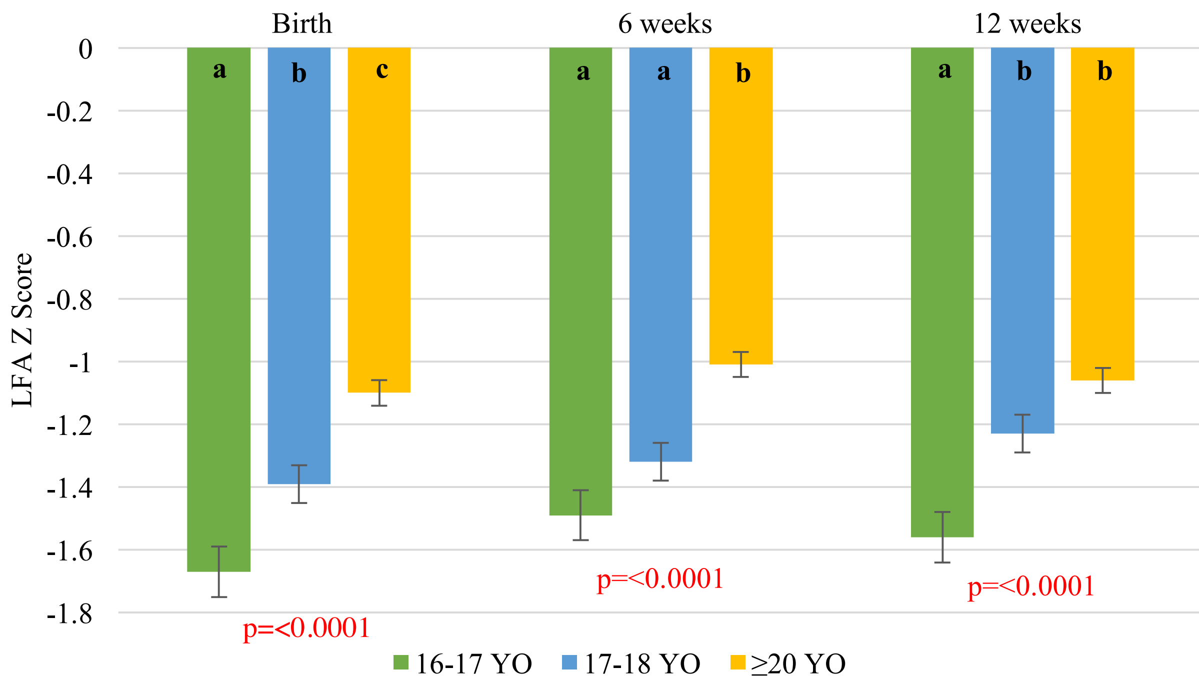


Figure 4.17 Infant LFA Z scores at birth, 6 weeks and 12 weeks, stratified by maternal age

Abbreviations: LFA, length-for-age

N at birth: 16-17 YO=229; 18-19 YO=446; ≥20 YO=724

N at 6 weeks: 16-17 YO=206; 18-19 YO=392; ≥20 YO=668

N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=675

[1]Values expressed as least square mean; error bars represent standard error

[2]Adjusted for BMI at enrollment and Fundal Height at enrollment

[3] *P* values for Maternal Age (Effects Likelihood Ratio Test)

Stunted

Consistent with the LFA Z scores seen in Figure 4.17, rates of stunting showed a similar pattern across all time points with infants of young adolescent mothers having the highest rates of stunting, infants of older adolescents having lower rates, and infants of adult mothers having the lowest rates of stunting (**Figure 4.18**). Rates of stunting found in the infants of young adolescent mothers were 106%, 75%, and 88% greater than rates of stunting of infants of adult mothers at birth, 6 weeks, and 12 weeks of age, respectively (p=<0.0001, p=0.0002, p=0.0002, respectively). At birth and 12 weeks of age, rates of stunting in each age category were significantly different from each other, however at 6 weeks, rates were similar between the infants of the younger and older adolescent mothers.

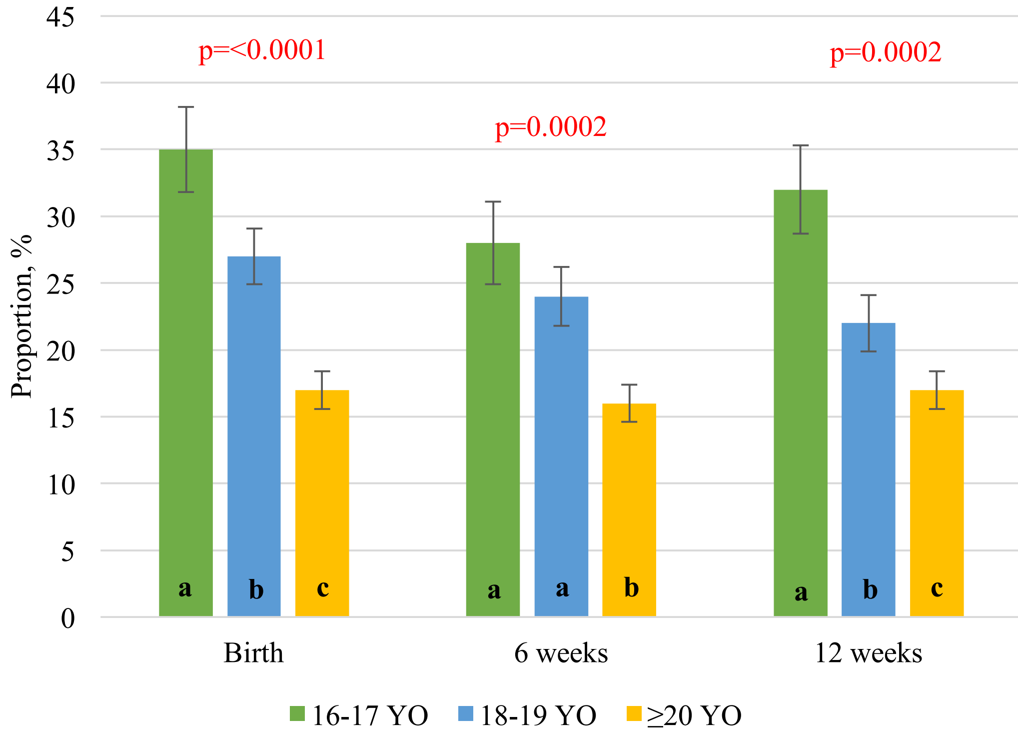


Figure 4.18 Proportions of stunted at birth, 6 weeks, and 12 weeks, stratified by maternal age

N at birth: 16-17 YO=229; 18-19 YO=446; ≥20 YO=724
N at 6 weeks: 16-17 YO=206; 18-19 YO=392; ≥20 YO=668
N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=675
[1]Values expressed as adjusted proportions; error bars represent standard error
[2]Adjusted for BMI and Fundal Height at enrollment
[3]*P* values for Maternal Age (Effects test)
[4]Stunting indicated by a LFA Z score <-2

Consistent with the results above, odds of having a stunted infant were significantly greater for the young adolescents compared to older adolescents and adults at birth, 6 weeks, and 12 weeks of age (**Table 4.18**). Specifically, the odds of having a stunted infant at birth, 6 weeks, and 12 weeks was 2.53, 2.10, and 2.23 times greater, respectively, for young adolescent mothers compared to adults (p=<0.0001, p=0.0001, p=<0.0001). Similarly, the odds of older adolescents having a stunted infant at birth, 6 weeks, and 12 weeks were 1.72, 1.62, and 1.38 times greater, respectively, than the adults (p=0.0002, p=0.0031, p=0.0485, respectively). At birth and 12 weeks, young adolescent mothers also had significantly higher odds of delivering a stunted infant compared to the older adolescent mothers (p=0.0298, p=0.0180, respectively).

Table 4.18 Odds of stunted at birth, 6 weeks, and 12 weeks, stratified by maternal age

	Age / Reference Age	Odds Ratio (95% CI)[2]	*P*
Birth	16-17 YO / ≥20 YO	2.53 (1.80-3.55)	<0.0001
	18-19 YO / ≥20 YO	1.72 (1.29-2.30)	0.0002
	16-17 YO / 18-19 YO	1.47 (1.04-2.07)	0.0298
6 weeks	16-17 YO / ≥20 YO	2.10 (1.44-3.05)	0.0001
	18-19 YO / ≥20 YO	1.62 (1.18-2.23)	0.0031
	16-17 YO / 18-19 YO	1.30 (0.88-1.90)	0.1833
12 weeks	16-17 YO / ≥20 YO	2.23 (1.53-3.23)	<0.0001
	18-19 YO / ≥20 YO	1.38 (1.00-1.91)	0.0485
	16-17 YO / 18-19 YO	1.61 (1.09-2.37)	0.0180

N at birth: 16-17 YO=229; 18-19 YO=446; ≥20 YO=724
N at 6 weeks: 16-17 YO=206; 18-19 YO=392; ≥20 YO=668
N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=675
[1]Stunting indicated by a LFA Z score <-2
[2]Tests and confidence intervals on odds ratios are likelihood ratio based

Severely Stunted

Rates of severe stunting were highest among the infants of younger and older adolescents across all time points, however significance was only met at birth and 12 weeks (p=0.0008, p=0.0242, respectively) (**Figure 4.19**). At birth, infants of younger and older adolescent mothers had statistically similar rates of severe stunting, and both were significantly greater than that of infants of adult mothers. By 12 weeks of age, infants of older adolescents reached statistical similarity to the infants of the adult mothers, however no catch up is seen in the infants of younger adolescents who still had 150% higher rates of severe stunting than the infants of adult mothers.

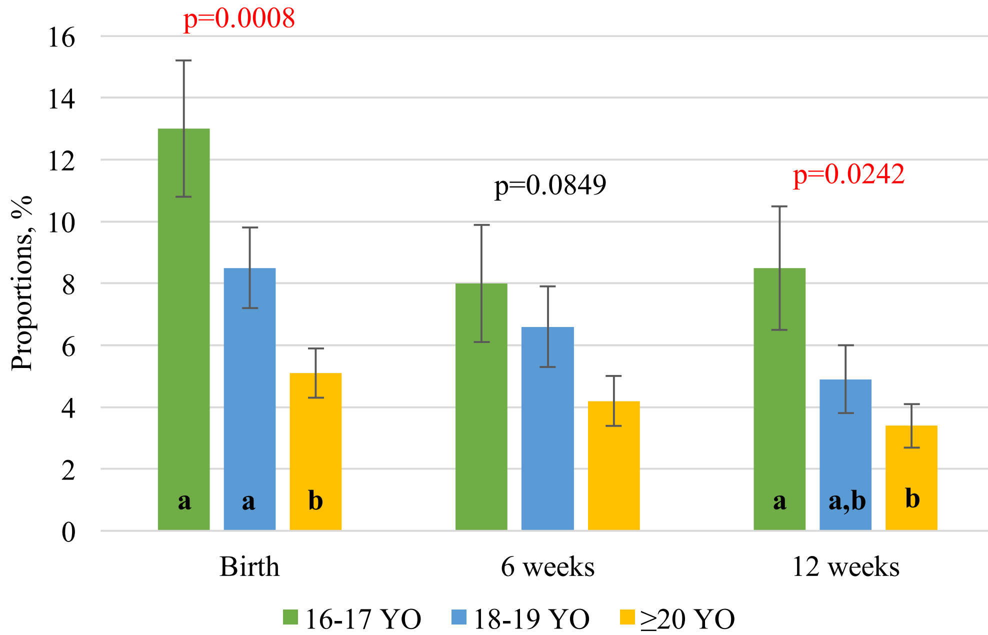


Figure 4.19 Proportions of severely stunted at birth, 6 weeks, and 12 weeks, stratified by maternal age

N at birth: 16-17 YO=229; 18-19 YO=446; ≥20 YO=724
N at 6 weeks: 16-17 YO=206; 18-19 YO=392; ≥20 YO=668
N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=675
[1]Values expressed as adjusted proportions; error bars represent standard error
[2]Adjusted for BMI and Fundal Height at enrollment
[3]*P* values for Maternal Age (Effects test)
[4]Stunting indicated by a LFA Z score <-3

The odds of having a severely stunted infant at birth, 6 weeks, and 12 weeks of age was significantly greater for the younger adolescents compared to adults (**Table 4.19**). Specifically, odds were 2.75, 1.97, and 2.65 times greater for the younger adolescents (p=0.0002, p=0.0438, p=0.0065, respectively). At birth, older adolescents also had 1.71 times greater odds of delivering a severely stunted infant compared to the adult mothers (p=0.0291). All other odds ratios were not significant.

Table 4.19 Odds of severely stunted at birth, 6 weeks, and 12 weeks, stratified by maternal age

	Age / Reference Age	Odds Ratio (95% CI)[2]	*p*
Birth	16-17 YO / ≥20 YO	2.75 (1.62-4.63)	0.0002
	18-19 YO / ≥20 YO	1.71 (1.06-2.76)	0.0291
	16-17 YO / 18-19 YO	1.61 (0.96-2.69)	0.0733
6 weeks	16-17 YO / ≥20 YO	1.97 (1.02-3.69)	0.0438
	18-19 YO / ≥20 YO	1.58 (0.90-2.77)	0.1090
	16-17 YO / 18-19 YO	1.24 (0.65-2.33)	0.5080
12 weeks	16-17 YO / ≥20 YO	2.65 (1.32-5.20)	0.0065
	18-19 YO / ≥20 YO	1.46 (0.76-2.76)	0.2500
	16-17 YO / 18-19 YO	1.81 (0.89-3.66)	0.0981

N at birth: 16-17 YO=229; 18-19 YO=446; ≥20 YO=724
N at 6 weeks: 16-17 YO=206; 18-19 YO=392; ≥20 YO=668
N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=675
[1]Stunting indicated by a LFA Z score <-3
[2]Tests and confidence intervals on odds ratios are likelihood ratio based

Weight-for-Length (WFL) Z score

A significant difference in WFL Z scores across all age groups was found at birth, but not at 6 or 12 weeks of age (**Figure 4.20**). At birth, mean WFL Z score was smallest for the infants of older adolescents compared to the infants of younger adolescents and adults, with infants of older adolescents being 0.1 and 0.28 smaller than the WFL Z scores of the infants of younger adolescents and adults, respectively (p=0.0001). From birth to 6 weeks, Z scores shifted from negative to positive. Mean WFL Z scores averaged 0.28 and 0.22 across all age groups at 6 and 12 weeks of age, respectively (p=0.5685, p=0.0902, respectively).

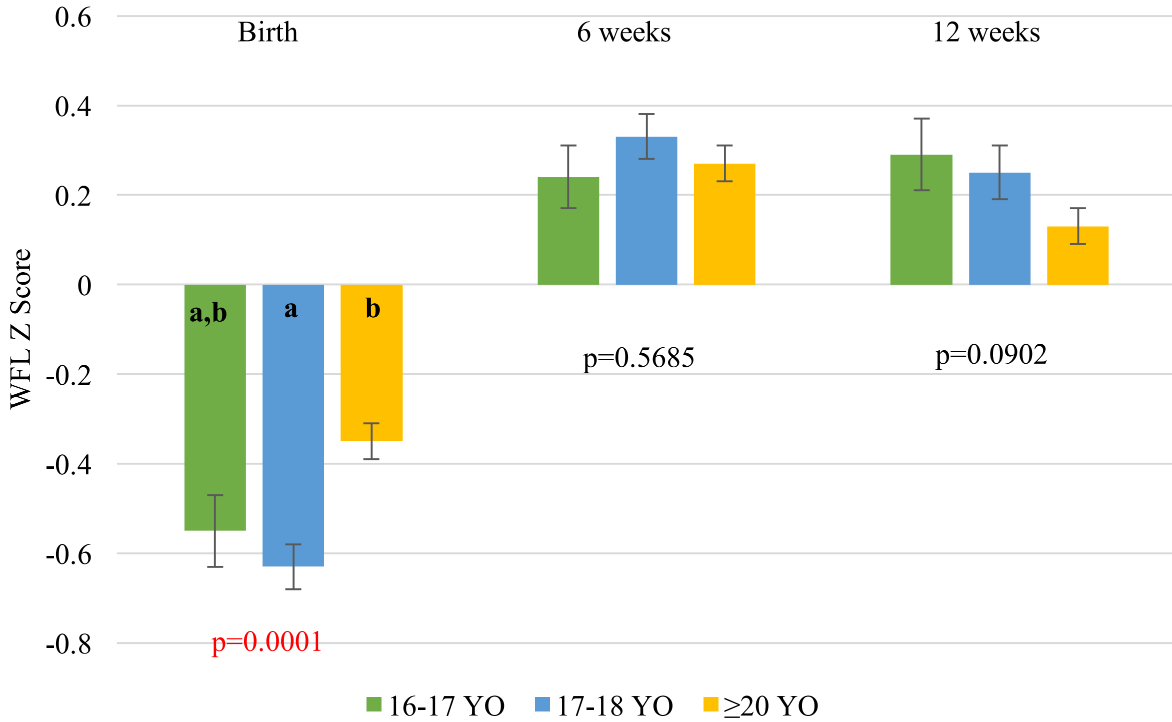


Figure 4. 20 Infant WFL Z scores at birth, 6 weeks and 12 weeks, stratified by maternal age

N at birth: 16-17 YO=182; 18-19 YO=379; ≥20 YO=652

N at 6 weeks: 16-17 YO=203; 18-19 YO=389; ≥20 YO=666

N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=675

Abbreviation: WFL, weight-for-length

[1]Values expressed as least square mean; error bars represent standard error

[2]Adjusted for BMI at enrollment and Fundal Height at enrollment

[3] *P* values for Maternal Age (Effects Likelihood Ratio Test)

[4]188 infants were excluded from WFL z-score because they were too short (<45.00 cm)

Wasted

Rates of wasting were low and did not significantly differ with maternal age stratification at birth, 6 weeks, or 12 weeks of age (p=0.1437, p=0.3565, p=0.0543, respectively) (**Figure 4.21**). At birth and 6 weeks, the average rates of wasting across all age groups were about 6% and 2%, respectively. Rates of wasting in the infants of younger adolescents and adults at 12 weeks were 200% higher than rates of wasting in the older adolescents, however this did not reach significance (p=0.0543).

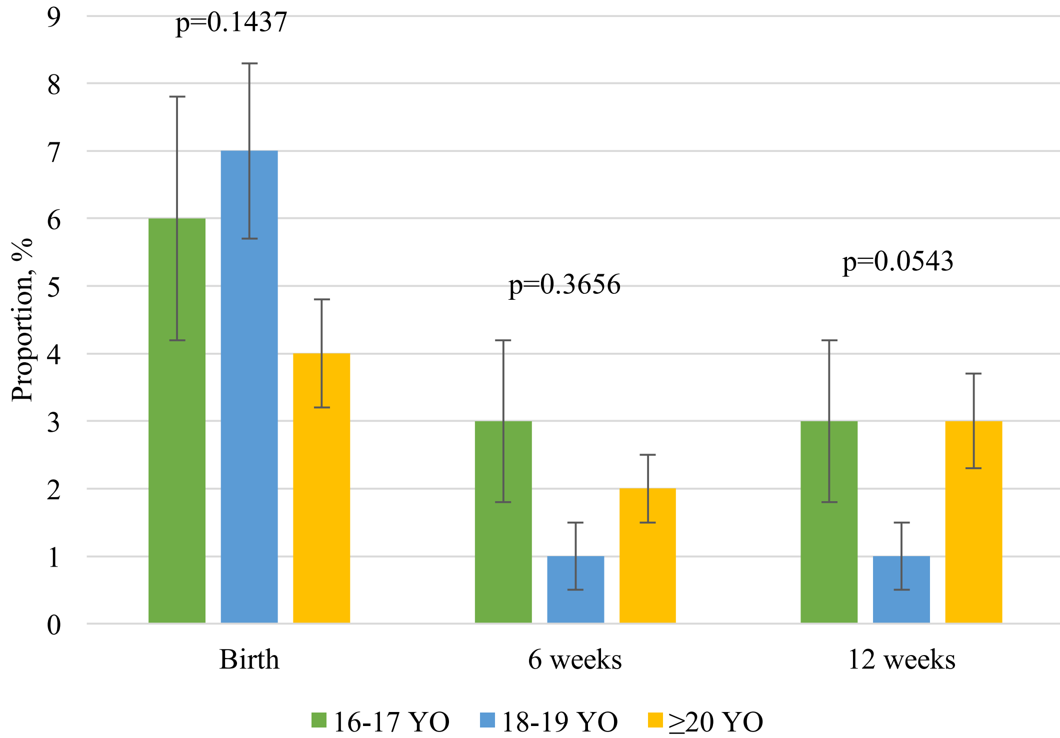


Figure 4.21 Proportions of wasted at birth, 6 weeks, and 12 weeks, stratified by maternal age

N at birth: 16-17 YO=182; 18-19 YO=379; ≥20 YO=652
N at 6 weeks: 16-17 YO=203; 18-19 YO=389; ≥20 YO=666
N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=675
[1]Values expressed as adjusted proportions; error bars represent standard error
[2]Adjusted for BMI and Fundal Height at enrollment
[3]*P* values for Maternal Age (Effects test)
[4]Wasted indicated by a WFL Z score <-2

At birth and 6 weeks of age, no age group had greater odds of having a wasted infant (**Table 4.20**). At 12 weeks, however, odds of wasting were greater for the infants of adult mothers compared to the infants of older adolescent mothers (p=0.0185).

Table 4.20 Odds of wasted at birth, 6 weeks, and 12 weeks, stratified by maternal age

	Age / Reference Age	Odds Ratio (95% CI)[2]	*p*
Birth	16-17 YO / ≥20 YO	1.50 (0.69-3.03)	0.2900
	18-19 YO / ≥20 YO	1.74 (0.99-3.04)	0.0555
	16-17 YO / 18-19 YO	0.86 (0.40-1.75)	0.6916
6 weeks	16-17 YO / ≥20 YO	1.5 (0.69-3.03)	0.2900
	18-19 YO / ≥20 YO	1.73 (1.0-3.05)	0.0555
	16-17 YO / 18-19 YO	0.86 (0.40-1.75)	0.6916
12 weeks	16-17 YO / ≥20 YO	0.96 (0.31-2.47)	0.9388
	18-19 YO / ≥20 YO	0.28 (0.06-0.82)	0.0185
	16-17 YO / 18-19 YO	3.46 (0.84-17.03)	0.0859

N at birth: 16-17 YO=182; 18-19 YO=379; ≥20 YO=652
N at 6 weeks: 16-17 YO=203; 18-19 YO=389; ≥20 YO=666
N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=675
[1]Wasted indicated by a WFL Z score <-2
[2]Tests and confidence intervals on odds ratios are likelihood ratio based

Severely Wasted

Rates of severe wasting were low for all infants at birth through 12 weeks of age (**Figure 4.22**) and did not statistically differ by age group. Average rates of severe wasting across all maternal ages were 1.5%, 0.3%, and 0.13% at birth, 6 weeks, and 12 weeks, respectively. The odds of severe wasting were no different by maternal age (**Table 4.21**).

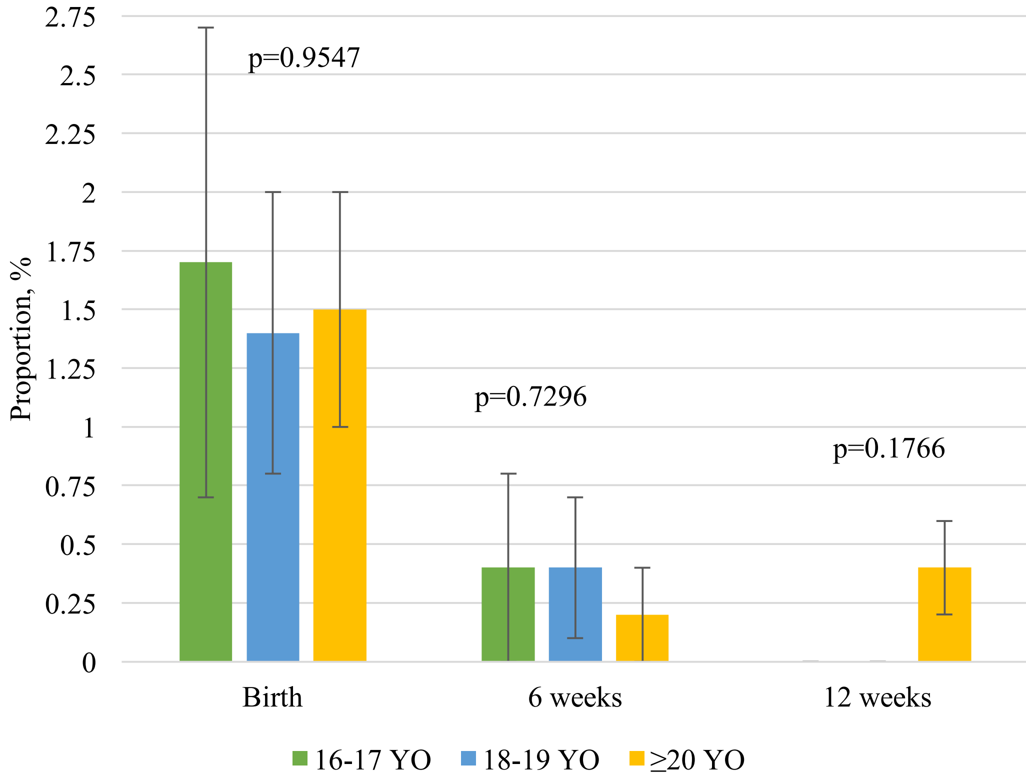


Figure 4.22 Proportions of severely wasted at birth, 6 weeks, and 12 weeks, stratified by maternal age

N at birth: 16-17 YO=182; 18-19 YO=379; ≥20 YO=652
N at 6 weeks: 16-17 YO=203; 18-19 YO=389; ≥20 YO=666
N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=675
[1]Values expressed as adjusted proportions; error bars represent standard error
[2]Adjusted for BMI and Fundal Height at enrollment
[3]*P* values for Maternal Age (Effects test)
[4]Severely wasted indicated by a WFL Z score <-3

Table 4.21 Odds of severe wasted at birth, 6 weeks, and 12 weeks, stratified by maternal age

	Age / Reference Age	Odds Ratio (95% CI)[2]	*p*
Birth	16-17 YO / ≥20 YO	1.17 (0.26-3.98)	0.8213
	18-19 YO / ≥20 YO	0.93 (0.28-2.71)	0.8984
	16-17 YO / 18-19 YO	1.25 (0.25-5.17)	0.7610
6 weeks	16-17 YO / ≥20 YO	2.09 (0.09-23.57)	0.5754
	18-19 YO / ≥20 YO	2.10 (0.24-18.18)	0.4736
	16-17 YO / 18-19 YO	1.00 (0.05-10.59)	0.9987
12 weeks	16-17 YO / ≥20 YO	1.17 (0.26-3.98)	0.8213
	18-19 YO / ≥20 YO	0.93 (0.28-2.71)	0.8984
	16-17 YO / 18-19 YO	1.25 (0.25-517)	0.7610

N at birth: 16-17 YO=182; 18-19 YO=379; ≥20 YO=652
N at 6 weeks: 16-17 YO=203; 18-19 YO=389; ≥20 YO=666
N at 12 weeks: 16-17 YO=197; 18-19 YO=380; ≥20 YO=675
[1]Severely wasted indicated by a WFL Z score <-3
[2]Tests and confidence intervals on odds ratios are likelihood ratio based

Head Circumference-for-Age Z score

Analysis of HCFA Z scores against maternal age stratification revealed that the infants of younger adolescents consistently had infants with the smallest HCFA Z score at birth, 6 weeks, and 12 weeks of age (**Figure 4.23**). At birth, mean HCFA Z score of infants of older adolescents was similar to the Z scores of infants of younger adolescents and adults, with those of younger adolescents having a 0.23 lower Z score than the adult mothers (p=0.0182). At 6 weeks, there is statistically significant evidence that the mean HCFA Z score is not the same for all three maternal age groups (p = 0.0345). In particular, the mean HCFA Z score at 6 weeks for the infants of the adult mothers was between 0.003 units less to 0.431 units more than infants of the young adolescents, with 95% confidence. At 12 weeks of age, infants of young adolescents had a Z score that was 0.30 lower than the average Z score of those of the older adolescents and adults (p= 0.0042). These results show that older adolescent HCFA Z scores were able to catch up to those of the adult mothers by 12 weeks of age.

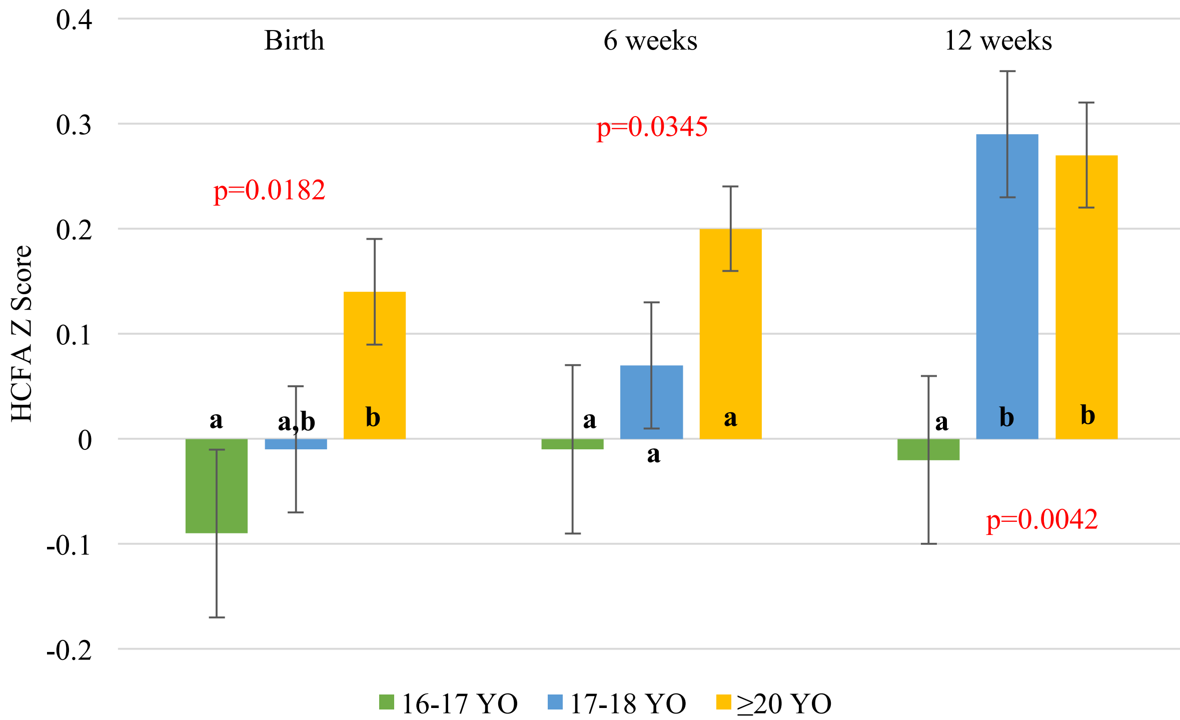


Figure 4.23 Infant HCFA Z scores at birth, 6 weeks and 12 weeks, stratified by maternal age

Abbreviation: HCFA, head circumference-for-age

N at birth: 16-17 YO=229; 18-19 YO=438; ≥20 YO=703

N at 6 weeks: 16-17 YO=205; 18-19 YO=391; ≥20 YO=665

N at 12 weeks: 16-17 YO=197; 18-19 YO=379; ≥20 YO=673

[1]Values expressed as least square mean; error bars represent standard error

[2]Adjusted for BMI at enrollment and Fundal Height at enrollment

[3] *P* values for Maternal Age (Effects Likelihood Ratio Test)

Small Head Circumference

Rates of small head circumference were significantly greater for the infants of younger adolescents compared to those of the older adolescents and adults, however significance was only met at birth (p=0.0294) (**Figure 4.24**). Specifically, rates were 100% and 167% greater in infants of the younger adolescents compared to those of the older adolescents and adults, respectively. Although rates remained higher for the infants of young adolescents, no statistical differences in rates of small head circumference were seen across the maternal age groups at 6 and 12 weeks of age (p=0.2159, p=0.1058).

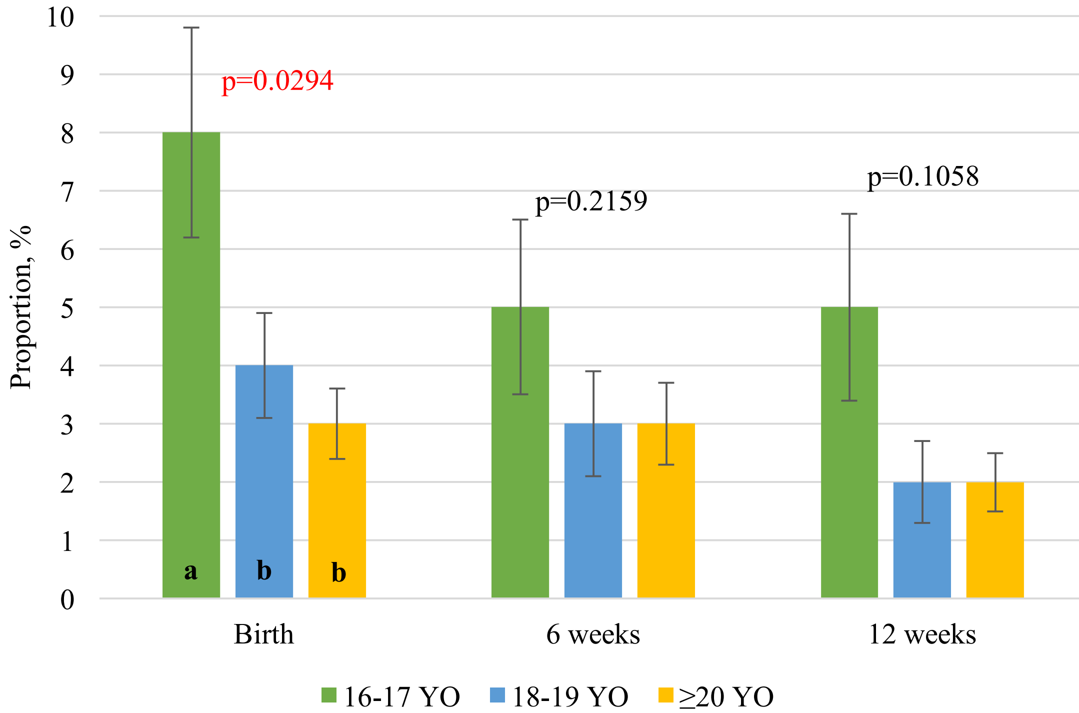


Figure 4.24 Proportions of small head circumference at birth, 6 weeks, and 12 weeks, stratified by maternal age

N at birth: 16-17 YO=229; 18-19 YO=438; ≥20 YO=703
N at 6 weeks: 16-17 YO=205; 18-19 YO=391; ≥20 YO=665
N at 12 weeks: 16-17 YO=197; 18-19 YO=379; ≥20 YO=673
[1]Values expressed as adjusted proportions; error bars represent standard error
[2]Adjusted for BMI and Fundal Height at enrollment
[3]*P* values for Maternal Age (Effects test)
[4]Small head circumference indicated by a HCFA Z score <-2

Odds of having an infant with small head circumference were 2.44 times greater for young adolescents compared to adults at birth (p=0.0084) (**Table 4.22**). While odds were higher for young adolescents compared to adults at 6 weeks of age, significance was not met (p=0.0912). At 12 weeks, odds were 3.04 times greater for younger adolescents compared to adults (p=0.0358).

Table 4.22 Odds of small head circumference at birth, 6 weeks, and 12 weeks, stratified by maternal age

	Age / Reference Age	Odds Ratio (95% CI)[2]	*P*
Birth	16-17 YO / ≥20 YO	2.44 (1.27-4.65)	0.0084
	18-19 YO / ≥20 YO	1.24 (0.65-2.31)	0.5131
	16-17 YO / 18-19 YO	1.98 (1.00-3.91)	0.0501
6 weeks	16-17 YO / ≥20 YO	2.03 (0.89-4.51)	0.0912
	18-19 YO / ≥20 YO	1.08 (0.48-2.36)	0.8479
	16-17 YO / 18-19 YO	1.88 (0.79-4.48)	0.1502
12 weeks	16-17 YO / ≥20 YO	2.05 (0.84-4.74)	0.1135
	18-19 YO / ≥20 YO	0.67 (0.24-1.67)	0.4058
	16-17 YO / 18-19 YO	3.04 (1.08-9.20)	0.0358

N at birth: 16-17 YO=229; 18-19 YO=438; ≥20 YO=703
N at 6 weeks: 16-17 YO=205; 18-19 YO=391; ≥20 YO=665
N at 12 weeks: 16-17 YO=197; 18-19 YO=379; ≥20 YO=673
[1]Small head circumference indicated by a HCFA Z score <-2
[2]Tests and confidence intervals on odds ratios are likelihood ratio based

Severely Small Head Circumference

While rates of severely small head circumference were consistently greatest for infants of young adolescent mothers at all time points, rates were not different by maternal age stratification at birth and 6 weeks of age (**Figure 4.25**). Rates of severely small head circumference in newborn infants of young adolescent mothers were 63% and 271% greater than rates seen in infants of the older adolescents and adults, respectively, however this did not reach significance (p=0.0720). At 12 weeks of age, rates of severely small head circumference were significantly greater for infants of young adolescent mothers compared to those of the older adolescents and adults (p=0.0006).

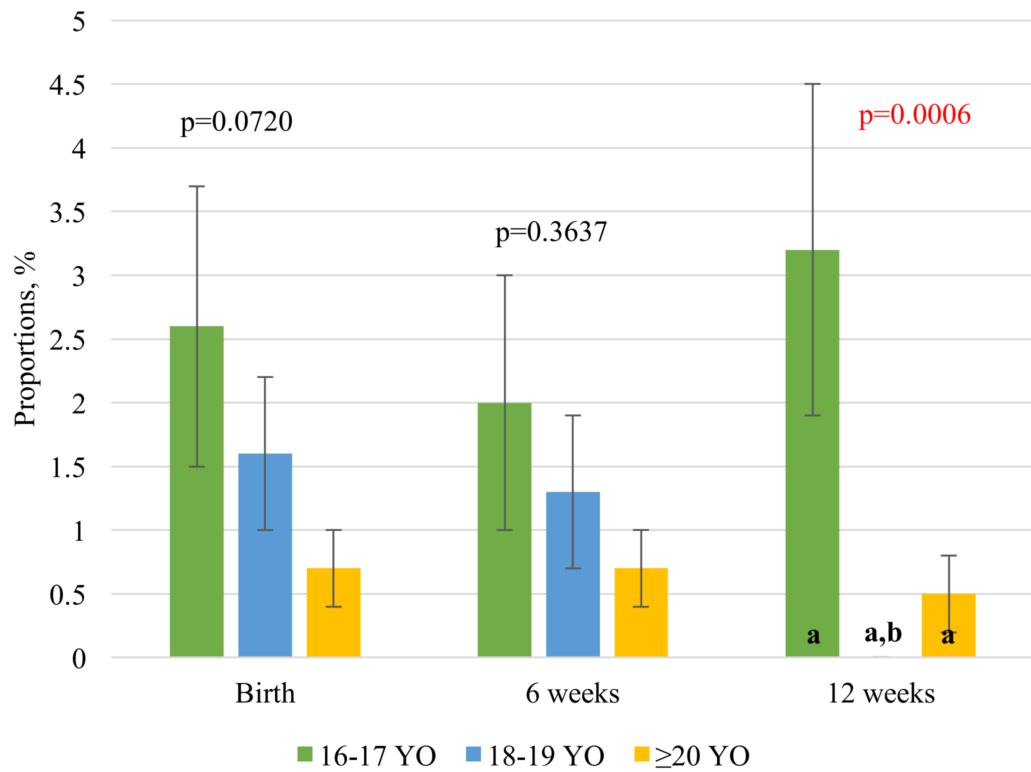


Figure 4.25 Proportions of severely small head circumference at birth, 6 weeks, and 12 weeks, stratified by maternal age

N at birth: 16-17 YO=229; 18-19 YO=438; ≥20 YO=703
N at 6 weeks: 16-17 YO=205; 18-19 YO=391; ≥20 YO=665
N at 12 weeks: 16-17 YO=197; 18-19 YO=379; ≥20 YO=673
[1]Values expressed as adjusted proportions; error bars represent standard error
[2]Adjusted for BMI and Fundal Height at enrollment
[3]*P* values for Maternal Age (Effects test)
[4]Severely small head circumference indicated by a HCFA Z score <-3

At birth, odds of delivering a newborn with severely small head circumference were 4.05 times greater for infants of young adolescent mothers compared to the infants of adult mothers (p=0.0281) (**Table 4.23**). All other odds ratios were nonsignificant at all other time points.

Table 4.23 Odds of severely small head circumference at birth, 6 weeks, and 12 weeks, stratified by maternal age

	Age / Reference Age	Odds Ratio (95% CI)[2]	*p*
Birth	16-17 YO / ≥20 YO	4.05 (1.17-14.66)	0.0281
	18-19 YO / ≥20 YO	2.44 (0.76-8.46)	0.1333
	16-17 YO / 18-19 YO	1.66 (0.53-5.07)	0.3755
6 weeks	16-17 YO / ≥20 YO	2.68 (0.64-10.63)	0.1680
	18-19 YO / ≥20 YO	1.73 (0.47-6.39)	0.3970
	16-17 YO / 18-19 YO	1.55 (0.38-5.93)	0.5236
12 weeks	16-17 YO / ≥20 YO	---	---
	18-19 YO / ≥20 YO	---	---
	16-17 YO / 18-19 YO	---	---

N at birth: 16-17 YO=229; 18-19 YO=438; ≥20 YO=703
N at 6 weeks: 16-17 YO=205; 18-19 YO=391; ≥20 YO=665
N at 12 weeks: 16-17 YO=197; 18-19 YO=379; ≥20 YO=673
[1]Severely small head circumference indicated by a HCFA Z score <-3
[2]Tests and confidence intervals on odds ratios are likelihood ratio based
[3]Odds ratios for severely small head circumference were not detected; no infants of older adolescents were classified as having severely small head circumference

Interaction Effects

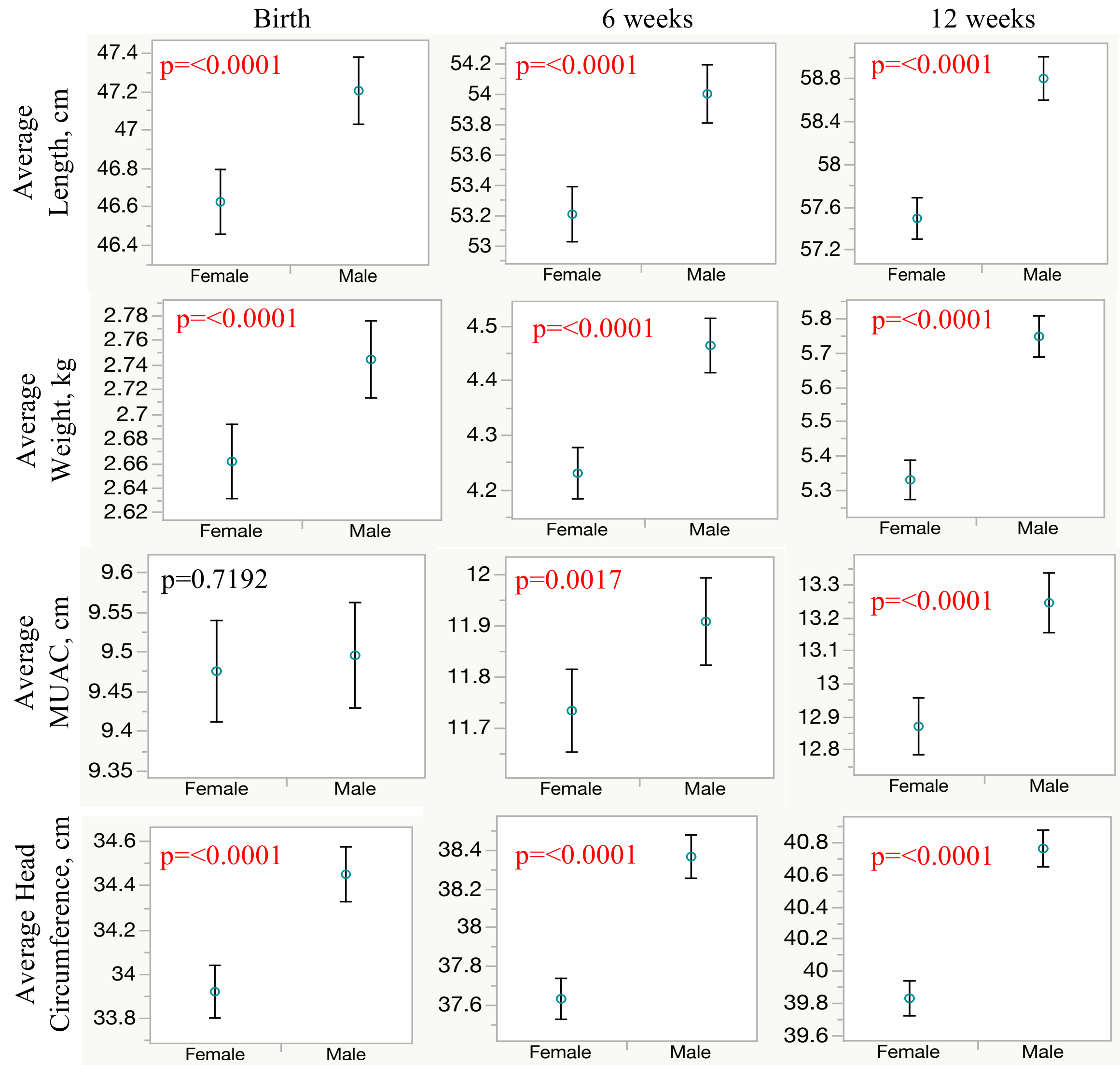
Analysis of infant Z score by intervention after controlling for BMI and FH at enrollment and maternal age showed that intervention had no consistent effect on infant Z scores at birth, 6 weeks, and 12 weeks (data not shown). Exceptions were WFA and LFA Z scores at 6 weeks (p=0.0480, p=0.0440, respectively). The interaction between intervention and maternal age also yielded non-significant results indicating that the relationship between maternal age and infant Z scores at birth, 6 weeks, and 12 weeks did not statistically differ by treatment.

Analysis of rates of underweight, stunting, wasted, and small head circumference against intervention also showed intervention to have inconsistent effects (data not shown). Exceptions were underweight at birth and stunting at 6 weeks (p=0.0364, p=0.0067, respectively). The interaction between intervention and maternal age also yielded non-significant results, again indicating that the relationship between maternal age and these markers of malnutrition at birth, 6 weeks, and 12 weeks did not statistically differ by treatment.

INFANT GENDER

Analysis of infant length, weight, MUAC and head circumference at birth, 6 weeks, and 12 weeks by infant gender revealed a consistent discrepancy in all anthropometric measures between male and female infants at birth, 6 weeks, and 12 weeks of age (**Figure 4.26**). Males were consistently larger in all measures; the only exception to this was MUAC at birth, where no difference was detected (p=0.6526). At birth, male infants were about 0.6 cm longer, weighed 80 g heavier, and had a head circumference that was 0.5 cm larger. At 6 weeks of age, male infants were about 0.8 cm longer, were 200 g heavier, and had a MUAC that was 0.2 cm larger and a head circumference that was 0.7 cm larger. At 12 weeks of age the discrepancies were even larger; male infants were about 1.3 cm longer, 400 g heavier, had a MUAC that was 0.4 cm longer, and a head circumference that was 0.9 cm larger.

Figure 4.26 Average infant length, weight, MUAC, and head circumference at birth, 6 weeks, and 12 weeks comparing infants of pooled treatment groups with young adolescents, older adolescents, and adult women, by infant gender



N: Male = 781; Female = 845
[1]Values expressed as LSM; error bar indicates SE
[2]Adjusted for BMI and Fundal Height at Enrollment and Maternal Age
[3]P values for Infant Gender (Effects test)

Despite anthropometric measures being consistently larger for male infants through 12 weeks of age, males were classified as having slightly lower percentiles for both LFA and WFA based on the WHO infant growth charts (**Figure 4.27**; **Figure 4.28**). At birth, LFA appeared similar in the male and female infants, with both falling between the 3rd and 15th percentiles. However, at 6 weeks, a noticeable difference was observed; male LFA was below the 15th percentile while female LFA was above the 15th percentile. LFA at 12 weeks of age also appeared similar, with females having a slightly higher LFA percentile. WFA at birth was just below the 15th percentile for both male and female infants. WFA at 6 and 12 weeks also appeared to be similar between male and female infants, with male infants having slightly lower WFA percentiles and with both falling between the 15th and 50th percentiles.

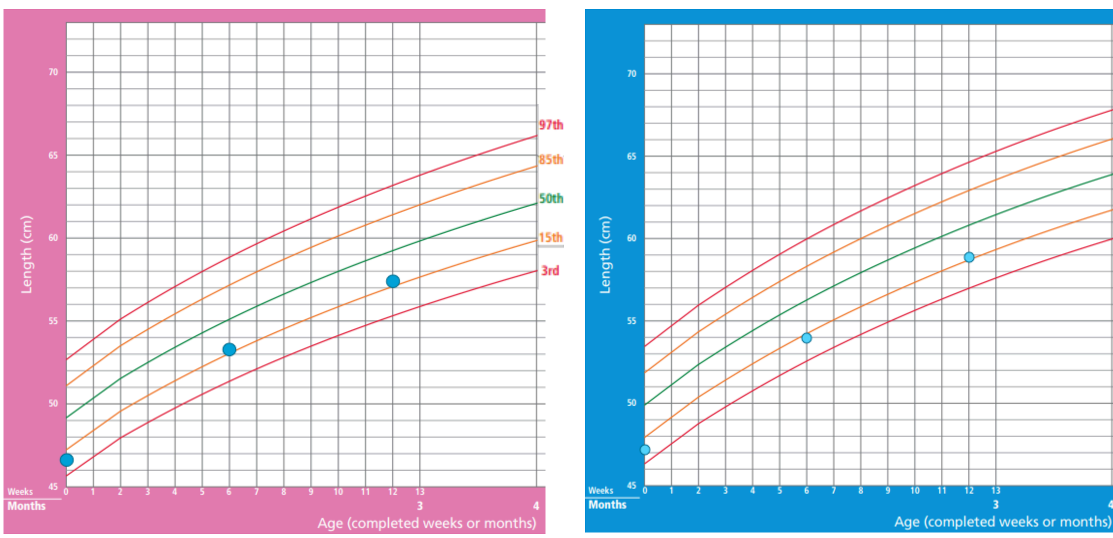


Figure 4.27 Length-for-Age WHO percentile classification of male and female infants
[1]Charts from: http://www.who.int/childgrowth/standards/en/

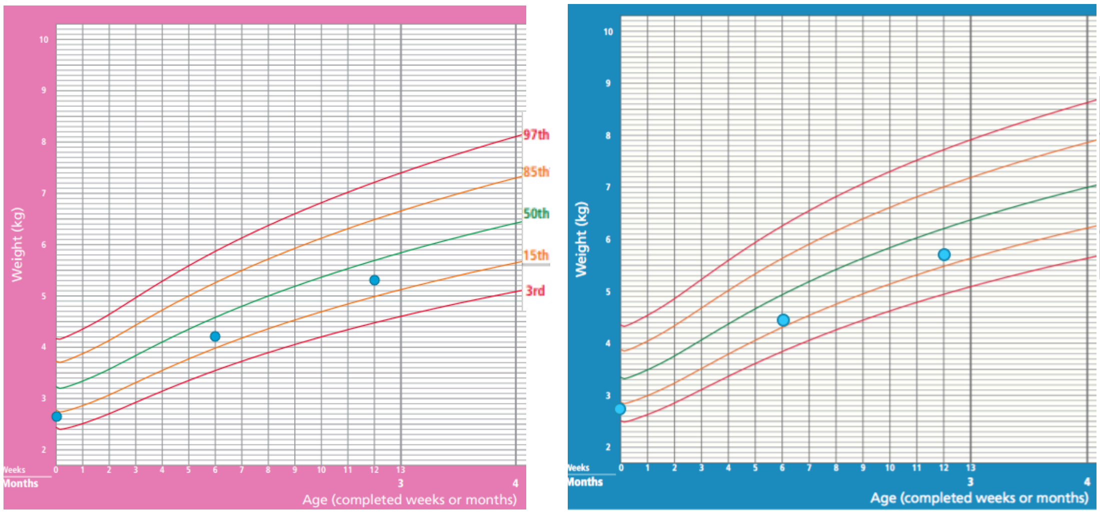


Figure 4.28 Weight-for-Age WHO percentile classification of male and female infants
[1]Charts from: http://www.who.int/childgrowth/standards/en/

At birth, neither males nor females had increased odds of underweight, stunting, wasting, or small head circumference (**Table 4.24**), however, this changed at 6 and 12 weeks. At 6 weeks of age, the odds of being underweight and stunted were 1.59 and 1.49 times greater, respectively, for the males compared to the females (0=0.0097, p=0.0048). Additionally, the odds of having a small head circumference were 2.58 times greater for the males compared to the females (p=0.0057). At 12 weeks of age, the odds of being underweight and stunted were 1.96 and 1.54 times greater, respectively, for the male infants compared to the female infants (p=0.0002, p=0.0021, respectively). The odds of being wasted at 12 weeks of age were 2.83 times greater for the male infants compared to the female infants (p=0.0066).

Table 4.24 Odds of male infants being underweight, stunted, wasted, and small head circumference at birth, 6 weeks, and 12 weeks of age compared to female infants

Outcome	P^1	Male / Female Odds Ratio (95% CI)
Birth		
Underweight, WFA < -2	0.7252	1.05 (0.80-1.37)
Stunted, LFA < -2	0.2942	1.14 (0.89-0.47)
Wasted, WFL < -2[3]	0.5230	0.85 (0.51-1.40)
Head Circumference Small, HCFA < -2	0.4111	1.24 (0.74-2.09)
6 weeks		
Underweight, WFA < -2	0.0097	1.59 (1.12-2.27)
Stunted, LFA < -2	0.0048	1.49 (1.13-1.97)
Wasted, WFL < -2[3]	0.1745	1.79 (0.77-4.35)
Head Circumference Small, HCFA < -2	0.0055	2.58 (1.31-5.36)
12 weeks		
Underweight, WFA < -2	0.0002	1.96 (1.37-2.80)
Stunted, LFA < -2	0.0021	1.54 (1.17-2.03)
Wasted, WFL < -2[3]	0.0066	2.83 (1.33-6.57)
Head Circumference Small, HCFA < -2	0.0730	1.92 (0.94-4.10)

N: Male = 781; Female = 845
[1]Adjusted for BMI and Fundal Height at Enrollment and Maternal Age
[2]*P* values for Infant Gender (Effect Likelihood Ratio Test)
[3]188 infants were excluded from WFL z-score because they were too short (<45.00 cm)

CHAPTER 5: DISCUSSION

In the secondary analysis of data from a randomized controlled clinical trial, results clearly indicated that young adolescent mothers and their infants had more severe consequences than the older, more mature mothers. Younger and older adolescent mothers experienced similar maternal outcomes compared to those of adult mothers. Adolescents ages 16-19 gained less weight on treatment, had smaller final MUACs and FHs, experienced a decrease in MUAC from enrollment to delivery, and had increased odds of extreme premature delivery compared to adult mothers. Additionally, the odds of delivering before recovery from moderate malnutrition (MUAC>23.0 cm) were higher for adolescent mothers, and the odds of recovering without relapse were lower compared to the adults, indicating that recovery was infrequent for the adolescent mothers.

Though the prevalence of adverse infant outcomes was higher for both younger and older adolescent mothers compared to the adults, the young adolescent women ages 16-17 years old had more severe outcomes. Infants of young adolescent mothers were the shortest, weighed the least, and had the smallest MUACs and head circumferences. These infants also had the smallest WFA and LFA Z scores compared to those of older adolescent and adult mothers from birth through 12 weeks of age, and the highest rates and odds of underweight and stunting at birth, 6 weeks, and 12 weeks compared to older adolescents and adults. Rates of LBW were also highest for the young adolescent mothers.

Although anthropometric measures at birth and 6 weeks were often similar for infants of younger and older adolescent mothers, infants of the older adolescents were consistently able to catch up anthropometrically to the infants of the adult mothers by 12 weeks of age. This indicates that anthropometric measures of young adolescents may continue to be lower, with

little to no catch up growth compared to the older adolescents and adults, suggesting an additional vulnerability in this age group.

While differences in maternal and infant outcomes were observed between the three maternal age groups, assessment of adolescent maternal and infant outcomes by treatment revealed no statistical differences between treatment groups, indicating that no treatment was better able to improve outcomes than the others. Additionally, in general, no statistical differences were detected between the younger and older adolescent mothers and their infants within each treatment group.

This sample of moderately malnourished pregnant women from the *Mamachiponde* study was young; 48% of the participants were classified as adolescents (≤ 19 YO), with about 16% being young adolescents (16-17 YO) and about 32% being older adolescents (18-19 YO). The inclusion criteria for age changed after initial enrollment had already begun in the primary *Mamachiponde* study. Initially, enrollment criteria stated that all participants needed to be ≥18 years of age, but was lowered to ≥16 years of age, allowing for younger adolescent women to enroll in the study. Figure 4.1 shows the age distribution of the *Mamachiponde* participants; according to this figure, about 18% of the participants reported being 18 years of age, the highest frequency seen out of all other ages. A possible explanation for this increased frequency at 18 years of age could be that women misreported their age to allow for enrollment into the study under the previous inclusion criteria.

Adolescents enrolled in treatment earlier in pregnancy and received more rations of supplementary food. Although rates of anemia were higher in the adolescents, adolescent mothers had lower rates of HIV, a 0.35 kg/m^2 larger BMI, on average, and fewer women were categorized as underweight (BMI <18.5 kg/m^2). Average BMI at enrollment for adolescent and

adult mothers ranged from 19.5-19.9 kg/m^2, classifying all age groups at the low end of normal. Although pre-pregnancy BMI was not measured since women typically enrolled at the end of their 2nd trimester, from 24-25 weeks' gestation, it was likely low given their BMI at this stage of pregnancy was at the low-end of normal. While maternal BMI is positively associated with birth weight for mothers of all ages, it can also serve as an indicator of biological immaturity in adolescents (Althabe et al., 2015; Wrottesley, et al., 2016). Underweight BMI in adolescents has been shown, specifically, to be associated with an increased risk for adverse outcomes, such as LBW, compared to adolescents classified as having a normal BMI (Han et al., 2010). The low BMI seen in the adolescent mothers of the current analysis likely contributed to the elevated rates and odds of LBW, stunting, wasting, and underweight seen in this analysis (Althabe et al., 2015; Wrottesley, et al., 2016; Frederick et al., 2007; Demographic and Health Survey (DHS), 2015-2016).

This population of moderately malnourished adolescents and adults was also short, with nearly 5% having very short stature (height <145 cm) and nearly 60% having short stature (height <155 cm). Although rates of short stature did not statistically differ by maternal age, its effects have been shown to yield more severe outcomes when the mother is classified as adolescent (Lao & Ho, 2000). Specifically, maternal short stature has been shown to be associated with a substantially higher risk of LBW, premature delivery, and infant underweight and stunting in both adult and adolescent pregnancies and likely contributed the outcomes observed in the present analysis (Katz et al. 2010; Ozaltin, Hill, and Subramanian, 2010).

Maternal Outcomes

Weight gain from enrollment to delivery was about 440 g greater for the adult women compared to both the younger and older adolescent mothers in the current analysis. Currently, evidence is insufficient to determine if IOM pregnancy weight gain recommendations are sufficient to optimize adolescent outcomes. Since using pediatric growth charts is impractical for pregnancy, it is recommended for adolescents to use the adult pre-pregnancy BMI cutoff points in spite of its limitations (Rasmussen, Yaktine, & IOM, 2009). The IOM recommends 12.5-18 kg of total weight gain for adult women classified as underweight by pre-pregnancy BMI (BMI <18.5 kg/m^2), with 10.8-17.3 kg gained from the beginning of the second trimester to the end of the third trimester (Rasmussen, Yaktine, & IOM, 2009). Specific recommendations for gestational weight gain in adolescent pregnancy have yet to be determined, however, adolescents are generally recommended to gain more weight than adult mothers to deliver the same sized infants (Rasmussen, Yaktine, & IOM, 2009). Since weight gain from enrollment to delivery averaged 2.8 kg in the adolescent mothers and 3.2 kg in the adults and most women enrolled at about 24 weeks gestation (end of the 2nd trimester), it is likely that weight gain across the entire pregnancy was inadequate. Additionally, more than 90% of the participants gained less than 454 g/week, an indicator of inadequate weekly weight gain.

The literature is inconsistent as to whether or not weight gain in adolescent pregnancy is greater or less than that of adult pregnancy. Thame et al. and Taiwo, Ogunkunle, and Sanusi both found adolescent weight gain in pregnancy to be significantly larger than that of the adult mothers (Thame et al, 2007; Taiwo, Ogunkunle, & Sanusi, 2014). However, this discrepancy in results can possibly be explained by the level of malnutrition at baseline; adolescents who

experienced greater maternal weight gain than the adults were more nutritionally adequate than the adolescent mothers who gained less weight than the adults.

It is possible that the limited gestational weight gain seen in the adolescent mothers (weight gain being an indication of increasing maternal nutrient reserves) was preferentially used as energy by the adolescent mother throughout pregnancy, rather than used to support fetal growth. Evidence suggests that breakdown of maternal fat stores is reduced in the 3^{rd} trimester of pregnancy, allowing the mother to use glucose for energy and thereby limiting the energy available for fetal growth (Scholl et al, 2000).

The weight gain observed in the adolescents may also be partly attributed to continued vertical growth of the mother. While adolescents in pregnancy have been shown to cease growth in a rural and undernourished population, it has also been shown to allow growth to continue at the expense of the infant (Rah et al, 2008; Scholl et al, 1994). Scholl et al. found that pregnant adolescents continued to grow during gestation, and although gestational weight gain was observed in this growing sample, the infants tended to be smaller (Scholl et al, 1994).

Maternal MUAC at enrollment did not significantly differ by age group in the current analysis (Table 4.2), however, MUAC at delivery was significantly lower in younger and older adolescents than in the adult mothers (Table 4.7). Additionally, when you look at the change in MUAC from enrollment to delivery, results showed that younger and older adolescents experienced greater losses in MUAC (Table 4.7) compared to the adult mothers who maintained MUAC across treatment. This indicates that the lean body mass of the adolescent mothers was depleted during pregnancy and maintained in adult pregnancy. Unlike the current analysis, Katz, et al. found that all pregnant Nepali women ≤ 25 years of age experienced a loss of MUAC from early pregnancy through postpartum (Katz et al. 2010). However, results were similar in that the

loss of MUAC seen in pregnant women ages 16-17 years of age was -0.21 cm greater than the loss of MUAC seen in the pregnant adults ages 20-25 years of age (-0.61 cm and -0.40 cm, respectively) (Katz et al. 2010).

Final fundal height at enrollment and delivery was significantly smaller in the younger and older adolescents compared to the adult mothers. Additionally, rates and odds of extreme premature delivery were significantly higher in the younger and older adolescents compared to the adult mothers (Table 4.7 and 4.8). The odds for extreme premature delivery were 2.84 and 1.79 times greater for the younger and older adolescents compared to the adults. The results of the current analysis were congruent with those found in the literature that the risk of delivering preterm (<37 weeks gestation) and very preterm (<32 weeks gestation) increase with decreasing maternal age (Conde-Agudelo et al., 2005; Thato, Rachukul, & Sopajaree, 2007; Thaithae & Thato, 2011; Momno-Ngoma et al, 2016; Althabe et al, 2015).

Interestingly, evidence also supports that vertical growth is ceased when undernourished adolescents become pregnant (Rah et al, 2008). Although maternal height throughout pregnancy up until 12 weeks postpartum was not recorded in the *Mamachiponde* study, it is possible that vertical growth was diminished by pregnancy thereby increasing the likelihood of short stature in the adolescent mothers later in life. Adult short stature compounded with malnutrition is known to exacerbate the intergenerational cycle of malnutrition (Figure 2.3), and increases the likelihood for adverse outcomes to occur in subsequent pregnancies.

Infant Anthropometric Outcomes

In the present analysis, infants of adolescent mothers ages 16-17 years of age were shorter, weighed the least, and had the smallest MUACs and head circumferences compared to

the older mothers through 12 weeks of age. At birth, the infants of the young adolescent mothers were about 46.4 cm in length, 2600 kg in weight, and had a MUAC and HC of 9.3 cm and 34.1 cm, respectively. In general, these outcomes are congruent with the literature, which shows infants of adolescents to be significantly smaller anthropometrically than infants of older, more mature mothers (Thame et al. 2007; Fall et al, 2015). Fall et al. found infants of adolescents ≤19 to weight about 100 g lighter at birth compared to infants of adult mothers ages 20-24 years old, about 150 g lighter compared to infants of adult mothers ages 25-29 years old, and about 200 g lighter compared to infants of adult mothers ages 30-34 years of age, using data collected from five low- to middle- income countries (Fall et al, 2015). These findings are similar to the current analysis, which found the infants of young adolescents to be about 200 g lighter at birth than infants of the adult mothers' ≥20 years of age.

In a study by Thame et al, newborn anthropometry was collected from infants of both adolescent and adult mothers living in Jamaica. While mean birth weight, mean crown-to-heel length, and mean head circumference of infants of adolescents and adults did not statistically differ (2990 g and 3040 g; 48.9 cm and 48.9 cm; and 34.2 cm and 34.2 cm, respectively), researchers found that the newborn infants born to adolescent mothers had a 0.3 cm smaller MUAC than the newborn infants of adult mothers ($p=0.02$) (10.3 cm and 10.6 cm, respectively) (Thame et al. 2007). Overall, the infants from the study by Thame et al. were larger anthropometrically compared to the infants in the current analysis, regardless of maternal age. A different study conducted in Peru found that young "still-growing" adolescent mothers had newborns that weighed less than the adult mothers, even after being matched for nutritional status (Frisancho, Matos, Leonard, & Yaroch, 1985). Frisancho, Matos, Leonard, & Yaroch determined the mean birth weight of infants of women ages 18-25 (3240 g) to be statistically

larger than the mean birth weight of infants born to the 12-13 YO, 14 YO, 15 YO, and 16 YO adolescents (2937 g, 3024 g, 3093g, and 3138 g, respectively) (Frisancho, Matos, Leonard, & Yaroch, 1985). However, mean birth weight of the infants of the 17 year old adolescents (3220 g) was not found to be statistically different than the adults. The infants in the studies by Thame et al. and Frisancho, Matos, Leonard, & Yaroch were larger overall compared to those in the current analysis, regarless of maternal age. A possible explanation for these discrepancies could be attributed to the nutritional status of the mothers at conception; neither study focused their efforts on malnourished pregnant women. Other possible explanations include access to prenatal care and food during pregnancy.

Additional analysis of the change in infant anthropometric measures from birth to 12 weeks of age revealed that infants of older adolescents had the largest increase in weight, MUAC, and head circumference compared to the infants of the younger adolescents and adults. These results support the notion that the infants of older adolescent mothers experienced catch up growth which allowed them to be anthropometrically similar to the infants of adult mothers at 12 weeks of age, with young adolescents experiencing little to no catch-up. Catch up growth refers to the growth that occurs following a period of growth failure, when the growth rate increases above the rate that was expected based on the growth deficit that was seen earlier in life (Griffin, 2015). Although catch up growth is commonly incomplete, meaning a defect still exists, it reduces the growth deficit between the subject and their expected body size (Griffin, 2015). Existing research on catch up growth tends to focus on children and adolescents in developing countries, with some studies showing that this growth occurs during in early childhood (Grantham-McGregor et al, 2007) and others finding it to occur during puberty (Prentice et al, 2013). Since catch up growth has been shown to occur from childhood through adolescence, it is

possible that infants born to both younger and older adolescent mothers will experience a catch up growth later in life if provided adequate nutrition. However, since catch up was not observed through 12 weeks of age in the infants of young adolescents, it is likely that their catch up growth later in life will still result in a greater deficit than that of the infants of older adolescents. Research on catch up growth in infants born to adolescent mothers in malnourished settings is lacking; additional research is needed to determine catch up growth in the infants born to malnourished adolescents and to determine if young maternal age limits this growth.

Comparison of mean anthropometric measures against the WHO infant growth charts indicated that infants of young adolescent mothers were consistently at the lowest percentile for LFA and WFA at birth, 6 weeks, and 12 weeks of age regardless of infant gender. The WHO growth charts are international standards showing how a healthy, breast-fed child should grow from birth to two years of age and were created using child growth data from a wide variety of different ethnic and cultural backgrounds (Brazil, Ghana, India, Norway, Oman, and the USA) (CDC, 2013). The WHO charts use the 2nd and 98th percentiles as the outer most cutoffs, with anything above or below these values indicating abnormal growth. Although the prevalence of underweight and stunting were high in infants of the young adolescent women based on the current analysis, plotting mean LFA and WFA on the WHO charts indicated that overall, infants in all age categories were not considered to have abnormal growth. This is consistent with the mean LFA and WFA Z scores calculated for each maternal age group which showed none of the mean Z scores to be less than -2.0.

Rates of low birth weight were significantly higher for younger and older adolescent mothers in the present analysis, compared to the adults. These results are consistent with the literature which shows adolescents, particularly young adolescents, to be the most strongly

associated with low birth weight in low- and middle-income countries (Taiwo, et al, 2014; Momno-Ngoma et al, 2016). In an observational study in sub-Saharan Africa by Mombo-Ngoma, et al., very young maternal age (≤ 16 years of age) was found to be associated with the highest risk for delivery of a LBW infant (Momno-Ngoma et al, 2016). Specifically, 14-16-year-old mothers had 2.06 (95% CI: 1.37-3.12) times greater odds of delivering a LBW infant compared to the adult reference group ages 20-30 after controlling for country, BMI, antenatal clinic, and MUAC (p=<0.0001) (Momno-Ngoma et al, 2016). These odds are similar to those in the present analysis, which determined young adolescents and older adolescents to have a 2.43 (95% CI: 1.75-3.36) and 2.00 (95% CI: 1.53-2.62) times greater odds, respectively, of delivering a LBW infant compared to the adult (≥ 20 YO) reference group. The lower odds ratio seen in the current analysis for the young adolescents could indicate that the young adolescents (16-17 YO) in the current analysis suffered from more severe moderate malnutrition compared to the 14-16 year olds in the Momno-Ngoma et al. study.

In the current analysis, rates and odds for stunting (LFA <-2) and severe stunting (LFA <-3) were greatest for adolescents, with young adolescents having the highest rates and odds compared to older adolescents and adults. These findings are consistent with the literature which consistently shows young adolescents having the strongest association with stunting. In an observational study by Fall, et al. where odds of stunting at 2 years of age was assessed in infants from five low- and middle-income countries, adolescents ≤ 19 years of age had 1.46 (95% CI: 1.25-1.70) times greater odds of having a stunted infant at 2 years of age compared to adult women 20-24 years of age (Fall et al, 2015). These results hint that the *Mamachiponde* infants born to adolescents, especially young adolescents, may likely be stunted through 2 years of age as well.

Interestingly, a study by Espo, et al. in rural Malawi found low infant weight from birth to 12 weeks of age, defined as a WFA Z score < -1, to be the strongest predictor of severe stunting at 12 months of age, with another independent predictor being maternal height under 150 cm (Espo et al, 2002). Mean WFA of the infants of young adolescent mothers in the current analysis was less than -1 Z score at birth, 6 weeks, and 12 weeks of age. This indicates that infants of young adolescents of the current analysis are likely to be severely stunted at 12 months of age given that their weight was consistently low in the first 12 weeks of life, as was seen in the study by Espo et al.

While the rates of underweight, stunted, and small head circumference in the infants were similar across maternal age groups at birth, 6 weeks, and 12 weeks, the pattern observed in Figure 4.21, depicting rates of wasting, is unique. At birth, about 7% of infants born to the older adolescent mothers were wasted, however, by 6 weeks of age, only 1% remained with this classification. This is compared to the infants of the young adolescents and adults who experienced a decrease in rates of wasting of about 2-3 percentages. This improvement could possibly be related to the catch up growth observed in the infants of the older adolescent mothers.

Possible Explanations for the Adverse Maternal and Infant Outcomes in Adolescent Pregnancy

There are multiple possible explanations for the more severe outcomes seen in the young adolescent mothers. A primary explanation for both the maternal and infant outcomes observed in the present study is the well-known hypothesis that a competition of nutrients exists between the adolescent mother and her fetus that results from altered nutrient partitioning (King, 2003).

Maternal nutritional status at the onset of pregnancy greatly influences how nutrients are distributed between the mother and fetus, with severe malnutrition resulting in a preferential energy supply to the mother at the expense of the fetus. This competition may account for the negative effect of young gynecological age on pregnancy outcomes (King, 2003). Additionally, even when gestational weight gain in the form of maternal fat stores is observed in the adolescent, evidence supports that this energy supply is primarily utilized by the mother (King, 2003).

Another possible explanation specifically for the more severe infant outcomes observed in the young adolescent mothers is related to the delayed onset of menses that occurs in the face of nutritional deficit (Soliman, Sanctis & Elalaily, 2014). Malnutrition has the ability to delay menarche for 1.5-2 years to allow the undernourished female an opportunity to continue growing (Leenstra et al, 2005). Research also supports that girls living in rural environments, such as those in the present analysis, have delayed age of menarche compared to girls living in urban settings (Odongkara Mpora et al, 2014). Since the average age of menarche is about 12-13 years of age in a healthy female in high-income countries (WHO, Recognizing Adolescence, 2014), it is possible that the adolescents of the current analysis did not experience menarche until 14.5-15 years of age, just before becoming pregnant. Although females are able to become pregnant after the onset of menarche, the pelvic structure does not reach adequate maturity to support an optimal pregnancy until two years post-menarche, at which point, the height and diameter of the pelvis reaches complete maturation (Kaplanoglu et al, 2015). Keeping this in mind, it is highly likely that the adolescent mothers in the *Mamachiponde* study were at a low gynecological age and did not have a fully matured pelvis which contributed to the poor outcomes seen in from these mothers.

Additionally, short maternal height is a likely contributor to the adverse infant outcomes seen in the adolescent mothers due to the fact that height also corresponds with pelvic development in adolescent females (Shirima et al, 2005). Young adolescent mothers have not attained their full adult height and the pelvis has not completed growing. A study of pregnant adolescent women in India showed that maternal short stature <145 cm to be strongly associated with poor infant outcomes, namely LBW (Bisai, 2010). Although rates of short stature of *Mamachiponde* women were found to be similar across age groups, it is likely that the compounded effects of short stature, malnutrition, and pregnancy in adolescence all contributed to the outcomes.

Another possible explanation for the severe infant outcomes seen in the current analysis is the inappropriate weight gain of the mothers. It is well-known that increased gestational weight gain leads to greater infant weight and that low gestational weight gain leads to reduced infant weight (King, 2003; Han et al, 2011). Adequate weight gain in pregnancy ensures sufficient energy stores are available to support the health of the mother and the health and development of her growing fetus.

Intervention

Although three different nutritional interventions were given with each providing about 900 kcal/day and double the RDA of most micronutrients, no one intervention was more helpful than another in determining maternal and infant outcomes in this population. The effect of supplementation on pregnancy outcomes largely depends on the nutritional status of the mother prior to pregnancy (King, 2003). When women with chronic moderate-to-severe malnutrition

are given a supplement, evidence shows that while they are able to improve their own nutritional status, nutrients are preferentially partitioned to the mother, to ensure her safety throughout pregnancy at the expense of the fetus (King, 2003). The inability of these interventions to improve outcomes highlights the extent of malnutrition present in this population and alludes to the notion that pre-pregnancy nutritional status should be a target for improvement. Nutritional interventions need to be more nutrient- and energy-dense than those used in the current analysis to more properly meet the needs of this population.

An observed effect of intervention on the adolescent women was seen when young adolescents and older adolescents were compared within treatment groups. Infants of young adolescents in the RUSF group were significantly shorter, weighed less and had significantly higher rates of underweight and stunting at 12 weeks of age compared to those of the older adolescent mothers on RUSF. While no consistent statistical differences between the infants of the younger and older adolescents were observed in the other treatment groups, the pattern observed in the RUSF groups is consistent with both the CSB-UNIMMAP and CSB-IFA groups at birth, 6 weeks, and 12 weeks of age. This indicates that while a significant difference was detected, it may not be clinically significant. Additionally, young adolescents may experience less of a benefit from supplementation compared to the older adolescent mothers. The reason behind these statistical differences at 12 weeks in the RUSF is unclear, since characteristics such as SES, education, diet diversity, and MUAC, BMI, and FH at enrollment were not significantly different between the two age groups at enrollment. It is possible that underlying micronutrient differences or supplementation adherence differed between the younger and older adolescents in this treatment group thereby causing these infant anthropometric variations to appear. While many studies have focused their efforts on improving birth outcomes and child health in

undernourished populations through supplementation, little to no evidence exists for supplementation of undernourished pregnant adolescents. In general, balanced protein-energy supplements have been shown to reduce the rate of SGA and LBW, and increased birth weight or infants (Papathakis et al, 2016). Additionally, maternal supplementation with lipid-based supplements have shown to increase birth weight of infants in an undernourished population (Adu-Afarwuah et al, 2015).

Specific energy intake recommendations have not been made for pregnant adolescents, however the general consensus is that energy intake should be greater in pregnant adolescents compared to pregnant adults, with young pregnant females having the highest needs (Story & Hermanson, 2000). Current recommendations for healthy adults suggest pregnant women should to increase their daily energy intake by 340 kcal/day in the second trimester, and 452 kcal/day in the third trimester, with most pregnant women consuming a total of 2200 to 2900 kcal/day.

Previous literature indicates that supplementation with about 900 kcal/day is likely insufficient to meet the energy needs of moderately malnourished pregnant adolescents (Singh et al, 1989; Heini et al, 1991). Women who live rurally in low-income countries, such as those in Malawi, often disproportionately participate in high levels of physical activity associated with agricultural work and various activities of daily living, such as water collection and travel to and from antenatal clinics (Rural Women and the Millenium Development Goals**).** Total energy expenditure of similar pregnant adult populations was calculated to range from 2408-2782 kcal/day depending on gestational age (Singh et al, 1989; Heini, Schutz, & Jequier, 1992). Additionally, a preliminary analysis from the *Mamachiponde* study revealed that energy intake, after the addition of supplementation, was varied across treatment groups with intakes being below 2000 kcal/day on average for each group. Specifically, the RUSF group consumed 1912

kcal/day, the CSB+ with UNIMMAP group consumed 1483 kcal/day, and the CSB+ with IFA consumed 1618 kcal/day. Based on the fact that energy requirements are elevated in pregnant adolescents and that energy expenditure is also higher in this population, nutritional interventions may not adequately meet their needs to support an optimal pregnancy.

Female adults and children also bear the main responsibility for collecting water in sub-Saharan Africa; UNICEF reported that this responsibility is given to 62% of women (≥ 15) compared to only 23% of men (≥ 15) in this region (UNICEF, 2003). Additionally, as an example, in rural Malawi, girls spend over three times more time than boys collecting wood and water, and collectively, in Sub-Saharan Africa, women spend about 40 billion hours a year collecting water (Rural Women and the Millenium Development Goals**)**. Studies looking at gender and age differences in these activities of daily living typically use 15 years of age as the cut-off to be classified as an adult (UNICEF, 2003; Graham, Hirai, & Kim, 2016). Although differentiating levels of physical activity between adolescents (16-19 YO) and adults (≥ 20) is not possible when using 15 years of age as the cut-off, female adolescents may be preferentially selected to participate in these activities. Elevated levels of physical activity could be a contributing factor in the adverse outcomes observed in adolescent pregnancy.

Infant Gender

In the present analysis, male infants consistently had significantly larger lengths, weights, MUACs and head circumferences than the female infants at birth, 6 weeks, and 12 weeks after controlling for appropriate variables. However, male infants had greater odds of being underweight and stunted at 6 and 12 weeks of age. These results are consistent with those of a meta-analysis by Wamami et al. that considered 16 demographic and health surveys from 10

countries in Sub-Saharan Africa containing information regarding stunting in children (<5 years of age) (Wamami et al, 2007). Wamami et al. reported that stunting prevalence was higher for males compared to females, and that overall, males had a 1.18 (95% CI: 1.14-1.22) times greater odds of being stunted after adjusting for child age and individual survey (Wamami et al, 2007). Specifically, the analysis reported that male infants in Malawi had a 1.11 (95% CI: 1.02-1.20) times greater odds of stunting compared to female infants (Wamami et al, 2007). The prevalence of stunting in Malawi was also identified as being more pronounced in the poorest socioeconomic group compared to individuals in the highest socioeconomic group (Wamami et al, 2007). The odds of stunting at 12 weeks for male infants compared to female infants in the current analysis was 1.54 (95% CI: 1.17-2.03), slightly higher than the odds ratio reported by Wamami et al. Based on the odds of stunting seen in male and female children in Malawi from Wamami et al.'s analysis, it is likely that the odds of stunting in males will remain greater than that of the females from the present analysis as they age and develop into children.

One possible explanation as to the increased rates of stunting in males is gender bias. The literature is conflicted regarding favoritism of child gender in Africa. One study suggested that daughters were more highly favored in regions of lower socioeconomic status, however another found that males were favored due to cultural views of male valor (Cronk, 1989; Crognier et al, 2006). In a report conducted using data from rural Malawi, male infants were found to have a higher mortality risk at 1-2 years of age compared to girls of the same age (Ashorn et al, 2002). This report highlighted the importance of females in Malawian families; unlike the males who move away to marry, females in Lungwena, Malawi tend to live near their parents for their whole lives and inherit their parents land (Ashorn et al, 2002). As a result, parental "investment" is higher for female children resulting in preferential care, namely greater

attention to vaccinations, of young females in this society (Ashorn et al, 2002). Although measurements were only taken up to 12 weeks in the current analysis, it is possible for gender bias behaviors to begin at birth.

Another possible explanation regarding increased rates of stunting in male infants is the biological differences between males and females. While the literature supports the notion that the male gender is associated with increased mortality and morbidity, the underlying mechanisms are unclear (Ashorn et al, 2002; Green et al 1992; Synnes et al, 1994). The results of the current analysis, as supported by previous literature, suggest that males through 5 years of age are more vulnerable to health inequalities compared to females of the same age.

Strengths and Limitations

There were many strengths of this study. One is that the primary study, *Mamachiponde*, was a randomized, controlled trial. Another strength was the fact that the *Mamachiponde* study team collected vast amounts of demographic, anthropometric, and health data, at enrollment, throughout treatment, at delivery, and up to 12 weeks postpartum. Having access to this data allowed this sub-study to explore many relationships relating to adolescent pregnancy in this setting. Specifically, the collection of infant anthropometric and health data at birth, 6 weeks, and 12 weeks was critical information for the creation of this substudy. Having data available at 3 postpartum time points allowed for a longitudinal analysis of infant health in each maternal age group. Extensive research team data collection training was another strength.

A limitation of this study was that no true control group was included. The current nutrition recommendations in Malawi recommend pregnant women with malnutrition receive CSB+ with IFA as supplementation. Due to this, it would have been unethical for moderately

malnourished women present at clinic to not receive any supplemental food, and as a result, it wasn't possible to compare intervention results against results of untreated moderately malnourished pregnant women.

Another limitation was the fact that double-blinding was not feasible. Although the researchers were blinded, it was not possible to blind the participants due to differing intake instructions and visible differences between the three interventions. Lack of double blinding likely did not affect the outcomes of the study. In addition, collection of all anthropometric measures by differing clinic technicians with varying amounts of training is another possible limitation. Although all measurements were collected either in duplicate or triplicate, the risk of error and variability remain relatively high.

The age requirements for study participation contributed a limitation. As stated previously, inclusion criteria for age changed after initial enrollment had already begun in the primary *Mamachiponde* study. We know that age 18 was reported at the highest frequency upon enrollment; it is possible that women intentionally misreported their age to allow for enrollment into the study under the previous inclusion criteria. Additionally, clinic workers encountered women did not know their age, and as a result provided their best guess. Since this analysis relied heavily on the age of the participants, this would be considered a limitation if women did not accurately report age upon enrollment.

Due to the study's location in rural Malawi, use of ultrasound to accurately assess gestational age was not an option, limiting the ability to enroll women at the same gestational age. Fundal height was used as a proxy for gestational age in this study. Lastly, since the current analysis was performed using only women with moderate malnutrition, we have no information about young adolescents with normal MUAC in this setting or about women less

than 16 years of age. It is also unlikely that these results can be generalizable to an adequately nourished or severely malnourished pregnant population.

CHAPTER 6: CONCLUSIONS

This analysis was unique in that it assessed maternal and infant outcomes of a sample of adolescents who were both moderately malnourished and pregnant. Observations from this secondary analysis support the hypothesis that the increased nutrient requirements present in adolescence and in pregnancy, have a compounded effect leading to a competition for nutrients between the young mother and her fetus. This competition may lead to limited growth of the fetus resulting in stunting at birth through 12 weeks of age. The additional burden of malnutrition increases the vulnerability of these adolescents through inadequate nutritional intake in the face of increased nutritional needs. Adolescent mothers, particularly young adolescent mothers <18 years of age, are a high-risk population and may have greater nutrient requirements compared to adults. Nutrition guidelines that focus on adolescent pregnancy, specifically young adolescent pregnancy, are limited. Given the global magnitude of adolescent pregnancy and the adverse outcomes associated with it, especially in low- and middle- income countries, it is essential for future research to focus their efforts on the nutrient requirements of pregnant young adolescents to help prevent, alleviate, or treat malnutrition, and to support optimal maternal and fetal health and development throughout pregnancy and postpartum.

This secondary analysis highlights the importance of expanding and enhancing public health efforts to delay the age of first pregnancy, which could benefit both the affected individual, their offspring, and their societies. Emphasis should be placed on expanding education on and access to modern contraceptive methods, as well as mandatory education on sexuality. Additional efforts should also focus on ensuring girls enroll and stay in school. Targeting adolescent women prior to pregnancy or early in pregnancy and providing adequate

nutritional support and education will help to prevent adolescent pregnancy and mitigate the adverse outcomes associated with it in malnourished populations.

Future research conducted in this population should include collection of anthropometric measurements throughout childhood to determine whether the rates and odds of stunting persist after 12 weeks of age. Additionally, this data would indicate if the rates and odds of stunting remain elevated in the children born to young adolescent mothers compared to the children born to the older, more mature mothers.

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APPENDIX: NUTRIENT CONTENT OF SUPPLEMENTARY FOODS

	RUSF[1]	CSB+ with UNIMMAP[2]	CSB + with IFA[3]	pregnancy, aged 19-30 YO	
Nutrient	Amt (% RDA)	Amt (% RDA)	Amt (% RDA)	RDA	UL
Energy, kcal	920	893	893		
Protein, g	36	33	33		
α-linolenic,g (Omega 3)	2.3 (161)	0.0 (0)	0.0 (0)	1.4	
linoleic,g (Omega 6)	14.0 (107)	0.0 (0)	0.0 (0)	13	
Docosahexaenoic acid, g	211	0	0		
Eicosapentaenoic acid, g	43	0	0		
Vitamin A, µg	2628 (341)	3210 (417)	2410 (312)	770	3000
Vitamin B1 (thiamine), mg	3.2 (228)	1.7 (121.5)	0.3 (20)	1.4	
Vitamin B2 (riboflavin), mg	3.8 (270)	4.7 (335)	3.3 (235)	1.4	
Niacin (B3), mg	35.0 (194)	36.8 (204)	18.8 (104)	18	35
Vitamin B6, mg	4.0 (210)	5.9 (198)	4.0 (210)	1.9	100
Vitamin B12, µg	5.5 (262)	7.3 (253)	4.7 (181)	2.6	
Folic acid, µg	574 (143)	659 (165)	659 (163)	400	1000
Vitamin C, mg	170 (200)	281 (331)	211 (249)	85	2000
Vitamin D, µg	30 (200)	31 (206)	25 (169)	15	100
Vitamin E, mg	39 (261)	30 (197)	20 (130)	15	1000
Vitamin K, µg	192 (213)	71 (78)	71 (78)	90	
Iodine, µg	300 (136)	244 (170)	94 (43)	220	1100
Copper, mg	2.4 (240)	2 (200)	0 (0)	1.0	10.0
Iron, mg	45 (170)	45 (181)	79 (292)	27	45
Zinc, mg	24.6 (223)	26.8 (243)	11.8 (107)	11	40
Magnesium, mg	327 (93)	400 (114)	400 (114)	350	350
Calcium, mg	1830 (183)	851 (85)	851 (85)	1000	2500
Selenium, µg	123 (205)	65 (108)	0 (0)	60	400

Abbreviations: RUSF, Ready-to-use supplemental food; CSB+, fortified corn soy blend; IFA, iron and folic acid (standard of care); RDA, recommended dietary allowance; UL, tolerable upper limit

[1] Assumes a daily portion of 175 g RUSF

[2] Assumes daily portion of 235 g CSB+/day with UNIMMAP.

[3] Assumes a daily portion of 235 g CSB+/day plus iron (60 mg) and folic acid (400 mcg).