Effects of Traditional Cereal Processing Methods on Complementary Meal Ingredients: Potential Risk Factors of Malnutrition amongst Children in Northern Ghana

Dissertation Submitted in Fulfilment of the Requirements for the Degree of Doctor of Philosophy (Public Health) to the School of Public Health, Bielefeld University, Bielefeld, Germany

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Bielefeld, January 2021

DECLARATION

School of Public Health

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Doctor of Philosophy (PhD), in the Discipline of Public Health

I, the undersigned, hereby declare that this dissertation is the result of my independent and original investigation in accordance with the rules of good academic practice, and that it has not been submitted in substance for any other degree, nor is it concurrently being submitted in candidature or achievement of any other degree at any other University.

A journal article (doi: 10.3390/nu12092565) based on the study objectives one and two of this dissertation has been published in the journal *Nutrients* (MDPI, Basel in Switzerland).

References to, quotations from, and discussions of the works of all other authors have been appropriately acknowledged and cited within the dissertation. I fully take responsibility for all errors and omissions identified in this dissertation.

Stephen Kofi Anin

Bielefeld, January 31, 2021.

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DEDICATION

To the glory of God, I gladly dedicate this dissertation to the memory and honour of the lives of my late parents, Mr. Peter Kwabena Twumasi Mensah (October 1949-December 2017) and Mrs. Faustina Adwoa Kyeremaa Mansa Mensah (July 1952-July 2019), who were both alive and well at the onset of the pursuit of this doctoral study but have all departed to eternity. For giving me the best of all they had and withholding nothing good from me, their legacies remain etched in my heart forever.

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LIST OF ABBREVIATIONS AND ACRONYMS

24HD/FR	Twenty-Four Hour Dietary/Food Recall
AAs	Amino Acids
ACF	Appropriate/Acceptable Complementary Feeding
ANFs	Anti-nutritional Factors
ASP	Animal Source Proteins
BCCE	Behaviour Change Communication and Education
BCEAAs	Branched-Chain Essential Amino Acids
BMI	Body Mass Index
CBF@1	Continuous Breastfeeding at Year One
CCFI	Composite Child Feeding Index
CEAAs	Conditionally Essential Amino Acids
CICs	Commercial Infant Cereals
CLBBs	Cereal-Legume-Based Blends
CLBs	Cereal-Legume Blends
CMIs	Complementary Meal Ingredients
COBI	Cereal-Only Based Ingredient
DCs	Developing Countries
DDS	Dietary Diversity Score
DIAAS	Digestible Indispensable Amino Acid Score
DQI	Dietary Quality Index
DRI	Dietary Reference Intake
EAAs	Essential Amino Acids
EBF	Exclusive Breastfeeding
EIBF	Early Initiation of Breastfeeding
FAO	Food and Agriculture Organization
FFQ	Food Frequency Questionnaire
GC-MS	Gas Chromatography-Mass Spectrometry
GDHS	Ghana Demographic and Health Survey
GHS	Ghana Health Service
GMD	Golm Metabolome Database
GSS	Ghana Statistical Service
HDDS	Household Dietary Diversity Score
HFI	Household Food Insecurity
HFRUPs	Habitual Food Resource Utilization Practices
HH	Hidden Hunger
HPLC	High Performance Liquid Chromatography
ICMJE	International Committee of Medical Journal Editors
IDDS	Individual Dietary Diversity Score
IMRAD	Introduction Methods Results and Discussion
IYCF	Infant and Young Child Feeding
L/HAZ	Length/Height-for-Age Z-Score
LC-MS/MS	Liquid Chromatography tandem Mass Spectrometry
LEAAs	Limiting Essential Amino Acids
LMICs	Low-and-Middle Income Countries
LPA	Linear Programming Analyses

MAD	Minimum Acceptable Diet
MDD	Minimum Dietary Diversity
MDGs	Millennium Development Goals
MDM	Micronutrient Deficiency Malnutrition
MICS	Multi Indicator Cluster Survey
MMF	Minimum Meal Frequency
MRF	Micronutrient Rich Foods
NCDs	Non-Communicable Diseases
NER	Nutritional Epidemiological Research
NIST	National Institute of Standards and Technology
PCBBs	Processed Cereal-Based Blends
PDCAAS	Protein Digestibility-Corrected Amino Acid Score
PEM	Protein Energy Malnutrition
PFAS	Per- and Polyflouroalkyl Substances
PHN	Public Health Nutrition
PPH	Precision Public Health
PSP	Plant Source Proteins
RCT	Randomized Controlled Trial
RDA	Recommended Daily Amount/Recommended Dietary Allowance
RDI/RNI	Recommended Dietary Intake/Recommended Nutrient Intake
SCEAAs	Sulphur-Containing Essential Amino Acids
SDGs	Sustainable Development Goals
SEA	South East Asia
SOFI	State of Food Insecurity in the World
SSA	Sub-saharan Africa
STROBE-Nut Epidemiology	Strengthening the Reporting of Observational Studies in Epidemiology- Nutritional
SUN	Scaling Up Nutrition
TCPMs	Traditional Cereal Processing Methods
TIBF	Timely Initiation of Breastfeeding
TICF	Timely Introduction to Complementary Feeding
UHP/UP-LC	Ultra High Performance/Ultra Perfomance-Liquid Chromatography
UNICEF	United Nations Children’s Fund
UNIGME	United Nations Inter-agency Group for Child Mortality Estimation
WASH	Water, Sanitation and Hygiene
WAZ	Weight-for-Age Z-Score
WFI	Weaning Food Ingredient
WHO	World Health Organization
WHZ	Weight-for-Height Z-Score

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STRUCTURE OF THE DISSERTATION

Table 1.1 Structure of the Dissertation

Section Name	Section	Contents
Front Matter		Cover Page, Title Page, Declaration, Dedication, Table of Contents, List of Tables, Figures, Abbreviations & Acronyms, Acknowledgement, Dissertation Structure and Abstract.
Introduction	1	Background to the Study and Purpose of Study.
Theoretical Background	2	Theoretical Framework (Concepts, Models, Methodological Approaches to Undernutrition Studies and Research Paradigms of Nutritional Epidemiology); Public Health Relevance of Undernutrition in Northern Ghana; State-of-the-Art (Empirical Application of Food Metabolomics to the Study of Undernutrition/Child Nutritional Health); Statement of the Research Problem (Justification of the Study).
Materials and Methods	3	Research Questions, Objectives, Hypotheses, Assumptions, Conceptual Framework, Research Paradigm, Research Phases & Components, Description of Definitive Analytical Cross-sectional Survey and Cereal Laboratory Analyses, Statistical Analyses, Ethical Clearance and Community Entry Protocols of the Study.
Results	4	**Objective I**: Prevalence of IYCF, HFRUP, TCPM indicators and nutritional status indicators (stunting, wasting and underweight) of children (6-23 months) in the Northern Region of Ghana.
	4	**Objective II:** Association between child food intake (WHO/UNICEF IYCF Indicators) and nutritional status (stunting and wasting) of children (6-23 months) in northern Ghana.
	4	**Objective III**: Association between HFRUP indicators and nutritional status (stunting and wasting) of children (6-23 months) in the Northern Region of Ghana.
	4	**Objective IV:** Effects of TCPMs on the nutritive and non-nutritive (antinutritional) constituents of cereal ingredients.
	4	**Objective V:** Association between the usage of TCPMs that effected nutritionally significant changes in the cereal ingredients (CMIs) and nutritional status (stunting, wasting and underweight) of children (6-23 months) in the Northern Region of Ghana.
Discussion	5	Discussion of inferences from study results in line with objectives, relevant studies, existing knowledge gap, strengths & limitations.
Conclusions and Recommendations	6	Conclusions, summary of key findings and recommendations for public health nutrition interventions, methodological approaches to undernutrition studies in DCs and further research required in the future.
Back Matter		References of cited works, supplementary tables and figures, instrument for data collection, study information brief, study consent form, ethical clearance for study protocol, phytosanitary certificates and research work plan.

ABSTRACT

Background of the Study: Food utilization, as one of the classical dimensions of household food insecurity (HFI) besides food availability, access, and stability, remains under-researched as potential determinants of undernutrition (stunting, wasting, and underweight status) amongst young children in developing countries (DCs). The usage indicators (preference, duration, type, or frequency) of traditional cereal processing methods (TCPMs) such as soaking, germination, dry milling, wet milling, and fermentation, in addition to habitual food resource utilization practices (HFRUPs) are two of the conceivable domains of the food utilization dimension of HFI. These indicators were hypothesized to be potentially significant contributors to the high prevalence of child undernutrition in northern Ghana. The premise was that, besides infant and young child feeding (IYCF) indicators as putative determinants of undernutrition, TCPMs could potentially cause nutritionally debilitative effects on the nutritional quality of complementary meal ingredients (CMIs) such as flour or dough, thus possibly contributing to child undernutrition in northern Ghana.

Objectives of the Study: The descriptive objective of the study was to find out the prevalence of IYCF practice indicators, TCPM usage indicators, and HFRUP indicators in addition to the nutritional status indicators of children (6-23 months) in the Northern Region of Ghana. The first analytical objective of the study was to examine the associations between the individual IYCF indicators and child nutritional status, accounting for potential confounders. The associations between some contextual HFRUP indicators and child nutritional status, as potential determinants of undernutrition were also examined, adjusting for putative confounders. The third inferential objective was to qualitatively evaluate the quantitative effects (relative and absolute concentrations) of some selected TCPMs (soaking, germination, dry milling, wet milling, and spontaneous fermentation) on the nutritive and non-nutritive (antinutritional) constituents of CMIs. The concluding analytical objective of the study was to examine the nutritional epidemiological significance of the usage of TCPMs, that effected nutritionally significant changes (net increases or decreases) in the nutritional quality of the CMIs (made traditionally from maize, sorghum, and millet), as potential determinants of stunting, wasting, and underweight status of young children.

Materials and Methods: Using a modified version of the UNICEF three-step hierarchical conceptual framework for the determinants of undernutrition in DCs, measures of IYCF, HFRUP, and TCPM usage indicators were operationalized as the explanatory variables of interest (Figure 3.1). Using a cross-sectional study design, an interviewer-administered survey of 581 mother-child pairs in the Northern Region of Ghana was conducted (24HFR) with a two-stage cluster sampling technique in June 2018, to obtain data on TCPM, HFRUP, and IYCF indicators. Stunting, wasting, and underweight status were measured as the outcome variables of interest as Z-scores of Length-to-Age, Weight-to-Length, and Weight-to-Age anthropometric growth indicators of the children. Using an experimental study design, lyophilized samples of TCPM-treated CMIs (soaked grains, germinated grains, flour, fresh dough, and fermented dough) were analyzed in technical triplicates using optimized high-throughput foodomics (food metabolomics) techniques. Premised on gas chromatography tandem mass spectrometry (GC-MS) and ultra high-performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS), the optimized analytical protocols were utilized for the compositional and nutritional analyses. The foodomics analytical results provided an operationally objective basis for the qualitative determination of the nutritional significance of TCPM treatments, guided by predefined criteria. The nutritional status (Z-scores) of the children were regressed on the usage indicators of the TCPMs obtained from the cross-sectional survey, to determine the nutritional epidemiological significance of the TCPMs.

Results: The prevalence of stunting, wasting, and underweight status of children (6-23 months) in the Northern Region was 33.2%, 14.1% and 27% respectively. The prevalence of the complementary feeding (CF)-related IYCF indicators (TICF, 66.4%; MMF, 69.4%; MAD, 38.9%; Vit A-rich food intake, 58% and Iron-rich food intake, 63.2%) had generally improved but did not correspondingly translate into improved child nutritional status. There was no significant association ($p < 0.05$) between the individual CF-related IYCF indicators and nutritional status except between the intake of iron-rich foods and stunting after adjusting for potential confounders. Child age and maternal height were associated with stunting status. Child age and gender were associated with wasting status. Of the mothers surveyed, 67.6% habitually always or very often used homemade dough for complementary meal preparation. Using a hierarchical multivariable binary logistic regression model, the HFRUP indicator found to be associated with stunting status ($p < 0.05$) was the type of container used for storing dough meant for complementary meal preparation. The HFRUP indicator found to be associated with wasting status was the duration of dough storage ($p < 0.05$) most preferably used habitually to prepare complementary meals for young children. Applying a 10% threshold of variability for determining nutritional significance, all the TCPMs examined were found to have effected both debilitative and facilitative nutritionally significant changes in relevant nutritive metabolites in the CMIs, especially the contents of essential amino acids (EAAs) such as lysine, isoleucine, valine, and histidine in maize, and methionine, threonine, phenylalanine, and tyrosine in millet, which are critical for infant and young child linear and ponderal growth and development. ANOVA and Dunnett's Posthoc tests on the absolute concentrations (nmol/mL) of the total contents of lysine (limiting EAAs in cereals) in the maize samples showed that the net losses due to the TCPM treatments were significant, F (5, 18) = 273,401, $p < 0.001$. Dry milling was a statistically significant predictor of stunting and underweight status ($p < 0.05$). Dry milling contributed an additional 1% each to the variance in stunting and underweight status over and above the variance accounted for by the proximal putative determinants of child nutritional status, with small effect sizes ($R^2 = 0.007$ and 0.008) respectively.

Conclusions: TCPMs have nutritionally significant effects on the nutritive contents of CMIs such as flour and dough, especially on the contents of essential amino acids. However, the overall nutritional epidemiological significance of the usage of TCPMs on the nutritional status of children was observed only between stunting regressed on dry milling usage indicators and underweight status regressed on dry milling usage indicators. The relationships between the individual CF-related IYCF indicators and child nutritional status are context-specific rather than generic across DCs. The container type habitually used for dough storage and the duration of dough storage for the preparation of complementary meals, were significantly associated with child nutritional status. Child undernutrition is still seriously prevalent in the Northern Region of Ghana.

Recommendations: Being a novel construct (TCPMs) under investigation, there is the need for further research to replicate and externally validate the preliminary hypothesis generated from this study. The nutritionally debilitative effects of dry milling could be mitigated through fortification of flour with lysine and other essential nutrients. Linear programming analyses (LPA) could be used to optimize the development of homemade CMIs from indigenous food resources such as staple cereal-legume blends, for nursing mothers' adoption and use for age-appropriate complementary feeding in northern Ghana. HFRUPs that are nutritionally debilitative to child nutritional status should be discouraged and reversed through behaviour change communication and education (BCCE). The conceptualization, operationalization, and validation of a multidimensional form (multi-item scale) of the main construct examined in this study (TCPMs), as a conceivable domain of household food utilization, should be undertaken (develop, validate, and standardize) for future use in nutritional epidemiological research (NER) studies. The development, validation, and standardization of a composite child feeding index (CCFI) from the individual IYCF indicators, would be useful to address more plausibly, inconsistencies in the predictive utility of the individual IYCF indicators for child nutritional status in DCs.

1 INTRODUCTION

1.1 Section Overview

This first section presents a synopsis of the dissertation format, background to the study, and the main purpose of the study. The dissertation is presented in eight parts with six main sections. These six main sections are introduction, theoretical background, materials and methods, results, discussion, and conclusions with some recommendations made from the study. As a guide on the scope of the dissertation, Table 1.1 provides a summary of the contents of the eight parts making up the front matter, the six main sections, and the back matter. The six main sections were guided and framed after an expanded format of IMRAD (Introduction, Methods, Results, and Discussion) used in most medical, public health, and life science publications as generally recommended by the International Committee of Medical Journal Editors (ICMJE), Strengthening the Reporting of Observational Studies in Epidemiology-nutritional epidemiology (STROBE-nut) statement, and other globally recognized stakeholders and advocates of good scientific communication in public health (Araújo, 2014; Barron, 2006; Belcher, 2016; Cuschieri, 2019; Elm et al., 2014; Lachat et al., 2016; Liumbruno, Velati, Pasqualetti, & Franchini, 2013; Oriokot, Buwembo, Munabi, & Kijjambu, 2011; Sollaci & Pereira, 2004).

The background to the study sub-section is a synthesis of the public health problem of undernutrition, particularly protein energy malnutrition (PEM) (hereafter measured as stunting, wasting, and underweight status) within the scope of this study in the Northern Region of Ghana and how foodomics (food metabolomics) could be applied conceptually and empirically to address the malady of malnutrition (undernutrition). The main aim of the study highlights the rationale for applying a multi-quantitative methodological approach, adopted in the definitive phase of the study to investigate the effects of traditional cereal processing methods (TCPMs) on the nutritional quality (particularly protein contents) of complementary meal ingredients (CMIs) also known as weaning food ingredients (WFIs), as potential determinants of undernutrition (nutritional status) amongst young children (6-23 months) in the Northern Region of Ghana.

The second major section of the dissertation namely theoretical background has four main sub-sections and presents a detailed review and synthesis of current literature relevant to this nutritional epidemiological research (NER) study. The third major section of the dissertation (materials and methods) provides an outline of the specific research questions, study objectives, hypotheses of the study, assumptions of the study, conceptual framework of the study, paradigms of the research methodology, phases of the study, study designs, operational definitions of the exposure (or explanatory) variables, potential and putative confounders (factors/covariates), and the outcome (or dependent) variables, a detailed description of the conduct of the definitive cross-sectional survey component and foodomics laboratory analyses component of the study, including the descriptive and inferential statistical analyses of the quantitative data sets obtained. The materials and methods section ends with a description of the study compliance with the required ethical clearance and community entry permit protocols, as recommended for good scientific conduct. The fourth, fifth, and sixth sections of the dissertation are made up of the results, discussions, and conclusions together with recommendations made from the study in line with the study objectives. The descriptive and analytical results are presented in an orderly textual narrative of the findings of the study, together with illustrative tables and charts. The results were soundly discussed in detail with relevant and comparable NER literature, logically plausible inferences, arguments, and interpretations of the study findings. Some unique strengths and limitations of the study, and challenges faced during the conduct of the entire study are also outlined. The conclusions drawn from the study are finally presented with some recommendations made for further research, methodological approaches to undernutrition research, and the development of interventions by relevant stakeholders of public health nutrition in Ghana and other similar resource-limited settings in DCs and/or LMICs.

1.2 Background to the Study

The global burden of malnutrition remains unacceptably high with about 150.8 million, 50.5 million and 38.3 million children under five years being stunted (too short for their ages: height for age Z-score (HAZ)/length for age Z-score (LAZ)), wasted (too thin for their weights: weight for height/length Z-score (WHZ/WLZ)) or overweight (too heavy for their heights/lengths: (WHZ/WLZ)) respectively (Development Initiatives, 2018; United Nations Children's Fund (UNICEF), World Health Organization, International Bank for Reconstruction and Development/The World Bank, 2019). There was generally a slowly progressive decline in stunting (chronic malnutrition) globally from 32.6% to about 22.2% over the Millennium Development Goals (MDG) era (2000-2015) up to 2017 (Development Initiatives, 2018). The current situation of malnutrition for the Sustainable Development Goals (SDG) period (2016-2025) especially in Sub-Saharan Africa (SSA) and South East Asia (SEA), shows the emergence of a double or multiple burden of the various forms of malnutrition (undernutrition and over-nutrition) in thirty-four (34) developing countries (Peng & Berry, 2018; United Nations Children's Fund (UNICEF), World Health Organization, International Bank for Reconstruction and Development/The World Bank, 2019). Despite general declines in undernutrition globally, several low-and-middle income countries (LMICs) or developing countries (DCs) without substantial improvements in context-specific interventions at the continental, regional, national, community and household levels, are likely to miss the 40% reduction in stunting targeted by WHO by 2025 (Kinyoki, Osgood-Zimmerman & Pickering et al., 2020; United Nations, 2020).

The consequences of undernutrition, in the form of Protein Energy Malnutrition (PEM) and Micronutrient Deficiency Malnutrition (MDM) among children in the first 1,000-day period (from pregnancy through to the 24th month of childhood) include high levels of child mortality, morbidity and impaired physical, cognitive, psychological, and potential socio-economic development within developing and emerging countries (Black et al., 2013; Fanzo, 2012)**.** PEM could manifest as stunting (chronic energy deficiency), wasting (acute energy deficiency) or underweight status (overall nutritional status due to chronic only, acute only or both types of energy deficiencies). MDM, also known as hidden hunger (HH) or micronutrient deficiency diseases or disorders (MDD) could manifest with specific clinical symptoms and adverse health outcomes depending on the deficient vitamin or mineral in question such as Vitamin A, Vitamin B12, Vitamin B3, Iron, Zinc, Folic acid, or Iodine. The term malnutrition is often interchangeably used with undernutrition in most NER literature within the context of LMICs to be erroneously synonymous, but malnutrition encompasses both undernutrition and overnutrition (Maleta, 2006; Shetty, 2003). Malnutrition, specifically undernutrition has been described as the underlying cause of over 45% of death globally amongst children under 5 years in LMICs (Black et al., 2013). Given the far-reaching and debilitating consequences of malnutrition, particularly undernutrition in DCs, the United Nations demonstrated its commitment to prioritizing efforts at addressing this public health menace, by declaring 2016 to 2025 as a Decade of Action on Nutrition (Peng & Berry, 2018; United Nations, 2020). The Lancet put nutrition and food-related health issues on the spotlight for all of its family of journals for the year 2019 in acknowledgement of the urgency and need to close the huge lacuna in our quest for new knowledge to address nutritional health issues globally (Lancet, 2019).

Although Ghana is described as a mature and stable democracy, classified as a lower-middle income country (LMIC), it remains one of the 34 high-burden countries (mostly from SSA and SEA) that contributes to 90% of global stunting among children under five years (Bhutta et al., 2013; USAID, 2020). In the Northern Region of Ghana, the estimated prevalence of stunting (chronic malnutrition) is 33.1% compared to a national average of 19% (Ghana Statistical Service

(GSS), Ghana Health Service (GHS), and ICF International, 2015). A stunting prevalence of 30% or above is considered serious, and thus suffices to be given premium attention as a public health concern (Onis et al., 2019; United Nations Children's Fund (UNICEF), World Health Organization, International Bank for Reconstruction and Development/The World Bank, 2019)**.**

Poor nutritional health status or undernutrition (stunting, wasting and underweight status) amongst children in DCs arising from inadequate intake of balanced, nutrient-rich, and diverse foods coupled with the high burden of infectious diseases (frequent and/or severe child morbidity), have been widely ascribed as the proximal determinants of undernutrition in developing and emerging countries in the last couple of decades (Arthur et al., 2015; Bhutta et al., 2013; Krämer, Kretzschmar, & Krickeberg, 2010; Müller & Krawinkel, 2005; White, Bégin, Kumapley, Murray, & Krasevec, 2017). Some underlying risk factors known to contribute to inadequate quantity and/or poor-quality food intake include household food insecurity (HFI), inadequate maternal childcare, poor parental status factors, inadequate medical healthcare services, and poor water, sanitation, hygiene (WASH) factors in LMICs (Bhutta et al., 2013; Boah, Azupogo, Amporfro, & Abada, 2019; Fanzo, 2012; Müller & Krawinkel, 2005). The optimal growth and development of infants and young children under five years is severely impaired when breastfeeding and complementary feeding are compromised, in synergy with or without other risk factors especially child morbidity (Bhutta et al., 2013; Shrimpton et al., 2001; Victora, Onis, Hallal, Blössner, & Shrimpton, 2010).

1.2.1 Food Insecurity, Food Utilization Domains, and Child Nutritional Status

Addressing the classical dimensions of food insecurity comprehensibly is considered one of the most viable and sustainable food-based approaches to tackling poor food and/or nutrient intake by children in order to address undernutrition (Barrett, 2010; Brian and Amoroso, 2014; Coates, 2013; Ham, 2020). The World Food Summit (WFS) defined food security as 'existing when all people, at all times, have physical, social, and economic access to sufficient, safe and nutritious food that meets their dietary needs and food preferences for an active and healthy life' (Food and Agriculture Organization, 2009; Peng & Berry, 2019). Over the MDG era (2000-2015), improvements in the four classical dimensions of food security (food availability, food access, food utilization and food stability) in developing countries (DCs) through various interventions, have contributed immensely to reducing undernutrition globally. Various studies that analyzed the relationship between food insecurity and child nutritional status at the household (meso) and individual (micro) levels from various representative countries across all regions of the world showed that food insecurity is a significant determinant of the different forms of malnutrition in all the countries studied (FAO, IFAD, UNICEF, WFP and WHO, 2019). Nonetheless, the food utilization dimension of household food insecurity (HFI) leaves a lot more to be desired in terms of its conceptualization, operationalization, and measurement.

Conceivable food utilization issues or domains related to child food intake (CFI) include traditional cereal processing methods (TCPMs), other indigenous or traditional food processing methods (gastronomy), indigenous food preferences, post-harvest food handling techniques, food stuff and meal storage techniques, food preservation practices, knowledge of child nutritional needs, portion allocation of meals to household members, knowledge of the nutritional values of indigenous plant and animal food resources, cultivation and usage of diverse nutrient-rich crops, knowledge of food quality, knowledge of food safety, food beliefs, cultural and customary practices, knowledge of appropriate child food preparation methods, knowledge of appropriate child feeding practices (IYCF), and other habitual food resource utilization practices (HFRUPs) (**Figure 1.1**). Some of these domains seem overlooked, unexplored, and underestimated in the fight against undernutrition in DCs. This is evidenced in the dearth of literature on this dimension of household food insecurity (Coates, 2013; Ham, 2020; Hwalla, El Labban, & Bahn, 2016; Mitchodigni et al., 2018).

TCPMs are simple, household-level, micro-level food processing technologies (or unit operations) such as sun drying, soaking, germination, roasting, dry milling, sieving, winnowing, wet milling, kneading, natural or spontaneous fermentation, and nixtamalization, among others. They are used to produce homemade complementary meal ingredients (CMIs) either as cereal-only-based ingredients (COBIs) or cereal-legume-based blends (CLBBs) contrary to the industrially made commercial infant cereals (CICs), which are formulated and produced in the form of flour, dough, grits, flakes, or groats. The nutritional quality and safety of the highly recommended and patronized CMIs (COBIs, CLBBs or CICs) have been a matter of concern and research due to either the ingredients used, processing technologies, safety certification regime, or inappropriate utilization by mothers in DCs for complementary feeding (Abeshu, Lelisa, & Geleta, 2016; Abizari, Ali, Essah, Agyeiwaa, & Amaniampong, 2017; Dimaria et al., 2018; Kwofie, Andrews, & Mensah, 2011; Masters, Nene, & Bell, 2017; Pee & Bloem, 2009; Saleh, Wang, Wang, Yang, & Xiao, 2019). CMIs have thus been implicated in the nutritional health outcomes of infants and young children even though there is no finality on these enquiries (Akinsola, Onabanjo, Idowu, & Ade-Omowaye, 2017; Masters et al., 2017; Mitchodigni et al., 2018).

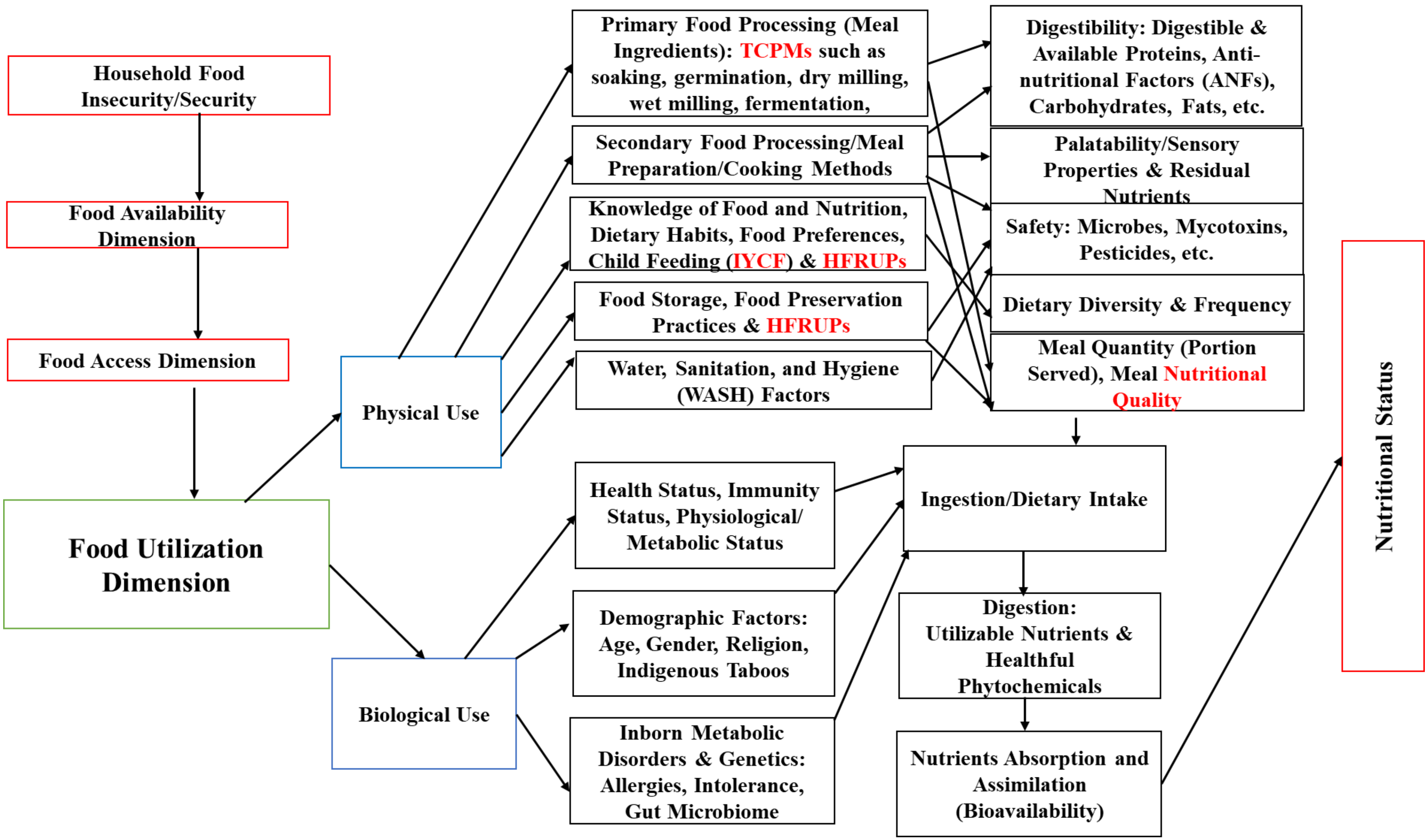

Figure 1.1: Conceptual Framework of the Conceivable Domains of Household and Individual Food Utilization

1.2.2 Evidence-Based Public Health Nutrition Interventions against Undernutrition in DCs

Evidence-based interventions developed by public health nutritionists out of the recommendations of several years of research by nutritional epidemiologists and nutritional scientists in partnership with international, regional, national, and local governmental institutions, non-governmental organizations (NGOs) and civil society organizations (CSOs), have contributed immensely to the progress made so far in the fight against malnutrition in DCs (Buttriss, Welch, Kearney, & Lanham-New, 2017). In the last half century, most if not all nutritional interventions were formulated from evidence garnered from various research activities of nutritional epidemiologists globally (FAO, 2013; FAO and WHO; FAO, IFAD, UNICEF, WFP and WHO, 2017). The recommendations from valid and reliable nutritional epidemiological research (NER) studies are often fed into the public health nutrition action cycle (assessment, policy formulation, implementation, and evaluation) to inform the development of various evidence-based food and nutrition interventions (Brownson, Fielding, & Green, 2018; Brownson, Fielding, & Maylahn, 2009). The food-based interventions against undernutrition in DCs currently in use widely include promotion of optimum breastfeeding (BF), promotion of appropriate or adequate complementary feeding (ACF), nutrition education (NE), dietary diversification (DD), food supplementation, food donations, micronutrient supplementation, food fortification, increased food and agricultural production and improved food distribution systems among others (Bhutta et al., 2013; Black et al., 2013). The huge lacuna that still exists despite the various public health nutrition interventions against undernutrition amongst children in DCs during the MDG era (2000-2015) and now the SDG era (2016-2030) requires more research, innovative solutions, and context-specific interventions.

The nutrition interventions developed in the last decade or more have been premised predominantly on the proximal putative determinants of undernutrition described as nutrition-specific risk factors by UNICEF and WHO. As a result, often, the focus of public health nutrition intervention development has been based on improving quality dietary intake, adequate nutrient intake, and reducing morbidity risk factors amongst children individually. Nutrition-sensitive interventions targeted at the underlying putative determinants of undernutrition particularly against household food insecurity (HFI) have also been overwhelmingly biased towards improving mostly the food availability, access, and stability dimensions of household food insecurity (HFI) and yet the efforts have only made modest contributions to the fight against undernutrition (Coates, 2013; Perez-Escamilla et al., 2018). The search therefore continues for more evidence-based recommendations from reliable and validated research findings, to inform the development of novel, context-relevant, pragmatic, and more cost-effective public health nutrition interventions against the seemingly intractable menace of undernutrition especially in DCs.

The WHO, UNICEF, and many experts in maternal and child nutritional health, have recommended the suitability of infant and young child feeding (IYCF) indicators as simple, highly cost-effective, and pragmatic nutrition-specific parameters (individual food utilization measures) for identifying populations at risk of malnutrition, monitoring the progress of child food intake (CFI), and guiding the development of appropriate interventions against child malnutrition in developing countries (Bhutta et al., 2013; White et al., 2017; WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2008). The core IYCF indicators include timely introduction to complementary feeding (TICF), minimum meal frequency (MMF) for specific child age groups, minimum dietary diversity (MDD), minimum acceptable diet (MAD), exclusive breastfeeding (EBF), early initiation of breastfeeding (EIBF), continued breastfeeding at one year (CBF@1), and adequate intake of micronutrient-rich foods (MRF), including Iron (Fe), Vitamin A, Zinc (Zn), and Iodine (I) (Bhutta et al., 2013; White et al., 2017; WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2010).

1.2.3 Methodological Deficits and Knowledge Gap: Determinants of Undernutrition

Self-reported child food intake (CFI) data collected over a defined period, such as 24-hour food recall (24HFR), remain widely used in observational studies (analytical cross-sectional surveys, case-control studies, and cohort studies) and intervention studies (randomized control trials) of malnutrition (under- and overnutrition), to measure infant and young child feeding (IYCF) indicators (Brouwer-Brolsma et al., 2017; FAO, 2018; Ghosh et al., 2019; Shim, Oh, & Kim, 2014; WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2010). The validity and reliability of these IYCF indicators and other such self-reported dietary intake metrics or indices for food intake quality, quantity, nutrient adequacy, and/or dietary diversity, however, still remain inconclusive among nutritional epidemiologists for studies across similar settings in DCs or LMICs (Archer, Lavie, & Hill, 2018; Habte & Krawinkel, 2016; Marshall, Burrows, & Collins, 2014; Miller, Webb, Micha, & Mozaffarian, 2020). Therefore, the question arises as to whether the IYCF indicators (breastfeeding and complementary feeding), which are postulated to be associated with chronic malnutrition (stunting) and acute malnutrition (wasting) as measures of impaired child anthropometric growth in low-and-middle income countries (LMICs), are viable monitoring and evaluation parameters to identify populations at risk of undernutrition. Besides, could there be other under-researched and potentially unexplored context-specific risk factors of undernutrition that require inquiry, given the relatively marginal improvements in child nutritional status in SSA and

SEA after so many decades and so many public health nutrition interventions locally and globally? White *et al* (2017) indicated that during the WHO-led development of the IYCF indicators, some food intake metrics adaptable to population-level assessment of other important domains of food utilization particularly complementary feeding (CF) were overlooked because they were deemed to be too complex to assess. As such, this gap in the child food intake (CFI) metrics also remain a challenge (Miller et al., 2020). Jones *et al* (2014) evinced the need for additional metrics of dietary quality and quantity, as a possible panacea to the limited specificity and sensitivity of some of the IYCF indicators (individual food utilization).

The seminal works of the Lancet Maternal and Child Nutrition Series estimated that, the top ten nutrition-specific evidence-based interventions (EBIs) together, if scaled up to 90% coverage (estimated to cost about 9.6 billion US Dollars), could significantly reduce the prevalence of child mortality, stunting and wasting in the 34 high-burden countries (where 90% of the world's malnourished children live) by about 15%, 20% and 60% respectively (Bhutta et al., 2013). Thus, these top ten EBIs that seek to address the proximal determinants of chronic malnutrition (stunting), acute undernutrition (wasting), and micronutrient deficiency malnutrition (hidden hunger) when prioritized and scaled up, have a significant chance of stemming the tide but not necessarily eliminating undernutrition or child anthropometric growth impairments between 2010 and 2025. This observation illustrates the large knowledge gap that still exists about the other possible risk factors of undernutrition and the related child growth impairments in DCs (Bhutta et al., 2013).

The plethora of research perspectives and methodological approaches towards unravelling the generic and context-specific determinants of child undernutrition in developing countries (DCs) and LMICs, continue to increase with just about five years or a decade left towards the World Health Organization/World Health Assembly (WHO/WHA) targets (2025) or SDG deadlines (2030) respectively (Boeing, 2013). For instance, the WHO Working Group of the International Agency for Research on Cancer (IARC) reported that evidence gleaned from epidemiological studies concerning the effects of mycotoxin exposure on child growth impairment, independent of, and together with, other risk factors suggest an association between mycotoxin exposure and stunting in children (Lombard, 2014; Wild & Gong, 2010). Other researchers similarly have found significant associations between mycotoxin exposure and stunting (Chen, Riley, & Wu, 2018; Wu, Groopman, & Pestka, 2014; Xu, Gong, & Routledge, 2018). Semba *et al.* (2016), also posit that children faced with a high risk of stunting may be strongly due to inadequate intake of dietary essential amino acids (EAAs). These quantity and quality perspectives of protein intake have also ignited a new wave of research into the roles and underlying mechanisms of essential amino acids in early childhood growth impairment particularly stunting (Ghosh, Suri, & Uauy, 2012; Millward, 2017; Rutherfurd & Moughan, 2012; Suri, Marcus, Ghosh, Kurpad, & Rosenberg, 2013; Uauy, Suri, Ghosh, Kurpad, & Rosenberg, 2016). Several nutritional epidemiologists are also employing new approaches to possibly overcome the limitations posed by measurement errors inarguably attributed to the current conventional methods of food intake measurements (dietary exposure) through the application of advanced food metabolomics (foodomics) and nutrimetabolomics (Boeing, 2013; Brouwer-Brolsma et al., 2017; Guasch-Ferré, Bhupathiraju, & Hu, 2018; Kim, Kim, Yun, & Kim, 2016; Nalbantoglu, 2019; Ulaszewska et al., 2019).

1.2.4 Household Processing Methods: Potential Risk Factors of Child Undernutrition

The essence of processing food ingredients is to transform raw food materials to become culinarily useful ingredients for the preparation of organoleptically ingestible meals (intake or consumption), digestible (breakable), absorbable (gastrointestinal tract uptake), bioavailable (physiological utilization) and safe from contaminants such as pathogens and/or toxins (mycotoxins) (Joye, 2019; Knorr & Watzke, 2019; Shobana Devi R, 2016). Traditional cereal processing methods (TCPMs) such as sun drying, soaking, germination, nixtamalization, dehulling, winnowing, roasting, dry milling, sieving, wet milling, kneading and spontaneous fermentation with the intent of achieving some of these goals, in the preparation of cereal ingredients (dough and/or flour) used for complementary meal preparation (CMIs), may potentially effect significant changes (increases or losses) in essential nutritive and non-nutritive (antinutritional) bioactive constituents (Beleggia et al., 2011; Hotz & Gibson, 2007; Mensah & Tomkins, 2003). The cereal ingredients such as dough and/or flour (hereafter called CMIs) used for the preparation of complementary meals such as porridge and/or gruels made at home for children in northern Ghana, could become nutritionally deficient, thus potentially contributing significantly to undernutrition (PEM). The correlation between such undesirable food compositional changes due to TCPMs and child nutritional health outcomes could be significant, given that infants and young children are routinely fed with such potentially low-quality complementary meals. This possibly implicates TCPMs as potential risk factors of malnutrition, given that TCPMs are routinely used in the production of dough and flour (CMIs) meant for the preparation of complementary meals for children in northern Ghana.

The various risk factors or determinants of malnutrition (undernutrition) identified from nutritional epidemiological studies in developing countries (DCs) such as poor food intake (quality and quantity), high burden of infectious diseases (child morbidity), household food insecurity (HFI), poor water, hygiene and sanitation services (WASH factors) coupled with poor maternal childcare, poor parental factors, and inadequate child healthcare services among others are inarguably all related to ignorance and poverty (Müller & Krawinkel, 2005; Perez-Escamilla et al., 2018). However, the strength of associations between these widely researched risk factors and nutritional health outcomes amongst children in northern Ghana, usually vary depending on the social, educational, economic, cultural, and geographical conditions (Saaka, Larbi, Mutaru, & Hoeschle-Zeledon, 2016). The limited insight into the context-specific determinants of malnutrition in a highly pluralistic region such as northern Ghana, calls for the application of other modern and innovative nutritional epidemiologic approaches such as the use of food metabolomics (foodomics) to better understand the determinants of malnutrition and other under-researched or unexplored, potentially novel risk factors such as TCPMs. This could help develop customized interventions premised on the novel concept of precision public health (PPH) because of the unique socio-economic and demographic outlook of northern Ghana and other similar settings in DCs.

1.2.5 Application of Food Metabolomics in Modern Nutritional Epidemiologic Studies

Modern nutritional epidemiologic studies are now going further to adopt the application of high-throughput, advanced, state-of-the-art technologies such as foodomics (food metabolomics) to replace, complement and/or improve on the accuracy of food, nutrient or dietary intake measurements directly (analysis of blood, faeces, urine, breast milk, gut microbiome or microbiota and other human biosamples) or by proxy (analysis of food ingredients, food byproducts, ready-to-eat meals) (Adebo, Njobeh, Adebiyi, Gbashi, & Kayitesi, 2017; Beleggia et al., 2011; Beleggia et al., 2016; Brody, 2020; Guasch-Ferré et al., 2018; Kim et al., 2016; Naska, Lagiou, & Lagiou, 2017; Ulaszewska et al., 2019; Wishart, 2008). Foodomics and nutrimetabolomics are helping researchers to understand better, the molecular transformations and biomechanisms of nutrients in food from farm to fork, the metabolic pathways and biochemical mechanisms of changes in food constituents upon consumption, to unravel the underlying mechanisms of the pathogenesis of diet-health relationships through the exposure levels of foods, meals, dietary habits, food groups, nutrients, antinutrients, mycotoxins, carcinogens, and gut microbiome in diet-health relationship studies (**Figure 1.2**) (Brennan, 2013; Cornelis & Hu, 2013; Kim et al., 2016; Ulaszewska et al., 2019). Thus, the combination of inferences drawn from foodomics laboratory data on the changes in constituent food metabolites (nutritive and non-nutritive food metabolome), serving as proxy measures of the potential external dose of exposure or surrogate dietary intake indicators of children (due to TCPM effects), together with population survey data on nutritional status (undernutrition), is viewed as a worthwhile approach to complement, supplement or compensate for some of the limitations of self-reported food intake assessment methods alone (Brouwer-Brolsma et al., 2017; Naska et al., 2017; Rollo et al., 2016).

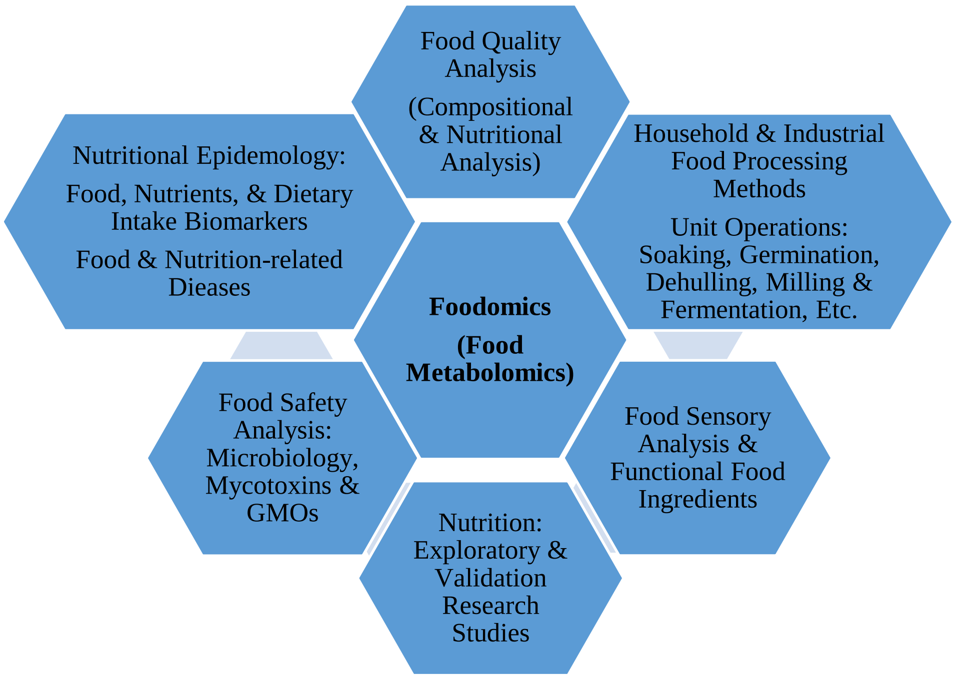

Figure 1.2: Scope of Applicability of Foodomics in Nutritional Epidemiology, Food Science, and Public Health Nutrition

Dietary quality indices (DQIs) have been developed based on qualitative and/or quantitative evaluations of nutrient adequacy, foods and/or food group serving adequacy, and a combination of other dietary quality factors, guided by recommended nutrient intake (RNI) references, food composition tables, recommended healthy diet guidelines, and recommended dietary lifestyles (Mediterranean and vegetarian diets) (Dalwood, Marshall, Burrows, McIntosh, & Collins, 2020; Gil, Martinez de Victoria, & Olza, 2015; Kourlaba & Panagiotakos, 2009; Marshall et al., 2014; Miller et al., 2020). These DQIs are used extensively in nutritional epidemiological studies as measures or indicators of the dietary exposure (explanatory) variables.

Foodomics (food metabolomics) has been defined as a discipline that studies the food and nutrition domains through the application and integration of advanced omics technologies and bioinformatics to improve consumer's well-being, health, and knowledge (Capozzi & Bordoni, 2013; Cifuentes, 2009; Herrero, Simó, García-Cañas, Ibáñez, & Cifuentes, 2012). Foodomics is a novel global discipline where advanced analytical laboratory techniques and bioinformatics are synergized to address research questions bothering on the relationships between diet or food intake as the exposure (explanatory) variable, and nutrition-related health outcomes such as stunting, wasting, obesity, cardiovascular diseases, some cancers, and diabetes (Brennan, 2013; Capozzi & Bordoni, 2013). Advanced analytical techniques and bioinformatics are applied in foodomics to characterize and/or quantify food components less than one kilo Dalton (1kDa) (Hu, 2011; Ibáñez, Simó, García-Cañas, Acunha, & Cifuentes, 2015). Food metabolites, be it exogenous or endogenous biomarkers of changes in food constituents and/or food intake, are intermediary downstream products of metabolism in biological systems. Food constituents such as sugars, sugar phosphates, sugar alcohols, organic acids, amines, amino acids, vitamins, minerals, peptides, nucleic acids, fatty acids, steroids, and antinutritional factors (ANFs) present in food materials are also metabolites that can be analyzed in nutrimetabolomics and/or foodomics studies. These serves as direct or otherwise, proxy (or surrogate) measures of dietary intake (potential external dose of exposure) respectively (Cornelis & Hu, 2013). Metabolomics uses complementary analytical methodologies such as Liquid Chromatography tandem Mass Spectrometry (LC-MS/MS), Gas Chromatography-Mass spectrometry (GC-MS) and/or Nuclear Magnetic Resonance (NMR), to separate, identify and quantify as many metabolites as possible in a biological sample, from a larger set of distinct compounds, both known and unknown (Castro-Puyana & Herrero, 2013; García-Cañas, Simó, Herrero, Ibáñez, & Cifuentes, 2012; Roessner & Bowne, 2009). A combination of foodomics laboratory data and population survey data with appropriate statistical computer modelling techniques represents the current approach to nutritional epidemiologic studies within the novel concept of precision public health (Boeing, 2013; Ibáñez et al., 2015). Notwithstanding its peculiar limitations, the advances in analytical laboratory technologies such as the use of GC-MS and LC-MS/MS to profile and/or target relevant food metabolites in bio-samples (food samples, blood samples, urine samples, etc.), present experimental nutritional epidemiologists more room for improvement in the multidisciplinary methodologies for nutritional epidemiological research (NER).

1.3 Purpose of the Study

The aim of this study was to unravel potential context-specific risk factors of child undernutrition at the household level of food utilization, which appears to have been overlooked or under-researched in the resource-limited settings of the Northern Region of Ghana. The general research question was that are the household unit operations of traditional cereal processing methods (dehulling, soaking, germination, dry milling, wet milling, and natural fermentation) used in the production of complementary meal ingredients (CMIs) such as dough and/or flour (used for complementary meal preparation), possibly complicit in the nutritional status of young children in northern Ghana? The main purpose of this epidemiological research was to determine the associations between the usage indicators (frequencies, preferences, or durations) of TCPMs such as dehulling, soaking, germination, dry milling, wet milling, and wet milling cum natural fermentation (exposure variables), and the nutritional status (outcome variables) of children (6-23 months) in the Northern Region of Ghana. The study sought to firstly find out the potential influence of TCPMs on the nutritional quality (nutritional and compositional metabolites) of the cereal ingredients (flour and/or dough) used for complementary meal preparation (mostly porridge or gruels), as potential determinants of undernutrition amongst children in northern Ghana. The high-throughput attributes, sensitivity, and specificity of food metabolomics techniques were harnessed to undertake the analyses of experimental cereal ingredient samples subjected to TCPMs.

The study was also aimed at unravelling the influence of some habitual food resource utilization practices (HFRUPs), as potential determinants of undernutrition in northern Ghana. These two unexplored domains (TCPMs and HFRUPs) of the food utilization dimension of household food insecurity (HFI) were examined as the exposure (explanatory) variables of interest in this NER. The study explored how analytical cross-sectional survey data could be synergized with foodomics laboratory data (GC-MS and UHPLC-MS/MS analyses) to ascertain the nutritional and epidemiological significance of TCPM usage, as potential risk factors of undernutrition (stunting, wasting and underweight) in northern Ghana using multivariable regression modelling (Boeing, 2013; Kaaks, 1997; Kimanya, Meulenaer, Roberfroid, Lachat, & Kolsteren, 2010; Krämer, Kupka, Subramanian, & Vollmer, 2016).

The WHO/UNICEF infant and young child feeding (IYCF) indicators are widely utilized as measures of the food utilization at the individual (proximal) level for epidemiological studies in paediatric populations. The conflicting findings or inconsistencies surrounding the putative utility of the widely recommended infant and young child feeding (IYCF) indicators developed by the WHO/UNICEF for the identification of populations at risk of malnutrition (undernutrition) and for monitoring child food intake (CFI) was also investigated within the context of the Northern Region of Ghana (Miller et al., 2020). This was aimed at validating or otherwise, the perceived generic applicability of these IYCF indicators across similar settings in LMICs or DCs irrespective of the plethora of inter-study variations reported in the NER literature.

2 THEORETICAL BACKGROUND

2.1 Section Overview

This second major section of the dissertation presents a comprehensive scope but compact narrative synthesis of relevant and thoroughly reviewed nutritional epidemiological research (NER) literature, covering four sub-sections. These sub-sections include the theoretical framework of the study (concepts, definitions, theories, models, methodological approaches to the study of child undernutrition, research paradigms and historical perspectives of nutritional epidemiology and public health nutrition impact), public health relevance of undernutrition and state-of-the-art (empirical application of foodomics techniques in NER studies). The fourth sub-section of the review concludes with the justification of the study by outlining the research problem under investigation. These literature syntheses are presented from broad perspectives and narrowed down to more specific and relevant sub-topics as applicable to the specific objectives and scope of the research (Grant & Booth, 2009).

The theoretical framework sub-section provides a descriptive and explanatory narrative of relevant theoretical concepts, models, constructs, definitions, terminologies, historical accounts, and philosophical underpinnings (research paradigms) applicable in discourses of studies in nutritional epidemiology and public health nutrition. A critical narrative literature review is also presented for the theoretical comprehension of the methodological approaches used in the study of undernutrition (child nutritional status) in relation to household food insecurity (HFI), dietary quality indices (DQIs), nutritional quality and cereal protein quality. The key explanatory variables of interest in this NER study as conceived domains of the food utilization dimension of HFI, namely traditional cereal processing methods (TCPMs), habitual food resource utilization practices (HFRUPs), and infant and young child feeding (IYCF) practices, all as potential determinants of the outcome variable (child undernutrition) were also reviewed. Various metrics of child undernutrition (child nutritional status) as applied in various NER studies were also reviewed.

The public health relevance of child undernutrition (prevalence, distribution, putative causes or determinants, consequences, and interventions against the menace) in the Northern Region of Ghana is broadly presented from the global level through to DCs or LMICs and then narrowed down specifically to undernutrition in the Northern Region of Ghana. Reports from recent Demographic and Health Survey (DHS), Multi Indicator Cluster Study (MICS), Knowledge, Attitude and Practice

(KAP) and other international, regional, national, and communal nutrition reports were reviewed and synthesized.

A review of the empirical application of state-of-the-art foodomics (food metabolomics) techniques in nutritional epidemiological studies was also conducted with the view to framing a suitable and pragmatic methodological approach, to examine the problem of undernutrition in the Northern Region of Ghana, with TCPMs as the focal exposure variables of interest. The potential to find valid and reliable answers to the research questions and thus contribute to the NER literature through the application of modern advances in high-throughput food metabolomics (foodomics) research techniques, have thus been reviewed also.

The theoretical background section ends with a sub-section on an exposition of the research knowledge gap identified from the review of relevant literature and situational analyses of the menace of undernutrition in the Northern Region of Ghana. This provided the needed justification for this study and clearly informed the description of the research problem and contextually posited the objectives, hypotheses, and purpose of the study.

2.2 Theoretical Framework of the Study

2.2.1 Theoretical Foundations: Nutritional Epidemiology and Public Health Nutrition

Since 1948 when the World Health Organization (WHO) enshrined its definition of health in its constitution, the meaning, and dimensions of the concept of health has also evolved (Sartorius, 2006). There is hardly any consensus on what constitutes health and what does not, at least amongst most researchers, scientists, policy makers and practitioners alike (Lancet, 2009; Sartorius, 2006). Bhopal (2002) defined health as ‘a desired ideal, which includes being alive and free of disease, disability, and infirmity, characterized by well-being and efficient functioning in society’. There is a generally accepted view of three main dimensions of health namely physical, mental, and social health status largely in line with the classical WHO definition, with their varied derivative domains, constructs and measurable outcome indicators or markers accordingly (Brüssow, 2013; Sartorius, 2006). Other domains of these health dimensions continue to evolve into distinct dimensions in their own right as the debate on the epistemological, ontological, and philosophical paradigms of health as a concept also continues (Godlee, 2011; Huber et al., 2011; Lancet, 2009). For instance, the concept of spiritual health and emotional health are perceived by their advocates as distinct dimensions from mental and social health respectively whiles others conceive wellness and social wellbeing in various dimensions and domains (Huber et al., 2011; Pratt, Hibberd, Cameron, & Maxwell, 2015; Stoewen, 2017).

Epidemiology is defined as a translational science or a scientific method applied to measure or determine the distribution (occurrence, frequency, pattern) and cause or determinants of a disease or health-related state or event, in order to control and/or prevent the occurrence of the disease or adverse health-related status in a defined population (Arnett & Claas, 2017; Frérot et al., 2018; Gordis, 2009; Krämer et al., 2010). Epidemiology, particularly infectious disease epidemiology, is considered as the core research discipline (foundational science) of preventive medical science, as related to the health status of populations (public health) (Arnett & Claas, 2017; Bhopal, 2002; Detels, Beaglehole, Lansang, & Gulliford, 2009; Krämer et al., 2010). The indicators or markers of disease, health status, health-related phenomenon or events, span across the various dimensions and/or domains of health including disability (functionality), growth impairment, injury, morbidity or disease state, mortality, well-being, quality of life (QoL), disability-adjusted life years (DALYs), mental state, emotional state, spiritual state, psychological state, social state, economic state, hospitalization, health service utilization, et cetera (Arnett & Claas, 2017).

Nutritional epidemiology, a nascent but important branch of epidemiology besides social epidemiology, pharmacoepidemiology, and environmental epidemiology among others, is defined as the study of the distribution, determinants, and health effects of dietary habits or food intake, for the purpose of guiding sound public health nutrition policy and practice (Margetts & Nelson, 1995; Stein, 1995). Nutritional epidemiological research (NER) has contributed immensely to the advances in public health nutrition in the last century and recent decades, all to the benefit of vulnerable sub-populations such as children under five years (U5), pregnant women, ageing persons (elderly), homeless persons, migrants, refugees, and persons with congenital conditions among others in developing, emerging, and industrialized countries (Alpers et al., 2014; Mao, Wang, & Li, 2019). Nutritional epidemiology also seeks to address the scope of five main questions of epidemiology associated with the study of the relationships between food or dietary intake and health status of a defined population. These five questions (five Ws for short) of epidemiology are premised on the descriptive dimension (distribution) which covers the disease occurrence (what), the time or temporal distribution (when), place or spatial distribution (where) and persons or people affected (who), whiles the analytic dimension covers the risk factors (determinants), that is the causes (etiology) and/or pathogenesis (mode of development) of the nutritional health outcome (why and how) (Arnett & Claas, 2017). Public health nutritionists then take over with the findings of the nutritional epidemiologists, to develop interventions, in order to control the adversity of the food or diet-related health outcome or disease state and also to prevent it from happening or occurring in other vulnerable members of the defined population (Buttriss et al., 2017; Kaufman, 1990; Stein, 1995). Public health nutrition interventions are developed from valid and reliable, evidence-based nutritional epidemiological findings drawn from basic research in biochemistry, nutritional sciences, medicine, physiology, and other related biosciences (Caballero, Trugo, & Finglas, 2003; Carpenter, 1983; Millward, 2017).

There is very little doubt that food, diet, or nutrient intake plays a major role in the overall health status of individuals and populations in general (Buttriss et al., 2017; Johanningsmeier, Harris, & Klevorn, 2016; Margetts & Nelson, 1995). However, generating indisputable evidence of the role of specific nutrients, non-nutritive (antinutritional) food constituents, meals, diets, foods, food supplements, food groups or dietary habits or patterns in the etiology and/or pathogenesis of food-related health outcomes, has been a major challenging undertaking for nutritional epidemiologists (Archer, Lavie et al., 2018; Archer, Marlow, & Lavie, 2018; Satija, Yu, Willett, & Hu, 2015). Dietary intake assessment is still challenging because diet is a complex mixture of substances (nutrients and non-nutrients) and it does not necessarily follow a linear dose-response paradigm (Satija et al., 2015; Schwingshackl et al., 2017). Food intake is also affected by several other confounding, mediating, interacting or moderating factors from the farm to fork; ingestion to digestion through to absorption and eventual assimilation of the nutrients and other bioactive substances for physiological and/or anatomical use in the human body (Satija et al., 2015). Among other reasons too, investigating food and/or nutrient intake may not be ethical and/or pragmatic in an effort to account for potential confounders, mediators, and/or moderators in the strictest sense of a robust scientific research. Notwithstanding, the discipline of nutritional epidemiology has developed acceptably reliable and reasonably valid study methods and designs over the years, which have provided seminal findings for the development of many relevant and impactful public health nutrition interventions (Alpers et al., 2014; Michels, 2003; Subar et al., 2015).

2.2.2 Types of Nutritional Epidemiological Study Methods and Designs

Nutritional epidemiologists employ appropriate versions of the two main types of study methods in descriptive and analytical epidemiological research, namely interventional (experimental) and observational (non-experimental) study methods (Arnett & Claas, 2017; Margetts & Nelson, 1995; Thiese, 2014). These methods and their study design types are chosen carefully in epidemiological studies, cognizant of their inherent strengths and weaknesses alike, in order to make them useful to conduct valid and reliable research (Cook & Thigpen, 2019; Krauss, 2018; Mariani & Pêgo-Fernandes, 2014; Thiese, 2014). The use of interventional study designs such as randomized controlled trials (RCTs), randomized cross-over clinical trials (RCCTs) and randomized controlled laboratory studies (RCLS) are relatively limited in several population-based studies compared to observational study methods and designs, even though RCTs are considered the gold standard methodological approach for generating evidence of causal relationships between exposures and health outcomes of interest in any epidemiological research (Black, 1999; Buttriss et al., 2017; Ferreira & Patino, 2016). The ethical, logistical, and pragmatic constraints among others, associated with the conduct of interventional studies largely explains why observational studies are complementary to experimental studies and would remain relevant and dominant in the NER literature, even though they provide lower level of evidence (Black, 1996; Buttriss et al., 2017; Mariani & Pêgo-Fernandes, 2014).

Cross-sectional studies are much more widely utilized besides the other types of observational study designs such as ecological, case-control, case-crossover, and cohort study designs in nutritional epidemiological studies in DCs or LMICs (Mann, 2003; Setia, 2016; Thiese, 2014; Wang & Cheng, 2020). The key issues that need addressing in observational studies to enhance validity and reliability of their findings include confounding, information bias, selection bias and interaction effects, whiles measuredly reporting the results and the unavoidable limitations (Arnett & Claas, 2017; Buttriss et al., 2017; Lachat et al., 2016; Liang, Zhao, & Lee, 2014).

2.2.3 Methodological Approaches to the Study of Undernutrition (Nutritional Status)

Depending on the goals of the NER study, either a qualitative or quantitative approach alone or a combination of both could be adopted in studies on undernutrition or nutritional status of any given population (Ahrens & Pigeot, 2014; Buttriss et al., 2017; Saks & Allsop, 2007). The qualitative approach, however, has often been used to generate an appreciation and in-depth understanding of the latent constructs, concepts and scope of food-related issues that potentially account for the nutritional health outcomes of defined populations of interest (Fade, 2003; Swift & Tischler, 2010). It has been recommended that an exploratory formative study precede the definitive quantitative study, when the exposure variables of interest in any NER are novel, under-researched or poorly understood, especially given the context of the study objectives and study settings (Anderson et al., 2001; Armar-Klemesu et al., 2018; Fade, 2003; Ghosh et al., 2014; Ham, 2020). Qualitative studies, be it ethnographic, phenomenological, grounded theory-based, critical theory-based or case study-oriented, help essentially to gain an understanding (how and why) of the food or nutrition issues or phenomenon of interest to the researcher, thus providing adequate basis for the conceptualization, operationalization and measurement of the concept or phenomenon of interest (Bhattacharya, 2017; Dodgson, 2017; Jackson, Drummond, & Camara, 2007). Most nutritional epidemiological studies employ the quantitative approach and more so in studies of undernutrition or poor nutritional status of mothers and children (Buttriss et al., 2017; Fade, 2003; Swift & Tischler, 2010)**.**

Nutritional status is defined as the physiological state of an individual, arising from the balance between nutrient intake (diet or food intake), the basal metabolic requirements of the individual to function optimally (maintenance, repair, growth and development) and the ability of the individual's body to utilize the nutrients or food (digest ingested food, absorb and, assimilate the required nutrients and healthful non-nutrients) to support the various life processes, typical of a living organism during its lifespan. Nutritional status is therefore viewed as a balance between nutrient or energy intake, basal metabolic nutrient or energy requirements, and the ability of the individual to utilize the nutrients or energy taken in, to optimize functionality and maintain internal equilibrium (homeostasis) (Pang, Xie, Chen, & Hu, 2014). The role of food or diet in determining the health status of an individual is an ancient concept or ideology captured in popular sayings such as 'eat your food as medicine', 'you are what you eat' and 'healthy mind in a healthy body' (Capozzi & Bordoni, 2013; Kleisiaris, Sfakianakis, & Papathanasiou, 2014; Krehl, 1983). Nutritional status is thus viewed as another measure or predictor of the health status of an individual because this physiological status due to nutrition could be telling on the physical, social, or mental state of the individual (National Research Council (U.S.), 1989). The nutritional status of an individual and for that matter a defined population, is considered widely by nutritional epidemiologists and other basic scientists including molecular nutritional scientists to be determined by the genetic potential (genotype) of the individual and other extrinsic factors namely the environment, social factors, economic factors, and geographical factors among others (National Research Council (U.S.), 1989; Svedberg, 2000). The genetic potential theorists posit that each individual has a genetic or inherent propensity to achieve their maximum growth, developmental and functional potential but is subject to extrinsic or 'environmental' factors including food or nutrient intake (Ferguson et al., 2016; Lango Allen et al., 2010; Perola, 2011; Stover & Caudill, 2008; Svedberg, 2000; Wilde, Petersen, & Niswander, 2014). Nutritional status therefore as a sum effect of all the intrinsic and extrinsic factors that influence the balance between nutrient and/or energy intake, basal metabolic requirements, and utilization (homeostasis or metabolic equilibrium), could be conceptualized, operationalized, and measured from different perspectives or paradigms (Bouma, 2017; Ridgway, Baker, Woods, & Lawrence, 2019).

The biological plausibility perspective considers the influence of the genetic potential (genotype) of the individual, together with the net effect of nutrient or energy intake balance on linear and/or ponderal growth (phenotype; physical expression of genes during growth), as a reflection of either the acute or chronic physiological state of the individual at any given time (Péter et al., 2015; Svedberg, 2000). There are dissenting views about the genetic potential theory to the effect that individuals who do not grow and develop according to their expected genetic prospects, cannot be considered to be physiologically challenged or impaired (‘small/short but healthy’), instead it would be erroneous to judge their developmental attainment on the basis of any growth or functionality reference or standard in the human population (Halfon, Forrest, Lerner, & Faustman, 2018; Lickliter, 2008). However, the WHO child growth standards 2006 (growth chart) vindicates the genetic potential theory or paradigm, in that irrespective of ethnicity (genetic disposition), socioeconomic status and type of feeding resources amongst other factors, under identical optimal environmental conditions, similar patterns of normal growth are possible in all humans (Garza, 2015; Onis, Garza, Onyango, & Rolland-Cachera, 2009). Infection or disease state for instance is considered as a perturbation factor that could influence the physiological state of an individual to the extent of altering growth, development, and functionality (Millward, 2017). Several studies have evinced the association between human biological development (physical, mental, social) and improved ‘environmental conditions’ such as nutrition, economy, and water, sanitation and hygiene (WASH) factors (Perkins, Subramanian, Davey Smith, & Özaltin, 2016). The height of well-nourished individuals and/or populations are thus putatively associated with proportionate improvements in the exposures experienced, in sync with the genetic potential paradigm of humans across the various geographical locations and racial disparities across the world (Deaton, 2007; Grasgruber, Cacek, Kalina, & Sebera, 2014).

An economic plausibility perspective considers nutritional status as an ‘input or cause’ measure of the ability to obtain adequate calories or energy, food, or diet (availability and access) for physical and biological utilization by individuals, often described in terms of food and nutrition security (Berry, Dernini, Burlingame, Meybeck, & Conforti, 2015; Peng & Berry, 2019; Svedberg, 2000). This input measure approach of the nutritional status of individuals and populations have several limitations compared to the ‘output or effect’ measure approach of nutritional status (Svedberg, 2000). The output or outcome measure approach takes account of the individual variations in genotypic dispositions, physiological perturbation factors and potentially any other source of unmeasured confounding and/or moderating effects in the individuals or the defined population. The biological plausibility perspective therefore dominates within the community of nutritional epidemiologists with anthropometry (physical growth) serving as a widely utilized measure of nutritional status in humans (Cole, 2012; Svedberg, 2000; Wit, Himes, van Buuren, Denno, & Suchdev, 2017). Anthropometry is currently the most widely utilized measure of nutritional status as a reflection of the physiological state of linear and/or ponderal growth and development of individuals especially amongst children under five years (Svedberg, 2000; Ulijaszek & Mascie-Taylor, 1994; Utkualp & Ercan, 2015). Nutritional epidemiological softwares useful for calculating and standardizing anthropometric measures of children, adolescents, and adults for both genders, based on validated human growth reference standards and classifications include ENA, WHO Anthro, Nutri-Survey, WHO AnthroPlus, OpenEpi and EpiInfo softwares. Other output or effect measures of nutritional status as a reflection of the physiological state of an individual, premised on the balance between nutrient or energy intake, basal metabolic requirements and actual utilization of the ingested, absorbed and assimilated nutrients, include examination of clinical signs, biochemical measurements, and environmental or geographic proxies of human growth or impairment (Shamah-Levy, Cuevas-Nasu, Rangel-Baltazar, & García-Feregrino, 2019; Upadhyay and Tripathi, 2017).

Most nutritional epidemiological studies on the determinants of undernutrition amongst children under five years in developing countries (DCs) or low-and-middle income countries (LMICs) often use the conventional epidemiological approach, by analyzing the correlation or association between the postulated dietary exposure variable of interest (food and/or nutrient intake) and nutritional status (food-related health outcome variable), after accounting for potential confounders and/or moderators (proximal, intermediate and distal risk factors and/or covariates), guided by a conceptual framework (Blaney et al., 2019; Boah et al., 2019; Hill, 2003; Victora, Huttly, Fuchs, and Olinto, 1997). There are various types of conceptual models and/or frameworks used within the community of nutritional epidemiologists, to undertake investigations of the possible causes or risk factors of food-related health outcomes and the pathogenesis underlying their occurrence (Lawrence, Forbat, & Zufferey, 2019; Oltersdorf, Boeing, Hendrichs, & Bodenstedt, 1989; Zeisel, 2019).

2.2.3.1 Theoretical Frameworks for Modelling Relationships: Dietary Exposures, Covariates, and Health Outcomes in NER Studies

In malnutrition studies, particularly undernutrition (PEM and MDM) in DCs and/or LMICs, the seminal UNICEF conceptual framework for the determinants of child nutritional status developed in 1990s (**Figure 2.1**), continues to dominate and has evolved over the years into its current form premised on a life-course approach (Bhutta et al., 2013; Black et al., 2008; Black et al., 2013; Black et al., 2017; UNICEF, 1998).

The current model is made up of a three-stage conceptual hierarchy of factors and/or covariates that are presumed to contribute to the prevalence of fetal and child nutritional status and development in developing country settings (**Figure 2.2**). The chronic and acute nutritional status of an infant or young child could then have medium to long-term growth, developmental and funtional consequences during their lives (adolescence through adulthood to senescence). The three tiers from the bottom upwards, correspond to community or distal risk factors and/or covariates (macro), household or intermediate risk factors and/or covariates (meso) and proximal or immediate risk factors and/or covariates (micro) respectively. The factors/covariates are conceived to act directly or indirectly (mediated) through the hierarchy of determinants according to the specific context of the defined population with some of the factors and/or covariates exerting confounding and/or interacting (moderating) effects on the child nutritional status (outcome health measure). From the fetal stage to neonatal, infant, and childhood stages (1000-day period) through adolescence to adulthood, the framework seeks to integrate the net effect of the relationships between the various factors and/or covariates at play, to present the best evidence-based interventions (EBIs) or actions needed to ensure optimal child growth and development, premised on food and nutrition among other factors (Bhutta et al., 2013; Black et al., 2013; Black, Lutter, & Trude, 2020; Garza, 2015).

New perspectives have been shed on the seminal UNICEF conceptual framework, suggesting the need to revise the model, albeit it remains fit-for-purpose, relevant, reliable, valid, and resilient for use in undertaking nutritional epidemiological research (NER) of maternal and child nutritional status especially in DCs and LMICs (Black et al., 2020; Garza, 2015; Haisma, Yousefzadeh, & van Boele Hensbroek, 2018; Raiten & Bremer, 2020).

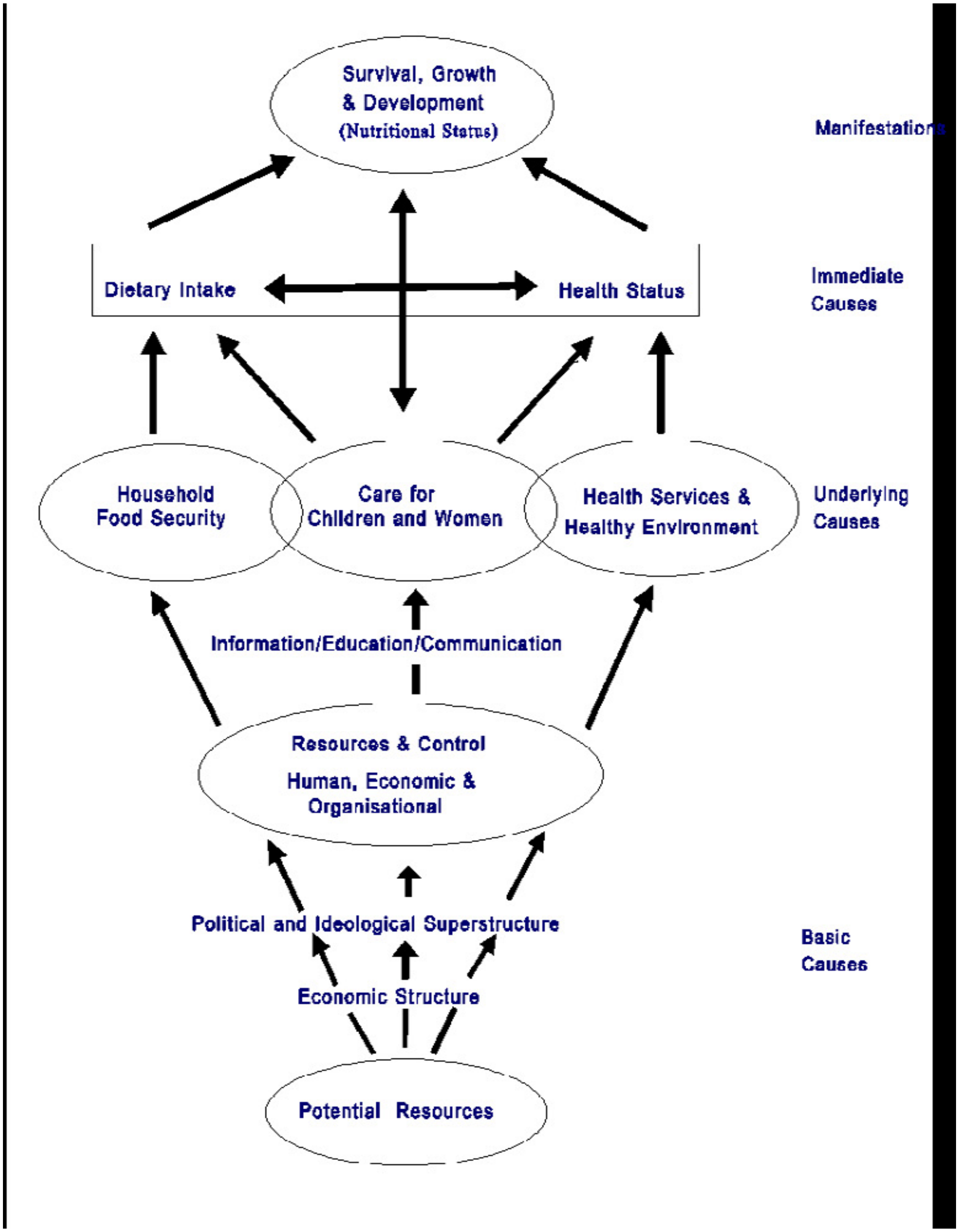

Figure 2.1: UNICEF's Seminal Conceptual Framework for the Determinants of Undernutrition in DCs Issued in the 1990s

Reproduced from UNICEF (1998)

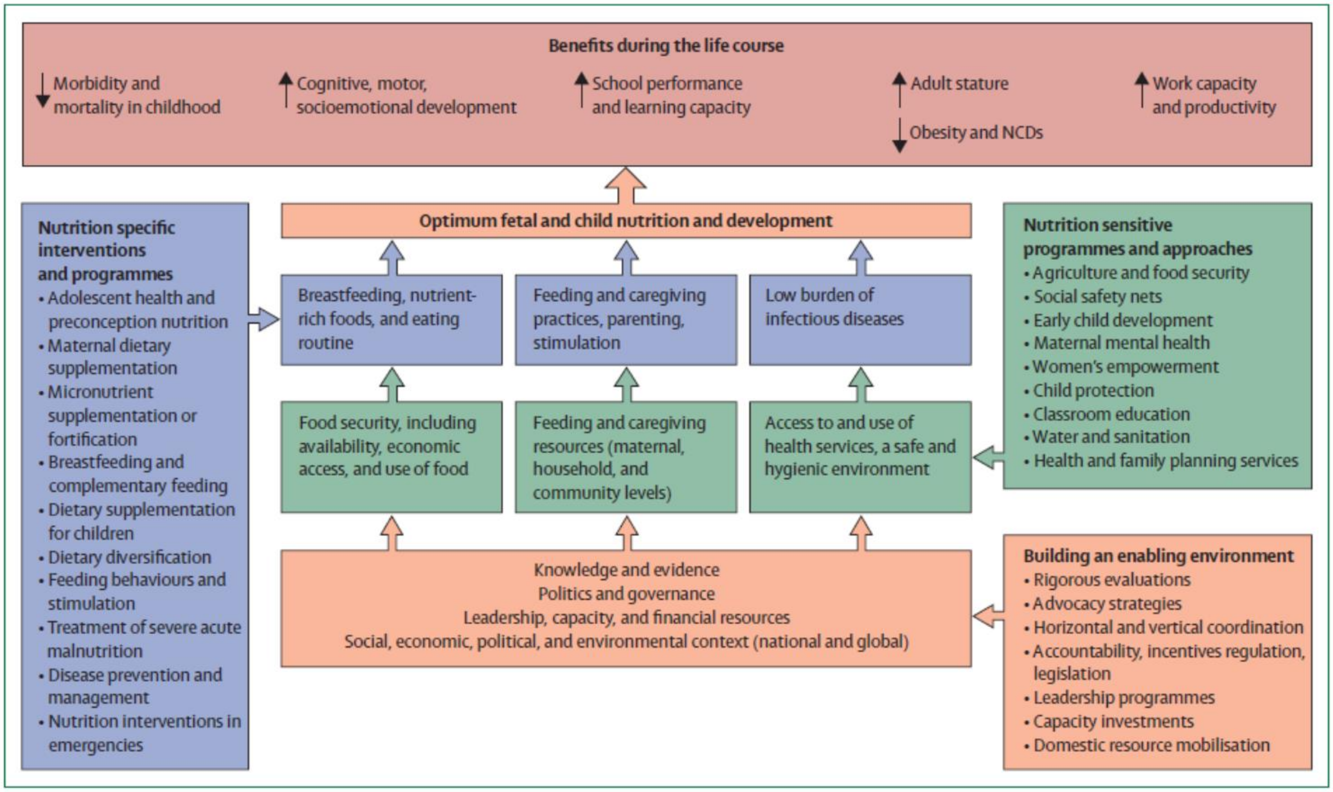

Figure 2.2: Framework for actions to achieve optimum fetal and child nutrition and development

Reproduced from Black et al. (2013)

Various novel and adapted versions of the seminal UNICEF conceptual framework of the determinants of child nutritional status have been churned out by various researchers over time (Black et al., 2008; Boah et al., 2019; Fanzo, 2012; Müller & Krawinkel, 2005). The main differences in all these adapted versions of the UNICEF conceptual framework are usually premised on the explanatory (exposure) and outcome variables of interest to the researchers, given the context of the study setting, how the explanatory variables, covariates and outcome variables are operationally defined and how the researchers conceive the determinants to interact either directly or indirectly (mediated) through the various factors/covariates at each hierarchy of the model (Chandrasekhar, Aguayo, Krishna, & Nair, 2017; Garcia, Sarmiento, Forde, & Velasco, 2013; Victora, Huttly, Fuchs, & Olinto, 1997).

For instance, Lin *et al* (2013) placed emphasis on investigating the role of water, sanitation, and hygiene (WASH) factors as determinants of child nutritional status. These environmental factors were percieved to exert their influence on the proximal risk factors through environmental enteric dysfunction (EED) or environmental enteropathy (EE) amongst the children alongside the parental factors and household food insecurity (HFI) factors at the household level (meso), to eventually determine the nutritional status of the children (Gera, Shah, & Sachdev, 2018; Merchant et al., 2003; Millward, 2017; Prendergast & Humphrey, 2014; Salameh et al., 2020). WASH indicators were considered as separate independent variables at the intermediate or underlying (household) level within the hierarchical conceptual framework used in this study in northern Ghana, rather than a sub-component or domain of the food utilization dimension of household food insecurity (HFI), as conceived by other researchers (Lin et al., 2013; Peng & Berry, 2019). Understandably, WASH indicators are associated with an increased propensity of child morbidity or childrens' experiences of enteric diseases such as diarrhoea which have been shown to impair appetite, ingestion of adequate food and/or adequate absorption of nutrients (Garcia et al., 2013; Lin et al., 2013).

Boah et al (2019) developed their version of a working conceptual framework for the examination of the contextual risk factors of undernutrition amongst children under five years in Ghana, by drawing on the UNICEF conceptual framework and those of other researchers of similar LMIC settings. A modified version of the UNICEF conceptual framework was used to examine the risk factors of undernutrition amongst children under five years in Ghana by classifying the explanatory variables into biological and non-biological variables (Welaga Miah & Awingura Apanga, 2016). In all these conceptual models, the researchers were required to make every effort to account for the limitations inherent in the study methods and designs, by addressing issues such as potential confounding, interaction, and bias among other issues, in order to eliminate or reduce significantly, the threat to validity and reliabilty (Greenland, Daniel, & Pearce, 2016; Liang et al., 2014; Sheean et al., 2011; Yan, Sun, Boivin, Kwon, & Li, 2016; Zeraatkar et al., 2019).

Conceptual frameworks or models serve as a guide to enable epidemiological researchers effectively and efficiently deal with all the complex interactions between the variables that conceptually matter for quantitative investigation, using multivariable analytical techniques to make sense of the data collected and results obtained, in the light of the contextual biological, environmental, social, economic, and political knowledge available (Kelly et al., 2009; Victora et al., 1997). Various statistical modelling approaches have been recommended as panacea to the propensity to churn out invalid and biased findings from quantitative epidemiological studies (Sheean et al., 2011; Ughade, 2013; Yan et al., 2016). These include explanatory modelling, predictive or diagnostic modelling and descriptive modelling which must be applied appropriately (Sainani, 2014; Shmueli, 2010). Candidate variables enlisted for data collection, the measurement of these variables in a given population and the variables that are selected eventually for statistical modelling, require very thoughtful considerations in order to obtain the most parsimonious model to churn out reliable and valid conclusions (Liang et al., 2014; Yan et al., 2016; Zeraatkar et al., 2019).

2.2.3.2 Measurement of Exposure Variables (Food and Nutrient Intake) in NER Studies

In nutritional epidemiological studies, the focal exposure (explanatory) variable of interest is food or nutrient intake. Measuring accurately, the current food or nutrient intake and/or the usual food or nutrient intake to correspond with the acute and/or chronic physiological states respectively of an individual or people in a defined population, has been theoretically, conceptually, and empirically challenging for nutritional epidemiologist, nutritional scientists, and public health nutritionists (Naska et al., 2017; Shim et al., 2014). Food or diet inarguably is a complex mixture of constituents made up of nutrients and the non-nutrititve components (Margetts & Nelson, 1995; Zhao & Singh, 2020). These food constituents are required and utilized differently under varying physiological or metabolic conditions (growth, ageing, pregnancy, infection, et cetera), they exhibit varying dose-response effects (linear and non-linear) in different people (age, gender, race, blood group, et cetera), exhibit varying attributes of bioavailability, multifuntionality, bioequivalence and interactions at different times and varying conditions coupled with the plethora of idiosycrasies in peoples' behaviours (smoking, alcohol intake, sleeping, socializing, working, physical activities, et cetera) (Margetts & Nelson, 1995). Nonetheless, nutritional epidemiologists and nutritional scientists have successfully developed reasonably valid and reliable food or dietary intake assessment methods, albeit against the odds of harsh criticisms of their usefulness and credibility (Archer & Blair, 2015; Archer, Lavie et al., 2018; Archer, Marlow et al., 2018; Archer, Pavela, & Lavie, 2015; Lachat et al., 2016; Margetts & Nelson, 1995; Naska et al., 2017; Subar et al., 2015).

There are currently two main approaches generally used to assess food or nutrient intake in an individual and/or persons in a defined population namely self-reported methods (subjective) and dietary biomarkers (objective) (Collins, McNamara, & Brennan, 2019; Jenab, Slimani, Bictash, Ferrari, & Bingham, 2009; Lachat et al., 2016; Naska et al., 2017). Both methods are used theoretically and empirically in observational and interventional studies to measure directly or indirectly as an alternative (proxy or surrogate), the presumed actual, habitual, current, or relative amounts of food or nutrients consumed by an individual or groups of people in a given population at a point in time, or over a defined period (Brouwer-Brolsma et al., 2017; Collins et al., 2019). Since observational studies still dominate the NER literature, and the costs associated with using dietary biomarkers are relatively higher, usage of the self-reported methods of food intake assessment also dominate in practice, albeit both methods have their peculiar limitations and strengths (Jenab et al., 2009; Lyu, Hsu, Chen, Lo, & Lin, 2014; Naska et al., 2017; Shim et al., 2014). In some well-resourced studies, both approaches are utilized to complement each other because there is a lack of an indisputable gold standard method to serve as reference for method validation (Archer, Lavie et al., 2018; Brouwer-Brolsma et al., 2017; Collins et al., 2019; Guasch-Ferré et al., 2018; Lachat et al., 2016).

In observational studies, self-reported food, or nutrient intake assessment methods for defined periods (a day, repeated days, weeks, months, a year, years or seasons), include methods of memory recalls such as 24-hour dietary recalls (24HDRs), dietary recall records (DRRs), food frequency questionnaires (FFQs) and dietary histories (DHs). The alternative methods premised on real-time self-reported recording of food or dietary intake such as food/dietary diaries (F/DDs) also known as food/dietary consumption records (F/DCRs) (with or without weighing) and the duplicate diet portion (DDP) method are used (Naska et al., 2017; Salvador Castell, Serra-Majem, & Ribas-Barba, 2015; Shim et al., 2014).

Food or dietary intake biomarkers are biochemical compounds which serve as objective indicators of the absolute or relative magnitude (quantitative) and/or presence or absence (qualitative) of the intake of a particular nutrient, food constituents, food ingredient or meal upon analytically examining the food material (biological material to be ingested) or alternatively biosamples such as blood, feces, or urine obtained from the study subjects or individuals (Biesalski et al., 2009; Corella & Ordovás, 2015; Dragsted et al., 2017; Gao et al., 2017; Jenab et al., 2009). Food or nutrient intake biomarkers have been variously classified based on a wide array of criteria such as recovery biomarkers, predictive biomarkers, concentration, and replacement dietary biomarkers. Other classifications include biomarkers of dietary exposure, biomarkers of nutritional status and biomarkers of health/disease state (Corella & Ordovás, 2015; Gao et al., 2017; Jenab et al., 2009; Rollo et al., 2016; Ulaszewska et al., 2019). The plethora of classification schemes and definitions of dietary intake biomarkers rather appears to create more confusion and ambiguity, thus the suggestions by Goa *et al* (2017) for a flexible classification scheme to address this ontological challenge (Dragsted et al., 2017).

High throughput analytical laboratory methods such as those applied in nutrimetabolomics (nutrition metabolomics), are used to measure compositional or constituent metabolites (nutritional and non-nutritional metabolome) in biosamples taken from individuals such as blood, urine, feces, hair, amniotic fluid, and breast milk, which can serve as biomarkers of food intake (Collins et al., 2019; Corella & Ordovás, 2015; Ulaszewska et al., 2019). Foodomics (food metabolomics) on other hand, also allows the measurement of food metabolites or dietary constituents in pre-processed (meal ingredients) and/or processed/prepared food biosamples (cooked meal), with the goal of establishing a link or association between the observed changes effected in the food metabolites in the food material, as a result of processing and some food-related health outcomes in individuals or a defined population (Gorzolka, Lissel, Kessler, Loch-Ahring, & Niehaus, 2012; Koistinen et al., 2018; Koistinen, Katina, Nordlund, Poutanen, & Hanhineva, 2016; Pinu, Goldansaz, & Jaine, 2019) Whether one employs a direct method (actual nutrient intake and/or usage measures) or indirect method (potential dose of nutrient exposure by proxies or surrogates) of assessment of food or dietary intake, reporting the findings has to be done, mindful of the complexities and limitations associated with measurement of food, diet (meal), nutrients, non-nutrients, foods, food groups, food patterns, food ingredient intake, and/or usage assessment methods (Collins et al., 2019; Poslusna, Ruprich, Vries, Jakubikova, & van't Veer, 2009; Potischman, 2003; Subar et al., 2015). Various methods have been propounded to account for systematic and random measurement errors (within-person and between-person variations) of food intake assessment methods whether by the use of biomarkers of food intake (direct or proxy), self-reported memory recall or real-time self-reported recording of dietary intake (Buttriss et al., 2017; Prentice & Huang, 2018).

2.2.3.3 Measurement of Outcome Variables (Nutritional Health Indicators) in NER

Anthropometry is widely recognized, and it is the most utilized measure within the community of nutritional epidemilogists, as a valid and reliable approach to conceiving and determining nutritional status of infants, young individuals and matured persons in a given population (Buttriss et al., 2017; Gorstein & Akré, 1988). The outcome variables usually measured in nutritional status studies include one or more of the various measures of protein energy malnutrition (PEM) namely stunting (height/length-to-age), wasting (weight-to-height/length), underweight (weight-to-age), skinfold thickness, and mid-upper arm circumference (MUAC) Z-scores among others (Bhattacharya, Pal, Mukherjee, & Roy, 2019; Buttriss et al., 2017). Various validated measures of hidden hunger (HH) or micronutrient deficiency malnutrition (MDM) namely iron deficiency anaemia, iodine deficiency, vitamin A deficiency and zinc deficiency are widely used in nutritional epidemiological studies as well (Dao et al., 2017).

2.2.4 Food Security Dimensions: Food Availability, Access, Utilization, and Stability

The definition of the concept of food security has evolved from ideas of hunger, famine, deprivation, starvation, undernourishment, livelihood, and the likes since the 1970s or earlier, coupled with a wide array of sometimes conflicting and confusing semantics used to describe the phenomenon over the years (Maxwell, 1996; Peng & Berry, 2019). Consequently, it currently still lacks a universally coherent, consistent, generally recognized, and utilized single measure for its assessment (Berry et al., 2015; Headey & Ecker, 2013; Hendriks, 2015; Peng & Berry, 2019). However, the current working definition most widely accepted and utilized globally also evolved from the World Food Summit (WFS) version in 1990 to the version issued by the Food and Agriculture Organization (FAO) at the WFS 2009. Food security is defined as the situation that exists when all people, at all times, have physical, social, and economic access to sufficient, safe, and nutritious food that meets their dietary needs and food preferences for an active and healthy life (Peng & Berry, 2019). Whether at the macro, meso or micro levels of society, the measurement of food security has been predominantly focused on the food availability and access dimensions (Leroy, Ruel, Frongillo, Harris, & Ballard, 2015). It has been seminally classified into four main dimensions (or pillars) namely food availability, food access, food utilization, and food stability (Lawlis, Islam, & Upton, 2018; Peng & Berry, 2019). A fifth dimension, premised on sustainability has been proposed for adoption into defining food security currently in line with the new understanding and perspectives (SDGs) of current human developmental issues, challenges, and the environment (climate change) (Berry et al., 2015). The current thinking about food security is unequivocal with regards to the need to be more comprehensive in the conceptualization, operationalization, and measurement of food security premised on all the conceivable dimensions (Barrett, 2010; Carr, 2006; Maxwell et al., 2013; Renzaho & Mellor, 2010).

A plethora of measures or indicators have been used by various researchers and analytical stakeholders to report on food security but the FAO as a global umbrella organization, has somewhat popularized the measurement of food security through its flagship periodic global report dubbed 'state of food insecurity in the world, SOFI', using a cocktail of indicators that span the four classical dimensions (Amarender Reddy, 2016; Berry et al., 2015; FAO, IFAD, UNICEF, WFP and WHO, 2020; FAO, 2013; Peng & Berry, 2019). Undernourishment and food inadequacy are two of the indicators of the food access dimension of food insecurity at the household level which are estimated based on meeting a set threshold of energy or calorie intake required to maintain an active and healthy life (FAO, IFAD, UNICEF, WFP and WHO, 2020; FAO, 2013). The prevalence of undernutrition (PoU) is estimated from the dietary energy supply (DES) in any given country and the coefficient of variation (CoV) of the distribution of food consumption, reflecting the level of unequal access to food. Other food and nutrition security researchers continue to use a wide array of other scales, measures or indicators to assess food insecurity premised predominantly on the food availability and access dimensions at the distal (local community, local regions, national, sub-regional, continental and global) and intermediate (household) levels, making it challenging to harmoniously compare, monitor and evaluate progress across various jurisdictions and hierarchies of society (Hendriks, 2015; Renzaho & Mellor, 2010).

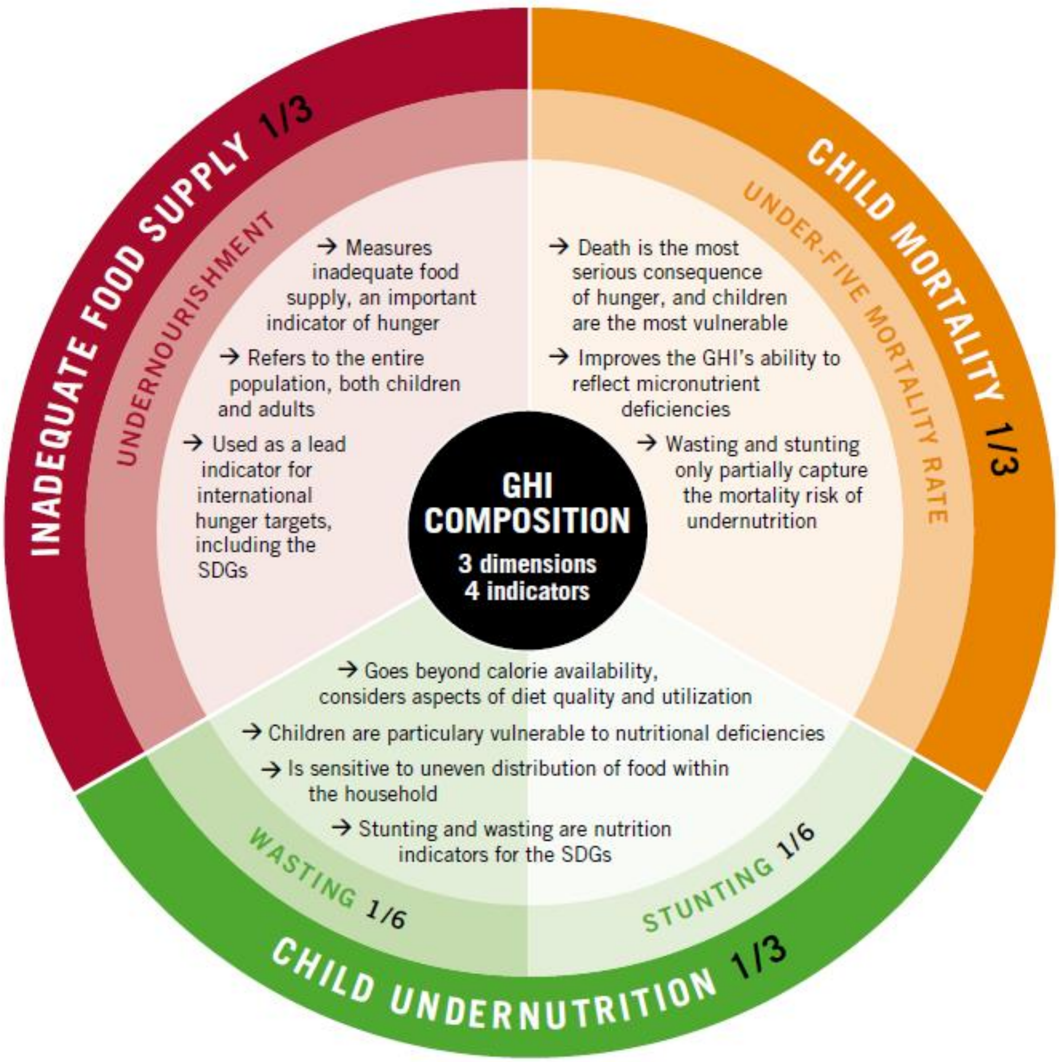

Figure 2.3: Composition of the global hunger index (GHI) used for score estimation

Reproduced from Grebmer (2019)

These include the household hunger scale (HHS), household food insecurity access Scale (HFIAS), household food consumption and expenditure surveys (HCES), food insecurity experience scale (FIES), food consumption score (FCS), Radimer-Cornell Instrument (RCI), global hunger index (GHI) and the coping strategies index (CSI) amongst others (Agbadi, Urke, & Mittelmark, 2017; Ali et al., 2013; Aurino, Wolf, & Tsinigo, 2020; Chandrasekhar et al., 2017; McKay, Haines, & Dunn, 2019; Saint Ville, Po, Sen, Bui, & Melgar-Quiñonez, 2019; Webb et al., 2006). Efforts continue to be made to develop simple, valid, reliable, composite (or aggregate) indices, given the multidimensional and multifaceted nature of the concept of food security (Caccavale & Giuffrida, 2020; Ren, Li, Wang, & Zhang, 2020). The global hunger index (GHI) for instance is calculated based on the standardization and aggregation of measures of child undernourishment (as estimated by FAO), child mortality (as estimated by UN IGME) and child undernutrition (as estimated by UNICEF and partners) resulting in scores on a 100-point scale, where 0 is the best score (no hunger) and 100 is the worst (**Figure 2.3**). A score of 100 means that the particular country in question meets the global thresholds set slightly above the recommended optimum levels observed for child undernourishment, child wasting, child stunting, and child mortality benchmarks recently (Grebmer, 2019).

2.2.5 Household Food Insecurity, Food Utilization, and Child Malnutrition

Undoubtedly, food insecurity is interrelated or associated with all the forms of undernutrition, as constraints to food availability, access, utilization and stability in any given vulnerable population would be telling on its nutritional status especially children under five years (**Figure 2.4**) (Berra, 2020; Fafard St-Germain & Siddiqi, 2019; FAO, IFAD, UNICEF, WFP and WHO, 2020; Hwalla et al., 2016; Moradi et al., 2019; Simelane & Worth, 2020; Sreeramareddy, Ramakrishnareddy, & Subramaniam, 2015). The utilization dimension of food insecurity is measured at the household and individual levels by FAO as a reflection of the nutritional status amongst children under five years (anemia, iodine deficiency, vitamin A-deficiency, stunting, wasting, underweight status) and adults (BMI of adults & anemia among pregnant women) (FAO, IFAD, UNICEF, WFP and WHO, 2017, 2020; FAO, 2013). The food utilization dimension of HFI as conceived in the definition of food security, is made up of a number of domains, some of which are often overlooked or minimally recognized by some researchers in the measurement instruments, scales and indicators used for household food insecurity assessments in DCs (Ashby, Kleve, McKechnie, & Palermo, 2016; Berry et al., 2015; Marques, Reichenheim, Moraes, Antunes, & Salles-Costa, 2015; Peng & Berry, 2019). Emphasis is often placed on the food access dimension with very little or none of the assessment indicators at all considering the food utilization dimension (Ashby et al., 2016; Hwalla et al., 2016; Leroy et al., 2015). Some of these food utilization domains (physical and biological use) may include food processing, meal preparation, food choices and preferences, food storage and preservation techniques, dietary habits and practices, and their effects on nutrient bioavailability, utilizable proteins, digestible proteins, anti-nutritional factors (ANFs) culminating in nutritional status. The WASH status and its effects on morbidity status, health status, and immunity status of the populations also are an important domain of food utilization (Joye, 2019; Peng & Berry, 2019; Rutherfurd & Moughan, 2012; Schönfeldt & Gibson Hall, 2012).

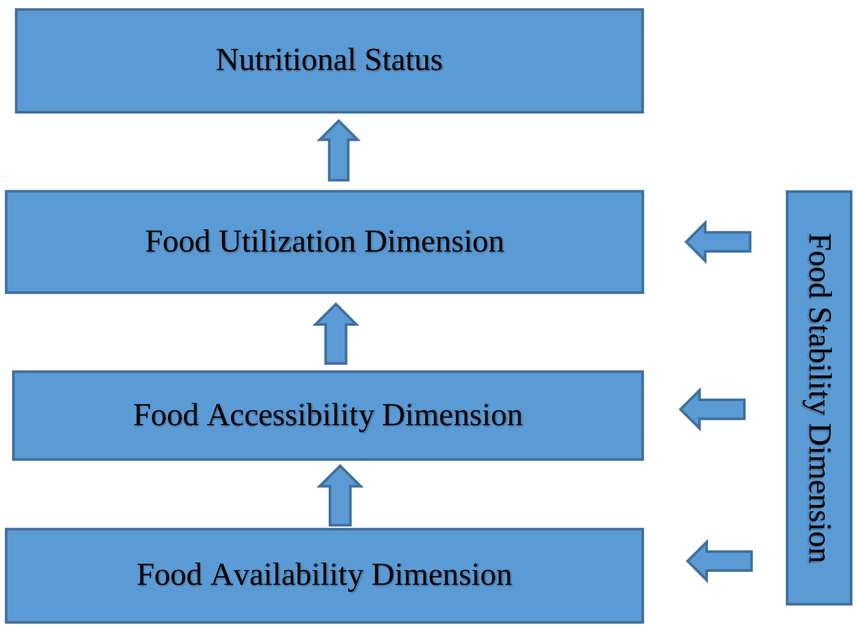

Figure 2.4: Conceptual Framework of Food Security in Relation to Nutritional Status
Adapted from Gross, Schoeneberger, Pfeifer and Preuss (2000).

In addition to the nutritional status measures or indicators, the FAO uses WASH factors as proxies to assess the morbidity status or burden of enteric diseases and safety of domestic food preparation practices as domains of HFI. These are conceptualized to be relatable to the optimal utilization of food supplies accessed within households (FAO, IFAD, UNICEF, WFP and WHO, 2017, 2020; FAO, 2013). However, this suite of indicators (WASH factors and nutritional status indicators) is not comprehensive enough to reflect the broad scope of domains that could possibly determine the optimal utilization of food resources accessed within households (Berry et al., 2015; Pangaribowo, Gerber & Torero, 2013; Peng & Berry, 2019).

TCPMs and HRFUPs constitute other possible conceivable domains of the food utilization dimension of HFI, which have been hypothesized in this study as potentially influential in determining the nutritional status of children under five years in the Northern Region of Ghana. Malnutrition is defined as inadequate or excess intake (imbalanced intake) of protein, energy (calories), and micronutrients resulting in physiological dysfunctions or disorders in the body (Ngo, Ortiz-Andrellucchi, & Serra-Majem, 2016)**.** There are two main sides to malnutrition, over-nutrition and undernutrition (Maleta, 2006). Undernutrition can be further categorized into two main broad groups, protein-energy malnutrition (PEM) and micronutrient deficiency malnutrition (MDM) or hidden hunger (HH) (Maleta, 2006; Ngo et al., 2016)**.** Malnutrition, particularly undernutrition as a major public health menace in developing countries, is an underlying cause of over 45% of child mortality associated with infectious diseases, and also results in other untoward health outcomes (Rice, Sacco, Hyder, & Black, 2000). This study thus conceptualized and operationalized the measurement of various constructs of some conceivable domains of food utilization (TCPMs and HFRUPs), considered to be under-researched for the purposes of finding out their potential associations with child nutritional status in the Northern Region of Ghana.

2.2.5.1 TCPM Indicators as Potential Risk Factors of Child Undernutrition

Traditional cereal processing methods (TCPMs) refer to household-level, low-level technological processing methods used customarily in resource-limited settings to convert cereals into semi-processed products (cereal meal ingredients) that require some domestic meal preparation or cooking methods to convert them into ready-to-eat meals (Hotz & Gibson, 2007; Oumarou, Ejoh, Ndjouenkeu, & Tanya, 2005). These include sun drying, dehulling, soaking, germination, roasting, dry milling, sieving, winnowing, wet milling, kneading, moulding and natural fermentation among others used especially for preparing complementary or weaning meals for children under five years and adult meals as well (Mensah & Tomkins, 2003). TCPM usage is widespread in many West African countries such as Ghana, Nigeria, Benin, and Burkina Faso where among other factors, the availability of the staple cereals (maize, sorghum, and millet), socio-economic conditions and traditional beliefs or customs play significant roles in how food is prepared. Various terminologies such as household-level technologies, traditional food-processing methods and indigenous processing methods are used by different authors to describe the same concept of TCPMs (Oumarou et al., 2005; Saleh et al., 2019; Saleh, Zhang, Chen, & Shen, 2013). Northern Ghana is home to several forms of cereal-based homemade food products of TCPMs from an equally heterogeneous mix of tribes, communities, and cultures (Ham, 2020).

TCPMs have been used routinely dating back several years but have also evolved to rapidly accommodate some modern technological advances in food processing such as the transition to motorized attrition milling (Nikanika) from the old-fashioned mortar-pestle pounding and/or stone grinding methods for pulverizing cereals into flour (Gwirtz & Garcia-Casal, 2014; Taylor, 2007; Taylor & Dewar, 2001). The propensity for sub-optimal flour volume yield, risk of nutrient loss, and contamination of finished cereal products are some of the potential drawbacks of TCPMs in resource-poor settings in DCs and LMICs (Gwirtz & Garcia-Casal, 2014; Pedersen & Eggum, 1983; Taylor, 2007). Potential contamination of cereal and cereal-based complementary meal ingredients with infectious diarrhoea-causing microbes and mycotoxins cannot be ruled out, given the high burden of pathogenic diseases, the low level of compliance with good hygienic practices (water, sanitation, and hygiene; WASH), coupled with under-resourced health facilities and services to many households in DCs. Due to the effects of TCPMs, the possibility of a decrease in nutritional quality of complementary meal ingredients (CMIs) produced for young children, is percieved as a major likelihood that could be contributing to the high prevalence of undernutrition (stunting, wasting and underweight status) in the Northern Region of Ghana. Some studies on traditionally processed cereals have reported a mix of both nutritionally facilitative and debilitative changes in the nutritional profiles of cereal products used in feeding infants and young children in monotonous cereal-only eating populations in DCs and LMICs (Oghbaei & Prakash, 2016).

2.2.5.2 Dietary Quality Indices, Nutritional Quality, and Cereal Protein Quality

Dietary quality indices (DQIs) are quantitative indicators, whose subjective (self-reported) and/or objective methods of evaluating compliance with the adequacy (quality and quantity) and/or variety of recommended reference diets, foods and/or nutrients, serve as a means of dietary intake assessment for population-based studies (Gil et al., 2015; Marshall et al., 2014; Miller et al., 2020; Naska et al., 2017; Shim et al., 2014). The application of dietary biomarkers as objective measures of food and/or nutrient intake, has also gained momentum recently in the generation of new DQIs to complement the more subjective self-reported methods (Brennan & Hu, 2019; Brouwer-Brolsma et al., 2017; Guasch-Ferré et al., 2018; Kim et al., 2016; Naska et al., 2017; Ulaszewska et al., 2019). The usage of DQIs are widespread as evidenced in the NER literature but still leaves more room for improvement especially with regards to their evaluation for external validity, reliability and associations with food-related health outcomes in paediatric populations of similar characteristics globally (Collins et al., 2015; Dalwood et al., 2020; Głąbska, Guzek, Ślązak, & Włodarek, 2017; Harahap, Sandjaja, Soekatri, Khouw, & Deurenberg, 2018; Miller et al., 2020; Owusu, Colecraft, Aryeetey, Vaccaro, & Huffman, 2017; Toffano et al., 2018). The concept of dietary quality evaluation is premised on various assumptions about the individual and/or synergistic roles of food constituents (nutrients and non-nutrients), foods and dietary patterns or lifestyles on the health of populations (Duncanson, Lee, Burrows, & Collins, 2017; Olza et al., 2019). There are three main types of DQIs namely nutrient-based indices, food/food group-based indices and an aggregate or combination of nutrient-food indices. Some have discretionary scoring systems, inclusion criteria and exclusion criteria which limits comparability of their usage across different settings, whiles others are standardized and/or validated for wider applicability (Gil et al., 2015; Olza et al., 2019; Toffano et al., 2018). Some well known DQIs include dietary diversity score (DDS), food variety score (FVS), healthy eating index (HEI), diet quality index (DQI), grain, fruit, and vegetable variety score (GFVS), the Chinese children dietary index (CCDI) and the Mediterranean diet quality index international (MedDQI-I) among others (Marshall et al., 2014). Majority of these DQIs use self-reported food intake assessment methods namely 24-hour dietary recall (24HDR), food frequency questionnaire (FFQ), food diary (FD), food record (FR) and dietary history (DH) (Dalwood et al., 2020; Habte & Krawinkel, 2016; Marshall et al., 2014; Tavakoli et al., 2016; Zhao et al., 2017). They have been very useful in nutritional epidemiological research in developing and developed nations over the years because of the methodological challenges nutritional epidemiologists still face with accurately measuring dietary intake as the exposure variable of interest (Dalwood et al., 2020; Duncanson et al., 2017). Nothwithstanding the significant progress with the use of dietary biomarkers in nutritional epidemiological studies recently, DQIs would remain indispensable and complementary to dietary biomarkers for the foreseable future (Brennan & Hu, 2019; Brouwer-Brolsma et al., 2017; Guasch-Ferré et al., 2018; Guertin et al., 2014).

The nutritional value or quality of any given food, food ingredient, meal or diet depends on its nutrient and non-nutrient composition (quantity and quality profile), sensorial acceptability, digestibility, and bioavailability (Wu, 2016). Optimal food value is however attained from animal and plant food sources only when there is an acceptable trade-off between the nutritional quality, functional characteristics (suitability for processing to obtain meal ingredients and/or meals), safety for consumption and acceptability or preference of its sensory attributes (Oghbaei & Prakash, 2016; Zhang, Zhang, Wang, & Qian, 2014). In the case of resource-poor communities or households, the priority would often be to obtain safe meals with as much nutritional value from the limited food resources, whiles most likely compromising on functional characteristics (such as swelling capacity, solubility, and water absorption index) and organoleptic properties (taste, aroma, viscousity, visual appeal) (Zhang et al., 2014). TCPMs are applied often with the intention to obtain that sort of balance during the production of complementary meal ingredients (CMIs) for weaning meal preparation, but they could paradoxically also contribute to the loss of significant amounts of essential nutrients, especially limiting essential amino acids (lysine, tryptophan and threonine) and some micronutrients (vitamins and minerals), whiles failing to improve protein digestibility significantly and the satisfactory elimination or reduction in the contents of antinutritional factors (Oghbaei & Prakash, 2016; Rutherfurd & Moughan, 2012).

Cereals are described as the edible grains or seeds of the grass family of plants (Gramineae), which provide the bulk of the calorie intake of humans and animals alike in developed and developing countries (DCs) (McKevith, 2004). Wheat, rice, maize, sorghum, millet, barley, oat, and rye remain the most widely cultivated and consumed cereals in the world, but maize, sorghum and millet are much more important food crops in sub-Saharan Africa (SSA). The tropical cultivars of these cereals are rich sources of carbohydrates (starch and fibre), fats, minerals, vitamins, healthful phytochemicals, and some appreciable amounts of proteins (Torbica et al., 2020). There are twenty proteinogenic amino acids in foods in addition to an array of non-proteinogenic AAs. Of these 20, nine of them are classified as essential or indispensable because they cannot be produced in the human body (in vivo) naturally from other biomolecular precursors in adequate or excess supply (de novo) (Bindels & Symposium, 1996; Coelho-Junior et al., 2020; Wu, 2016). These nine EAAs are lysine, tryptophan, threonine, methionine, leucine, isoleucine, valine, phenylalanine, and histidine which must be provided through diet (Semba et al., 2016). However, most of these cereals lack nutritionally adequate amounts of the essential amino acids (EAAs) or indispensable amino acids (IAAs), which therefore need to be provided through diet, especially the limiting EAAs lysine, tryptophan, and threonine. Lysine is the first limiting EAA in all these cereals (ICAAS, 2020; Leinonen et al., 2019). Animal source proteins are considered superior to plant source proteins because they are richer in the diversity of key essential amino acids (branched-chain essential amino acids, BCEAA; sulphur-containing essential amino acids, SCEAAs and limiting essential amino acids, LEAAs profile) and exhibit higher protein digestibility (Bailey & Stein, 2020; Joye, 2019; van Vliet, Burd, & van Loon, 2015; Wu, 2016). Various EAAs have been shown to be involved in the master growth regulation pathway (human growth mechanism), the underlying mechanism targeted by rapamycin complex C1 (mTORC1) (Laplante & Sabatini, 2012; Pang et al., 2014; Semba et al., 2016). The BCEAAs include leucine (the most characterized EAA sensed by mTORC1), isoleucine and valine whiles methionine and cysteine are the SCEAAs (Brosnan &

Brosnan, 2006; Coelho-Junior et al., 2020; Holeček, 2018). Deficiencies in specific EAAs such as leucine alter anabolism or synthesis of proteins and lipids as well as cellular growth, thus affecting linear and ponderal growth of children through the constraints imposed on bone growth (chondoral growth plate regulated by mTORC1) (Kim et al., 2009; Laplante & Sabatini, 2012).

Cereal protein quality depends on the composition (profile or types of AAs and their quantities) and digestibility of the cereal proteins (Joye, 2019). Consumption of predominantly cereal-only-based complementary meals is widespread amongst children under five years in resource-poor settings in DCs and LMICs, resulting in Kwashiokor, a clinical manifestation of protein-energy malnutrition (PEM) mainly due to poor protein ingestion (utilizable or digestible dietary protein and AAs), poor digestion (dietary amino acids), poor ileal absorption (available amino acids) and/or assimilation (Otten, Hellwig, & Meyers, 2006; Rutherfurd & Moughan, 2012; Semba et al., 2016; Uauy et al., 2016). Besides the relatively poor quality of cereal proteins due to the inadequacy of some EAAs and the limiting EAAs (lysine, threonine, and tryptophan), some cereal proteins have very poor digestibility (digestible dietary amino acids). This is especially so with the storage proteins (kafirins) in sorghum due to high hydrophobicity, grain structure, high isopeptide and disulphide cross-linking during wet cooking, and antinutritional factors (ANFs) such as protease inhibitors, polyphenols, tannins, and phytates (Duodu et al., 2002; Duodu, Taylor, Belton, & Hamaker, 2003; Joye, 2019; Rutherfurd & Moughan, 2012).

Efforts at addressing poor cereal protein quality include the application of traditional cereal processing methods (TCPMs) such as fermentation and germination, genetic engineering, and fortification of cereal products with limiting EAAs (lysine, threonine and tryptophan) and other EAAs (Chaves-López, Rossi, Maggio, Paparella, & Serio, 2020; Galili & Amir, 2013; Joye, 2019; Le, Chu, & Le, 2016; Nkhata, Ayua, Kamau, & Shingiro, 2018; Oghbaei & Prakash, 2016; Saleh et al., 2013; Suri, Tano-Debrah, & Ghosh, 2014). TCPMs may exert their quality-improving influence on cereal protein by enhancing protein digestibility, increasing AAs yield, and decreasing ANF contents (Oghbaei & Prakash, 2016). Protein quality is currently being evaluated using the newly recommended digestible indispensable amino acid score (DIAAS), thus replacing the protein digestibility-corrected amino acids score (PDCAAS) system which has been in use since the turn of the 21st century (FAO, 2013; Ghosh, 2016; Joye, 2019; Leser, 2013; Schaafsma, 2000). The DIAAS method is based on a comparism between the level of all digestible EAAs in the protein content (per gram) of the test food material and the level of those digestible EAAs in a reference protein such as egg albumin or milk proteins. The limiting essential amino acid (LEAA) in the test protein is then used in the computation of the DIAAS (FAO, 2013; Ghosh, 2016; Leser, 2013; Rutherfurd, Fanning, Miller, & Moughan, 2015). With this new protein quality evaluation formular or approach, the relative cereal protein quality of various CMIs and other foods can also be compared, rated, and classified as good sources of proteins or not. Based on this new formular, most cereals and pseudo-cereals assessed so far are rated as poor protein quality sources due to their suboptimal essential amino acid contents (LEAAs, SCEAAs, BCEAAs) and protein digestibility drawbacks (Cervantes-Pahm, Liu, & Stein, 2014; Han et al., 2019; Joye, 2019).

2.2.5.3 HFRUP Indicators as Potential Risk Factors of Child Undernutrition

Habitual food resource utilization practice (HFRUP) is operationally defined in this study as any activity carried out routinely in the domestic or home setting during the production of complementary meal ingredients (CMIs) such as flour and dough, used for the preparation of complementary meals for infants and young children. As a novel construct conceived for this study, it was also operationally defined as the indigenous household choices made and/or domestic unit operations used routinely in the processing of staple cereals into complementary meal ingredients (CMIs), the storage or preservation methods, and/or cooking techniques used for the preparation of complementary meals for infants and young children. These may include the preferred choice of cereal type (maize, sorghum, millet, or rice), CMI form (flour, fresh dough, and fermented dough), dough storage duration, dough storage container types preferably used often, and source of dough (homemade or otherwise) among others. Cultural norms and traditions, religious beliefs, heritage, socio-economic conditions, and exposure or otherwise to technological advancements may have an influence on HFRUPs (McLaughlin, Tarasuk, & Kreiger, 2003; Smith, Dunton, Pinard, & Yaroch, 2016).

The context-specific idiosyncracies of various households, communities, and societal settings in DCs appear to have an influence on the nutritional status of infants and young children (Khanam, Shimul, & Sarker, 2019). Presumably, routine attitudes based on the body of knowlede held in various resource-limited populations, influence their practices and behaviours with regards to food resources (HFRUPs) and could then potentially have effects on the adequacy and quality of food intake of their infants and young children. Even in similar settings, some children exposed to the same debilitative conditions are found to be resilient against the adverse health outcomes that other children become victims of. Positive nutritional deviance has been explored by some researchers to help understand some of the contextual factors that tend to be protective of some children against undernutrition whiles others yield to the risk factors of poor child nutritional status. The current understanding is that positive deviance in child anthropometric growth is not a simple converse phenomenon (Saaka & Mutaru, 2014).

2.2.5.4 IYCF Indicators as Putative Determinants of Child Undernutrition in DCs

The United Nations Children's Fund (UNICEF) in partnership with the World Health Organization (WHO), and other experts in maternal and child nutritional health developed a set of fifteen (15) indicators to aid the simple, valid, and reliable assessment, evaluation, and monitoring of infant and young child feeding practices (Daelmans, Dewey, & Arimond, 2009; Marriott, White, Hadden, Davies, & Wallingford, 2012; WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2010). Analytical cross-sectional surveys in DCs and LMICs often employ single or repeated 24HDRs in nutritional epidemiological studies, to measure the eight (8) core infant and young child feeding (IYCF) practice indicators namely timely intiation of breeastfeeding (TIBF) or early initiation of breastfeeding (EIBF), exclusive breastfeeding (EBF), continued breastfeeding at year one (CBF@1), timely introduction to complementary feeding (TICF), minimum meal frequency (MMF), minimum dietary diversity (MDD), minimum acceptable diet (MAD), intake of micronutrient-rich foods (Vitamin A and iron-rich foods) (WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2008). Though these dietary exposure measurement methods have acknowledged limitations due to the complex nature of diet or food itself and measurement errors arising from possible recall bias, the conventional use of data from self-reported food intake assessment methods remain widely prevalent amongst nutritional epidemiologists. They are also generally considered to be validated, reliable, and pragmatic currently for the purposes of NER studies in resource-limited settings in DCs (Brouwer-Brolsma et al., 2017; Shim et al., 2014; White et al., 2017). MMF serves as a proxy measure for adequate energy intake from non-breast milk sources whiles MDD serves as a proxy measure for micronutrient density or adequacy of foods and liquids other than breast milk (Habte & Krawinkel, 2016; WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2010). TICF conceptually measures the timeliness of the inception of complementary feeding (CF), in that growth faltering was found to predominantly occur during CF when breast milk alone was not enough to provide the required nourishment for infants and young children (Victora et al., 2010).

The IYCF indicators are routinely used to report on the prevalence and trends of food intake around the world amongst infants and young children especially in DCs or LMICs (Daelmans et al., 2009; White et al., 2017). The putative hypothesis is that these indices as measures of child food intake, are associated with nutritional status of children. Several studies have been in sync with this postulate but there are equally a significant array of inconsistencies, partularly between the individual indicators and the measures of child nutritional status across similar settings in DCs and LMICs (Anin, Saaka, Fischer, & Kraemer, 2020; Reinbott et al., 2015). The new school of thought is that aggregate or composite child food intake indices (CCFIs) developed from these individual indicators, would be plausibly more reflective of the various dimensions of child food intake. A good number of studies are churning out composite indices from these WHO/UNICEF IYCF indicators, but they are currently mostly based on discretionary criteria, making them somewhat incomaparable across different and even similar study population settings. The inconsistencies and ambiguities in the NER literature about the associations between the IYCF indicators and child nutritional status continues to garner and drive more interest in researching into this putative causal relationship (Reinbott et al., 2015).

2.2.6 Nutritional Epidemiology: Epistemological Paradigms, Historical Perspectives, and Impact on Public Health Nutrition

Epistemologically, there are two main schools of thought about the measurement approaches to food or nutrient intake as the main exposure variable of interest and diet-related health outcomes in nutritional epidemiological research (NER) studies. These are the reductionist paradigm and the holistic paradigm (Fardet & Rock, 2014, 2015; Fardet & Rock, 2016; Hoffmann, 2003; Jacobs, Tapsell, & Temple, 2011; Michels, 2003). The reductionist paradigm is of the view that food or diet is made up of several constituent nutrients and non-nutrients which perform different roles metabolically with unique underlying mechanisms in determining the health of humans and other living organisms (Fardet & Rock, 2014, 2015). The holistic paradigm is of the view that even though food or diet is made up of several constituent nutrients and non-nutrients which perform different roles metabolically with unique underlying mechanisms in the health of humans and other living organisms, the constituents act in synergy and not in isolation (Jacobs et al., 2011; Jacobs & Tapsell, 2013). This means nutritional roles of food or dietary intake in the health outcomes of living organisms and humans should be viewed as a whole. This ecological approach, also dubbed the Eastern philosophical perspective to food and nutrition finds expression in Chinese and Indian medical and pharmacological philosophy towards diseases. The state of health is perceived by the patrons of holism as an ecological physiological state, which can only be maintained or restored into harmony or homeostasis after experiencing any form of perturbation, by whole medicines or foods (Cheung, Kwan, Chan, Sea, & Woo, 2016; Fardet & Rock, 2015). The holistic view is subscribed to by nutritional scientists and researchers who are strong advocates of studying dietary patterns, lifestyles, and behaviours as a measure of food intake such as amongst vegetarians and patrons of Mediterranean diets (Jacobs et al., 2011; Jacobs & Tapsell, 2013). In their opinion, food or diet is a complex mixture of various constituents and thus individual nutrients cannot be simply analyzed on the premise of a linear cause-effect relationship which is rather applicable in the drug trial paradigm (Fardet & Rock, 2014; Jacobs & Tapsell, 2013; Satija et al., 2015).

The reductionist paradigm, also dubbed as the Western philosophical approach to food and nutrition, continues to dominate owing to the discovery of individual nutrients such as vitamins in the early nineteenth century, the rapid advances in nutritional science knowledge about individual nutrients, and other healthful non-nutritive constituents of food, coupled with recent advances in the analytical laboratory chemistry methods (omics technologies) for separating, identifying, and quantifying very small biologically active molecules in foods (foodome and food metabolome) and food-related biological systems (Carpenter, 2003; Cheung et al., 2016; Cifuentes, 2012; Mozaffarian, Rosenberg, & Uauy, 2018; Semba, 2012; Ulaszewska et al., 2019). FAO has recently endorsed a new method of evaluating protein quality called Digestible Indispensable Amino Acid Score (DIAAS) to replace the former system called Protein Digestibility-Corrected Amino Acid Score (PDCAAS) (FAO, 2013; Joye, 2019; Leser, 2013; Wolfe, Rutherfurd, Kim, & Moughan, 2016). One of the key epistemological positions for advancing this new method of evaluating protein quality in foods is that constituent nutrients and non-nutritive bioactive biomolecules should be examined individually with regards to their metabolism and functions in the human body in the light of their actual and/or potential effects on human health. Food product labels should as much as much possible indicate the constituent nutrients and bioactive non-nutrients and not just the ingredients for the product formulation (FAO, 2013; Ghosh, 2016; Joye, 2019; Leser, 2013; Wolfe et al., 2016). The unilateral influence of a single nutrient like lysine, a limiting essential amino acid in cereals, on the linear and ponderal growth of infants and young children in DCs and LMICs, is indicative in addition to the many other reasons why the reductionist paradigm may continue to dominate the methodological approaches to food and nutrition research (Hussain, Abbas, Khan, & Scrimshaw, 2004; Mozaffarian et al., 2018; Uauy et al., 2015). Generally, the traditional quantitative or positivist orientation of the principles guiding the conduct of epidemiological studies of infectious diseases lends itself to nutritional epidemiological studies too, where causal inferences and interpretations are the ultimate goals of most NER studies (Broadbent, 2013; Hansson, 2014). Given the influence of the dichotomy of philosophical perspectives on the relationships between food intake and health status of individuals and defined populations, other researchers have suggested an integrated, multidisciplinary and/or interdisciplinary approach to addressing research questions in nutritional epidemiology, as criticisms against its methodological approaches are unrelenting (Archer et al., 2015; Archer, Lavie et al., 2018; Archer, Marlow et al., 2018; Boeing, 2013; Satija et al., 2015; Tapsell, Neale, Satija, & Hu, 2016).

The impact of the nutritional sciences and nutritional epidemiological studies on public health nutrition, and by extension human population health globally in the 20th and 21st century is well documented (Carpenter, 2003). From the earliest recorded evidence of a randomized control trial (RCT) with diet on humans in the Bible (Daniel and his friends), to the unravelling of the mystery behind scurvy (Vitamin C deficiency disease) in 1747 by Captain James Lind, and the later discovery of vitamins in 1921, through to the conduct of other scientific enquiries into the influence of diet on human health and diet-related diseases in modern times, the lives and health of millions of people have been saved through nutritional epidemiology and public health nutrition interventions (Humphreys, 2009; Michels, 2003; Mooney, Knox, & Morabia, 2014). The contributions of the nutritional sciences and nutritional epidemiology in particular, to the etiology and/or pathogenesis of dietary deficiency diseases such as pellagra, beriberi, Kwashiorkor, scurvy, rickets, phenylketonuria (PKU), anemia, neural tube defect (NTD), and goiter among others are immeasurable, yet these putative dietary diseases and others like diabetes, some cancers, and cardiovascular diseases (CVDs) are still not fully understood till date (Alpers et al., 2014; Stein, 1995). Notwithstanding, nutritional epidemiological research has contributed immensely to the various public health nutrition interventions that have saved millions of lives over the years, reduced morbidity, extended life expectancy, enhanced the quality of life (QoL), wellbeing, and health in general, in both developing and advanced countries (Alpers et al., 2014; Boeing, 2013; Satija et al., 2015). The relatively nascent discipline of nutritional epidemiology continues to develop rapidly as it persistently fends off the myriads of constructive and somewhat debilitative criticisms, especially with regards to the limitations inherent in some methodological approaches to the measurement of dietary intake (Archer, Lavie et al., 2018; Archer, Marlow et al., 2018; Cannon, 2008; Satija et al., 2015).

2.2.7 Pellagra Epidemic: Stigma, Mystery and Misery of a Dietary Deficiency Disease

The stigma, mystery and misery experienced from the pellagra epidemic in the southern regions of the USA between 1900 and 1940, resulted in the four Ds, dermatitis, diarrhea, dementia, and death (Carpenter, 1981; Mooney et al., 2014). Over 100,000 people died of pellagra in the southern states where food availability, access, and variety (dietary diversity) were relatively limited coupled with the period of the introduction of new mechanized attrition mills to replace the gristmills. The new milling technology significantly dehulled and/or degermed the cornmeal to improve the shelf life and visual appeal compared to the so-called obsolete gristmills that instead retained much of the niacin and tryptophan-rich germ and pericarp portions (Marks, 2003; Sydenstricker, 1958). The socio-economic conditions of these southern states mirror the present-day resource-poor settings of most DCs and LMICs where malnutrition (undernutrition) is largely perceived to be a consequence of extreme poverty and underdevelopment alongside the putative risk of morbidity (disease) and the consumption of poor quality, monotonous cereal-based diets (Carpenter, 1983; Müller & Krawinkel, 2005).

However, the seminal epidemiological and clinical research work of Joseph Goldberger and other scientists, precisely uncovered the deficiency of niacin (Vitamin B3) in the predominantly corn-based diets of the poor southerners, as the cause of pellagra (Brenton & Paine, 2007; Sebrell, 1981). The dietary deficiency disease had been erroneously presumed by physicians, public health officials and politicians to be caused by an infectious pathogen or spoiled corn and even failed to notice and/or acknowledge the social epidemiological underpinnings of race, gender, and economic status as risk factors in the etiology and/or pathogenesis of the nutrient deficiency disease (Marks, 2003; Mooney et al., 2014; Rajakumar, 2000). The victims were predominantly African American and over two-thirds were women who lived and worked under very poor conditions in the cotton, tobacco and corn growing countryside of the southern states of the USA (Marks, 2003; Park, Sempos, Barton, Vanderveen, & Yetley, 2000).

It took deliberate public health nutrition interventions premised mainly on the fortification of wheat flour, cornmeal, and grits with niacin (Vitamin B3) to eradicate the dietary disease in the United States by 1950 (Humphreys, 2009; Park et al., 2000). Tryptophan, a limiting essential amino acid (EAA), is a precursor for the synthesis of niacin in the human body (Carpenter, 1983; Friedman, 2018; Krehl, 1981; Park et al., 2000). Nixtamalization, a Mesoamerican ancient technology which involves the boiling of maize grains in alkaline solution (lime solution), is especially common in Mexico and most of Latin America, which aids in the liberation of proteins and also improves the bioavailability of calcium and niacin (Wacher, 2003). The Spanish explorers who took Mesoamerican corn with them from Latin America back home, could have avoided the massively debilitative consequences of pellagra on millions of Europeans, had they been aware of the import and usefulness of nixtamalization commonly used by the Latin Americans to process maize into nixtamal dough, popularly used for the production of delicacies like tortillas (Rajakumar, 2000).

Scientists of today are falling on the lessons from the miserable experiences of the influenza flu pandemic of 1918-1919 and other epidemics of the 20th and 21st century, as historical precedents of the global Covid 19 pandemic, to think outside the box and harness the prowess of modern advances in science and technology to map out very comprehensive mitigating measures to end this pandemic (Gaeta, Fornaciari, & Giuffra, 2020; Martini, Gazzaniga, Bragazzi, & Barberis, 2019; Wheelock, 2020). Perhaps, the various domains of the food utilization dimension of household food insecurity (HFI) in DCs such as household-level food processing and preparation methods, which have been overlooked for the most part of the 20th and 21st century in the fight against malnutrition (undernutrition), holds the panacea to undernutrition in DCs.

2.3 Public Health Relevance of Undernutrition

Given the subjective meanings ascribed to the concept of 'public health relevance' in the scientific literature, it was operationally defined in this study, premised on the scope of issues covered by classical epidemiology and public health nutrition (Bhopal, 2002; Buttriss et al., 2017). In this nutritional epidemiological study, public health relevance was described premised on four main criteria. These are the prevalence (magnitude or burden) and trends of undernutrition; the putative causes, risk factors or determinants of undernutrition; the consequences or effects of undernutrition on infants and young children, and the various public health interventions implemented to address undernutrition as a malady at the various organizational levels of society (local community, national, sub-regional, continental, and global). The main sources of reliable and valid information on the epidemiology and public health relevance of malnutrition (M), hunger (H) and food insecurity (FI) include representative community, national, and regional surveys, and special reports from national and global agencies such as the Ghana Health Service (GHS), Institute of Health Metrics and Evaluation (IHME), Welt Hunger Hilfe (WHH), Concern Worldwide (CW), USAID, UNICEF, FAO, WHO, IFAD, WFP, the World Bank Group, and well-designed and conducted systematic reviews and primary studies (**Table 2.1**) (Buttriss et al., 2017). Relevant nutritional epidemiological and public health nutrition questions were addressed from these sources to highlight the public health relevance of undernutrition. These questions include;

- **i.** How serious is the nutritional health issue in the population (severity, burden, magnitude, or prevalence, and trend)?
- **ii.** Who are the most vulnerable persons, groups of persons, or subjects in the defined population, affected by the nutritional problem (distribution)?

iii. What are the possible causes, risk factors, or determinants of child undernutrition also known as child nutritional status?

iv. What are the consequences, effects, or adverse health outcomes of poor child nutritional status?

v. What has been done or can be done to reduce, prevent, or eliminate the occurrence of poor child nutritional status?

vi. Have certain evidence-based interventions (EBIs) made the situation better or eradicated the adverse nutritional health consequences to justify the efforts, time, finances, logistics, research, and other resources invested?

Table 2.1: Sources of information on malnutrition (M), hunger (H), and food insecurity (FI) at the global, regional, and national levels

Study	**DHS**	**MICS**	**GBD**	**KAP**	**SMART**	**GNR**	**GHS-DHIMS**	**SR & ES**	**GHI**	**SOFI**
Funding/ Facilitators/ Authors	USAID	UNICEF	Bill & Melinda Gates Foundation/ IHME	USAID	Network of Humanitarian Agencies & Governments	Varies: Donors & Philanthropists	GoG & DPs/ Ghana Health Service	Varies	Welt Hunger Hilfe & Concern Worldwide	FAO, IFAD, UNICEF, WFP & WHO
Year Started	1984	1995	1990	2011	2002	2013	2012	Varies	2006	1996
Method of Measurement	Quantitative Survey	Quantitative Survey	Quantitative Survey	Quantitative Survey	Quantitative Survey	Secondary Data Synthesis	Electronic Real-time	Synthesis of ES & R	Aggregate Scores	Cocktail of GPHI
Study Design	Cross-sectional	Cross-sectional	Nested Cross-sectional	Cross-sectional	Cross-sectional	Nested Cross-sectional	Longitudinal	Varies	NA	NA
Age Range	All Ages	All Ages	All Ages	All Ages	U5	All Ages	All Ages	All Ages	U5	All Ages
Purpose	M, H, FI & GPHI	M, H, FI and GPHI	Burden of Diseases, Injuries & RFs	Baseline GPHI for M&E	Nutritional Status & Mortality	Tracking (M&E) Global Nutrition Targets	GPHI	M, H, FI & GPHI	H Food & Nutrition	M,H,FI Food & Nutrition
Target Population	National: DCs & LMICs	National: DCs & LMICs (Women & Children), Men (2011)	Global	Households, Communities & National	National: Communities, Regions & Countries in Crisis	Global	National: Residents in Ghana	Community, National & Global	Global	Global

DHS, Demographic and Health Survey; **MICS**, Multi Indicator Cluster Survey; **GBD**, Global Burden of Disease Study; **KAP**, Knowledge, Attitude and Practice; **SMART**, Standardized Monitoring and Assessment of Relief and Transition; **GPHI**, General Public Health Indicators; **GNR**, Global Nutrition Report; **GHS-DHIMS**, Ghana Health Service-Data Health Information Management System; **SR & ES**, Systematic Reviews and Empirical Studies, **GHI**; Global Hunger Index; **SOFI**, State of Food Insecurity in the World; **NA**, Not Applicable; **IHME**, Institute of Health Metrics and Evaluation; **DPs**, Development Partners; **RFs**, Risk Factors; **GoG**, Government of Ghana; WFP World Food Programme; **U5**, Children under five years, **FI**, Food Insecurity

2.3.1 Prevalence and Trends of Child Nutritional Status (Child Undernutrition)

According to the global nutrition report of 2018 (GNR), 150.8 million and 50.5 million children under five years were stunted or wasted respectively (Development Initiatives, 2018). In 2019, a joint child malnutrition report estimated by the UNICEF, WHO and World Bank Group indicated that 149 million (21.9%) and 49 million (7.3%) children under five years (6-59 months) were stunted or wasted respectively (United Nations Children's Fund (UNICEF), World Health Organization, International Bank for Reconstruction and Development/The World Bank, 2019). Generally, there has been a relatively marginal decline in stunting globally, with South East Asia (SEA) and sub-Saharan Africa (SSA) contributing the most to the slow progress made. Particularly in SSA, even though there has been a decline in percentage terms (38% to 30%) between 2000 and 2017, an increase in the paediatric population in SSA has accordingly shot up the absolute number of children under five years who are stunted (Development Initiatives, 2018). Southern Asia however still ranks first in terms of prevalence rate based on socio-economic classification of the countries of stunted children globally, underscoring the underlying role of poverty in malnutrition (**Figure 2.4**).

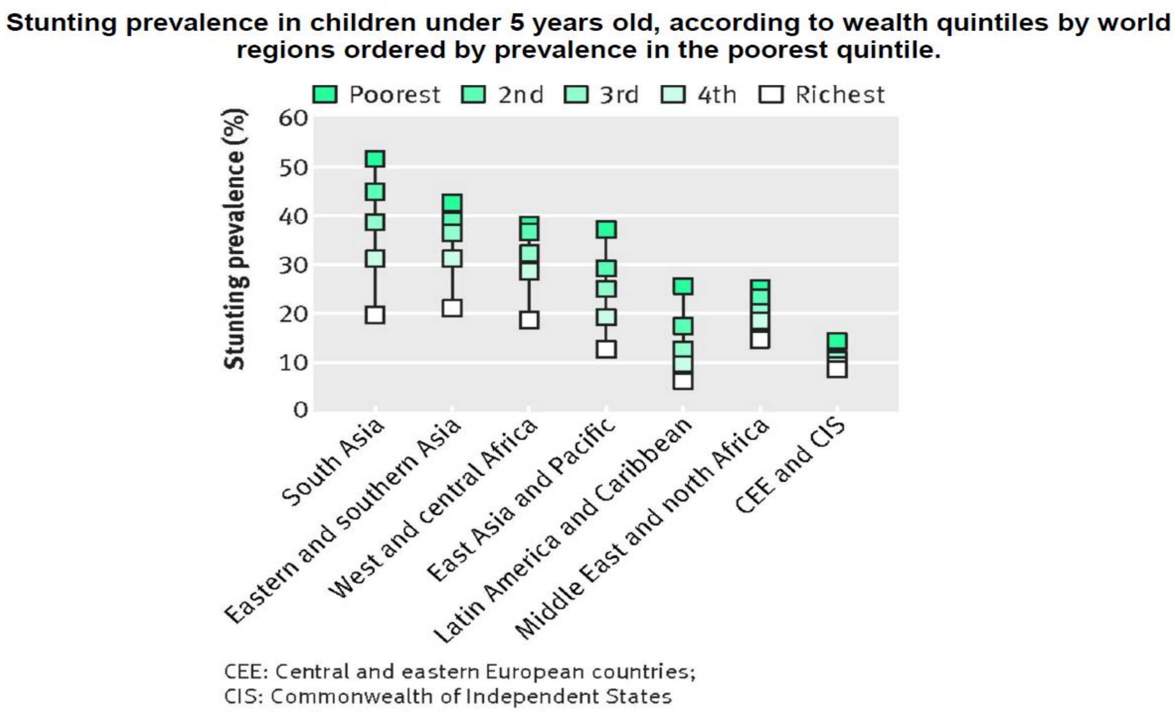

Figure 2.4: Global stunting prevalence among children under five years based on socio-economic classification of 80 countries by UNICEF regions.

Reproduced from Perez-Escamilla et al. (2018)

Visual illustrations of the geospatial data of stunting prevalence in 51 African countries (**Figure 2.5**), depicts that the probability of stunting reduction in countries that met the WHO target between 2000 and 2015 was low in most of west, central, and eastern Africa even though some coastal nations showed rather impressive performances such as in Ghana, Gabon, and Equatorial Guinea. Similarly, the relative annualized decrease in stunting prevalence was in concordance with the trend of improvements in the nutritional status of children under five years in those regions (Development Initiatives, 2018; Osgood-Zimmerman et al., 2018).

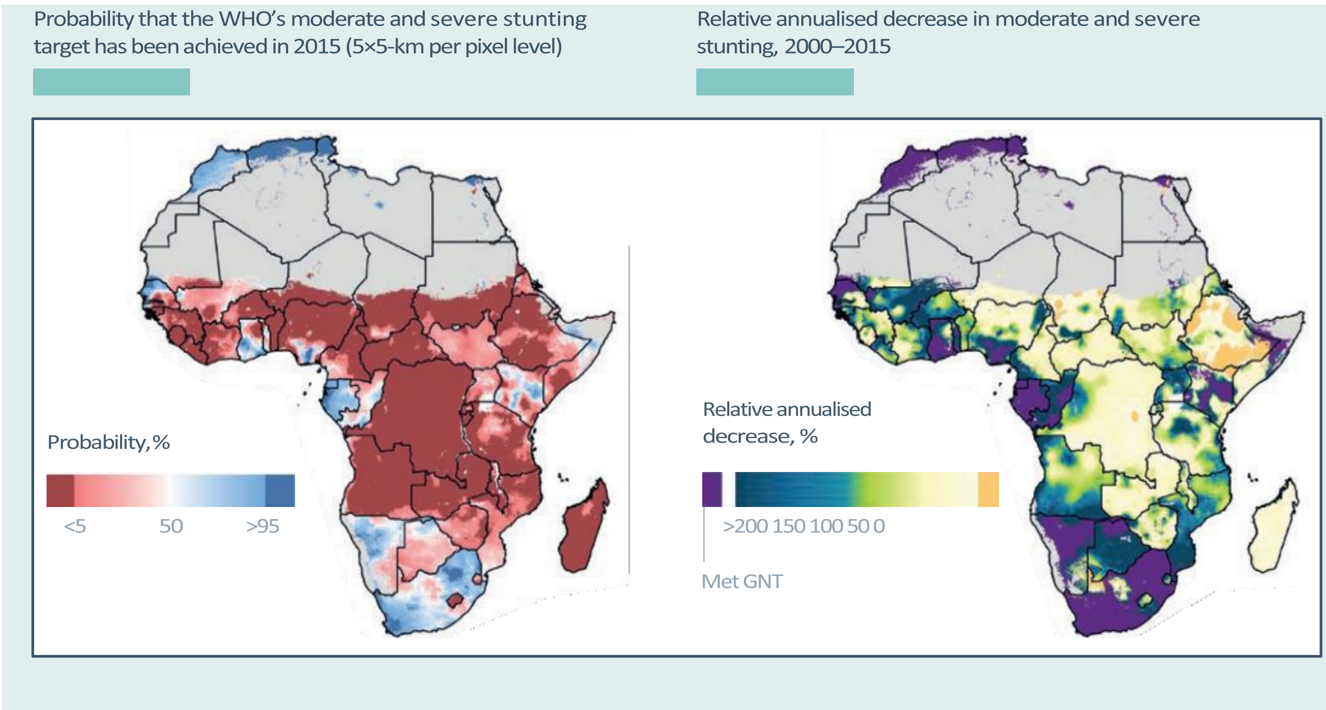

Figure 2.5: Geospatial data illustration of the trends of stunting across 51 African countries (2000-2015)

Reproduced from Osgood-Zimmerman et al. (2018) GNT: Global Nutrition Target.

According to the Global Burden of Diseases, Injuries, and Risk Factors Study 2016 (GBD 2016), 36.6% of children under five years were stunted, 8.6% were wasted and 19.5% were underweight in sub-Saharan Africa (SSA) in 2015 (Gakidou et al., 2017). Almost half (47.2%) of stunted children globally is from three highly populated countries in SEA and SSA namely India (46.6 million), Nigeria (13.9%) and Pakistan (10.7%) (Development Initiatives, 2018). The number of children who are wasted also come from these same regions (SEA and SSA) namely India (25.5 million), Nigeria (3.4 million) and Indonesia (3.3 million). Stunting prevalence on average was reported to be higher amongst boys (25.6%) than girls (22.6%) globally. Similarly, on average

6.8% of boys compared to 5.7% girls were reported to be wasted globally in 2017 (Development Initiatives, 2018).

Southern Asia and sub-Saharan Africa (SSA) had the highest 2019 global hunger index (GHI) scores, at 29.3 and 28.4 respectively, which is in congruence with the prevalence of undernutrition in these regions (Grebmer, 2019). Ghana's GHI score of 14 in 2019 places the country as the best performer of the 15 countries evaluated in the West African sub-region with a classification of moderate hunger (≤9.9 low, 10-19.9 moderate, 20-34.9 serious, 35-49.9 alarming and ≥50 extremely alarming) (**Figure 2.6**) (Grebmer, 2019). The constraints to rapid improvements in the nutritional status of children under five years are attributed to the three northern regions and the Central region in Ghana, where the disparity indices between communities in these areas and other parts of Ghana are quite stark (Ghana Statistical Service, 2018; Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015).

According to the Ghana Demographic and Health Survey (GDHS) findings, stunting status amongst children under five years decreased successively from 35% (2003), 28% (2008) to 19% (2014). Correspondingly, Ghana' global hunger index (GHI) score decreased successively from 28.7 (2000), 22 (2005), 18.3 (2010) to 14 (2019) (Grebmer, 2019). However, another nationally representative survey, the Multi Indicator Cluster Survey Six (MICS 6) conducted in 2017/2018 reported a national prevalence of 18%, 7% and 13% for stunting, wasting and underweight status respectively (Ghana Statistical Service, 2018). This points to a worsening situation of wasting and underweight status contrary to the previous trend in the last decade. According to Black et al (2008), Ghana was one of the 34 countries globally with a high burden of malnutrition. These countries accounted for 90% of the global burden of malnutrition.

In northern Ghana, the estimated prevalence of chronic malnutrition (stunting) is 33.1% compared to a national average of 19% (Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015). According to a survey conducted in five districts in the northern regions of Ghana in November 2013, the prevalence rates of stunting, wasting and underweight amongst children under five years were 23.3%, 2.2% and 21.1% respectively (Saaka, M, Asamoah, L, Hoeschle-Zeledon, I and Appiah, B., 2015). The GDHS 2014 report also indicated the average prevalence rates of stunting, wasting and underweight status amongst children under five years as 33%, 6.3% and 20% respectively in northern Ghana (Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015).

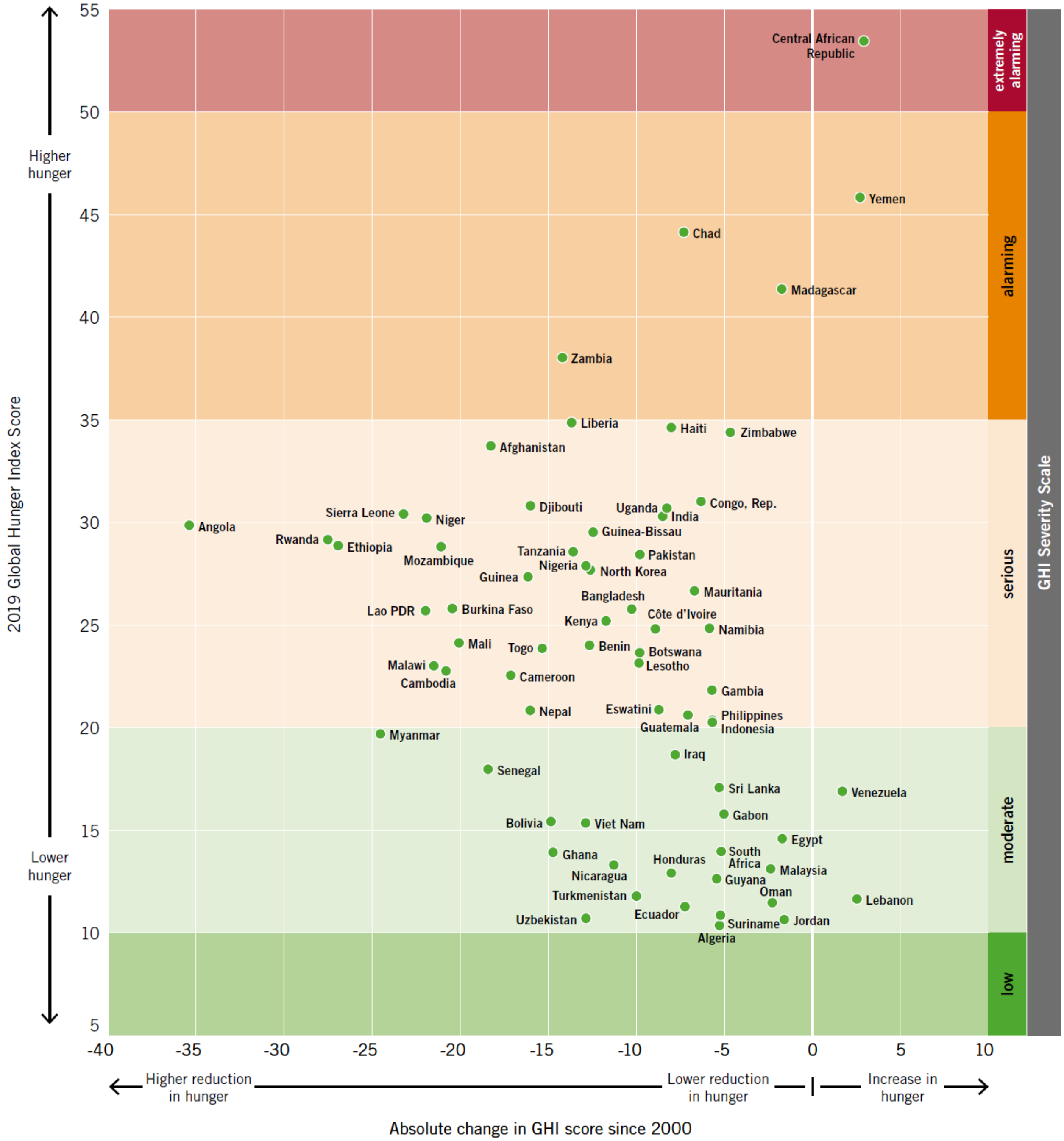

Figure 2.6: 2019 GHI Scores and Country Progression since 2000

Reproduced from Grebmer (2019)

The pervasiveness and seemingly intractable nature of chronic and acute undernutrition in northern Ghana is of immense public health concern that requires urgent attention and sustainable interventions. In the Northern Region of Ghana where many resource-poor communities exist, the synergy between poor dietary or nutrient intake and high morbidity (infectious diseases and mycotoxin exposure), threaten the public health of many nutritionally vulnerable infants and young children. Northern Ghana continues to record the worst indices of nutritional status among children under five nationally**.** Several studies conducted in the northern regions of Ghana in relation to nutrition have sought to determine the prevalence of malnutrition and to establish the associations between nutritional status of young children and various risk factors or causal variables (Groot, Handa, Ragno, & Spadafora, 2020).

2.3.2 Putative Causes or Risk Factors of Child Undernutrition in Developing Countries

Several studies have shown varying associations between child nutritional status and some risk factors and/or covariates classified as proximal, underlying, and distal determinants (Glover-Amengor et al., 2016). The proximal, immediate, or micro-level risk factors and/or covariates identified from various studies include inadequate and low-quality food and/or nutrient intake (IYCF), child morbidity (infectious diseases, child immunity status and mycotoxin exposure), low birth weight (LBW), premature birth, child age and gender (Arthur et al., 2015; Lombard, 2014). The inconsistencies in the NER literature across different and similar settings in DCs, point to the inference that these risk factors and/covariates are context specific. Nonetheless, child age and gender have been reported almost always by most studies as predictors of nutritional status, irrespective of the study design and study settings (Anin et al., 2020; Darteh, Acquah, & Kumi-Kyereme, 2014; Sienso & Lyford, 2018).

The intermediate, underlying, household or meso-level risk factors and/covariates identified from various studies include household food insecurity (HFI), child medical health care, parental factors, child caregiving factors and environmental sanitation and personal hygiene practices (WASH Factors) (Ali, Saaka, Adams, Kamwininaang, & Abizari, 2017; Tariq, Sajjad, Zakar, Zakar, & Fischer, 2018). Various measures of socio-economic status and poor hygiene have been reported frequently as underlying causes of undermatron in DCs (Tette, Sifah, & Nartey, 2015; van Cooten, Bilal, Gebremedhin, & Spigt, 2019). However, given the plethora of indicators used in the assessment of these potential household determinants coupled with the influence of context-specific factors in the aetiology of child nutritional status in DCs or LMICs, the NER literature is replete with myriads of predictors (Shrestha, Six, Dahal, Marks, & Meierhofer, 2020). The distal, macro-level or community risk factors and/or covariates identified from various studies include socio-economic status or community wealth index, agricultural outputs, geographical location of communities, climate change vulnerability index and type of community (rural, semi-rural or urban) among others (Müller & Krawinkel, 2005).

2.3.3 Consequences or Effects of Child Undernutrition in Developing Countries

Child growth failure described by the indicators of undernutrition (stunting, wasting and underweight status) excluding MDM amongst children under five years, was classified as the second leading risk factor for child mortality in SSA, and was attributed to 23% of child death in the sub-region (Gakidou et al., 2017; Osgood-Zimmerman et al., 2018). The risk of all-cause mortality amongst children under five was elevated by the concurrent prevalence of multiple deficits in various forms of undernutrition (McDonald et al., 2013). Undernutrition, the more prevalent form of malnutrition in DC or LMICs is well documented as a strong underlying cause of child mortality, poor physical growth and disability linked to frequent or severe infectious diseases (Black et al., 2008). Impaired linear and ponderal growth potential of children under five years is the most commonly reported effect of undernutrition in DCs (Richard, Black, & Checkley, 2012). The mental, cognitive, motor and intellectual growth and developmental potential of children especially during the first 1000 days, have been copiously reported (Pollitt, Gorman, Engle, Rivera, & Martorell, 1995; Udani, 1992). From a life course approach, impaired socio-economic growth potential of individual children and the cumulative and cyclical consequences and economic losses on whole communities and nations has been documented as well (Martorell, 2017; Martorell & Zongrone, 2012).

2.3.4 Evidence-Based Public Health Nutrition Interventions against Undernutrition

A historical overview of the relationship between nutrition, hunger, and population health, particularly in DCs shows that the priority of world and national leaders after the Second World War until about the early 1970s, was to ramp up the production of staple foods to counter hunger and protein energy malnutrition (Semba, 2008). The attention was shifted to micronutrient deficiency malnutrition (MDM) or hidden hunger (HH) from the 1970s up until the close of the 20th century, when more evidence begun to point towards escalating prevalence rates and the devastating consequences of inadequate intake of micronutrients in DCs or LMICs (Mozaffarian et al., 2018; Semba, 2008). Besides, it appeared that protein intake had become adequate and more of the world's resources especially from global development partners had to be prioritized to address the most pressing needs at the time (Mozaffarian et al., 2018; Semba, 2008).

During the period of the Millennium Development Goals (2000-2015), most efforts on 'Goal One' were focused on improving the food availability and access dimensions of food security with less attention to food utilization (Amarender Reddy, 2016). Many researchers and nutrition policy advocates, recommended a conscientious effort to boost food production and supply, increase food supplementation, promote breastfeeding and complementary feeding programmes, improve sanitation and water supply, improve parental and health care services for children, address diarrhea-related diseases and other infectious diseases, empower women to be part of household decision-making, reduce poverty through strengthened linkage between agriculture and food security, to address the undernutrition challenge particularly in developing countries (Müller & Krawinkel, 2005; Pawlak & Kołodziejczak, 2020). In the wake of the modest progress made prior to 2016 premised on the goodwill demonstrated by global leaders during the Millennium Development Goals era (MDGs: 2000 to 2015) to address hunger and malnutrition, the new Sustainable Development Goals era (SDGs: 2016-2030) has garnered more commitments globally to furthermore need the inputs of nutritional epidemiologists and other key stakeholders to inform more context-specific interventions against malnutrition, in midst of the double burden (Development Initiatives, 2018).

Whiles 'sustainability' is now the buzz word since the launching of the SDGs, all countries across the globe are faced with a herculean challenge posed by the nutrition transitions occurring, with DC or LMICs in particular having to deal with a double burden of malnutrition (Popkin, Corvalan, & Grummer-Strawn, 2020; Wells et al., 2020). The co-existence of more than one of the various forms of malnutrition (undernutrition and over-nutrition) in DCs and the escalating prevalence of over-nutrition (overweight, obesity, diabetes, hypertension, and other related dietary diseases) has driven the formulation of comprehensive nutrition interventions premised on sustainability (Pawlak & Kołodziejczak, 2020). According to the global nutrition report (GNR) 2018, the world is much more resourced than ever before to deal with the menace of malnutrition premised on the increased level of scientific knowledge and access to scientific literature, political will, and commitments to finance evidence-based interventions (EBIs) by global, sub-regional and national leaders and the availability of higher quality data on malnutrition. Stakeholders are positioned now to make better decisions and provide more effective and efficient public health nutrition interventions (Development Initiatives, 2018).

In 2018, USD 21.8 billion was disbursed by ten large donors towards EBIs in DCs (Development Initiatives, 2018). If the USD 9.6 billion estimated as the cost of 90% coverage in 34 countries, for the successful implementation of the top ten evidence-based public health nutrition interventions outlined by UNICEF, WHO and other experts on maternal and child nutritional health is made available, at least 45% of child mortality, 60% child wasting, 20% child stunting would be avoided (Bhutta et al., 2013; Black et al., 2013). These EBIs are to be channelled through policies and programmes at global, regional, and national levels following the identification and prioritization of countries and populations at the highest risk of undernutrition. The nutrition-specific interventions recommended to mitigate the proximal risk factors and secure optimum fetal and child nutrition and development are micronutrient supplementation or fortification, breastfeeding and complementary feeding promotion, dietary supplementation for children, dietary diversification, feeding behaviours and stimulation, treatment of severe acute malnutrition (SAM), disease prevention and management, nutrition interventions in emergencies, adolescent health and preconception nutrition, and maternal dietary supplementation (Bhutta et al., 2013). The nutrition-sensitive interventions recommended by UNICEF and its partners to mitigate the household risk factors include agriculture and food security, social safety nets, early child development, maternal mental health, women's empowerment, child protection, classroom education, water, sanitation, and hygiene (WASH) factors coupled with health and family planning services (immunization, deworming, et cetera) (Bhutta et al., 2013).

With geospatial data and the availability of advanced information technology resources, precision public health nutrition interventions are now a reality (Seal, 2018). Beyond the aggregate outlook which tends to hide the context-specific issues within countries, communities, and specific sub-populations across various geographical locations, nutritional epidemiologists, and public health nutritionists in partnership with other stakeholders can now zero in on precise locations and households faced with specific nutritional challenges, to provide the needed interventions to turn the tide around (Osgood-Zimmerman et al., 2018). Continued scientific research to drive the development of efficient nutrition solutions globally and in DCs in particular, are key interventions. Areas of research interest in the last decade and into the future include investigating the potential roles of mycotoxin exposure, household (traditional) and industrial production of complementary meal ingredients (CMIs), environmental enteric dysfunction (EED), effects of domestic food preparation methods for children, protein and micronutrient intake (quality and inadequacies) from plant and animal sources, epigenetics, gut microbiome, and mechanisms underlying the roles of amino acids in the aetiology and/or pathogenesis of child undernutrition in DCs (Kiprop Choge, 2020; Smith & Haddad, 2015).

In Ghana and in particular the northern regions, interventions implemented by government and its development partners in the last decade include Feed the Future (FTF) and Africa Research in Sustainable Intensification for the Next Generation (Africa RISING), Strengthening Parnerships, Results, and Innovations in Nutrition Globally (SPRING) programmes among others (; Saaka, M, Asamoah, L, Hoeschle-Zeledon, I and Appiah, B., 2015; SPRING, 2018; Yawson et al., 2017). FTF, SPRING, and Africa RISING were geared towards improving the nutritional status of the most vulnerable children. The interventions sought to create opportunities for smallholder farm households to move out of hunger and poverty through sustainably intensified farming systems to improve food, nutrition, and income security especially for women (Saaka, Asamoah, Hoeschle-Zeledon, and Appiah, 2015). The implementation of these and other UNICEF/WHO-recommended public health nutrition intervention policies and programmes coupled with the general improvement in the socio-economic outlook of Ghana, most likely accounts for some of the impressive performances recorded, albeit the disparities between the north and south remain largely (SPRING, 2018).

2.4 State-of-the-Art: Application of Foodomics in Nutritional Epidemiological Research

The suitability of the measurement methods of food, dietary, or nutrient intake as the exposure variable of interest in any nutritional epidemiological research (NER) is key to the validity and reliability of the study findings (Lachat et al., 2016; Subar et al., 2015). However, given the pros and cons associated with any choice of measurement approach available so far, nutritional epidemiological researchers have had to be mindful of the various limitations and their consequences on study conclusions (Lachat et al., 2016). The application of foodomics (food metabolomics) in the assessment of food, diet, or nutrient intake in relation to its consequences on the health outcomes of individuals and populations, takes many forms and approaches. These include the analytical laboratory measurements of dietary biomarkers, nutritional quality/values of selected foods and food ingredients, and the profiling of biochemical changes that take place in food materials during farm harvesting through storage, food processing and domestic food preparation (Beleggia et al., 2011; Beleggia et al., 2016; Cifuentes, 2012; Guasch-Ferré et al., 2018; Kim et al., 2016). Nutrimetabolomics researchers then take over from the point of food consumption or ingestion in relation to health outcomes (Ulaszewska et al., 2019). The application of foodomics (food metabolomics) in the assessment of food, diet, or nutrient intake by proxies or surrogates (potential external dose of intake), as measures of the exposure variable of interest in NER studies, is currently rife alongside the more preferred nutrimetabolomics approach (Capozzi & Bordoni, 2013; García-Cañas et al., 2012; Subar et al., 2015; Ulaszewska et al., 2019). The foodomics and nutrimetabolomics approaches, however, also have their own limitations vis-a-vis the most popularly and widely used traditional dietary intake assessment methods (self-reported dietary intake) in most observational and intervention studies (Keyzer et al., 2011; Naska et al., 2017; Shim et al., 2014; Subar et al., 2015; Ulaszewska et al., 2019).

The differences between foodomics (food metabolomics) and nutrimetabolomics (nutrition metabolomics) corresponds with the differences between the scientific disciplines of food science and nutritional science and the bio-samples that are usually subjected to laboratory examination, using the high-throughput, state-of-the-art omics analytical chemistry set of techniques (García-Cañas et al., 2012; Herrero et al., 2012; Herrero, Ibáñez, Cifuentes, & Bernal, 2009; Morrison et al., 2006; Ulaszewska et al., 2019). Nutritional science begins where food science ends, in that food science addresses the body of scientific knowledge from farm to fork, whiles the discipline of nutrition embodies the study of nutrients and the non-nutritive constituents of foods together with how the nutrients are utilized in the body to maintain life processes, growth, development, health and well-being (Vaclavik & Christian, 2008).

Foodomics researchers are well positioned to harness the high-throughput, sensitivity, and specificity attributes of metabolomics to measure the biochemical, metabolic, or physiological changes (identities and/or quantities) effected on the constituents of food ingredients or diets. Inferences from such laboratory investigations could then be extended (biologic correlate) to the potential health outcomes, well-being or health status of individuals or populations, upon consuming such food ingredients or diets (García-Cañas et al., 2012). Nutrimetabolomics researchers on the other hand, conventionally measure biochemical, metabolic, or physiological changes (identities and/or quantities) effected on dietary biomarkers (food intake metabolites) in the biosamples (blood, urine, et cetera) obtained from the subjects of investigation, in order to draw inferences about the individuals or subjects, from whom the biosamples were drawn (Bub et al., 2016). Due to ethical constraints, costs, research question of interest and other factors, applying foodomics as a first line method of investigating of the potential relationship between dietary intake and health status, may be the most pragmatic and appropriate approach in NER studies. For instance, Kimanya (2008) applied a foodomics approach first to determine the potential dose of exposure to fumonisins from home grown maize amongst predominantly maize-eating adults in Tanzania and subsequently examined the possibility of mycotoxin exposure in maize-based complementary meals as potential predictors of the nutritional status (growth retardation) of infants in Tanzania (Kimanya et al., 2009; Kimanya et al., 2010). Chilaka *et al* (2016) also applied the foodomics approach to investigate the occurrence of *Fusarium* mycotoxins in CMIs from three Nigerian cereals. Similar NER studies as conducted by Kimanya et al (2010) were undertaken in

Tanzania, Benin, Guinea and other similar LMIC settings, but were carried out using the nutrimetabolomics approach, with blood samples of the children taken as biosamples to investigate the dietary intake biomarkers of mycotoxins (Gong et al., 2004; Gong, Watson, & Routledge, 2016; Lombard, 2014; Shirima et al., 2013; Watson, Chen, Sylla, Routledge, & Gong, 2016). Beleggia et al (2011) applied food metabolomics to profile changes in the nutritional and non-nutritional constituents of cereal products during processing and cooking and discussed the potential implications of the molecular transformations that occurred as correlates of consumer health (Beleggia et al., 2016).

2.4.1 Food Metabolome and Foodomics (Food Metabolomics)

From the perspective of food or dietary material (biosample) as a whole or partial organism (plant or animal source foods), food metabolome has been defined as the complete set of dietary metabolites or food constituents in any food material (Cevallos-Cevallos & Reyes-De-Corcuera, 2012; Wishart, 2008). Alternatively, from the perspective of humans as host organisms of a wide array of food metabolites contributed to the human metabolome from foods eaten and other sources of metabolites (drugs, pollutants, etcetera), it is viewed as the sum of all the possible metabolites derived from the digestion of foods or diets, their absorption in the gastrointestinal tract, and the eventual biochemical transformations that take place in the human being together with its constituent microbiome (Bub et al., 2016; Cevallos-Cevallos & Reyes-De-Corcuera, 2012; Scalbert et al., 2014; Wishart, 2008). An analytical assessment of any aspect of the food metabolome, provides insightful inferences that can be correlated to the potential consequences on the health status of individuals and defined populations (Brennan & Hu, 2019; Scalbert et al., 2014; Ulaszewska et al., 2019).

Conventional food compositional analysis involves several separate analytical chemistry methods to assay the constituent proteins, fats, carbohydrates, fiber, vitamins, minerals, and non-nutritive bioactive compounds (James, 1995). Foodomics (food metabolomics) however, has been defined as the application of metabolomics (advanced high-throughput analytical omics techniques combined with bioinformatics) in food systems ranging from farm to fork, for the purposes of studying nutrition and dietary-related health outcomes (**Figure 2.7**) (Cifuentes, 2012; Ibáñez et al., 2015; Kim et al., 2016; Wishart, 2008). Metabolomics refers to the study of endogenous and exogenous metabolites (low-molecular-weight molecules less than 1 kilo Dalton) in living organisms, organs, tissues, cells, biofluids, biosamples (blood, urine, milk, feces, et cetera) or any biological material such as food (Collins et al., 2019; Nalbantoglu, 2019).

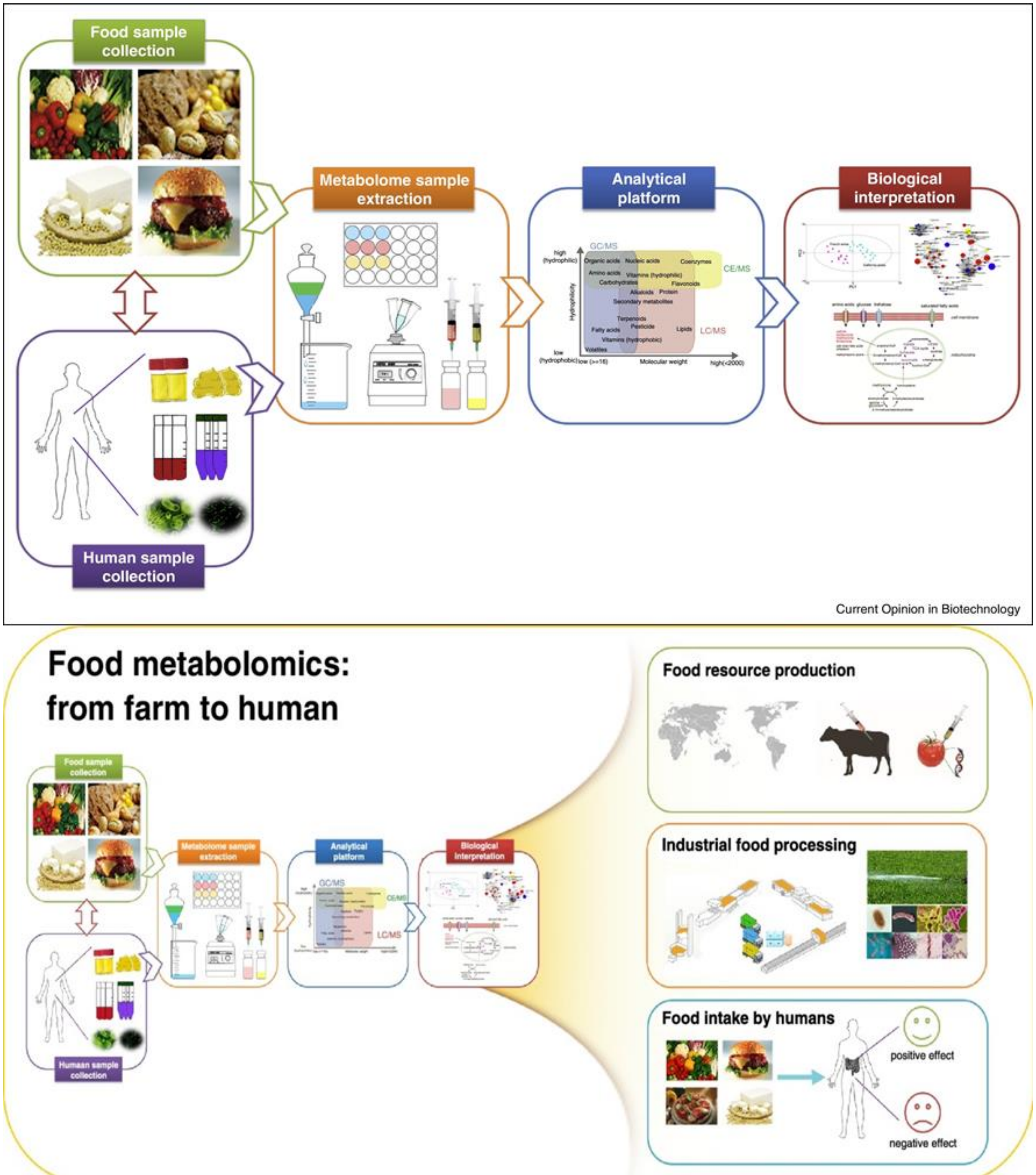

Figure 2.7 Application of food metabolomics in food systems and nutritional epidemiology

Reproduced with permission from Kim et al. (2016).

In food metabolomics (foodomics), metabolites such as amino acids (AAs), sugars, fatty acids, vitamins, minerals, phenolics, tannins, and all kinds of bioactive nutritive and non-nutritive constituents of various food materials containing biomarkers or biochemical indicators of food, are examined comprehensively to objectively and precisely identify and/or quantify these metabolites (Adebo et al., 2017; Kim et al., 2016; Nalbantoglu, 2019; Ulaszewska et al., 2019). The issues of interest in food systems may include but not limited to the effects of food production and processing methods on food safety, food quality, nutritional quality, food traceability, food bioactivity, organoleptic or sensory properties of foods or food ingredients (food science), and the eventual implications of these changes upon consumption of the food, diet, or nutrients (dietetics and nutrition) on the well-being and health status of individuals and/or defined populations at the molecular and sub-molecular levels (Capozzi & Bordoni, 2013; Diez-Simon, Mumm, & Hall, 2019). In this NER study, foodomics was applied to determine the quantitative effects of TCPMs on the nutritive and non-nutritive (ANFs) constituents of cereal ingredients for the purposes of biologically correlating the potential consequences of the debilitative or facilitative changes in the cereal nutritional quality, on the nutritional status of children in the Northern Region of Ghana.

2.4.2 Analytical Laboratory Methods: Gas Chromatography-Mass Spectrometry (GC-MS) and Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

GC-MS, LC-MS and capillary electrophoresis (CE) are currently the most robust, sensitive, specific, high-throughput and rapid analytical techniques for the separation, identification and quantitative analysis of biological molecules (metabolites) in complex biological matrices such as food (Barderas et al., 2011; Cifuentes, 2012). Despite some peculiar limitations of each of these state-of-art analytical techniques, their wide applicability to myriads of metabolites of varying chemical and biological characteristics, makes their resourcefulness to any modern analytical laboratory unparalleled (Cifuentes, 2012; Jacobs, van den Berg, & Hall, 2020). Acceptable analytical chemistry methods used in the analysis of food and food-related constituents continue to evolve over the years, but the official methods for quantitative and qualitative analysis of the major and minor food constituents (nutritive and non-nutritive), still remain the reference methods for validation (James, 1995). The development of advanced, high-throughput analytical techniques and instrumentation (semi-manual and fully automated), continues to provide food analysts, nutritional scientists and other basic and applied bioscience researchers more capacity to undertake research studies within much shorter times at relatively lesser cost simultaneously with higher precision, sensitivity, specificity, validity, reproducibility and many other advantageous attributes (Adebo et al., 2017; James, 1995; Lisec, Schauer, Kopka, Willmitzer, & Fernie, 2006; Pitt, 2009).

Advanced molecular separation methods such as ultra high performance liquid chromatography (UHPLC), gas chromatography (GC) and capillary electrophoresis (CE) coupled with bioinformatics and advanced molecular detection technologies/instrumentation such as high-resolution mass spectrometry (MS), nuclear magnetic resonance (NMR), fourier transformation infrared spectroscopy (FTIRS) and ultraviolet (UV)/ visible light absorbance, flouresence or luminesence, have led to an explosion in the amounts and quality of analytical laboratory outputs applicable to food and nutrition-related health research (foodomics and nutrimetabolomics) (Barderas et al., 2011; Capozzi & Bordoni, 2013). The state-of-the-art separation, analytical detection, identification and quantification capacities of LC-MS/MS and GC-MS for low-molecular weight small molecules or metabolites, less than 1 kilo Dalton (metabolomics) is being harnessed and exploited in the novel foodomics and nutrimetabolomics sub-disciplines (Beleggia et al., 2011; Brennan & Hu, 2019; Capozzi & Bordoni, 2013; Cifuentes, 2012; Guasch-Ferré et al., 2018; Ulaszewska et al., 2019).

In GC-MS set ups, the mixture of volatile and thermally stable biological compounds or metabolites are separated on the basis of relative vapour pressure and polarity (ion-exchange of the ionized and vapourized metabolites) between a gaseous mobile phase (inert carrier gas) and a liquid (GLC) or solid (GSC) stationary phase (packed column or capillary column), and the subsequent transfer of the ionized and vapourized metabolites to be further separated and detected as spectral fragmentation patterns (mass-to-charge ratio) by mass spectrometry (MS) (Kopka, Fernie, Weckwerth, Gibon, & Stitt, 2004; Pitt, 2009). Mass spectrometers operate on the principle of converting metabolites into ions (charged molecules) following the application of an appropriate ionization technique such as electrospray ionization (ESI), electron ionization (EI), chemical ionization (CI), atmospheric pressure chemical ionization (APCI), matrix assisted laser desorption ionization (MALDI) or atmospheric pressure photoionization (APPI) to the derivatived constituent metabolites (Nalbantoglu, 2019; Rosenberg, 2003). Metabolites with good thermostability and molecular weight (MW) below 500 Da are well-suited for GC-MS analysis, as decomposition of the parent metabolites following the ionization procedure would be counter-productive in GC-MS (Roessner & Bowne, 2009). Derivatization involves the chemical transformation (alkylation, acylation and silylation) of the parent constituent metabolites in the analytical sample into derivative compounds that have the attributes of enhanced volatility and decreased polarity (reduced ion suppression), allowing for their rapid separation and feasible ionization of volatile organic compounds (VOCs) such as fatty acids, alcohols, aldehydes, furans, pyrroles, terpenes and ketones (Nalbantoglu, 2019; Rodrigues et al., 2018; Zarate et al., 2016).

The general workflow of GC-MS analysis involves six main steps (Kopka et al., 2004; Lisec et al., 2006; Nalbantoglu, 2019; Rubert, Zachariasova, & Hajslova, 2015).

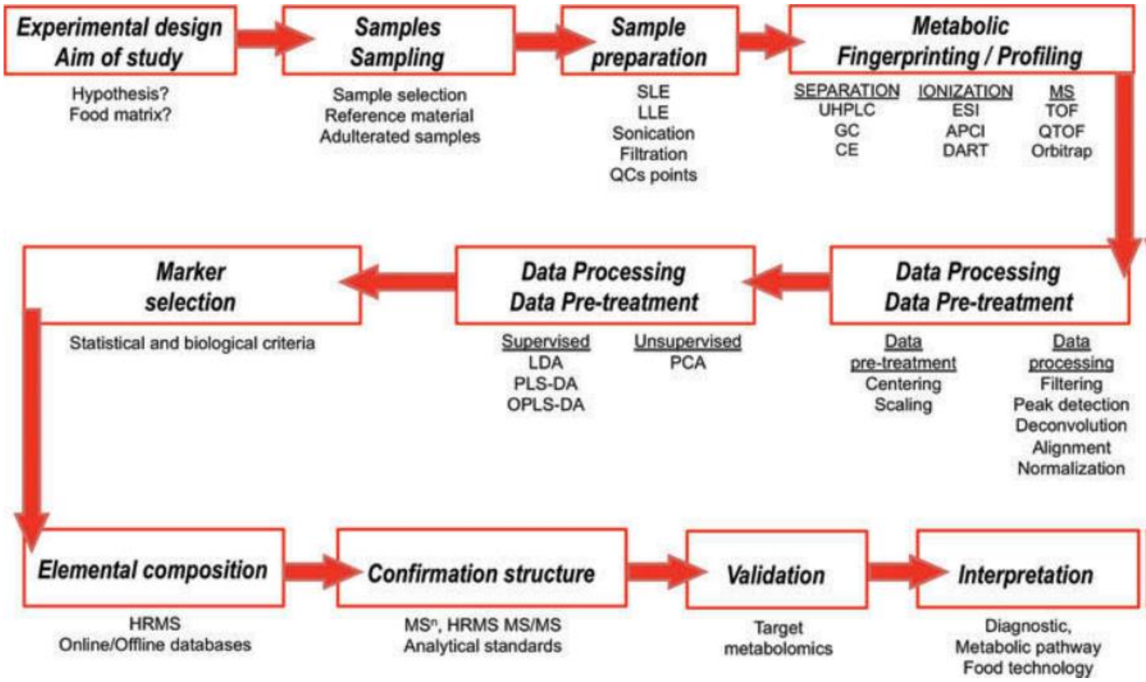

Figure 2.8: General Process Workflow of Metabolomics

Reproduced with permission from Rubert et al. (2015).

These include extraction of the mixture of metabolites (polar and non-polar) from the analytical food material matrix, derivatization to render the metabolites volatile, gas chromatographic (GC) separation of the derivatized metabolites (controlled gas-flow, temperature settings and standardized column specifications), and ionization of the separated metabolite derivatives to generate highly reproducible spectral fragmentation patterns from their molecular ions (Kopka et al., 2004; Tranchida, 2019). These molecular ions are then transfered from the GC exit channel through a vacuum for detection of the metabolite or compound-specific mass spectral fragmentation patterns by mass-detection devices (quadrupole, QUAD; ion-trap technology, TRAP; time-of-light, TOF and orbitals detectors) and the evaluation of the identity of each metabolite by matching its chromatographic retention time (CRT) with mass-spectral fragmentation patterns based on mass to charge ratio (m/z) of known compounds available in standardized databases (Kopka et al., 2004; Lisec et al., 2006). Quantification can be carried out based on the response factor and/or relative response factor of the analyte or metabolite relative to an internal standard or a standard solution (known concentration) of the targeted metabolite using a calibration curve (Tranchida, 2019).

In LC-MS/MS set ups, the workflow is similar to GC-MS except that the metabolites in the sample extract is usually not derivatized but instead after exiting the LC unit (liquid mobile phase) based on solubility differentials in the mobile phase, the metabolites (usually larger and more polar than in GC) are introduced into the mass spectral detector unit (MS) in a gaseous mobile phase after ionization (electrospray ionization, ESI; atmospheric pressure chemical ionization, APCI) as a single (MS) or multiples of charged molecules (MS/MS), transportable in an electrical field. These charged molecular ions are detected based on their mass-to-charge ratios and chromatographic retention times (CRT) matched against known mass spectral fragmentation patterns of compounds in standardized databases (Kopka et al., 2004; Pitt, 2009). Absolute quantification when using LC-MS, is best carried out with standard calibration curves (Dahal, Jones, Davis, & Rock, 2011; Kim, Achcar, Breitling, Burgess, & Barrett, 2015).

2.4.3 Application of Foodomics (Food Metabolomics) to Assess Usage Effects of TCPMs on Nutritional Quality of Cereals

Food, food groups, dietary patterns, and individual nutrient intake, conceptually, theoretically, and empirically can be measured directly or indirectly using dietary biomarkers by applying metabolomics and nutrimetabolomics techniques (Brennan, 2013; Brennan & Hu, 2019; Guasch-Ferré et al., 2018). Based on the biological knowledge of the relevant biomolecules (nutritive and non-nutritive metabolites) under different physiological or metabolic conditions, these biomarkers could serve as biologic correlates of food or dietary intake in nutritional epidemiological studies, where biosamples from individuals in a given population are analysed using metabolomics (Brennan & Hu, 2019; Gibbons & Brennan, 2017; Guasch-Ferré et al., 2018; Guertin et al., 2014). However, in foodomics and nutrimetabolomics, the availability of validated dietary intake biomarkers to obtain estimates that can be considered to be accurate, reliable, and valid measures of food or nutrient intake is limited (Corella & Ordovás, 2015; Dragsted et al., 2017).

Alternatively, targeted and untargeted food metabolomics (foodomics) could be employed to measure the constituent metabolites (nutritive and non-nutritive) in particular foods or ingredients (raw, semi-processed or ready-to-eat), to generate a nutrient-adequacy-based dietary quality index (DQI) guided by an a prior criteria, as a proxy measure of the estimated potential nutrient intake, dietary exposure, or dietary habit, instead of analyzing biosamples (blood, urine, feces) from the population subjects (Beleggia et al., 2016; Dalwood et al., 2020; Gil et al., 2015; González-Domínguez, González-Domínguez, Sayago, & Fernández-Recamales, 2020; Koistinen et al., 2018; Marshall et al., 2014; Olza et al., 2019; Saia, Fragasso, Vita, & Beleggia, 2019). Such indirect deterministic approaches to dietary exposure measurement (qualitative and/or surrogate), could then be applied in nutritional epidemiological studies to examine the associations between dietary intake and health-related paediatric outcomes (Dalwood et al., 2020). Various habitual food resource utilization practices (HFRUPs) and/or factors such as choice of food ingredients, cereal processing methods (TCPMs), food packaging, preservation and/or storage techniques, and domestic food preparation methods could affect the nutritional quality of diets or meals prepared at home especially for children under five years (Beleggia et al., 2011; Dewettinck et al., 2008; Griffith, Castell-Perez, & Griffith, 1998; Oghbaei & Prakash, 2016; Poutanen, Flander, & Katina, 2009). Ethical, logistical, study objectives, and other pragmatic reasons could limit the use of metabolomics for the analysis of human biosamples (blood, urine, etc.) from the subjects of interest in a given population when investigating for instance, the effects of processing on the nutritional value of a given food ingredient, and consequently its potential effects on the health or nutritional status of a defined population. In such situations, it would be appropriate to substitute the subjects' biosamples (blood, urine, feces, and et cetera) with food, meal, or dietary samples as proxy measures of the potential external dose of exposure. Predefined nutrient-adequacy-based criteria could be used to generate dietary quality indices (DQIs) of 'significant or non-significant effects' of the processing methods on the nutritional quality and value of the meal or CMI, based on metabolomics analytical laboratory findings on the experimental food samples. In combination with self-reported indices of the usage of such processed food products and/or methods (TCPMs), the nutritional epidemiological significance of the intake of diet made from such food ingredients (CMIs) in question can then be evaluated (Dalwood et al., 2020; Gil et al., 2015).

2.5 Statement of the Research Problem (Justification of the Study)

Public health interventions developed to address malnutrition among children under five years, particularly undernutrition in Africa, contributed to a modest but significant reduction in stunting from 38% to 30% between 2000 and 2018 whiles globally stunting was reduced from 32.5% to 21.9% for the same period (United Nations Children's Fund (UNICEF), World Health Organization, International Bank for Reconstruction and Development/The World Bank, 2019). This accomplishment notwithstanding, the yawning gap or lacuna leaves more to be desired given that stunting amongst children under five years remains high in SEA, SSA, Ghana and the Northern Region of Ghana in particular (Jager, Giller, & Brouwer, 2018). A scale up to 90% coverage of the top ten (10) evidence-based, public health nutrition-specific interventions recommended by WHO, UNICEF and other nutritional health experts against child undernutrition, in the most endemic countries, would be able to explain only about 15%, 20% and 60% of the variance in child mortality, stunting and wasting respectively according to Bhutta et al. (2013). This suggests that there are other potentially significant determinants, risk factors, predictors or covariates that could account for stunting and wasting but are either unknown, overlooked, or widely under-researched (Raiten & Bremer, 2020).

The risk factors or determinants of undernutrition among children in DCs are diverse, multifaceted, and context-specific even though several studies putatively attribute the immediate causes of child undernutrition to poor food intake (low quality and inadequate quantity) and child morbidity (infectious diseases, poor immune status, low birth weight or exposure to mycotoxins) amongst vulnerable children (Arthur et al., 2015; Bhutta et al., 2013; Gong et al., 2016; Müller & Krawinkel, 2005). The quality of food, diet or nutrient intake by infants and young children can be influenced by several factors including processing methods of the complementary meal ingredients (CMIs), habitual food resource utilization practices (HFRUPs), limited dietary diversity and other household food insecurity (HFI) factors (Hotz & Gibson, 2007; Reddy & Love, 1999). Sub-optimal HFRUPs may potentially result in significant reduction in the quality of food intake or losses in essential nutrients (nutritional value) due to household cereal processing methods, complementary meal preparation methods, food ingredient preferences, and food preservation methods among other factors (Ekpa, Palacios-Rojas, Kruseman, Fogliano, & Linnemann, 2019). This should be a major concern for household food insecurity (HFI) and consequently child nutritional status especially in DCs or LMICs. Even though traditional cereal processing methods (TCPMs) such as sun drying, soaking, germination, dehulling, roasting, dry milling, wet milling, and natural fermentation are used routinely, they may have undesirable or debilitating effects on the limited essential nutrients of the cereal dough and/or flour used in the preparation of most complementary meals for infants and young children in developing countries such as in northern Ghana. The almost routine need for nutrient fortification of most, if not all industrially processed paediatric food ingredients affirms the putative effects of processing on the constituents of processed foods (Reddy & Love, 1999; Satyanarayana, Pindi, & singh, 2012).

Even though several nutritional epidemiological studies have explored several conventional risk factors of undernutrition (stunting, wasting and underweight status) amongst infants and young children, no study so far to the best of my knowledge has attempted to apply foodomics (food metabolomics) to investigate the potential roles of the usage of TCPMs on the nutritional quality of complementary meal ingredients (CMIs), as potential determinants or risk factors of undernutrition in Ghana and LMICs in general. This study portends to trigger an interest in exploring other unconventional potential risk factors or determinants of undernutrition such as TCPMs and HFRUPs. These conceivable domains (TCPMs and HFRUPs) of the food utilization dimension of household food insecurity (HFI) have not been given meaningful attention, particularly their conceptualization, operationalization, and measurement in developing countries (DCs) such as Ghana. Such unconventional food-based risk factors within households could possibly account for the knowledge gap that still exists amongst nutritional epidemiologists and public health nutritionists with regards to the development of feasible contextual solutions. Discovering these other potentially significant determinants of undernutrition, could possibly complement the development of other viable ways of combating undernutrition in DCs or LMICs (Raiten & Bremer, 2020). The scientific literature is replete with a significantly varied number of measures for the food availability and access dimensions of HFI on food insecurity, malnutrition, hunger, and undernourishment (Cafiero, Melgar-Quiñonez, Ballard, & Kepple, 2014; FAO, 2013; Maxwell, D., Coates, J. and Vaitla, B., 2013). However, the infant and young child feeding (IYCF) indicators conceived and developed by UNICEF and WHO is are the dominant, validated, and most widely utilized measure of food utilization for epidemiological studies of peadriatic populations. According to White et al (2017) indicators adaptable to population-based assessment of key complementary feeding domains such as responsive feeding, adequate food texture, portion size, and safe food preparation and storage were not addressed during the development of the IYCF indicators, because they were deemed too complex. TCPMs and HFRUPs constitute some of these domains of the food utilization dimension of HFI.

Indicators of infant and young child feeding (IYCF) practices have been widely found to be protective against undernutrition in some settings and therefore postulated to be associated with child nutritional status. These indicators are generally recommended by WHO/UNICEF and other experts in paediatric nutritional health issues, to be useful and cost-effective parameters for monitoring child anthropometric growth and for the identification of paediatric populations at risk of malnutrition in developing countries (DCs). However, given that there are still inconsistencies or no conclusiveness in the nutritional epidemiological research (NER) literature concerning the associations between the individual IYCF indicators and nutritional status (stunting, wasting and underweight) of children in DCs or LMICs, this postulate was also investigated within the context of the Northern Region of Ghana.

3 MATERIALS AND METHODS

3.1 Section Overview

This third major section of the dissertation encompasses the empirical considerations and descriptions of the methodological approaches and procedures adopted in this NER study. The research questions and specific research objectives that guided the scope of the study and the hypotheses that were tested, are presented also under this section of the dissertation. It furthermore provides detailed accounts of how the choice of study method and study designs were implemented. How the relevant quantitative data were acquired for statistical analyses in order to address the purpose of this research are described in detail. The conceptual framework and operational definitions that were used to provide context and comprehensible meanings to the variables investigated, and how inferences were drawn from the variables measured, have also been described in detail in this section of the dissertation. The philosophical, ontological, and epistemological underpinnings that informed and justifies the choice of research method and research designs have been briefly explained as well. The study setting, population of interest, survey sampling method, survey sample size, survey data collection instrument and the data collection procedures for the definitive cross-sectional survey of the study are presented under this section. The experimental cereal samples' collection, samples' handling, or storage, foodomics analytical laboratory procedures, laboratory instruments, laboratory supplies, laboratory data acquisition methods, methods of data evaluation, validation, analyses, and interpretation for addressing the research questions of this study have also been presented under this section. This third section of the dissertation also outlines pragmatic measures adopted to ensure high data quality (reliability and validity) whiles outlining some limitations and challenges faced during the research, for the choices of materials, methods and designs used. The section ends with an account of the ethical clearance compliance and community entry permit protocols used for the study as required of good scientific practice and conduct.

The study was conducted in two phases, the formative, and the definitive phases. The formative study phase was made up of recruitment and training of a field research support team, organization of auxiliary field materials, obtaining ethical clearance, obtaining community entry permit, qualitative pilot study (FGD: focused group discussions and IDIs: in-depth interviews), pre-testing of the draft survey data collection instrument, quantitative pilot cross-sectional survey, trial cereal samples' collection, cereal samples' handling and laboratory protocol optimization trials on the cereal samples collected. The formative study phase informed and guided the development of a context-appropriate and standardized survey instrument (interviewer-administered questionnaire), the cereal samples' collection protocols and optimized experimental foodomics laboratory protocols for the definitive phase of the study. The definitive research study consisted of two main parts, a community-based analytical cross-sectional survey and foodomics (food metabolomics) experimental laboratory analyses parts. The definitive cross-sectional survey provided quantitative data for the measurement of all the independent variables including the main exposure variables of interest (usage indicators of the various TCPMs) and the other explanatory variables (HFRUP and IYCF indicators). The anthropometric measurements provided the data which was used to calculate Z-scores as measures of the primary outcome variables (stunting, wasting and underweight status) of the study population of interest (children 6-23 months). The foodomics experimental laboratory analyses (GC-MS and UHPLC-MS/MS) were performed to qualitatively determine the TCPMs (soaking, germination, dry milling, wet milling only and wet milling cum natural/spontaneous fermentation) that effected nutritionally significant changes in some relevant nutritive and non-nutritive (antinutritional) constituents of the cereal ingredients (soaked grains, germinated grains, dry-milled grains, wet-milled grains and wet-milled grains cum fermentation). A determinant operational criterion, guided by the principles for estimating the recommended daily allowance (RDA) or recommended nutrient intake (RNI) of various food nutrients and components, was used to determine qualitatively which traditional cereal processing methods (TCPMs) were nutritionally significant or not from the foodomics laboratory data. Sun-dried (laboratory-milled) grains served as the control or reference samples for the experimental investigation. Statistical analyses of the cross-sectional survey data were conducted, adjusting for relevant potential and putative confounders where applicable using Statistical Package for Social Science (SPSS) software (Version 25). Arithmetical computations and generation of illustrative charts were conducted with the foodomics laboratory data using Microsoft Excel software (2016 version) following data exportation (chromatograms) from the XCalibur (Thermo Scientific, Germany) and Compass DataAnalytics (CDA) softwares (Bruker Daltonics, Germany).

3.2 Research Questions of the Study

The significance of the main research question and the derivative questions that arose from the formative study and brainstorming on the seemingly intractable problem of undernutrition in northern Ghana, in addition to a critical review of the available literature, are reflective of the appropriateness of decisions made about the purpose of the study, the study population of interest, study design, data collected and how the datasets were analyzed (Farrugia, Petrisor, Farrokhyar, & Bhandari, 2010). The research questions of the study were;

i. What is the prevalence of the IYCF, HFRUP, TCPM and nutritional status indicators in the Northern Region of Ghana?

ii. What is the association between the WHO/UNICEF complementary feeding (CF)-related IYCF indicators and nutritional status (stunting and wasting) of children (6-23 months) in the Northern Region of Ghana?

iii. What is the association between the habitual food resource utilization practices (HFRUPs) and nutritional status (stunting and wasting) of children (6-23 months) in the Northern Region of Ghana?

iv. From the foodomics experimental laboratory data, what are the effects of TCPMs (soaking, germination, dry milling, wet milling and wet milling cum fermentation) on the nutritive and non-nutritive (anti-nutritional) contents of the experimental cereal ingredients (soaked grains, germinated grains, flour, fresh dough, and fermented dough) from maize, sorghum and millet?

v. What is the association between the usage indicators (frequencies, preferences or durations) of the TCPMs that are found to effect nutritionally significant changes in the experimental cereal ingredients, and the nutritional status (stunting, wasting and underweight) of children (6-23 months) in the Northern Region of Ghana?

3.3 Objectives of the Study

The objectives of the study were to;

i. measure the prevalence of IYCF, HFRUP, TCPM indicators and nutritional status indicators (stunting, wasting and underweight) of children (6-23 months) in the Northern Region of Ghana.

ii. ascertain the association between the WHO/UNICEF complementary feeding (CF)-related Infant and Young Child Feeding (IYCF) indicators and nutritional status (stunting and wasting) of children (6-23 months) in the Northern Region of Ghana.

iii. examine the association between habitual food resource utilization practice (HFRUP) indicators and nutritional status (stunting and wasting) of children (6-23 months) in the Northern Region of Ghana.

iv. analyze from foodomics experimental laboratory data, the effects of TCPMs (soaking, germination, dry milling, wet milling only and wet milling cum natural fermentation) on the essential nutritive and non-nutritive (antinutritional) constituents of cereal ingredients (soaked grains, germinated grains, flour, fresh dough, and fermented dough) of maize, sorghum, and millet.

v. examine the associations between the usage (frequencies, preferences or durations) of the TCPMs that are found to effect nutritionally significant changes in the complementary meal ingredients (flour and dough) as determinants of undernutrition (nutritional status) amongst children (6-23 months) in the Northern Region of Ghana.

3.4 Hypotheses of the Study

It was postulated in this study that, TCPMs such as soaking, germination, dry milling, wet milling only and wet milling cum fermentation would result in significant changes (≥10% increases or depletion) in the nutritive and non-nutritive (antinutritional) contents of the experimental cereal samples with consequential epidemiological significance expressed as statistical associations with stunting, wasting and/or underweight status of the children. The usage indicators (frequencies, preferences, or durations) of the TCPMs in the production of complementary meal ingredients (CMIs: flour, fresh dough, and fermented dough) for the preparation of complementary meals for children, was thus postulated to be associated with the nutritional status (stunting, wasting and underweight) of children under five years in northern Ghana. In addition to the usage of TCPMs, the epidemiological significance of IYCF practice indicators and HFRUP indicators as predictors of nutritional status (stunting and wasting) was explored to help identify the paediatric population at risk of undernutrition based on these exposures. The hypotheses tested were:

Null Hypothesis 1 (H_0): There is no significant association between the WHO/UNICEF complementary feeding (CF)-related Infant and Young Child Feeding (IYCF) indicators and nutritional status (stunting and wasting) of children under five years in the Northern Region of Ghana.

Alternative Hypothesis 1 (H_1): There is a significant association between the WHO/UNICEF CF-related Infant and Young Child Feeding (IYCF) indicators and nutritional status (stunting and wasting) of children under five years in the Northern Region of Ghana.

Null Hypothesis 2 (H_0): There is no significant association between habitual food resource utilization practice (HFRUP) indicators and nutritional status (stunting and wasting) of children under five years in the Northern Region of Ghana.

Alternative Hypothesis 2 (H_1): There is a significant association between habitual food resource utilization practice (HFRUP) indicators and nutritional status (stunting and wasting) of children under five years in the Northern Region of Ghana.

Null Hypothesis 3 (H_0): There is no significant difference between the effects of the TCPMs (soaking, germination, dry milling, wet milling, and wet milling cum fermentation) on essential nutritive and non-nutritive constituents of the experimental cereal ingredients (soaked grains, germinated grains, flour, fresh dough and fermented dough) and the control cereal samples.

Alternative Hypothesis 3 (H_1): There is a significant difference between the effects of the TCPMs (soaking, germination, dry milling, wet milling, and wet milling cum fermentation) on essential nutritive and non-nutritive constituents of the experimental cereal ingredients (soaked grains, germinated grains, flour, fresh dough and fermented dough) and the control cereal samples.

Null Hypothesis 4 (H_0): There is no significant association between the usage (frequencies, preferences, or durations) of TCPMs for complementary meal ingredient (CMI) preparation by mother-child pairs and the nutritional status of their children.

Alternative Hypothesis 4 (H_1): There is a significant association between the usage (frequencies, preferences, or durations) of TCPMs for complementary meal ingredient (CMI) preparation by mother-child pairs and the nutritional status of their children.

3.5 Assumptions of the Study

The postulate that informed the main hypothesis of the study (hypothesis four) was premised on the key assumption that, TCPMs could be significant determinants or risk factors of the seemingly intractable menace of undernutrition in northern Ghana, given their routine or habitual usage for the production of complementary meal ingredients (dough and/or flour) used for complementary meal preparation for infants and young children. This assumption is also predicated on the following assumptions;

i. there is a high prevalence of the intake of cereal-only-based complementary meals (made from indigenous staples such as maize, sorghum and millet), characterized by inadequate, limited or depleted levels of macronutrients (carbohydrate, protein and fat) and micronutrients (vitamins, minerals and healthful phytochemicals), together with little or no nutrient-rich accompaniments especially during the lean season of food supply, amongst children under five years in several households and communities in northern Ghana and similar settings in DCs (Adeoti & Osundahunsi, 2012; Oladiran & Emmambux, 2020; Saaka, Wemakor, Abizari, & Aryee, 2015; Suri et al., 2014; Uauy et al., 2016)**.**

ii. Homemade meals from cereal-only-based CMIs and even cereal-legume blended CMIs, have low protein quality due to limiting essential amino acids (LEAAs) such as Lysine, Threonine, Tryptophan and sulphur-containing EAAs (Methionine and Cysteine) needed by infants and young children to avert the development of stunting, wasting and/or underweight status. High prevalence of child morbidity due to repeated infections and/or exposure to mycotoxins may predispose children in northern Ghana and DCs to limited intake and absorption of indispensable amino acids (IAAs) and other healthful nutrients and non-nutritive (antinutritional factors, ANFs) food constituents. Worse still, LEAAs are either absent or inadequate in most cereal-only-based meals (Ghosh et al., 2012; Ghosh, 2016; Lombard, 2014; Millward, 2017; Semba et al., 2016; Suri et al., 2014; Uauy et al., 2016).

iii. studies of resource-poor households and/or communities in northern Ghana have reported low dietary diversity scores (DDS) especially amongst children under five years with a rather highly skewed intake of micronutrient-poor, protein-poor and high-calorie-containing complementary meals (Saaka et al., 2015)**.**

iv. consumption of protein-rich and micronutrient-rich foods amongst children under five years remains poor with as many as 80% fed on predominantly cereal-only-based meals; less than 12% consumption of complete protein source foods (flesh meat, fish and eggs) and only 32.9 % households consumed legumes and nuts as reported in a nutritional epidemiological study in the Northern Region of Ghana (Saaka, Asamoah, Hoeschle-Zeledon, and Appiah, 2015)**.**

v. various household unit operations of traditional cereal processing methods (TCPMs) such as soaking, germination, dehulling, winnowing, sieving, roasting, dry milling, wet milling, kneading and fermentation are customary or habitual practices in households, communities and various regions in developing and emerging countries like Ghana (Oniang'o, Mutuku, & Malaba, 2003).

vi. routine usage (frequencies, preferences, or durations) of TCPMs (exposures) within households could potentially reduce significantly, the quantitative and qualitative nutritional value of constituents such as essential nutrients especially indispensable limiting amino acids including Lysine, Tryptophan, and Threonine in the cereal-only-based complementary meal ingredients (CMIs).

vii. changes in the nutritive and non-nutritive (antinutritional factors, ANFs) contents of the cereal ingredients (flour, fresh dough and fermented dough) used to prepare complementary meals for infants and young children, can be quantitatively (relative and absolute) and objectively determined using food metabolomics or foodomics analytical methods (Cornelis & Hu, 2013; Ibáñez et al., 2015; Nalbantoglu, 2019). Metabolomics premised on the high-resolution separation capacities of advanced chromatographic analytical techniques (LC and GC) coupled with the high precison, sensitivity, reproducibility attributes of advanced mass spectrometry, is the gold standard currently for identifying and quantifying hitherto impossible marginal changes in biological materials and systems.

viii. the usage of TCPMs (exposures), qualitatively determined to have made nutritionally significant changes or had significant effects on the nutritive and non-nutritive contents of the cereal ingredients used within resource-poor households and/or communities, could be analytically correlated with the nutritional status or nutritional health outcomes of children, using a hierarchical conceptual framework (Hill, 2003; Victora et al., 1997).

The study presumes therefore that if all the resource-poor mothers of children in the Northern Region of Ghana have available to feed their children on routinely, is predominantly cereal-only-based (poor nutritional quality), any significant depletion of the residual essential nutrients (especially limiting essential amino acids in cereals) in the complementary meal ingredients (flour and/or dough) due to TCPMs, would more likely worsen the nutritional value of the complementary meals made from the cereal ingredients. In synergy with high child morbidity due to the high prevalence of infectious diseases (malaria, diarrhoea and acute respiratory infections) in northern Ghana, poorly fed infants and young children in the Northern Region are more likely to be stunted, wasted and/or underweight.

3.6 Conceptual Framework of the Study

The conceptual frameworks for the determinants of malnutrition (undernutrition) in DCs as described by various maternal and child nutritional health researchers, were adopted and customized for the development of the conceptual framework used in the definitive phase of this study (Arthur et al., 2015; Bhutta et al., 2013; Black et al., 2008; Fanzo, 2012; Hotz & Gibson, 2007; Mensah & Tomkins, 2003; Müller & Krawinkel, 2005; UNICEF, 1998). The model illustrates the relationships and interactions between the risk factors of malnutrition (undernutrition) and the nutritional status indicators (stunting, wasting and underweight) of children in a three-step conceptual hierarchy. The spectrum of factors and/or covariates of child undernutrition for this analytical cross-sectional survey were classified into distal, intermediate and proximal risk factors (Arthur et al., 2015). The hierarchies, from the conical base to the top were made up of the distal (societal or macro level), intermediate (underlying, environmental, household, family or meso level) and proximal (immediate, biological, individual, or micro level) risk factors. In the adapted conceptual framework (Figure 3.1) of this study, the associations between the postulated risk factors of undernutrition including the usage of traditional cereal processing methods (TCPMs) and nutritional status of children (measured as LAZ/HAZ, WLZ/WHZ and WAZ scores for stunting, wasting and underweight respectively) were analyzed. The main outcome variable or dependent variable was the nutritional status of the children under five years.

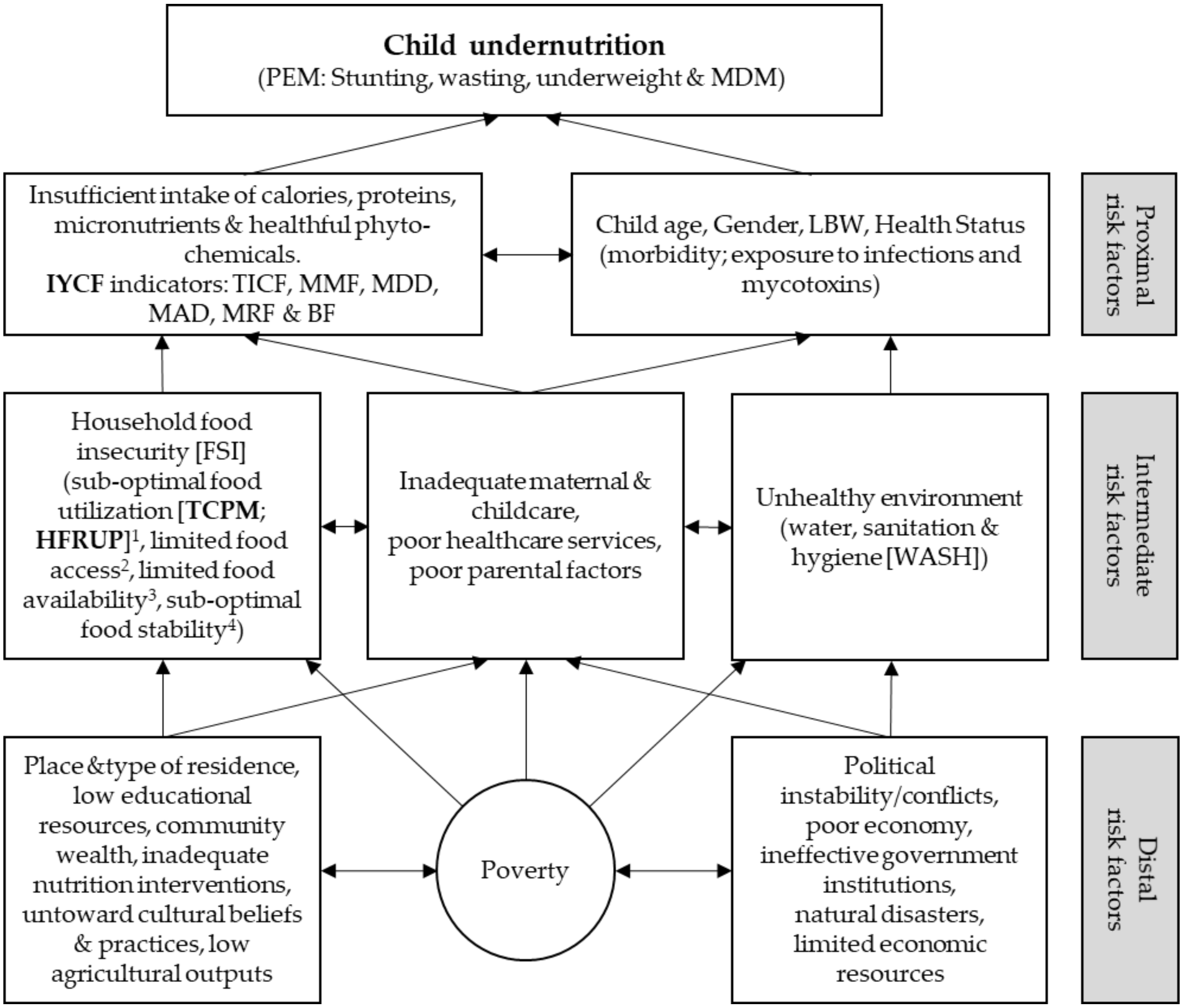

Figure 3.1: Conceptual Framework for the Determinants of Malnutrition (Undernutrition) in northern Ghana

(Adapted from **Bhutta *et al*, 2013; Black *et al*, 2008; Fanzo, 2012, Müller and Krawinkel, 2005 and UNICEF, 1998**). [1]**Sub-optimal food utilization**: debilitating food processing and preparation methods including usage of nutritionally debilitative complementary meal ingredient (**CMI**) production practices such as some Traditional Cereal Processing Methods (**TCPMs**), debilitating Habitual Food Resource Utilization Practices (**HFRUPs**) such as some indigenous meal preparation methods, unhealthful food preferences, inequitable household meal distribution, meal spoilage via poor storage practices, post-harvest losses, poor knowledge of nutrition and untoward cultural beliefs and practices among other factors; [2]**Limited food access (HDDS):** low purchasing power, poor transportation systems and limited diversity of plant and animal food resources; [3]**Limited food availability:** inadequate food production/imports and/or supply to households; [4]**Sub-optimal food stability**: inconsistency in food production, supply, availability, access and utilization due to economic, social, political and/or natural crisis or instability; **BF**: Breastfeeding; **HFI**: Household Food Insecurity (Food Availability, Access, Utilization and Stability Dimensions); **HDDS**: Household Dietary Diversity Score; **IYCF**: Infant and Young Child Feeding; **LBW**: Low Birth Weight; **MAD**: Minimum Acceptable Diet; **MDD**: Minimum Dietary Diversity; **MDM**: Micronutrient Deficiency Malnutrition; **MMF**: Minimum Meal Frequency; **MRF**: Micronutrient-Rich Foods; **PEM**: Protein Energy Malnutrition; **TICF**: Timely Introduction to Complementary Feeding

The main exposure or explanatory variables of interest (TCPM usage indicators and HFRUP indicators) in this study were considered as intermediate risk factors at the household, family or meso level. The focus of this study was therefore on the domains of the food utilization dimension out of the four classical dimensions of the concept of household food security as defined by the World Food Summit (WFS), FAO or USAID (Peng & Berry, 2019). The child food intake measures (WHO/UNICEF IYCF indicators) putatively deemed to be associated with child nutritional status were considered as proximal risk factors within this conceptual framework. The proximal determinants that were measured include the IYCF core indicators (EIBF, EBF, CBF@1, TICF, MMF, MDD, MAD, & Iron intake), ACF, Vitamin A intake, frequency of child morbidity, types of illnesses or infections recently experienced (child morbidity type), oedema, birth weight, child age, and sex of child.

Changes in the relative and absolute quantities of relevant nutritive and non-nutritive (antinutritional) metabolites from the foodomics laboratory analyses, were used to qualitatively determine and classify the usage of each TCPM (soaking, germination, dry milling, wet milling, and wet milling cum fermentation) as nutritionally significant or not. Intermediate risk factors that were measured during the survey included usage (frequencies, preferences or durations) indicators of TCPMs, HFRUPs indicators, WASH indicators (type of sanitary facilities used, sources of drinking water, hygiene practices), mother's age at birth of child, number of children catered for in the household, mother's educational status, mother's body mass index (BMI), household wealth index (HWI) or socio-economic status (SES), types of maternal healthcare services (such as immunization, ANC-antenatal care, PNC-postnatal care) and observance or compliance with recommended maternal child caregiving practices. The distal determinants that were measured include district of residence, type of community (rural, semi-rural/peri-urban, urban), name of community and community wealth index (CWI).

3.7 Research Philosophy, Epistemology, Methodology, and Study Design

The positivist paradigm was applied in this study because it lends itself to quantifiable and observable phenomena independent of the study subjects in the study population of interest or experimental material. Nutritional epidemiology is steeped in the philosophical orientation of the natural sciences, where objectivity and realism are the preferred path to the generation and/or validation of knowledge (Johnston et al., 2019). The main research question informed the purpose of the study which were broken down into four main analytical research objectives (**Figure 3.2**). These specific research objectives were converted into the corresponding hypotheses which required statistical analytical testing and deductive inferencing based on the adapted conceptual framework of the study (**Figure 3.1**), to arrive at objective conclusions (Farrugia et al., 2010).

The quantitative method was adopted because it lends itself to fact, reproducibility, and objectivity. Traditionally, it is widely utilized within the discipline of nutritional epidemiology, food science, nutrition, and public health nutrition, and thus allows for comparison of results were applicable. The quantitative observational study methods, particularly analytical cross-sectional study design was used for this research because it is widely utilized by nutritional epidemiologists, recommended as valid and reliable if well executed, relatively inexpensive, and contextually appropriate for resource-limited settings and studies (Setia, 2016; Thiese, 2014). In addition, logistical, feasibility, pragmatic research duration, and ethical considerations made the choice of quantitative study method and the analytical cross-sectional research design appropriate for the definitive study. Analytical cross-sectional study designs are the most widely used of the observational study designs besides cohort study and case control study designs particularly for the generation of hypotheses and the needed muse for more robust, indepth and comprehensive research (Funai, Rosenbush, Lee, & Del, 2001).

Analytical cross-sectional designs are suitably well placed as a first-line of preliminary evidence within the matrix or hierarchy of evidence produced from epidemiological studies and health-related research (Funai et al., 2001; Hill, 1965; Thiese, 2014). Anglemyer, Horvath and Bero (2014) demonstrated in their review of methodological reviews' study, which compared the effectiveness (effect estimate differences) of randomized controlled trials (RCTs) with observational studies in arriving at the same conclusion, that the choice of study design alone should not be enough criteria for assessing the validity and reliability of a study (Rychetnik, Frommer, Hawe, & Shiell, 2002). Indeed, they found no significant differences between the results of studies conducted using RCT compared to observational study designs for the same research question, regardless of even heterogeneity or inclusion of drug studies. Most importantly, once the researcher addresses adequately, the inherent weaknesses of any choice of study design, the results should pan out to be valid and reliable (Fischer, 2016; Ioannidis, Haidich, & Lau, 2001; Rychetnik et al., 2002). In the case of observational studies, confounding effect and various other biases tend to be the most significant drawbacks in determining study validity and reliability (Grimes & Schulz, 2002; Mariani & Pêgo-Fernandes, 2014; Setia, 2016). Potential confounding effects were addressed at the data analysis stage through the application of multivariable regression analyses (Howards, 2018). Observational studies namely cross-sectional designs, cohort studies, and case-control studies dominate the literature as they are commonly utilized to generate preliminary postulates or foundational-level evidence (or hypothesis) in epidemiological and health-related research (Burns, Rohrich, & Chung, 2011; Funai et al., 2001; Murad, Asi, Alsawas, & Alahdab, 2016).

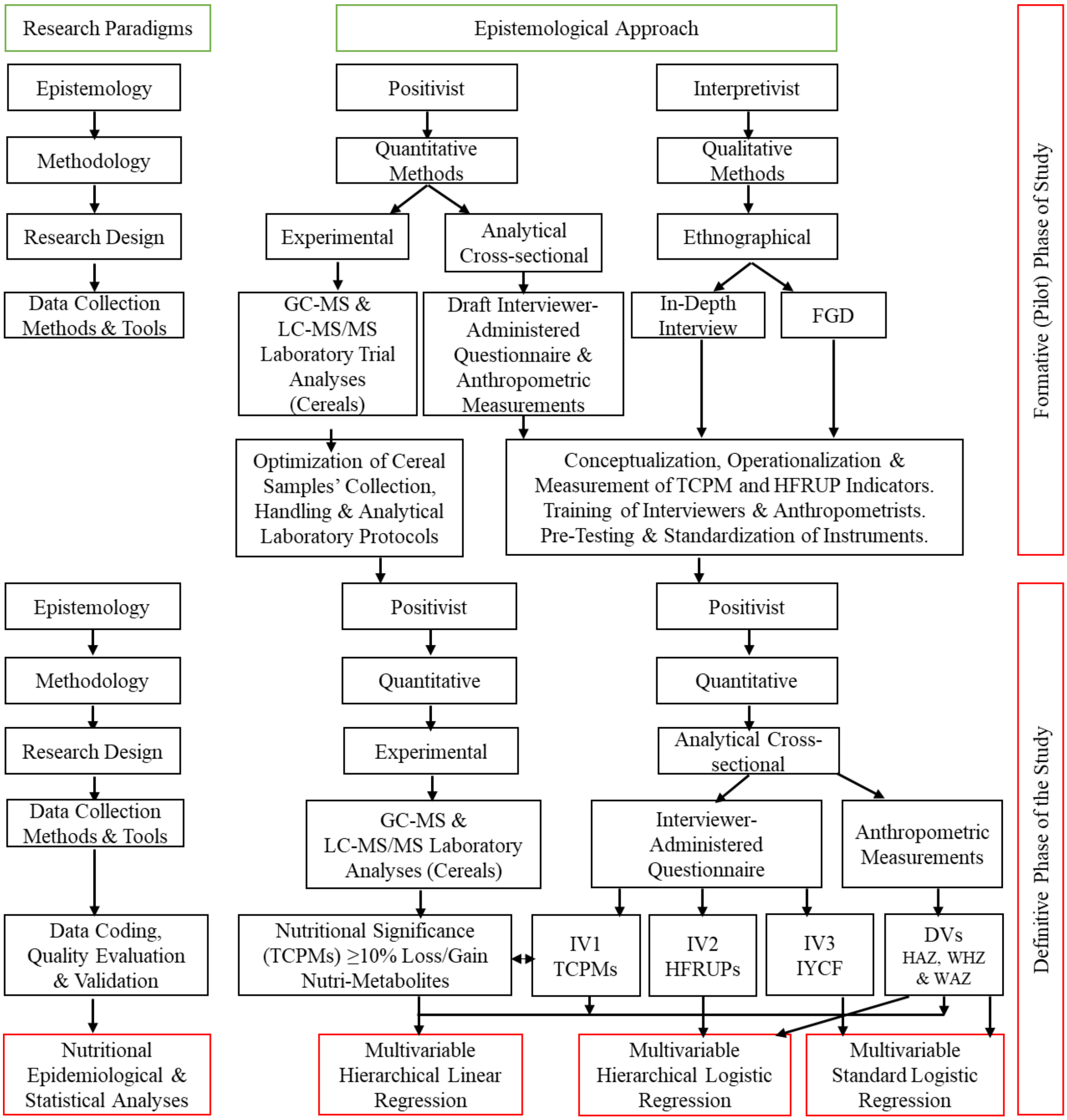

Figure 3.2: Schematic Summary of the Research Methodological Approach of the Study

DVs, Dependent Variables; **FGD**, Focused Group Discussion; **GC-MS**, Gas Chromatography-Mass Spectrometry; **HAZ**, Height-to Age Z-Score; **HFRUP**, Habitual Food Resource Utilization Practices; **IV**, Independent Variable;

IYCF, Infant and Young Child Feeding; **LC-MS**, Liquid Chromatography-Mass Spectrometry; **TCPM**, Traditional Cereal Processing Methods; **WAZ**, Weight-to Age Z-Score; **WHZ**, Weight-to Height Z-Score

Being the first attempt by any researcher to explore this concept (or phenomenon) as the main exposure (or explanatory) variable of interest (TCPMs), it was considered a logical, ethical, pragmatic, cost-effective, and suitable methodological approach (Mann, 2003; Thiese, 2014). This methodological approach was thus deemed as scientifically sound and an acceptable decision to leverage the synergy between the strengths of modern experimental omics technologies (UHPLC-MS/MS and GC-MS) and the advantages of the analytical cross-sectional study design, as a trade-off with a resource-constrained study setting such as northern Ghana.

3.8 Formative Phase of the Study

3.8.1 Recruitment and Training of Field Support Team

The field research support team made up of personnel with a minimum of a bachelor's degree in Community Nutrition, namely data enumerators, supervisors, and data entry clerks were recruited from the Northern Region. They were trained prior to the pilot and definitive phases of the study. The training agenda included general study purpose, survey purpose, sampling procedures, field procedures (community and household entry protocols, systematic random household selection, data collection/recording, cereal samples' collection, storage, and handling), interviewing techniques, timeliness, ethics, correct interpretation of questions from English to the local languages and vice versa, taking anthropometric measurements (height/length and weight), and identification of bilateral pitting oedema and other clinical symptoms of child morbidity. The training was conducted by the principal researcher (PI) together with an experienced senior researcher with specialization in nutritional epidemiology (community nutrition) and public health nutrition based at the University for Development Studies, Tamale in the Northern Region of Ghana. The supervisors engaged for the study were public health nutritionists from the Maternal and Child Health Department of the Ghana Health Service (GHS) in Tamale, Ghana. The theoretical, illustrative, and hands-on training programme was followed up with pre-testing of a draft focused group discussion (FGD) guide, in-depth interview (IDI) guide, cereal samples' collection guide, and a quantitative interviewer-administered questionnaire in three communities at Tamale, Ghana. The formative phase of the study was made up of a qualitative pilot study component (FGD and IDI), collection of cereal samples (grains and complementary meal ingredients) for trial laboratory analyses, and a pilot quantitative cross-sectional survey, conducted over a one-week period.

3.8.2 Qualitative Pilot Study

In-depth interviews (IDIs) and focussed group discussions (FGDs) were conducted with fifteen nurses and community health workers, and fifteen nursing mother-groups respectively in three out of the five communities selected in each of the five study districts to elicit relevant grass root information on infant and young child feeding (IYCF) practices, habitual food resource utilization practices (HFRUPs), traditional cereal processing methods (TCPMs), and other perceived determinants of malnutrition (undernutrition). These activities served to inform inputs (conceptualization, operationalization, and measurement of constructs/variables) and revisions in the quantitative interviewer-administered questionnaire used for the cross-sectional survey, and the development of the cereal samples collection guide/matrix during the quantitative pilot study. The most commonly used varieties (or cultivars) of the staple cereals and the most commonly used TCPMs to produce complementary meal ingredients (CMIs) such as dough and flour, meant for preparing porridge and other similar complementary meals for children in northern Ghana, were ascertained from the focused group discussions and in-depth interviews conducted in the communities and health facilities, respectively. Content analysis of the responses received from the IDIs and FGDs gave helpful ideas and inputs for the conceptualization and operationalization of TCPMs and HFRUPs as constructs of food utilization. Refinement of the draft composite, interviewer-administered questionnaire for the pilot quantitative cross-sectional survey was thus enhanced (Fade & Swift, 2011; Hsieh & Shannon, 2005; Onwuegbuzie, Bustamante, & Nelson, 2010).

3.8.3 Quantitative Pilot Study

Using a two-stage cluster sampling technique, 350 mother-child pairs were selected from households in the Northern Region of Ghana for a cross-sectional survey as preparatory activities to achieve high instrument validity and reliability in the definitive cross-sectional survey. The composite, interviewer-administered, survey instrument was revised with inputs from the preceding qualitative study activities, literature review, and expert views. Validity assessment of the survey instrument was conducted using the feedback from experts. The internal consistency and equivalence reliability of the instrument were also assessed accordingly. Additionally, cereal samples were collected from some households for trial foodomics laboratory analyses, to optimize the GC-MS and UHPLC-MS/MS protocols. Various experiences on the field also informed various revisions and strategies implemented during the definitive phase of the quantitative cross-sectional survey, cereal samples' collection exercise, and foodomics laboratory analyses at the Center for

Biotechnology, Bielefeld University, Bielefeld (Germany). This dissertation presents a detailed report of mainly the definitive phase of the study.

3.9 Definitive Phase of the Study (Quantitative Cross-Sectional Survey)

3.9.1 Study Setting

Ghana has a population of almost 31.1 million people and is described as a mature and stable model democracy in Africa (Ghana Statistical Service, 2018; Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015; USAID, 2020). The population of infants and young children under five years (U5) in Ghana is about 4.6 million (approximately 15% of the total population) and about 555 thousand for the Northern Region (Ghana Statistical Service, 2018). The country is classified as a lower-middle-income country, but it is one of the 34 high-burden countries (mostly from SSA and SEA) that accounts for 90% of global stunting amongst children under five years of age (Bhutta et al., 2013; USAID, 2020). Ghana is an English-speaking country located in West Africa, surrounded by French-speaking countries, Ivory Coast to the west, Burkina Faso to the north, Togo to the east and to the south along the Gulf of Guinea, the north-eastern side of the tropical Atlantic Ocean. The country covers an estimated 238,535 km^2 of land and water bodies. Ghana is the first country in Sub-Saharan Africa (SSA) to gain independence from British colonial rule on 6^{th} March 1957 which was previously called Gold Coast due to its vast natural mineral wealth particularly gold, diamond, manganese, and bauxite.

There are four major ethnic groupings besides other minority groups that make up Ghana. These include the Akans (47.5%), Mole-Dagbon (16.6%), the Ewes (13.9%), the Ga-Adangbe (7.4%), other smaller ethnic groups (Bassare, Konkomba, Guan) and foreigners (Ghana Statistical Service, 2018; Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015). There are over 70 languages and dialects spoken by various ethnic groups and tribes in Ghana, but twenty-one (21) indigenous languages are officially recognized and taught in the formal school system. Arabic, though not native to Ghana is widely taught in the predominantly Muslim communities and Islamic schools from the primary to the tertiary levels. Ghana is a mostly Christian country (71.2%**)** with Muslims (17.6%**)**, adherents to the African Traditional Religion (6.2%) and other religions or no belief systems (5%) constituting the minority groups.

Ghana has operated a free, compulsory, universal and basic education (FCUBE) policy nationally for more than three decades and recently in September 2017, the government introduced a free, compulsory, universal senior high school education policy nationwide. The literacy rate in Ghana stands at 71-82% (Female: Male) as of 2015. With over 70% enrolment currently nationwide, a national health insurance (NHI) policy has been implemented since 2003 replacing the former cash-and-carry system (Nsiah-Boateng, Prah Ruger, & Nonvignon, 2019). During the ongoing battle against Covid-19 globally, Ghana was ranked among the top 5 out of the 54 countries in Africa with one of the lowest death rates and highest testing rates as at June, 2020 even though it had high rates of community infections following the first confirmed positive case on March 12, 2020 (Bonful et al., 2020; Gyasi, 2020; Sibiri, Prah, & Zankawah, 2020).

Ghana was ranked 59th out of 192 countries in 2008 based on the global nutrition index (GNI) and was a significant contributor to the general reduction in the indices for hunger, prevalence of undernourishment and the GNI for the Sub-Sahara African (SSA) region between 1990 and 2015 (Peng & Berry, 2018; Rosenbloom, Kaluski, & Berry, 2008). Structurally, agriculture used to be the highest contributor (over 50%) to Ghana's GDP premised on cocoa and other agricultural exports. Currently the service sector has taken over as the highest (44%) contributor to Ghana's workforce premised on tourism, finance, ICT, aviation, education, and health services. Ghana was described as the fastest growing economy in the world in 2011. Electricity penetration rate is over 80% (Ghana Statistical Service, 2018). The 400th year of the end of slavery was commemorated in 2019 globally culminating in the hosting of a memorial Pan-African event dubbed "The Year of Return" which attracted over one million visitors to Ghana especially from the diaspora in 2019 (Boateng, Okoe, & Hinson, 2018). Still serving as the gateway and preferred destination to Sub-Saharan Africa (SSA) as a tourism, education, health, aviation, finance, and ICT hub of West Africa, being a pioneering and leading member of the African Union (AU), Ghana hosts the permanent secretariat of the Africa Free Trade Area (AFTA) launched in 2019. AFTA has been described as the largest single market in the world and holds the promise for massive and rapid socio-economic transformation of the African continent premised on the largest intra-African trade era if diligently implemented (Abrego et al., 2020).

Notwithstanding the modestly impressive political, social, and economic transformations that have taken place in Ghana over the last three decades, there remains a huge lacuna and unequal distribution of these gains across the country. There is a historically apparent socio-economic development gap between the northern savannah ecological zones and the mid-southern regions of Ghana over the 63 years of its independence as a state. The mid-southern regions are made up of savannah transition rain forest, high rain forest and savannah coastal agro-ecological zones. The northern savannah regions have one short but major raining season which supports agricultural activities and a long dry Harmattan season characterized by dry winds and desert-like heat.

The northern area of Ghana was made up of three politically demarcated regions until February 2019 namely Northern Region (NR), Upper East Region (UER) and Upper West Region (UWR). The Northern Region has now been split into three regions, namely Savannah, North East and Northern regions following a recent regional referendum. The survey was conducted across the former Northern Region which has the highest prevalence rate of stunting (33%) according to the Ghana Demographic and Health Survey 2014 report (Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015). The under-five (U5) population of infants and young children in the Northern Region of Ghana was estimated to be about 555, 000. February and March are usually the hottest months of the year in northern Ghana. There are two climatic seasons in the northern regions namely the short rainy season (May-August) and the long dry season (September-April) characterized by dry Harmattan winds. Majority of the inhabitants are engaged in agriculture with a significant proportion involved in trading. The harvesting season is usually from October to December when there is usually abundance of staple foods such as maize, sorghum, millet, and yam.

3.9.2 Survey Population of Interest

The population of interest in this study was mother-child pairs living in the Northern Region of Ghana where the prevalence of the key outcome variable of interest (stunting) is highest out of the 10 regions (as at 2018) in Ghana. The study participants were drawn from 25 communities in 5 out of the 10 districts in the Northern Region of Ghana with relatively high prevalence of stunting (≥ 30%) amongst children under five years. The shortlisting of districts was based on a Nutrition Surveillance Report (NSR) on the Northern Region of Ghana conducted by the Ghana Health Service (GHS) and the University for Development Studies (UDS), Tamale in November, 2013 and additional information from the Ghana Demographic and Health Survey (GDHS) 2014 summary report of the Northern Region (Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015).

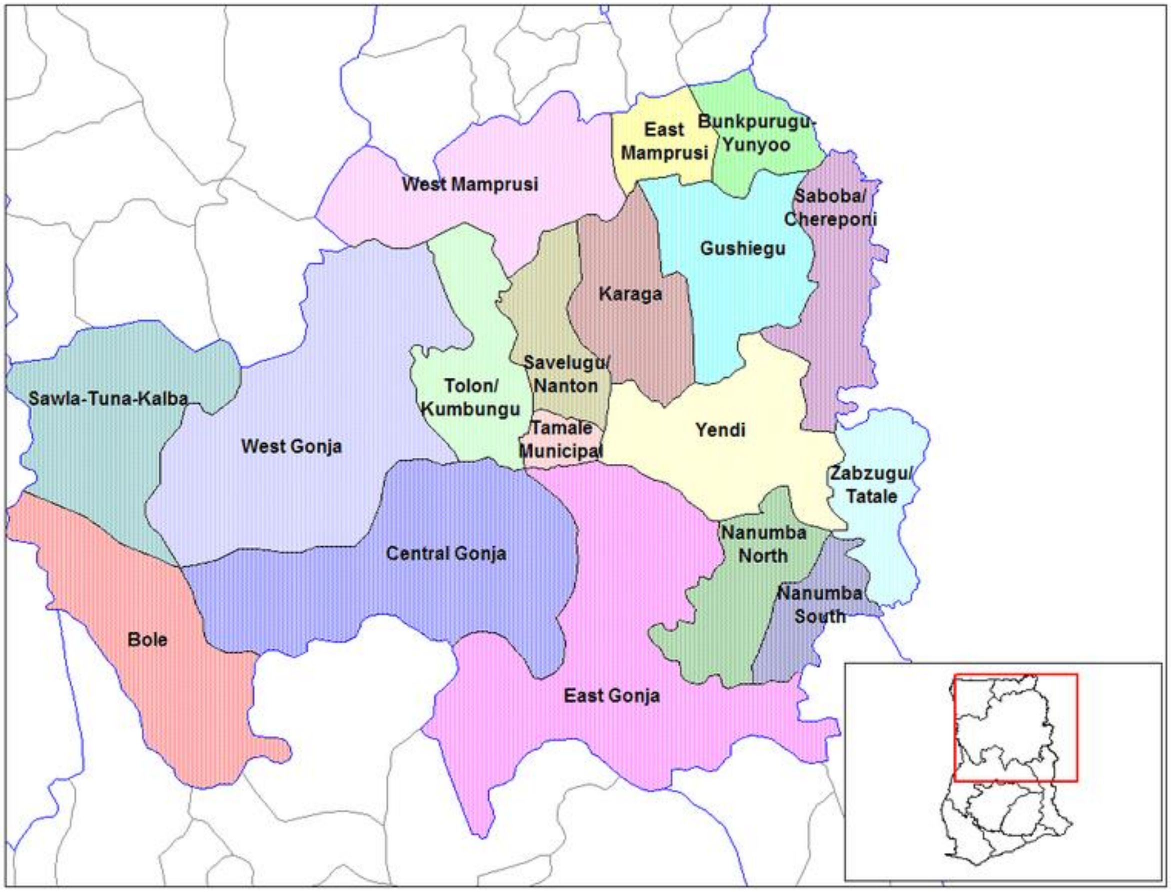

Figure 3.3 Illustrative Map of the Northern Region of Ghana (source: www.ghanaweb.com**)**

The districts which were purposively selected based on the prevalence of stunting were Tamale Metropolis (35%), Karaga District (41.7%), Nanumba North District (39.7%), Tolon-Kumbungu District (43.1%) and Central Gonja District (22.0%). Besides the prevalence of stunting, the district selection was also based on geographical spread around the capital of the Northern Region (Tamale), proximity to the Tamale Metropolis and other pragmatic and logistical reasons to attain adequate representativeness of the 10 shortlisted districts (prevalence of stunting ≥ 30%). The distribution of the selected districts with Tamale Metropolis as the center of the compass points are to the North-West (Tolon-Kumbungu), North-East (Karaga), South-West (Central Gonja) and South-East (Nanumba North) (**Figure 3.3**). There are several languages and dialects spoken in northern Ghana. However, the major languages spoken in the selected study districts are Dagbani (Dagombas), Gonja and Nanumba.

3.9.3 Inclusion and Exclusion Criteria for the Study Participants

Mothers of reproductive age (15-49 years) who were not pregnant and were caring for their children aged between 5 and 24 months were included in the study. Children who were sick at the time of the conduct of the survey were excluded. Mothers selected for the study were expected to be providing complementary feeding (CF) together with or without breastfeeding to their children. Only mother-child pairs who consented in writing to participate in the study together with the consent of the household heads were included in the study. Households and/or mother child-pairs that participated in the pilot study were not included in the definitive survey.

3.9.4 Sample Size of the Survey

The sample size (N) was calculated based on the standard formula for one-point sample estimation (Glover-Amengor et al., 2016; Kumar, Rai, Basu, Dash, & Singh, 2008; Saaka, Oladele, Larbi, & Hoeschle-Zeledon, 2017). The standard formular is given by the equation: $n = \frac{t^2 \times p\,(1-p)}{m^2}$ where *n* is the required sample size, *t* is the Z-score value at 95% confidence level, *m* is the margin of error at statistical significance level of 5% (α =0.05) and *p* is the estimated prevalence of the outcome variable of interest in the study. For a standard normal distribution, the standard value of $t = Z_{\alpha/2}$ =1.96, where Z is the Z-score (critical value) at 95% confidence level and α =0.05. The primary outcome variable that was used to estimate the required sample size (*n*) was the prevalence rate or population proportion of chronic malnutrition (stunting) based on a Nutrition Surveillance (NS) report of the Northern Region and the Ghana Demographic and Health Survey (GDHS) 2014 report of the Northern Region (Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015).

The GDHS 2014 and NS study reported 33.1% (survey from September-December 2014) and 28.3% (survey in November 2013) respectively for stunting in the Northern Region. With an estimated 20% of the total population of the Northern Region being children less than five years and a 33.1% prevalence of chronic malnutrition (Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015), premised on 80% power and an absolute precision of 5% (α= 0.05) at the 95 % confidence level, the sample size (*n*) determined was 284. Assuming a correction factor of 2.0 (the design effect) for cluster sampling, the required minimum sample size was 568 (Saaka et al., 2016). Allowing for a 5% non-response rate covering limiting circumstances such as missing values, implausible data, damages, or loss of completed questionnaires, and withdrawal from the interview and/or anthropometric measurement exercise, the overall sample size (N) was adjusted to 600.

3.9.5 Survey Sampling Method

A two-stage cluster sampling procedure was used to select the study participants. At the first stage, five communities from the list of communities in each selected district, were selected randomly using lottery (fishbowl) sampling whiles ensuring adequate geographical spread to obtain 25 clusters (communities) in total as recommended for community-based cluster sampling surveys (Saaka et al., 2015). The five communities (clusters) per district served as the primary sampling units (PSUs). The communities (clusters) selected were also guided by the Nutrition Surveillance 2014 report on the Northern Region of Ghana together with some validation information from the Ghana Demographic and Health Survey 2014 report on the Northern Region and the 2010 Population Census updated master list of communities and districts managed by the Metropolitan Health Directorates in the Northern Region.

At the second stage, all the households with eligible mother-child pairs were enlisted in a census for selection using systematic random sampling (SyRS) method, thus serving as the secondary sampling units (SSUs) of the participants. This stage of the sampling involved selecting the required 24 households from each cluster to meet the estimated sample size of 600 for the study. The eligible households (6- to 23-month-old child; 15- to 49-year-old, non-pregnant mother) were identified and serially enlisted in a census with the assistance of community volunteers who usually had prior knowledge of the household characteristics and thus served as community entry guides on the field. After determining the sampling interval by dividing the number of eligible households by 24, any sampling interval was randomly selected as a starting point for the first household to visit after which the subsequent houses were selected by adding the sampling interval to the first number selected. This was continued until all the twenty-four (24) households required per community or cluster were selected for the definitive study. Based on the consent of the selected household to participate in the survey, mother-child pairs were selected for interview. In households where more than one child qualified (6-23 months), a child between 6-12 months was selected randomly or discretely since complementary feeding is recommended to begin after the 5th month and stunting is relatively less prevalent amongst much younger children in the study age group who were ideally expected to be breastfeeding (Saaka et al., 2015; WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2008).

3.9.6 Survey Data Collection Instrument

The quantitative data collection instrument (interviewer-administered questionnaire) developed for the pilot study was a composite instrument. It was made from the combination of validated and standardized questionnaires used for assessing child food intake (IYCF) in malnutrition studies and food insecurity studies in DCs by the FAO, WHO, and UNICEF, in addition to the section developed from the qualitative study to conceptualize and operationalize the measurement of TCPMs and HFRUPs as unidimentional constructs of food utilization (Ali et al., 2017; FAO, 2018; WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2008). The final version of the quantitative survey instrument was produced after reviewing inputs from the training programme, pre-testing excercise, pilot qualitative study, pilot quantitative field study activities, and expert views. The survey instrument validity (construct and content) and reliability (internal consistency and equivalence) were evaluated in accordance with recommended best practices as applicable (Bastos, Duquia, González-Chica, Mesa, & Bonamigo, 2014; Boateng, G. O., Neilands, T. B., Frongillo, E. A., Melgar-Quiñonez, H. R., & Young, S. L., 2018; Heale & Twycross, 2015; Souza, Alexandre, & Guirardello, 2017). The data collection instrument was made up of four main sections with other sub-sections (**Appendix C1**). The main sections were used to elicit;

i. socio-demographic data of the mother-child pairs

ii. nutritional status data (anthropometric measurements) of the mother-child pairs

iii. food intake data (IYCF practice indicators) of the mother-child pairs

iv. the focal explanatory (exposure) variable of interest in this NER study (TCPMs) and other independent variables were considered as potential risk factors and/or covariates of undernutrition (proximal, intermediate, and distal variables). The explanatory variables conceived as measures of the food utilization dimension of household food insecurity (HFI) in this study, included indicators of habitual food resource utilization practices (HFRUPs) and usage indicators of traditional cereal processing methods (TCPMs), considered as intermediate risk factors (**Figure 3.1**). The TCPM and HFRUP indicators (food utilization dimension measures of HFI), together with the IYCP indicators were the explanatory (or exposure) variables of interest in this NER study.

The first section of the questionnaire was made up of close-ended questions that elicited data on the socio-demographics of the mother-child dyads such as maternal age, religion, marital status, ethnicity, sources of income, maternal educational attainment, number of children under five years being catered for, type of community mother resides in, child’s gender, child’s pre-schooling status, and child age.

The next section of the questionnaire was used to record data on the anthropometric measurements of the mother-child pairs. These included child's height, child's current weight, birthweight, and monthly weights from birth to the 24th month in addition to maternal height and maternal weight which were used to estimate the maternal body mass index (BMI).

The third section of the questionnaire was made up of mostly binary questions (Yes/No) that were used to capture data on the intake of any drink or meal including snacks in the last 24 hours (24HFR) of the survey, whose ingredients were from any of the 17-food groups (FAO classification). These 17-food groups were re-classified into 7-food groups (WHO/UNICEF classification) during the data analyses. The 17-food groups included cereals (1), white roots and tubers (2), Vitamin A-rich vegetables and tubers (3), dark green leafy vegetables (4), other vegetables (5), Vitamin A-rich fruits (6), other fruits (7), organ meats (8), flesh meats (9), eggs (10), fish and sea foods (11), pulses, nuts, and seeds (12), milk and milk products (13), oils and fats (14), red palm products (15), sweets (16) and spices, condiments, and beverages (17). The 7-food groups (WHO/UNICEF classification) were G1-Grains, Roots and Tubers; G2-Vitamin A-Rich Fruits and Vegetables; G3- Other Fruits and Vegetables; G4- Flesh Foods; G5- Eggs; G6- Legumes and Nuts and G7- Dairy Products. In addition to these binary questions for the food groups, there were questions on breastfeeding status, feeding frequency, pregnancy status, morbidity status, and involvement in any recent celebration that could have had an influence on the regular food intake of the mother-child pairs, and thus were considered in the computation of food intake indicators.

The fourth section of the composite data collection instrument (questionnaire) was made up of questions that elicited data on the other potential determinants of undernutrition. The independent variables were classified as proximal, intermediate, and distal risk factors/covariates (**Figure 3.1**). The proximal risk factors included two groups of indicators. The first group of proximal risk factors were factors related to the health status of the children namely bilateral pitting oedema, frequency of child sickness in the last two weeks and six months, type of sicknesses experienced, immunization status, and usage of insect-treated nets (ITN). The second group of potential proximal risk factors were the measures of infant and young child feeding (IYCF) indicators derived from the WHO/UNICEF 7-food groups (MMF, MDD, MAD, Vit A and Fe) in addition to questions that were used to elicit other IYCF indicators namely timely initiation of breastfeeding (TIBF), exclusive breastfeeding (EBF), continued breastfeeding at one year (CBF@1) and timely initiation of complementary feeding (TICF). The intermediate risk factors included three groups of indicators (or variables) measured from the survey data collection instrument. The first set of questions were used to elicit binary and/or multiple responses to acquire data on the household wealth index (HWI), habitual food resource utilization practices (HFRUPs), and the usage of selected traditional cereal processing methods (TCPMs). HFRUP indicators and TCPM usage indicators were the measures adopted in this study to operationalize various domains of the food utilization concept (or phenomenon) of household food insecurity (HFI) in the study population. The HWI was estimated from the ownership of durable household assets (house type, radio/audio player, TV, sewing machine, bed/mattress, refrigerator, bicycle/tricycle, computer/printing accessories, electric fan/air-conditioner, telephone, vehicle (car/truck/van/motor cycle), animal-drawn cart or donkey, crop farm and poultry/livestock farm, household utilities (source of household drinking water, type of household toilet facility, type of fuel for cooking and source of power for lighting the household) and the adequacy of household space (number of rooms per household, number of people per household and the number of people sharing a room).

The HFRUPs were made of six (6) main items which included cereal-only-based complementary meal feeding, cereal type preferably or often used for the production of complementary meal ingredients (flour and dough) by the mothers for complementary feeding, cereal form (flour, fresh dough or fermented dough) preferably or often used by the mothers for complementary meal preparation, duration of dough storage for complementary meal preparation, dough storage containers often used, and the source of dough (home-made or purchased) for complementary meal preparation by mothers for their children. The usage indicators of TCPMs were assessed from the questions that elicited usage (frequencies, preferences, or durations) of soaking, dehulling, dry milling, wet milling, and wet milling cum fermentation in the production of complementary meal ingredients (CMIs; flour and dough), used for the preparation of complementary meals for children. The second set of intermediate risk factors measured from the fourth section of the data collection instrument were the maternal childcare and healthcare services indicators. These questions elicited data on the attendance to antenatal care (ANC) services, postnatal care (PNC) services, place of childbirth, and maternal health indicators during pregnancy. The third set of intermediate risk factors measured from the fourth section of the interviewer-administered questionnaire were indicators of access to and/or usage of water, hygiene, and sanitation (WASH) practices. The distal risk factors were measured from the questions that addressed the district of residence, name of community of residence, type of community of residence (rural, semi-rural or urban), and community wealth index (CWI).

3.9.7 Survey Data Collection Method

With an estimated working sample size of 600 from 25 clusters (communities), a minimum of 24 mother-child pairs were interviewed in each community in June 2018. The trained field research support team (data enumerators, supervisors and data-entry clerks), who were recruited mostly from the Northern Region, conducted in-person or face-to-face collection of the survey data and anthropometric measurements from household to household. The interviewer-administered questionnaire was used to elicit data from eligible mother-child pairs over a 24-hour recall period (**Appendix C1**). The standardized quantitative questionnaire was interpreted in the local languages to obtain socio-demographic data, self-reported dietary intake data, and data on the potential proximal, intermediate, and distal determinants of undernutrition as illustrated in Figure 3.1.

3.9.8 Operational Definitions: Outcome Variables of the Study

The nutritional status measures WAZ (weight-for-age), LAZ (length-for-age) and WLZ (weight-for-length) Z-scores of the children were the dependent or outcome variables in this study (**Figure 3.1**). Anthropometric measurements were carried out to determine the nutritional status of the children and mothers by measuring their heights/lengths and weights. The data collected were used to calculate the anthropometric indicators of underweight, stunting, wasting and overweight status respectively: WAZ (weight-for-age), LAZ (length-for-age), WLZ (weight-for-length < -2SD) and WLZ (weight-for-length >+2SD) for the children and BMI (Body Mass Index) for the mothers using the WHO Anthro Software Version 3. Children who fell below minus two standard deviations (-2 SD) from the median of the reference population for LAZ, WAZ and WLZ were classified as stunted, underweight, and wasted respectively whiles those who fell below minus three standard deviations (-3 SD) from the reference population median were considered severely stunted, underweight, and wasted. A child was classified as overweight when WLZ was above plus two standard deviations (+2 SD) from the median of the reference population (Onis, 2006)**.** The data was exported to SPSS version 25 software for further analysis. The Z scores were based on the 2006 WHO growth standards expressed as standard deviation units from the median value for the WHO growth reference groups (Onis, 2006). Implausible Z-scores (scores falling outside the WHO flags): WLZ -5 to 5; LAZ -6 to 6 and WAZ -6 to 5 were excluded from the data set. The maternal and child weights were measured using standard electronic scale sensitive to the nearest 100g (Seca 890). The recumbent length of each child was measured in a supine position to the nearest 0.1cm with a portable Infantometer. This supine measurement was done by placing each child on his or her back between the slanting sides ensuring that the child's head was placed gently against the fixed top end. The child's knees were held down gently by the anthropometrist whiles the movable foot-piece of the Infantometer was drawn to touch the child's feet at right angle orientation against the legs (Onis, Onyango, van den Broeck, Chumlea, & Martorell, 2004; Saaka et al., 2015). Some of the children who could stand appropriately were measured standing. The WHO Anthro software automatically converts height to length for children less than 24 months (WHO, 2009). For the mothers, height was measured in a standing position using a Seca microtoise stadiometer to the nearest 0.1cm.

3.9.9 Operational Definitions: Explanatory Variables of the Study

Given the iterative nature of the body of knowledge in nutritional sciences and the relatively nascent status of nutritional epidemiology and public health nutrition as academic disciplines and professions, it is useful to provide the operational definitions of the exposure variables developed from the concepts (phenomenon) or constructs under investigation, as used in this study, in addition to classical definitions of some other frequently used nutritional epidemiological terms (Buttriss et al., 2017; Dragsted et al., 2017; Lawrence & Worsley, 2007).

The three main exposure (explanatory) variables of interest in this study were the complementary feeding (CF)-related food intake measures of infant and young child feeding practices (IYCF indicators) and measures of two domains of the food utilization dimension of household food insecurity (HFI), namely habitual food resource utilization practices (HFRUP indicators) and the usage (frequencies, preferences, or durations) of traditional cereal processing methods (TCPM indicators) (**Figure 3.1**). The IYCF practice indicators were conceptualized, defined, and measured in consonance with their usual usage as recommended by WHO/UNICEF and most researchers of maternal and child nutritional health (Daelmans et al., 2009). Traditional cereal processing methods (TCPMs) have several terminologies used to describe them in the NER literature. These include domestic cereal processing methods, low-level cereal processing technologies, indigenous cereal treatment methods, domestic unit operations of cereal processing, primary cereal processing methods, household-level processing technologies, and traditional household food processing technologies among others (Berhanu, Mesfin, Kebebu, Henery, & Whiting, 2015; Hotz & Gibson, 2007; Mensah & Tomkins, 2003; Oumarou et al., 2005; Samtiya, Aluko, & Dhewa, 2020). For the purpose of this study, TCPMs were defined as household-level cereal processing unit operations such as sun-drying, dehulling/debranning, soaking/steeping, germination/sprouting, winnowing, roasting, dry milling, wet milling, kneading, and natural/spontaneous fermentation. These are carried out customarily in most rural and peri-urban settings where advanced food processing technologies may not be available or accessible for the production of homemade food ingredients. The third explanatory variable, habitual food resource utilization practices (HFRUPs) was defined as any activity carried out habitually (customarily) in the domestic or home setting towards the preparation of complementary meal ingredients (CMIs) such as flour and dough, used for the preparation of complementary meals for infants and young children. As a construct, it was also operationally defined to include the indigenous household choices made and/or domestic unit operations used in the preservation and/or processing of staple cereals into complementary meal ingredients (CMIs) such as flour and dough. CMIs are used for the preparation of complementary meals for infants and young children. These included the preferred choice of cereal type (maize, sorghum, millet, or rice), CMI form (flour, fresh dough, and fermented dough), dough storage duration, dough storage container types preferred, and source of dough (homemade or otherwise) among others. TCPMs and HFRUPs were viewed as domains of the food utilization dimension of household food insecurity (HFI) whose usage by mothers habitually or customarily, could be associated with the nutritional health status of their children. Habitual food resource utilization practices (HFRUPs) were also further operationally defined as the indigenous, customary or habitual practices that are routinely undertaken by resource-limited mothers with the food resources available and accessible to them during the care, feeding, and upkeep of their children. It also includes the handling and/or processing activities habitually carried out on indigenous plant food resources (raw or semi-processed) obtained and the preferential choices made about food resources by resource-poor households in order to maximize their culinary, organoleptic, nutritional, and health benefits. For the purposes of this study, usage of the term CMIs refers to homemade cereal-only-based complementary meal ingredients which excludes composite weaning meal ingredients (WMIs) made from cereal-legume blends.

3.9.9.1 Proxy Food Intake Assessment (IYCF Indicators) at the Individual Level

The complementary feeding (CF)-related UNICEF/WHO IYCF indicators (TICF, MMF, MDD, MAD, ACF, Vitamin A intake and Iron intake) were estimated from self-reported 24-hour food recall (24HFR). Each mother was asked to recall the number of times, in the past 24 hours prior to the survey, her child had received any type of meal, snack or drink (complementary feeding), aside breast milk from the seven (7) food groups as classified by WHO (Ghosh et al., 2019; Saaka et al., 2015; WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2010). Timely introduction of complementary feeding (TICF) refers to the commencement of complementary feeding (introduction of solid, semi-solid and soft foods besides breast milk) at six months of birth. Dietary diversity score (DDS) refers to the score on the number of food groups out of the 7 food groups, each child is fed from in the last 24 hours, 7 being the highest and 0 being the lowest score. Minimum dietary diversity (MDD) refers to the proportion of children (6-23 months) who received foods from at least 4 out of the 7 food groups. Minimum meal frequency (MMF) refers to the proportion of children (6-23 months) who received the minimum recommended number of times of complementary feeding in the last 24 hours depending on the child' age as classified by WHO (CF $\geq$ 2 times for 6-8 months and $\geq$ 3 times for 9-23 months plus snacks for breastfeeding children and $\geq$ 4 times in 24 hours for non-breastfeeding children). Minimum acceptable diet (MAD) refers to the proportion of children who received both the MMF and MDD for their age category as classified by WHO. Appropriate complementary feeding (ACF) is an aggregate indicator that was additionally derived from TICF, MMF and MDD (Kassa, Meshesha, Haji, & Ebrahim, 2016; Saaka et al., 2016). ACF as a composite index in this study, refers to the proportion of children who received the MMF, MDD and commenced complementary feeding at 6 months of birth (TICF) as recommended by WHO. Intake of Micronutrient-rich foods (MRF) was also estimated for Vitamin A and Iron (Fe) using the 17 food groups as classified by FAO (FAO, 2018; FAO, 2013). Children who received meals from at least one out of the three iron-rich food groups were classified as having had adequate iron (Fe) intake. Children were classified as having received none (0), low (1-3) or high (more than 4) Vitamin A intake out of the seven Vitamin A-rich food groups from the self-reported 24-hour food recalls (24HFRs).

3.9.9.2 Proxy Food Intake Assessment (HFRUP Indicators) at Household Level

The HFRUP measures explored in this study following the findings of the formative phase of the study (FGD and IDI) included the feeding or otherwise of infants and young children with cereal-only-based complementary meals, type of staple cereals (maize, sorghum, millet, rice or others) habitually used preferably for complementary meal preparation, cereal form (flour, fresh dough or fermented dough) preferably used by the mothers for complementary meal preparation, the habitual duration of storage of dough used for complementary meal preparation, source of the complementary meal ingredients (self-preparation at home or purchased), and type of container (plastic, metal, calabash or jute sacks) habitually used for the storage of dough used for complementary meal preparation. These indicators were assessed from self-reported responses to sets of close-ended questions during the cross-sectional survey (**Appendix C1**). As proxy or surrogate measures of the usage of complementary meal ingredients (CMIs), the HFRUP indicators served as a means of assessing the association between some routine food utilization practices and child nutritional status in the Northern region. HFI was considered as a potential intermediate risk factor (RF) at the meso or household level in the three-step hierarchical framework (**Figure 3.1**).

3.9.9.3 Proxy Residual Nutrient Intake Assessment (TCPM Indicators) at Household Level

Traditional cereal processing methods (TCPMs) as the main explanatory variable of interest in this study, was considered as another domain of the food utilization dimension of household food insecurity (HFI). The TCPM indicators for the usage (frequencies, preferences, or durations) of dehulling, soaking, dry milling (flour), wet milling only (fresh dough), and wet milling cum fermentation (fermented dough) in the preparation of complementary meal ingredients (CMIs) for infants and young children, were assessed from self-reported responses to sets of close-ended questions during the cross-sectional survey (**Appendix C1**). As proxy (or surrogate) measures of food or nutrient intake, the TCPM usage indicators served as a means of qualitatively assessing the potential dose of exposure to the residual nutritive and non-nutritive (antinutritional) constituents of the complementary meal ingredients, namely flour and/or dough. The quantitative effects of the TCPMs on the nutritional metabolites (foodmics laboratory analyses), provided an objective basis for the qualitative assessment of the CMIs, using a nutrient adequacy-based dietary quality index (DQI) criterion.

3.9.9.4 Body Mass Index (BMI)

Body Mass Index (BMI) was calculated for the mothers as an indicator of nutritional status reflecting chronic energy deficiency or sufficiency. BMI was calculated as weight (kg) divided by the individual's height (meters) squared. A BMI $\leq$ 18.5 was categorized as underweight or chronically energy deficient, BMI between 18.5 and 24.9 was classified as normal, BMI between 25 and 30 was classified as adequately nourished but overweight, and BMI > 30 was obese.

3.9.9.5 Bilateral Pitting Oedema

Oedema was assessed in the children by placing both thumbs on the upper section of the child's feet and applied some pressure for about 2-3 seconds. Oedema was considered to be present when the skin depression on both feet remained after the pressure was released.

3.9.9.6 Household Wealth Index (HWI)

The socio-economic status of each mother-child pair was determined using the first component from the Principal Component Analysis (PCA) of the household ownership of certain durable assets, type of utilities and household space adequacy (Doku, Koivusilta, & Rimpelä, 2010; Filmer

& Pritchett, 2001; Reinbott et al., 2015). The ownership of durable assets assessed include house type, radio/audio player, TV, sewing machine, bed/mattress, refrigerator, bicycle/tricycle, computer/printing accessories, electric fan/air-conditioner, telephone, car/truck/van/motorcycle, animal-drawn cart/donkey, farm (crop) and farm (poultry/livestock). The utilities assessed were the source of household drinking water, type of household toilet facility, type of fuel for cooking, and source of power for lighting the household and operating electrical and/or electronic gadgets. The adequacy of household space was assessed from the number of rooms per household, number of people per household, and the number of people sharing a room.

3.9.10 Classification of the Independent Variables of the Survey

The potential risk factors or determinants of undernutrition were classified into proximal, intermediate, and distal factors or covariates which served as the independent variables of the study based on a modified version of the UNICEF hierarchical conceptual framework (**Figure 3.1**) (Bhutta et al., 2013; Fanzo, 2012; Müller & Krawinkel, 2005; UNICEF, 1998). These independent variables or covariates were identified and enlisted from previous studies conducted in the Northern Region of Ghana and other DCs or LMICs with similar settings as northern Ghana (Tariq et al., 2018; Zeraatkar et al., 2019).

3.9.10.1 Proximal Factors or Covariates

Nutrition-specific interventions and programmes are often targeted at the immediate determinants of undernutrition (Black et al., 2013). The proximal independent variables measured and explored in this study include the WHO/UNICEF infant and young child feeding (IYCF) indicators (TICF, MMF, MDD, MAD, EIBF, EBF, CBF@1 and Iron intake), ACF, Vitamin A intake, child morbidity (frequency of illnesses or infections, types of illnesses experienced by the child recently and bilateral pitting oedema), birth weight, age and sex of child (Bhutta et al., 2013; Black et al., 2008; Fanzo, 2012; UNICEF, 1998; WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2008)

3.9.10.2 Intermediate Factors or Covariates

Nutrition-sensitive interventions and programmes are often targeted at the underlying determinants of undernutrition (Black et al., 2013; Ruel & Alderman, 2013). The intermediate independent variables measured were the habitual food resource utilization practice (HFRUP) indicators, traditional cereal processing method (TCPM) indicators, household wealth index (HWI), type of fuel used for cooking, WASH indicators (type of sanitary facility/toilet used, sources of drinking water and hygiene practices), maternal child care indices (child pre-school attendance, number of children under five years catered for, and usage of insecticide-treated nets- ITN), mother's age, mother's height, marital status, mother's educational status, religion, ethnicity, maternal BMI, maternal and child healthcare services' usage (place of delivery, vaccination status, antenatal care- ANC and post-natal care- PNC) and parental occupation or income sources (Bhutta et al., 2013; Black et al., 2008; Fanzo, 2012; UNICEF, 1998)

3.9.10.3 Distal Factors or Covariates

The distal independent variables considered include district of residence, name of community, type of community (rural, peri-urban/semi-rural and urban) and community wealth index (CWI) (Bhutta et al., 2013; Black et al., 2008; Fanzo, 2012; UNICEF, 1998).

3.9.11 Statistical Analyses of the Cross-Sectional Survey Data

The questionnaires received from the trained interviewers and anthropometrists were thoroughly inspected and screened for completeness and consistency. The responses from the interviewer-administered questionnaires (N=634) were coded appropriately and double-entered using the Statistical Package for Social Sciences software (SPSS Version 25). Questions with binary responses (yes/no; male/female, et cetera) were coded with Yes=1 and No=0. The other questions that had more than two possible choices of responses were coded serially with ordinal discrete numbers or codes starting from 1 to the maximum corresponding number in the SPSS data file. Derivative variables were computed from other primary variables by direct summation of scores, recoding or by conditional arithmetic based on the recommended formula as applicable to the variable of interest. In the case of the IYCF indicators, the recommended formulas for their computations were used (WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2010). Wherever there was a count of less than five (5) cases or observations for any level of the categorical or nominal variables, the level was collapsed and merged appropriately with the next most suitable level or sub-category (Field, 2013; Pallant, 2011). The WHO Anthro software (Version 3) was used for the Z-scores computations from the anthropometric measurements of the children.

The data set was prescreened (N=634), cleaned (N=581) and tested for compliance with the key assumptions underlying the multivariable regression analysis techniques used (standard multiple binary logistic regression, hierarchical multiple binary logistic regression, and hierarchical multiple linear regression). The diagnostics included sample size adequacy, missing values, univariate outliers, multivariate outliers, normality of data distribution, instrument internal reliability and reliability, equality or homogeneity of variance, multicollinearity, and independence of variance. Technical corrections were made where applicable following the observation of any significant violation of any of the assumptions. This was to ensure statistically valid estimates and inferences from the data set.

Univariate (or descriptive) statistical analyses were performed to estimate the prevalence of nutritional status (stunting, wasting, underweight, and overweight), IYCF indicators, HFRUP indicators, TCPM indicators, and the frequency distributions of the other independent variables (covariates and/or factors). The univariate (descriptive) analyses were followed up with bivariate analyses (Pearson's Chi square, Pearson correlation, and simple regression) to determine the relationships between the independent and dependent variables (stunting, wasting and underweight status). The absolute frequencies, relative frequencies (percentages), p-values (statistical significance), confidence intervals (CI), Chi-square values (χ^2), correlation coefficients, coefficient of determination, and other relevant statistics were reported for the bivariate statistical analyses for the measures of associations where applicable. Bivariate analyses for all the categorical risk factors were performed using Pearson's Chi-square (χ^2) test to measure the strength and significance of associations with the binary form of the dependent variables (DVs) at $p<0.10$ for the IYCF indicators, HFRUP indicators and TCPM indicators (Ughade, 2013; Zhang, 2016). Bivariate analyses for all the other categorical or nominal independent variables (factors) were performed using Pearson's Chi-square (χ^2) test (binary form of DVs) to measure the significance of associations at $p<0.05$ (Bewick, Cheek, & Ball, 2003b; McHugh, 2013). Pearson correlation (r) and simple linear regression were used to measure the strength, direction, and significance of correlations with the continuous form of the DVs at $p<0.05$, for the covariates (continuous or non-categorical independent variables) (Bewick, Cheek, & Ball, 2003a). Distribution of the data was inspected visually using histograms, Q-Q plots, and boxplots, and were also statistically tested for normality using Shapiro–Wilk test and Kolmogorov–Smirnov test (Akoglu, 2018; Bertani, Di Paola, Russo, & Tuzzolino, 2018; Bursac, Gauss, Williams, & Hosmer, 2008; Schober, Boer, & Schwarte, 2018; Ughade, 2013; Zhang, 2016).

The IYCF indicators were hypothesized to be associated with stunting (chronic malnutrition) and wasting (acute malnutrition) status, as the indicators of child anthropometric growth impairment in the Northern Region of Ghana. The IYCF indicators were considered as potentially viable monitoring parameters for identifying sub-groups of the child population at risk of the various adverse nutritional health outcomes (Ghana Statistical Service (GSS), Ghana Health Service

(GHS), and ICF International, 2015; WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2010). To address this question, the first set of inferential statistical analyses were conducted using standard multivariable binary logistic regression analyses at $p<0.05$ level of significance. The purpose of this set of analyses were to determine the associations between the individual IYCF indicators and nutritional status (stunting and wasting) amongst the children (6–23 months) in the Northern Region of Ghana, after adjusting for potential confounders. To produce a parsimonious model, multicollinearity was assessed amongst the significant variables selected from the bivariate analyses, using variance inflation factor (VIF) with a threshold of three (3) for nominal variables and ten (10) for non-categorical variables (O'brien, 2007). ACF and MAD violated the assumption of singularity because they are derived from a combination formular of TICF-MAD and MMF-MDD, respectively. Furthermore, ACF and MAD showed multicollinearity with other core IYCF indicators and were thus not included in the regression modelling. Intake of iron-rich foods was included in the regression model because of its biological and statistical significance ($p<0.10$) (Ughade, 2013; Zeraatkar et al., 2019; Zhang, 2016). The overall model performance and calibration were assessed using the Hosmer-Lemeshow goodness of fit (GOF) test and variance explained by the significant predictors (coefficient of determination) was reported using the Nagelkerke R^2 (Tabachnick and Fidell, 2007). The independent variables found to be significantly associated with each of the dependent variables (stunting and wasting status) in the bivariate analyses were selected in addition to other variables identified from literature as potential determinants (biological significance) and used in the standard multivariable binary logistic regression modelling. The selection of potential confounders (covariates and/or factors) was thus conducted using both data-driven and knowledge-based approaches for the standard multivariable binary logistic regression modelling (VanderWeele, 2019). Adjusted Odds Ratios (AOR), 95% Confidence Intervals (CI) and other statistics were reported at $p<0.05$ level of significance.

The second set of inferential statistical analyses conducted with the cross-sectional survey data was hierarchical multivariable binary logistic regression to determine the associations between habitual food resource utilization practice (HFRUP) indicators and child undernutrition (stunting and wasting), adjusting for putative confounders identified from literature and the conceptual framework (**Figure 3.1**). This statistical technique was employed to determine the proportion of variance in child undernutrition explained by the HFRUP indicators, over and above the variance in the dependent variables accounted for, by the proximal risk factors of child nutritional status. The coefficient of determination (R^2), the change in R^2, standardized regression coefficients, standard error (SE), test of model parsimony (Hosmer and Lemeshow test), VIF range (multicollinearity check), and statistical significance test statistic (*p* values) were reported (Kindermann et al., 2020).

The third set of inferential statistical analyses on the quantitative cross-sectional survey data was hierarchical multivariable linear regression to determine the strength, direction, and significance of the associations between the usage indicators (preferences, duration, or frequencies) of each nutritionally significant TCPM, and child undernutrition (stunting, wasting and underweight status; Z-scores), accounting for only the proximal or individual risk factors and/or covariates (**Figure 3.1**). The TCPMs were considered as potential intermediate risk factors of undernutrition, operationalized as the conceived constructs (or measurable indicators) of the food utilization dimension of household food insecurity (HFI) in this study. The relative contribution of each nutritionally significant TCPM was determined from the hierarchical multivariable linear regression analyses, accounting for the variance in stunting status (HAZ/LAZ scores), wasting status (WHZ/WLZ scores), and underweight status (WAZ scores), over and beyond that of the proximal factors and/or covariates (Hagan, 2018; Yap, Nasir, Tan, & Lau, 2019). The nutritional significance of each TCPM was determined from the foodomics laboratory analyses (≥ 10% loss in EAA; DQI, Yes =1 and No= 0).

3.10 Definitive Phase of the Study (Foodomics Experimental Laboratory Analyses)

3.10.1 Research Design and Analytical Procedures

A quantitative laboratory-based randomized control study design was used for the foodomics (food metabolomics) study component of this research project to undertake nutritional and compositional analyses of three staple cereals. Experimental laboratory samples of the staple cereals (maize, sorghum and millet) were collected from the study households in the Northern Region of Ghana during the cross-sectional survey and analyzed using food metabolomics techniques namely Gas Chromatography-Mass Spectrometry (GC-MS) and Ultra High Performance Liquid Chromatography tandem Mass Spectrometry (UHPLC-MS/MS) (Gorzolka et al., 2012; Kopka et al., 2004; Nalbantoglu, 2019; Persicke et al., 2012; Zörb, Langenkämper, Betsche, Niehaus, & Barsch, 2006). The purpose of the foodomics laboratory analysis was to qualitatively determine the quantitative effects (relative and absolute) of the TCPMs on the nutritive and non-nutritive (anti-nutritional) constituents of the experimental cereal samples. This provided an objective basis to analyze the nutritional epidemiological significance of the usage of these TCPMs which are usually used in the production of complementary meal ingredients (flour and dough). There are a number of different cultivars or varieties of the three staple cereals in the northern regions of Ghana selected for this study. These include local yellow maize and the improved maize varieties namely Obaatanpa, Okomasa, Mamaba, Popcorn, Golden Crystal, Dobidi, Dodzi, Laposta, Abeleehi and Dorke SR for *Zea mays* (maize); Mankariga, Kapala, Kadaga, Pannar, Fremida, Local 29, NSV-1 and NSV-2 for *Sorghum bicolor* (sorghum); Early maturing millet (Naara) and Late-maturing millet (Zea) for *Pennisetum glaucum (L)* (Pearl millet). The most popularly available and widely consumed cultivar or variety of maize, sorghum and millet that were collected for the study were Okomasa-Obaatanpa mix, Kapala and Naara respectively. The cereal grains collected from the households were visually assessed thoroughly to ensure that they were free from foreign materials, visible mould growth, damage or brokenness and were reasonably dry. The choice of these cultivars was informed by the findings from the qualitative study (the focused group discussions, FGD and in-depth-interviews, IDI) during the pilot phase of the research project.

The relative and absolute quantities of relevant nutritive and non-nutritive constituents (metabolites) of the cereals were analyzed using state-of-the-art GC-MS and UHPLC-MS/MS techniques, respectively. This served to measure the relative and absolute quantitative changes in the cereal constituents through the effects of the TCPMs. The metabolic profiling and targeting of relevant metabolites of the nutritive and non-nutritive constituents of the cereals were conducted at the Metabolomics Laboratories of the Center for Biotechnology (CeBiTech) at Bielefeld University, Bielefeld, Germany. Trial foodomics analyses (food metabolite analyses) on some of the cereal samples were conducted to optimize the validity and reliability of the analytical GC-MS and UHPLC-MS/MS laboratory protocols, chromatography-mass spectrometry instrument performance, metabolite reference databases and targeted metabolite standards (AAs standard solutions for the calibration curves), before applying the optimized analytical protocols to the cereal samples in the definitive study.

3.10.2 Sample Collection and Preparation for Foodomics Laboratory Analyses

The cereal samples in the form of dried whole grains (control/reference samples), flour (ground with local attrition milling machine called Nikanika), soaked/steeped grains, germinated/sprouted grains, fresh dough (freshly wet-milled) and fermented dough (wet-milled cum naturally fermented during storage) were collected from the study households of communities in the Northern Region of Ghana for the experimental laboratory analyses during the cross-sectional survey exercise and packaged into sterile biological sample bags (**Table 3.1**). The germinated and soaked grain samples were prepared by some designated households to simulate the usual household preparation practices in the communities (**Figure 3.4**). The samples were made from portions of the dried grains of each cereal under the prescribed conditions for experimental purposes to ensure uniformity of the batches of samples collected from the households (Getenesh, Addisalem, Afework, Susan, & Carol, 2014; Mensah & Tomkins, 2003).

Table 3.1 Cereal Sample Collection Matrix for Foodomics Laboratory Analyses

Cereal Samples	**Treatment Variations of Cereals**		
	Maize	Sorghum	Millet
Sun-Dried & Laboratory-milled Grains (Control)	Popular Cultivar (Obaatanpa-Okomasa Mix)	Popular Cultivar (Kapala)	Popular Cultivar (Naara)
Steeped/Soaked Grains	72 Hours (3 Days)	48 Hours (2 Days)	24 Hours (1 Day)
Germinated/Sprouted Grains	≥72 Hrs ≤ 84Hrs	≥ 72 Hrs ≤78 Hrs	≥ 24 Hrs ≤30 Hrs
Flour: Dry-milled Grains	Public Motorized Dry milling (Nika-nika)	Public Motorized Dry milling (Nika-nika)	Public Motorized Dry milling (Nika-nika)
Fresh Dough: Wet-milled Grains	Public Motorized Wet milling ≤48 Hours storage	Public Motorized Wet milling ≤48 Hours storage	Public Motorized Wet milling ≤48 Hours storage
Fermented Dough: Wet-milled grains cum fermented (spontaneous/natural)	Public Motorized Wet milling >48 Hours storage	Public Motorized Wet milling >48 Hours storage	Public Motorized Wet milling >48 Hours storage

The sample bags were organized and stored under appropriate conditions before the package was swiftly transported within an hour by air travel from Tamale in the Northern Region to the Biotechnology Laboratory, Faculty of Agriculture at the University of Ghana (Legon) in Accra. The cereal samples collected (whole grains) were sorted out further into composite representative analytical samples using a laboratory sample mixer to thoroughly mix the contents of the bags of sun-dried grains, soaked grains, germinated grains, flour, fresh dough, and fermented dough (Kimanya et al., 2010).

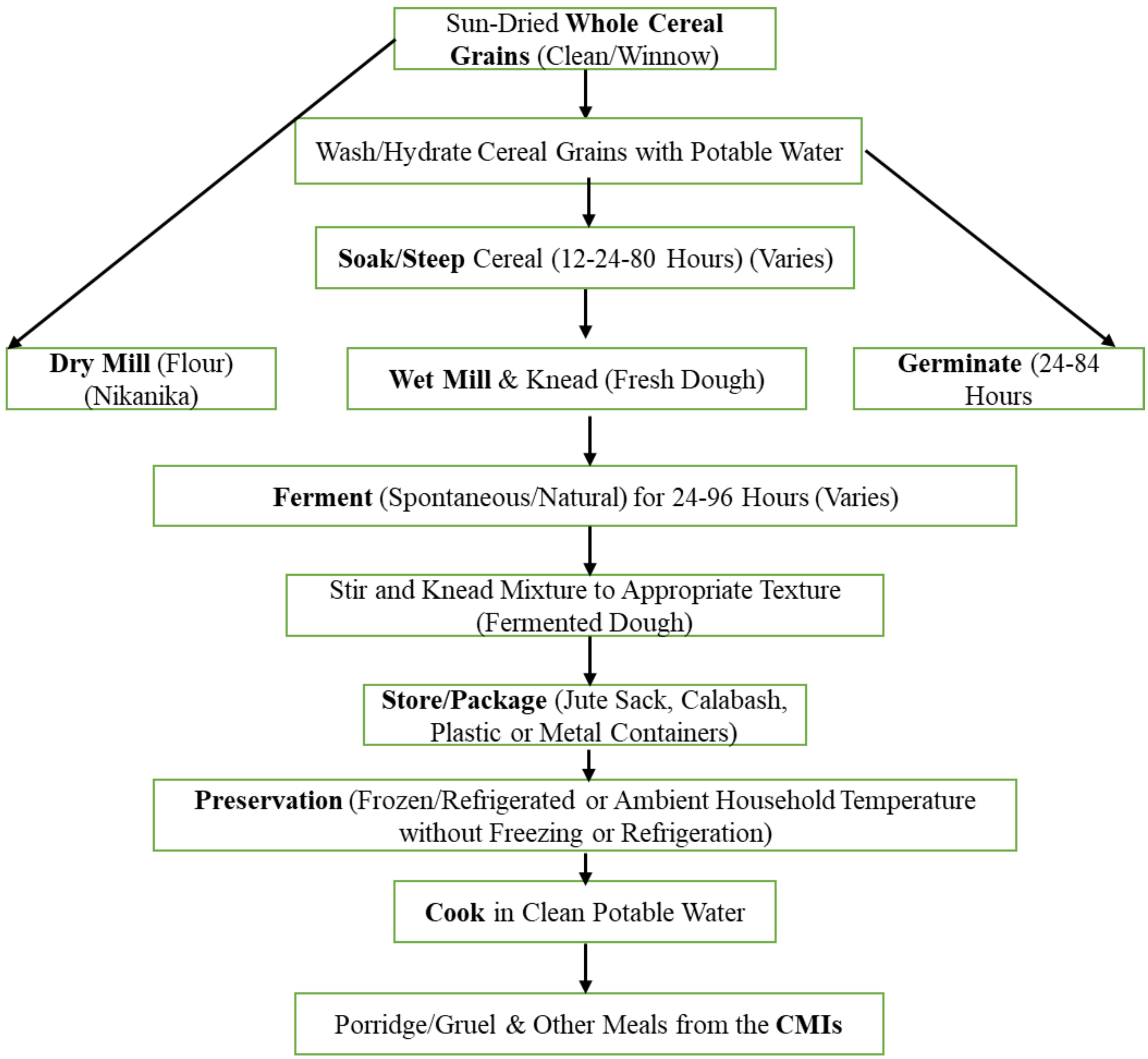

Figure 3.4 Production Flow Diagram of Cereal Ingredients Examined in the Laboratory

Sun-dried Whole Grains (Control), Soaked Grains, Germinated Grains, Dry-milled Grains (flour), Wet-milled Grains (Fresh Dough) and Wet-milled Grains cum Fermented (Fermented Dough)

The samples were then preliminarily lyophilized (freeze-dried) and stored at -20°C away from light until carried to Bielefeld, Germany. The screw-capped tubes were then wrapped in aluminium foils and kept in LDPE Ziplock bags for onward travel arrangements. At the CeBiTech Laboratory (Bielefeld University, Germany), the samples were deep-frozen as duplicate composite samples at -80°C in sterile, non-pyrogenic 50ml Sarstedt screw cap tubes. The deep-frozen samples were lyophilized thoroughly (Christ Alpha 1-4 Plus Freeze Dryer, Germany), milled into fine flour (Rotor Mill, KIKA-WERKE® GmBH and Co KG, Germany) and re-packed into sterile, non-pyrogenic 50ml Sarstedt screw cap tubes as ready-for-analysis samples on the GC-MS and UHPLC-MS/MS setups.

3.10.3 Optimization of the Food Metabolomics Analytical Laboratory Protocols

Cereal samples (maize, sorghum, and millet) were collected and analyzed to ascertain the validity and reliability of the analytical protocols, instrumentation, internal standards, metabolite databases and standard solutions of targeted metabolites using different sample weights of 5mg and 10mg (Satorius TE214S Analytical Weighing Balance). The results of the trials informed revisions in the GC-MS and UHPLC-MS/MS analytical laboratory protocols that were used for the definitive analyses.

3.10.4 Relative Quantification of Cereal Metabolites (GC-MS)

The samples were analyzed in technical triplicates using 10 mg cereal samples (Satorius TE214S Analytical Weighing Balance, Central Europe) as determined from the trials during optimization assays of the analytical protocols. The sun-dried whole grains served as the control or reference samples for the experimental cereal samples. The relative quantities of the metabolites that were determined include amino acids, sugars, sugar alcohols, sugar phosphates, organic acids and other metabolites as described by Gorzolka et al. (2012) and Zörb et al. (2006)**.** The GC-MS analysis was used as a generic simultaneous assay of the physiological contents of the hydrophilic metabolites (water-soluble compounds) present in the cereal samples due to the TCPM treatments. The GC-MS analysis as a generic snapshot assay, was thus a qualitative means of assessing whether the TCPM treatments were facilitative (improved the nutritive value or decreased the anti-nutrient contents) or debilitative (depleted the nutritive constituents or increased the anti-nutrient contents).

3.10.4.1 Methanolic Metabolite Extraction from the Cereal Samples (GC-MS)

The metabolites (nutritive and non-nutritive constituents) were extracted from 10mg cereal samples (Satorius TE214S Analytical Weighing Balance, Central Europe) with 1 mL 80% methanol, containing 10µM Ribitol as internal standard (IS) in a homogenizer (Precellys® 24 Instrument: Peqlab, Erlangen, Germany), using 1mm zirconia/silica beads (Roth, Karlsruhe, Germany). The methanolic extracts were treated three times at 6.5 m/s for 45 seconds to homogenize the cereal samples. After 20 minutes of centrifugation at 15,000g at room temperature, 750µL clear supernatant were each transferred into 1mL glass vials (Supelco, Bellfonte, Carlifonia, USA) and evaporated in a nitrogen stream until it was satisfactorily dry (Gorzolka et al., 2012; Lisec et al., 2006; Zörb et al., 2006).

3.10.4.2 Derivatization of Metabolites from the Aqueous Methanolic Extract (GC-MS)

The metabolites were derivatised with 50µL methoxylamine hydrochloride in pyridine (20 mg/mL; g/v) for 90 minutes at 37°C together with 50 µL N-Methyl-N-(trimethylsilyl) trifluoroacetamide (MSTFA) and 20 µL alkane standard for 30 minutes at 37°C. All chemicals and standard compounds were purchased from Sigma-Aldrich-Fluka (Taufkirchen, Germany), MercK (Darmstadt, Germany) and Macherey-Nagel (Düren, Germany) (Gorzolka et al., 2012; Lisec et al., 2006; Zörb et al., 2006). The GC-MS derivatization step is necessary for the conversion of the extracted metabolites (nutritive and non-nutritive analytes) into well vapourizable state (preferably undecomposed). During the process, mainly hydrophobic functional groups are converted into vapourizable analytes in an aqueous methanolic extract.

3.10.4.3 GC-MS Instrumental Analysis of Derivatized Metabolites

Sample volumes of 1µL were analyzed with a TraceGC gas chromatograph coupled to a PolarisQ ion trap mass (TRAP) spectrometer equipped with an AS2000 auto sampler (Thermo Electron, Dreieich, Germany). The derivatised metabolites were evaporated at 250°C in splitless mode and separated on a 30 x 0.25mm RTX-5MS capillary column with 0.25 µm coating equipped with an integrated 10m guard column (Restek, Bad Homburg, Germany). Helium carrier gas flow was adjusted to 1mL/minute. The interface temperature was set to 250°C and ion source temperature to 220°C. The oven temperature was kept constant for 3 minutes at 80°C and subsequently raised to 325°C at 5°C/minute. The system was equilibrated for 2 minutes at 80°C after each analysis. The mass spectra were recorded at 1 scan/second with a scanning range of 50-650 m/z (Gorzolka et al., 2012; Lisec et al., 2006; Persicke et al., 2012; Zörb et al., 2006).

3.10.4.4 Data Mining, Metabolite Identification, and Relative Quantification (GC-MS)

The data set of the metabolites selected for data mining to serve as the relevant indicators of the nutritive and non-nutritive (antinutritional) contents of the cereal samples were manually inspected to effect correction (where necessary) in mis-identified metabolites from the updated databases used by XCalibur™ software (Thermo Electron, Dreieich, Germany). Metabolites were identified by matching their chromatographic retention times (RT) and mass-spectral fragmentation patterns using their mass-charge (m/z) ratio in the updated metabolome databases (GMD 2008 & NIST 2009) of the XCalibur™ software at the CeBiTech Laboratory, Bielefeld, Germany. The meticulous processes of chromatogram identification, calibration, data acquisition, peak integration, data extraction, data transformation/conversion, data cross-checking, validation, and data exportation into a user-friendly data file format in Microsoft Excel (XLSX) and/or a metabolomics data management and statistical analysis software such as MeltDB constituted the data mining process (Gorzolka et al., 2012; Persicke et al., 2012; Zörb et al., 2006). These processes were painstakingly carried out to identify and estimate the relative quantities of the selected metabolites that served as quantitative indices of the nutritive and non-nutritive contents of the cereal samples. The relative quantities of the metabolites were estimated using the raw data files generated from the mass spectrometer (molecular ion detector), converted to computable document files (cdf) in the Xcalibur™ software (Thermo Scientific™, Germany). By integrating the peak areas of the metabolite ions, the relative response ratios were calculated by normalizing each metabolite's peak area to the peak area of the internal standard (Ribitol) and dividing the value by the dry weight of the sample from which the metabolites were extracted (Gorzolka et al., 2012; Persicke et al., 2012; Zörb et al., 2006).

3.10.4.5 Nutritional Significance Evaluation and Classification of TCPMs (GC-MS)

From the foodomics experimental data, the magnitude of changes (fold change) in the relative quantities of the relevant metabolites (nutrients and non-nutrients) present in the experimental cereal samples compared to the reference (or control) samples, were estimated using Microsoft Excel software (Version 2016). The TCPMs that effected more than 10% net changes (increase or decrease) in the relative quantities of the selected nutrients and non-nutrients were qualitatively determined guided by the a priori defined criteria premised on the principles for the recommended nutrient intake (RNI) values (non-validated) and biological relevance of the changes (Buttriss et al., 2017; European Food Safety Authority, 2011; Semba et al., 2016). The TCPMs were qualitatively classified as having effected nutritionally significant changes in the relevant metabolites or not ($\geq$ 10% loss, Yes =1 and No= 0).

3.10.5 Absolute Quantification of Total Amino Acids in Cereals (UHPLC-MS/MS)

The effects of the TCPMs on the absolute quantities or concentrations (nmol/mL) of essential amino acids in the cereal samples were also determined using UHPLC-MS/MS to complement the determination of the nutritional significance evaluation of each TCPM from the results of the GC-MS analyses. Trial foodomics (food metabolomics) analyses on some of the cereal samples were conducted to optimize the accuracy and reliability of the analytical UHPLC-MS/MS laboratory protocols, instrumentation, and amino acid standards (calibration curve) before applying the optimized protocols to the cereal samples in the definitive study. Sun-dried whole grains of each of the three cereals were laboratory-milled and served as the control or reference samples for the experimental samples. The acid-hydrolyzed samples were analyzed in three technical replicates (triplicates) using 50 mg of each biological sample (Satorius TE214S Analytical Weighing Balance, Central Europe) as determined from the optimized analytical protocol. 100mg was used for the analysis of the physiologically free EAAs in the cereal samples also in technical triplicates. The absolute quantities of essential and non-essential amino acids were determined using the Phenomenex® EZ Faast™ amino acid analysis kits and protocols (Phenomenex®, Carlifornia, USA). The UHPLC-MS/MS Phenomenex® EZ Faast™ analytical protocol (targeted metabolomics) was specifically developed for the determination of the absolute concentrations (nmol/mL) of over 70 proteinogenic (protein-forming) and non-proteinogenic (non-protein-forming) amino acids (AAs) in either the physiologically free or totally free state (total AAs present in protein or peptide-bound hydrolysates plus the physiologically free AAs) in various biological samples. The sample preparation with the Phenomenex analytical protocol was made up of a fast SPE (solid phase extraction) step (ion exchange in resin-packed pipet tips), derivatization with propyl chroloformate and followed up with a clean-up by liquid-liquid extraction (biphasic aqueous/iso-octane mixture). The SPE involved entrapping the free amino acids into resin-packed sorbent tips in a meticulous procedure outlined in the Phenomenex® EZ Faast™ amino acids analytical manual. Derivatization involved getting the metabolites (amino acids) of interest transformed into a form (chemical reaction) that allowed it to be easily vapourized and ionizable. The derivatized total amino acids were separated into an organic layer (liquid-liquid extraction) to free it of interfering compounds and the supernatant was dried over nitrogen stream (≤10 minutes maximum after drying) in autosampler vials in readiness for the UHPLC-MS/MS analysis. The dried samples of extracted amino acids (stored away from light) were each reconstituted as a concentration step, with 100µL of 68% methanol (MeOH) containing 10mM ammonium formate.

3.10.5.1 Extraction of Total Amino Acids from the Cereal Samples

Metabolite (total amino acids) extraction involves the separation of the metabolites into a medium or solution from which the metabolites could be chemically transformed in the derivatized form for further analysis. The total amino acid contents in the cereal proteins were extracted from 50 mg of each cereal sample (Satorius TE214S Analytical Weighing Balance, Central Europe). The samples were each firstly acid-hydrolyzed using 2.5 mL 6N HCl in micro-reaction glass vials (10 mL) incubated at 110°C in an oven (Memmert, Germany) over a 24-hour period. The acid-hydrolyzed sample (protein hydrolysate) was allowed to cool down to room temperature and allowed to settle to obtain a clear supernatant (stored at -20°C).

3.10.5.2 SPE, Derivatization and Liquid-Liquid Extraction of Amino Acids

The EZ Faast™ amino acids analyses were carried out according to the Phenomenex® EZ Faast™ amino acids analytical protocols outlined in the accompanying manual to the test kits (Phenomenex®, Carlifornia, USA). 700µL of the protein hydrolysate supernatant (instead of 100 µL) was pipetted into each sample glass vial and 200µL of Reagent 2 (Sodium Carbonate Solution) was added and mixed briefly to neutralize the acid (pH ≥2 ≤5). 100µL of Reagent 1 (Internal Amino Acid Standard Solutions) was added to 25 µL of each sample mixture in the flat-bottom sample reaction glass vials (8 x 40 mm: 1mL). The solid phase extraction (SPE), derivatization and liquid-liquid extraction procedures were carried out as outlined in the Phenomenex® EZ Faast™ amino acids analytical manual. Freshly prepared elution medium (Reagent 3A and 3B) was used for the SPE. Propyl chloroform was used for the derivatization of the total amino acids in the sample. N-Propanol was used in place of UHPLC grade water in the procedure. The derivatized amino acids which were freed from possible interfering compounds in an organic layer (liquid-liquid extraction), were centrifuged at 1,300-1,500 rpm for 2 minutes. 100 µL of the supernatant (clear organic layer) was transferred using a Pasteur glass pipette into the autosampler vials carefully avoiding a transfer of the aqueous layer along with the organic layer. The organic supernatant was dried over nitrogen stream (≤10 minutes maximum after drying) in the autosampler vials in readiness for the UHPLC-MS/MS analyses.

3.10.5.3 UHPLC-MS/MS Instrumental Analyses of Total Amino Acids in Cereal Proteins

The dried total amino acids were re-dissolved (or re-constituted) with 100 µL of the LC mobile phase eluent (mixture of 68% methanol containing 10mM of Ammonium formate in Milli-Q water and 83% methanol containing ammonium formate) and transferred into autosampler vial inserts. The solution was vortexed for about 10 seconds three (3) or four (4) times until the samples were completely dissolved, placed in the autosampler vial inserts in the autosampler vials and covered in readiness for the UHPLC-MS/MS instrumental analysis. The autosampler vials were randomly arranged on the auto-sampling UHPLC-MS/MS instrumentation set up as a quality control measure to ensure that the results were not order-influenced.

2µL of sample volume of in the autosampler vials were injected and analyzed with a liquid chromatograph coupled to a micrOTOF-Q mass spectrometer (Bruker Daltonics, Bremen, Germany) equipped with a Dionex Ultimate 3000 Autosampler (Thermo Scientific, Germany) with a scan range of 100-600m/z. The derivatised metabolites (AAs) after the separation phase in the UHPLC column, were evaporated at 250°C in splitless mode and ionized (electrospray inonization, ESI) for detection on the mass spectrometer. The elution medium or mobile phase eluent (mixture of 68% methanol containing 10mM of ammonium formate in Milli-Q water and 83% methanol containing ammonium formate) was used for the separation of the total amino acids on the appropriate EZ Faast™ UHPLC column (250 x 2.0mm; AAA-MS; 0.25mL/minute for 2.0mm ID column; column temperature 35°C; polar endcapped C18 column packing) because the flow rate is most compatible with the UHPLC-MS/MS system used.

3.10.5.4 Data Mining, Amino Acid Identification and Absolute Quantification

The data set of the selected essential and non-essential amino acids was exported from the UHPLC-MS instrumentation software into the Compass Data Analysis (CDA) software (Version 4, Bruker Daltonics, Germany) at CeBiTech, Bielefeld. Each amino acid was preliminarily identified using its retention index by matching the Extracted Ion Chromatogram (EIC) retention times (RT) and mass-spectral fragmentation patterns using their mass-charge (m/z) ratio (molecular weight of the derivative reaction product). The identity of each metabolite (amino acid) in the Compass Data Analysis software was confirmed by its MS/MS (M2 or MS^2) chromatographic retention times (RT) and mass-spectral fragmentation patterns if MS (MS1 or MS^1) was in doubt due to multiple metabolites eluted exactly at, or around the same time. The meticulous processes of Extracted Ion Chromatogram (EIC) identification, calibration, data extraction, peak integration, data transformation/conversion, isotope correction, data cross-checking, data validation and data exportation into a user-friendly metabolomics bioinformatics data management and statistical analysis interface (QualAnalysis and QuantAnalysis Version 4.0) constituted the data mining process. These processes were painstakingly carried out to identify and calculate the absolute quantities of the essential amino acids. The QuantAnalysis Version 4.0 interface of the Compass Data Analysis software controlling the outputs of the UHPLC-MS/MS analytical instrument, performed the auto-calculation of the absolute concentrations of the amino acids based on the concentrations of the internal standards (IS), standard AAs mixture and inputs of other key parameters. The internal standard (IS) used was a mixture of 0.2mM Homoarginine (HARG) for early eluting AAs, 0.2mM Methionine-d3 for medium retention time (RT) AAs and 0.2mM of Homophenylalanine (HPHE) for the late eluting AAs. Quantification was performed on peak areas of each amino acid's derivative product, normalized to the internal standard (IS), dilution factor and cereal material dry weight. The protein hydrolysate amino acid standard mixture (SD) used was composed of 20 AAs of 200 nmol/mL each. The concentrations of the calibration standard solutions (SD) used were SD1= 20 nmol/mL, SD2= 100 nmol/mL, and SD3= 200 nmol/mL, respectively. The results were reported in nmol/mL (µmol/L).

3.10.5.5 Statistical Analyses: Total Amino Acids in the Cereal Proteins (UHPLC-MS/MS)

Computation of the percentage (%) changes in the essential amino acid (EAA) concentrations were conducted in the Microsoft Excel (2016) spreadsheet exported from the QuantAnalysis interface of the Compass Data Analysis (CDA) software (Version 4, Bruker Daltonics, Germany). The absolute quantities (nmol/mL) of selected essential amino acids in the experimental cereal samples were statistically analysed to determine mean group differences between the reference or control samples and the experimental cereal samples using One-Way ANOVA and Dunnett's Post-hoc test using SPSS software (version 25). The illustrative results of lysine (limiting EAA in cereals) were presented in tables and figures.

3.10.6 Interpretation of Foodomics Laboratory Data (GC-MS/UHPLC-MS/MS)

It was postulated in this study that TCPMs such as soaking, germination, dry milling, wet milling only, and wet milling cum spontaneous fermentation would result in significant changes (≥10% increases or depletion) in the nutritive and non-nutritive (antinutritional) concentrations of the cereal samples, with consequential epidemiological significance. Table 3.2 summarizes the operationally predefined criteria for qualitatively determining the nutritional significance of the effects of each TCPM, on the nutritive and non-nutritive contents of the experimental cereals. The operationally predefined criteria served to generate a dietary quality index (DQI) for the purposes of modelling the potential epidemiological significance of the usage of the TCPMs.

A change in concentration of the relevant nutritive metabolite of at least 10% was used as a basis to determine the DQI (≥ 10% loss in EAA, Yes =1 and No= 0) of complementary meals that could potentially be made from the CMIs due to the TCPM effects (facilitative being ≥ 10% gain in nutrients or EAAs, debilitative being ≥ 10% loss in EAAs, and debilitative being ≥ 10% gain in ANFs). The standard deviation of most biological variables is between 10-15%, an equivalent of 1.2 or 1.3 standard deviation score (SDS) units respectively based on a normally distributed (Gaussian or bell-shape) population data (Buttriss et al., 2017). The operationally set 10% threshold or cut off in this study was guided by the statistical philosophy and principles of biological relevance for the interpretation of population reference charts (PRC) and standard deviation scores

(SDS) used for estimating cut-off points for body mass index (BMI), waist circumference (WC), recommended nutrient intake (RNI) or recommended dietary/daily allowance (RDA), toxicity thresholds, and biologically relevant differences, et cetera in the absence of a validated benchmark, as used in most epidemiological studies (Buttriss et al., 2017; Cole, 2012; Kaufman, 1990; Semba et al., 2016).

Table 3.2 Criteria for Qualitatively Determining Nutritional Significance of the TCPMs

#	Net Change in the Relative/Absolute Quantity of Metabolite	Meaning
1	≥10% loss in relative/absolute quantity of nutritive metabolite (nutrient) was considered nutritionally significant.	Debilitative
2	≥10% gain in relative/absolute quantity of undesirable non-nutritive metabolite (antinutritional factor, ANF) was considered nutritionally significant.	Debilitative
3	≥10% gain in relative/absolute quantity of nutritive metabolite (nutrient) was considered nutritionally significant.	Facilitative
4	TCPM treatment that resulted in ≥1 nutritionally significant loss in nutrients and ≥1 nutritionally significant gain in an undesirable non-nutritive metabolite (ANF) was considered to have potential epidemiological significance for inclusion in the hierarchical linear regression modelling of the analytical cross-sectional survey data.	Potentially debilitative
5	TCPM treatment that resulted in ≥2 nutritionally debilitative changes (≥10 % gain in ANFs or ≥10% loss of EAAs) was considered to have potential epidemiological significance for inclusion in the hierarchical linear regression modelling of the analytical cross-sectional survey data.	Potentially debilitative

RDA/RNI = EAR ± 2SD (adequate nutrient intake for 97.5% of study population), where a net change in the relative (GC-MS) or absolute (UHPLC-MS/MS) concentrations of EAAs or ANFs in the experimental cereal samples was considered nutritionally significant (Buttriss et al., 2017; Kennedy & Meyers, 2005; Lawrence & Worsley, 2007).

RNI is defined as the daily recommended intake of a nutrient, set at the Estimated Average Requirement (EAR) plus 2 standard deviations (SD), which meets the nutrient requirements of almost all (97.5%) apparently healthy individuals in an age- and gender-specific population following a normal distribution or pattern (Gaussian or bell-shaped) (Buttriss et al., 2017; Kaufman, 1990; Roman-Viñas & Serra-Majem, 2019). Where the absolute nutrient requirement values are unknown, a Gaussian or normal distribution can be assumed where EAR plus two standard deviations (2 SDs) would be adequate for the nutrient needs of 97.5% of the population. A standard deviation score (SDS) corresponds mathematically to an equivalent percentile on a population reference chart (Buttriss et al., 2017). An operational criterion, guided by the statistical philosophy and principles for estimating the cut-off points for the recommended daily allowance (RDA) of various food nutrients and components, was used to determine which TCPMs were nutritionally significant or not. A variation between the original (sun-dried cereal) and after TCPM-treatment contents of any given nutrient (EAAs) or non-nutritive constituent (ANF) in the experimental cereals from the foodomics analyses, with greater than or equal to 10% percent as threshold (≥10%), was considered nutritionally significant. This premise as applied, quantitatively translates ≥10% increase or depletion (± 10.0%) in the nutritive (EAAs) and non-nutritive (ANFs) contents of the cereals to mean that any variation beyond plus or minus two standard deviations (±2SD) exceeds the RNI or falls short of the RNI lower threshold respectively (Buttriss et al., 2017; Cole, 2012; FAO & WHO, 2006; Gernand, Schulze, Stewart, West, & Christian, 2016; Kaufman, 1990; Kennedy & Meyers, 2005; Lawrence & Worsley, 2007; Otten et al., 2006; Roman-Viñas & Serra-Majem, 2019; WHO, 2007). Besides, a 10% loss in a limiting EAA such as lysine could potentially have biological relevance with possible nutritional epidemiological significance on the nutritional status of vulnerable infants and young children.

3.11 Epidemiological Regression Analyses of the Nutritionally Significant TCPMs

Following the qualitative determination of the nutritional significance of each of the TCPM usage indicators (frequencies, preferences, or durations) from the evaluation of the GC-MS and UHPLC-MS/MS results, the association between the usage responses (Yes=1; No=0) of the TCPM indicators by the mothers for complementary meal ingredient preparation (grains, flour, and dough) and the nutritional status (stunting, wasting and underweight status) of the children, were analysed. Responses to enquiries on the usage (frequencies, preferences, or durations) of the TCPMs by the mothers from the cross-sectional survey were regressed on the anthropometric Z-scores (LAZ-stunting, WLZ-wasting and WAZ-underweight). The proximal risk factors of undernutrition guided by the three-step hierarchical conceptual framework of the study (**Figure 3.1**) were adjusted for, to determine the additional variance contributed by the TCPM usage indicators over and above the variance explained by the putative proximal risk factors.

Bivariate association analyses and multivariable hierarchical linear regression analyses of the relationships between the usage of the nutritionally significant TCPMs (exposure) and undernutrition status (stunting, wasting and underweight status of the children as the outcome variable), with adjustment made for confounding effects of the putative proximal risk factors and/or covariates of undernutrition were then conducted using SPSS (Version 25). The additional variance accounted for by the usage of each TCPM over and above the variance contributed by the proximal determinants of child nutritional status was examined.

3.12 Ethical Clearance and Community Entry Permit Protocols for the Study

Ethical clearance was secured from the Ghana Health Service Ethics Review Committee (GHS-ERC: 011/11/17) in Accra, Ghana for the pilot study and the Ethics Committee of Bielefeld University (EUB 2018-083) in Bielefeld, Germany for the definitive study. The study information brief and consent form which was developed in compliance with the requirements for the study's ethical clearance, outlines the profile of the principal researcher (PR), purpose of the research, the responsibilities and expectations of the principal researcher, the responsibilities and rights of the participants and a section for participant's signature or thumb printing to indicate consent (**Appendix B**).

After explaining the purpose and scope of the study to the participants in their local languages, written informed consent prior to enrolment was obtained from each mother (endorsed with a thumb print or signature on the consent form), in addition to verbal consent from the household heads. Community entry permit protocols for the study area were followed as provided by the District Assemblies and local opinion leaders. Participants were assured of confidentiality and anonymity, right to withdrawal without consequences and voluntary participation in the study. Coding of the data obtained coupled with restricted access to the survey data ensured anonymity and confidentiality of respondents' information and responses, respectively.

4 RESULTS

4.1 Section Overview

The results section of this dissertation presents textual and graphic outputs of the analyses of both the quantitative cross-sectional survey and foodomics laboratory data sets. Results of diagnosis of the suitability of the data sets obtained (assumptions underlying the statistical techniques), quality of the data collection instrument (validity and reliability), quality of the optimized foodomics analytical laboratory protocols and instrumentation, and the main descriptive and analytical study findings in line with the research objectives, constitute this section. The descriptive results are made up of the prevalence of the IYCF indicators, HFRUP indicators, TCPM indicators, and child nutritional status (stunting, wasting and underweight status). The analytical results comprise of the bivariate associations between the focal explanatory variables (IYCF, HFRUP and TCPM) and the dependent variables (child nutritional status), the multivariable associations between IYCF indicators and dependent variables (stunting and wasting), the multivariable associations between HFRUP indicators and dependent variables (stunting and wasting), the quantitative changes in the concentrations of cereal metabolites due to the effects of TCPMs (GC-MS and UHPLC-MS), and the multivariable associations between the TCPM indicators and child nutritional status.

4.2 Diagnostics of Assumptions Underlying Statistical Methods and Instrument Quality

The prescreening, statistical tests, and analyses run for the diagnostics of the various assumptions underlying the statistical methods (multiple linear regression and multiple logistic regression) applied to the analytical cross-sectional survey data, during the data curation process showed that all the assumptions and prerequisites for univariate (descriptive), bivariate, and multivariable analyses were satisfactorily met. These include the suitability of data types or forms of the independent and dependent variables (categorical or continuous, and scale of measurement), normality of data distribution (Q-Q Plots and Shapiro-Wilk tests), sample size adequacy, missing cases, univariate outliers, multivariate outliers (Mahalanobis and Cook's distance), multicollinearity (Variance Inflation Factor, VIF), linearity (scatter plots), normality of the residuals, independence of residuals (or independence of observations), homoscedasticity of residuals or equality of variances (residual and scatter plots), and the survey instrument validity, and reliability (Field, 2013; Ghasemi & Zahediasl, 2012; Hair, Black, Babin, & Anderson, 2014; Tabachnick, G. Barbara and Fidell, S. Linda, 2007). The response rate of the survey was 100% comparable to similar community-based household surveys in Northern Ghana (Ghana Statistical

Service, 2018; Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015). Fifty-three (53) cases were deleted from the original dataset (N=634) due to missing cases, implausible Z-scores (anthropometric measurements) and other outliers resulting in a sample size of 581. The Kuder-Richardson-20 coefficient alpha value (K-R20 α-value) for the food intake assessment section (food groups' classification sub-scale) of the composite survey instrument was 0.70. The domains (or scope) of the explanatory variables (TCPMs and HFRUPs) conceived and operationalized as parts of the food utilization dimension of household food insecurity (HFI) were judged qualitatively to be reasonably adequate and theoretically plausible by expert views. The validity (content and construct) and reliability (internal consistency and equivalence) of all the sub-sections of the composite data collection instrument (interviewer-administered survey questionnaire) were all deemed satisfactory (Bountziouka & Panagiotakos, 2010; Field, 2013; Heale & Twycross, 2015; Scholtes, Terwee, & Poolman, 2011; Souza et al., 2017; Tabachnick and Fidell, 2007).

The statistical tests run on the foodomics laboratory data also met the required assumptions underlying the use of the parametric F-test (One-Way ANOVA) and the Post hoc test (Dunnett). Assumptions of normality, independence of observation, and equality or homogeneity of variance (determined by the Levene's test) were not violated (Du Prel, Röhrig, Hommel, & Blettner, 2010; Field, 2013; Ghasemi & Zahediasl, 2012; Lee & Lee, 2018; McHugh, 2011; Yan et al., 2016).

4.3 Descriptive Results of the Cross-Sectional Survey

4.3.1 Characteristics of the Study Participants

The data for the 581 study participants from the five districts used for the analyses showed that they were mostly (68.2%) from the Dagomba ethnic group (**Table 8.1, Appendix A**). The mean (±SD) maternal and child ages were 29.31 ±6.40 years and 13.25 ±5.09 months respectively (**Table 4.1 and Table 4.2**). Of the children, 51.8% were males and 41.7% were in the age range 6–11 months old. Of the mothers, 90.2% were Muslims and a little over half (55.2%) were between 25 and 34 years of age. Almost all (97.7%) were married and most (94.3%) had basic education (completed only primary/junior high school) or had no formal schooling at all (**Table 4.1 and Table 4.2**). The majority (86.9%) of the mother–child pairs had no access to improved toilet facilities in their households. A little over half (52.2%) of the study participants had household access to improved sources of drinking water. A significant majority (91%) had access to electricity as a means of lighting their homes and powering electrical devices (**Table 8.1, Appendix A**).

Using principal component analysis (PCA) of the ownership of some durable household assets, access to utilities and household space adequacy, 39.9% and 40.3% of the study participants were classified as being of low and medium-level socio-economic status (SES) respectively. Of the households surveyed, 44.8% had 6–10 occupants (**Table 8.1, Appendix A**).

Table 4.1 Maternal Characteristics

Characteristics	Frequency	%
Age *		
15–24 years	136	23.4
25–34 years	321	55.2
35–49 years	124	21.3
Marital Status		
Not married	16	2.8
Married	565	97.2
Maternal Height		
160 cm and above	282	48.5
Below 160 cm	299	51.5
Occupation		
Trader/Vendor/Manual Labourer	166	28.6
Farmer	323	55.6
Vocational/Skilled Service Worker	48	8.3
Unemployed	44	7.6
Number of Postnatal Care (PNC) Visits		
Fewer than 4 times	106	8.2
At least 4 times	475	81.8
Number of Antenatal Care (ANC) Visits		
Fewer than 4 times	34	5.9
At least 4 times	547	94.1
Currently Breastfeeding		
Yes	560	96.4
No	21	3.6

Data Source: June, 2018 * Mean maternal age (± standard deviation) was 29.31 ± 6.40 years. N=581

Table 4.2 Child Characteristics

Characteristics	Frequency	%
Age *		
6–11 months	242	41.7
12–17 months	185	31.8
18–23 months	154	26.5
Gender		
Male	301	51.8
Female	280	48.2
Immunisation Status		
Up to date	373	64.2
Not up to date	208	35.8
Place of Birth		
Family Home/Residence	225	38.7
Community-Based Health Planning and Services (CHPS) Compound/Traditional Maternity Home	45	7.7
Clinic/Health Centre	153	26.3
Hospital	158	27.2
Usage of Insecticide-Treated Net (ITN)		
Yes	518	89.2
No	63	10.8
Recent Illness/Morbidity (within the two weeks immediately prior to the survey)		
Yes	215	37.0
No	366	63.0
Child's Birth Weight (*n* = 274)		
Less than 2.5 kg	246	89.8
More than 2.5 kg	28	10.2

Data Source: June, 2018 * Mean child age was 13.25 ± 5.09 months. N = 581

4.3.2 Prevalence of IYCF Indicators in the Northern Region of Ghana

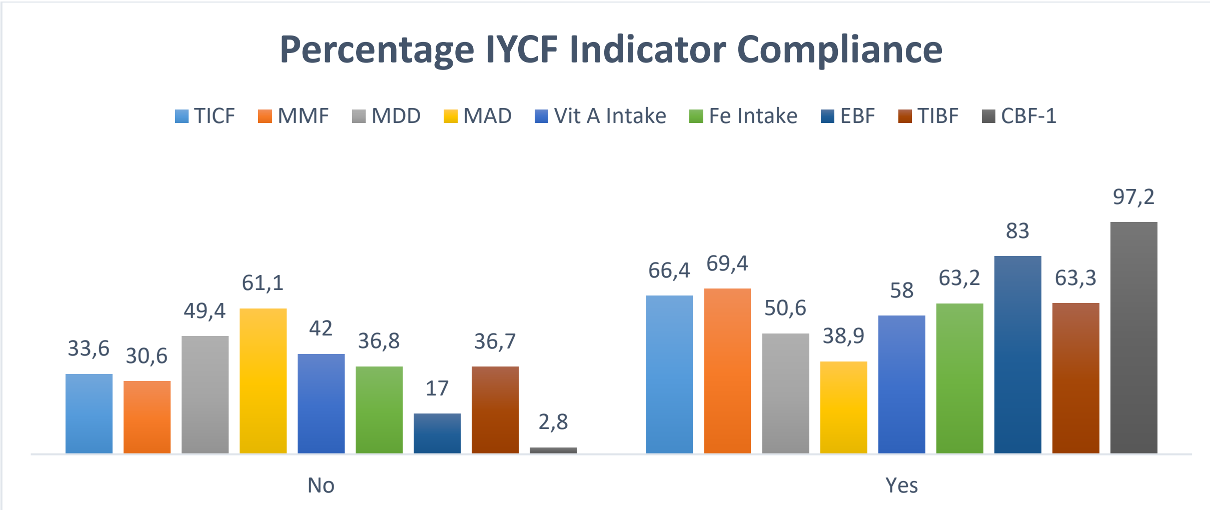

Figure 4.1 Percentage Level of Compliance with IYCF Indicators by the Children

MMF was the CF-related IYCF indicator with the highest level of compliance (69.4%) among the eight core WHO/UNICEF IYCF indicators whiles continuous breastfeeding at year one was the BF-related IYCF indicator with the highest level of compliance (97.2%) (**Figure 4.1**). Timely initiation of breastfeeding (TIBF) that is, breastfeeding within an hour of birth was the BF-related indicator with the lowest level (63.3%) of compliance whiles MAD was the CF-related IYCF indicator with the lowest level of compliance (38.9%) (**Figure 4.1**).

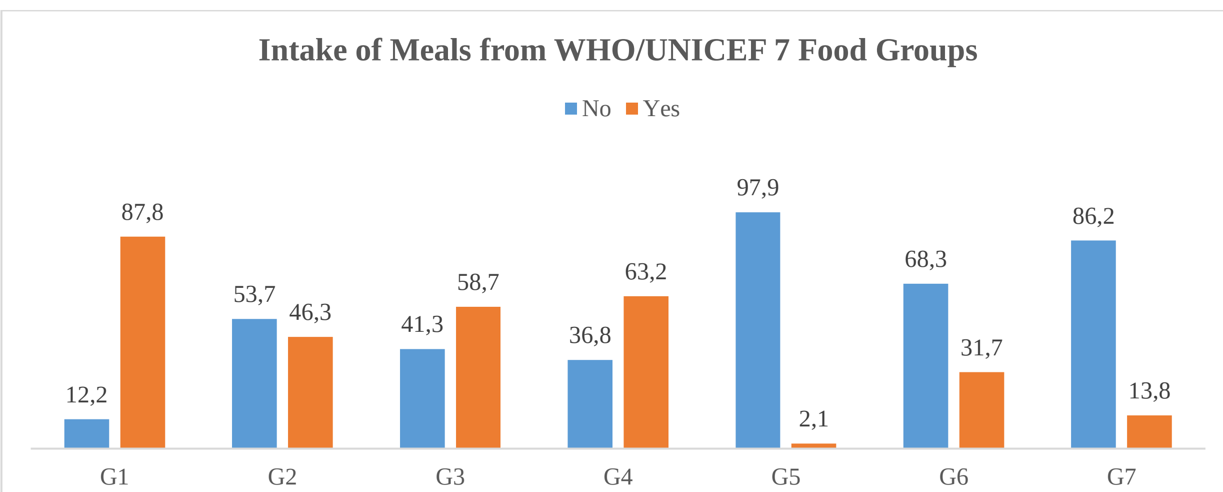

Figure 4.2 Percentage of Children Fed with Meals from the Seven Food Groups (24HFR)

Food Groups: G1- Grains, Roots and Tubers; G2- Vitamin A-Rich Fruits and Vegetables; G3- Other Fruits and Vegetables; G4- Flesh Foods; G5- Eggs; G6- Legumes and Nuts; G7- Dairy Products

Figure 4.2 shows the level of intake by the children of meals made from food ingredients belonging to the seven food groups as classified by WHO/UNICEF. G1 food group (cereals, roots, and tubers) followed by G4 food group (meat, fish, and offal) and G3 food group (non-Vitamin A-rich fruits and vegetables) had the highest to high level intake of 87.8%, 63.2% and 58.7% respectively whiles intake of Eggs (G5), the gold standard for complete protein source had the lowest level of food intake (2.1%).

4.3.3 Frequency Distribution: Food Utilization Practices (HFRUP Indicators)

Table 4.3 presents six selected habitual food resource utilization practice (HFRUP) indicators as one of the domains of the food utilization dimension of household food insecurity (HFI) examined in this study. The habitual usage of three specific staple cereals were inquired about for cereal type preferred or often used.

Of the 581 mother-child dyads interviewed, 78% indicated that they fed their children habitually with complementary meals made from predominantly cereal-only-based ingredients. Fermented dough (39.6%) followed by fresh dough (36.5%) were the most preferred forms of the cereal ingredients habitually used for the preparations of complementary meals for the children in the Northern Region of Ghana. Maize was the most preferred type of cereal (74.5%) habitually used in the preparation of complementary meals for the children by their mothers.

Majority of the mothers (63.3%) indicated that they habitually stored dough meant for the preparation of complementary meals for their children for 3 days or less whiles an additional 28.4% customarily tended to store the dough from 4 days to a maximum of one week. Of the various types of containers or vessels used to store dough meant for the preparation of complementary meals for their children, 85.7% of the mothers indicated that they habitually used plastic containers. Dough meant for the preparation of complementary meals for the children were always or very often made habitually at home by 67.6% of the mothers interviewed. The remaining 32.3% occasionally purchased dough meant for the preparation of complementary meals for their children from the open market or sourced dough from their neighbours.

Table 4.3 Prevalence of HFRUP Indicators in the Northern Region of Ghana

HFRUP Indicators	Usage Response	Frequency	%
Intake of Cereal-Only-Based Complementary Meals	Yes, always	137	23.6
	Yes, very often	129	22.2
	Yes, sometimes/occasionally	187	32.2
	No	128	22.0
Cereal Form Preferably/Often Used	Fermented dough	230	39.6
	Fresh dough	212	36.5
	Flour	139	23.9
Cereal Type Preferably/Often Used (Maize)	Always/very often	433	74.5
	Occasionally	114	19.6
	Not at all	34	5.9
Cereal Type Preferably/Often Used (Sorghum)	Always/very often	89	15.3
	Occasionally	140	24.1
	Not at all	352	60.6
Cereal Type Preferably/Often Used (Millet)	Always/very often	100	17.2
	Occasionally	201	34.6
	Not at all	280	48.2
Dough Storage Duration	3 Days or Less	368	63.3
	4-7 days Max	165	28.4
	More than 7 days	48	8.3
Dough Storage Container Type Used	Calabash/Jute Sacks	11	1.9
	Metal Containers	72	12.4
	Plastic Containers	498	85.7
Source of Dough (Homemade)	Yes, always	264	45.4
	Yes, very often	129	22.2
	Yes, sometimes/occasionally	150	25.8
	No	38	6.5

HFRUP: Habitual Food Resource Utilization Practices (Data Source: June, 2018)

4.3.4 Frequency Distribution: Food Utilization Practices (TCPM Usage Indicators)

Table 4.4 presents five of the unit operations of some traditional cereal processing methods (TCPMs) as the focal domain of the food utilization dimension of household food insecurity (HFI) that was examined in this nutritional epidemiological research (NER). Majority (57.7%) of the mothers surveyed indicated that they did not dehull the cereal grains used for the preparation of the complementary meal ingredients (flour or dough) meant for the preparation of complementary meals for their children.

Table 4.4 Prevalence of TCPM Usage Indicators in the Northern Region of Ghana

TCPM Indicator	Usage Response	Frequency	%
Dehulling	Yes, always	64	11
	Yes, very often	19	3.3
	Yes, sometimes/occasionally	163	28.1
	No	335	57.7
Dry-Milling	No- Purchased imported flour/**used other milling methods	25	4.3
	Yes- *Nikanika	556	95.7
Soaking	Less than 6 hours/Quarter Day	98	16.9
	12 hours/Half Day	91	15.7
	More than 12 hours (Half Day) up to 24 hours (1 Day)	204	35.1
	More than 24 hours (1 day) up to 48 hours (2 Days)	138	23.8
	More than 48 hours (2 Days)	50	8.6
Wet-Milling & Spontaneous Fermentation	Less than 6 hours/Quarter day	359	61.8
	12 hours/Half Day	177	30.5
	More than 12 hours up to 24 hours	18	3.1
	More than 24 hours up to 48 hours/2 Days	17	2.9
	More than 48 hours/2 Days	10	1.7

*Commercial Local Attrition Mill **Domestic Pounding (mortar-pestle)/Milling-Grinding Stone

Only 4.4% always or very often dehulled the cereal grains before using it for the preparation of the complementary meal ingredients. Majority of the mothers (95.7%) obtained or sourced their dry-milled flour meant for complementary meal preparation for their children from the services of the local attrition mill called ‘Nikanika’. This milling machine is commonly available as a commercial service to the communities. The rest used the laborious method of domestic mortar-pestle pounding, stone grinding, or purchased already-made flour (imported) for use in the preparation of complementary meals for their children. The ‘Nikanika’ service is also utilized for wet milling. Majority (67.7%) of the mothers who prepared the complementary meal ingredient (dough) at home, usually soaked the cereal grain of choice for up to a maximum of 24 hours before wet milling to obtain the dough. Out of all the mothers interviewed during the survey, 35.1% indicated that they soaked the grains between 12-24 hours. Only 8.6% of the mothers indicated that they usually soaked their grains for more than 48 hours before wet milling. Of the mothers interviewed, 92.3% indicated that they perceived that (alcoholic aroma or sour taste) spontaneous or natural fermentation begun to take place in fresh dough, 12 hours or less after wet milling their soaked grains.

4.3.5 Nutritional Status of the Children by Age

The prevalence of stunting (LAZ<-2SD), wasting (WLZ<-2SD), underweight (WAZ<-2SD) and overweight (WLZ>+2SD) status amongst children in the Northern Region of Ghana was 33.2%, 14.1%, 27% and 2.6% respectively. Of these children classified as stunted, wasted, underweight or overweight, 79.3%, 65.9%, 70.7% and 60% respectively were aged 12–23 months (**Table 4.5**).

Table 4.5 Nutritional Status of Children by Age

		Child Age						Total	
		6–8 months		9–11 months		12–23 months			
Nutritional Status		n	%	n	%	n	%	N	%
Stunting (LAZ)	No	120	30.9	82	21.1	186	47.9	388	66.8
	Yes	21	10.9	19	9.8	153	79.3	193	33.2*
Wasting (WLZ)	No	126	25.3	88	17.6	285	57.1	499	85.9
	Yes	15	18.3	13	15.9	54	65.9	82	14.1*
Underweight (WAZ)	No	116	27.4	80	18.9	228	53.8	424	73.0
	Yes	25	15.9	21	13.4	111	70.7	157	27.0*
Overweight (WLZ)	No	135	23.9	101	17. 8	330	58.3	566	97.4
	Yes	6	40.0	0	0.0	9	60.0	15	2.6*

*Prevalence of Nutritional Status Indicator. Row % of cross tabulation are presented in the table, except for Total % of *N* in the last column. (N=581)

4.3.6 Prevalence of IYCF Indicators by Age of Children in Northern Ghana

Of all the IYCF indicators, majority of the children who were compliant with MDD (42.2%), MAD (44.7%), ACF (45.7%), intake of iron-rich foods (42%) and intake of Vitamin A-rich foods (38.8%) were in the age group 12-17 months. Majority of the children who were TICF (43.3%) and MMF (36.7%) compliant were in the 6-11 months age group (**Table 4.6**).

Table 4.6 Prevalence of IYCF indicators by child age

IYFC Indicators		Child Age 6–11 months		12–17 months		18–23 months		Total (IYCF)	
		n	**%**	**N**	**%**	**n**	**%**	**N**	**%**
TICF: Timely Introduction to Complementary Feeding	No	75	38.5	64	32.8	56	28.7	195	33.6
	Yes	167	43.3	121	31.3	98	25.4	386	66.4 *
MMF: Minimum Meal Frequency	No	94	52.8	48	27.0	36	20.2	178	30.6
	Yes	148	36.7	137	34.0	118	29.3	403	69.4 *
MDD: Minimum Dietary Diversity	No	177	61.7	61	21.3	49	17.1	287	49.4
	Yes	65	22.1	124	42.2	105	35.7	294	50.6 *
MAD: Minimum Acceptable Diet	No	193	54.4	84	23.7	78	22.0	355	61.1
	Yes	49	21.7	101	44.7	76	33.6	226	38.9 *
ACF: Appropriate Complementary Feeding	No	200	48.0	110	26.4	107	25.7	417	71.8
	Yes	42	25.6	75	45.7	47	28.7	164	28.2 *
Intake of Iron-rich Foods	No	155	72.4	31	14.5	28	13.1	214	36.8
	Yes	87	23.7	154	42.0	126	34.3	367	63.2 *
Intake of Vitamin A-rich Foods	No	145	59.4	59	24.2	40	16.4	244	42.0
	Low	93	28.6	126	38.8	106	32.6	325	55.9 *
	High	4	33.3	0	0.0	8	66.7	12	2.1 *

* Prevalence of complementary feeding (CF)-related IYCF indicator. Row % of cross tabulation are presented in the table, except for Total % of *N* in the last column. (N = 581)

4.4 Results of Bivariate Analyses

4.4.1 Bivariate Association between IYCF Indicators and Child Stunting Status

In the bivariate analysis, intake of Vitamin A-rich foods (Vit A), MDD and MAD were significantly associated with stunting at $p<0.05$ whiles ACF and Fe were significantly associated with stunting at $p<0.1$ (**Table 4.7**). The covariates or factors found to be significantly associated with stunting ($p<0.05$) include the district of residence, maternal age, religion, tribe, child age group, maternal height, number of postnatal care (PNC) visits, usage of insecticide-treated nets (ITN) and number of occupants per household (**Table 8.2, Appendix A**).

Table 4.7 Bivariate Analysis: Association between IYCF Indicators and Stunting Status

IYCF Indicators		Nutritional Status (n)%		Total (N)%	Test Statistic	
		Normal	Stunted			
TICF	No	(128) 65.6	(67) 34.4	(195) 100.0	$\chi^2 = 0.172$	p=0.678
	Yes	(260) 67.4	(126) 32.6	(386) 100.0		
MMF	No	(124) 69.7	(54) 30.3	(178) 100.0	$\chi^2 = 0.960$	p=0.327
	Yes	(264) 65.5	(139) 34.5	(403) 100.0		
MDD	<4 foods	(212) 73.9	(75) 26.1	(287) 100.0	$\chi^2 = 12.838$	$p<0.001^{*}$
	≥ 4 foods	(176) 59.9	(118) 40.1	(294) 100.0		
MAD	No	(251) 70.7	(104) 29.3	(355) 100.0	$\chi^2 = 6.331$	$p=0.012^{*}$
	Yes	(137) 60.6	(89) 39.4	(226) 100.0		
ACF	No	(287) 68.8	(130) 31.2	(417) 100.0	$\chi^2 = 2.781$	$p=0.095^{**}$
	Yes	(101) 61.6	(63) 38.4	(164) 100.0		
Fe Intake	No	(153) 71.5	(61) 28.5	(214) 100.0	$\chi^2 = 3.394$	$p=0.065^{**}$
	Yes	(235) 64.0	(132) 36.0	(367) 100.0		
Vitamin A	No Intake	(183) 75.0	(61) 25.0	(244) 100.0	$\chi^2 = 14.868$	$p=0.001^{*}$
	Low intake	(200) 61.5	(125) 38.5	(325) 100.0		
	High intake	(5) 41.7	(7) 58.3	(12) 100.0		

Significant at *p<0.05 and **p<0.10 *N*=581

4.4.2 Bivariate Association between IYCF Indicators and Child Wasting Status

None of the IYCF indicators was significantly associated with acute undernutrition (wasting) in the bivariate analysis at p<0.10 (**Table 8.3, Appendix A**). The covariates or factors found to be significantly associated with wasting (p<0.05) include religion, marital status, tribe, child gender, child age group, maternal BMI and the utility power source used for lighting households. However, child morbidity (any sickness two weeks prior to the survey), frequency of diarrhoea during the previous six months, child immunisation status and postnatal visits to a healthcare facility were associated with wasting at p<0.10 (**Table 8.4, Appendix A**).

4.4.3 Bivariate Association between HFRUP Indicators and Child Stunting Status

Table 8.5 shows the results of the analysis of the bivariate associations between the HFRUP indicators and stunting status (**Appendix A**). The habitually preferred or often used cereal form, cereal type (sorghum), cereal type (millet) and source of dough (homemade) meant for the preparation of complementary meals for the children were significantly associated with stunting at p<0.10 respectively ($\chi2 = 6.244$, p=0.044; $\chi2 = 10.965$, p=0.004; $\chi2 = 18.951$, p<0.001; $\chi2 = 6.348$, p<0.096).

4.4.4 Bivariate Association between HFRUP Indicators and Child Wasting Status

Table 8.6 shows the results of the analysis of the bivariate associations between the HFRUP indicators and wasting status (**Appendix A**). The habitually preferred or often used cereal form, duration of dough storage and intake of cereal-only-based complementary meals by the children were significantly associated with wasting at p<0.10 respectively ($\chi2$ = 6.519, p=0.089; $\chi2$ = 7.570, p=0.023; $\chi2$ = 4.634, p=0.099).

4.4.5 Bivariate Association between TCPM Usage Indicators and Nutritional Status

Of all the five TCPM indicators, only dry milling was strongly associated (p<0.05) with stunting in the bivariate analysis, F (1, 579) = 6.45, (β= -.81, P=0.011; R^2=0.011, R^2 adjusted=0.009) (**Table 8.7, Appendix A**). Of all the five TCPM indicators, none was significantly associated with wasting status in the bivariate analysis. Dry milling again was the only TCPM strongly associated with underweight status, F (1, 579) = 5.34, (β= -.74, P=0.021; R^2=0.009, R^2 adjusted=0.007) (**Table 8.8, Appendix A**).

4.5 Multivariable Association between IYCF Indicators and Child Stunting (LAZ)

None of the IYCF indicators was significantly associated with stunting after adjusting for potential confounders except intake of iron-rich foods (Fe). Child age group and maternal height were significantly associated with stunting among the children studied in the Northern Region. These predictors explained 27.3% (Nagelkerke R^2 =0.273) of the variance in the outcome of stunting. The Hosmer and Lemeshow goodness of fit (GOF) test for the final model was not statistically significant (p=0.885), confirming parsimony of the regression model (**Table 4.8**). Compared to children who did not receive any meal containing iron-rich foods, children who did receive meals containing iron-rich foods were 50% less likely to be stunted (AOR=0.479, 95% CI: 0.252–0.912, p=0.025). Compared to children aged 6–11 months, children aged 12–17 months were a little over four times more likely to be stunted (AOR=4.399, 95% CI: 2.518–7.686, p<0.001). Compared to children aged 6–11 months, children aged 18–23 months were almost nine times as likely to be stunted (AOR=8.656, 95% CI: 4.846–15.462, p=0.001).

Table 4.8 Multivariable binary logistic regression analysis of predictors of stunting

						95% CI	
Factors and/or Covariates	**B**	**SE**	**Wald**	**Sig.**	**AOR**	**Lower**	**Upper**
Intake of Iron-rich foods (Yes)	−0.735	0.328	5.028	0.025 *	0.479	0.252	0.912
Child's Age (6–11 Months)			53.576	<0.001 *			
Child's Age (12–17 Months)	1.481	0.285	27.078	<0.001 *	4.399	2.518	7.686
Child's Age (18–23 Months)	2.158	0.296	53.169	<0.001 *	8.656	4.846	15.462
Mother's Height (Below 160cm)	0.535	0.203	6.926	0.008 *	1.708	1.146	2.545
Constant	−2.507	0.766	10.701	<0.001	0.082		

* Significance at $p < 0.05$; AOR: Adjusted Odds Ratio; B: Beta value; SE: Standard error; CI: Confidence interval

Compared to children whose mothers were 160cm tall or more, children whose mothers were below 160cm in height were almost twice as likely to be stunted (AOR=1.708, 95% CI: 1.146–2.545, p=0.008). Child age group contributed the most to the variance in stunting (Wald=53.576, p<0.001).

4.6 Multivariable Association between IYCF Indicators and Wasting (WLZ)

None of the IYCF indicators was significantly associated with wasting after adjusting for potential confounders. Child gender, child age group and source of power for lighting households were significant predictors (p<0.05) of wasting among the children studied in the Northern Region (**Table 4.9**). These factors explained 17.4% (Nagelkerke R^2=0.174) of the variance in the outcome of wasting among the children. The Hosmer and Lemeshow goodness of fit (GOF) test for the final model was not statistically significant (*p*=0.272), confirming parsimony of the regression model.

Compared to male children, female children were about 0.42 times (42%) less likely to be wasted (AOR=0.424, 95% CI: 0.248–0.725, *p*=0.002). Compared to children aged 6–11 months, children aged 12–17 months were almost twice more likely to be wasted (AOR=1.977, 95% CI: 1.048–3.730, *p*=0.035).

Compared to children from households with electricity to power lighting and other electrical devices, children who lived in households without electricity were 0.35 times (35%) less likely to be wasted (AOR=0.353, 95% CI: 0.164–0.761, *p*=0.008. Child age contributed the most to the variance in wasting (Wald=11.23, *p*=0.004).

Table 4.9 Multivariable binary logistic regression analysis of predictors of wasting

Factors and/or Covariates	B	SE	Wald	Sig.	AOR	95% CI	
						Lower	Upper
Child's Gender (Female)	−0.858	0.274	9.800	0.002 *	0.424	0.248	0.725
Child's Age (6–11 Months)			11.234	0.004 *			
Child's Age (12–17 Months)	0.681	0.324	4.425	0.035	1.977	1.048	3.730
Child's Age (18–23 Months)	−0.473	0.401	1.391	0.238	0.623	0.284	1.367
Power Source for Light (No Electricity)	−1.041	0.391	7.070	0.008 *	0.353	0.164	0.761
Constant	0.591	0.946	0.390	0.532	1.805		

* Significance at $p < 0.05$; AOR: Adjusted Odds Ratio; B: Beta value; SE: Standard error; CI: Confidence interval.

4.7 Multivariable Association between HFRUP Indicators and Stunting (LAZ)

Multivariable hierarchical binary logistic regression analysis was conducted to examine the association between the HFRUP indicators and stunting status of the children (**Table 4.10**). The type of storage container used by the mothers for storing dough meant for the preparation of complementary meals for their children was the only HFRUP indicator that was statistically significant together with child age group, maternal height, child morbidity status (diarrhoea in the last 6 months) and intake of iron-rich foods. Together, these statistically significant factors at step one accounted for 25-35% variance in stunting status. Child age group contributed the most to the variance in stunting status, Wald (df= 2, N=581) = 51.11, $p < 0.001$. The type of storage container used by the mothers for storing dough meant for the preparation of complementary meals for their children contributed an additional 4% variance, χ^2 (df= 56, N=581) = 168.40, $p < 0.001$ to the variance in stunting status over and above the variance accounted for by the variables in step one of the hierarchical regression model. Compared to children whose mothers stored their dough in calabash and/or jute sacks, children whose mothers stored their dough in metal containers were 38% less likely to be stunted. Compared to children whose mothers stored their dough in calabash and/or jute sacks, children whose mothers stored their dough in plastic containers were 102% more likely to be stunted.

Table 4.10 Hierarchical Multivariable Binary Logistic Regression Analysis (HFRUP Indicators and Stunting)

Model 1: Stunting Status (Stunted vrs Normal)													
		Step 1						Step 2					
Variables		Beta	Wald	Sig	AOR	CI		Beta	Wald	Sig	AOR	CI	
Dough Storage Container	Calabash-Jute sack$^{\Phi}$								6.594	.037**			
	Metal Containers							-.98	.966	.326	.375	.053	2.65
	Plastics Containers							.015	.932	.987	1.02	.163	6.31
Child Age	6-11 months$^{\Phi}$		52.20	.000*					51.11	.000*			
	12-17 months	1.48	26.17	.000*	4.40	2.50	7.75	1.61	27.62	.000*	4.98	2.74	9.07
	18-23 months	2.21	51.66	.000*	9.08	4.98	16.58	2.36	50.24	.000*	10.60	5.52	20.35
Maternal Height	(< 160cm)	.53	6.50	.011**	1.70	1.13	2.56	.52	5.64	.018**	1.68	1.10	2.58
Child Morbidity (Diarrhoea in last 6 months)	None$^{\Phi}$		10.03	.018**					9.34	.025**			
	Once	-.15	.31	.578	.86	.51	1.46	-.27	.90	.342	.76	.43	1.34
	2-3 times	.56	4.11	.043**	1.75	1.02	3.01	.48	2.75	.097***	1.62	.92	2.86
	Every month	-.66	1.43	.232	.52	.18	1.53	-.71	1.45	.229	.49	.16	1.56
Intake of Iron-rich Foods	Yes	-.82	5.77	.016**	.44	.23	.86	-.86	5.76	.016**	.43	.21	.86
Constant		-3.50	19.136	.000*	.03			-2.24	2.094	.148	.106		
Model Summary													
HL Test: χ^2(df=8)	8.95, *p*=.35								7.29, *p*=.51				
Nagelkerke Pseudo R^2	.31								.35				
Cox & Snell Pseudo R^2	.23								.25				
ΔR^2 (Nagelkerke)	.31								.04				
LR Test: χ^2(df)	147.83 (35)*								168.40 (56)*				
% Correct Overall Classification	74.5								75.9				

Significant at $*p < 0.001$, $**p < 0.05$ and $***p < 0.10$; $N = 581$; **AOR**, Adjusted Odds Ratio with **CI**=95% confidence interval; **df**, degree of freedom; **Φ**, Reference category for contrast; **LR**, Likelihood ratio test for comparing with the null-model/previous model; **HL**= Hosmer and Lemeshow test (non-significant means good model fit); **HFRUP**, Habitual Food Resource Utilization Practices; $\mathbf{R^2}$, Coefficient of Determination (Variance in Nutritional Status Explained); $\Delta \mathbf{R^2}$, Change in R Squared (Variance Accounted for due to Addition of HFRUP Indicators)

4.8 Multivariable Association between HFRUP Indicators and Wasting (WLZ)

Multivariable hierarchical binary logistic regression analysis was conducted to examine the association between the HFRUP indicators and wasting status of the children (**Table 4.11**). The cereal form preferably or mostly used ($p < 0.1$) for the preparation of complementary meals by the mothers for their children and the duration of dough storage ($p < 0.05$) are the HFRUP indicators that were statistically significant predictors together with child age group, child gender, child morbidity status (sick in the last two weeks) and utility source of power for lighting their households. Together, these predictors at step 1 accounted for 15-27% variance in wasting status. Child gender contributed the most to the variance in wasting status, Wald (df=1, N=581) =10.49, $p < 0.05$. The cereal form preferably or mostly used habitually for the preparation of complementary meals by the mothers for their children and the duration of dough storage contributed an additional 7% variance, χ^2 (44, N=581) = 93.61, $p < 0.01$ to the variance in wasting status over and above the variance accounted for by the variables in step 1 of the hierarchical logistic regression model. Compared to children whose mothers preferably or mostly used fermented dough for the preparation of complementary meals, children whose mothers preferably or mostly used fresh dough were 44% less likely to be wasted. Compared to children whose mothers preferably or mostly used fermented dough (dough stored for more than 3 days) habitually for the preparation of complementary meals, children whose mothers preferably or mostly used flour were 55% less likely to be wasted. Compared to children whose mothers often used dough stored for 3 days or less for the preparation of complementary meals, children whose mothers often used dough stored for 4 to 7 days were 39% less likely to be wasted. Compared to children whose mothers often used dough stored for 3 days or less habitually for the preparation of complementary meals, children whose mothers often used dough stored for 7 days or more were 111% more likely to be wasted.

Table 4.11 Hierarchical Multivariable Binary Logistic Regression Analysis (HFRUP Indicators and Wasting)

Model 2: Wasting Status (Wasted versus Normal)													
		Step 1						Step 2					
Variables		**Beta**	**Wald**	**Sig**	**AOR**	**CI**		**Beta**	**Wald**	**Sig**	**AOR**	**CI**	
Cereal form preferably or mostly used	Fermented Dough$^{\Phi}$								5.468	0.065***			
	Fresh Dough							-0.820	5.310	0.021**	0.440	0.219	0.885
	Flour							-0.597	2.006	0.157	0.550	0.241	1.258
Dough Storage Duration	≤3 days$^{\Phi}$								6.266	0.044**			
	4-7 days							-0.940	5.903	0.015**	0.391	0.183	0.834
	> 7 days							0.104	0.040	0.842	1.110	0.400	3.077
Child Gender	Female	-0.836	9.114	0.003*	0.434	0.252	0.746	-0.961	10.488	0.001*	0.382	0.214	0.684
Child Age (Months)	6-11$^{\Phi}$		9.476	0.009*					9.667	0.008*			
	12-17	0.654	4.026	0.045**	1.923	1.015	3.642	0.687	3.897	0.048**	1.988	1.005	3.932
	18-23	-0.373	0.854	0.355	0.689	0.312	1.519	-0.417	0.903	0.342	0.659	0.279	1.558
Child Morbidity (Sick in the last 2 weeks)	Yes	0.616	4.787	0.029**	1.852	1.066	3.216	0.709	5.338	0.021**	2.031	1.113	3.705
Utility: Power Source for lighting household	Yes	-0.971	6.384	0.012**	0.379	0.178	0.804	-0.925	4.703	0.030**	0.396	0.172	0.915
Constant		0.406	0.184	0.668	1.500			0.333	0.034	0.853	1.396		
Model Summary													
HL Test: χ^2(df=8)	7.33. p=.50								7.47. p=.49				
Nagelkerke Pseudo R^2	.20								.27				
Cox & Snell Pseudo R^2	.11								.15				
ΔR^2 (Nagelkerke)	.20								.07				
LR Test: χ^2(df)	69.34 (21)$^{\lambda}$								93.61 (44)$^{\lambda}$				
% Correct Overall Classification	86.7								86.6				

Significant at $^{\lambda}p < 0.001$, $*p < 0.01$, $**p < 0.05$ and $***p < 0.10$; ***N*** = 581; **AOR**, Adjusted Odds Ratio with **CI**=95% confidence interval; **df,** degree of freedom; **Φ**, Reference category for contrast; **LR**, Likelihood ratio test for comparing with the null-model/previous model; **HL**= Hosmer and Lemeshow test (non-significant means good model fit); **HFRUP**, Habitual Food Resource Utilization Practice; **R^2**, Coefficient of Determination (Variance in Nutritional Status Explained); **ΔR^2**, Change in R Squared (Variance Accounted for due to Addition of HFRUP Indicators)

4.9 Analytical Results of the Experimental Foodomics Laboratory Study (GC/LC-MS^2)

The high-throughput GC-MS analyses were successfully used to detect and quantify 102 nutritive and non-nutritive metabolites in the generic hydrophilic extracts (water-soluble) from the experimental cereal samples (TCPM treatments). All the metabolites in the GC-MS experimental cereal samples were analysed in their physiological free state (as is basis) without any metabolite-targeting treatments. Some of the 102 metabolites were eluted at different retention times (RT) even though they were derivatives of the same compounds. For instance, Fructose was eluted as Fructose-MeOX1 and Fructose-MeOX2 because the methoxylamin-hydrochloride (MeOX) derivatization creates two peaks for reducing sugars with the same mass-to-charge ratio (m/z) but different Kovats retention indices (RI). Out of these 102 physiologically free metabolites, the relative quantities (or concentrations) of 12 amino acids (9 essential and 3 conditionally essential), 4 sugars, 2 sugar phosphates, 3 sugar alcohols, and 3 organic acids were presented for this study. The optimized metabolomics analytical GC-MS protocol used could not characterize and quantify the most researched antinutritional phytochemical (non-nutritive constituent) of major bioactive or physiological significance nutritionally in cereals for this study, namely phytate or phytic acid (*myo*-inositol-1,2,3,4,5,6-hexakis dihydrogen phosphate, or IP6). However, low relative concentrations of other antinutritional factors (ANFs) such as phenolics (Ferulic acid, p-Coumaric acid, Sinapic acid, Caffeic acid and their esters) and lower *myo*-inositol phosphates (m/z: 305 and 318) were characterized and quantified but not reported in this study due to their relative insignificance as ANFs.

Based on the three reference standard solutions (SD) of amino acids mixtures used (SD1=20 nmol/mL, SD2=100 nmol/mL and SD3=200 nmol/mL), the calibration plots for the amino acids analyses showed very satisfactory linearity of detection (LoD) for all the essential amino acids (metabolites) presented in this study as prescribed by the UHPLC-MS/MS Phenomenex® analytical protocol. The relative changes (coefficient of variation) in the concentrations (200nmol/mL each) of the internal standards used (Homoarginine-Methionine-d_3-Homophenylalanine mixture) were below 10%, which was also deemed very satisfactory. The absolute quantities or concentrations (nmol/mL) of 8 total essential amino acids (EAAs) and 2 total conditionally essential amino acids (CEAAs) have been presented in this study due to their nutritional relevance in cereals amongst all the other amino acids. The absolute concentration (nmol/mL) of the total contents of tryptophan (limiting EAA in cereals) and Cysteine (CEAAs) were not determined using the UHPLC-MS/MS Phenomenex® analytical protocol due to the effect of the acid-hydrolysis treatment on their stability and recovery as noted in the manufacturer's manual in line with hydrolysis chemistry of these amino acids.

From the GC-MS analyses, Figures 4.3 to 4.11 present a summary of the net changes (% change: 1-fold corresponds to 100%) in the relative concentrations or quantities of some relevant physiologically free essential amino acids, sugars, sugar phosphates, sugar alcohols and organic acids present in the cereal samples. Tables 4.12 to 4.14 and Figures 8.1 to 8.6 (**Appendix A**) from the UHPLC-MS/MS analyses, present a summary of the net changes in the absolute concentrations (nmol/mL) of eight (8) essential amino acids (EAAs) and two (2) conditionally essential amino acids (CEAAs) in the cereal samples analysed that were most relevant for this nutritional epidemiological study.

4.9.1 Results of Physiologically Free Untargeted Metabolites in the Cereal Samples

Generally, the TCPMs resulted in net increases in the relative quantities (or levels) of almost all the amino acids, maltose and pinitol in all the three cereals analysed as illustrated in Figures 4.3a to 4.5c. Almost all the reducing sugars, sugar alcohols and sugar phosphates were depleted in all the three cereals except Maltose, Fructose, Fructose-6-Phosphate, and β-alanine in the maize samples and whiles Pinitol was depleted in almost all the three cereals. The amino acids, maltose and pinitol increased by 10-100 folds, 110-700 folds and 12-100 folds respectively in the three cereals. Leucine, phenylalanine, and lysine levels were the highest in the dry-milled sorghum samples (flour). The highest relative quantities or levels of fold increases in the physiologically free essential amino acids (PF-EAAs) were in maize particularly for phenylalanine, methionine, and lysine when maize was freshly wet-milled (fresh dough). The cysteine, histidine, tryptophan, lysine, tyrosine, and arginine contents were generally the most depleted for the three cereals except in the sorghum samples where the lysine levels contrarily showed relatively higher increases except for the germinated samples. Lysine being a limiting essential amino acid in most cereals, was depleted the most by germination in all three cereals.

The increase in Maltose was highest in the fermented cereal samples. A 12 to 110-fold spike in the level of Pinitol was observed in the germinated samples of sorghum and millet but was relatively lower in the maize samples. The levels of β-Alanine, a precursor of Pantothenic acid (Vitamin B5) synthesis in plants, were depleted in the sorghum and millet samples but increased by almost 2-9 folds in only the maize samples under all the five TCPM treatments.

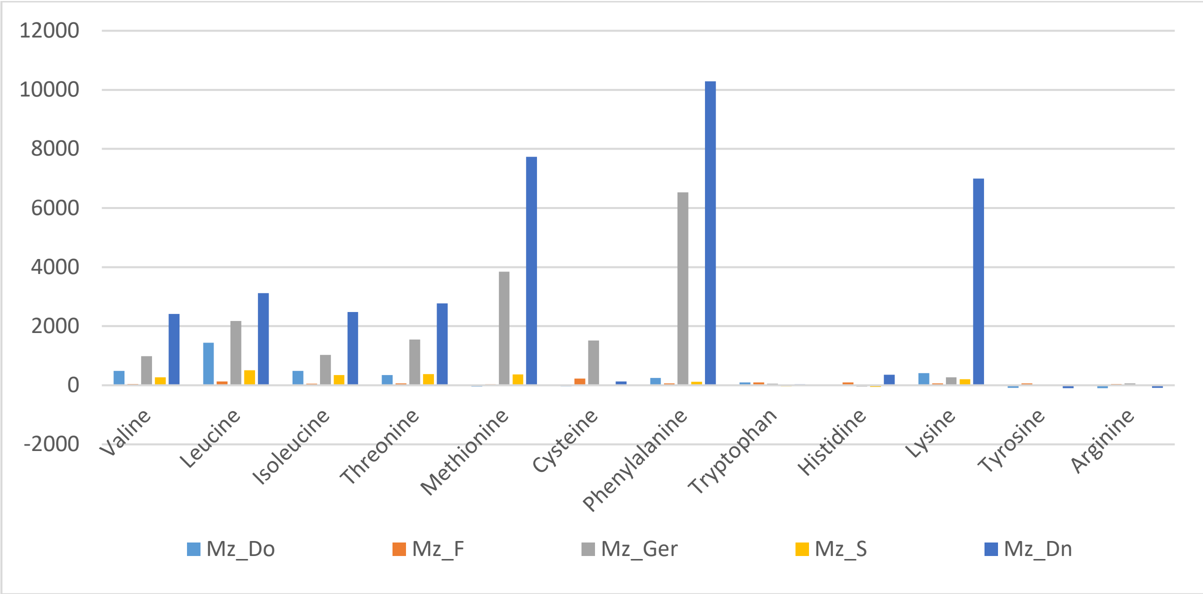

Figure 4.3 Change in the Relative Concentration of Physiologically Free EAAs in Maize

Mz_Do, Maize Fermented Dough; **Mz_F**, Maize Dry-milled (Flour); **Mz_Ger**, Maize Germinated; **Mz_S**, Maize Soaked; **Mz_Dn**, Maize Fresh Dough

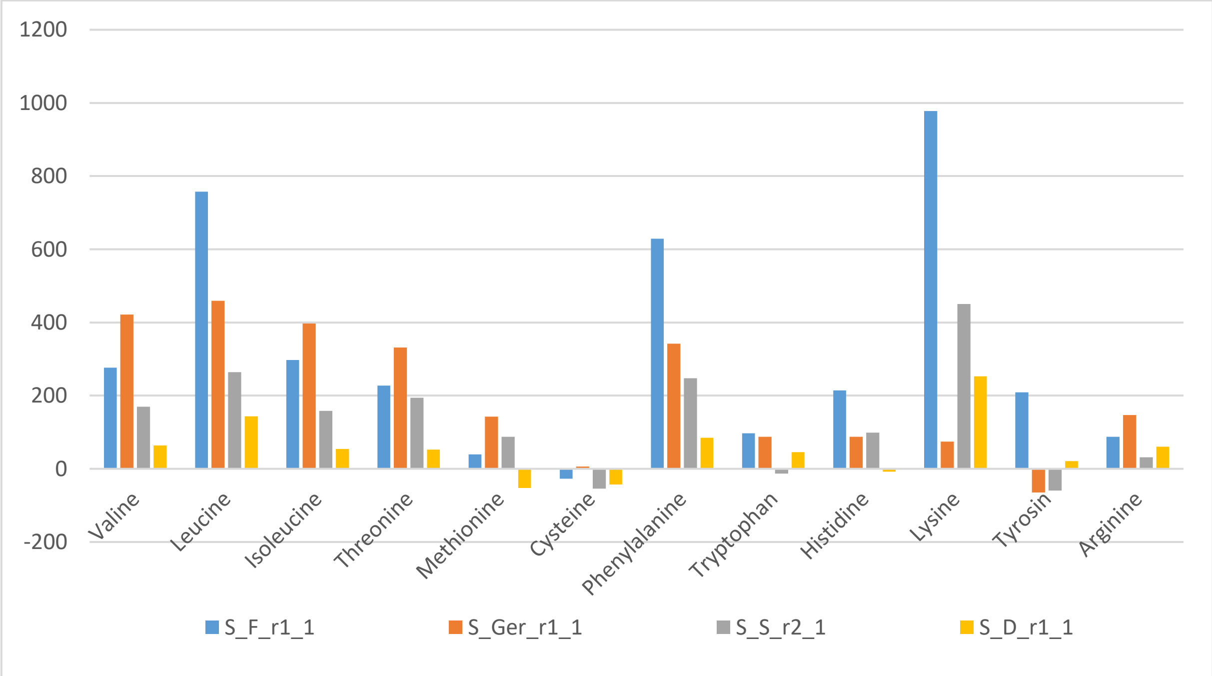

Figure 4.4 Change in the Relative Concentration of Physiologically Free EAAs in Sorghum

S_F, Sorghum Dry-milled (Flour); **S_Ger**, Sorghum Germinated; **S_S**, Sorghum Soaked; **S_D**, Fermented Dough

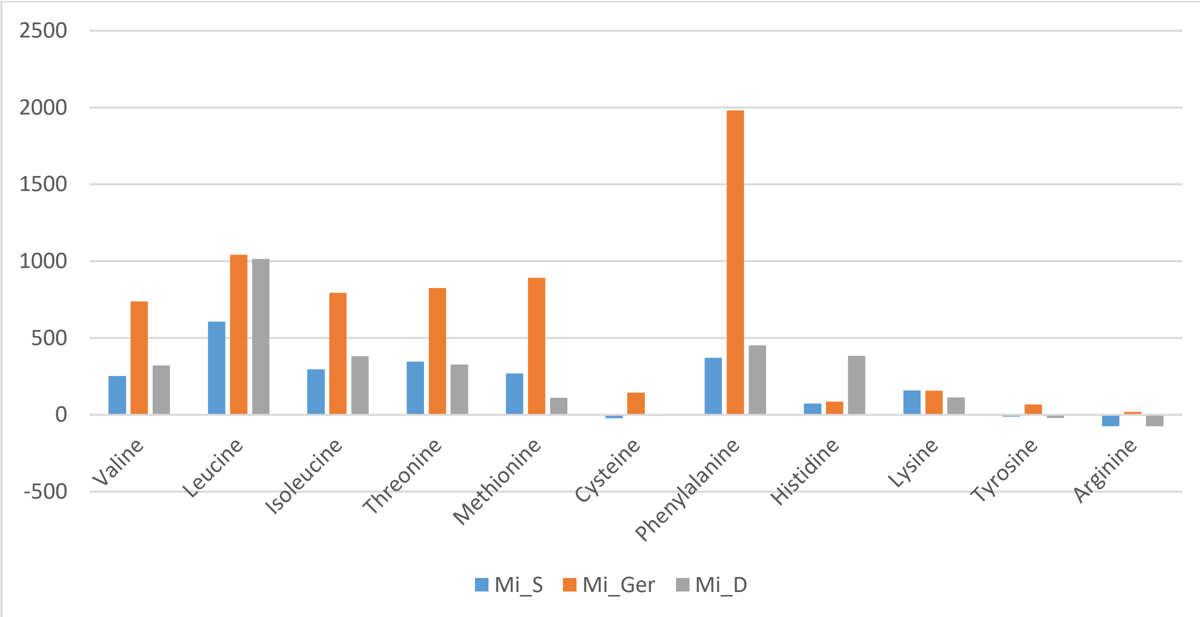

Figure 4.5 Change in the Relative Concentration of Physiologically Free EAAs in Millet

Mi_S, Millet Soaked; **Mi_Ger**, Millet Germinated; **Mi_D**, Millet Fermented Dough

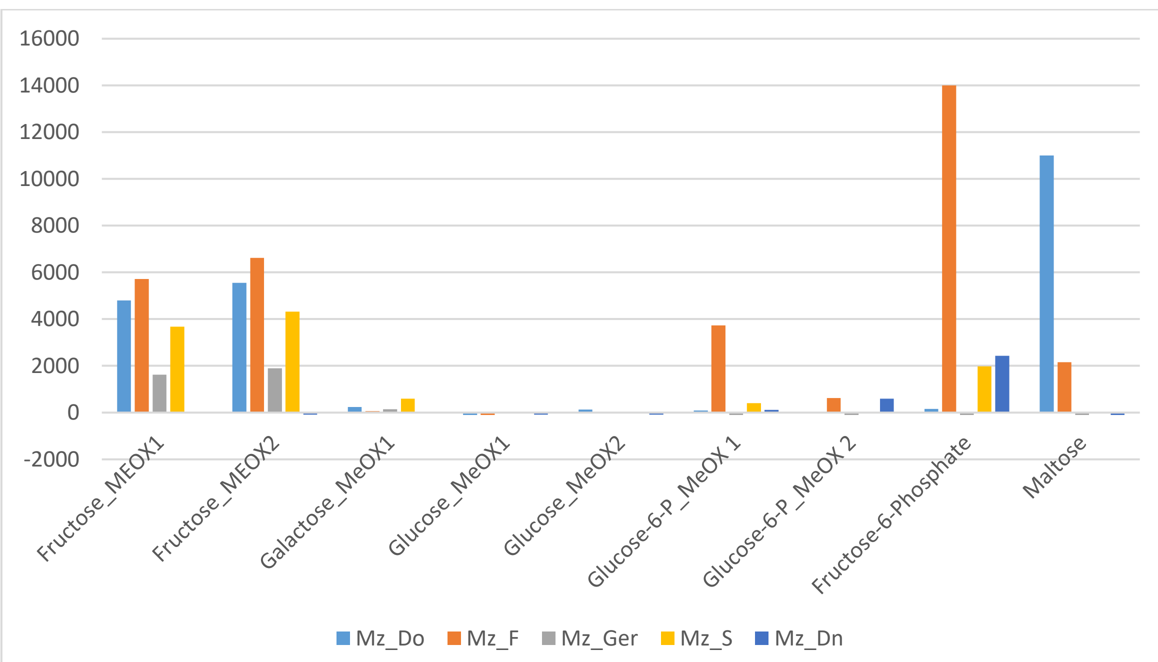

Figure 4.6 Change in the Relative Conc. of Physiologically Free Sugars in Maize

Mz_Do, Maize Fermented Dough; **Mz_F**, Maize Dry-milled (Flour); **Mz_Ger**, Maize Germinated; **Mz_S**, Maize Soaked; **Mz_Dn**, Maize Fresh Dough

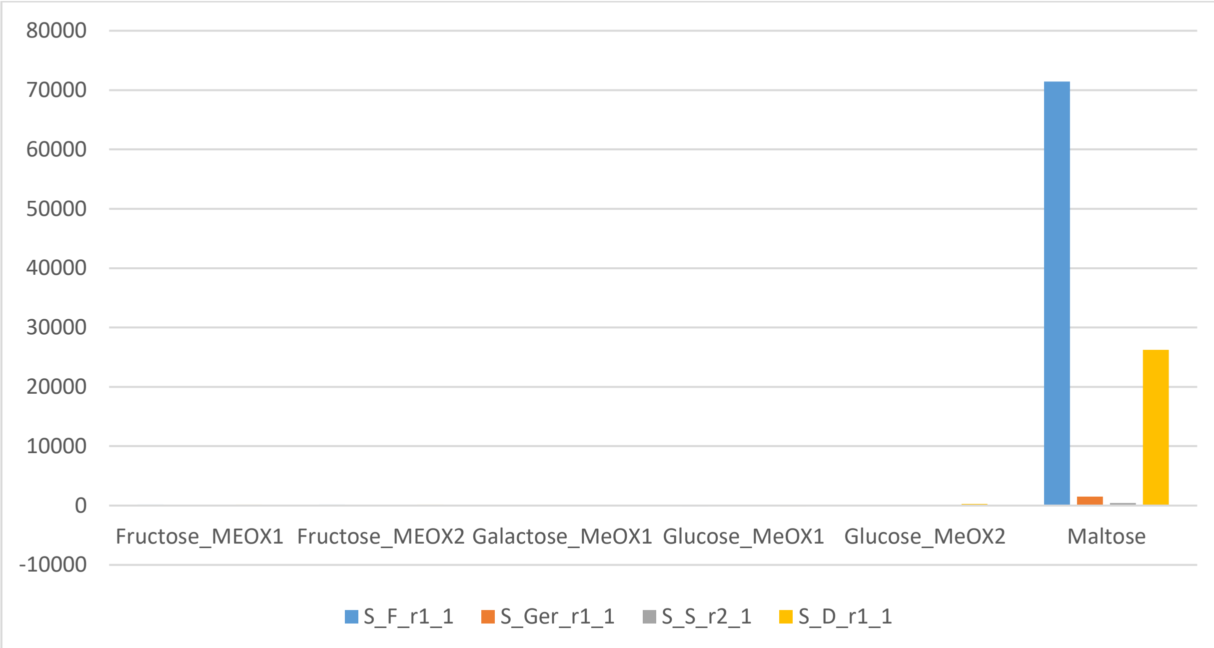

Figure 4.7 Change in the Relative Conc. of Physiologically Free Sugars in Sorghum

S_F, Sorghum Dry-milled (Flour); **S_Ger**, Sorghum Germinated; **S_S**, Sorghum Soaked; **S_D**, Fermented Dough

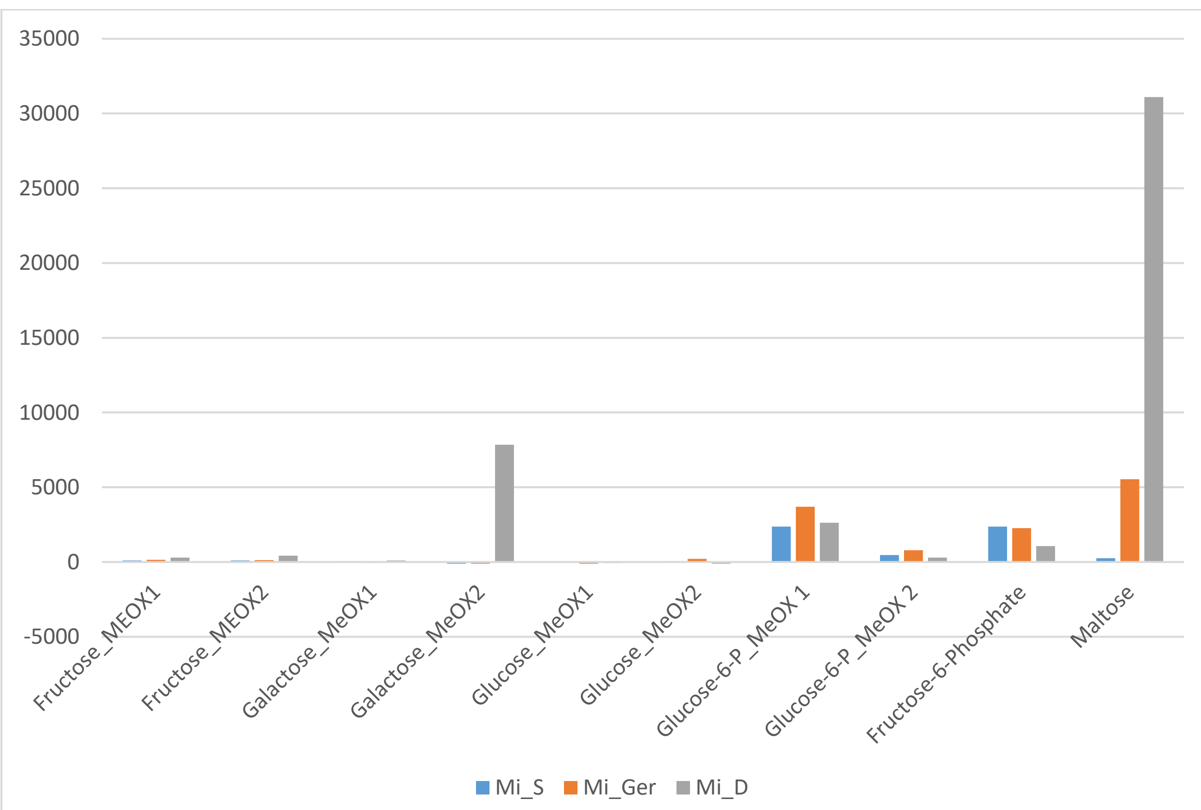

Figure 4.8 Change in the Relative Conc. of Physiologically Free Sugars in Millet

Mi_S, Millet Soaked; **Mi_Ger**, Millet Germinated; **Mi_D**, Millet Fermented Dough

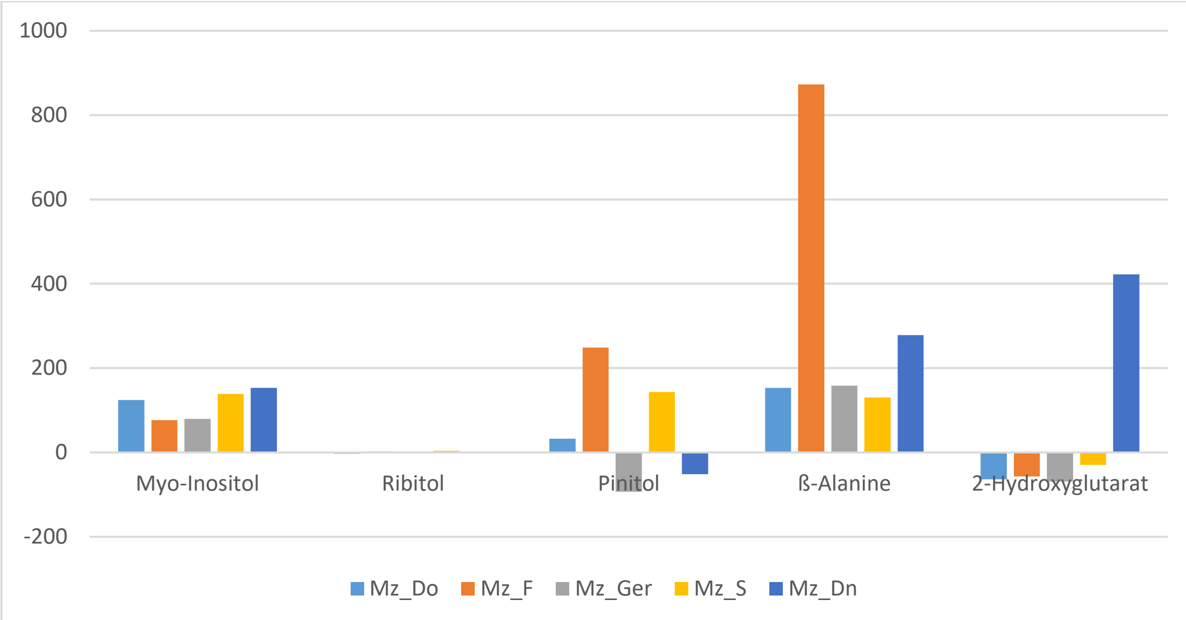

Figure 4.9 Change in the Relative Conc. of Physiologically Free Sugar Alcohols and Organic Acids in Maize

Mz_Do, Maize Fermented Dough; **Mz_F**, Maize Dry-milled (Flour); **Mz_Ger**, Maize Germinated; **Mz_S**, Maize Soaked; **Mz_Dn**, Maize Fresh Dough

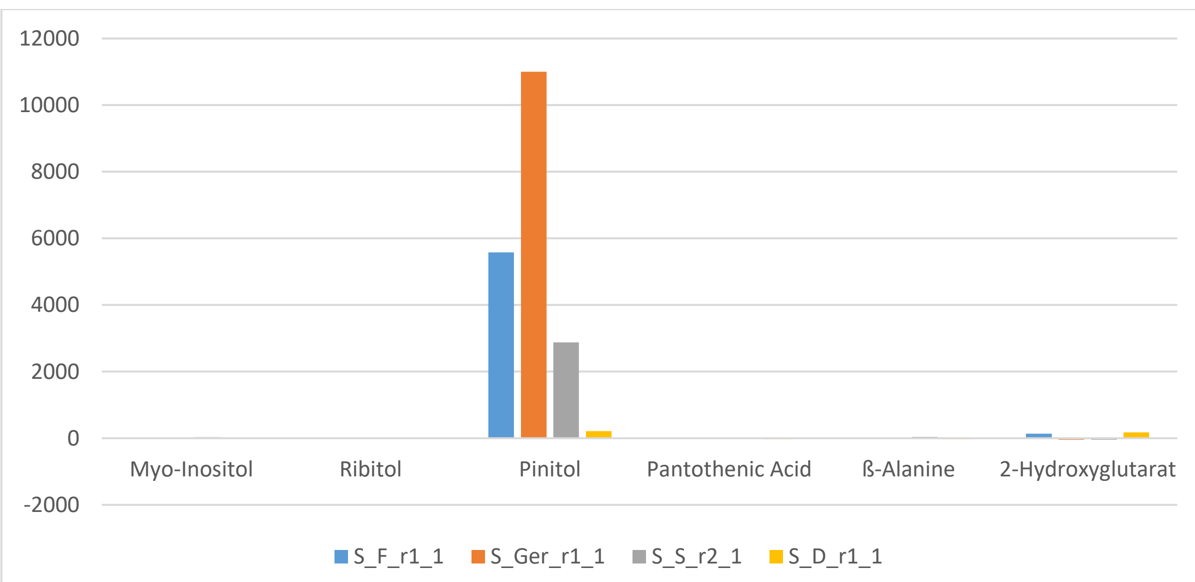

Figure 4.10 Change in the Relative Conc. of Physiologically Free Sugar Alcohols and Organic Acids in Sorghum

S_F, Sorghum Dry-milled (Flour); **S_Ger**, Sorghum Germinated; **S_S**, Sorghum Soaked; **S_D**, Fermented Dough

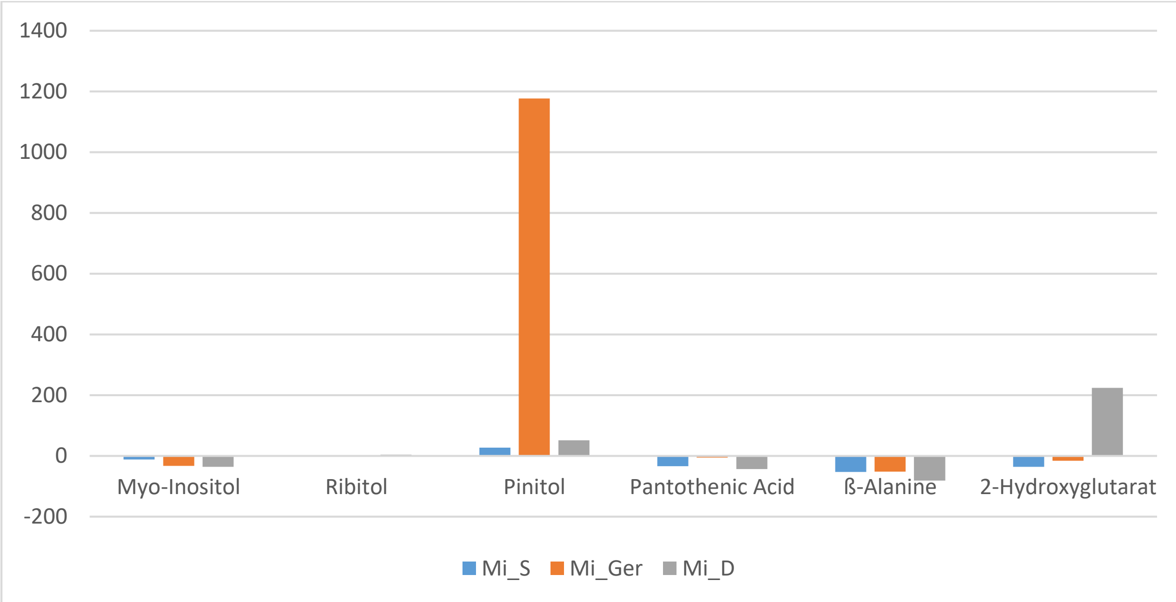

Figure 4.11 Change in the Relative Conc. of Physiologically Free Sugar Alcohols and Organic Acids in Millet

Mi_S, Millet Soaked; **Mi_Ger**, Millet Germinated; **Mi_D**, Millet Fermented Dough

Pantothenic acid (Vitamin B5) was virtually wiped out in all the three cereals under all the TCPM conditions examined. 2-Hydroxyglutarate levels appear to have been enhanced by fermentation (millet and maize samples). Generally, soaking, and spontaneous fermentation seem to have had the most debilitative effects (negative nutritionally significant changes) on the relative net levels of physiologically free essential amino acids (PF-EAAs) in the cereal samples.

4.9.2 UHPLC-MS Results: Total Essential Amino Acids in the Cereal Samples

The TCPMs generally resulted in net increases in the absolute concentrations (nmol/mL) of most of the total essential amino acids (T-EAAs) in the acid-hydrolysed sorghum samples. Contrarily, there were a mix of some net increases and net decreases in the T-EAAs in the acid-hydrolysed maize and millet samples (**Tables 4.12 to 4.14; Figures 8.1 to 8.6, Appendix A**).

Methionine, threonine, phenylalanine, leucine, tyrosine, and arginine generally showed net increases in their absolute concentrations in the acid-hydrolysed maize samples. The TCPMs generally had debilitative effects (negative nutritionally significant changes: ≥10% net decreases) on the absolute concentrations (mmol/mL) of at least three of the total essential amino acids (T-EAAs) in the acid-hydrolysed maize samples. The TCPMs resulted in negative nutritionally significant changes (≥10% net losses) in the concentrations of totally free methionine, lysine, isoleucine, leucine, valine, histidine, and tyrosine in almost all the acid-hydrolysed maize samples.

Lysine, a limiting essential amino acid, and Valine, a branched chain amino acid (BCAA) revealed the nutritionally significant debilitative effects of all the five TCPM-treatments in the maize samples (**Table 4.12**).

Lysine, isoleucine, valine, histidine, and arginine generally showed net increases in the absolute concentrations (nmol/mL) in the acid-hydrolysed millet samples. The TCPMs had debilitative net effects on the absolute concentrations (nmol/mL) of at least four of the total EAAs in the acid-hydrolysed millet samples. The TCPMs resulted in negative nutritionally significant changes (≥10% net losses) in the absolute concentrations (nmol/mL) of total methionine, threonine, phenylalanine, and tyrosine in almost all the acid-hydrolysed millet samples (**Table 4.13**).

All the T-EAAs in the acid-hydrolysed sorghum samples generally showed net increases in the absolute concentrations (nmol/mL) by the TCPM treatments. Only germination resulted in a negative nutritionally significant change (≥10% net loss), which was observed in only histidine (**Table 4.14**).

For the physiologically free essential amino acids (PF-EAAs) in the maize and millet samples (LC-MS/MS), the TCPMs resulted in general net increases in the absolute concentrations (nmol/mL). On the contrary, there was a general net decrease in the physiologically free EAAs in all the sorghum samples except in valine for the fermented sample (**Figure 8.4, Appendix A**). The facilitative effects (net increases) of the TCPMs observed in the physiologically free essential amino acids (PF-EAAs) in the maize and millet samples, were similarly observed in the PF-EAAs in the maize and millet samples analysed by GC-MS. Interestingly however, the sorghum samples rather showed negative nutritionally significant changes (≥10% net decreases) in the absolute concentrations (nmol/mL) of the PF-EAAs analysed by LC-MS/MS contrary to the generally positive changes or net increases in the relative concentrations of the physiologically free essential amino acids (PF-EAAs) in the sorghum samples analysed by GC-MS.

Table 4.12 % Change in the Absolute Concentration (nmol/mL) of Total Essential Amino Acids in Maize Samples

TCPM Cereal Sample	Essential Amino Acids								Conditionally Essential Amino Acids	
	Methionine	Lysine	Threonine	Isoleucine	Phenylalanine	Leucine	Valine	Histidine	**Tyrosine	**Arginine
Maize_Germinated	-18.69*	-18.83*	-6.47	-13.79*	10.33	-4.78	-55.27	54.67	11.41	-4.95
Maize_Soaked	468.24	-60.18*	7.43	19.95	5.82	8.19	-59.03*	-20.08*	-11.29*	16.91
Maize_Dry-Milled (Flour)	221.82	-58.44*	10.37	-23.32*	24.59	-3.59	-75.69*	-63.86*	50.67	29.56
Maize_Dough (Fresh)	297.16	-70.53*	64.61	-57.30*	85.81	-14.56*	-80.30*	-19.05*	133.15	33.84
Maize_Dough (Fermented)	269.47	-60.72*	10.21	-1.39	23.80	6.03	-69.26*	-15.68*	46.00	3.88

EAAs- Essential Amino Acids; ****CEAAs-** Conditionally Essential Amino Acids; **LC-MS-** Liquid Chromatography-Mass Spectrometry
TCPM- Traditional Cereal Processing Methods; ***Nutritionally Significant Debilitative TCPM Effects** (-2SD or ≥ 10% net loss in the nutritional metabolite from the LC-MS Analysis)

Table 4.13 % Change in the Absolute Concentration (nmol/mL) of Total Essential Amino Acids in Sorghum Samples

TCPM Cereal Sample	Essential Amino Acids								Conditionally Essential Amino Acids	
	Methionine	**Lysine**	**Threonine**	**Isoleucine**	**Phenylalanine**	**Leucine**	**Valine**	**Histidine**	****Tyrosine**	****Arginine**
Sorghum_Germinated	114.58	-7.65	12.03	63.19	52.76	40.86	-6.58	-11.66*	0.01	12.07
Sorghum_Soaked	718.32	136.99	161.29	67.10	183.39	106.19	36.80	109.35	108.79	128.25
Sorghum_Dry-Milled (Flour)	229.04	93.28	63.53	25.60	105.25	53.57	28.92	106.26	68.47	71.24
Sorghum_Dough (Fermented)	83.44	81.29	24.60	49.95	105.19	63.99	94.21	46.34	37.76	29.16

EAAs- Essential Amino Acids; ****CEAAs**- Conditionally Essential Amino Acids; **LC-MS**- Liquid Chromatography-Mass Spectrometry
TCPM- Traditional Cereal Processing Methods; ***Nutritionally Significant Debilitative TCPM Effects** (-2SD or ≥ 10% net loss in the nutritional metabolite from the LC-MS Analysis)

Table 4.14 % Change in the Absolute Concentration (nmol/mL) of Total Essential Amino Acids in Millet Samples

TCPM Cereal Sample	Essential Amino Acids								Conditionally Essential Amino Acids	
	Methionine	**Lysine**	**Threonine**	**Isoleucine**	**Phenylalanine**	**Leucine**	**Valine**	**Histidine**	****Tyrosine**	****Arginine**
Millet_Germinated	7.05	26.91	-19.30*	13.87	-26.57*	-10.75*	45.83	35.18	-37.20*	0.55
Millet_Soaked	-19.29*	-16.19*	-11.78*	66.70	-25.36*	8.47	174.40	-55.64*	-24.17*	-0.69
Millet_Dough (Fermented)	-69.41*	81.88	-18.06*	43.35	-18.96*	5.97	189.02	94.23	-32.98*	-15.77*

EAAs- Essential Amino Acids**; **CEAAs-** Conditionally Essential Amino Acids**; LC-MS-** Liquid Chromatography-Mass Spectrometry**; TCPM-** Traditional Cereal Processing Methods**; *Nutritionally Significant Debilitative TCPM Effects** (-2SD or ≥ 10% net loss in the nutritional metabolite from the LC-MS Analysis)

Table 8.13 (**Appendix A**) presents the results of omnibus one-way ANOVA and Dunnett's Post-Hoc test for the determination of the statistical significance of the changes in the mean absolute concentrations (nmol/mL) of total lysine, a limiting essential amino acid (L-EAA) in maize. Lysine was purposefully selected for this illustrative analysis on the basis of its widely researched and documented nutritional and clinical significance (biological relevance) in child anthropometric growth studies in DCs (**Figure 4.12**).

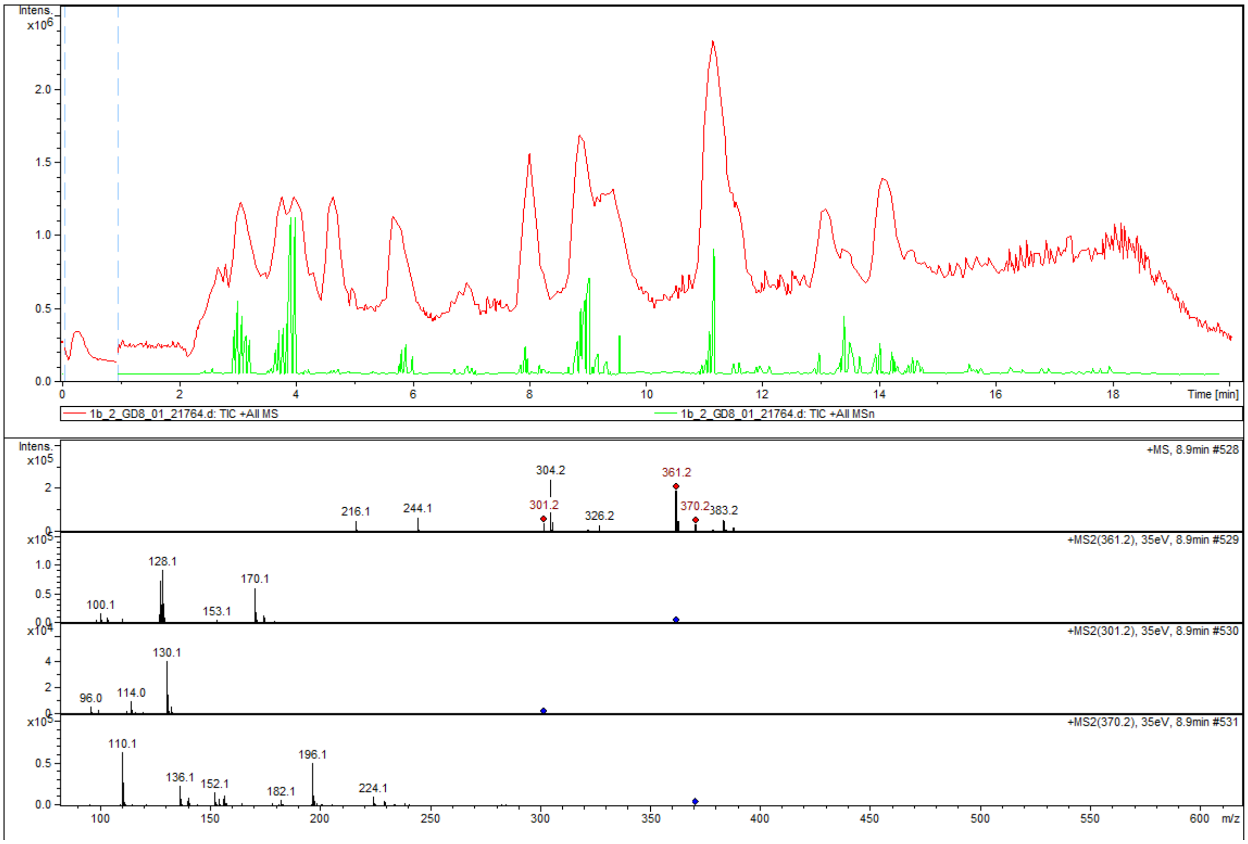

Figure 4.12 UHPLC-MS Total Ion Chromatograms (TIC) of EAAs and Sprectrum View of Extracted Ion Chromatograms (EIC) of Lysine's Derivative MS2 Ions in Maize Sample

Lysine (m/z= 361.2 eluted at 8.9 minutes); Derivative metabolite ions of Lys (m/z=301.2 and m/z=170.1); Red chromatograms are for the cereal sample analytes and green chromatograms are for the standard AAs solution used for calibration.

The interest in lysine was also stoked by the fact that all the five TCPMs examined, effected significant nutritionally debilitative changes (≥10% loss in EAAs) in the absolute concentrations of total lysine in maize, with maize also being the most preferably utilized cereal for CMI production in the Northern Region of Ghana. There was a significant effect of the five TCPMs examined (germination, soaking, dry milling, wet milling only, and wet milling cum fermentation) on the net concentrations (nmol/mL) of total lysine in the TCPM-treated acid-hydrolyzed maize samples, F (5, 18) = 273,401, p < 0.001. The effect size calculated using eta squared, was 0.99 indicating very strong or large effects on the actual differences in mean concentrations (nmol/mL) of lysine between the control maize samples and the treatment samples. Post-hoc comparisons using Dunnett's test (2-tailed) indicated that the mean differences between the concentration of total lysine (nmol/mL) in the control maize grain samples (M=13,675.98, SD= 537.10) and the germinated (M=11,100.49, SD= 412.47), soaked (M= 5,446.41, SD= 278.37), dry-milled (M= 5683.86, SD= 104.60), wet milled-only (M= 4,029.82, SD= 461.68) and wet-milled cum fermented (M= 5,371.45, SD= 479.30) maize grains were all statistically significant respectively.

Table 4.15 presents a summary evaluation of the TCPMs that effected negative nutritionally significant changes (≥10% loss in EAAs) in the concentrations of at least two of the total EAAs analyzed in the acid-hydrolyzed cereal samples. All the five TCPM-treated samples of maize and millet effected a mix of both debilitative (negative) and facilitative (positive) nutritional effects on the absolute net quantities or concentrations (nmol/mL) of the essential amino acids assayed using the Phenomenex® EZ Faast™ Amino Acids analytical protocol. All the TCPMs effected facilitative effects on the sorghum samples assayed except for histidine in the germinated samples unlike in the maize and millet samples where a mix of net nutritionally significant increases and decreases were observed for all the TCPMs. On the basis of the operationally predefined criteria for this study, premised on the principles for the estimation of the thresholds for non-validated nutrient reference values (or recommended nutrient intake), all the TCPMs were considered to have nutritionally significant effects on the nutritive metabolites (particularly the EAAs).

Table 4.15 Summary Evaluation of the Nutritional Significance of the TCPMs

TCPMs	**Cereals**		
	Maize	**Sorghum**	**Millet**
	Did the TCPM Effect Nutritionally Significant Changes in the Total Essential Amino Acids?		
Soaking	Yes (+/-)	Yes (+)	Yes (+/-)
Germination	Yes (+/-)	Yes (+)	Yes (+/-)
Dry milling	Yes (+/-)	Yes (+)	ND
Wet milling Only (Fresh Dough)	Yes (+/-)	ND	ND
Wet milling cum Fermentation (Fermented Dough)	Yes (+/-)	Yes (+)	Yes (+/-)

(+/-) Direction of nutritional significance in brackets: Positive nutritional significance denotes a net increase in the absolute quantities of at least two of the totally free essential amino acids due to TCPM effects and vice versa.
ND: Laboratory analysis of the totally free EAAs was not determined.
DQI for any CMI produced using each of the TCPMs would be significantly affected (Yes =1, No =0).

4.10 Multivariable Association between TCPMs and Child Nutritional Status

A two-stage hierarchical multiple linear regression analysis was conducted with stunting (length-to-age Z-score) as the dependent variable (**Table 4.16**). The proximal risk factors of undernutrition (Figure 3.1) were entered at step one of the regression model.

Table 4.16 Hierarchical Linear Regression Analysis of Dry milling Usage and Stunting

	Regresssion Model (Step 1)				**Regression Model (Step 2)**			
Variables	**B**	**SE**	**β**	**t**	**B**	**SE**	**β**	**t**
Constant	-0.71	0.17		-4.12	0.09	0.33		1.93
MMF	0.22	0.14	0.06	1.58	0.24	0.14	0.07*	1.78
TICF	0.05	0.13	0.02	0.40	0.06	0.13	0.02	0.55
MDD	-0.31	0.19	-0.10*	-1.68	-0.28	0.19	-0.10	-1.66
Vit A	-0.32	0.14	-0.11**	-2.20	-0.33	0.14	-0.11**	-2.29
Fe	0.59	0.18	0.18***	2.87	0.57	0.18	0.15**	2.74
Child Age	-0.72	0.08	-0.37***	-8.64	-0.71	0.08	-0.40***	-8.60
Child Gender	-0.19	0.12	0.06	1.55	-0.18	0.12	0.05	1.42
Child Morbidity	0.03	0.13	0.01	0.25	-0.01	0.13	0.00	-0.04
Dry Milling					-0.67	0.30	-0.09**	-2.24
R^2	.175				.182			
ΔR^2	.175				.007			
VIF Range		1.02-2.40						
Durbin-Watson		1.77			1.74			

Significance at $*p < 0.10$; $**p < 0.05$; $***p < 0.01$; **B**, Unstandardized Beta Coefficient; **SE**, Standard Error (B); **β**, Standardized Beta Coefficient; **t**, t-test statistic; **VIF**, Variance Inflation Factor; **R^2**, Coefficient of Determination (Variance Explained); **ΔR^2**, Change in Variance Explained; **MMF**, Minimum Meal Frequency; **TICF**, Timely Introduction to Complementary Feeding; **MDD**, Minimum Dietary Diversity; **Vit A**, Intake of Vitamin A-rich Foods; **Fe,** Intake of Iron-rich Foods

These proximal variables accounted for 17.5% in the variance of stunting status of the children (R^2=0.175, R^2adj =0.160). MDD, intake of Vitamin-A rich foods, intake of iron-rich foods and child age were statistically significant predictors of stunting, F (10, 570) =12.05, $p < 0.001$. The model showed that child age, t (581) = -8.64, $p < 0.01$ contributed the most to the variance in stunting amongst the significant predictors at Step 1. Usage indicators (preference, duration, or frequency) of the TCPMs were each entered in separate models at Step 2.

Of all the TCPMs examined in the regression models, only dry milling usage was a statistically significant predictor of stunting, F (11, 569) =11.50, $p < 0.001$, with a small effect size (R^2=0.007) (**Table 4.16**). It contributed marginally, an additional 1% variance in stunting status of the children. Dry milling was negatively associated with stunting (β= -0.09, p < 0.05).

A two-stage hierarchical multiple linear regression was conducted with underweight status (weight-to-age Z-score) as the dependent variable (**Table 4.17**). The proximal risk factors of undernutrition (Figure 3.1) were entered at Step 1 of the regression model. These variables accounted for 9.4% in the variance of underweight status of the children (R^2=0.094, R^2 adj= 0.078). Intake of Vitamin-A rich foods, intake of iron-rich foods, child gender, and child age were statistically significant predictors of underweight status, F (10, 570) =5.90, $p < 0.001$. The model showed that child gender, t (581) = -3.26, $p < 0.01$ contributed the most to the variance in underweight status amongst the significant predictors at Step 1.

Table 4.17 Hierarchical Linear Regression Analysis of Dry Milling Usage and Underweight Status

	Regression Model (Step 1)				Regression Model (Step 2)			
Variables	**B**	**SE**	**β**	**t**	**B**	**SE**	**β**	**t**
Constant	-0.61	0.14		-4.53	-0.13	0.26		0.52
MMF	-0.04	0.11	-0.02	-0.35	-0.02	0.11	-0.01	-0.15
TICF	0.02	0.10	0.01	0.19	0.03	0.10	0.01	0.25
MDD	0.04	0.15	0.02	0.29	0.06	0.15	0.03	0.44
Vit A	-0.22	0.11	-0.10*	-1.88	-0.23	0.12	-0.10*	-1.87
Fe	-0.01	0.14	-0.01	-0.01	-0.02	0.14	-0.01	-0.16
Child Age	-0.20	0.07	-0.14***	-3.06	-0.20	0.07	-0.15***	-3.01
Child Gender	0.31	0.10	0.13***	-3.33	0.31	0.09	0.13***	-3.29
Child Morbidity	-0.21	0.10	-0.09**	-2.18	-0.24	0.10	-0.10**	-2.39
Dry milling					-0.51	0.23	-0.09**	-2.20
R^2	.094				.101			
ΔR^2	.094				.008			
VIF Range		1.03-2.40						
Durbin-Watson		1.87			1.89			

Significance at *$p < 0.10$; **$p < 0.05$; ***$p < 0.01$; **B**, Unstandardized Beta Coefficient; **SE**, Standard Error (B); **β**, Standardized Beta Coefficient; **t**, t-test statistic; **VIF**, Variance Inflation Factor; **R^2**, Coefficient of Determination (Variance Explained); **ΔR^2**, Change in Variance Explained; **MMF**, Minimum Meal Frequency; **TICF**, Timely Introduction to Complementary Feeding; **MDD**, Minimum Dietary Diversity; **Vit A**, Intake of Vitamin A-rich Foods; **Fe,** Intake of Iron-rich Foods

Usage (preference, duration, or frequency) of the TCPM indicators were each entered in separate models at Step 2. Dry milling usage was a statistically significant predictor of underweight status of the children, F (11, 569) =5.84, $p < 0.001$, with a small effect size (R^2=0.008) (**Table 4.17**). It contributed marginally an additional 1% variance to underweight status. Dry milling was negatively associated with underweight status (β= -0.09, p < 0.05).

Table 4.18 presents an overview of the main purpose of this NER study. Of all the TCPM usage indicators examined only dry milling was found to be significantly associated with child undernutrition (stunting and underweight status) in the Northern Region of Ghana. Even though all the five TCPMs (soaking, germination, dry milling- flour, wet milling only- fresh dough, and wet milling cum spontaneous fermentation- fermented dough) were found to have resulted in debilitative effects (negative net nutritionally significant losses) on at least two essential nutritive metabolites (essential amino acids) in all the three cereals as deduced from the UHPLC-MS/MS analyses, only dry milling showed overall nutritional epidemiological significance. The effects were minimal or marginal generally (R^2, coefficient of determination ≤ 0.3).

Table 4.18 Summary of Evaluation: Epidemiological Significance of the TCPM Indicators vis-à-vis the Nutritional Status of the Children in the Northern Region of Ghana

	Nutritional Status		
TCPMs	**Stunting**	**Wasting**	**Underweight**
	TCPM indicator epidemiologically significant?		
Dehulling	No (ND)	No (ND)	No (ND)
Germination	ND (+/-)	ND (+/-)	ND (+/-)
Soaking	No (+/-)	No (+/-)	No (+/-)
Dry milling (Flour)	**Yes** (+/-)	No (+/-)	**Yes** (+/-)
Wet milling only (Fresh Dough)	No (+/-)	No (+/-)	No (+/-)
Wet milling cum Fermentation (Fermented Dough)	No (+/-)	No (+/-)	No (+/-)

(+/-) Nutritional significance in brackets: Positive nutritional significance denotes a net increase in the absolute quantities of at least two of the totally free essential amino acids (EAAs) due to TCPM effects and vice versa.
ND: Laboratory analysis of the free EAAs was not determined or survey of TCPM usage was not determined

5 DISCUSSION

5.1 Section Overview

The descriptive (univariate) analyses of the survey data sought to measure the prevalence of complementary feeding (CF)-related IYCF indicators, HFRUP indicators, TCPM indicators and nutritional status indicators (stunting, wasting and underweight status) amongst children (6–23 months) in the Northern Region of Ghana. A discussion of the implications of the single time point estimate of the prevalence rates of the three main explanatory (exposure) variables and outcome (dependent) variables of interest in this study conducted in June 2018 has been provided. The bivariate analyses sought to examine the significance and strength of the relationships between the explanatory variables (IYCF, HFRUP and TCPM indicators) and the outcome variables (nutritional status) of children (6–23 months) in the Northern Region of Ghana.

The first multivariable analysis of the analytical cross-sectional study sought to examine the associations between the individual CF-related IYCF indicators and the nutritional status (stunting and wasting) of children in the Northern Region of Ghana, after adjusting for potential confounders. Standard multivariable binary logistic regression was used for these inferential statistical analyses (parameter estimation and hypothesis testing). The second inferential statistical analyses sought to examine the context-specific determinants of undernutrition (stunting and wasting status) by examining the multivariable associations between indicators of habitual food resource utilization practices (HFRUPs) and undernutrition (nutritional status), after adjusting for potential confounders. The third part of the analytical study examined the effects of TCPMs on the quantities (relative and absolute) of nutritive and non-nutritive (anti-nutritional) contents of the experimental cereal samples (soaked grains, germinated grains, dry-milled grains or flour, wet-milled grains or fresh dough, and wet-milled grains cum fermented or fermented dough). GC-MS foodomics laboratory analyses were used to evaluate the net fold changes (effects of the TCPM treatments) in the relative quantities of selected physiologically free metabolites (nutrients and non-nutrients present in the cereal samples on an as-is-basis). UHPLC-MS/MS foodomics laboratory analyses were also used to evaluate the net percentage changes (effects of the TCPM treatments) in the absolute concentrations (nmol/mL) of eight (8) essential amino acids (EAAs) and two (2) conditionally essential amino acids (CEAAs) in the experimental cereal samples. The statistical significance of the mean differences in the absolute concentrations (nmol/mL) of lysine, a limiting EAA in cereals was examined using One-Way ANOVA (two-tailed) and Dunnett Post hoc tests.

The magnitude and direction of changes due to the effects of the TCPMs on the relative (GC-MS) and absolute (UHPLC-MS/MS) quantities of the examined metabolites, served as a basis for qualitatively determining the nutritional significance of each TCPM, guided by the operationally predefined (a prior) criteria. The fourth inferential statistical analysis of the study was used to examine the main research question and hypothesis of the study. The analyses sought to determine the significance, direction, and magnitude of the associations between the usage indicators (frequencies, preferences, or durations) of the nutritionally significant TCPMs (qualitatively determined from the foodomics analyses) and child nutritional status (stunting, wasting and underweight status). The epidemiological significance of the nutritionally significant TCPMs were determined using hierarchical multivariable linear regression analyses as a function of the TCPM usage indicators. Some identifiable strengths and limitations of the study have also been presented in the discussion whiles some of the challenges faced during the study have also been outlined and discussed in this penultimate chapter of the dissertation.

5.2 Prevalence and Implications of IYCF Indicators and Intake of Meals (Food Groups)

One of the findings of the first objective of this study was that generally, the prevalence of the CF-related IYCF indicators estimated in the Northern Region of Ghana were relatively higher compared to the northern regional findings of the GDHS 2014 (Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015). The IYCF indicators are nutrition-specific indicators recommended by the WHO, UNICEF, and other maternal and child nutritional health experts as being simple, reliable, valid, suitable, highly cost-effective, evidence-based, and pragmatic parameters for monitoring and evaluating progress in child food intake, child nutritional status and also for identifying populations at risk of malnutrition. These indicators help to inform the development of context-appropriate interventions against the various forms of malnutrition (Bhutta et al., 2013; WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2008). The findings of this study showed some interesting similarities and disparities compared with the IYCF indicators reported in some recent studies conducted both in the Northern Region of Ghana and nationally. The Multiple Indicator Cluster Survey Six (MICS 6), conducted between 2017 and 2018, reported a national prevalence of 79%, 41%, 23% and 12% respectively for TICF, MMF, MDD and MAD amongst children aged 6–23 months (Ghana Statistical Service, 2018). The Ghana Demographic and Health Survey (GDHS) 2014, conducted in 2013, reported prevalence rates of 45.2%, 17.9%, 14.1%, 47.7% and 55.9% for MMF, MDD, MAD, Fe and Vit A respectively amongst children (6–59 months) in the Northern Region (Ghana Statistical Service (GSS), Ghana

Health Service (GHS), and ICF International, 2015). The indicators from this study were generally higher compared with the GDHS 2014 findings for the Northern Region (**Figure 4.1**). In a Nutrition Surveillance (NS) study, conducted in November 2013, of the three northern regions of Ghana, Saaka et al (2015) also reported prevalence rates of 48.8%, 58.2%, 34.8%, 27.8% and 15.7% for TICF, MMF, MDD, MAD and ACF respectively amongst children aged 6–59 months. The general improvements in IYCF indicators reported from this study could possibly reflect the various nutrition intervention strategies implemented in northern Ghana by the Government of Ghana and development partners over the period between 2010 and 2018, within which this study was conducted in June 2018 (Cooke, 2020). These may have contributed to improvements in the knowledge, attitudes, and practices (KAP) of infant and young child feeding amongst mothers and caregivers in the region.

The intake of meals made from ingredients belonging to food group one (G1- grains, roots, and tubers), group four (G4- flesh foods) and group three (G3- other fruits and vegetables) were all above 50% whiles intake of meals made from protein-rich and micronutrient-rich ingredients belonging to food group five (G5- eggs), food group six (G6- legume and nuts) and food group seven (G7- dairy products) were below 32% (**Figure 4.2**). The food group intake trend observed in this study was similar but higher than the national GDHS 2014 findings except for intake of eggs (2.1% versus 18%) for breastfeeding children (6-23 months). The consumption of eggs within households in northern Ghana has been reported to be low. Even though over 80% of households surveyed in the three northern regions kept chickens, ducks and other birds for meat or sale, only between 23-33% raised these birds for their eggs (Saaka, Asamoah, Hoeschle-Zeledon and Appiah, 2015).

From the recent Ethiopia DHS 2016, intake of meals from G6 and G7 food groups were generally higher than the national intake by breastfed children (6-23 months) in Ghana and almost the same for G5 but the MDD prevalence for Ethiopia was 13.8% compared to 28.1% for Ghana and 17.9% for the Northern Region from the Ghana DHS 2014 (Central Statistical Agency - CSA/Ethiopia & ICF, 2017; Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015). Comparing the prevalence of stunting and wasting status of children (6-59 months) in Ethiopia (38.4%, 9.9%) with those in Ghana (19%, 5%) and further with the Northern Region (33.1%, 6.3%) respectively, the inference is that despite the seemingly higher intake of G6 and G7 food groups and almost the same for G5 food groups (which are supposed to be protein-rich and micro-nutrient rich), the overall nutritional status indicators (stunting and wasting) of Ethiopian children nationally compared to both Ghana nationally and the Northern Region were poorer. This may suggest that, indeed an improvement in dietary diversity or intake of meals from micronutrient-rich and/or protein-rich food groups might not necessarily translate into significantly observable improvements in child nutritional status just as observed in this study. A similar inference was made from a study conducted in Cambodia that even though an educational intervention implemented in an RCT study improved minimum dietary diversity (MDD), this did not translate into an improvement in the overall nutritional status of the children (Kuchenbecker, Reinbott, Mtimuni, Krawinkel, & Jordan, 2017; Reinbott et al., 2015).

It is not surprising that the consumption of meat and flesh foods was relatively higher in the Northern Region given that the Ghanaian meat supply system through local production and imports has seen increases between the year 2001 and 2010 (Adzitey, 2013). The northern regions are also key contributors of livestock and other flesh and meat sources nationally. Besides, in the three northern regions of Ghana, more than 50% of households on average rear cattle, goats, sheep or dogs for their meat or sale (Saaka, Asamoah, Hoeschle-Zeledon and Appiah 2015). Even though egg production trails chicken meat production, production of eggs has also seen an increase, though cost remains a barrier to patronage (Nyantakyi-Frimpong et al., 2018). However, the regional production of eggs is concentrated in the mid-to-southern section of the country (Greater Accra, Ashanti and Brong Ahafo). Inefficient transportation systems for eggs and the relatively expensive nature of poultry and egg production, makes the northern regions less lucrative for the enterprise. Interventions to ensure the provision of at least one egg a day per child for children under five years in the Northern Region could prove very helpful to improve the intake of eggs as a rich protein source (Morris, Beesabathuni, & Headey, 2018). The availability and access dimensions of household food security for affordable eggs within resource-limited households in the Northern Region could remain a mirage in the foreseeable future unless drastic interventions are implemented. The effects of potentially novel risk factors of child undernutrition such as TCPMs, HFRUPs, and the putative proximal risk factors of undernutrition such as child morbidity (or health status) and child age group could become significantly more apparent given the dire nature of the food insecurity situation in the Northern Region (Adu, Yawson, Armah, Abano, & Quansah, 2018).

5.3 Prevalence and Implications of HFRUPs in the Northern Region of Ghana

HFRUP as a domain of the food utilization dimension of HFI, was operationally defined in this study as the household handling, processing, and/or usage activities habitually carried out on indigenous food resources (raw or semi-processed) obtained by resource-limited households. They also include the choices made on these predominantly plant food resources by the resource-poor households to maximize the culinary, organoleptic, nutritional, and/or health benefits of these limited food resources. Six main HFRUPs were examined in this study (**Table 4.3**). The monotonous feeding with cereal-only-based complementary meals to young children in the Northern Region was high (55.8%). Findings reported on the intake of complementary meals by young children in DCs habitually from G1 food groups have always been distinctly the highest amongst the seven food groupings (Aguayo, 2017; Armar-Klemesu et al., 2018; Belew, Ali, Abebe, & Dachew, 2017; Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015; Kassa et al., 2016; Saaka, Asamoah, Hoeschle-Zeledon and Appiah, 2015; Teji Roba, 2016). Cereals are the most available and accessible high-calorie food sources for most resource-limited developing country settings. Besides, utilization of cereals for the production of homemade complementary meal ingredients (CMIs) for complementary meal preparation for young children, is driven probably by familiarity with the indigenous knowledge of their usage in food preparation, customary habits and traditions, food beliefs, relative affordability (access), limited diversity (availability limitations), limited knowledge of alternative nutrient-rich accompaniments of complementary meals, and mothers' possibly parochial perceptions about their nutritional quality for young children (Armar-Klemesu et al., 2018). However, for various reasons, habitually feeding infants and young children with cereal-only-based complementary meals with or without breastfeeding would more likely deny children the nutritional adequacy critical for optimum growth and development (Akinsola et al., 2017). Various studies on the nutritional composition of CMIs suggest their significant nutritional contents but they would still not be adequate to meet the nutritional needs of infants and young children unless ingredients from other nutrient-rich food groups (proteins and micronutrients) are incorporated for complementary meal preparation (Adeoti & Osundahunsi 2012; Makori, Kassim, Kinabo, & Matemu, 2017). During the formative and definitive phases of this study, it was observed that homemade single-cereal-based dough or flour was mostly used as compared to composite or blended CMIs from different cereals or a mix of cereals and legumes in the Northern Region of Ghana. A similar trend of the dominance of cereal-only-based or non-composite CMIs over commercial infant cereals (CICs) was observed in both rural and urban settings. In these settings, the promotion of composite industrially made CMIs (cereal-legumes) or CICs popularly called Weanimix in Ghana through behaviour change communication (BCC) interventions, have not been very successful in displacing the status quo of child feeding preferences of mothers for homemade CMIs (Masters, Kuwornu, &

Sarpong, Daniel, 2011; Pelto & Armar-Klemesu, 2011; Pelto, Armar-Klemesu, Siekmann, & Schofield, 2013). Abizari *et al* (2017) however, reported a high usage of CICs amongst mothers of young children mostly between 6-12 months in the urban settings of Tamale in the Northern Region of Ghana albeit in combination with other homemade CMIs. Concerns have also been raised about the potential increase in exposure to aflatoxin intake by infants and young children if the safety of homemade composite CMIs (cereal-legume) is not prioritized in their promotion over nutritional quality, given that mycotoxins have been widely implicated in the menace of undernutrition in DCs (Atongbiik Achaglinkame, Opoku, & Amagloh, 2017; Lombard, 2014; Makori, Matemu, Kimanya, & Kassim, 2019; Masters et al. 2011). Furthermore, some children are allergic to some legumes especially peanuts and soya beans. Advocacy for the combination of protein and micronutrient-rich legumes in composite CMIs should therefore be done also mindful of these possible drawbacks (Ho et al., 2008; Ierodiakonou et al., 2016; Peters et al., 2015).

Dough was preferred over flour (76% versus 24%) but the most preferred form of the homemade CMIs habitually used by the mothers in northern Ghana to prepare complementary meals for their children was fermented dough (39.6%) (**Table 4.3**). This could possibly be due to the influence of cultural antecedents of child complementary feeding in the Northern Region as well as the food preferences and dietary habits of most children at this age towards meals made from fermented dough compared to fresh dough (Armar-Klemesu et al., 2018; Meyer-Rochow, 2009). Shorter fermentation time together with long steeping of maize was reported to have resulted in low stickiness, high fineness of the wet-milled maize flour, low acidic taste, and low ethanolic odour of the dough (Oduro-Yeboah et al., 2016). These organoleptic attributes of fermented dough may be the reason for its sensory appeal. Tano-Debrah *et al* (2019) observed a significant preference by mothers of young children for homemade Koko (porridge made from fermented maize dough) with lower consistency (lightness) which is enhanced by the natural or spontaneous fermentation unit operation during the production of the homemade CMIs.

Maize was the most preferred cereal type for the production of CMIs habitually used by mothers in the Northern Region of Ghana to prepare complementary meals for their children as observed also widely across Ghana, Malawi, and most of Sub-Saharan Africa (Armar-Klemesu et al., 2018; Ekpa et al., 2019; Ghosh et al., 2014; Kuchenbecker et al., 2017). The cereal preference is likely to be influenced predominantly by local production volumes or importation (availability), affordability (access), familiarity with the meals made from them and customary food beliefs among other reasons (Armar-Klemesu et al., 2018; Chakona & Shackleton, 2019; Martínez Pérez

& Pascual García, 2013; McNamara & Wood, 2019; Meyer-Rochow, 2009; Reddy & Anitha, 2015). During the formative phase of the study in the Northern Region, some households indicated their abstinence from the use of certain cereals (sorghum and millet) purely on the basis of their cultural beliefs in taboos associated with these cereals even though some of them also indicated that they believed, perceived, or knew that these cereals were nutritious.

Majority of the mothers (63.3%) indicated that they habitually used only dough stored for a maximum of three days under normal household temperature conditions for the preparation of complementary meals for their children (**Table 4.3**). Only an additional 28.4% of the mothers habitually used dough stored for a maximum of 7 days under ambient temperature and household conditions. This could probably be due to the development of undesirable taste and aroma compounds (alcohol or acetic acids) in the dough which may be detected by the mothers (or children) as off-flavours, off-colours, or unpleasant sour taste. These undesirable developments during the storage of dough, however, could negatively affect the sensory appeal of the complementary meals (CMs) to children.

The storage containers used to keep dough meant for the preparation of CMs for children could affect the safety and sensory appeal of the dough. Majority (85.7%) of the mothers indicated their usage of plastic containers for the storage of dough. Plastic containers especially made from low- and high-density polyethylene (LHDPE) have inert effects on fresh or processed food materials or ingredients if their surfaces are not contaminated. Compliance with basic hygiene, sanitary, and safety practices is likely therefore to be more influential than the storage containers alone in determining the safety and/or sensory qualities of dough or any homemade CMI meant for the preparation of complementary meals for infants and young children.

Majority of the mothers (67.7%) surveyed indicated that they always or very often made the CMIs (dough) meant for complementary meal preparation at home by themselves. The pros and cons of homemade CMIs could therefore be profound on the nutritional health of infants and young children (Dimaria et al., 2018). Only 6.5% of the mothers indicated that they sourced their dough from outside the home by purchasing CMIs that are either imported or locally made. Often due to the commercial interests of industrial manufacturers of commercial CMIs, the complementary meal products (imported and locally manufactured) are labelled and marketed most probably with a somewhat biased projection of the commercial CMIs as being nutritionally superior to the homemade ones. Some studies have shown that this projected nutritional superiority of CICs is not often the case and rather smacks of exploitative tendencies against the already vulnerable resource-limited segments of society (Dimaria et al., 2018; Masters et al. 2011; Pelto et al., 2013). The limited availability and purchasing power of resource-poor mothers of young children in the Northern Region of Ghana probably accounts for the high level of homemade production of CMIs, as found in the study across West Africa (Dimaria et al., 2018). These industrially processed cereal-legume-based blends (CLBBs) and/or commercial infant cereals (CICs) were found to be two to three times more expensive than the homemade CMIs across West Africa (Dimaria et al., 2018). Notwithstanding, mothers in northern Ghana who still sacrificed their meagre resources to patronize the industrially made CMIs (CLBBs or CICs) did so mostly on the basis of the rather misleading assumption of nutritional superiority over the homemade CMIs as Akerlof (1970) posits about the relationship between branding and quality perception (Abizari et al., 2017).

5.4 Prevalence and Implications of TCPM Usage in the Northern Region of Ghana

The use of TCPMs for the production of homemade CMIs in northern Ghana and generally in West Africa is pervasive (Abeshu et al., 2016; Masters et al., 2017; Tano-Debrah et al., 2019). Homemade CMI usage have been implicated in the nutritional status of infants and young children in such developing country settings (Mitchodigni et al., 2018). Majority of the mothers surveyed (57.7%) indicated that they do not dehull their cereal grains before using it for CMI production (**Table 4.4**). Descriptive studies on the prevalence of TCPM usage in northern Ghana and West Africa in general is not replete in the NER literature for the purposes of comparison with the findings of this study. Dehulling or debranning has generally been discouraged as a unit operation during the production of CMIs for infants and young children in Ghana possibly because of the putative losses of essential proteins, micronutrients, other healthful nutrients, and non-nutrients. Dehulling has been found to be more debilitative than facilitative with regards to the dietary fibre and healthful phytochemical contents (anticancer, anti-oxidative, and gastrointestinal functions) in cereals especially for adults but not yet widely researched for CMIs in the case of infants and young children (Klerks et al., 2019; Slavin, Jacobs, & Marquart, 2000). The removal of the bran or hull of cereal grains (debranning or dehulling) is usually aimed at getting rid of the pericarp and/or outer layers whose constituents depending on the cereal, may also impart off-colours and undesirable bitter tasting compounds (Bassey & Schmidt, 1989). Some phytochemicals such as C-glycosyl flavones and other flavonoids found in millet may be associated with the prevalence of goitre (Gaitan et al., 1989; Sartelet et al., 1996). Phytic acid (*myo*-inositol-1,2,3,4,5,6-hexakis dihydrogen phosphate) also called inositol hexaphosphate (IP6) is a secondary metabolite richly present in cereals, legumes, and oilseeds, which is known to exhibit anti-nutritional properties against proteins, enzymatic activities, and the optimal absorption of nutritionally relevant polyvalent cations such of Iron, Calcium, Magnesium, and Zinc (Schlemmer, Frølich, Prieto, & Grases, 2009). IP6 content is however reduced significantly through dehulling (Samtiya et al., 2020; Schlemmer et al., 2009). The consumption of whole grains by children may be paradoxical as it could prove somewhat beneficial to infants and young children better than refined cereals when used for CMI production only if the phytate drawback is dealt with through suitable TCPMs (Hotz & Gibson, 2007). In addition, the sensory acceptability of whole grains during childhood could be transitioned into adolescence and adulthood as well (Alexy, Zorn, & Kersting, 2010; Haro-Vicente et al., 2017). Dry milling is a necessary unit operation in the production of flour and other pulverised products from cereals. A significant majority (95.7%) of the mothers surveyed indicated that they obtained their flour from the commercial plate attrition miller services (locally called Nikanika) available in or near their communities or residences. A few of them however purchased already made and packaged commercial cereal flour (imported or locally made) or they produced the flour (CMI) using the laborious mortar-pestle pounding method or stone grinding method at home. Technically, the use of motorized machines for cereal milling purposes would however not qualify to be described as a TCPM within the context of this study. Even though they are traditional or customary practices, the Nikanika services are not performed at home with low-level processing technologies indigenous to the Northern Region. Small-scale commercial attrition millers were widely introduced and made available in most urban and now rural settings across West African countries from as far back as the 1980s (Bassey & Schmidt, 1989). Obtaining machine dry-milled flour were within the reach of a good proportion of the households and communities surveyed in the Northern Region, where electricity was available to run these milling machines but may possibly not be affordable to every household. The electricity penetration rate in Ghana is about 80% nationally but still many communities where most of the resource-poor communities are located, are likely to be without access to electricity (Ghana Statistical Service, 2018). Dry milling with the more modern usage of electricity-run attrition mills (Nikanika) has thus become generally more pervasive and may be obliviating the traditional household production of flour through mortar-pestle pounding and/or stone grinding methods in the Northern Region of Ghana. Some studies have however raised concerns over potential heavy metal contamination in the cereal flour products from these attrition mills (Nikanika) through the wear and tear of the grinding metal plates (Kwofie et al., 2011; Kwofie & Chandler, 2007; Larsen, Cobbina, Ofori, & Addo, 2020; Ofori, Tortoe, Akonor, & Ampah, 2016).

A little over a third of the mothers (35.1%) indicated that soaking or steeping of the cereal grains was done for at least 12 hours but not more than 24 hours before being wet milled (**Table 4.4**). About 32% of the mothers also habitually soaked their cereal grains for more than 24 hours. Only a dearth of literature was available to compare the prevalence of different regimes of household-level soaking or steeping duration practices and other similar or additional hydration conditions (such as nixtamalization, temperature variations) of cereals for the production of CMIs in the Northern Region of Ghana. However, a minimum of 12 hours (overnight) and an average of 24 hours duration of soaking at room temperature appears to be the popular practice. This time range (12-24 hours) is also mostly recommended as optimal for homemade CMIs, industrial CMI production and also the popular discretionary practice in experimental laboratory analyses of cereal grains (Apotiola, 2013; Brožková et al., 2018; Chiang & Yeh, 2002; Ertaş & Türker, 2014; Mahgoub & Elhag, 1998; Oduro-Yeboah et al., 2016; Onwuka, 2006). The duration of soaking appears to be determined by the attributes of the cereal product desired in terms of particle size, dough or flour form, texture (stickiness, grittiness, or fineness), dryness, taste (sourness or blandness), aroma and digestibility. For instance, extended soaking time resulted in finer flour, decreased stickiness and higher viscosity of wet-milled maize and rice grains (Chiang & Yeh, 2002; Oduro-Yeboah et al., 2016). Hydration or water uptake that instigates the release of enzymes for enzymatic activities and other metabolites in maize grains was reported to have become saturated between 8-10 hours (Oduro-Yeboah et al., 2016). The rate of grain hydration is a function of the cereal form (level of exposed surface area: whole, grit or degermed), cereal type, grain structure and temperature amongst other factors (Afolabi, 2014; Duodu et al., 2003; Hamaker, Kirleis, Mertz, & Axtell, 1986; Wong et al., 2009). Whole, dehulled (also degermed) or coarsely dry-milled (grits) maize grains got hydrated in increasing order of kinetics respectively during soaking until saturation point with about 45-50% moisture content (wet basis) between 10 hours and 1 hour respectively (Nche, Odamtten, Nout, & Rombouts, 1994; Oduro-Yeboah et al., 2016). All these physico-biochemical modifications would have direct influences on the nutritional quality and organoleptic characteristics of the CMI produced due to the soaking treatment regime. As noted, longer steeping time was facilitative for hydrolases and proteases, finer texture, and fairly bland taste (milder sourness preferred by children) (Oduro-Yeboah et al., 2016).

Wet milling usage was observed during the pilot study and was also reported by the mothers surveyed in this definitive study as a practice carried out mostly if the purpose ideally were to produce CMIs or cereal dough for other purposes. Majority of the mothers interviewed (92.3%)

indicated that they could perceive the onset and significant progression of spontaneous fermentation from about 6-12 hours after wet milling (**Table 4.4**). However, in northern Ghana, the mothers usually considered dough that was prepared three days or less after wet milling to be fresh dough, or otherwise it was considered fermented dough, if it was beyond the third day of storage (**Table 4.3**). The higher preference for fermented dough for complementary feeding of young children in the Northern Region, is suggestive of its sensory appeal to children and the perceived nutritionally facilitative benefits to children according to the mothers. The use of homemade fermented CMIs for feeding infants and young children have been reported to be decreasing in Tanzania and South Africa in favour of commercial infant cereals (CICs) even though fermented complementary meals are recommended to be generally more nutritious than unfermented complementary meals (Chelule, Mokgatle, Zungu, & Chaponda, 2014; Lorri & Svanberg, 1995). The use of whole grains for Tuo Zaafi (main local cereal delicacy in the Northern Region) flour production was preferred to the use of dehulled grains (Ham, 2020). This is in sync with the observation that majority of the mothers surveyed indicated that they do not dehull their cereal grains for CMI production. Wet milled grains usually have moisture content of between 35-45 % (wet basis) but would usually be kneaded with the addition of water to obtain moist cereal dough (Oduro-Yeboah et al., 2016). The amount of water added, kneading, atmospheric temperature, storage or holding time, exposed surface area, concentration of the starter culture (natural flora or microbiota) in the containers used for storage or holding the cereal meal or within the immediate atmosphere, and the volume of the cereal meal all could have an influence on the onset and rate of spontaneous or natural fermentation (Chaves-López et al., 2020).

5.5 Prevalence and Implications of Nutritional Status of Children in Northern Ghana

The prevalence of undernutrition in the Northern Region generally has not improved significantly compared to that found in recent studies. For instance, compared to the estimated prevalence of stunting (33.1%), wasting (6.3%) and underweight (20%) in the GDHS 2014 study among children (6–59 months) in the Northern Region of Ghana, stunting estimated in this study remained the same (33.2%), wasting increased by a factor of a little over two (14.1%) and underweight has also increased (27%), by almost one-third (Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015). The Multiple Indicator Cluster Survey Five (MICS 5), conducted in 2011, reported 37.4%, 8.1%, 24.2% and 1.1% for stunting, wasting, underweight and overweight prevalence respectively in the Northern Region (Ghana Statistical Service, 2011). MICS 6, conducted in 2017–18, reported 29%, 9% and 1% for stunting, wasting and overweight among children (6–59 months) in the Northern Region, which is indicative also of only a marginal change in prevalence (Ghana Statistical Service, 2018). Saaka et al. (2015) reported a prevalence of 20.5%, 11.5% and 21.1% for stunting, wasting and underweight respectively in a survey of 44 districts in the three northern regions of Ghana conducted in November 2013 among children aged 6–23 months. The disparities could be attributed to the age ranges of the children surveyed in these studies or the periods of the surveys, among other reasons. A disaggregation of the prevalence rates for children under two years of age (6–24 months) from the GDHS 2014 and the MICS 5 and 6 studies would be optimal for comparison with this study. Nonetheless, chronic undernutrition (LAZ), seems intractable in the Northern Region of Ghana. The majority of the stunted, wasted, underweight and overweight children were aged 12–23 months (Table 3). This observation supports the hypothesis that the peak period for complementary feeding among growing children, with or without continued breastfeeding and comorbidities, is critical to optimal child linear and ponderal growth (Lassi, Das, Zahid, Imdad, & Bhutta, 2013).

Compared to the GDHS 2014, MICS 5 and MICS 6, the prevalence of wasting (WAZ) in this study of the Northern Region has increased (Ghana Statistical Service, 2011, 2018; Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015). Acute undernutrition or wasting (WLZ), which reflects the effect of acute inadequate nourishment among children, is a more useful measure in emergency situations than stunting, which reflects an impairment of growth due to prolonged inadequate nutrient intake. The level of wasting estimated in this study (14.1%) is sufficient to be classified as serious (10–14%) based on the WHO cut-off values for public health significance (Onis et al., 2019; United Nations Children’s Fund (UNICEF), World Health Organization, International Bank for Reconstruction and Development/The World Bank, 2019). This is probably due to the period of the survey (June), during which the onset of rain ushers in the planting season, which is known for scarcity of food and increase in infectious diseases such as malaria and cholera.

Underweight (WAZ) and overweight (WLZ) status were both present in this study population, at 27% and 2.6% respectively. Falling within the high prevalence category according to the WHO public health significance cut-off (20–29%), the level of underweight is a phenomenon reflective of the overall nutritional health of children, which is usually premised on one or both chronic growth impairment and acute growth impairment due to prolonged famine, acute hunger or frequent or recurrent illnesses, among other causes (Onis et al., 2019; United Nations Children’s Fund (UNICEF), World Health Organization, International Bank for Reconstruction and

Development/The World Bank, 2019). Although the prevalence of overweight status among the children was relatively low, the emerging phenomenon of the double or multiple burdens of malnutrition in developing countries calls for efforts to stem the tide before it becomes too widespread in the Northern Region. Even though the prevalence of the IYCF indicators in this study are relatively higher, these changes did not translate into a corresponding decrease in the prevalence of stunting or wasting status of the children in northern Ghana. Instead, the indicators of undernutrition were either similar to the GDHS 2014 findings or worse than before. Appropriate, context-specific interventions are therefore needed to address this public health menace in the Northern Region of Ghana.

5.6 Association between IYCF Indicators and Undernutrition (Stunting and Wasting)

Intake of iron-rich foods (Fe), child age group and maternal height were significant predictors ($p<0.05$) of stunting among the children studied in the Northern Region. Child gender, child age and the source of power for lighting in households were significant predictors ($p<0.05$) of wasting among the children. None of the IYCF indicators showed a significant association with stunting or wasting after adjusting for potential confounders in the models, except intake of iron-rich foods for stunting (**Tables 4.8 and 4.9**). This apparent lack of significant correlation between the IYCF indicators and child nutritional status may also be due to insignificant variations in the child feeding practices of the study population generally. The study was conducted during the lean season and dietary diversity may be altered during this period because most rural households depend on their own production of subsistence crops, livestock, and birds. The lack of association observed between the IYCF indicators and child nutritional status may also be attributed to the method of child food intake measurement. A single 24HFR may not be reflective of the usual intake of food by the children and thus probably explaining why the study failed to reveal any significant associations (Krasevec, An, Kumapley, Bégin, & Frongillo, 2017; Mya, Kyaw, & Tun, 2019). However, some studies in SSA and SEA countries found strong relationships between some of the complementary feeding (CF)-related indicators and nutritional status, while others reported no significant associations (Bork, Cames, Barigou, Cournil, & Diallo, 2012; Jones et al., 2014; Krasevec et al., 2017; Marriott et al., 2012; Reinbott et al., 2015). The inconsistent findings about the relationship between the CF-related IYCF indicators and child anthropometric growth indicators (LAZ, WLZ and WAZ) may thus be context-specific and moderated by other factors and/or covariates (Beal, Tumilowicz, Sutrisna, Izwardy, & Neufeld, 2018; Bhutta et al., 2013; Stewart, Iannotti, Dewey, Michaelsen, & Onyango, 2013; Vossenaar et al., 2017).

Similar to this study, Saaka et al. (2015), in their quest to ascertain the relationship between the IYCF indicators and nutritional status of children in northern Ghana, found that none of the core CF-related indicators was a significant predictor of stunting (LAZ), except TICF. Interestingly, in this same study by Saaka et al. (2015), ACF, a composite food intake (CFI) metric estimated from TICF, MMF and MDD, was a significant predictor of wasting, but not stunting. Reinbott et al (2015) posit that a composite child feeding index (CCFI), computed from a combination of the IYCF core indicators, is superior to the individual IYCF indicators in explaining stunting among children in DCs. The predictive utility of variously computed CCFIs from the individual IYCF indicators should be further investigated to validate or disprove the hypothesis that CCFIs are more resilient metrics than the individual IYCF indicators for predicting and monitoring progress in child nutritional health status, as postulated (Bork et al., 2012; Chaudhary, Govil, Lala, & Yagnik, 2018; Khatoon, Mollah, Choudhury, Islam, & Rahman, 2011; Lohia & Udipi, 2014; Reinbott et al., 2015). Standardizing the formula for CCFIs would also prove useful for comparability purposes (Chowdhury, Rahman, & Khan, 2016). Also, in consonance with the findings of this study, none of the individual IYCF indicators was associated with LAZ in recent studies conducted in Cambodia and southern Ethiopia (Reinbott et al., 2015; Tessema, Belachew, & Ersino, 2013). The fact that the general improvement in the individual IYCF indicators in the Northern Region found in this study did not necessarily show a corresponding improvement in the nutritional status of the children, is suggestive of a weak or non-existent association between the individual IYCF indicators and undernutrition (stunting and wasting). The predictive utility of the IYCF indicators individually for stunting and wasting may thus be limited. This buttresses the observation that, although a prolonged state of limited or inadequate food intake has been implicated as a major cause of stunting, some emerging evidence now suggests that stunting could continue to prevail even in food-secure households (nutritionally negative deviant children) or vice versa in food-insecure households (nutritionally positive deviant children). This suggests that, among other things, sub-optimal food utilisation, in synergy with other proximal and intermediate risk factors, may potentially play a significant role in children’s nutritional status (Chen et al., 2018; Saaka & Mutaru, 2014; Semba et al., 2016).

The generally accepted cut-off point of a minimum of four food groups (MDD ≥4) for the intake of meals made from ingredients belonging to the seven food groups as classified by WHO/UNICEF, seems justified given that most children in DCs generally show high intake of meals from G1, G4 and G3 food groups almost always (Figure 4.2). An additional intake of meals made from ingredients belonging to at least G2, G5, G6 or G7 to complement G1, G4 and G3 should thus suffice in providing the minimum level of proteins and/or micronutrients required for adequate growth and development of young children in DCs (Arimond & Ruel, 2004; Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF International, 2015; Habte & Krawinkel, 2016; WHO/UNICEF/IFPRI/UCDavis/FANTA/AED/USAID, 2008, 2010). Several studies have reported an association between dietary diversity (DD) and stunting (Krasevec et al., 2017; Marriott et al., 2012; Reinbott et al., 2015). On that premise, it is often expected that an improvement in dietary diversity measured as dietary diversity score (DDS) or minimum dietary diversity (MDD) would correspondingly result in an improvement in child nutritional status. Indeed, some researchers have reported DDS or MDD as a good measure of nutritional adequacy, healthy dietary intake or micronutrient intake adequacy (Arimond et al., 2010; Gewa, Murphy, Weiss, & Neumann, 2014; Habte & Krawinkel, 2016; Kennedy, Pedro, Seghieri, Nantel, & Brouwer, 2007; Rathnayake, Madushani, & Silva, 2012; Torheim et al., 2004). However, even though the prevalence of MDD (a reflection of the diversity of food consumption from the WHO/UNICEF seven food groupings) in this study was relatively higher than the findings from the GDHS 2014 study, this did not necessarily translate into improved nutritional status of the children in the Northern Region of Ghana. MDD was strongly associated with stunting status but not wasting status of the children in only the bivariate analyses but not in the multivariable analyses of this study. However, this finding is inconsistent with some inferences drawn from a similar study in India (Chandrasekhar et al., 2017). There is the need also to assess across several LMICs and DCs, the association between the usage of the WHO/UNICEF seven food groupings and nutritional status as well as the most appropriate thresholds for determining nutritional adequacy in various vulnerable sub-populations (age, gender, breastfeeding status, etc) towards tracking progress in IYCF indicators and nutritional status. The recommendation for revisions in some definitions and formulas particularly for MDD recently by the technical expert advisory group on nutrition monitoring needs further evaluation for the other IYCF parameters too (WHO, 2020).

Intake of foods rich in iron has been reported as a significant determinant of anaemia, but not often for stunting among children in DCs (Mohammed, Larijani, & Esmaillzadeh, 2019; Mya et al., 2019; Sachdev, Gera, & Nestel, 2006). Kubuga *et al.*, in a 12-week, community-based feeding trial study in northern Ghana, found the consumption of iron-rich native *Hibiscus sabdariffa* leaf meal to be significantly associated with anaemia in women of reproductive age (15–49 years) and had a protective effect against stunting amongst toddlers (Kubuga, Hong, & Song, 2019). This observation may be of interest and relevance in developing dual-purpose nutritional intervention programmes aimed at addressing both stunting and anaemia.

The finding about age as a significant risk factor for stunting is consistent with similar nutritional studies in northern Ghana and other DCs (Ali et al., 2017; Saaka et al., 2016; Tariq et al., 2018). Compared to children in the youngest age range (6–11 months), older children especially had a significantly higher risk of stunting. During this period, complementary feeding tends to be compromised, leading to adverse child anthropometric growth, while babies aged 6–11 months appear to benefit from the nutrient-rich and protective effect of breastfeeding. Maternal height has been reported as significantly associated with stunting by studies in similar settings (Ali et al., 2017; Beal et al., 2018; Victora et al., 2010). The epigenetic and intergenerational influence of maternal height tends to underscore the role of genes and the environment on phenotypic expressions in children, even though the WHO child growth standards depict that all children follow a similar growth pattern, irrespective of their race, type of feeding, wealth or social status, among other factors, under optimal environmental circumstances all around the world (Aguayo, Nair, Badgaiyan, & Krishna, 2016; Martorell & Zongrone, 2012; Onis, 2006).

The covariates or risk factors that were significantly associated with wasting after adjusting for confounders were child gender, child age group and source of power for lighting the household (**Table 4.9**). Acute undernutrition (wasting) tends to be relatively more pronounced in male children, probably due to diarrhoeal diseases arising from the greater tendencies of male children to explore their environment as they begin to crawl, toddle and/or walk (Ali et al., 2017; Glover-Amengor et al., 2016; Saaka et al., 2015; Sahn & Stifel, 2002). Females are also genetically more resilient to stressors than males in early life (Wamani, Astrøm, Peterson, Tumwine, & Tylleskär, 2007; Wells, 2000). Child age group was associated with wasting, as reported in a similar study in northern Ghana (Sienso & Lyford, 2018). Young children in resource-poor settings, upon commencement of complementary feeding, are more acutely vulnerable to diarrhoeal infections and acute food inadequacies than other children much younger or older. Besides being introduced to complementary meals, breastfeeding provides babies or infants (much younger children) with the required nourishment and protection against infections, whilst the relatively older children can better ingest the often more nutritious household meals than children in the intermediate age groups (12–17 months). More often than not, these family meals are more nutritious than the often-monotonous cereal-based-only porridge fed to young children (Sienso & Lyford, 2018). Households without access to electricity are likely to have limited capacity to safely and properly preserve food ingredients and unused meals meant for their children, thus increasing the children's vulnerability to unsafe food intake.

5.7 Association between HFRUP Indicators and Undernutrition (Stunting and Wasting)

Six HFRUP indicators were examined in this study (**Table 4.3**). Even though the cereal form, cereal type (sorghum and millet) and source of dough (homemade) were found to be associated with stunting status in the bivariate analyses (**Table 8.5, Appendix A**), upon adjusting for the proximal covariates and/or factors in the multivariable hierarchical logistic regression analysis, only the type of storage container used habitually by the mothers for keeping dough meant for complementary meal preparation was significantly associated with child stunting status (**Table 4.10**). Interestingly, children of mothers who indicated that they used plastic containers for the storage of dough meant for complementary meal preparation for their children were 102% more likely to be stunted compared to those that used jute sacks or calabash. The likelihood of stunting amongst metal container users was also about 38% more compared to the jute sack or calabash users. Studies conducted on the efficiency of the packaging functions of plastic and metal materials suitable for infant and young child meal ingredients rather vindicates plastics and metals as being effective, safe, and convenient. It was expected instead that the use of jute sacks or calabash would rather be facilitative for the likelihood of stunting status amongst the children, given that these containers may be potential reservoirs of diarrheagenic pathogens in a resource-limited setting where sanitation and hygiene practices may not be optimal. Child morbidity status due to exposure to mycotoxins and/or pathogenic agents especially diarrheagenic microbes have been implicated in the nutritional status of infants and young children in DCs (Ferdous et al., 2013; Lombard, 2014). The use of plastic and metal containers therefore may have contributed to the conditions ideal for the generation of mycotoxins and the presence of enteropathogens in the CMIs during storage.

Given the strong advocacy for cereal-legume blends as a means of improving nutritional quality, the drawbacks associated with potential mycotoxin exposure should be of concern. Mycotoxin (aflatoxin and fumonisin) production in cereal grains have been reported to be more pronounced during harvest (on-farm heap) and post-harvest (post-drying) storage of grains under favourable conditions of grain moisture (22-33%), insect pest infestation, high temperature (35±10°C) and high relative humidity (>80%) (Danso et al., 2017; Enyiukwu, Awurum, & Nwaneri, 2014; Fandohani, Hell, Marasas, and Wingfield, 2003; Hell, Mutegi, & Fandohan, 2010). However, to the best of my knowledge, not much scholarly research, if any at all has been published on the possible production of mycotoxins during storage of domestically or industrially processed cereal products (flour or dough) or CMIs meant for homemade meal preparation, beyond post-harvest cereal drying and storage. Mycotoxins are known to be stable even under cooking temperatures (~100°C) and are usually produced before harvest, during harvest, and/or post-harvest (post-drying) storage prior to potentially being carried over along the value chain of cereal processing unit operations. Scholarly literature on the possible influence of traditional or domestic storage containers and/or conditions of CMIs or homemade cereal-legume-based blends (CLBBs) on child stunting status is thus very scanty which calls for research to fill this gap. The presence of enteropathogens in the CMIs (dough or flour) during storage could also be enhanced not only by the use of plastic or metal containers per se but also the water, sanitation, and hygiene (WASH) conditions and practices during complementary food preparation and feeding of infants and young children.

The habitually preferred cereal form, duration of dough storage, and intake of cereal-only-based complementary meals were associated with child wasting status in the bivariate analysis (**Table 8.6**) but upon accounting for the proximal covariates and/or factors in the multivariable hierarchical logistic regression analysis, only cereal form preferred, and dough storage duration were weakly significant and strongly significant in relation to child wasting status respectively (**Table 4.11**). This study found that children in the Northern Region whose mothers habitually used fresh dough or flour for complementary meal preparation were between 44-55% less likely to be wasted compared to those fed with fermented dough. Paradoxicaly, fermented dough is preferably recommended for complementary meal preparation given the well-documented nutritional quality attributes (improved protein digestibility, improved bioavailability of essential nutrients, and reduced anti-nutrient contents) and improved organoleptic properties (consistency) it has over fresh dough (Chaves-López et al., 2020). Furthermore, intake of porridge or gruels made from fermented dough by children has been found to be protective against diarrhoeal episodes (enteropathogens) and thus helps to prevent inadequate intake of meal servings due to loss of appetite usually experienced by sick children (Ferdous et al., 2013; Kingamkono, Sjögren, & Svanberg, 1999; Kingamkono, Sjögren, Svanberg, & Kaijser, 1994; Lorri & Svanberg, 1994). This finding thus contradicts the putative paradigm, but the association observed between dough storage duration and child wasting status in this study further affirms this rather unusual observation. Compared to children who were habitually fed with dough stored for 3 days or less, children who were fed with dough stored for more than 7 days were 110% more likely to be wasted, whiles those habitually fed with dough stored for a duration between 4-7 days were about 40% less likely to be wasted

(**Table 4.11**). Excessively prolonged fermentation of dough could possibly be counter-protective and result in unpalatable products (sourness) as observed by Oduro-Yeboah et al (2016) in the production of white kenkey (nsiho, a mildly sour stiff dumpling). To obtain similarly desirable sensory attributes such as the mild sour taste (relatively bland), finer or lower consistency, smooth texture, less stickiness, and lower solids contents of soft porridge (Koko), the study recommended that the fermentation time be shorter (12 hours) and the soaking duration be longer (48 hours) (Oduro-Yeboah et al., 2016; Tano-Debrah et al., 2019). Theses attributes may possibly be more organoleptically desirable to infants and young children just as the white kenkey.

5.8 Effects of TCPMs on the Relative Quantities of Physiologically Free Metabolites

In order to ascertain the general effects of the TCPMs on the nutritive and non-nutritive (ANFs) constituents of the three cereals, an optimized, simultaneous (single-run) GC-MS analytical protocol was used to profile the wide range of possible physiological free state (as-is-basis) metabolites in the hydrophilic (water-soluble), methanolic extracts of the experimental cereal samples, without any metabolite-targeting treatments (Filee, Schoos, & Boemer, 2014; Rohloff, 2015; Zörb et al., 2006). The net changes in the relative quantities of nine essential amino acids (EAAs) including the limiting essential amino acids (LEAAs) in cereals (lysine, tryptophan, and threonine) and three conditionally essential amino acids (CEAAs) of children (tyrosine, arginine, and cysteine) together with some carbohydrates (sugars, sugar phosphates and sugar alcohols) and organic acids analyzed from the GC-MS laboratory assays, were evaluated. Even though it is well-known that there are wide variations in the concentrations of the various nutritive and non-nutritive constituents in the main segments of cereal grain structure (pericarp, germ and endosperm), across the three cereals examined (maize, sorghum and millet), the intention of this evaluation from the GC-MS analyses was to note and discuss the patterns of directional changes (increases or decreases) and the magnitude of net fold changes in the physiologically free metabolites in these staple tropical cereals generally, rather than individually for each cereal (Duodu et al., 2002; Duodu et al., 2003; McKevith, 2004; Suri & Tanumihardjo, 2016; Welti-Chanes, Serna-Saldívar, Campanella, & Tejada-Ortigoza, 2020; Zörb et al., 2006).

The GC-MS analyses generally revealed net increases in the relative quantities of most of the essential amino acids in all the three cereals by about 0.06 to 103-fold, including the branched chain essential amino acids (BCAAs; leucine, isoleucine and valine) under almost all the five TCPMs examined (Koistinen et al., 2018). The highest increases in the EAAs were mostly under germination and fermentation conditions. Almost all the sugars (highly abundant in cereals), sugar alcohols (lowly abundant in cereals) and sugar phosphates (lowly abundant in cereals) were generally depleted in the three cereals except maltose, fructose, and fructose-6-phosphate in the maize samples alongside only maltose in the sorghum and millet grains. Pinitol was also increased in almost all the three cereals by between 0.27 and 110-fold, most significantly under germination except in the maize grains. The variable effects of mostly increases and a few decreases observed in the dominant metabolites eluted (amino acids and sugars) were indicative of the variable catabolic and anabolic changes that occurred within the composition of the cereals under the various TCPM treatments (Gorzolka et al., 2012; Koistinen et al., 2018). The exact metabolic pathways, optimal physicochemical conditions, and the enzymes involved in these changes are not apparent from the GC-MC analyses. However, it is clear that the TCPMs examined did elicit net production and release of significant amounts of physiologically free and some peptide-bound amino acids respectively in the three cereals whiles the free monosaccharides (fructose, glucose, and galactose) were mostly used up except for fructose in the maize samples. A combination of the early onset and progression of grain water uptake (hydration) and leaching of free metabolites from the soaked grains, stimulation, or induction of enzymatic hydrolysis of the moiety and membrane-bound biopolymers in the germinated grains and the spontaneous fermentation of the wet-milled cereals, probably accounts for the variable changes in these water-soluble compounds of the cereal metabolome (Gorzolka et al., 2012; Koistinen et al., 2018; Oduro-Yeboah et al., 2016). These observations were mostly in tandem with the findings reported of the time-dependent effects of similar TCPM unit operations (steeping and germination) during industrial malting of barley whole seeds (including endosperm and embryo or germ portions) and sourdough production (yeast and lactic acid bacteria fermentation) from wheat and rye (Gorzolka et al., 2012; Koistinen et al., 2018). Dry milling is reported to liberate membrane-bound metabolites as the cell walls of the cereal grains are raptured by the pulverization process (Taylor, 2007). As a result of these generally observed pattern of net increases in nutritionally essential cereal metabolites (amino acids), TCPMs and such other cereal processing methods are generally perceived to be nutritionally more facilitative and less debilitative, if the processing conditions are optimized (Chaves-López et al., 2020; Mensah & Tomkins, 2003; Nkhata et al., 2018; Oghbaei & Prakash, 2016; Saleh et al., 2013).

Cereals are considered to be very rich sources of energy nutrients (carbohydrates and fats) and healthful phytochemicals but not proteins, vitamins, and minerals (McKevith, 2004). However, for consumers who are predominantly dependent on cereals for their nourishment, any significant amount of nutrient loss could be viewed as nutritionally relevant. Essential nutrients must necessarily be provided in diet because they cannot be produced de novo and in vivo from other nutrients in adequate or excess supply from dietary intake (Awika, Piironen, & Bean, 2011). Therefore, the nutritional epidemiological significance of the adverse loss or inadequacy of even a single essential nutrient such as the limiting essential amino acids in cereals (lysine, threonine and tryptophan) or alternatively a significant increase in the presence of even a single antinutritional factor (ANF) in the diet of especially nutritionally vulnerable populations, are critical public health nutrition concerns (Awika et al., 2011; Ghosh et al., 2012; Ghosh et al., 2015; Ghosh, 2016; Millward, 2017).

Spontaneous or natural fermentation induced mostly increases in the physiologically free amino acids by about 0.2 to 14.3-fold (Koistinen et al., 2018). However, fermentation also resulted in a net nutritionally significant loss (≥10% loss in EAAs) of methionine, cysteine, tyrosine, and arginine in maize; methionine and cysteine in sorghum; tyrosine and arginine in the millet samples examined respectively from the GC-MS analyses. The net losses in cysteine, tyrosine and arginine, being conditionally essential amino acids (CEAAs) for infants and young children, may be considered nutritionally imperative only under certain metabolic or physiological states of the children such as during infections and digestive disorders (Bindels, Goedhart, & Visser, 1996; Millward, 2017). The time-dependent effects of fermentation on the physiologically free sulphur-containing amino acids (methionine and cysteine) in maize-soya bean blends has been reported with similar magnitudes of changes, albeit in variable directions (increases and decreases) at different time points of the fermentation process (Ng'ong'ola-Manani, Ostlie, Mwangwela, & Wicklund, 2014). Sulphur-containing amino acids are critical in child growth, development and maintenance particularly because of their vital functions in protein synthesis, protein structural integrity and metabolic regulation (Brosnan & Brosnan, 2006; Willke, 2014). Methionine and cysteine are richly present in cereals but significantly lacking in legumes, thus justifying the advocacy for cereal-legume blended CMIs (Ng'ong'ola-Manani et al., 2014; Palanisamy, Rajendran, Sathyaseelan, Bhat, & Venkatesan, 2012).

Soaking or steeping also induced mostly increases in the physiologically free amino acids in all the three cereals by about 0.32 to 6.06-fold but also resulted in a net nutritionally significant loss (≥10% loss in EAAs) of cysteine, tryptophan, histidine, tyrosine, and arginine in maize; cysteine, tryptophan, and tyrosine in sorghum; cysteine, tyrosine and arginine in millet samples examined respectively in the GC-MS analyses. This observation was most likely due to seed water uptake leading to leaching especially of cysteine, tryptophan and tyrosine as noted in at least two of the cereals (Swantson & Taylor, 1990).

Wet milling induced mostly increases in the physiologically free amino acids by about 0.37 to 103-fold but also resulted in a net nutritionally significant loss (≥10% loss in EAAs) of only tyrosine in maize. This is most likely due to the disruption of the grains thus releasing some free amino acids entrapped within the various matrices of the endosperm and germ of the cereal grains (Jones, Adams, Harriman, Miller, & van der Kamp, 2015).

Germination induced mostly increases in the physiologically free amino acids in all the three cereals by about 0.06 to 65.3-fold but notably also resulted in a net nutritionally significant loss (≥10% loss in EAAs) of histidine in maize and tyrosine in sorghum. This nutritionally facilitative change in the free amino acid profile of the cereals is most likely due to the hydrolysis of the storage proteins (albumins, globulins, glutelins and prolamins) by naturally present proteolytic enzymes in the embryo or germ of the cereal grains, thus making available more free amino acids as germination was elicited and progressed (Benincasa, Falcinelli, Lutts, Stagnari, & Galieni, 2019; Chiba et al., 2012; Phiarais, Schehl, & Arendt, 2008; van Hung, Maeda, Yamamoto, & Morita, 2012). The duration of germination, temperature, and cereal type has been noted to influence the free amino acid profile of cereal grains (Benincasa et al., 2019; Chiba et al., 2012; Wijngaard, Ulmer, & Arendt, 2006).

Dry milling induced mostly increases in the physiologically free amino acids by about 0.34 to 9.80-fold but also resulted in a net nutritionally significant loss (≥10% loss in EAAs) of only cysteine in the experimental sorghum samples. This is most probably due the liberation of some peptide-bound amino acids in addition to the physiologically free amino acids**.** Without the replacement or supplementation of the indispensable nutrients lost due to milling, the consequences could be significant given the routine usage of such products by the already nutritionally vulnerable communities and households. A classic example is the fortification of cereals with niacin (Vitamin B3) and/or tryptophan (endogenous precursor of niacin), which was implemented in the case of the pellagra malady in the southern states of the United States of America. Refining (debranning, de-husking, decortication or dehulling and degerming) and milling of corn flour was found to be nutritionally debilitative and thus complicit in the inadequacy of niacin in the corn-based diets of the southerners (Humphreys, 2009; Millward, 2017; Mooney et al., 2014; Nyumuah et al., 2012; Sasa Redzic & Vikas Gupta, 2020; Welti-Chanes et al., 2020).

From the GC-MS experimental cereal sample analyses, the relative quantities of the carbohydrate contents (sugars, sugar alcohols and sugar phosphates) generally showed net increases in all the three cereals under the five TCPMs examined**.** These observations are biologically plausible due to the induction and progression of hydrolytic activities of carbohydrate enzymes (amylases) (Georg-Kraemer, Mundstock, & Cavalli-Molina, 2001). The carbohydrate contents of the starchy endosperm of the cereal grains were hydrolzed or degraded into the successively smaller composite units of starch such as the oligosaccharides (raffinose and stachyose), disaccharide (maltose), monosaccharides (glucose, fructose, and galactose), their derivative sugar alcohols (galactitol and mannitol) and sugar phosphates (Gorzolka et al., 2012).

The non-nutritive constituents, particularly the antinutritional factors (ANFs) detected and quantified, included relatively minor quantities of physiologically free phenolic compounds (ferulic acid, p-coumaric acid, sinapic acid and caffeic acid). The levels of these hydroxyl cinnamic acid derivatives (phenolic acids) in sorghum and millet are however much higher than in maize (Gani, Wani, Masoodi & Gousia, 2012). The relatively low levels of these phenolic compounds in whole wheat (non-hydrolysed) were also reported by Gorzolka et al. (2012). These phenolics were reportedly reduced significantly after fermentation of wheat and rye whole grains in a sourdough production study (Koistinen et al., 2018). Ferulic acid, which is considered the most abundant of the hydroxyl cinnamic acid derivatives (phenolic compounds) in most cereals, was also present in relatively low quantities in the three cereal samples analysed (data not shown). This was most probably because the cereal samples were not subjected to hydrolysis treatments (acid, alkaline or enzyme) to liberate these phenolics, most of which are predominantly ester-bound to the cell walls of the grains (Gani et al., 2012; Khakimov, Jespersen, & Engelsen, 2014; Ragaee, Seetharaman, & Abdel-Aal, 2014; Rohloff, 2015). From the GC-MS analyses, these phenolics in the context of this study were considered to be of little or no nutritional and physiological significance with regards to the antinutritional attributes of polyphenols (Gani et al., 2012).

Phytate is considered the most nutritionally important ANF present in the three cereals analysed in this study but phytate could not be analysed with the optimized generic GC-MS protocol used for the separation and relative quantification of water-soluble metabolites in the methanolic extract of the three cereals (Duong, Clark, Lapsley, & Pegg, 2017; Park et al., 2006; Romero-Aguilera, Alonso-Esteban, Torija-Isasa, Cámara, & Sánchez-Mata, 2017; Schlemmer et al., 2009; Zhang et al., 2017). Despite the many strengths of GC-MS analytical techniques, one of its drawbacks during untargeted metabolomics analysis is the need for a trade-off between some metabolites of interest that could be analysed under a common sample preparation treatment or condition (extraction and derivatization) and other compounds, given the wide range of metabolites that could be profiled simultaneously in a single run (Brennan, 2013; Castro-Puyana & Herrero, 2013; Kopka et al., 2004). Myo-inositol and myo-inositol-1-phosphate were detected and quantified, but these are lower inositol phosphate derivatives (precursory anabolites or consequent catabolites of phytic acid) which do not possess the antinutritional attributes of phytic acid (IP6) (Coulibaly, Kouakou, & Chen, 2010; Schlemmer et al., 2009). Generally, fermentation, soaking and germination have been reported to be the most effective traditional cereal processing methods for reducing the nutritionally debilitative potency of phytates in cereals and legumes through the activation of endogenous phytases under optimal acidic pH conditions. Cereal refining processes (dehulling or decortication and milling) in addition, are able to significantly reduce phytate contents (ANF) following cereal pericarp removal (Gupta, Gangoliya, & Singh, 2015; Popova & Mihaylova, 2019; Reale, Konietzny, Coppola, Sorrentino, & Greiner, 2007; Samtiya et al., 2020; Schlemmer et al., 2009).

Yobi *et al* (2020) concluded that only the 1-10% physiologically free amino acids in plant seeds undergo alteration under water stress conditions (and possibly so under other exogenous stress conditions) whiles the approximately 90-99% of the total protein or peptide-bound amino acids in plant seeds, remain intact as a metabolic and physiological acclimation measure (Muehlbauer, Gengenbach, Somers, & Donovan, 1994). This suggests that the stress effect exerted by TCPMs might not affect the total protein-bound amino acid contents in the tropical cereals examined. Could changes in the physiologically free amino acid contents in the cereals therefore alter the total dietary amino acid contents for the purposes of nutritional value or protein quality evaluation? Given the current putative hypothesis in plant physiology, of the adaptive metabolic mechanisms employed by plants under various stress conditions, the quantities and composition (types of AAs) of the physiologically free amino acids could not have been altered accordingly by the various TCPMs in this study. Furthermore, the peptide or protein-bound amino acids in the cereal grains were expected to remain unaltered under the strenuous conditions of the TCPM treatments (Yobi et al., 2020).

The concentration of physiologically free metabolites (nutritionally critical) such as the essential amino acids, in the case of these three cereals analysed (GC-MS analyses), or any food material for that matter, are not reflective of its comprehensive nutritional value or protein quality (van Sadelhoff et al., 2018; Wu et al., 2016). Protein quality evaluation is based on the total quantitative contents of AAs (physiologically free amino acids plus the protein or peptide-bound amino acids), the proteinogenic amino acid composition (types and proportions of the relevant anabolic amino acids) and protein digestibility in the food material (Anitha, Govindaraj, & Kane-Potaka, 2020; Hoffman & Falvo, 2004; Joye, 2019; Reeds, Schaafsma, Tomé, & Young, 2000). The digestible dietary amino acid content is thus determined from the total protein hydrolysate in the food material (Rutherfurd & Gilani, 2009; Rutherfurd & Moughan, 2012). The UHPLC-MS/MS analyses (acid-hydrolysed cereal samples) in this study was conducted to provide a more definitive and comprehensive outlook of the potential protein quality variations (protein value) from the total amino acids (TAAs) contents of the three cereals as a function of the TCPM effects. This served to distinguish between the effects of the TCPMs on the physiologically free amino acids (as-is-basis) compared with the total digestible dietary amino acids (acid-hydrolysed total amino acid contents) (Rutherfurd & Moughan, 2012; van Sadelhoff et al., 2018).

5.9 Effects of TCPMs on the Absolute Quantities of Total EAAs in the Cereals

In order to determine qualitatively, the nutritional significance of each of the five TCPMs examined (soaking, germination, dry milling, wet milling only and wet milling cum spontaneous fermentation) on the three experimental cereals in this study, the net loss (absolute quantities in nmol/mL) in at least two of the essential amino acids (EAAs) were evaluated based on the predefined operational criteria (Buttriss et al., 2017; Kaufman, 1990). Eight essential amino acids (EAAs) including the limiting essential amino acids (LEAAs) in the cereals (lysine, tryptophan, and threonine) and two conditionally essential amino acids (CEAAs) of children (tyrosine and arginine), were prioritized in the laboratory assays of the experimental cereals because of their potentially consequential effects on infant and young child growth and development (Bindels et al., 1996; Dewey, Beaton, Fjeld, Lönnerdal, & Reeds, 1996; Holt & Snyderman, 1965; Rigo & Ziegler, 2006).

From the UHPLC-MS/MS analyses, there were generally a mix of changes observed in the magnitudes (absolute quantities in nmol/mL) and directions of the pattern of variations (increases and/or decreases) in these EAAs in all three cereals. These could be due to several factors ranging from choice of cereal types and type of cultivars to the TCPM variations among others (Bai et al., 2015; Cui, Li, & Liu, 2012; Gwirtz & Garcia-Casal, 2014; Liyanaarachchi, Mahanama, Somasiri, Punyasiri, & Kottawa-Arachchi, 2020; Oghbaei & Prakash, 2016; Thielecke, Lecerf, & Nugent, 2020). However, all the five TCPMs examined, unequivocally effected debilitative nutritionally significant changes (≥10% loss in EAAs) in the absolute contents (nmol/mL) of at least two of the constituent total essential amino acids (EAAs). Dietary deficiency diseases can be caused by significant inadequacy or the lack of even just a single essential nutrient in the diet of vulnerable persons (Kaufman, 1990). The impact of the lack of, or inadequacy of an individual nutrient, or a combination of a few essential nutrients especially limiting essential amino acids (LEAAs), vitamins and minerals in cereals, if not supplemented by some viable means with the preformed essential nutrient such as through dietary fortification, it could prove to be nutritionally problematic (Kaufman, 1990). Pellagra, scurvy, beriberi, rickets, and Kwashiorkor are examples of dietary deficiency diseases owing to the lack of, or inadequate intake of one, or a few combinations of some critical nutrients (Elmore & Feinstein, 1994; Martin & Humphreys, 2006; Rajakumar, 2000). Dry milling with Nikanika (disc plate motorized attrition mill used for flour production) in northern Ghana, resulted in nutritionally significant losses (≥10% loss in EAAs) of lysine, isoleucine, valine, and histidine in the experimental maize flour samples. The significant loss in these essential amino acids especially lysine (first limiting amino acid in cereals) has also been reported in some studies on milled cereals (Pedersen & Eggum, 1983). The maize flour samples were possibly degermed during the dry milling process resulting in the loss of the lysine and tryptophan-rich metabolic proteins (albumins and globulins) concentrated in the germ or embryo portions of the grains (Ai & Jane, 2016; Gwirtz & Garcia-Casal, 2014). Even though about 50% of the storage proteins (zein also called prolamins and glutelins) are located predominantly in the starchy endosperm of maize grains, the storage proteins contain relatively lower amounts of lysine and tryptophan (but high amounts of methionine and cysteine) contrary to the germ or embryo portion which is relatively richer in lysine and tryptophan (Azevedo & Lea, 2001; Shewry & Halford, 2002). The laboratory-milled whole maize grains which served as the reference (or control) samples, upon pulverization of all the grain segments (bran or pericarp, germ, or embryo, aleurone and endosperm), most likely retained all of its physiologically free amino acids, peptide and/or protein-bound amino acids stored in the starchy endosperm, germ, bran, and aleurone (Balandrán-Quintana, 2018; Shewry & Halford, 2002; Sylvester-Bradley & Folkes, 1976). The likelihood of degerming occurring during milling of maize with the commercial attrition mills (Nikanika) in the Northern Region of Ghana, possibly accounts for the net losses in lysine, isoleucine, valine, and histidine in the maize flour samples (Gwirtz & Garcia-Casal, 2014). Maillard reaction has been reported also as a possible reason for amino acid loss in cereals after milling (Ashoor & Zent, 1984; Lund & Ray, 2017). Milling possibly increases the exposure levels of reducing sugars and amino acid moieties to one another, thus facilitating Maillard reactions.

In the experimental sorghum flour samples, dry milling (using the commercial attrition mills called Nikanika) mostly exerted facilitative nutritional significance (≥10% gain in EAA) for all the EAAs, from the UHPLC-MS/MS analyses. The processing of sorghum grains to obtain flour is very challenging compared to maize and other tropical cereal grains even when the grains are tempered to improve degermination and debranning before milling of the mainly starchy endosperm. This is due to the desiccated crumbly bran (pericarp), relatively larger germ or embryo portion and the wide range of starchy endosperm matrix properties of sorghum (Saleh et al., 2013; Taylor & Dewar, 2001). The flour yield from sorghum grains is usually affected by the milling method employed, be it mortar-pestle pounding, abrasive-decortication hammer milling, Nikanika-type disc attrition milling (used in northern Ghana) or roller milling with or without tempering (Larsen et al., 2020; Taylor, 2007). Besides, sorghum has a uniquely poor protein digestibility attribute compared to other tropical cereals due to some endogenous and exogenous factors (Duodu et al., 2002; Duodu et al., 2003). This attribute possibly facilitated maximum retention of most of all the proteins in the various grain segments during dry milling with Nikanika which may have resulted in minimal degerming of the sorghum grains. Ideally, the total contents of the amino acids in both the reference flour (laboratory-milled sorghum grains) and the experimental sorghum grain flour (Nikanika-milled) should have been the same but the net increase in the absolute concentrations (nmol/mL) of the total essential amino acids contents suggests that the experimental sorghum flour collected from the various households besides minimal degerming, may have been subjected to some amino acid-generating and/or protein yield-enhancing treatments before the dry milling process. No sample of the dry-milled millet grains was obtained from the households in the Northern region for this study.

Soaking or steeping of the cereal grains in water induced mostly increases in the total amino acids (protein metabolites) in all the three cereals but also resulted in the nutritionally significant loss (≥10% loss in EAAs) of lysine, valine, histidine, and tyrosine in the experimental maize grain samples as well as methionine, lysine, threonine, phenylalanine, histidine, and tyrosine in the experimental millet grain samples. This significant loss in some of the essential amino acids especially lysine (first limiting essential amino acid in cereals) has also been reported in some analytical studies on soaked tropical cereals. This loss observed was probably due to leaching of the physiologically free essential amino acids (P-FEAAs) into the water during steeping and additional amino acids that may have been liberated and/or synthesized from the bound peptide or protein moieties in the maize and millet experimental samples. Hydrolases and proteases responsible for these possible hydrolytic liberations of AAs are predominantly concentrated in the embryo or germ of cereal grains. Soaking of sorghum grains mostly resulted in net increases in all the eight essential amino acids (EAAs) and the two conditionally essential amino acids (CEAAs) examined. This significant net gain in the essential amino acids especially methionine, lysine, threonine, phenylalanine, and arginine has also been reported of some EAAs in similar analytical studies on tropical cereals. The unique behaviour of the storage proteins in sorghum (karifins) has been a subject of research to unravel the mechanisms underlying its unusual characteristics (Duodu et al., 2002; Duodu et al., 2003). The net increase in the absolute concentrations of these EAAs may be due to the resilience of the peptide and/or protein bound EAAs during soaking against enzymatic hydrolysis (hydrolases and proteases), which may have prevented leaching of its EAAs. Wet milling only of the maize grains (fresh dough production) resulted in the nutritionally significant loss (≥10% loss in EAAs) of lysine, isoleucine, leucine, valine, and histidine. The branched chain amino acids (BCAAs) leucine, isoleucine and valine are recognized to be very important in muscle anabolism and other metabolic processes, facilitated in synergy with the other EAAs (Martínez Sanz, Norte Navarro, Salinas García, & Sospedra López, 2019). The fresh maize dough produced from soaked maize may also have lost these EAAs due to leaching and hydrolysis in a similar fashion as observed with the soaked maize and millet grains.

Natural fermentation of the cereal grains (fermented dough production) induced variable changes (increases and decreases) in the total free amino acids (total protein metabolites) in the maize and millet grains whiles only net increases in the total EAAs were observed in the sorghum grains. Notably also, natural fermentation resulted in the nutritionally significant loss (≥10% loss in EAAs) of lysine, valine, and histidine in the maize samples as well as methionine, lysine, threonine, phenylalanine, histidine, and tyrosine in the millet samples. This significant loss in these essential amino acids especially lysine (first limiting amino acid in cereals) again is in tandem with similar analytical studies on fermented cereals. However, some studies on different maize cultivars and other cereals indicated that fermentation resulted in an increase in the protein and amino acid contents, including lysine (Cui et al., 2012; Hamad & Fields, 1979; Mohiedeen, El Tinay, Elkhalifa, Babiker, & Mallasy, 2010). The disparity observed between this study and these other studies could possibly be due to the differences in the cultivars analysed and the time-dependent variations in the steady-state levels of total amino acids as the metabolic processes of fermentation progressed. The time point during the fermentation at which the analytical samples are collected could affect the EAAs estimated (Ng'ong'ola-Manani et al., 2014). Fermentation, as one of the oldest biotechnological food processing methods, is generally perceived as more nutritionally facilitative than debilitative, if at all due to the several benefits it confers on cereal and other food products (Chaves-López et al., 2020; Nkhata et al., 2018; Singh, Rehal, Kaur, & Jyot, 2015).

Sprouting or germination of the cereal grains induced variable changes (increases and decreases) in the total amino acid contents (total proteins) in all the three cereals but also notably resulted in nutritionally significant loss (≥10% loss in EAAs) of methionine, lysine, isoleucine, and valine in the maize samples; histidine in sorghum; threonine, phenylalanine, and tyrosine in the millet samples. This is possibly due to changes in the amino acid profile of seeds during germination as reported in some studies, as a reflection of the physiological transitions that facilitate the seed germination process. Some of the amino acids were increased most likely through synthesis in the seed and/or the breakdown of some bound proteins or peptides (Fait et al., 2006; Gorzolka et al., 2012; Singh et al., 2015). Sprouting or germination of cereal grains for the production of homemade CMIs was however not evaluated for its usage or practice by the mothers during the survey of this study and was thus not examined in the nutritional epidemiological analysis. This TCPM is however highly recommended by the WHO/UNICEF and other experts in maternal and child nutritional health as a means of improving the nutritional quality of complementary meal ingredients (Lay & Fields, 1981; Mensah & Tomkins, 2003; Mohamed Nour, Mohamed Ahmed, Babiker, & Yagoub, 2010; Nkhata et al., 2018).

Consistently, all the five TCPMs resulted in nutritionally significant losses of at least two essential amino acids in the maize grains, including lysine which is the first limiting amino acid in all the three staple tropical cereals examined. Lysine fortification has been advocated as a panacea to the debilitating phenomenon of undernutrition amongst monotonous cereal-eating paediatric populations in DCs. Fortification would be especially needful in the Northern Region of Ghana where cereal-only-based CMIs abound (Backstrand, 2002; Ghosh et al., 2008; Ghosh et al., 2014; Gwirtz & Garcia-Casal, 2014; Huo et al., 2011; Hussain et al., 2004; Suri et al., 2014; Zhao et al., 2004). However, fortification of cereals with essential nutrients such as lysine, vitamins, and iron to replace, augment, and/or supplement their loss through processing may not be cost-effective and sustainable on a small scale as a public health nutrition intervention if not properly implemented (Assunção, Santos, Barros, Gigante, & Victora, 2012; Dary, Freire, & Kim, 2002; Gwirtz & Garcia-Casal, 2014). Flour fortification with essential nutrients is also a costly industrial process whose CMI products most likely would be pragmatically inaccessible to the most vulnerable children whose parents (or guardians) predominantly lack the economic wherewithal (or purchasing power) now and possibly in the foreseeable future if they were even made available to their communities (Abeshu et al., 2016; Gwirtz & Garcia-Casal, 2014; Pelto & Armar-Klemesu, 2011; Suri et al., 2014; Tano-Debrah et al., 2019).

Lysine (Lys), histidine (His) and valine (Val) were all significantly reduced under all the five TCPMs examined in the maize samples except germination for histidine. Valine, an important branched-chain amino acid (BCAA) was also significantly reduced in all the five TCPMs. Maize is the most used cereal for complementary feeding of infants and young children in the Northern Region of Ghana. Threonine, phenylalanine, and tyrosine were all significantly reduced under all the three TCPMs examined on the experimental millet samples except methionine under germination. Millet generally has the highest level of proteins among these three staple cereals which is traditionally patronized also quite highly in the northern region of Ghana for complementary feeding of infants and young children (Saleh et al., 2013). Developing optimal blends of these cereals with high quality protein-rich legumes which are locally available in the Northern Region of Ghana, could contribute significantly to addressing the concerns about the possibility of adverse losses in the essential nutrients, especially limiting EAAs due to TCPM effects. Legumes are rich in lysine and tryptophan whiles the cereals are rich sources of sulphur-containing essential amino acids (SCEAAs), namely methionine and cysteine (Singh, 2017). The quantitiy of leucine in the three cereals are generally higher even though a nutritionally significant loss was observed in the freshly wet-milled maize experimental sample (fresh dough). Leucine happens to be the most elucidated EAA, responsive to the mechanistic target of rapamycin complex C1 (mTOR1), which is involved in the regulation of linear and ponderal growth in humans (Laplante & Sabatini, 2012; Semba et al., 2016).

5.10 Association between TCPM Usage Indicators and Undernutrition

Multivariable hierarchical linear regression analyses were conducted to determine the association between the usage of TCPMs and child undernutrition (stunting, wasting and underweight status), after accounting for the proximal putative determinants of child undernutrition. Only dry milling was a significant predictor of child stunting status with a small effect size ($R^2 = 0.007$). Dry milling was again found to be a significant predictor of child underweight status with a small effect size ($R^2= 0.008$) (Sullivan & Feinn, 2012). Even though the effect size appears to be small, it may have marked biological relevance, particularly for limiting essential amino acids such as lysine (European Food Safety Authority, 2011; Maher, Markey, & Ebert-May, 2013; Pavlovic, Prentice, Thorsdottir, Wolfram, & Branca, 2007). Dry milling was not associated with wasting probably because of the fleeting or temporal nature of this nutritional health indicator compared with stunting and underweight status which are conceptually reflective of chronic and aggregate nutritional health measures, respectively. Even though dry milling is an inevitable unit operation of cereal processing to produce flour or cereal meal, the effects on nutritional quality are reported to be generally more nutritionally facilitative than debilitative if the unrefined form or whole grains of the cereal is used compared to milling the polished or refined grains (Heshe, Haki, Woldegiorgis, & Gemede, 2016). Milling is defined as a mechanical size reduction unit operation or a pulverization process whereby grains are ground into flour or meal (Bender, Bender, & Bender, 2006). The milling method, type of equipment, and sequence of pre-treatments prior to milling also play a role in the compositional and nutritional changes of the cereal (Gwirtz & Garcia-Casal, 2014; Oghbaei & Prakash, 2016). Even though dry milling of cereals has been shown to generally reduce the levels of antinutritional factors (ANFs) especially phytic acid (IP6), phenolics, and tannins, the loss of some essential amino acids, vitamins, minerals, and other healthful phytochemicals alongside may also be significant with undesirable consequences (Hotz & Gibson, 2007; Saleh et al., 2013). This rather paradoxical phenomenon buttresses why fortification of flour with essential nutrients especially limiting amino acids such as lysine in cereals, is critical at the household level and/or industrial formulation and production of CMIs, CICs, or PCBBs (Datta & Vitolins, 2016; De-Regil, Suchdev, Vist, Walleser, & Peña-Rosas, 2013; Ghosh, 2016; Pellett & Ghosh, 2004). Intake of lysine (lysine-fortified flour or lysine-fortified capsules) showed a significant association with linear growth of children, desirable immunologic indices, decreased stress-related anxiety, and additionally exhibited positive effects on diarrhoeal morbidity in children (Ghosh et al., 2008; Ghosh et al., 2010; Hussain et al., 2004; Smriga et al., 2007; Smriga, Ghosh, Mouneimne, Pellett, & Scrimshaw, 2004; Zhao et al., 2004). At the household level in resource-poor settings such as the Northern Region of Ghana, fortification of homemade CMIs with limiting essential amino acids and key micronutrients could be achieved pragmatically through blending or composite formulation of cereals with legumes such as groundnuts, cowpeas, lentils, chickpeas, and green peas. These legumes are rich in micronutrients and some essential amino acids like lysine, arginine, and valine (Iqbal, Khalil, Ateeq, & Sayyar Khan, 2006). This is why dry milling, even though it is an inevitable unit operation (TCPM) in the production of flour, it may possibly be wreaking havoc on the nutritional health status of children in northern Ghana. In this resource-constrained setting, the compensatory and/or complementary sources of lysine, other essential amino acids (EAAs), and micronutrients are not widely available, accessible, and sufficiently being utilized to meet the recommended nutrient intake (RNI) or nutrient adequacy of the vulnerable children. The possibly significant level of inadequacy of lysine intake from the complementary meals of children in the Northern Region needs urgent attention (Jager et al., 2018; Jager, Borgonjen-van den Berg, Giller, & Brouwer, 2019).

The nutritional epidemiologic significance of dry milling may be exacerbated by other food utilization domains of HFI. Furthermore, nutritional limitations could be exerted by the other possible iterative biochemical reactions in the homemade CMIs and complementary meals during production and preparation, respectively. Meal preparation unit operations such as cooking, though culinarily inevitable, could cause Maillard reactions and racemisation resulting in the non-bioavailability of some essential amino acids (Liardon & Ledermann, 1986; Rutherfurd & Gilani, 2009; Rutherfurd & Moughan, 2012). Bioavailability drawbacks on especially amino acids, vitamins, and minerals could also constrain the optimal utilization of complementary meals. This could be due to successive gastrointestinal tract (GIT) factors during ingestion, aggregate digestibility of the consumed complementary meal, and ileal absorption and assimilation of the essential and limiting nutrients (Rutherfurd & Moughan, 2012).

However small the effect size of dry milling in association with undernutrition may apperar to be, this finding could be translated into relevant nutrition interventions, even though is has to be externally validated (Ialongo, 2016; Maher et al., 2013). Various interventions aimed at addressing the public health menace of undernutrition in the northern regions of Ghana, particularly food-based approaches premised on improving dietary diversity (especially legume intake), dietary fortification, and dietary supplementation among others continue to show improved nutritional quality of complementary meals and worthwhile nutritional health outcomes but still fall short of the RNI of some essential nutrients (Ghosh et al., 2010; Ghosh et al., 2014; Jager et al., 2019). However, there still remains a huge lacuna to be filled possibly if optimization of TCPMs for the production of homemade CMIs are given the due attention. Some studies have reported improvement in protein and micronutrient intake among infants and young children through the consumption of traditional cereal-legume blends (CLBs), industrially processed cereal-based blends (PCBBs), and commercial infant cereals (CICs) compared with cereal-only-based fermented dough porridge (Koko) or complementary foods but still fall short of the RNI thresholds or nutrient adequacy for a good number of key nutrients. Besides, the homemade CMIs are still mostly preferred, and patronized by nursing mothers (Abizari et al., 2017; Dimaria et al., 2018; Ferguson, Chege, Kimiywe, Wiesmann, & Hotz, 2015; Masters et al., 2017; Suri et al., 2014).

For instance, optimization of the cereal-legume blended CMIs made from locally available and accessible ingredients within the limits of the resource-poor settings of DCs and LMICs are also being explored with linear programming analyses (LPA) to develop context-specific food-based complementary recommendations (FBCFRs), food-based recommendations (FBRs) and food-based dietary guidelines (FBDGs) in some DCs and LMICs (Ferguson et al., 2015; Jager et al., 2019; Santika, Fahmida, & Ferguson, 2009; Suri et al., 2014). LPA in this context, is an application of the philosophy and some principles of precision public health (PPH) whereby, mathematical or statistical modelling techniques are used to obtain the most optimal solutions for real-life food and nutrition problems, given our knowledge of the multiple theoretical and empirical factors that could contribute to and/or constrain attainment of those optimal nutritional goals (Dantzig & Thapa, 1997-2003; Maillot, Vieux, Amiot, & Darmon, 2010; van Dooren, 2018). The usage of homemade or traditionally produced CMIs, be it solely cereal-only-based or composite cereal-legume blends, are likely to continue to dominate compared to the patronage of industrially processed CICs especially in the rural areas even though patronage of CICs and industrially processed CLBBs is higher in the urban centres. This is mainly due to limited availability of the CLBBs and/or CICs in the rural areas and the relatively weaker purchasing power of mothers and/or households in such small towns and villages. To meet the minimum RNI adequacy for all the key nutrients needed by infants and young children therefore, how these homemade or traditional CMIs are processed could be very key to addressing undernutrition in the Northern Region of Ghana. For instance, what is the optimal combination of household soaking, germination, wet milling, dry milling, and natural fermentation conditions (duration, cereal type, legume type, pre-treatments, et cetera) for the production of fermented or unfermented composite cereal-legume flour or dough in order to harness the full nutritional potential of the locally available and preferred cereals and legumes?

Harnessing and extending the optimization functions of linear programming analyses (LPA) to account for the potentially debilitative effects of sub-optimal TCPMs such as dry milling could go a long way to fill the gap possibly missing in the quest to reverse the problem of undernutrition in the Northern Region of Ghana and other similar settings in DCs. Application of linear programming analyses, cognisant of the influence of TCPMs on the nutritional quality of the locally available ingredients for the traditional production of CMIs, could be worthwhile. Studies on the debilitative and facilitative effects of various household cereal processing (TCPM) regimes or conditions on nutritional quality continue to increase in the NER literature (Joye, 2019; Thielecke et al., 2020). However, studies on the optimal combination of these TCPMs to maximize the potential benefits of the nutritive and non-nutritive (ANFs and healthful phytochemicals) constituents in cereals, legumes, and other ingredients for CMI production are lacking (Hotz & Gibson, 2007). When these optimization studies are done, linear programming analyses (LPA) could then be implemented, incorporating the findings to account for the drawbacks or constraints of sub-optimal TCPMs such as dry milling in the formulation and development of optimal, context-specific, pragmatic, and easily transferable household cereal processing technologies to mothers and care givers of infants and young children, for the production of homemade CMIs that meet the minimum RNIs. For instance, the constraining factors of yield and nutrient retention due to food preparation, were accounted for during the application of linear programming analyses (LPA) to develop food-based dietary guidelines (FBDGs) aimed at optimizing the role of legume grains on protein and micronutrient adequacy of complementary diets of children in rural northern Ghana (Bergström, 1996; Jager et al., 2019). The superiority of animal source proteins (ASPs) over plant source proteins (PSPs) is well documented and therefore the promotion of ASP intake as a more viable panacea to the child undernutrition malady is well-founded as advocated by some researchers (Hoppe et al., 2008; Millward, 2017; Wu, 2016). However, given the economic and environmental limitations and consequences respectively that such a potentially efficacious intervention could present to the target communities in the Northern Region of Ghana, addressing the potential drawbacks associated with cereal-legume based CMIs due to TCPM effects and other constrains, would be a better alternative instead (Leinonen et al., 2019; Pelto & Armar-Klemesu, 2011; Suri et al., 2014).

5.11 Challenges Faced During the Study

The domains (HFRUPs and TCPMs) conceived of the food utilization dimension of HFI, which were examined in this study are novel constructs. Consequently, due to the lack of precedence to guide the conceptualization, operationalization, and measurement of the HFRUP and TCPM indicators, a formative study (qualitative and quantitative pilot study) had to be conducted to help frame and operationalize the concepts (phenomenon) as constructs in simple, reliable, validly suitable, and pragmatic terms within the specific contexts of the Northern Region of Ghana. There was no standardized and/or validated instrument available that was suitable for the measurement of these newly conceived constructs (HFRUPs and TCPMs) of the food utilization dimension of HFI. The definitive interviewer-administered questionnaire was therefore developed out of the formative study and extensive literature review. The draft composite data collection instrument had to be pre-tested and piloted to standardize and/or validate it before its application in the definitive cross-sectional survey. The iterative processes leading to the development of the definitive interviewer-administered data collection instrument proved to be a challenging task with regards to the doctoral study duration, funding resources, timing for the mobilization of the research support team, and mobilization and sensitization of the study participants and communities.

The need to optimize the foodomics analytical protocols (GC-MS and UHPLC-MS/MS) in a series of repeated trial analyses on the cereal samples, made the research process more time-consuming and laborious. This prolonged the timelines required for the conduct of the entire definitive cross-sectional survey and experimental laboratory components of the study. The study was faced with occasional delays due to occasional supply challenges of critical test kits and laboratory equipment break down and/or routine maintenance services, which limited laboratory bench time and space from time to time. Notwithstanding, the research project was eventually completed successfully.

5.12 Strengths and Limitations of the Study

This study is the first to the best of my knowledge and the literature reviewed so far, to investigate these defined constructs or domains (TCPMs and HFRUPs) of the food utilization dimension of household food insecurity (HFI), as potential risk factors of child nutritional status in a developing country setting. The study was successful in generating an intriguing hypothesis (or postulate) about the probable association between the effects of TCPMs on the nutritional quality of complementary meal ingredients (such as flour and dough) and child nutritional health status. This study therefore provides the needed muse for further and broader inquiry into the potential influence of domestic (or household) food ingredient processing methods and meal preparation methods on the nutritional health outcomes of infants and young children, especially during the transition period from exclusive breastfeeding to complementary feeding (weaning).

This study also adds to the dearth of literature on the quality of complementary meal ingredients (CMIs) or weaning food ingredients (WFIs), particularly homemade CMIs compared to the relatively much more researched, industrially processed cereal-legume-based blends (CLBBs) and/or commercial infant cereals (CICs). This remains as an area of research concern in the combat against the malady of undernutrition amongst infants and young children in resource-limited settings. Some specific strengths and limitations are further discussed in the subsequent section with regards to the methodological approach to the cross-sectional survey and the foodomics analytical laboratory components of the study.

5.12.1 Strengths of the Methodological Approach: Survey Component of the Study

Every pragmatic and rigorous effort was made to obtain high quality primary survey data, which involved the recruitment and standard training of the field research support personnel (interviewers, anthropometrists, data entry clerks, and supervisors) with the requisite academic and professional backgrounds. This ensured high intra and inter-rater reliability (IRR). In addition, a pilot study (formative study phase) was conducted for both the analytical cross-sectional survey and foodomics laboratory analyses components of the study. The sample size for the cross-sectional survey was large and representative enough (80% power) of children aged 6–23 months in the Northern Region, in order to satisfactorily generalize the findings of the research questions. The putative and potential confounders identified from the NER literature on the Northern Region and similar resource-constrained settings in DCs as well as the formative study findings, were accounted for in the definitive study (VanderWeele, 2019). The survey data collection instrument was rigorously revised until it was deemed adequately suitable, valid, and reliable with the support and inputs from community nutrition research experts and inferences from the psychometric analyses (Rousson, Gasser, & Seifert, 2002; Scholtes et al., 2011).

5.12.2 Limitations of the Methodological Approach: Survey Component of the Study

Being an analytical cross-sectional study, causality cannot be inferred from the results of such an observational study design (Wang & Cheng, 2020). Due to the limited availability of similar studies conducted in northern Ghana for the child age range of interest in this study (6–23 months), some comparisons of the IYCF indicators were not ideal. Some of the studies from which findings were compared with this study, involved children (24–59 months) who were outside the age range of children targeted in this study.

Despite the widely utilized and putatively accepted validity and reliability of data obtained from self-reported, interviewer-administered 24HFR in nutritional epidemiological studies, measurement errors due to recall bias arising from socially desirable responses and forgetfulness, still poses a challenge and may thus have affected some of the findings (Ahrens & Pigeot, 2014; Carroll, 2014). The seasonal variations in potential time-variant confounders (inter-temporal effects) such as changes in the food security situations and dietary diversity in the study setting was not accounted for. The use of a 24HFR to assess the usual intake of food by the children from this single time point survey may not have captured the actual dietary intake as theoretically intended. These possibly may have had effects on the associations observed between the exposure (explanatory) and outcome variables in this study, including residual confounding despite measures taken to eliminate confounding effects through the statistical techniques of the data analysis (Lee & Burstyn, 2016; Liang et al., 2014).

The explanatory (exposure) variables, potential confounders, and covariates/factors explored in this study may not be exhaustive, and thus the understanding or insight gained from the relationships between the exposure variables (IYCF indicators, HFRUP indicators and TCPM indicators) and child undernutrition (outcome variable) in northern Ghana may be limited by those variables unaccounted for (unmeasured potential confounding effect) (Agogo & van der Voet, 2016). The scope of the study did not cover for instance the usage of industrially made CICs nor PCBBs, compared to homemade CMIs to be able to account for, or adjust the influence of the level of utilization of these different complementary feeding ingredients in the Northern Region of Ghana. Besides, sensitivity analysis was not undertaken to further examine the robustness of the analytical methods, definitions and measurement of the explanatory variables, statistical models, assumptions, and/or unmeasured confounders in the study (Ding & VanderWeele, 2016; Greenland, 1996).

Child malnutrition (undernutrition) is composed of two main dimensions, protein energy malnutrition (PEM) and micronutrient deficiency malnutrition (MDM). Even though MDM is also a serious public health nutrition concern in the Northern Region of Ghana, measures of MDM such as anemia, iron deficiency, iron deficiency anemia, zinc deficiency and Vitamin A deficiency amongst others were not included in the study (Petry et al., 2020; Wegmüller et al., 2020). This thus limits the knowledge and understanding gained about the effects of TCPMs as potential determinants of child undernutrition status comprehensively, given that the most widely documented effects of processing on nutritional quality are mostly about micronutrients (Gwirtz & Garcia-Casal, 2014; Oghbaei & Prakash, 2016).

TCPM, as a construct conceived from the NER literature search and the formative research study to reflect the unit operations commonly utilized by mothers in the Northern Region of Ghana for the production of CMIs (flour/dough), was each defined by either preferences, duration, or frequency of usage unidimensionally. The conceptualization of HFRUPs and TCPMs as unidimensional constructs rather than multidimensional constructs was intended to simplify the indicators used as the explanatory variables (domains of the food utilization dimension of HFI). This was intended to assess the potential dose of exposure (food or nutrient intake) by children at the household level. However, based on the self-reported responses of the mothers (proxy or surrogate measures), these unidimensional indicators may not be accurate measures of food or nutrient intake compared to the use of direct biomarker measurement methods from the subjects' individual bio-samples (such as blood, urine, or feces) (Carroll, 2014). Notwithstanding, biomarkers mostly used in nutrimetabolomics also have significant limitations (Corella & Ordovás, 2015; Dragsted et al., 2017; Prentice, Sugar, Wang, Neuhouser, & Patterson, 2002; Rollo et al., 2016). The use of biomarkers in nutrimetabolomics studies rather than food metabolomics (foodomics) would also have been constrained by the lack of suitably validated biomarkers of the intake of these tropical cereals (maize, sorghum, and millet). In addition to pragmatic resource challenges (state-of-art analytical laboratory resources) and ethical constraints associated with recruiting participants for such a NER study, the application of food intake biomarkers still largely have significant limitations.

5.12.3 Strengths of the Food Metabolomics Analytical Laboratory Methods

The unique strengths that distinguish foodomics analyses (UHPLC-MS/MS and GC-MS) were harnessed. These include the high throughput attribute in a simultaneous single-run, efficiency, sensitivity to low concentrations of metabolites, specificity of the separation and detection capabilities, validity, and reliability of experimental study results. UHPLC-MS/MS analytical protocols currently are considered the gold standard for amino acid analysis (Koistinen et al., 2018; Semba et al., 2016).

5.12.4 Limitations of the Foodomics Laboratory Methods and Experimental Design

The methodological approach adopted towards synergizing the findings of the foodomics (cereal metabolomics) laboratory study component with the analytical cross-sectional survey data were premised on some assumptions. The limitations inherent in some of the assumptions may have confounded some of the findings of the study. For instance, it was assumed that the conditions under which the soaked and/or germinated cereal samples were collected for this study, were representative of the average or typical physiological and/or metabolic state of all soaked and/or germinated cereals used in the study households. However, malting studies (controlled steeping and optimized germination of cereals) by Gorzolka *et al* (2012) and Frank *et al* (2011) illustrate the time-dependent changes in the metabolite profiles of the constituent biomarker compounds (metabolites) between the onset of steeping, progression of germination, and termination of germination by kilning of the barley grains. This phenomenon is replete in plant physiology of cereal grains and thus suggests that the metabolite profiles of the three cereals examined in this study, are limited by, or subject to their metabolic states from the collection time until analysed.

However, the necessary pragmatic precautions were taken to minimize or avoid stark changes in the cereal samples collected for analyses in this study.

The wide range of possible processing conditions of cereals (TCPMs) for the production of homemade CMIs that were examined in the foodomics laboratory were not exhaustive and thus the study findings may not be reflective of the diversity of specific cereal processing conditions used in the various households. For instance, only one regime of soaking duration (72 hours for maize, 48 hours for sorghum and 24 hours for millet) out of the variety of possible soaking durations used by the various households in the communities was sampled and analysed in the laboratory. This choice of soaking regime was decided on from the formative study but certainly may not completely be reflective of the diversity of soaking regimes nor the various TCPM conditions possibly used by the mothers for CMI production.

The TCPMs examined in this study were not exhaustive. Other TCPMs such as roasting or kilning, nixtamalization, winnowing or sieving, and kneading which may be utilized in the Northern Region of Ghana and other similar settings in DCs for the production of homemade CMIs were not investigated in this study. Some of these TCPMs have been reported in some laboratory studies as having significant quantitative effects on the compositional and nutritional constituents of cereals and other related food materials (Geervani, Vimala, Pradeep, & Devi, 1996; Tiwari & Awasthi, 2014).

The sample pre-treatments and foodomics analytical laboratory methods (protocols) used in this study have their peculiar limitations, some of which could not pragmatically be fully accounted for or corrected in the computation of the relative and absolute quantities (concentrations) of the metabolites examined. Sample pre-treatments such as the collection, handling, transportation, and storage conditions were managed optimally within the limits of the resources and situations of the study, and study settings but errors arising from flaws in any of these cannot be ruled out completely.

Acid hydrolysis has effects on the accuracy of measurement of some amino acids as indicated by the manufacturers of the analytical test kits and/or prescribed analytical protocols, and also from literature (Rowan, Moughan, & Wilson, 1992; Rutherfurd & Gilani, 2009). Amino acids tryptophan and cysteine were completely destroyed during the acid hydrolysis as part of the sample preparation procedures for the UHPLC-MS/MS analyses and were therefore not included in the UHPLC-MS/MS results. The yield and recovery of leucine, isoleucine, and valine (hydrophobic AAs) due to their strong peptide bonds (thus requiring longer hydrolysis time) and, threonine and tyrosine (hydroxyl and sulphur-containing AAs) due to the possible effects of residual oxygen in the hydrolysis vials, may have been affected.

Though the optimized GC-MS and UHPLC-MS/MS analytical methods (protocols) both showed very satisfactory performance (relative standard deviation, RSD, or coefficient of variation, CoV <10%) and the optimal linearity of detection (LoD) from the metabolites based on the metabolome databases and amino acid standards used respectively, the inherent limitations in these analytical procedures and instrumentation cannot also be ruled out completely (Koek, Jellema, van der Greef, Tas, & Hankemeier, 2011; Zarate et al., 2016). However, standard techniques such as data normalization, data validation, and uniform treatments of all the biological samples and their technical replicates during the assays, served as a good basis for confidence in the study results (Fernie et al., 2011).

6 CONCLUSIONS AND RECOMMENDATIONS

6.1 Section Overview

This section of the dissertation presents a highlight of the main study findings and the conclusions drawn from the discussions within the context of the existing body of scientific knowledge. The main inferences drawn from the study results are presented for each of the five research questions. Recommendations have been made for public health nutrition interventions against undernutrition in northern Ghana and similar settings, methodological approaches to the study of child undernutrition in LMICs (or DCs), and further research studies which could be carried out in future.

6.2 Conclusions of the Study

The nutritional status of children in the Northern Region of Ghana has not changed significantly compared to the GDHS 2014 findings. The prevalence of each of the IYCF indicators was relatively higher than the GDHS 2014 findings but did not necessarily translate into improved nutritional status of the children. None of the individual CF-related core IYCF indicators showed a significant association with undernutrition, except intake of iron-rich foods for stunting. The relationships between the individual CF-related IYCF indicators and child nutritional status are context-specific rather than generic across DCs. Child age showed consistent associations with stunting and wasting, thus supporting the need for age-appropriate feeding interventions for young children.

The type of container habitually used for dough storage, the cereal form habitually preferred, and the duration of storage of dough meant for the preparation of complementary meals (HFRUPs) by mothers and/or caregivers were significantly associated with child nutritional status. TCPMs have very large nutritionally significant effects on the nutritive contents of CMIs such as flour and dough, especially on the contents of essential amino acids (lysine and valine), which are considered very important for linear and ponderal growth and development of infants and young children. However, the overall nutritional epidemiological significance of the usage of TCPMs on the nutritional status of children was observed only between dry milling usage versus stunting and dry milling usage versus underweight status. The effect sizes of the associations between the dry milling and child nutritional status were small based on the coefficient of determination ($R^2 < 0.3$)

Notwithstanding the limitations inherent in the multitude and mix of approaches used for measuring directly or by proxy, the rather complex exposure variable of interest (food and/or nutrient intake) in nutritional epidemiological research (NER) studies, the methodological approach used in this observational study has generated a preliminary but worthwhile hypothesis, that warrants external validation studies and further research. The exploration of various measures (indicators) of two conceivable domains or constructs (HFRUP and TCPM indicators) of the food utilization dimension of household food insecurity (HFI), as potential determinants of child undernutrition was insightful.

6.2.1 Prevalence of IYCF, HFRUP, TCPM Indicators, and Child Undernutrition

The prevalence of the IYCF indicators TICF, MMF, MDD, MAD, Vit A intake, Fe intake, EBF, TIBF and CBF@1 of children (6-23 months) in the Northern Region of Ghana were 66.4%, 69.4%, 50.6%, 38.9%, 58%, 63.3%, 83%, 63.3% and 97.3% respectively.

Of the mothers interviewed, 48.8% indicated that they fed their children predominantly with cereal-only-based complementary meals. Majority of the mothers (76%) habitually preferred to feed their children with complementary meals made from dough (wet-milled cereals) compared to flour (dry-milled cereals). Of all the mothers interviewed, 39.6% preferred the naturally fermented dough form of CMIs compared to fresh dough and flour cereal form. Maize was the most preferred cereal (74.5%) for the production of complementary meal ingredients (CMIs) at home in the Northern Region of Ghana. Majority of the mothers surveyed (63.3%), habitually preferred to feed their children with dough which has been stored under ambient household storage conditions (non-refrigerated or non-frozen) for three days or less. However, only 8.3% of them still used dough stored under ambient household storage conditions (non-refrigerated or non-frozen) for more than seven days, to prepare complementary meals for their children. Plastic containers were the commonest storage vessels used for keeping dough (wet-milled cereals) under ambient household storage conditions (non-refrigerated or non-frozen). Of the mothers surveyed during the cross-sectional study, 67.6% of them habitually (always or very often) made the CMIs for their children at home. Only 6.5% of them sourced already-made CMIs or weaning food ingredients (WFIs), or commercial infant cereals (CICs) outside their homes to prepare meals for their infants and young children.

Of the mothers interviewed during the study, majority of them (85.8%) used whole cereal grains in the preparation of CMIs for their children due to reduced yield after milling, if they used dehulled cereal grains instead. Majority of the mothers (95.7%) indicated that they produced their flour (sun-dried and dry-milled cereals) by patronizing the local plate attrition milling services (Nikanika) in their communities. The rest either purchased already-made flour (imported or commercially produced in Ghana), or they used the laborious mortar-pestle method of pounding or stone milling of cereal grains into flour. Majority of the mothers (67.7%) indicated that they habitually soaked their cereal grains in potable water for a maximum of 24 hours before wet milling during the production of fresh or fermented dough at home. Majority of the mothers interviewed (92.3%) during the cross-sectional survey indicated that after wet milling their cereal grains, the fresh dough usually begun to spontaneously ferment within 12 hours under ambient household storage conditions (non-refrigerated or non-frozen).

The prevalence of stunting, wasting, and underweight status of children (6-23 months) in the Northern Region of Ghana was 33.2%, 14.1% and 27% respectively.

6.2.2 Association between IYCF Indicators and Child Undernutrition

In the bivariate analysis, intake of Vitamin A-rich foods (Vit A), MDD and MAD were significantly associated with chronic undernutrition (stunting) at $p<0.05$ whiles intake of iron-rich foods (Fe) was significantly associated with chronic undernutrition (stunting) at $p<0.10$. None of the individual CF-related IYCF indicators (TICF, MMF, MDD, MAD, Vitamin A intake) showed a significant association with undernutrition (stunting and wasting) in the multivariable regression analyses, after adjusting for potential confounders, except intake of iron-rich foods (Fe intake) for child stunting status. None of the IYCF indicators was significantly associated with acute undernutrition (wasting) in the bivariate and multivariable regression analyses conducted.

6.2.3 Association between HFRUP Indicators and Child Undernutrition

The type of container habitually used for dough storage (plastic, metal, or calabash/jute sack) was significantly associated with child stunting status at $p<0.05$, after adjusting for the putative proximal risk factors. The cereal form habitually preferred (fermented dough, fresh dough, or flour) and the duration of storage of dough (3 days or less, 4-7 days, or more than 7 days) meant for the preparation of complementary meals, were significantly associated with child wasting status at $p<0.05$ and $p<0.10$, respectively, after adjusting for the putative risk factors of child undernutrition.

6.2.4 Effects of TCPMs on Nutritive and Non-Nutritive Constituents of Cereals

The TCPMs effected nutritionally significant changes to the relative quanties of untargeted physiologically free nutritive and non-nutritive metabolites in the three cereals (maize, sorghum and milled) examined from the foodomics (food metabolomics) laboratory analyses. Additionally, the TCPMs effected nutritionally debilitative changes (≥10% net loss) in the absolute concentrations (nmol/mL) of some of the essential amino acids (EAAs) in the three cereal samples examined. An analysis of the variance (ANOVA) of the net changes in the absolute concentrations of lysine (limiting esential amino acid, LEAA) due to the TCPM effects on the maize grain samples, were nutritionally debilitative (≥10% net loss in EAAs) and found to be statistically significant at $P< 0.001$. Given the biological relevance of any deficiency in even a single essential nutrient on the physiological state and/or metabolic processes that underpin the health status of infants and young children, such nutritionally debilitative changes in the main source of LEAAs could be critical.

6.2.5 Association between TCPM Indicators and Stunting, Wasting, and Underweight

The overall nutritional epidemiological significance of the usage of TCPMs on the nutritional status of children in the Northern Region of Ghana was observed only between dry milling usage versus stunting and dry milling usage versus underweight status. The effect size of the significant associations between dry milling and undernutrition (stunting and underweight status) were considered to be small (R^2=0.007 and 0.008 respectively) but are potentially significant in terms of the biological relevance of the loss of lysine.

6.3 Recommendations of the Study

6.3.1 Recommended Public Health Interventions: Undernutrition in Northern Ghana

Stunting is reflective of chronic undernutrition, and thus the risk factors identified in this study informed the suggested interventions accordingly. The evidence that consumption of iron-rich foods makes a difference to stunting gives an indication of the need for some micronutrients for optimal protein energy balance. Nutritional interventions that improve the intake of iron-rich foods could serve the dual purpose of reducing both child stunting and anaemia. Increasing dietary diversity is a potentially viable approach to reduce the burden of stunting amongst young children, given that dietary diversity scores are widely acceptable predictors of the adequacy of micronutrient intake (Kennedy et al., 2007; Mallard et al., 2016; Zhao et al., 2017).

While further prospective studies are needed to determine the effects of feeding practices on linear growth, food-based interventions (including diversifying food production, dietary supplementation of animal source proteins, micronutrient supplementation, dietary diversification, and biofortification) have great potential to ensure food and nutrition security, combat micronutrient deficiencies, improve dietary quality, and raise the levels of nutrition, especially for children under five years of age (Brian and Amoroso, 2014). In addition, communication programmes promoting livelihood and social behaviour change that support the increased production and consumption of nutrient-rich foods (such as green leafy vegetables, fruits, and animal source proteins) are needed to bring about positive behavioural changes relating to child food intake. Furthermore, interventions that address dietary diversity, such as unconditional cash transfers and the community-based promotion of improved infant and young child feeding practices, should be pursued, together with public health efforts to reduce the burden of infectious diseases, such as seasonal malaria chemoprevention and usage of insecticide-treated nets (ITNs).

Strong advocacy by local, national, and international stakeholders who are engaged in sustainable human capital development in developing nations is recommended to improve children's diets during the first two years of life, as a priority area. The Government of Ghana needs to ensure that the country's Food and Nutrition Security policies are locally relevant and factually appropriate but aligned with internationally validated recommendations in order to protect, promote, and support age-appropriate complementary feeding practices for infants and young children. The government and its development partners, including health-related NGOs, need to better coordinate efforts in order to implement multisectoral, large-scale, evidence-based programmes for the promotion and support of improved complementary feeding for children aged 6–23 months. Just as focused food security and livelihood interventions implemented recently by the Government of Ghana such as planting for food and jobs, one district one factory, one village one dam, et cetera have shown tremendous positively facilitative improvements in the livelihoods and food security situation of various resource-limited communities across the country, adoption of a 'one child, one egg' policy for children under five years in the Northern Region of Ghana could significantly contribute to improving dietary diversity and potentially the nutritional status of young children.

Because wasting is reflective of acute undernutrition, it requires situational interventions. Nutrition-sensitive interventions, such as child vaccination programmes and recommended water, sanitation, and hygiene (WASH) practices to reduce the burden of infectious diseases, policies and programmes targeted at improving agriculture and food security (the availability and/or supply of food, purchasing power and optimal utilisation of limited food resources) in households, should be implemented and scaled up. These could more sustainably address the limitations inherent in the overreliance on food donation and micronutrient supplementation programmes in northern Ghana to address the undesirable trend of acute child nutritional status.

Nutrition-sensitive interventions, such a behaviour change communication (BCC) and nutrition education (NE) targeted at improving nutrition-specific IYCF practices, should be carried out. Feeding and caregiving aimed especially at male children to minimise morbidity, and nutrition education targeted at dietary diversification to improve the intake of nutrient-rich meals, should be adopted, and scaled up especially during periods of food shortages or famine. The timing of such interventions should coincide with the period of highest food insecurity and highest vulnerability to infectious diseases, which is usually at the onset of the major planting season (May–August). Given that lysine is a limiting essential amino acid in the staple cereals in northern Ghana, fortification of both homemade and industrially processed CMIs with lysine should be implemented and scaled up as being explored and advocated by Suri *et al.* (2014) and Gosh *et al*. (2019)

6.3.2 Recommendations for Methodological Approach: Undernutrition Studies

IYCF practices, TCPMs, and HFRUPs are conceivably complex constructs (phenomenon) or concepts because of their multidimensionality (Law, Wong, & Mobley, 1998). Given the novelty of TCPM and HFRUPs as constructs of food utilization, there was a lack of study precedence and thus no validated survey instrument available with suitable indicators (or measures) adaptable for this study. The operationalization of TCPM and HFRUP for the purposes of nutritional epidemiological research studies in the future would require a battery of questions (multi-item questionnaire scale revision and re-development) in order to possibly capture comprehensively, the entire scope of latent variables and other underlying concepts. The operationalization of the TCPM and HFRUP concepts (constructs) appears to have been oversimplified in this study. It is recommended that multidimensional measures (or indicators) be explored in place of the unidimensional measures or indicators. Principal component analysis (PCA) and exploratory factor analysis (EFA) as dimension reduction statistical techniques should be applied during the re-development of the TCPM and HFRUP sub-scales (multi-question question items and/or indicators) of the composite interviewer-adminstered survey questionnaire (Alavi et al., 2020). There is the need therefore for further methodological exploration of these concepts (constructs) for optimal operationalization and measurement of the latent and observable variables of the various underlying domains of food utilization at the household level. These could be further developed for adoption at the global level by FAO for instance to improve reporting on the food utilization dimension of household food insecurity in its flagship global report updates (state of the world's food insecurity, SOFI).

The validity, reliability, and comparability of evidence-based public health nutrition interventions developed from these concepts (constructs) of the various domains of the food utilization dimension and IYCF practices as explanatory variables, would depend on universally standardized formulars and nomalization methods in NER studies. A case in hand is the lack of a universally adopted formular for the computation of a composite index for child food intake from the individual

IYCF indicators. This would help make up for the inconsistencies replete in the NER literature, of the predictive utility of the individual WHO/UNICEF-recommended IYCF practice indicators for child nutritional status in DCs. There is the need to develop a universally applicable composite child food intake (CCFI) index from the core WHO-UNICEF IYCF indicators. This could then be used to compare the results of child feeding practices in relation to undernutrition across developing and emerging countries, for the purposes of monitoring and evaluating progress, and identifying populations at risk of undernutrition, irrespective of the different population contexts. Standardizing the formula for CCFIs universally would also prove useful for comparability purposes given the varieties of scoring formulars being used currently by different researchers for these computations (Chowdhury et al., 2016; Reinbott et al., 2015).

Identification of the contextually relevant idiosyncrasies and unique nuances of various study settings have been advocated by various researchers (Armar-Klemesu et al., 2018; Ham, 2020). There is the need to undertake comprehensive formative research prior to the conceptualization and operationalization of potentially novel explanatory variables of interest in any nutritional epidemiological research (NER) study, especially in a pluralistic setting such as the northern regions of Ghana, where cultural diversity is starkly expressed in the food preferences and indigenous gastronomy of various segments of the northern Ghanaian society (Ham, 2020). Identification of contextually facilitative and debilitative factors relevant to child nutritional health outcomes through formative research, may prove to be a better epistemological approach to complement the conventional approaches to the conduct of nutritional epidemiological studies in the Northern Region of Ghana and other similar settings in DCs (Armar-Klemesu et al., 2018; Pelto et al., 2013). The impact of nutrition interventions premised only on predominantly increasing the quantity of food (such as the Feed the Future, FTF programme) with little or no attention paid to the potentially debilitative factors of food quality (due to some TCPMs and HFRUPs), may partly account for the marginal improvements in nutritional health outcomes (or nutritional status) of children in the northern regions of Ghana (Ham, 2020).

6.3.3 Recommendations for Further NER Studies

The preliminary hypothesis (postulate) generated from this study requires further research with more robust study designs in other similar resource-limited study settings (DCs and LMICs), to validate its generalizability. It is recommended therefore that an iterative approach be adopted to experimentally test this preliminary postulate by harnessing a synergy between the strengths of food metabolomics and the more robust nutritional epidemiological study designs especially longitudinal study designs to account for potential time-variant confounders, if any (Stein, 1995).

The influence of child gender, maternal height, and dough storage conditions on child undernutrition remains poorly understood and warrants further research. Alongside the conventionally known and widely researched determinants of undernutrition in developing countries (DCs), other potentially novel risk factors of undernutrition should also be investigated to ascertain their possible associations with the nutritional health outcomes of children in northern Ghana and other similar settings in DCs (Hotz & Gibson, 2007; Weerasooriya, Bean, Nugusu, Ioerger, & Tesso, 2018). Such other potential determinants of undernutrition in northern Ghana incude mycotoxin exposure and epigenetic factors that need to be further researched to help fill the huge knowledge gap (or lacuna) that currently exists with regards to the aetiology and/or pathogenesis of undernutrition in the Northern Region of Ghana and other similar settings in DCs and LMICs (Bautista-García, González-López, Esparza, & Castillo-Rosas, 2017; Greco, Lenzi, Migliaccio, & Gessani, 2019). The influence of cultural beliefs and practices, and food preferences relating to child feeding and caregiving as potential risk factors for undernutrition, could also be explored.

The advocacy for cereal-legume-based blends (CLBBs) may also come along with some drawbacks such as potentially increased exposure to mycotoxins. Mycotoxin exposure as a potential risk factor for child growth impairment has been under investigation in some DCs for the last decade and should also be researched further in the northern regions of Ghana (Chen et al., 2018; Gong et al., 2016; Shirima et al., 2013; Wild & Gong, 2010; Wu et al., 2014). These other potential risk factors of child nutritional status can then be adjusted or accounted for, to fully evaluate the magnitude and significance of the variance in child nutritional status contributed by TCPMs and HFRUPs.

It is recommended that further studies be conducted on the effects of other traditional (or household) and industrial cereal processing methods (such as roasting, nixtamalization, and kneading) on the nutritive and anti-nutritive constituents of the various types/cultivars of cereals, and forms of cereals (flour, fresh dough, fermented dough et cetera). This could be conducted with different analytical research methods to ascertain if the compositional and nutritional changes observed in this study are generic or otherwise specific, given the wide range of findings (facilitative and debilitative) reported in the NER literature (Gwirtz & Garcia-Casal, 2014).

Studies on the optimal combination of the various possible regimes of TCPM application to maximize the potential benefits of the nutritive and non-nutritive constituents (ANFs and healthful phytochemicals) in cereals, legumes, and other ingredients for CMI production are lacking (Hotz & Gibson, 2007). Optimization studies on the application of various TCPMs for the production of CMIs in resource-constrained settings (DCs) are needed similar to studies conducted by Min *et al* (2020) for the optimization of soaking and temperature regimes for the production of the eco-friendly and protein-rich soy foods in the Republic of Korea. Linear programming analyses (LPA) could then be implemented, incorporating the findings to account for the drawbacks of sub-optimal TCPMs such as dry milling in the formulation and development of optimal, context-specific, pragmatic, and easily transferable household cereal processing technologies to mothers and care givers of infants and young children, for the production of homemade CMIs that meet the minimum RNIs (Jager et al., 2019; Ryan et al., 2014; Suri et al., 2014; Suri & Tanumihardjo, 2016).

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8 APPENDIX

8.1 Appendix A: Supplementary Tables and Figures

Table 8.1 Socio-demographic and Household Characteristics of Study Participants (N=581)

Sociodemographic Characteristics	Frequency (n)	%
Communal Characteristics		
District		
Tamale	118	20.3
Karaga	125	21.5
Nanumba North	116	20.0
Tolon-Kumbungu	118	20.3
Central Gonja	104	17.9
Religion		
Islam	524	90.2
Christianity	36	6.2
Traditional African Religion (ATR)	21	3.6
Ethnicity		
Gonja	63	10.8
Dagomba	396	68.2
Nanumba	48	8.3
Kokomba	52	9.0
Others	22	3.8
Residence/Community Type		
Rural	421	72.5
Semi-rural	142	24.4
Urban	18	3.1
Household Characteristics		
Type of Toilet Used		
Improved	76	13.1
Not Improved	505	86.9
Main Source of Drinking Water		
Improved	303	52.2
Not Improved	278	47.8
Main Source of Power for Lighting		
Electricity	529	91
Others (Kerosene Lamp. Etc.)	52	9
Fuel Used for Cooking		
Modern (Electricity. LPG)	5	0.9
Others (Charcoal. Firewood)	576	99.1
Household Wealth Index (HWI) or Socio-Economic Status (SES)		
Low wealth (Poor)	232	39.9
Medium wealth (Average)	234	40.3
High wealth (Rich)	115	19.8
Number of People Living in the Household		
1-5 people	104	17.9
6-10 people	260	44.8
11 or more people	217	37.3
Number of Rooms per Household		
4 or Less	275	47.3
5-8	237	40.8
9 or More	69	11.9
Number of People per Room		
3 or Less	502	86.4
4 or more people	79	13.6

Table 8.2: Bivariate analysis of the association between factors/covariates and Stunting

Factors		Nutritional Status (n)%		Total (N)%	Test Statistic	
		Normal	Stunted			
District of Residence	Tamale	(79) 66.9	(39) 33.1	(118) 100.0	χ^2 = 31.874	*P*< 0.001
	Tolon	(72) 61.0	(46) 39.0	(118) 100.0		
	Gonja Central	(75) 72.1	(29) 27.9	(104) 100.0		
	Nanumba North	(98) 84.5	(18) 15.5	(116) 100.0		
	Karaga	(65) 52.0	(60) 48.0	(125) 100.0		
Maternal Age (Years)	15-24	(107) 78.7	(29) 21.3	(136) 100.0	χ^2 = 12.089	*P*= 0.002
	25-34	(208) 64.8	(113) 35.2	(321) 100.0		
	35-50	(74) 59.7	(50) 40.3	(124)100.0		
Religion	Islam	(340) 64.9	(184)35.1	(524) 100.0	χ^2 = 10.325	*P*= 0.006
	Christianity	(31) 86.1	(5) 13.9	(36) 100.0		
	ATR	(18) 67.0	(3) 14.3	(21) 100.0		
Tribe	Gonja	(49) 77.8	(14) 22.2	(63) 100.0	χ^2 = 25.343	*P*< 0.001
	Dagomba	(239) 60.4	(157) 39.6	(396) 100.0		
	Nanumba	(40) 83.3	(8) 16.7	(48) 100.0		
	Komkoba	(44) 84.6	(8) 15.4	(52) 100.0		
	Others	(17) 77.3	(5) 22.7	(22) 100.0		
Child Age (Months)	6-11	(203) 83.9	(39) 16.1	(242) 100.0	χ^2 = 62.131	*P*< 0.001
	12-17	(114) 61.6	(71) 38.4	(185) 100.0		
	18-23	(72) 46.8	(82) 53.2	(154) 100.0		
Maternal Height (cm)	≥160 cm	(204) 72.3	(78) 27.7	(282) 100.0	χ^2 = 7.187	*P*= 0.007
	Below 160cm	(185) 61.9	(114) 38.1	(299) 100.0		
PNC	< 4 Times	(82) 77.4	(24) 22.6	(106) 100.0	χ^2 = 6.344	*P*= 0.012
	≥ 4 Times	(307) 64.6	(168) 35.4	(475) 100.0		
ITN	No	(35) 55.6	(28) 44.4	(63) 100.0	χ^2 = 4.149	*P*= 0.042
	Yes	(354) 68.3	(164) 31.7	(518)100.0		
Number of Occupants Per Household	**7 people or less**	(153) 71.8	(60) 28.2	(213) 100.0	χ^2 = 3.616	*P*= 0.057**
	> 7 people	(236) 64.1	(132) 35.9	(368) 100.0		

Significance at **p<0.10 and p<0.05

Table 8.3 Bivariate analysis of the Association between IYCF indicators and Wasting

IYCF Indicators		Nutritional Status (n)%		Total (N)%	Test Statistic	
		Not Wasted	Wasted			
TICF	No	(167)28.74	(28)4.82	(195)33.56	χ^2 = 0.015	*P*= 0.904
	Yes	(332)57.14	(54)9.29	(386)66.44		
MMF	No	(156)26.85	(22)3.79	(178)30.64	χ^2 = 0.651	*P*= 0.420
	Yes	(343)59.04	(60)10.33	(403)69.36		
MDD	<4 foods	(246)42.34	(41)7.06	(287)49.40	χ^2 = 0.014	*P*= 0.906
	≥ 4 foods	(253)43.55	(41)7.06	(294)50.60		
MAD	No	(309)53.18	(46)7.92	(355)61.10	χ^2 = 1.006	*P*= 0.316
	Yes	(190)32.70	(36)6.20	(226)38.90		
ACF	No	(362)62.31	(55)9.47	(417)71.77	χ^2 = 1.041	*P*= 0.308
	Yes	(137)23.58	(27)4.65	(164)28.23		
Fe Intake	No	(188)32.36	(26)4.48	(214)36.83	χ^2 = 1.078	*P*= 0.299
	Yes	(311)53.53	(56)9.64	(367)63.17		
Vitamin A	No Intake	(211)36.32	(33)5.70	(244)42.00	χ^2 = 0.167	*P*= 0.920
	Low intake	(278)47.85	(47)8.09	(325)55.94		
	High intake	(10)1.72	(2)0.34	(12)2.07		

Significance at p<0.10 and p<0.05

Table 8.4 Bivariate analysis of the association between factors/covariates and wasting

Factors		Nutritional Status (n)%		Total (N)%	Test Statistic	
		Normal	Wasted			
Religion	Islam	(459) 87.6	(65) 12.4	(524) 100.0	χ^2 = 17.529	P< 0.001**
	Christianity					
	ATR					
Marital Status	Single	(11)68.8	(5) 31.3	(16) 100.0	χ^2 = 3.986	P= 0.046**
	Married	(488) 86.4	(77) 13.6	(565) 100.0		
Tribe	Gonja	(57) 90.5	(6) 9.5	(63) 100.0	χ^2 = 15.996	P= 0.003**
	Dagomba	(341) 86.1	(55) 13.9	(396) 100.0		
	Nanumba	(44) 91.7	(4) 8.3	(48) 100.0		
	Komkoba	(36) 69.2	(16) 30.8	(52) 100.0		
	Others	(21) 95.5	(1) 4.5	(22) 100.0		
Gender	Female	(255) 91.1	(25) 8.9	(280) 100.0	χ^2 = 11.987	P= 0.001**
	Male	(244) 81.1	(57) 18.9	(301) 100		
Child Age (Months)	6-11	(214) 88.4	(28) 11.6	(242)	χ^2 = 15.265	P= 0.001**
	12-17	(144) 77.8	(41) 22.2	(185) 100.0		
	18-23	(141) 91.6	(13) 8.4	(154) 100.0		
Maternal BMI	Underweight	(53) 76.8	(16) 23.2	(69) 100.0	χ^2 = 9.336	P= 0.025**
	Normal	(359) 86.1	(58) 13.9	(417) 100.0		
	Overweight	(61) 88.4	(8) 11.6	(69) 100.0		
	Obese	(26) 100.0	(0) 0.0	(26) 100.0		
Utility Power Source for Lighting	Non-Electricity	(37) 71.2	(15) 28.8	(52) 100.0	χ^2 = 10.226	P= 0.001**
	Electricity	(462) 87.3	(67) 12.7	(529) 100.0		
Child Morbidity (recent 2 weeks)	No	(322) 88.0	(44) 12.0	(366) 100.0	χ^2 = 3.570	P= 0.059*
	Yes	(177) 82.3	(38) 17.7	(215) 100.0		
Child Morbidity (Diarrhoea frequency in last 6 months)	None	(163) 87.6	(23) 12.4	(186) 100.0	χ^2 = 6.272	P= 0.099*
	Only once	(171) 87.2	(25) 12.8	(196) 100.0		
	2-3 times	(146) 84.9	(26) 15.1	(172) 100.0		
	Every month	(19) 70.4	(8) 29.6	(27) 100.0		
Child Immunization Status	Not Up to Date	(171) 82.2	(37) 17.8	(208) 100.0	χ^2 = 3.610	P= 0.057*
	Up to Date	(328) 87.9	(45) 12.1	(373) 100.0		
PNC	< 4 Times	(85) 80.2	(21) 19.8	(106) 100.0	χ^2 = 3.472	P= 0.062*
	≥ 4 Times	(414) 87.2	(61) 12.8	(475) 100.0		
Consumption of Cereal-Only-Based Meals	Yes. Always	(119) 86.9	(18) 13.1	(137) 100.0	χ^2 = 6.519	P= 0.089*
	Yes. Very Often	(116) 89.9	(13) 10.1	(129) 100.0		
	Yes. Sometimes	(151) 80.7	(36) 19.3	(187) 100.0		
	No	(113) 88.3	(15) 11.7	(128) 100.0		

Significance at $^{*}p<0.10$ and $^{**}p<0.05$ ATR-African Traditional Religion BMI-Body Mass Index

Table 8.5 Bivariate analysis of the association between HFRUP Indicators and Stunting

		Nutritional Status			Test Statistic	
HFRUP Indicator	**Response**	**Normal**	**Stunted**	**Total (N)%**	**$\chi 2$**	***P* value**
Intake of Cereal-Only-Meal	Yes, always	95 (69.3)	42(30.7)	137(100)	3.184	P=0.364
	Yes, very often	78(60.5)	51(39.5)	129(100)		
	Yes sometimes/occasionally	128 (68.4)	59(31.6)	187(100)		
	No	88(68.8)	40(31.3)	128(100)		
Cereal Form Preffered	Fermented Dough	161(70.0)	69(30.0)	230(100)	6.244	P=0.044
	Fresh Dough	147(69.3)	65(30.7)	212(100)		
	Flour	81(58.3)	58(41.7)	139(100)		
Cereal Type (Maize)	Yes, Always/Very Often	284(65.6)	149(34.4)	433(100)	2.207	p=0.332
	Yes, Occasionally	83(72.8)	31(27.2)	114(100)		
	No	22(64.7)	12(35.3)	34(100)		
Cereal Type (Sorghum)	Yes, Always/Very Often	48(53.9)	41(46.1)	89(100)	10.965	p=0.004
	Yes, Occasionally	89(63.6)	51(36.4)	140(100)		
	No	252(71.6)	100(28.4)	352(100)		
Cereal Type (Millet)	Yes, Always/Very Often	49(49.0)	51(51.0)	100(100)	18.951	p< 0.001
	Yes, Occasionally	148(73.6)	53(26.4)	201(100)		
	No	192(68.6)	88(31.4)	280(100)		
Storage Duration (Dough)	3 Days or Less	251(68.2)	117(31.8)	368(100)	1.345	p=0.719
	4-7 Days	105(63.6)	60(36.4)	165(100)		
	More than 7 Days	30(69.8)	13(30.2)	43(100)		
Storage Container (Dough)	Calabash-Jute Sacs	8(72.7)	3(27.3)	11(100)	3.564	p=0.168
	Metal Containers	55(76.4)	17(23.6)	72(100)		
	Plastic Containers	326(65.5)	172(34.5)	498(100)		
Dough Source (Home-made)	Yes, always	170(64.4)	94(35.6)	264(100)	6.348	p=0.096
	Yes, very often	80(62.0)	49(38.0)	129(100)		
	Yes sometimes/occasionally	111(74.0)	39(26.0)	150(100)		
	No	28(73.7)	10(26.3)	38(100)		

Table 8.6 Bivariate analysis of the association between HFRUP Indicators and Wasting

		Nutritional Status			Test Statistic	
HFRUP Indicator	**Response**	**Normal**	**Wasted**	**Total (N)%**	$\chi 2$	***P* value**
Intake of Cereal-Only-Meal	Yes, always	119(86.9)	18(13.1)	137(100)	6.519	P=0.089
	Yes, very often	116(89.9)	13(10.1)	129(100)		
	Yes sometimes/occasionally	151(80.7)	36(19.3)	187(100)		
	No	113(88.3)	15(11.7)	128(100)		
Cereal Form Preferred	Fermented Dough	189(82.2)	41(17.8)	230(100)	4.634	P=0.099
	Fresh Dough	189(89.2)	23(10.3)	212(100)		
	Flour	121(87.1)	18(12.9)	139(100)		
Cereal Type (Maize)	Yes, Always/Very Often	378(87.3)	55(12.7)	433(100)	2.807	p=0.246
	Yes, Occasionally	93(81.6)	21(18.4)	114(100)		
	No	28(82.4)	6(17.6)	34(100)		
Cereal Type (Sorghum)	Yes, Always/Very Often	82(92.1)	7(7.9)	89(100)	3.395	p=0.183
	Yes, Occasionally	119(85.0)	21(15.0)	140(100)		
	No	298(84.7)	54(15.3)	352(100)		
Cereal Type (Millet)	Yes, Always/Very Often	88(88.0)	12(12)	100(100)	2.035	p= 0.362
	Yes, Occasionally	167(83.1)	34(16.9)	201(100)		
	No	244(87.1)	36(12.9)	280(100)		
Storage Duration (Dough)	3 Days or Less	306(83.2)	62(16.8)	368(100)	7.570	p=0.023
	4-7 Days	152(92.1)	13(7.9)	165(100)		
	More than 7 Days	41(85.4)	7(14.6)	48(100)		
Storage Container (Dough)	Calabash-Jute Sacs	9(81.8)	2(18.2)	11(100)	0.313	p=0.855
	Metal Containers	63(87.5)	9(12.5)	72(100)		
	Plastic Containers	427(85.7)	71(14.3)	498(100)		
Dough Source (Home-made)	Yes, always	228(86.4)	36(13.6)	264(100)	4.377	p=0.224
	Yes, very often	116(89.9)	13(10.1)	129(100)		
	Yes sometimes/occasionally	122(81.3)	28(18.7)	150(100)		
	No	33(86.8)	5(13.2)	38(100)		

Table 8.7 : Bivariate analysis of the association between TCPM Indicators and Stunting

					95% CI for B		Test Statistic	
TCPM Indicator	**Response**	**R^2**	**R^2 Adj**	**B**	**Lower Bound**	**Upper Bound**	**F-Statistic**	***P*-value**
Dehulling	Yes, always			.30	-.12	.72	F (3, 577) =0.83	0.478
	Yes, very often			.01	-.73	.72		
	Yes, sometimes/ occasionally			.15	-.14	.45		
	No	.004	-.001	-1.38	-1.55	-1.21		
Soaking	≤ 6 hours/ Quarter day			-.18	-.72	.35	F (4, 576) =1.52	0.195
	12 hours/ Half Day			.08	-.46	.62		
	> 12 hours up to 24 hours			.25	-.24	.73		
	>24 hours up to 48 hours/2 Days			-.06	-.57	.45		
	> 48 hours	.010	.004	-1.36	-1.79	-.92		
Dry-Milling	Other milling methods & purchased imported flour			-.53	-1.14	0.09	F (1, 579) =6.45	0.011
	Commercial attrition Mill (Nikanika)	.011	.009	-.81	-1.44	-0.18		
Wet-Milling cum Spontaneous Fermentation	≤ 6 hours/ Quarter day			.19	-.80	1.18	F (4, 576) =0.70	0.595
	12 hours/Half Day			.40	-.60	1.41		
	>12 hours up to 24 hours			.06	-1.16	1.28		
	> 24 hours up to 48 hours/2 Days			.32	-.92	1.55		
	> 48 hours	.005	-.002	-1.55	-2.53	-.58		

CI, Confidence Interval; **LAZ**, Length-to-Age Z-Score; **R^2**, Coefficient of Determination; **R^2 Adj**, adjusted R squared; **B**, Unstandardized Coefficient;

Table 8.8 : Bivariate analysis of the association between TCPM Indicators and Underweight

					95% CI for B		Test Statistic	
TCPM Indicator	**Response**	**R^2**	**R^2 Adj**	**B**	**Lower Bound**	**Upper Bound**	**F-Statistic**	***P*-value**
Dehulling	Yes, always			.39	.07	.70	F(3, 577) = 2.08	0.102
	Yes, very often			.19	-.35	.73		
	Yes, sometimes/ occasionally			.11	-.11	.33		
	No	.011	.006	-1.35	-1.47	-1.22		
Soaking	≤ 6 hours/ Quarter day			-.15	-.55	.25	F(4, 576) = 2.31	0.057
	12 hours/ Half Day			.03	-.38	.43		
	> 12 hours up to 24 hours			.25	-.18	.61		
	>24 hours up to 48 hours/2 Days			-.03	-.41	.35		
	> 48 hours	.016	.009	-1.33	-1.65	-1.00		
Dry-Milling	Other milling methods & purchased imported flour			-.55	-1.02	-.28	F(1, 579) = 5.34	0.021
	Commercial Attrition Mill (Nikanika)	.009	.007	-.74	-1.20	-.28		
Wet-Milling cum Spontaneous Fermentation	≤ 6 hours/ Quarter day			-.17	-.90	.57	F(4, 576) = 2.06	0.085
	12 hours/Half Day			.11	-.64	.85		
	>12 hours up to 24 hours			.21	-.69	1.12		
	> 24 hours up to 48 hours/2 Days			-.31	-1.23	.60		
	> 48 hours	.014	.007	-1.19	-1.92	-.47		

CI, Confidence Interval; **WAZ**, Weight-to-Age Z-Score; **R^2**, Coefficient of Determination; **R^2 Adj**, adjusted R squared; **B**, Unstandardized Coefficient

Table 8.9: Mean concentration (nmol/mL) of Total Free Amino Acids in Acid-Hydrolysed Maize Samples due to TCPM Effects

TCPM Cereal Sample	Methionine	Lysine	Threonine	Isoleucine	Phenylalanine	Leucine	Valine	Histidine	Tyrosine**	Arginine**
Maize_Grain (**Reference**)	280.53	13675.98	603.02	10372.19	1801.72	8336.36	567465.35	5226.98	792.15	2260.38
Maize_Germinated	228.11	11100.49	564.00	8941.67	1987.76	7937.52	253821.31	8084.55	882.51	2148.50
Maize_Soaked	1594.05	5446.41	647.84	12441.61	1906.62	9019.38	232480.75	4177.41	702.70	2642.68
Maize_Dry-Milled (Flour)	902.80	5683.85	665.56	7953.08	2244.82	8037.32	137942.84	1889.25	1193.55	2928.54
Maize_Dough (Fresh)	1114.13	4029.82	992.63	4428.81	3347.80	7122.73	111772.21	4231.37	1846.92	3025.34
Maize_Dough (Fermented)	1036.45	5371.45	664.60	10228.16	2230.56	8839.41	174413.26	4407.22	1156.56	2348.12

EAAs- Essential Amino Acids; ****CEAAs-** Conditionally Essential Amino Acids; **LC-MS-** Liquid Chromatography-Mass Spectrometry
TCPM- Traditional Cereal Processing Methods; *Nutritionally Significant TCPM Effects (-2SD or ≥ 10% net loss in the nutritional metabolite from the LC-MS Analysis

Table 8.10 Mean concentration (nmol/mL) of Total Amino Acids in Acid-Hydrolysed Sorghum Samples due to TCPM Effects

TCPM Cereal Sample	Methionine	Lysine	Threonine	Isoleucine	Phenylalanine	Leucine	Valine	Histidine	Tyrosine**	Arginine**
Sorghum_Grain **(Reference)**	324.70	6051.05	511.95	9554.93	1158.30	6650.49	301334.58	3843.11	743.78	1917.61
Sorghum_Germinated	696.75	5587.99	573.55	15592.90	1769.37	9368.02	281492.38	3395.17	743.85	2149.08
Sorghum_Soaked	2657.07	14340.10	1337.66	15966.45	3282.56	13712.69	412226.08	8045.50	1552.95	4376.95
Sorghum_Dry-Milled (Flour)	1068.40	11695.52	837.18	12001.45	2377.37	10213.37	388490.04	7926.79	1253.04	3283.70
Sorghum_Dough	595.61	10970.17	637.88	14327.62	2376.70	10906.13	585209.15	5624.01	1024.61	2476.72

EAAs- Essential Amino Acids; ****CEAAs-** Conditionally Essential Amino Acids; **LC-MS-** Liquid Chromatography-Mass Spectrometry
TCPM- Traditional Cereal Processing Methods; *Nutritionally Significant TCPM Effects (-2SD or ≥ 10% net loss in the nutritional metabolite from the LC-MS Analysis

Table 8.11 Mean Concentration (nmol/mL) of Total Amino Acids in Acid-Hydrolysed Millet Samples due to TCPM Effects

TCPM Cereal Sample	Methionine	Lysine	Threonine	Isoleucine	Phenylalanine	Leucine	Valine	Histidine	Tyrosine**	Arginine**
Millet_Grain **(Reference)**	1892.45	9073.52	1107.49	11122.10	2814.83	9134.99	236870.35	4302.71	1411.79	3416.33
Millet_Germinated	2025.86	11515.54	893.77	12664.24	2067.07	8152.90	345426.75	5816.34	886.61	3435.12
Millet_Soaked	1527.47	7604.45	977.05	18540.52	2101.10	9908.65	649962.08	1908.84	1070.52	3392.62
Millet_Dough	578.92	16502.70	907.50	15943.56	2281.04	9679.99	684593.48	8357.12	946.12	2877.51

EAAs- Essential Amino Acids; ****CEAAs-** Conditionally Essential Amino Acids; **LC-MS-** Liquid Chromatography-Mass Spectrometry
TCPM- Traditional Cereal Processing Methods; *Nutritionally Significant TCPM Effects (-2SD or ≥ 10% net loss in the nutritional metabolite from the LC-MS Analysis

Table 8.12 ANOVA and Dunnett's Post-Hoc Test Results for Lysine Concentration

TCPMs	Control Group	Mean Difference	SE	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Maize Germ	Maize Grain	-2575,495582349082000*	331,6484755	<0.001	-3537,69356	-1613,297605
Maize Soaked	Maize Grain	-8229,569220169595000*	331,6484755	<0.001	-9191,767197	-7267,371243
Maize Dry-milled (Flour)	Maize Grain	-7992,126038078250000*	331,6484755	<0.001	-8954,324015	-7029,928061
Maize Wet-milled (Dough Fresh)	Maize Grain	-9223,372036854777000*	331,6484755	<0.001	-10608,35563	-8683,959671
Maize Wet milled cum Fermented (Fermente d Dough)	Maize Grain	-8304,527024656774000*	331,6484755	<0.001	-9266,725002	-7342,329047
* The mean difference is significant at the 0.05 level. **SE**: Standard Error						
[a] Dunnett-T-Tests treat one group as a control and compare all other groups against it.						

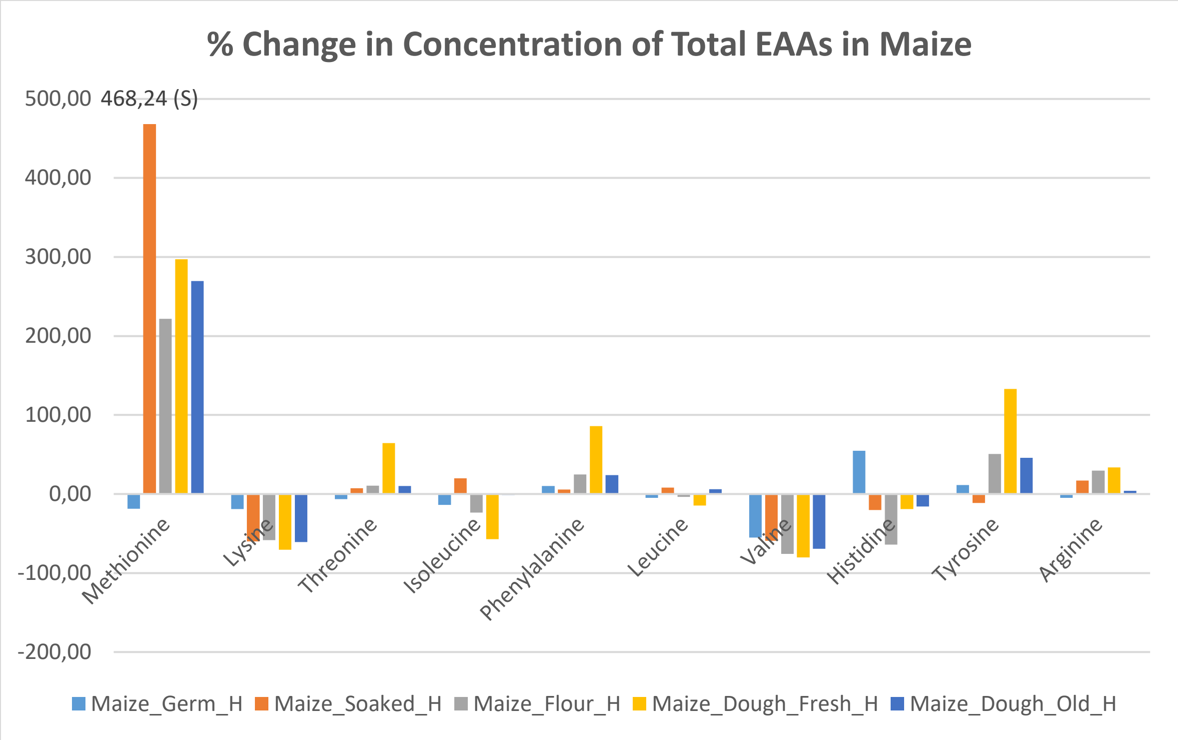

Figure 8.1 % Change in Conc. (nmol/mL) of Total Essential Amino Acids in Maize

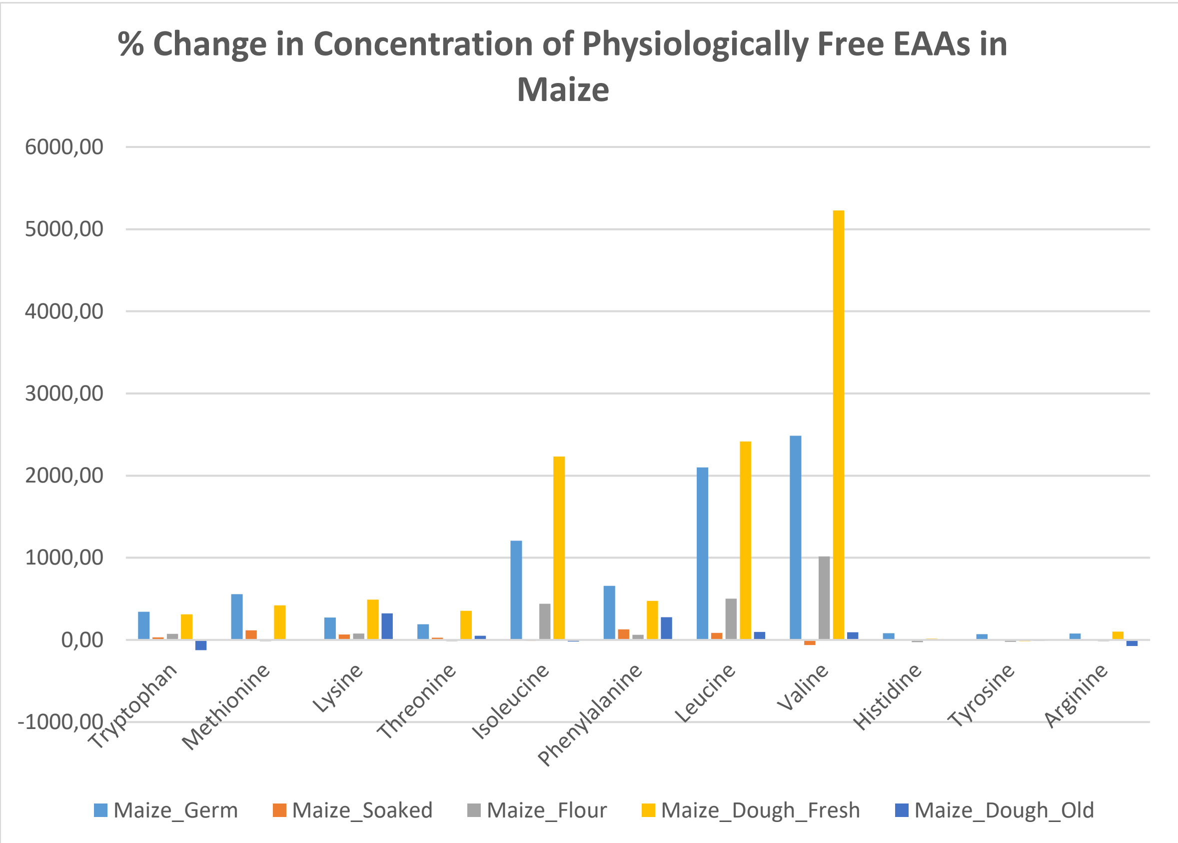

Figure 8.2 % Change in Relative Conc. of Physiologically Free EAAs in Maize

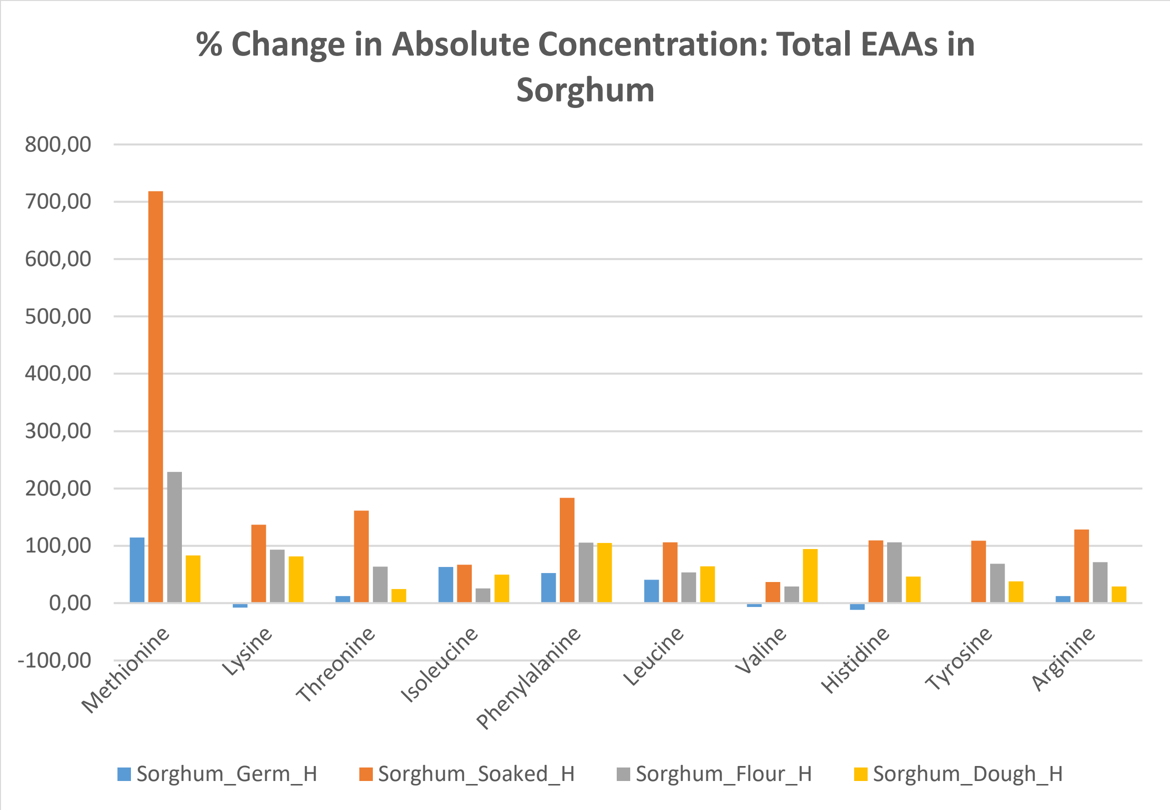

Figure 8.3 % Change in Conc. (nmol/mL) of Total Essential Amino Acids in Sorghum

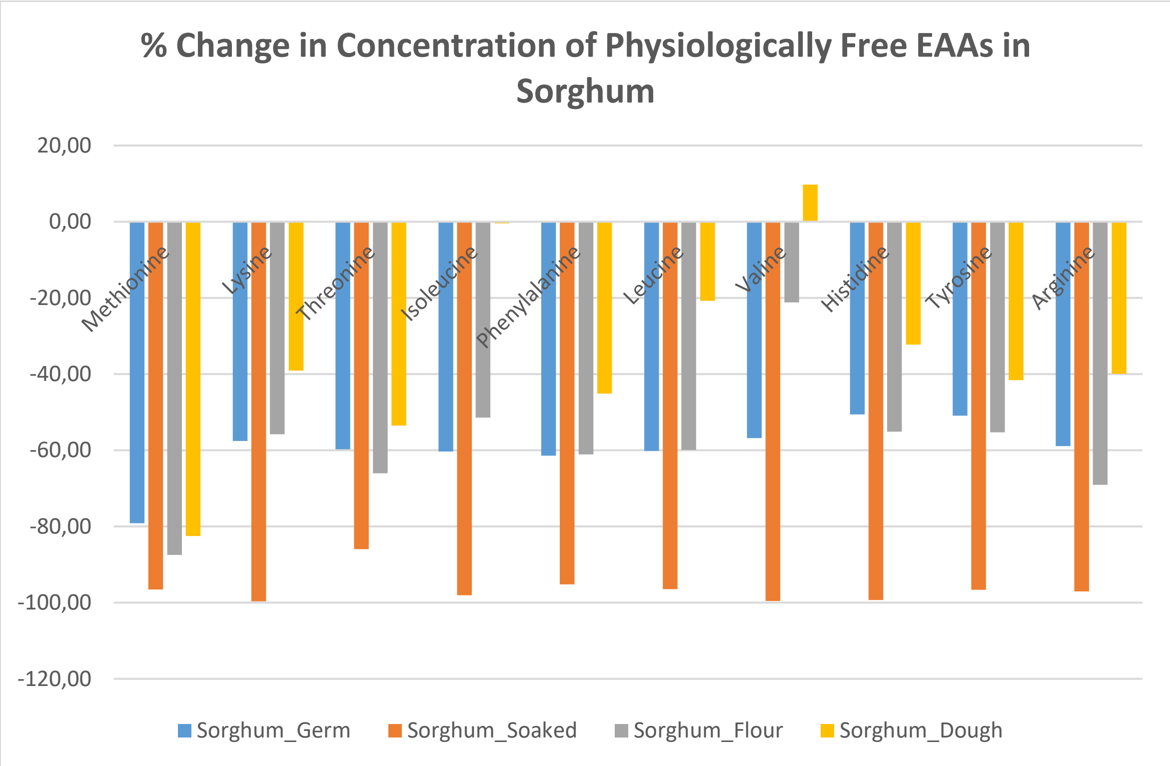

Figure 8.4 % Change in Relative Conc. of Physiologically Free EAAs in Sorghum

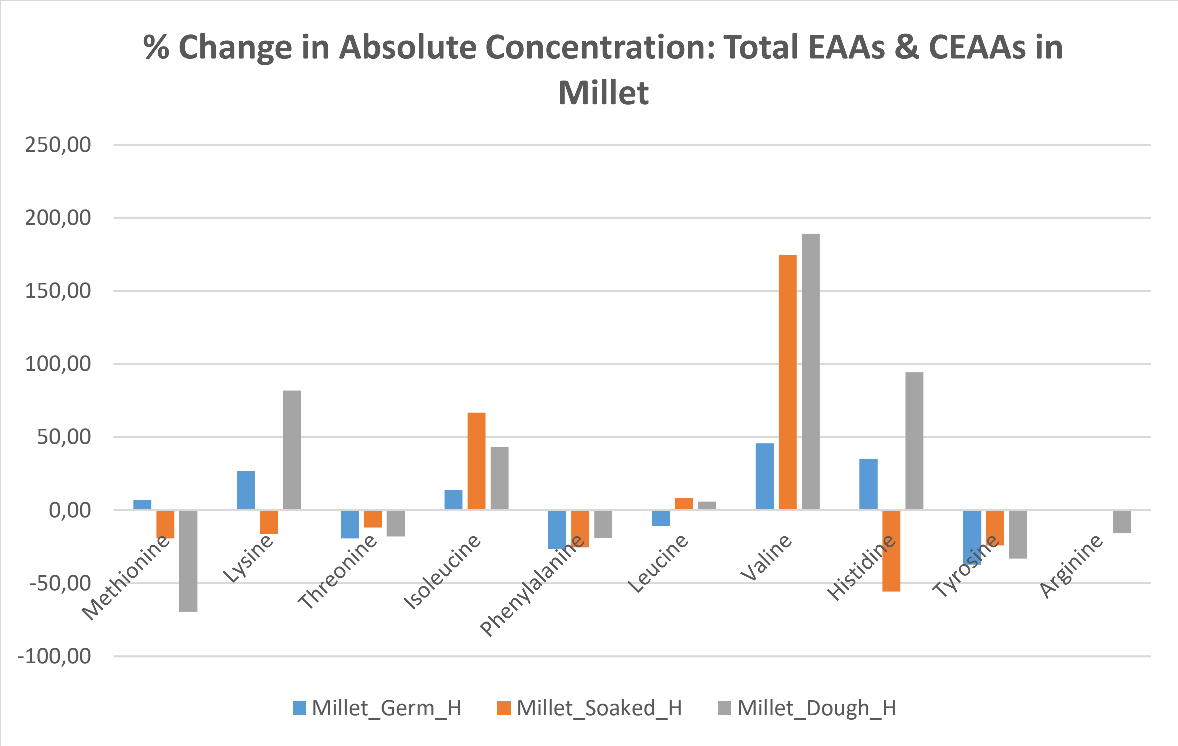

Figure 8.5 % Change in Conc. (nmol/mL) of Total Essential Amino Acids in Millet

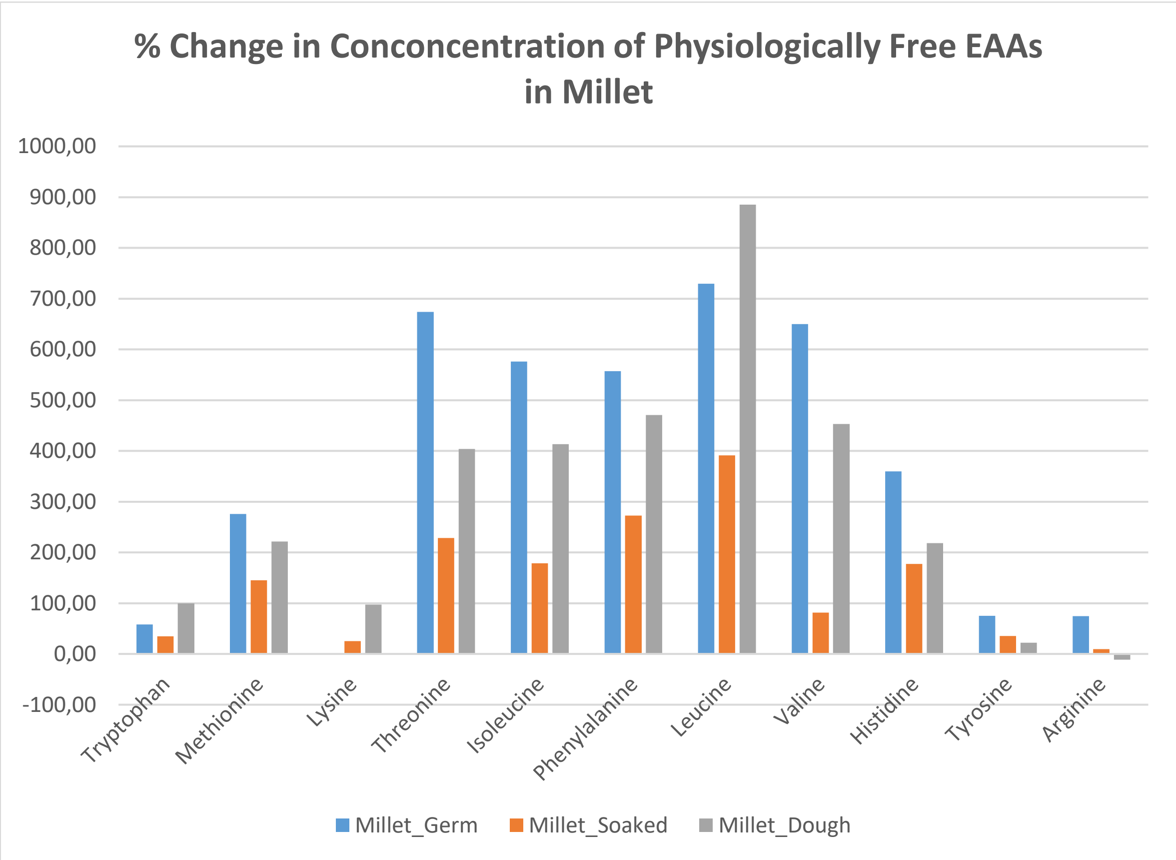

Figure 8.6 % Change in Relative Conc. of Physiologically Free EAAs in Millet

8.2 Appendix B1: Ethical Clearance for the Study (Bielefeld University. Germany)

Universität Bielefeld Ethik-Kommission

Ethik-Kommission der Universität Bielefeld
Postfach 10 01 31 | D-33501 Bielefeld

Der Vorsitzende

Geschäftsstelle:
Fatma Akkaya-Willis
Raum: T5-239
Tel.: 0521 106-4436
ethikkommission@uni-bielefeld.de
Az.: 1266

Bielefeld, 18. Mai 2018
Seite 1 von 1

Stellungnahme der Ethik-Kommission der Universität Bielefeld zu Antrag Nr. EUB 2018-083 vom 17.04.2018

Kurzbezeichnung der Studie:	Traditional Cereal Processing Methods (TCPMs) as Potential Determinants of Malnutrition among Children in Ghana
Hauptansprechpartner:	Stephen K. Anin
Betreuer:	Prof. Dr. Alexander Krämer

Die Ethikkommission der Universität Bielefeld hat den Antrag nach den ethischen Richtlinien der Deutschen Gesellschaft für Psychologie e.V. und des Berufsverbands Deutscher Psychologinnen und Psychologen e.V. begutachtet.

Sie hält die Durchführung der Studie auf der Grundlage der eingereichten Unterlagen für ethisch unbedenklich.

Für die Ethik-Kommission

Vorsitzender

8.3 Appendix B2: Ethical Clearance for the Study (Ghana Health Service, Ghana)

GHANA HEALTH SERVICE ETHICS REVIEW COMMITTEE

In case of reply the
number and date of this
Letter should be quoted.

Research & Development Division
Ghana Health Service
P. O. Box MB 190
Accra
Tel: +233-302-681109
Fax + 233-302-685424
Email: ghserc@gmail.com
4th December, 2017

MyRef. GHS/RDD/ERC/Admin/App / 866
Your Ref. No.

Stephen Kofi Anin
Takoradi Technical University
School of Applied Sciences
Takoradi

The Ghana Health Service Ethics Review Committee has reviewed and given approval for the implementation of your Study Protocol.

GHS-ERC Number	**GHS-ERC: 011/11/17**
Project Title	Effects of Traditional Cereal Processing Methods (TCPM) on Complementary Meals: Potential Risk Factor of Malnutrition among Children in Northern Ghana
Approval Date	29th November, 2017
Expiry Date	28th November, 2018
GHS-ERC Decision	**Approved**

This approval requires the following from the Principal Investigator

- Submission of yearly progress report of the study to the Ethics Review Committee (ERC)
- Renewal of ethical approval if the study lasts for more than 12 months,
- Reporting of all serious adverse events related to this study to the ERC within three days verbally and seven days in writing.
- Submission of a final report **after completion** of the study
- Informing ERC if study cannot be implemented or is discontinued and reasons why
- Informing the ERC and your sponsor (where applicable) before any publication of the research findings.

Please note that any modification of the study without ERC approval of the amendment is invalid.

The ERC may observe or cause to be observed procedures and records of the study during and after implementation.

Kindly quote the protocol identification number in all future correspondence in relation to this approved protocol

SIGNED...
DR. CYNTHIA BANNERMAN
(GHS-ERC CHAIRPERSON)

Cc: The Director, Research & Development Division, Ghana Health Service, Accra

8.4 Appendix B3: Community Entry Permit for Research

TAMALE METRO. ASSEMBLY

Office of the Metropolitan Assembly, Box 4, Tamale

Tel: 0372-22653/22795/22950
e-mail: tamalemetro@yahoo.com
Fax:0372-22653

Your Ref: ....

Our Ref: AB.226/226/26/98

Date: 08/12/17

RE:REQUEST FOR PERMISSION TO UNDERTAKE ACADEMIC RESEARCH STUDY: APPLICATION FOR ETHICAL CLEARANCE AT GHS-ERC FOR RESEARCH STUDY IN NORTHERN REGION, GHANA

We wish to refer to your request to undertake an Academic Research Study in pursuit of your PhD on the topic "Effects of Traditional Cereal Processing Methods on Complementary Meals: Potential Risk Factor of Malnutrition among children in Northern Ghana" in some selected communities in the Tamale Metropolis.

We find your area of research very relevant to us as malnutrition among children is a serious health challenge.

Permission is therefore granted you to undertake the study, the outcome of which we know will be of much relevance to us.

Our cooperation to ensure smooth and effective study is assured.

Thank you.

For: METROPOLITAN CHIEF EXECUTIVE
(SARFO-AGYAPONG KANTANKA)
METROPOLITAN COORDINATING DIRECTOR

MR. STEPHEN KOFI ANNI
TAKORADI TECHNICAL UNIVERSITY
DEPARTMENT OF INDUSTRIAL AND HEALTH SCIENCES
P. O. BOX 256
TAKORADI

8.5 Appendix C1: Interviewer-Administered Survey Questionnaire

QUESTIONNAIRE FOR CROSS-SECTIONAL SURVEY

Please **tick** (√) or **fill** in responses where applicable.

Questionnaire No ……………….. Date of Interview: _/ _ _/ _ _ _ _ (DD/MM/YYYY)

District Name: …………………… Community Name: ……….…………………………

GPS Address of the Household ……………………………………………………………….

SECTION A1: DEMOGRAPHIC DATA OF MOTHER

1. Age of mother …………………………………………(complete years)

2. Religion

a) Islam
b) Christianity
c) Traditional African Religion
d) Others (specify):…………………………………………………………

3. Marital Status

a) Single
b) Married
c) Divorced
d) Widow
e) Separated

4. Ethnicity

a) Gonja
b) Dagomba
c) Nanumba
d) Kokomba
e) Other (specify)………………………………………………………….,

5. Source of income (occupation)

Income Source	Mother	Household Head
Trader/vendor		
Farmer		
Vocational/skilled service worker (Hairdresser, Etc.)		
Teacher/Educationist/ Office worker		
Healthcare worker		
Domestic/Housekeeping Service/Manual Labourer		
Unemployed/Jobless		
Other (specify)…………………………………….		

6. Mother's highest educational attainment

a) None/Pre-School/Primary/Elementary/Middle School/Junior High School
b) Senior Secondary School/Certificated Vocational & Technical School
c) Tertiary/Formal Post-Secondary Professional School

7. How many children less than five years do you cater for in your household? ………

8. Type of community the mother resides in: a) Rural b) Semi-rural c) Urban

SECTION A2: DEMOGRAPHIC DATA OF CHILD

9. Child's Gender (a) Male (b) Female

10. Is your child in pre-school (kindergarten/nursery/crèche) or under any outside-the-home care service? [a] Yes [b] No

11. Age of Child: …..... (Months) Date of Birth _ _ / _ _/ _ _ _ _ (DD/MM/YYYY)

SECTION B: NUTRITIONAL STATUS DATA OF MOTHER AND CHILD

Anthropometric Measurements of Mother

12. Height: ……………………………..cm

13. Weight: ……………………………..kg

14. BMI..kg/m^2

Anthropometric Measurements of Child

15. Height: ………………………………cm

16. Weight: …………………………….....kg

17. Birthweight: ………………………kg

18. Record of child weight from 1st to 24th month in the **GHS Child Health Booklet**:

Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Weight (Kg)												
Month	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**
Weight (Kg)												

SECTION C1: FOOD SECURITY STATUS (FOOD INTAKE) DATA OF MOTHER

SECTION C1.1 : DIETARY DIVERSITY SURVEY FOR MOTHERS
19. Are you currently breastfeeding? *(Yes or No)* Yes=1 No=0
20. Are you currently pregnant? *(Yes or No)* Yes=1 No=0
21. Did you suffer any illness that prevented you from eating as usual yesterday? **(**Yes=1 No=0**) If no, go to Question 23** **22. If yes, did this illness that prevented you from eating as usual last for more than 3 days?** **(**Yes=1 No=0**)**
23. Was yesterday a celebration day (festival, baptism, marriage or funeral) or a market day? **(**Yes=1 No=0**) If no, go to open recall (Section C1.2)** **24. If yes, has this celebration or market day been lasting for several days? (**Yes=1 No=0**)**

SECTION C1.2 : DIETARY DIVERSITY SURVEY FOR MOTHERS
25. Please describe all foods (meals and snacks) that you ate or drank yesterday during the day and night, whether at home or outside the home. Start with the first food in the morning.

Meal/Snack Time	Name of Dish/Meal	Detailed List of Ingredients
Breakfast		
Snack before lunch		
Lunch		
Snack before dinner		
Dinner/Supper		
Snack after dinner/supper		
Drinks taken during the day/night		

26. From the meals mentioned by the mother, indicate whether she ate from the following food groups during the past 24 hours whether at home or outside the home. Please indicate with **Yes, No or Not Applicable (N/A)**

SECTION C1.3: DIETARY DIVERSITY SURVEY FOR MOTHERS			
#	**Food Groups**	**Examples of Foods**	**Consumption** **No = 0** **Yes = 1** **N/A = 9**
26.1	**CEREALS**	Sorghum, maize, millet, wheat, rice (porridge, fritters, couscous, flour/broken cereal, toasted, bread, etc)	| |
26.2	**WHITE ROOTS AND TUBERS**	White-fleshed sweet potato, potato, cassava, cocoyam, plantain, yam, etc	| |
26.3	**VITAMIN A RICH VEGETABLES AND TUBERS**	Carrot, red pepper, orange-fleshed sweet potatoes, etc	| |
26.4	**DARK GREEN LEAFY VEGETABLES**	Baobab leaves, dark-green shallot leaves, onion leaves, squash leaves, bean leaves, *cocoyam leaves*, potato leaves, spinach, dark-green lettuce, any dark-green wild leaves, etc	| |
26.5	**OTHER VEGETABLES**	Fresh tomato, fresh or dried okra, eggplant, local eggplant (*jaxatus* or *goyo*), zucchini, cucumber, cabbage, onion, shallot, green pepper, green beans, beets, lettuce (light-green leaves), green peas, etc	| |
26.6	**VITAMIN A RICH FRUITS**	Mango, papaya, orange-fleshed melon, fruit of African locust bean, powder made from the fruit of African locust bean, etc	| |
26.7	**OTHER FRUITS**	Watermelon, orange, lemon, wild dates, dates, pineapple, apple, banana, guava, avocados, wild fruits (monkey- bread, baobab fruit), shea fruit pulp, cashew nut fruit, fresh fruit juices, plum fruit juice, grape, etc	| |
26.8	**ORGAN MEAT**	Liver, kidneys, heart, lungs, or any other organ meat (from calf, mutton, goat, camel, poultry), entrails (entrails soup), coagulated blood	| |
26.9	**FLESH MEATS**	Beef, mutton, goat, rabbit, bush meat, chicken, guinea fowl, camel, bird, gazelle, goose, duck, varan, turtle, insects, caterpillars/worms, lizard, wild rats, bush rats, squirrels, partridges, snake, mouse, warthogs, deer, etc	| |
26.10	**EGGS**	Chicken, turkey, guinea fowl or varan or duck eggs, etc	| |
26.11	**FISH AND SEAFOOD**	Fresh fish, smoked fish, salted fish, dried fish (except pinch of powder), canned fish (sardines, tuna..), all shellfish and seafood (shrimp, squid, octopus, lobster..), dried or smoked fish powder (in large quantities)	| |
26.12	**PULSES, NUTS AND SEEDS**	Beans (cowpeas), peanut (paste or plain), sesame, bambara groundnut, sweet peas, African locust bean (in large quantities for sauce), cashew nuts, wild nuts, chickpea, lentil, water lily seeds, other dried pulses	| |
26.13	**MILK AND MILK PRODUCTS**	Fresh milk, milk powder, condensed milk (sweetened or not), curd, yogurt, cheese	| |
26.14	**OILS AND FATS**	Vegetable oil (peanut, sesame, coconut, wild date oil, seasonings, frying, fritter), shea butter/oi), vegetable fats/margarine, mayonnaise, sour cream, fresh cream, lard, etc	| |

26.15	**RED PALM PRODUCTS**	Red palm oil, red palm nuts	| |
26.16	**SWEETS**	Sugar, lump sugar (in tea, coffee, porridge, fritter), soft drinks (sweetened soda, hibiscus juice/sobolo drink, sweetened ginger juice, tamarind leaf or fruit sweetened juice, monkey bread juice, lemon juice), fresh palm wine, honey, jam, candy, biscuits, etc	| |
26.17	**SPICES, CONDIMENTS** **BEVERAGES**	**Spices, condiments** : chili, pepper, vinegar, garlic, mix spices, cinnamon, salt, Monosodium Glutamate (Maggi cube, white Maggi, Royco, etc), tomato paste, condiment made from seeds, leaves or pulp), condiment made from onion or dried/processed onion leaves or from dried shallots, condiment made from turnip roots, condiment made from soy, kola nut, etc **Small quantity** of fish powder, of okra powder, of dried baobab leaf powder, of pepper powder, of *leafy* powder, of African locust bean powder, yeast Tea- "*lipton*", coffee, *chicory, kinkeliba*, lemon grass, unsweetened tamarind leaf or fruit juice, unsweetened ginger juice, unsweetened hibiscus pulp juice, unsweetened fermented millet bran water, etc	| |
26.18	**Did you eat anything (meal or snack) outside the home yesterday? yes=1, no=0**		| |
26.19	**Did anyone in your household eat anything (meal or snack) outside the home yesterday? yes=1, no=0**		| |

SECTION C2: FOOD SECURITY STATUS (FOOD INTAKE) DATA OF THE CHILD

i) Dietary Diversity Survey (DDS)

SECTION C2.1 : DIETARY DIVERSITY SURVEY FOR CHILDREN AGED 6-24 MONTHS

27. **Yesterday, was the child breastfed (directly from the breast) during the day or the night? (**Yes=1 No=0**)**

28. **If no, did the child receive breast milk in a different way, for example by spoon, cup or bottle or from another woman (wet nurse), yesterday during the day and the night? (**Yes=1 No=0**)**

29. **Yesterday, how many times did the child eat any meal or snack (food) during the day and the night? ? ……………………………………………**

30. **Did the child suffer any illness that prevented him/her from eating as usual yesterday? (**Yes=1 No=0**)**

31. **Was yesterday a celebration day (festival, baptism, marriage or funeral) or a market day? (**Yes=1 No=0**)**

If no, go to open recall (Section C2.2)

32. **If yes, has this celebration or market been lasting for several days? (**Yes=1 No=0**)**

SECTION C2.2 : DIETARY DIVERSITY SURVEY FOR CHILDREN AGED 6-24 MONTHS		
33. Please describe all foods (meals and snacks) that your child ate or drank yesterday during the day and night, whether at home or outside the home. Start with food in the morning.		
Meal/Snack Time	**Name of Dish/Meal**	**Detailed List of Ingredients**
Breakfast		
Snack before lunch		
Lunch		
Snack before dinner		
Dinner/Supper		
Snack after dinner/supper		
Drinks taken during the day/night		

34. **From the meals mentioned by the mother, indicate whether the child ate any meal or snack from the following food groups during the past 24 hours whether at home or outside the home.** Please indicate with **Yes, No or Not Applicable (N/A).**

SECTION C2.3: DIETARY DIVERSITY SURVEY FOR CHILDREN (6-24 MONTHS)			
#	**Food Groups**	**Examples of Foods**	**Consumption** **No = 0** **Yes = 1** **N/A = 9**
34.1	**CEREALS**	Sorghum, maize, millet, wheat, rice (porridge, fritters, couscous, flour/broken cereal, toasted, bread, etc)	| |
34.2	**WHITE ROOTS AND TUBERS**	White-fleshed sweet potato, potato, cassava, cocoyam, plantain, yam, etc	| |
34.3	**VITAMIN A RICH VEGETABLES AND TUBERS**	Carrot, red pepper, orange-fleshed sweet potatoes, etc	| |
34.4	**DARK GREEN LEAFY VEGETABLES**	Baobab leaves, dark-green shallot leaves, onion leaves, squash leaves, bean leaves, *cocoyam leaves*, potato leaves, spinach, dark-green lettuce, any dark-green wild leaves, etc	| |
34.5	**OTHER VEGETABLES**	Fresh tomato, fresh or dried okra, eggplant, local eggplant (*jaxatus* or *goyo*), zucchini, cucumber, cabbage, onion, shallot, green pepper, green beans, beets, lettuce (light-green leaves), green peas, etc	| |
34.6	**VITAMIN A RICH FRUITS**	Mango, papaya, orange-fleshed melon, fruit of African locust bean, powder made from the fruit of African locust bean, etc	| |
34.7	**OTHER FRUITS**	Watermelon, orange, lemon, wild dates, dates, pineapple, apple, banana, guava, avocados, wild fruits (monkey- bread, baobab fruit), shea fruit pulp, cashew nut fruit, fresh fruit juices, plum fruit juice, grape, etc	| |
34.8	**ORGAN MEAT**	Liver, kidneys, heart, lungs, or any other organ meat (from calf, mutton, goat, camel, poultry), entrails (entrails soup), coagulated blood	| |
34.9	**FLESH MEATS**	Beef, mutton, goat, rabbit, bush meat, chicken, guinea fowl, camel, bird, gazelle, goose, duck, varan, turtle, insects, caterpillars/worms, lizard, wild rats, bush rats, squirrels, partridges, snake, mouse, warthogs, deer, etc	| |
34.10	**EGGS**	Chicken, turkey, guinea fowl or varan or duck eggs, etc	| |
34.11	**FISH AND SEAFOOD**	Fresh fish, smoked fish, salted fish, dried fish (except pinch of powder), canned fish (sardines, tuna..), all shellfish and seafood (shrimp, squid, octopus, lobster..), dried or smoked fish powder (in large quantities)	| |
34.12	**PULSES, NUTS AND SEEDS**	Beans (cowpeas), peanut (paste or plain), sesame, bambara groundnut, sweet peas, African locust bean (in large quantities for sauce), cashew nuts, wild nuts, chickpea, lentil, water lily seeds, other dried pulses	| |
34.13	**MILK AND MILK PRODUCTS**	Fresh milk, milk powder, condensed milk (sweetened or not), curd, yogurt, cheese	| |
34.14	**OILS AND FATS**	Vegetable oil (peanut, sesame, coconut, wild date oil, seasonings, frying, fritter), shea butter/oi), vegetable fats/margarine, mayonnaise, sour cream, fresh cream, lard, etc	| |
34.15	**RED PALM PRODUCTS**	Red palm oil, red palm nuts	| |

34.16	**SWEETS**	Sugar, lump sugar (in tea, coffee, porridge, fritter), soft drinks (sweetened soda, hibiscus juice/sobolo drink, sweetened ginger juice, tamarind leaf or fruit sweetened juice, monkey bread juice, lemon juice), fresh palm wine, honey, jam, candy, biscuits, etc	| |
34.17	**SPICES, CONDIMENTS** **BEVERAGES**	**Spices, condiments** : chili, pepper, vinegar, garlic, mix spices, cinnamon, salt, Monosodium Glutamate (Maggi cube, white Maggi, Royco, etc), tomato paste, condiment made from seeds, leaves or pulp, condiment made from onion or dried/processed onion leaves or from dried shallots, condiment made from turnip roots, condiment made from soy, kola nut, etc **Small quantity** of fish powder, of okra powder, of dried baobab leaf powder, of pepper powder, of *leafy* powder, of African locust bean powder, yeast Tea- "*lipton*", coffee, *chicory*, *kinkeliba*, lemon grass, unsweetened tamarind leaf or fruit juice, unsweetened ginger juice, unsweetened hibiscus pulp juice, unsweetened fermented millet bran water, etc	| |
34.18	**Did your child eat anything (meal or snack) outside the home yesterday? yes=1, no=0**		| |

SECTION D: RISK FACTORS OF MALNUTRITION (UNDERNUTRITION)

i) Proximal Risk Factors **Use** Yes=1 No=0

a) Child Morbidity Indicators

35. Does the child have bilateral pitting oodema? [a] Yes [b] No

36. Has the child been sick in the last two weeks? [a] Yes [b] No

37. If yes, what was the type of sickness the child suffered from?

a) Malaria/Fever **b)** Diarrhea **c)** Flu and/or Cough **d)** Other……………………………….

38. How frequently has the child been sick of the following illnesses in the last 6 months?

Illness	None	Only Once	2-3 Times	Every Month
Malaria/Fever				
Cough and/or Flu				
Diarrhea/Stomach Upset				

39. Is the immunization of the child up to date? [a] Yes [b] No

40. Does the child sleep under Insect Treated Nets (ITN)? [a] Yes [b] No

41. Does the child use feeding bottle (s) [a] Yes [b] No

b) Adequacy of Food Intake: Infant and Young Child Feeding Practices (IYCFP)

42. After delivery of your child, how long did it take you to breastfeed your child for the first time?

a) Within first hour of delivery
b) 2 to 23 hours after delivery
c) The next day (More than 24 hours)
d) Do not remember

43. Before putting your child to the breast for the first time after delivery, what was your child given to drink? (Multiple responses possible)

a) Nothing
b) Fresh Milk (Other than breast milk)
c) Plain water

d) Sugar or glucose solution
e) Gripe water
f) Sugar-salt solution
g) Fruit juice
h) Cocoa-based beverage
i) Infant formula
j) Honey
k) Other (specify) ______________

44. When you delivered your child, what did you do with the first yellowish breast milk?

(a) Gave it to the baby (**b**) Discarded it **(c)** Other (Specify) ______________

45. Did you exclusively feed your child with breastmilk (without water) from birth to at least 6 months of age? **(a)** Yes **(b)** No

46. At what age did you first introduce solid or semi-solid food to your child?

a) Before 6 months
b) At Six months
c) Seven to 9 months
d) After nine months
e) Yet to start

47. Is your child currently breastfeeding? **(a)** Yes **(b)** No If yes, go to 54

48. If your child is **not** breastfeeding, when did you wean him off breastmilk? ……………………….. (Complete months).

ii) Intermediate Risk Factors

A) Maternal Childcare and Maternal Healthcare-Seeking Behaviour Factors

49. Where did you deliver your child?

a) At Home
b) CHPS Compound
c) Clinic/ Health Centre
d) Accredited Maternity Home
e) Hospital
f) Traditional Birth Attendant
g) Other (specify)……………………………………………………………….

Using the health records from mother's Antenatal Card (ANC):

50. Number of times mother visited a Health Care Facility for prenatal care: ………...

51. Number of times mother has visited a Health Care Facility for postnatal care: ……

B) Food Utilization Factors I: Habitual Food Resource Utilization Practices (HFRUPs) for Complementary Meal Preparation or Complementary Feeding

52. Do you feed your child habitually with porridge **without** any other ingredient (rich sources of proteins, fats, vitamins, and minerals) as a complete meal?

a) Yes, always **b)** Yes, very often **c)** Yes sometimes/occasionally **d)** No

53. Which of these cereal forms habitually is most preferred or often used for complementary meal preparation for your child?

a) Fermented Dough **b)** Fresh Dough **c)** Flour

54. Do you habitually prepare the dough for your child's porridge/gruel yourself at home?

a) Yes, always **b)** Yes, very often **c)** Yes sometimes/occasionally **d)** No

55. Do you purchase or source dough habitually from outside your home to prepare food for your child?

a) Yes, always b) Yes, very often b) Yes sometimes/occasionally c) No

56. How long do you habitually store dough meant for preparing food for your child?

a) 3 Days or Less b) 4-7 Days Maximum c) More than 7 Days to 3 weeks d) >3 weeks

57. Which storage container is most habitually preferred or often used for storing complementary meal ingredients (dough) for complementary meal preparation for your child?

a) Gourd/Calabash **b)** Metal Containers **c)** Plastic Containers **d)** Jute Sacks

58. How frequently do you habitually use these cereals in food preparation for your child?

Usage for Child's Meals Cereal	**Always/Very Often (> 4 Days/Week)**	**Occasionally (1-3 Days/Week)**	**Not at All**
a. Maize			
b. Sorghum			
c. Millet			
d. Rice			

C) Food Utilization Factors II: Traditional Cereal Processing Methods (TCPMs) for the Preparation of Complementary Meal Ingredients (Flour & Dough)

Which of these traditional/household cereal processing methods do you preferably or often use for the preparation of dough/flour from cereals for your child's meals (porridge, gruels)?

59. Dehulling or Removal of Cereal Coat/Grain Skin

a) Yes, always **b)** Yes, very often **c)** Yes sometimes/occasionally **d)** No

60. Dry Milling of Grains (Flour):

a) Domestic/Home Pounding (Mortar-Pestle) **b)** Grinding/Milling Stone **c)** Commercial Non-machine Pounding (Mortar-Pestle) **d)** Commercial Machine Milling ('Nikanika') **e)** No (Purchased imported flour)

61. Steeping/Soaking of Grains:

a) Less than 6 hours/Quarter day **b)** 12 hours/Half Day **c)** More than 12 hours up to 24 hours **d)** More than 24 hours up to 48 hours/2 Days **e)** More than 48 hours

62. Wet milling of Grains cum Natural/Spontaneous Fermentation (Dough)

Aroma or smell of alcohol and/or taste of alcohol in dough sample can be perceived in:

a) Less than 24 hours **b)** 24 hours or more up to 7 Days **c)** More than 7 Days

D) Environmental/WASH Factors (Water, Sanitation and Hygiene):

63. What is the main source of **drinking water** for members of your household? (Only one response).

a) Piped/Industrially-treated water
b) Borehole
c) Protected well
d) Unprotected well
e) Surface water (river, stream, dam, lake, pond, canal, irrigation channel)
f) Rain water

64. Are you satisfied with the **drinking water** supply in this community? (If answer is **No,** go to question **65.** If answer is **Yes,** go to question **66)**.
a) Yes
b) No
c) Partially/Indifferent

65. What is the main reason you are **not** satisfied with the water supply?
a) Not enough
b) Long waiting queue
c) Long distance
d) Irregular supply
e) Water is not drinkable (bad taste/smell/colour)
f) Water cannot be used for domestic activities
g) Other (specify)…………………………………………………………………………

66. What kind of toilet facility does this household use?
a) Flushed water closet type
b) Simple pit latrine with floor/slab
c) Pit latrine without floor/slab
d) No facility: open field, bush, plastic bag, etc

67. The last time your child passed stool, how did you **dispose off** the stool?
a) Child used toilet/latrine
b) Put/rinsed into toilet or latrine
c) Buried
d) Thrown into garbage
e) Put/rinsed into drain or ditch
f) Left in the open
g) Other (specify)…………………………………………………………………………

68. At what moments did you wash your hands in the last 24 hours? (Multiple answers possible)
a) Before preparation of food
b) After using the toilet
c) After cleaning the home (sweeping, scrubbing, mopping, etc)
d) Before eating meals/snacks
e) After eating meals/snacks
f) Before feeding my child
g) Other (Specify) ………………………………………………………………………

E) Household Wealth Index (HWI)/Household Socioeconomic Status (HSES)

69. What type of house do members of the household dwell in?

a) Block house (b) Brick house (c) Mud house (d) Other (specify) ………………

70. How many people live in your household? ....

71. How many rooms are in your household? …………………

72. What is the main source of power for lighting the household?

a) Electricity (b) Solar/Sunlight (c) Kerosene Lamps (d) Other (specify) …………

73. What type of fuel does your household mainly use for cooking?

a) Electricity
b) Liquefied Petroleum Gas (LPG)
c) Charcoal
d) Kerosene
e) Firewood
f) Other (specify) ………………………………………………………………

Does your household have any of these assets? Tick **Yes=1** or **No**=0

ITEM	**YES**	**NO**
74. Radio/DVD/VCD/ Audio Player		
75. Color/Black & White TV/Satellite Dish		
76. Sewing Machine		
77. Mattress/Bed		
78. Refrigerator		
79. Bicycle/Tricycle		
80. Computer/Printer/Photocopier		
81. Electric Fan/Air conditioner		
82. Mobile Telephone/Home Phone		
83. Car/Truck/Van/Motorcycle		
84. Animal-drawn cart/Donkey		
85. Farm (crop production)		
86. Farm (poultry/livestock production)		

iii) Distal Risk Factors

Communal Wealth Index (CWI)/Communal Socioeconomic Status (CSES)

Does your community have any of these amenities/services? Tick **Yes=1** or **No=0**

ITEM	YES	NO
87. Basic/Elementary School		
88. Health Center/Clinic		
89. Designated Refuse Dump/Site		
90. Milling Machine ('Nikanika')		
91. Sheltered Market		
92. Public Toilet Facility		
93. Sheltered Community Center		
94. Motorable Roads		
95. Electricity Supply Services		
96. Motorized Transport Service		
97. Banking/Financial Services		
98. Telephone/Internet Service		
99. Antenatal Care Services		
100. Immunization Services		
101. Nutrition Education Services		
102. Potable Water Supply Service		
103. Welfare Assistance (Free Food, Clothes, Medication, Building Materials, etc)		

THANK YOU!! **END OF INTERVIEW**

8.6 Appendix C2: Study Information Brief

Research Participants Information Brief (Mothers/Caregivers/Community Leaders)

i. **About the Researcher/Principal Investigator (PI):**

I am a PhD student undertaking a research study in Public Health Nutrition (Nutritional Epidemiology) and a Lecturer from Takoradi Technical University, Takoradi, Ghana. I would be working with a support team of research assistants namely supervisors, interviewers, anthropometrists and community volunteers.

ii. **Topic:**

I am conducting an academic research as part of my PhD study on malnutrition amongst children in northern Ghana titled '**Effects of Traditional Cereal Processing Methods (TCPMs) on Complementary Meal Ingredients: Potential Risk Factors of Malnutrition among Children in northern Ghana'.**

iii. **Purpose of Study:**

The purpose of this study is to ascertain the significance of traditional or household cereal processing methods (such as dehulling, soaking/steeping, germination/sprouting, dry/wet-milling, fermentation, and storage) as potential determinants or risk factors of the nutritional status of children in northern Ghana. The effects of TCPMs on the nutritional quality of dough and flour made from staple tropical cereals for complementary feeding of children in northern Ghana would be analyzed.

iv. **Duration and Scope of Activities:**

Mothers/Caregiver: You and your child (6-24 months) have been selected to be part of this study to respond to a set of questions and allow for physical examinations and some bodily measurements (height and weight) to be taken which may take about 45 minutes in total. Samples of cereal grains (maize, sorghum, and millet) and their products (dough and flour) would also be collected from your household for laboratory analysis.

v. **Potential Risks:**

There is no known physical or psychological harm associated with the enquiries and/or the measurements to be made/taken from you.

vi. **Benefits and Importance of the Study**

The results of the study could be useful to provide insights into developing context-specific interventions with regards to appropriate infant and young child cereal processing and food preparation practices to address malnutrition in northern Ghana.

vii. **Costs**

There would be no cost ordinarily incurred by you. However, should the research team collect samples of cereals and cereal products from your household, the costs associated shall be paid to you.

viii. **Compensation**

You are expected to freely accept to participate in this study at no fee. However, you would be given an incentive or token of appreciation for your time offered to us if you do not mind. You shall be given feedback on the research if you are interested.

ix. **Confidentiality:**

Utmost care would be taken to respect your privacy. Your identity, related information and responses shall remain strictly confidential and thus would not be linked up to your identity or publicly accessible to any unauthorized person. The responses obtained from you shall be coded and/or anonymized to ensure confidentiality. No audio, photo or video records of you or other participants or related activities shall be taken.

x. Respect for Participant and Voluntary Participation:

You are assured of the utmost respect for your privacy, religious beliefs, cultural values, opinions, and voluntary participation in this study. You are free to refuse to answer any question in particular and free to withdraw from continuing in the enquiry process. You shall not be penalized for refusing to participate in this study.

xi. Data Protection, Outcomes and Feedback:

The data obtained shall be kept with the researcher under controlled/restricted access for up to 10 years in accordance with international best practices at the Bielefeld University Data Depository, Germany or at any other suitable data storage means. The data would be analyzed and used to generate reports, publications in peer-reviewed journals, PhD dissertation, and dissemination for non-commercial purposes. Participants shall be given feedback if anyone requests for it. In situations where a child or mother is found to be severely malnourished, the participant shall be referred to a health facility for professional medical attention.

xii. Funding

The costs associated with all the field data collection activities are self-financed by the PI.

xiii. Conflict of Interest

The data obtained from this study would be the sole property of the researcher (PI) but access shall be granted for its use following an appropriate and reasonable request by any organization or individual for the general public good.

xiv. Contact details in case of any question or feedback needed:

Principal Investigator (PI): Mr. Stephen Kofi Anin	**Local Research Advisor: Dr Mahama Saaka**	**Ghana Health Service: Ms. Hannah Frimpong**
Takoradi Technical University, Faculty of Applied Sciences, Department of Industrial and Health Sciences, P. O. Box 256, Takoradi, Ghana. **Phone:** +233-244-410-127 **Email**: stephen36anin@gmail.com	University for Development Studies, School of Allied Health Sciences, Department of Community Nutrition, P.O. Box 1883, Tamale, Ghana **Phone**:+233-207061136 **Email:**mmsaaka@gmail.com msaaka@uds.edu.gh	The ERC Administrator, Research and Development Division, Ghana Health Service, P.O. Box MB 190, Accra, Ghana. **Phone:** +233-507041223 **Email:** ghserc@gmail.com

Please sign/thumb-print this form if you **understand the information related to participating in this study and agree** to willfully participate. Thank you.

Date……………………………………… Signature…………………………………………..

Thumbprint……………………….……….. Witness …………………………………………..

8.7 Appendix C3: Informed Consent Form

INFORMED CONSENT FORM
(Cross-Sectional Survey of Mothers/Caregivers)

Research Title: Effects of Traditional Cereal Processing Methods (TCPM) on Complementary Meal Ingredients: Potential Risk Factors of Malnutrition among Children in northern Ghana.

Statement of Consent to Participate

"I have read the participant information about this study or it has been read and explained to me in a language I understand. I have been assured of the opportunity to ask questions during the survey. I have had the opportunity to ask questions and received answers satisfactorily before proceeding with the interview. I consent to voluntarily participate in the study with my child and household. I understand that I have the right to withdraw from the study at any time without any reason and without any consequence to me''.

"I am assured of the utmost respect for my privacy, religious beliefs, cultural values, opinions and voluntary participation in this study at no fee. However, I would be given an incentive or a token of appreciation for participating in the study if it is acceptable to me. My child and I have been selected to be part of this study to be interviewed and I would allow some body measurements to be taken which may take about 45 minutes''.

'I understand that there is no known physical or psychological harm associated with the measurements, physical examination, and enquiries to be made from me. I shall be given feedback on the research if I am interested''.

Signature/Thumbprint…………………………………… Date: ……………………………

Signature of Witness for Illiterate Participant………………………………………………

Investigator Statement and Signature

'I hereby certify that the participant has been given enough information to make the informed choice and is willing to participate in this study''.

Name:…………………………………………………………………………………

Signature…………………………………. Date: …………………………………………….

Signature of Person who Sought Participant's Consent:…………………………………..

Thank you for agreeing to participate in this study.

8.8 Appendix D1: Phytosanitary Certificate of the Cereal Samples (Pilot Study)

Original

REPUBLIC OF GHANA

MINISTRY OF FOOD AND AGRICULTURE
PLANT PROTECTION & REGULATORY SERVICES DIRECTORATE
(PLANT EXPORTATION REGULATIONS)

PHYTOSANITARY CERTIFICATE

PC No: 0035670

TO: Plant Protection Organisation(s) of....GERMANY....

I. Description of Consignment

Name and address of Exporter:....ANIN STEPHEN KOFI
....TAKORADI TECH. UNIV, TAKORADI....

Declared name and address of Consignee....AS ABOVE
....DUSSELDORF....

Number and description of packages....ONE (1) BAG

Distinguishing marks....NONE

Place of origin....GHANA

Declared means of conveyance....BY AIR

Declared point of entry....DUSSELDORF

Name of produce and quantity declared....CORN DOUGH, SORGHUM, MILLET
....

Botanical name of plants....ZEA MAYS; SORGHUM SP; PENNISETUM SP

This is to certify that the plants, plant products or other regulated articles described herein have been inspected and/or tested according to appropriate official procedures and are considered to be free from the quarantine pests specified by the importing contracting party and to conform with the current phytosanitary requirements of the importing contracting party, including those for regulated non-quarantine pests.

They are deemed to be practically free from other pests.

II. Additional Declaration

III. Disinfestation and/or Disinfection Treatment

Date........Treatment........Chemical (active ingredient)........

Duration and temperature........

Concentration........

Additional information........

(Stamp of Organisation) PLANT PROTECTION & REGULATORY SERVICES DIRECTORATE GHANA — 0035670 — PHYTOSANITARY PERMIT — Date: 22/01/18

Place of issue....KIA - ACCRA

Name of authorized officer....MOSES KPORMEGBE

Date....22ND JAN, 2018 .... *(Signature)*

No financial liability with respect to this certificate shall attach to PPRSD or to any of its officers or representatives*
*Optional clause

8.9 Appendix D2: Phytosanitary Certificate of the Cereal Samples (Definitive Study)

Original

REPUBLIC OF GHANA

MINISTRY OF FOOD AND AGRICULTURE
PLANT PROTECTION & REGULATORY SERVICES DIRECTORATE
(PLANT EXPORTATION REGULATIONS)

PHYTOSANITARY CERTIFICATE

PC No: 0003399

TO: Plant Protection Organisation(s) of GERMANY

I. Description of Consignment

Name and address of the Exporter: ANIN STEPHEN KOFI
T.T.U P.O BOX 256 TAKORADI

Declared name and address of Consignee: AS ABOVE
DUSSELDORF

Number and description of packages: ONE (1) BAG

Distinguishing marks: NONE

Place of origin: GHANA

Declared means of conveyance: BY AIR

Declared point of entry: DUSSELDORF

Name of produce and quantity declared: FOOD ITEM (S)

Botanical name of plants: ZEA SP, SORGHUM SP, PENNISETUM SP

This is to certify that the plants, plant products or other regulated articles described herein have been inspected and/or tested according to appropriate official procedures and are considered to be free from the quarantine pests specified by the importing contracting party and to conform with the current phytosanitary requirements of the importing contracting party, including those for regulated non-quarantine pests

They are deemed to be practically free from other pests.

II. Additional Declaration

III. Disinfestation and/or Disinfection Treatment

Date:................Treatment..............................Chemical (active ingredient)..............................

Duration and temperature..............................

Concentration..............................

Additional information..............................

(Stamp of Organisation) PLANT PROTECTION & REGULATORY SERVICES DIRECTORATE GHANA — PHYTOSANITARY PERMIT — Date 17/7/18

Place of issue: KIA - ACCRA

Name of authorized officer: EDWIN A PAINTSIL

Date: 17th JULY 2018

(Signature)

No financial liability with respect to this certificate shall attach to PPRSD or to any of its officers or representatives*
*Optional clause

8.10 Appendix E: Timelines for Doctoral Research Study

*Blocks	Programme/Activities	2016		2017				2018				2019				2020				2021
	Quarters of the Year	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**
Block 1&2	**Conceptualization of Study:** **QP1** (Expose on Research Topic) and **QP2** (Public Health Relevance of the Study)		■																	
Block 3&4	**QP3** (Specifying the Research Questions of the Study) and **QP4** (State of Research/State-of-the-Art of the Study)			■	■															
Block 5, 6, &7	**QP5** (Theoretical and Conceptual Framework of the Study) and **QP6** (Methodology I/Methodological Considerations of the Study)				■	■														
	Formative (Pilot) Phase and Operationalization of Study: Survey Instrument Development and Testing, Ethical Clearance, Recruitment & Training of Field Research Support Team, Cross-sectional Survey Data Collection in Ghana, Cross-sectional Survey Data Analysis, Trial Cereal Samples' Collection, Foodomics Laboratory Analysis, Data Analysis & Optimization of Analytical Laboratory Protocols						■	■	■											
Block 8	**QP7 (**Methodology II/Methodological Approach to the Study)								■											
	Definitive and Completion Phase of Study: Cross-sectional Survey Data Collection and Experimental Cereal Samples' Collection in Ghana								■											
Block 9, 10 & 11	**QP8** (Methods of Data Analysis & Preliminary Results of the Pilot Study), **QP9** (Protocol of the Definitive Study) and **QP10** (Descriptive Results of the Definitive Cross-sectional Survey)									■	■	■								
	Cross-sectional Survey Data Evaluation, Validation, Curation & Analysis GC-MS Foodomics Laboratory Analyses for the Relative Quantification of Nutritive and Non-nutritive Metabolites in Cereal Samples									■	■	■	■	■	■					
	Drafting, Reviewing, and Publication of Journal Article in *Nutrients*														■	■	■	■		
	UHPLC-MS/MS Foodomics Laboratory Analyses for the Absolute Quantification of Total Essential Amino Acids (Total Cereal Proteins)													■	■	■	■			
	GC-MS & UHPLC-MS/MS Data Evaluation, Validation, and Inferencing										■	■	■	■	■	■	■	■		
	Writing, Reviewing, Editing and Submission of Dissertation															■	■	■	■	■

*Doctoral Blocks; **QPs**, Qualifying Papers Submitted for Doctoral Block Seminars

"Printed on Permanent Paper °° ISO 9706"