

**Transition phase feeding in infants and children
(6–59 months) treated for severe acute
malnutrition in Ghanaian referral hospitals: the
SAMAC study**

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Dissertation submitted in fulfilment of the requirements for the
degree *Masters of Science in Dietetics*
at the North-West University

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Graduation:	July 2021
Student number:	33471177

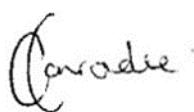
PREFACE

This mini-dissertation comprises four chapters written in article format. Chapter 1 is an introductory chapter that provides the aims, objectives of this study. Chapter 2 is a comprehensive review of the literature on the topic. Chapter 3 is an article to be submitted to the South African Journal of Clinical Nutrition titled “*Transition phase feeding in infants and children (6–59 months) treated for severe acute malnutrition in Ghana*,” written by Humphrey Chatenga, MSc student, according to the authors' instructions of the journal, and co-authored by Mrs Cornelia Conradie, Mrs Philna Neethling, Miss Sanele Nkomani, Mr Geoge Mwenyephiri and Dr Martani Lombard. All have agreed to the article's inclusion in this mini-dissertation, to examination and completion of the Master of Science degree in Dietetics. Chapter 4 discusses the findings of the study together with recommendations and conclusions of the study. The acknowledging of the references is at the end of each chapter.

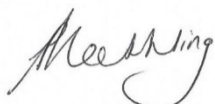
I, Humphrey Chatenga, hereby declare that with the exemption of the acknowledged references, I conducted the research to write this mini-dissertation at the Centre of Excellence for Nutrition at the North-West University under the supervision and guidance of Mrs Cornelia Conradie, together with Mrs Philna Neethling also from the Centre of Excellence for Nutrition at North-West University and Miss Sanele Nkomani of the Lilongwe University of Agriculture and Natural Resources in Malawi.



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Sanele Nkomani (Assistant-Supervisor)

ACKNOWLEDGEMENT

Glory and honour is onto you Lord for the grace, passion, patience, perseverance and energy granted upon me to complete this mini-dissertation.

My profound gratitude goes to the following people for their contribution in this research work:

- Mrs Cornelia Conradie, my supervisor, thank you for all the time you spent guiding, challenging and inspiring me, even during your maternity leave. The journey was winding, bumpy and rocky, but you made me the researcher I am today, I am honoured to learn from you.
- My co-supervisors, Mrs Philna Neethling and Miss Sanele Nkomani: thank you for your contribution on this work.
- Mr George Mwenyephiri, thank you for reviewing the statistics in this work.
- Dr Tani Lombard, thank you for your support and guidance during protocol development and article writing.
- To my colleagues, post-graduate students working on the SAMAC project – Doris, Luizer, Sunita and Magriet – do not give up, the daunting task has paid off.
- To the former MSc students, Hanna and Janet, and community health workers. Thank you for gathering data used in this study.
- To all my family members, Doris, Bernard, Mercy, Veronica, Martha and the Mndoliro's, especially Samuel, thank you for the motivation and prayers.
- The Supporting Nutrition Research in Africa and National Research Foundation, South Africa; thank you for the grants to study and funding the research work.

To my parents: thank you for your endless players, love, care and motivation.

Finally, I dedicate this work to my wife Lustia and my daughters Honorina and Faustina for your motivation, support and never-ending love. Thank you for you are always there for me, God bless you.

ABSTRACT

Introduction: Childhood wasting is a major public health problem owing to its associated risk for death from infectious diseases such as diarrhoea, pneumonia, and measles. Severe acute malnutrition (SAM), a severe form of wasting, affects 14.3 million children globally and is responsible for nearly half a million deaths of children under 5 years of age annually. Children with SAM who present with medical complications should be treated in hospitals or medical facilities as their mortality increases by 11-fold compared to non-wasted children. To reduce high case fatalities due to complicated SAM, the World Health Organization (WHO) developed therapeutic feeding guidelines for the treatment of complicated SAM. These guidelines, commonly known as “the ten steps,” are implemented in a two-phase approach, namely the stabilisation and rehabilitation phases. A gradual transition phase is proposed between these two steps to avoid feeding complications. However, there are no clear guidelines on ensuring that nutrition requirements are met during the transition phase due to a lack of data at the time the guidelines were updated. Gradual feeding is necessary, as a rapid introduction of a large amount of feed may cause, amongst others, poor feed tolerance. The WHO, hence, suggests the use of formula-100 (F-100) and/or ready-to-use therapeutic food (RUTF) during the transition phase with the number and skills of staff available supervising and monitoring feeds to ensure that nutritional requirements are met. The implementation of the transition phase in Ghanaian referral hospitals remains, as yet, unknown. Therefore, this study's evidence contributes to a better understanding of the transitional phase feeding practices applied in children with complicated SAM in Ghana. Additionally, this study will provide insight into how these practices link to clinical outcomes.

Methods: This study forms part of the SAMAC study, of which the protocol was previously published. The SAMAC study is an observational, multi-country, multi-hospital study coordinated by the Centre of Excellence for Nutrition at the North-West University in South Africa. Data for this sub-study was collected from medical records of children aged 6 to 59 months in three randomly selected referral hospitals in Ghana from January 2013 to June 2018. Data was captured into Microsoft Access and analysed using version 26 of IBM SPSS.

Results: Medical records of 380 children with complicated SAM were included in the analysis. The majority (54%) of children included were boys. Two hundred and twenty (58%) study participants were admitted at TTH, 94 (25%) at PML, and 66 (17%) at KATH. The median age of children at admission was 15 months (IQR: 10.0; 24.0 months), and the majority (41%) of those with SAM were within the 12 to 23 months age group. Nearly half (49%) of the children with complicated SAM presented with diarrhoea, 48% with vomiting, and 43% with dehydration on

admission. During the transition phase, the majority (40%) of children with complicated SAM, and treated at Ghanaian referral hospitals, were prescribed F-100, 32% were prescribed RUTF, 24% RUTF + F-75, and 2% were prescribed “other foods”. The median energy prescribed per kilogram body weight during the transition phase was 153.2 kcal/kg/day (IQR: 102.3; 208.3 kcal/kg/day), which was higher than the recommended 100 to 135 kcal/kg/day for the transition phase. Over-prescription of energy was present in 58% of children treated for complicated SAM while 26.8% had under-prescription of energy. Children aged 6 to 11 months across all the hospitals were prescribed the highest energy quantities, with a median of 172.4 kcal/kg/day (IQR 110.20; 219.96 kcal/kg/day). During the transition phase, 74 (21%) children had diarrhoea, and 26 (8%) children vomited. The majority (72%) of children with complicated SAM failed the transition phase on the first attempt. There were though no significant associations found between the transition feeding regimens and diarrhoea status, vomiting, and length of the transition. However, oedematous malnutrition, vomiting and diarrhoea during admission, and an HIV positive status were found to be predictors of vomiting and diarrhoea during the transition period, as well as increased length of the transition phase.

Conclusion: Most children treated for complicated SAM in Ghana were given WHO-recommended feeds during the transition phase. However, these transition feeding regimens were not significantly associated with diarrhoea status, vomiting, and length of the transition phase. In addition, the current transition feeding regimens recommended by WHO appeared to have a low transition success rate due to over-prescriptions which resulted in overfeeding and poor digestibility, as observed from previous studies. As we can predict that children with complicated SAM presenting with oedematous malnutrition, diarrhoea, vomiting and HIV at admission are likely to have a longer and more complicated transition, these populations could benefit from specialised feeds, for example, lactose free or a more cautious transition phase. Therefore, this calls for a study in this specific population to develop guidelines specific to them. We also recommend a large multi-hospital and rigorous controlled prospective study to explore the actual consumption and improvements in monitoring and documentation for children treated for complicated SAM.

Key terms: Severe acute malnutrition; transition feeding regimens; diarrhoea; vomiting; length of transition; referral hospitals.

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LIST OF ABBREVIATIONS

B.Sc.	Bachelor of Science
CEN	Centre of Excellence for Nutrition
CRF	Case Fatality Rate
Dr	Doctor
F-100	Formula 100
F-75	Formula 75
GHS	Ghana Health Service
GHS-ERC	Ghana Health Service Ethical Review Committee
GSS	Ghana Statistical Service
HAZ/LAZ	Height-for-Age Z-score/Length-for-Age Z-score
HIV	Human Immune Virus
HPCSA	Health Professions Council of South Africa
HREC	Health Research and Ethics Committee
ICF International	Inner-City Fund International
KATH	Komfo Anokye Teaching Hospital
MSc	Master of Science
MSF	Médecins Sans Frontières
MUAC	Mid-Upper Arm Circumference
NWU	North-West University
PEM	Protein Energy Malnutrition
PhD.	Doctor of Philosophy

LIST OF ABBREVIATIONS

PI	Primary Investigator
PML	Princess Marie Louise Children's Hospital
RD	Registered Dietitian
RUTF	Ready-to-Use Therapeutic Food
SAM	Severe Acute Malnutrition
SAMAC	Severe Acute Malnutrition in African Children
SD	Standard Deviation
SDG	Sustainable Development Goals
SPSS	Statistical Package for Social Science
SUNREA	Supporting Nutrition Research in Africa
TB	Tuberculosis
TTH	Tamale Teaching Hospital
UN	United Nations
UNDP	United Nations Development Programme
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
WAZ	Weight-for-Age Z-score
WHA	World Health Assembly
WHO	World Health Organization
WLZ/WHZ	Weight-for-Length/Height Z-score

LIST OF SYMBOLS AND UNITS

%	percentage
~	approximately
+	plus
<	less than
>	greater than
±	plus or minus
≤	less than or equal to
≥	greater than or equal to
cm	centimetre
e.g.	example
g	grams
g/kg	grams per kilogram
g/kg/day	grams per kilogram body weight per day
kcal	kilocalorie
kcal/kg/day	kilocalories per kilogram body weight per day
kg	kilogram
ml	millilitre
mmol	milli mole
α	alpha
β	beta

CHAPTER 1 INTRODUCTION

1.1 Introduction

The global rates in wasting (6.9%), severe wasting (2.1%), stunting (21.3%), and overweight (5.6%) among children under 5 years of age is insufficient to meet the 2025 World Health Assembly (WHA) global targets (Micha *et al.*, 2020; WHO, 2012). The 65th WHA global targets for childhood wasting, stunting, and overweight are 5%, 14.7%, and 10.6%, respectively (WHO, 2012). According to the Levels and Trends in Child Malnutrition (2018), severe acute malnutrition (SAM) affects 17 million (7.3%) children worldwide and is responsible for nearly half a million deaths of children under 5 years of age every year (UNICEF/WHO/World Bank Group, 2018). In sub-Saharan Africa, SAM affects 6.4% of children under 5 years of age (UNICEF/WHO/World Bank Group, 2020), while in Ghana, a country in Western Africa, 5.3% of children under 5 years of age are wasted and 1% have SAM (Boah *et al.*, 2019).

Research shows optimal nutrition alongside health, learning, responsive caregiving, security, and safety in children under 5 years of age allows them to survive and thrive and contribute to a country's development (Black *et al.*, 2020). Conversely, malnutrition robs children of their futures and leaves young lives hanging in the balance (UNICEF/WHO/World Bank Group, 2020). The Maternal Infant and Young Child (MIYC) nutrition targets for wasting are to attain a rate of less than 5% by 2025 and bring the level of wasting to less than 3% by 2030 (UNICEF, 2018; WHO/UNICEF/WFP, 2014). For childhood stunting, the MIYC nutrition target for 2025 is 14.7%, while the 2030 target is to reduce the number of stunted children by 50% globally. The 2025 MIYC nutrition target for childhood overweight is to maintain its prevalence at 6% and reduce it to less than 3% by 2030 (UNICEF, 2018).

Africa and Asia bear the greatest burden of all forms of malnutrition (UNICEF/WHO/World Bank Group, 2020). According to the Levels and Trends in Child Malnutrition: Key Findings of the 2020 Edition of the Joint Child Malnutrition Estimates, in Africa, 40%, 27%, and 24% of children under 5 years are stunted, wasted and overweight, respectively. Ghana shows a progressive decline in all forms of undernutrition from 2003 to 2019, where wasting declined from 8% in 2003 to 5.3% in 2019. Stunting has also declined from 35% in 2003 to 18.4% in 2019 (Boah *et al.*, 2019).

Undernutrition, specifically wasting, remains a major global health concern, as it is associated with frequent illnesses and deaths owing to excessive weight loss (Bhan *et al.*, 2003; UNICEF, 2018). Children with a severe form of wasting, which is also referred to as SAM, are 11 times more likely to die than their healthy counterparts (McDonald *et al.*, 2013). The (WHA) highlights

that if wasting is not managed appropriately alongside reducing hunger, it will be difficult to continue improving child survival rates (UNICEF, 2018).

Wasting refers to thinness measured by a weight-for-height/length z-score (WH/LZ) of less than -2 standard deviation (SD) of the World Health Organization (WHO) growth standards (WHO, 2013). A WHZ score of less than -3 SD of the WHO growth standards is indicative of SAM (Briend, 2018; WHO, 2013). Severe acute malnutrition can also be diagnosed based on a mid-upper arm circumference of less than 115 mm, or by the presence of bilateral pitting oedema in children 6-59 months old (WHO, 2013).

1.2 WHO guidelines for the treatment of SAM

The treatment of SAM depends on the child's clinical presentation (Ashworth *et al.*, 2003). Infants and children with SAM who present without medical complications are classified as uncomplicated SAM, and are treated in the community (Ashworth *et al.*, 2003; WHO, 2013). However, those with SAM who present with medical complications are classified as complicated SAM (Ashworth *et al.*, 2003) and are treated in a hospital or a medical facility (Ashworth *et al.*, 2003; WHO, 2013); these medical complications include bilateral pitting oedema, poor appetite, infections such as pneumonia, malaria, diarrhoea, measles, fever, among other integrated management of childhood illnesses. Children with complicated SAM have altered functionality in the body systems (Ashworth *et al.*, 2003; National Department of Health, 2015). This change reduces a child's adaptation responses to life-threatening complications such as infections, inappropriate fluid replacements, and feeding optimally (National Department of Health, 2015; Rytter *et al.*, 2017).

Children with SAM require systematic medical treatment for underlying infections and a dietary treatment with specially formulated therapeutic foods (Ashworth *et al.*, 2003; National Department of Health, 2015). Hence, the WHO formulated specific guidelines for the treatment of complicated SAM in 1999, which were updated in 2003 and 2013 to reduce poor case-fatality rates associated with therapeutic fluid replacements and feeding practices (Ashworth *et al.*, 2003); these guidelines are referred to as the 'WHO 10-Step Plan for the Management of Complicated SAM,' also known as 'The Ten Steps' (Ashworth *et al.*, 2003). These ten-steps are accomplished using two phases, namely the stabilisation phase and the rehabilitation phase. A successful change from the initial stabilisation to the rehabilitation phase in children with complicated SAM requires a gradual transition period, referred to as the transition phase (Ashworth *et al.*, 2003). The gradual transition phase is important as it reduces feeding complications associated with a rapid intake of a large amount of feed, such as diarrhoea, vomiting, and electrolyte imbalance (Manary *et al.*, 2012; WHO, 2013).

The most common feeding complication observed in children with complicated SAM is osmotic diarrhoea. Osmotic diarrhoea refers to increased faecal flow volume and frequency because of the ingestion of a poorly absorbed solute that inhibits normal water and electrolyte absorption (Frothingham & Sethi, 2018). In infants and children with SAM, osmotic diarrhoea is attributable to the insufficient intestinal absorption capacity of nutrients because of villous atrophy and pancreatic insufficiency (Bandsma *et al.*, 2019; Golden & Grellety, 2011).

1.3 Study rationale

The WHO indicates that by adhering to its 10-Step plan to manage complicated SAM, a case fatality rate of less than 10% could be achieved (Ashworth *et al.*, 2003; Sphere Association, 2018). However, health centres and hospitals in sub-Saharan Africa have reported mortality rates ranging between 10 and 40% among infants and children with complicated SAM (Fergusson & Tomkins, 2009; Kerac *et al.*, 2014). Nevertheless, in Ghana, the complicated SAM mortality rate in hospitals decreased significantly from 5.8% in 2015 to 1.9% in 2017 (Choi *et al.*, 2020), which is within the acceptable national standards for mortality rate (less than 10%) (Sphere Association, 2018). Besides this progress, the therapeutic feeding practice for children treated for complicated SAM, especially during the transition period in Ghanaian hospitals, has not been evaluated (Akparibo *et al.*, 2017).

The rapid introduction of high-protein and high-energy diets, such as RUTF and F-100, has been associated with feeding complications (WHO, 2013). These complications include vomiting, diarrhoea, abdominal distention, electrolyte imbalance and sudden death (Mbethe & Mda, 2017; Okinyi, 2018; WHO, 2013). Hence, the WHO recommends a gradual transition of feeding between the stabilisation and rehabilitation phases to avoid these feeding complications (WHO, 2013). However, the WHO's guideline development group failed to provide a straightforward feeding approach to meet optimal nutrition requirements of 100–130 kcal/kg/day for the transition phase due to a lack of research to support this guideline's formulation (WHO, 2013).

The transition phase feeding recommendations were initially made based on clinical experience and the understanding of human physiology due to the absence of trial-based evidence (Manary *et al.*, 2012). The WHO made the last updates to the guidelines for the transition phase in 2013. During this update, a systematic review was conducted, which reported there were no trials that critically examined the transition phase feeding practice regarding either having the transition phase approach or an alternative approach without the transition phase. Also, there were no comparative trials identified that examined the composition or amounts of food offered upon completion of the stabilisation phase (Manary *et al.*, 2012).

CHAPTER 1 INTRODUCTION

Since 2012, there are only two clinical trials published on therapeutic feeding during the transition phase in children with complicated SAM (Lanyero *et al.*, 2017; Versloot *et al.*, 2017). In the study by Lanyero *et al.* (2017), the testing of the transition from F-75 to RUTF was with 400 children treated for complicated SAM in Uganda. In this study, children received half of the nutrients required during the transition phase from RUTF and the other half from F-75; RUTF was gradually increased to be the only source of energy. Only 65% of children completed the transition phase within the recommended 2–3 days on the first attempt recommended by WHO. Younger children, severely wasted, HIV-infected children, and those with severe illness were predictors of failure to transition. In this study, a child was classified to have failed the transition if he or she failed the appetite test, developed profuse diarrhoea or vomiting when RUTF was ingested, or those who had progressively reduced RUTF intake during the subsequent days (Lanyero *et al.*, 2017).

According to Versloot *et al.* (2017), the effectiveness of the three transition feeding approaches, F-100, RUTF, and RUTF + F-75, were tested in 74 children with complicated SAM (Versloot *et al.*, 2017). In this trial, clinical outcomes, such as diarrhoea incidence, weight gain, length of hospital stay and mortality, were similar among the three groups of children treated for complicated SAM at the nutrition rehabilitation unit in Malawi (Versloot *et al.*, 2017). However, this study did not explore the actual implementation in terms of the composition or amounts of therapeutic diet offered during the transition phase, noted in the 2012 systematic review (Manary *et al.*, 2012; Versloot *et al.*, 2017).

Based on current evidence, data on the composition or amounts of food offered during the transition phase for children treated for complicated SAM are limited (WHO, 2013), with evidence informing the practice of transition phase feeding being inadequate (WHO, 2013). This study, which focuses on the transition phase of the WHO's ten steps, is part of a larger study called Severe Acute Malnutrition in African Children (SAMAC). The larger study aims to evaluate the admission criteria and treatment guidelines in children diagnosed with complicated SAM (Carboo *et al.*, 2020). However, this SAMAC sub-study explores different transition feeding approaches used in Ghana to establish associations between the feeding approaches and clinical outcomes, such as vomiting, diarrhoea status, and length of the transition phase. This study's evidence contributes to a better understanding of the transitional phase feeding practices applied in children with complicated SAM in Ghana. In addition, this study will provide insight into how these practices link to clinical outcomes.

1.4 Research aim and objectives

This sub-study aimed to determine the associations of the feeding regimens used during the transition phase with vomiting, diarrhoea status, and the duration of the transition phase in infants and children (6–59 months) treated for complicated SAM in three Ghanaian referral hospitals.

The objectives of this study were to:

- 1 Identify the transition feeding regimes used for the management of children (6–59 months) with complicated SAM in three Ghanaian referral hospitals
- 2 Describe:
 - a. the total energy prescribed per kilogram body weight (kcal/kg/day) by considering the volume of transition feed prescribed;
 - b. vomiting and diarrhoea that developed during the transition phase;
 - c. the number of days spent in the transition phase
- 3 Determine the associations of the transition feeding regimens with vomiting, diarrhoea, and length of the transition phase.

The discussion and reporting of the results of this sub-study are as pooled data and per hospital, gender, and age group (6–11 months; 12–23 months; 24–59 months).

1.5 Overview of the SAMAC study

This study forms part of the SAMAC larger study of which the protocol was previously published (Carboo *et al.*, 2020). The SAMAC study is a multi-country, multi-hospital study coordinated by the Centre for Excellence for Nutrition at the North-West University in South Africa. This study works in South Africa, Ghana, Botswana, Kenya, and Malawi. In brief, the SAMAC study collects data from medical records of infants and children aged 0–59 months treated for complicated SAM from the five countries.

The SAMAC study extracts data from medical records for children diagnosed with conditions or diseases related to complicated SAM, provided they had a WH/LZ of less than -3 SD, MUAC of less than 115mm, or generalised pitting oedema. These conditions included recurring infections, malaria, dehydration, diarrhoea, TB, parasite infestations, cholera, etc. Children admitted with medical problems unrelated to complicated SAM had their medical records excluded, including those with unspecified metabolic neurodevelopmental conditions or any other growth disorders, as their nutrition needs differed from children with SAM without these other disorders. Medical records of children with multiple admissions were noted as new cases. Data for the SAMAC study was collected by trained research assistants using a research tool adapted from the WHO admission criteria and treatment guidelines to treat SAM (WHO, 2010).

The study used secondary data for medical records of children aged 6-59 months, extracted from Ghanaian referral hospitals between 2013 and 2018. These hospitals were Komfo Anokye Teaching Hospital (KATH), Princess Marie Louise (PML) Children's Hospital, and the Tamale Teaching Hospital (TTH). Excluded were children without a documented transition feeding record, and multiple admissions.

1.6 Ethical approval

The SAMAC larger study, of which this study forms part, received approval from the Health Research and Ethics Committee (HREC) at North-West University (NWU) (NWU-00063-17-A1) (Annexure 1). The HREC granted ethical approval (NWU-00063-17-A1-08) (Annexure 2). Additional ethical clearance was also obtained from the Ghana Health Ethics Review Committee (GHS-ERC) (GHS-ERC 09/06/2017) and the School of Medical Sciences, Komfo Anokye Teaching Hospital Committee on Human Research, Publication and Ethics (CHRPE/AP/374/17) in Ghana (Annexure 3 and 4). Letters of approval were also obtained from KATH, PML and TTH (Annexure 5, 6, and 7).

1.7 The research team and their contributions

Table 1.1 provides a summary of the research team members involved in this sub-study and their contribution. None of the research team members had a conflict of interest to declare.

Table 1-1: Research team members and their roles

Name of Partner	Team member	Qualification	Professional registration	Role and responsibilities
North-West University (South Africa)	Mr Humphrey Chatenga	Postgraduate Diploma in Clinical Dietetics	Registered Dietitian (RD) Medical Council of Malawi	Responsible for the planning, implementation, and management of this project He compiled the literature review, statistical analysis, interpretation of data, and writing-up of this mini-dissertation.
	Mrs Cornelia Conradie	MSc Dietetics	RD, Health Professions Council of South Africa (HPCSA)	The primary investigator (PI) of SAMAC larger study Supervisor for this sub-study Postgraduate supervision
	Mrs Philna Neethling	MSc Dietetics	RD, HPCSA	Co-supervisor Postgraduate supervision
	Dr Martani Lombard	PhD Dietetics	RD, HPCSA	PI-SAMAC larger study Oversaw the data analysis
Lilongwe University of Agriculture and Natural Resources (Malawi)	Miss Sanele Nkomani	MSc Nutrition BSc Dietetics	RD, Medical Council of Malawi	Assistant-supervisor Postgraduate supervision

1.8 Structure of this mini-dissertation

Chapter 1 is the introduction chapter and comprises the general overview of childhood malnutrition globally and in Ghana. The chapter also discusses the study rationale, aim, and specific objectives of this sub-study. Chapter 2 comprises the literature review. This chapter provides a detailed understanding of malnutrition, its classifications and determinants, and further discusses childhood malnutrition trends in Ghana and current management protocols for complicated SAM in Ghana. Finally, the chapter discusses studies reporting feeding practices for children with complicated SAM. Chapter 3 comprises the article for publication, entitled “*Transition phase feeding in infants and children (6–59 months) treated for severe acute malnutrition in Ghana.*” The article will be submitted for publication in the South African Journal of Clinical Nutrition. In this chapter, all references and language formats are according to the authors' specifications by the journal (Annexure 11). Chapter 4 concludes the mini-dissertation. It provides a summary of the study, along with proposed recommendations and future research. The citations' references appear at the end of each chapter in the modified Harvard style, as required by the North-West University.

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CHAPTER 2 LITERATURE REVIEW

2.1 Introduction

According to the World Health Organization (WHO), childhood malnutrition remains a public health burden, especially in low- and middle-income countries (WHO, 2020a). The United Nations Children's Fund (UNICEF) estimated that every year, 3 million children's lives (45%) under 5 years of age are lost unnecessarily because of malnutrition (UNICEF/WHO/World Bank Group, 2018; WHO, 2019). The WHO defines malnutrition as an imbalance between nutrient requirements and dietary intake that results in deficits or excess in energy, protein, and micronutrient stores (WHO, 2020b). Malnutrition includes both overnutrition and undernutrition (Lenters *et al.*, 2016; WHO, 2020b). Overnutrition is associated with overweight, obesity, and diet-related non-communicable diseases (such as heart diseases, stroke, diabetes, and cancer). Undernutrition encompasses acute, chronic, and micronutrient malnutrition (Lenters *et al.*, 2016; Mehta *et al.*, 2017). This literature review focuses on undernutrition, particularly severe acute malnutrition (SAM).

In understanding SAM in children under 5 years of age, this literature review firstly summarises the classification of childhood undernutrition. Secondly, it explores the causes or determinants of childhood undernutrition in children under 5 years of age. Thirdly, it discusses the status of childhood malnutrition in Ghana. This review further deliberates SAM in terms of definition, pathophysiology, and its current management protocols. Finally, the review highlights the studies that report feeding practices in children treated for complicated SAM in a hospital setting.

2.2 Classification of childhood malnutrition

The WHO classifies childhood undernutrition into four broad categories: underweight, stunting, wasting, and micronutrient deficiencies (WHO, 2020b). The basis for these classifications is on three anthropometric indices, namely length/height-for-age -score (LAZ/HAZ), weight-for-age z-score (WAZ), and weight-for-length/height z-score (WHZ/WLZ), respectively. These WHO indices are used to measure growth standards, which essentially determine the degree to which physiological needs for growth and development are met during critical periods of childhood growth and development (WHO, 2006). The WHO growth standards were developed using data collected in the WHO Multicentre Growth Reference Study, which included 8500 children from widely different ethnic backgrounds and cultural settings, and reflected ideal conditions for growth in Brazil, Ghana, India, Norway, Oman and the USA (WHO, WHO, 2020). A z-score, or standard deviation (SD), is the deviation of the value for an individual from the median value of the reference population, divided by the standard deviation for the reference population in the WHO

growth standards (WHO, 2006). A child may present with one or a combination of the forms of undernutrition (WHO, 2020b). The following section, briefly explains each form of childhood malnutrition.

2.2.1 Underweight

The definition of underweight is a WAZ below -2 SD and severe underweight as a WAZ below -3 SD of the WHO growth standards (WHO, 2016). Since underweight only requires a child's weight, which is relatively simple to measure, this is the indicator for which most data were collected in nutrition surveys in the past (WHO, 2010). However, as length/height is not considered, underweight is a composite indicator, as it may reflect either stunting, wasting, or both (FAO, 2007; WHO, 2016; WHO, 2020b). Underweight therefore has a high positive predictive value as an indicator of child malnutrition in lower-and middle-income countries (Fishman *et al.*, 2004). According to the WHO, the global prevalence of underweight has declined from 28% in 1990 to 17% in 2013, but persists in lower-and middle-income countries where poverty is a strong underlying determinant (Fishman *et al.*, 2004; WHO, 2018).

2.2.2 Stunting

Stunting indicates a restriction of a child's potential linear growth and is a reflection of chronic malnutrition (Black *et al.*, 2008). A child with a LAZ/HAZ of less than -2 SD is classified as moderately stunted, and one with a LAZ/HAZ of less than -3 SD as severely stunted (UNICEF, 2013; WHO, 1997). Stunting may begin in utero and continue through early childhood if nutrient requirements are persistently unmet (Bhutta *et al.*, 2008). Stunting is associated with poor socioeconomic conditions, which are directly linked with unsafe water, lack of hygiene and sanitation, poor maternal health and nutrition, frequent illness, and/or inappropriate infant and young child feeding and care in early life (UNICEF/WHO/World Bank Group, 2020; WHO, 2020b). The effects of stunting are not always immediately visible (Black *et al.*, 2008). However, stunted children begin their lives at a marked disadvantage and may never attain their full physical and cognitive potential because of two plausible reasons (Leroy & Frongillo, 2019; UNICEF/WHO/World Bank Group, 2020; WHO, 2020b). Firstly, stunted children have reduced motor activity, which is related to their smaller body size (Leroy & Frongillo, 2019); this limits the child's ability to explore and access stimulation, thereby reducing the opportunities for language, socioemotional, and cognitive development (Larson & Yousafzai, 2017; Sudfeld *et al.*, 2015). Secondly, short child stature lowers caregivers' expectations about children's developmental potential, especially in societies where a number of children suffer from some degree of linear growth retardation (Aboud & Aisha, 2015); eventually, these children receive minimal stimulation from caregivers (Aboud & Aisha, 2015).

The prevalence of stunting among children under 5 years of age has reduced globally from 32.2% in 2000 to 21.3% in 2019 (UNICEF/WHO/World Bank Group, 2020). This reduction is attributed to improvements in household income, which leads to improved access to nutritious food, clean water, sanitation facilities and medical care (Vaivada *et al.*, 2020). In addition, improvements in maternal educational attainment and lower fertility rates have also contributed to this reduction (Headey, 2013; Vaivada *et al.*, 2020). Current statistics show that stunting has reduced by over two-thirds, mainly in upper-middle-income countries, because of improvements in maternal and paternal education, household socioeconomic status, sanitation conditions, maternal health services access, and family planning (Vaivada *et al.*, 2020). In Africa, however, the number of stunted children has risen from 49.7 million in 2000 to 57.5 million in 2019 (UNICEF/WHO/World Bank Group, 2018; UNICEF/WHO/World Bank Group, 2020). The United Nations Children's Fund and Vaivada *et al.* ascribed a rise in stunting in Africa to slow rates of stunting reduction by individual countries and high fertility rates (UNICEF, 2019; Vaivada *et al.*, 2020). In Africa, only 3 to 39% of children aged 6 to 23 months receive minimum acceptable diets, and 36% of households have poor access to clean and adequate water and sanitation facilities (UNICEF, 2019). This leads to a higher incidence of infectious diseases, including diarrhoea and worm infestation, which are associated with stunting (Goyal & Canning, 2017; Ikeda *et al.*, 2013).

2.2.3 Wasting

Wasting refers to thinness measured by a low WH/LZ compared to WHO growth standards (WHO, 2016) and represents acute malnutrition. If a child's WH/LZ is less than -2 SD but more than -3 SD, their classification is moderate wasting or moderate acute malnutrition (MAM). If a child has a WH/LZ of less than or equal to -3 SD, the classification is severely wasted, also known as SAM (WHO, 2020b). Wasting indicates acute malnutrition resulting from a recent weight loss or failure to gain weight (Lenters *et al.*, 2016). Childhood wasting results from poor access to appropriate, timely and affordable, healthcare, dietary inadequacy, inadequate caring practices, maternal stature and inappropriate complementary feeding practices (Arimond & Ruel, 2004; Özaltın *et al.*, 2010; Richard *et al.*, 2013). Wasting can also result from infectious diseases, such as malaria or cholera. These diseases often trigger weight loss because of diarrhoea and poor appetite (Black *et al.*, 2008; Lenters *et al.*, 2013; Smith & Haddad, 2000). Severe weight loss weakens a child's immune system, increases long-term developmental delays, and increases the risk of death (UNICEF/WHO/World Bank Group, 2020). Poor immunity resulting from wasting, fuels the vicious cycle of wasting and infection (Black *et al.*, 2008). When wasting becomes severe, the child develops severe health consequences, such as bilateral pitting oedema, because of the interaction between nutrient deprivation, infection and the immune response (Golden, 2015; Harding *et al.*, 2018).

Figure 2-1 shows the prevalence of wasting in the United Nations regions (UNICEF/WHO/World Bank Group, 2020). Currently, 47 million (6.9%) children under 5 years of age are wasted, of which 14.3 million are severely wasted. Among the severely wasted children, 3.5 million (6.4%) live in Africa (UNICEF/WHO/World Bank Group, 2020). The global nutrition targets for wasting on Maternal Infant and Young Child nutrition (MIYC) is to reduce and maintain childhood wasting to less than 5% by 2025 (WHO/UNICEF, 2019; WHO/UNICEF/WFP, 2014), whereas the proposed MIYC target for wasting for 2030 is to bring the level to less than 3% (WHO/UNICEF, 2019). Countries with a childhood wasting prevalence of 5 to 9% are perceived as having achieved medium progress toward eradicating wasting (De Onis *et al.*, 2019; Micha *et al.*, 2020). These countries require a 2% or greater annual rate of reduction to achieve the 2025 global target for wasting reduction, and then maintain childhood wasting levels below 5% (Micha *et al.*, 2020; WHO/UNICEF/WFP, 2014).

Wasting is a major health problem due to its associated risks for death from infectious diseases, such as diarrhoea, pneumonia and measles (Pelletier *et al.*, 2013). The WHA indicates that to improve rates of child survival among those who are wasted, it is essential to provide timely life-saving treatment, alongside reductions in the number of children becoming wasted in the first place (WHO/UNICEF/WFP, 2014). Children who are wasted require promotion and support for breastfeeding to the mother, nutrition counselling for families regarding complementary feeding practices, and food supplements, otherwise moderately wasted children deteriorate into SAM, which increases their risk of death (Chang *et al.*, 2013; James *et al.*, 2016).

While countries agree that tackling malnutrition is critical in achieving sustainable development goals (SDGs), gaps in understanding severe forms of wasting exist (Mogeni *et al.*, 2011; UN, 2015). For example, in countries such as Bangladesh, Niger, Chad and South Sudan, the prevalence of wasting fluctuated around 15% in the last decade despite substantial humanitarian efforts (Micha *et al.*, 2020). The prevalence of wasting has remained high in Western Africa despite the decline from 11.6% in 1990 to 7.1% in 2017 (Akombi *et al.*, 2017a; UNICEF/WHO/World Bank Group, 2012; WHO, 2019). Additionally, studies show that hospitals in sub-Saharan Africa have continued to report high rates of mortality (10–40%) among infants and children with severe wasting, this questions the practicality in the implementation of the ten-steps by the hospitals (Fergusson & Tomkins, 2009; Kerac *et al.*, 2014; Tickell & Denno, 2016). In Ghana, a country in Western Africa, 5.3% of children under 5 years of age are wasted (Boah *et al.*, 2019). In 2012, Princess Marie Louise Children's Hospital (PML), one of the randomly selected hospitals for this study in Ghana, reported a mortality rate of 11.2% for children treated for complicated SAM (Tette *et al.*, 2015); this mortality rate was above the acceptable standard of less than 10% (Sphere Association, 2018).

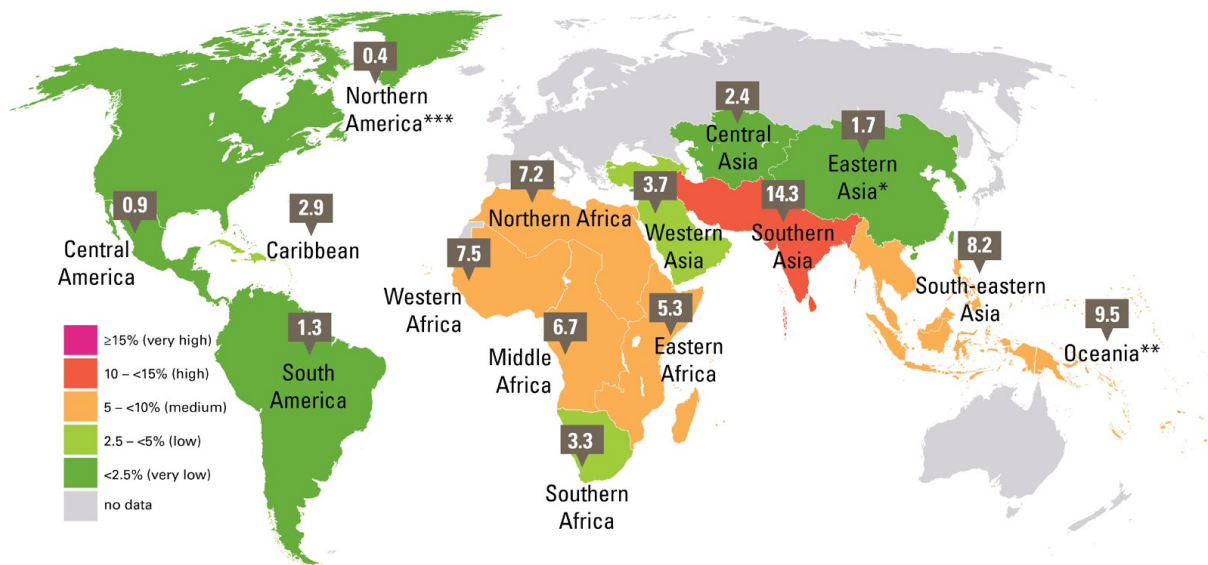


Figure 2-1: Percentage of wasted children under 5 years of age by United Nations sub-region 2019

Source: UNICEF, WHO, World Bank Group joint malnutrition estimates, 2020 edition. Note: *Eastern Asia excluding Japan; **Oceania excluding Australia and New Zealand; ***Northern America sub-regional estimate based on United States data.

2.2.4 Deficiencies in vitamins and minerals

Ritchie and Roser (2017) define micronutrient deficiencies as a lack of essential vitamins and minerals required in small amounts by the body for optimal growth and development, and they are also known as “hidden hunger” (Bailey *et al.*, 2015; USAID/UNICEF/WHO/World Bank, 2009; WHO, 2020b). Micronutrients enable the body to produce enzymes, hormones and other substances essential for optimal growth and development (WHO, 2020b). The causes of micronutrient deficiencies include intake of food with insufficient nutrient content coupled with insufficient absorption, poor sanitation, infection, and/or lack of education and healthcare (UNICEF, 2013; USAID/UNICEF/WHO/World Bank, 2009). Micronutrient deficiencies contribute to poor health and development in children under 5 years of age (Bailey *et al.*, 2015; Black *et al.*, 2008). Micronutrient deficiencies are frequent complications encountered by children with complicated SAM (Bailey *et al.*, 2015; Black *et al.*, 2013).

Vitamin A, iron and iodine are the most important micronutrients in global public health terms (WHO, 2020b). Deficiencies of these micronutrients, mainly in children and pregnant women, represent a major threat to health and development in low-income countries (WHO, 2020b). In Ghana, 80 to 95% of children under 5 years of age with SAM present with iron deficiency anaemia (GSS/GHS/ICF International, 2015). The causes of iron deficiency in Ghanaian children include inadequate intake from the diet, malaria, and/or intestinal worm infestations (GSS/GHS/ICF

International, 2015; WHO, 2011). According to Balley *et al.* (2015), individuals with iron deficiency anaemia have impaired work capacity, decreased immunity and endocrine functions. The prevalence of vitamin A deficiency is not well documented in Ghana, nevertheless, children under 5 years of age receive vitamin A supplements (GSS/GHS/ICF International, 2015).

2.3 Determinants of childhood malnutrition

Childhood malnutrition is the result of multifactorial determinants, including inadequate and non-nutritious food, frequent illness, poor care practices, and lack of access to health and other social services (Smith & Haddad, 2000; UNICEF, 2013; UNICEF, 2015). These determinants were first outlined in a conceptual framework two decades ago by UNICEF (UNICEF, 2010). The UNICEF conceptual framework has been widely adopted by both the development and humanitarian spheres (WHO., 2020). However, the framework requires adaptation to address the gaps that would allow children to grow and develop to their potential; these gaps include nutrition, learning, responsive caregiving, safety and security (Black *et al.*, 2020; H., 2020). In the UNICEF framework, malnutrition causes are expressed as either immediate, underlying or basic (UNICEF, 2013).

2.3.1 Immediate causes of undernutrition

The immediate causes of malnutrition, influenced by the basic and underlying causes, can manifest at an individual level because of inadequate food intake and/or disease (UNICEF, 2013; UNICEF, 2015). These causes create a vicious cycle of malnutrition, in which the disease and inadequate dietary intake exacerbate each other (UNICEF, 2013). Rodríguez *et al.* (2011) and UNICEF (2015) indicated that acute infections increases catabolism and malabsorption while decreasing appetite, this may induce malnutrition or exacerbate pre-existing malnutrition. Likewise, undernutrition decreases immune functions thereby increasing the child's susceptibility to infections and mortality (Black *et al.*, 2013). Thus, for a successful recovery of malnutrition, both food intake and disease must be addressed (UNICEF, 2013).

2.3.2 Underlying causes of undernutrition

The underlying causes of malnutrition are affected by the basic causes, including inadequate food supply, income and poverty, maternal education, investment in health services, infrastructure, and social protection schemes (UNICEF, 2013). Underlying causes of undernutrition include inadequate household food security (limited access or availability of food), inadequate social and care environments in the household and local community for women and children. Underlying causes of malnutrition result from limited access to adequate health services and/or inadequate environmental health conditions (including access to safe water and sanitation facilities) (Akombi

CHAPTER 2 LITERATURE REVIEW

et al., 2017b; Black *et al.*, 2013). The underlying causes of childhood malnutrition lead to immediate causes of malnutrition (Smith & Haddad, 2000; UNICEF, 2015).

According to the World Bank, food security is achieved when a person can access enough food to lead an active and healthy life (World Bank, 1986). Globally, 690 million people were food insecure in 2019, which showed impeding optimal nutrition to children (FAO/IFAD/UNICEF/WFP/WHO, 2019). Childhood undernutrition can begin in the womb and propagate across generations when a mother, who does not meet nutrition intake requirements during pregnancy, gives birth to an already stunted infant (Black *et al.*, 2008; Reinhardt & Fanzo, 2014). The halting of the intergeneration cycle of malnutrition can occur if the mother and child's health is optimised (Akombi *et al.*, 2017b; Black *et al.*, 2013; UN, 2015). Households access food through food production, income for food purchases, or in-kind transfers of food (whether from other private citizens, national or foreign governments, or international institutions) (UNICEF, 2015).

The second underlying determinant for childhood undernutrition is care. In children under the age of five years, care includes child feeding, health-seeking behaviours, support and cognitive stimulation for children, and care and support for mothers during pregnancy and lactation (Smith & Haddad, 2000; UNICEF, 2015). These caring practices ensure optimal growth and development in children (Smith & Haddad, 2000). However, such care's adequacy is determined by the caregiver's control of economic resources, autonomy in decision making, and physical and mental status (Smith & Haddad, 2000).

The third underlying determinant of child undernutrition is a healthy environment and services (Smith & Haddad, 2000; UNICEF, 2015). This determinant rests on the availability of safe water, sanitation, healthcare and environmental safety, including shelter (Smith & Haddad, 2000; UNICEF, 2015). In 2016, the United Nations Development Program (UNDP) estimated that 400 million people lacked access to basic healthcare services and therefore failed to achieve optimal care for children (UNDP, 2016). Poor sanitation and inadequate healthcare facilities increase the risk of infection, leading to malnutrition (Rodríguez *et al.*, 2011). The UN has included increased access to quality essential healthcare services and access to safe, effective, quality, and affordable essential medicines and vaccines in its SDG number three (UN, 2015). Research has shown that childhood malnutrition reduces productivity and family income, as adults spend more money and time caring for a malnourished child who gets infections frequently (Rodríguez *et al.*, 2011).

Poverty is a crucial factor affecting all underlying causes of childhood malnutrition (Smith & Haddad, 2000). When households lack basic needs such as food, health, water, shelter, primary education, and community participation, they are classified under the absolute poverty bracket (Frankenberger, 1996). The effects of poverty on child malnutrition are persistent. Thus, poor households and individuals cannot achieve food security, have inadequate resources for care, and cannot utilise (or contribute to the creation of) resources for health sustainably (Smith & Haddad, 2000).

2.3.3 Basic causes of undernutrition

The basic causes of undernutrition address systematic level challenges that reflect the structural and political process at society level (UNICEF, 1990). Basic causes also influence child undernutrition's underlying causes (Smith & Haddad, 2000; UNICEF, 1990; UNICEF, 2015). Basic causes of undernutrition include the societal structures and processes that neglect human rights and perpetuate poverty. In addition, the basic causes of undernutrition limit the access of vulnerable populations to essential resources and social, economic, and political factors that have a long-term influence on maternal and childhood undernutrition (Bellamy, 1998; UNICEF, 1990; UNICEF, 2013). All these basic factors influence the nutrition status of an individual (UNICEF, 2015).

Firstly, societal structures such as land (for food production), education, employment, and income, available to a country or community are limited by the natural environment, access to technology, and human resources quality (Smith & Haddad, 2000; UNICEF, 1990). However, these structures are affected by their governance and allocation by communities (UNICEF, 1990). Lack of these resources at community level denies households access to essential resources for food production and healthcare (UNICEF, 2015). It is common knowledge that childhood undernutrition is most common in underprivileged households as they lack the resources to buy enough food and healthcare services (Black *et al.*, 2008; Ricci *et al.*, 2019).

Secondly, childhood undernutrition results from inadequate financial, human, physical, and social capital resources (Smith & Haddad, 2000; UNICEF, 2015). In this context, children most affected by malnutrition come from households with the lowest incomes, who are most economically and socially marginalised, and whose livelihoods are most eroded (FAO, 2015). The 2007 review by Banerjee and Duflo also highlighted inadequate financial resources. Banerjee & Duflo (2007) reported that households that are underprivileged are less likely to buy food, invest little or none of their income in education, and take loans at higher interest rates. These factors limit household knowledge on nutritious food choices, sanitation, and healthcare choices (Banerjee & Duflo, 2007).

Finally, at household and national levels, the distribution of resources depends on the political, economic, and social factors (UNICEF, 1990). For instance, policy decisions and economic situations caused by inflation or war, can cause undernutrition (UNICEF, 2015); for example, war can lead to insufficient food production as people migrate from their production land, whereas high inflation can lead to high production costs. These factors will all contribute to poor access to food by the households leading to malnutrition (FMOH, 2011; Smith & Haddad, 2000; UNICEF, 2015). According to the 2014 Demographic and Health Survey (DHS) report, the following basic predictors were associated with childhood undernutrition in Ghana: wealth index of the household, paternal educational status, and residence region (Boah *et al.*, 2019). Children from households with middle to higher wealth index had increased access to household dietary needs, healthcare services, and better living conditions (Boah *et al.*, 2019; GSS/GHS/ICF International, 2015); in addition, children from middle-income households had low rates of childhood undernutrition. Children born from fathers with less education had an increased risk of undernutrition, resulting in low household wealth status, food insecurity, and poor general living conditions. High rates of childhood malnutrition in Ghana's Northern region were also associated with ecological constraints, food insecurity and poverty (Boah *et al.*, 2019; GSS/GHS/ICF International, 2015).

2.4 Childhood malnutrition in Ghana

Trends in Ghana show a progressive decline in all forms of malnutrition in children under 5 years of age from 2003 to 2014. **Figure 2-2** shows stunting, wasting, and underweight trends in Ghanaian children under 5 years of age based on the DHS of 2003, 2008, and 2014 (GSS/GHS/ICF International, 2015). The 2014 DHS shows that wasting and underweight in Ghanaian children posed a medium level of importance, according to WHO classification for assessing the severity of malnutrition by prevalence (WHO, 2020a). However, these trends do not provide contentment grounds until childhood malnutrition is eradicated (Micha *et al.*, 2020; UN, 2015).

Underweight affects 11%, while severely underweight affects 2% of children under 5 years of age in Ghana (GSS/GHS/ICF International, 2015). Currently, 5.3% of Ghanaian children under 5 years of age are wasted, of which 1% are severely wasted (Boah *et al.*, 2019). To achieve the MIYCN targets for wasting levels of less than 5% by 2025 (WHO/UNICEF, 2019) and to bring the level of wasting to less than 3% by 2030 (WHO/UNICEF, 2019; WHO/UNICEF/WFP, 2014), Ghana needs a reduction of greater than 2% in wasting prevalence annually (Micha *et al.*, 2020). In the 2014 DHS report for Ghana, the prevalence of wasting was highest (11%) among children aged 9–11 months old, and children with the lowest prevalence of wasting aged between 36–47 months (GSS/GHS/ICF International, 2015). Ghanaian girls were more likely to be wasted (5%) than boys

(4%), and wasting was more common among children residing in rural areas (6%) rather than in those from urban areas (4%) (GSS/GHS/ICF International, 2015).

An emerging concern towards the fight against malnutrition in Ghana is the decline in breastfeeding (from 63% in 2008, 52% in 2014, and 42.9% in 2020) and an increase in bottle-feeding (from 11% in 2003, 12% in 2008 to 16% in 2014) among infants of less than 6 months of age (GSS/GHS/ICF International, 2015; Micha *et al.*, 2020). Breastfeeding is the best natural resource to improve childhood nutrition throughout the world (Biesalski & Black, 2016). Hence, a decline in breastfeeding and an increase in formula feeding in children, particularly in low- and middle-income countries, have increased the risk of malnutrition (Kuchenbecker *et al.*, 2015; Nisar *et al.*, 2016). As reported by Aheto *et al.*, (2015), 40% of deaths in children under 5 years of age in Ghana are attributed to malnutrition. Additionally, the Coronavirus disease 2019 (COVID-19) pandemic is expected to increase the risk of malnutrition globally due to reduced access to food, disruption of health services during lockdowns, and economic and food systems crises (Akseer *et al.*, 2020; Busch-Hallen *et al.*, 2020). Due to lockdown and school closure, 1.7 million Ghanaian children who were relying on a school feeding programme, a very important source of daily nutrition, struggled to access a nutritious meal as of April 2020 (WFP, 2019; WFP, 2020).

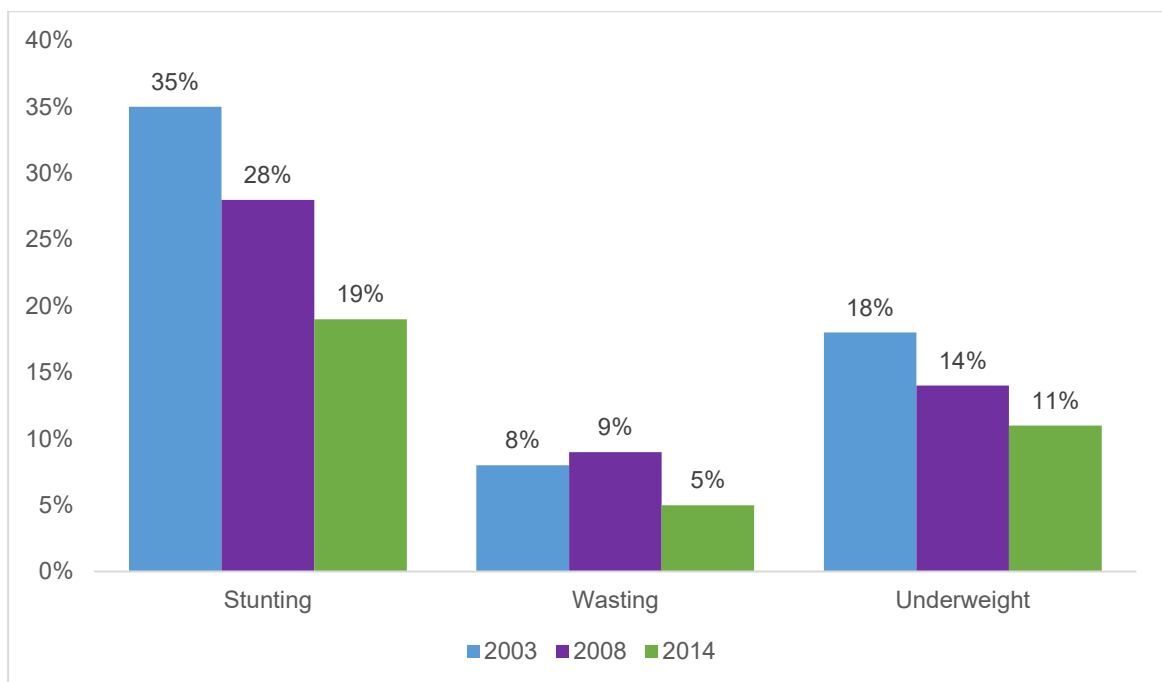


Figure 2-2: Trends of childhood malnutrition in Ghana, 2003 to 2014

Source: National Demographic Health Survey (GSS/GHS/ICF International, 2015).

2.5 Severe acute malnutrition

Severe acute malnutrition is defined by a WHZ/WLZ of less than or equal to -3 SD, or a mid-upper arm circumference of less than 115 mm, or by bilateral pitting oedema in infants and children aged 6–59 months (WHO, 2013). Infants and children with SAM who are clinically well without signs of infections or other hospital admission indications, with a retained appetite ('passed an appetite test'), are classified as uncomplicated SAM (GHS, 2010; WHO, 2013). An appetite test is a sensitive indicator for determining whether the child with SAM should be treated as an outpatient or admitted for in-hospital management (Golden & Grellety, 2011). In this test, the child receives ready-to-use therapeutic food (RUTF) to eat according to their weight category; children who retain their appetite show the absence of severe metabolic disturbance (Golden & Grellety, 2011; WHO, 2013). Also in line with the WHO's recommendations is that infants and children with SAM who present with clinical features of infection, metabolic disturbance, severe oedema, hypothermia, vomiting, severe dehydration, severe anaemia, or a lack of appetite are classified as complicated SAM, and treated in a hospital or medical facility (Ashworth *et al.*, 2003; GHS, 2010; WHO, 2013).

2.6 Pathophysiology of complicated SAM

Complicated SAM results in severely disturbed metabolic, physiological and anatomical changes in body tissues (Bhan *et al.*, 2003; Rytter *et al.*, 2017). These changes cause alterations in physiological processes in the body, known as reductive adaptation (Bhan *et al.*, 2003). Reductive adaptation refers to the slowing down of the body's systems, enabling the body to survive on limited nutrients and energy (Bhan *et al.*, 2003; MOH, 2016; National Department of Health, 2015; Rytter *et al.*, 2017). Due to reductive adaptation, a rapid increase in the amount of nutrition given to a child with complicated SAM can lead to electrolyte disequilibrium, referred to as refeeding syndrome (WHO, 2013). Refeeding syndrome is a potentially fatal complication of SAM caused by electrolyte changes that occur once feeding starts too rapidly (Golden & Grellety, 2011; Mbethe & Mda, 2017; Okinyi, 2018). Rapid feed initiation reduces the already depleted plasma phosphorus, potassium, and magnesium in patients (Golden & Grellety, 2011; Okinyi, 2018). Low serum phosphorus (hypophosphatemia) is the hallmark biomarker of refeeding syndrome. Hypophosphatemia affects 40 to 60% of infants and children with complicated SAM in the first three days of admission, and continues throughout the admission period (Chanchal *et al.*, 2019; Hother *et al.*, 2016). Hypophosphatemia makes cautious feeding crucial (Ashworth *et al.*, 2003). Refeeding syndrome impairs cardiac, pulmonary and neurological functions and can cause sudden death (WHO, 2013).

Table 2-1: Body system changes resulting from complicated SAM

Body system	Alterations because of complicated SAM
Cardiovascular system	• Cardiac output and stroke volume are reduced • Blood pressure is low • Renal perfusion and circulation time are reduced • Plasma volume is usually normal, and red cell volume is reduced
Gastrointestinal system	• Production of gastric acid is reduced • Intestinal motility is reduced • The pancreas is atrophied and the production of digestive enzymes reduced • The small intestinal mucosa is atrophied and the secretion of digestive enzymes is reduced • The absorption of nutrients is reduced
Liver function	• The synthesis of all proteins is reduced • Abnormal metabolites of amino acids are produced • The capacity of the liver to take up metabolise and excrete toxins is severely reduced • Energy production from galactose and fructose is much slower than normal • Gluconeogenesis is reduced with a high risk of hypoglycaemia during infection • Bile secretion is reduced
Genitourinary system	• Glomerular filtration is reduced • The capacity of the kidney to excrete excess acid or water is reduced • Urinary phosphate output is low • Sodium excretion is reduced • Urinary tract infection is common.
Circulatory system	• The basic metabolic rate is reduced by about 30% • Energy expenditure because of activity is very low • Both heat generation and heat loss are impaired • The child becomes hypothermic in an inhospitable environment and hyperthermic in a hot environment
Endocrine system	• Insulin levels are reduced and the child has glucose intolerance • IGF-1 levels are reduced • Growth hormone levels are increased • Cortisol levels are usually increased
Immune system	• All aspects of immunity are diminished • Lymph glands, tonsils, and thymus are atrophied • Ig-A levels in secretions are reduced • Complement components are low. • Phagocytes do not kill ingested bacteria efficiently. • Tissue damage does not result in inflammation or migration of white cells to the affected area • The acute phase immune response is diminished, and the cell-mediated immunity severely depressed • Typical signs of infection, such as an increased white cell count and fever, are frequently absent

Body system	Alterations because of complicated SAM
	Hypoglycaemia and hypothermia are signs of severe infection usually associated with septic shock

Note: Ig-A = Immunoglobulin A; IGF-1= Insulin growth factor -1.

Adapted from: Briend (2018) and Jordanian Ministry of Health (2013)

Children with complicated SAM usually present with non-specific signs and symptoms because of body system changes. For example, a child with complicated SAM may present with no fever or hypothermia, hypoglycaemia, and normal white cell count, despite the severity of the disease (Ashworth *et al.*, 2003; Rytter *et al.*, 2017; WHO, 1999). Often, infections in children with complicated SAM present with hypothermia (Black *et al.*, 2008; UNICEF, 2013a). To reduce complications associated with the management of complicated SAM, the WHO recommends a standard treatment protocol known as the WHO's ten-step guidelines for inpatient management of complicated SAM (Ashworth *et al.*, 2003; WHO, 1999; WHO, 2013).

2.7 The World Health Organization's ten-step guidelines for inpatient management of complicated SAM

In 2003, the WHO published a ten-step guide for inpatient management of complicated SAM to combat the high case fatality rates (CFRs) in some health facilities (Ashworth *et al.*, 2003). These guidelines were updated in 2013 (WHO, 2013). However, the group that updated the guidelines noted that some recommendations in the guidelines lacked enough evidence, as they were made based on low-quality research supplemented by best practices and expert opinion (Lenters *et al.*, 2016; WHO, 2013). **Table 2-2** presents the ten-step plan for inpatient management of SAM.

Table 2-2: Outline of the WHO's ten-steps for inpatient management of complicated SAM

Step	PHASE		
	STABILISATION		REHABILITATION
	Days 1-2	Days 3-7	Weeks 2-6
1. Treat/prevent hypoglycaemia	→		
2. Treat/prevent hypothermia	→		
3. Treat/prevent dehydration	→		
4. Correct electrolyte imbalance	→	→	→
5. Treat/prevent Infections	→	→	
6. Correct micronutrient deficiencies		no iron	with iron
7. Start cautious feeding	→	→	
8. Achieve catch-up growth			→
9. Provide sensory stimulation and emotional support	→	→	→
10. Prepare for follow-up after recovery			→

Source: Adapted from Ashworth *et al.*, (2003).

Accomplishing the WHO's ten-steps is through two phases, the stabilisation phase and the rehabilitation phase. These guidelines recommend a transition period between the two phases (Ashworth *et al.*, 2003). This two-phase approach aims to successfully treat children with complicated SAM and introduce therapeutic products and the management of the complications (Ashworth *et al.*, 2003; WHO, 2013). In this approach, therapeutic nutrition products, such as Formula 75 (F-75), Formula (F-100) and RUTF, are used during the stabilisation and rehabilitation phases to promote recovery of normal metabolic functions, electrolyte balance and rapid weight gain (WHO, 2013). The WHO indicates that facilities that adhere to these guidelines can achieve a CFR of less than 10% in children with complicated SAM (Ashworth *et al.*, 2003; Sphere Association, 2018).

2.8 Feeding approaches during the different phases of the treatment of complicated SAM in children 6–59 months

2.8.1 Stabilisation phase

The stabilisation phase refers to the initial phase of the inpatient treatment of complicated SAM (WHO, 2013). This phase aims to effectively treat and correct infections and metabolic abnormalities (Ashworth *et al.*, 2003; WHO, 1999; WHO, 2013). During the stabilisation phase, a cautious feeding approach is required since the child with SAM has a compromised physiological state and reduced capacity to metabolise large amounts of food (Ashworth *et al.*, 2003). Cautious feeding refers to giving small, frequent feeds of low osmolality and low lactose (Ashworth *et al.*, 2003). This feeding approach begins immediately after admission or resuscitation (Ashworth *et al.*, 2003; WHO, 2013). The recommended feed for the stabilisation phase is F-75, (commercial and home made). Commercial F-75 is a pre packaged powder formula which is reconstituted by adding only boiled water while home made F-75 is made at the hospital by mixing full cream cows milk, sugar, oil, combined mineral vitamin mix, and water using a standardised recipe (Ashworth *et al.*, 2003). Home made F-75 is usually used when commercial F-75 is not available (Ashworth *et al.*, 2003). In this study only commercial F-75 was used in the treatment of complicated SAM. Formula 75 provides 75 kcal/100 ml, of which 5% of energy comes from protein, and 35% comes from fat. Every 100 g of F-75 contains 11 g of lactose, which is much lower than F-100 (34 g) and RUTF (19.5 g) (Versloot *et al.*, 2017). Low lactose improves tolerance and digestibility of the feed (MacLean & Graham, 1975). The carbohydrate (58 g per 100 g) used in the formulation of F-75 is maltodextrin, which is easy to digest by a child with complicated SAM (Eichenberger *et al.*, 1984). F-75 provides high potassium (4.0 mmol/100 ml) and magnesium (0.43 mmol/100 ml) for the treatment of electrolyte disturbances that often manifest in starved states and can be fatal (Golden & Grellety, 2011; Manary *et al.*, 2012; WHO, 1999) and promotes the repair of

physiological and metabolic functions and restore electrolyte balance, thereby reducing the risk of refeeding syndrome (WHO, 1999; WHO, 2013).

For children with complicated SAM, F-75 should be given at 80 kcal/kg to 100 kcal/kg per day (WHO, 1999; WHO, 2013). If less than 80 kcal/kg per day is given the child with SAM will continue to lose weight, if over 100 kcal/kg per day is given the child may develop a severe metabolic imbalance (WHO, 2013). The quantity of F-75 given can be determined using the WHO's feed reference tables, which are available and recommended in settings where healthcare providers have limited clinical experience and knowledge in managing SAM (Ashworth *et al.*, 2003; WHO, 1999; WHO, 2013). The calculated quantities of F-75 in the feed reference tables are to provide 80–100 kcal/kg per day of energy, 1–1.5 g/kg per day of protein, and 130 ml/kg per day of fluid. Children with oedematous malnutrition should receive 75 kcal/kg of energy per day and 100 ml/kg per day of fluid using specific reference tables for children with oedema (Ashworth *et al.*, 2003; WHO, 1999; WHO, 2013).

The recommended feeding schedule for a child with SAM should start with two-hourly feeds, proceeding to three- or four-hourly feedings; however, this progression mainly depends on the volume of feed tolerated by the child and staff availability to prepare, distribute and monitor feeding (Ashworth *et al.*, 2003; Golden & Grellety, 2011). During the stabilisation phase, if the child vomits the feed, both the amount of F-75 given at each feed and the interval between feeds should be reduced (WHO, 2013). If the child tolerates the feeds, the frequency of F-75 should gradually be decreased from two-hourly to three- and four-hourly feeds, while concurrently increasing the volume of each feed to maintain a required total volume of 130 ml/kg per day (Ashworth *et al.*, 2003). Infants and children unable to feed orally or unwilling to eat should be fed through a nasogastric tube (Golden & Grellety, 2011; WHO, 2013).

The stabilisation phase continues until the child's vital signs, such as temperature, heart rate, and respiratory rate have stabilised and the appetite returns. The stabilisation phase usually takes about two to seven days (WHO, 1999; WHO, 2013); if the stabilisation phase takes longer than 10 days, the child is failing to respond to treatment and additional measures are required (Ashworth *et al.*, 2003; WHO, 1999). Besides the return of appetite, other medical complications, such as oedema and infections, need resolving (Golden & Grellety, 2011; WHO, 2013). During the stabilisation phase, the child's weight is usually static. The quantity of F-75 gives sufficient energy to maintain the basic physiological processes and not weight gain for a child with complicated SAM (Behrens, 1993; Golden & Grellety, 2011). Hence, children with oedematous malnutrition lose weight during this phase as they lose fluid from extracellular space as the oedema resolves (Ashworth *et al.*, 2003; WHO, 1999). After stabilisation, the child is transitioned

into the rehabilitation phase, where catch-up growth should occur (Ashworth *et al.*, 2003; WHO, 2013).

2.8.2 Transition phase

The period between the initial stabilisation phase to the nutritional rehabilitation phase in children with complicated SAM is referred to as the transition phase (Brown *et al.*, 2009; Manary *et al.*, 2012). The transition phase feeding was introduced for inpatients because a sudden change to large amounts of nutrition before the physiological function with complicated SAM is restored can be dangerous, and lead to electrolyte disequilibrium (Golden & Grellety, 2011; WHO, 2013); this phase should last one to three days (WHO, 2013). If the transition phase goes beyond 10 days from admission, this indicates the child is failing to respond to treatment (Golden & Grellety, 2011). During this phase, children with complicated SAM require 100–135 kcal/kg/day of energy and 130 ml/kg/day of fluid (Ashworth *et al.*, 2003; WHO, 2013). Rapid transition feeding may cause, amongst others, poor feed tolerance characterised by vomiting, osmotic diarrhoea and abdominal distention, which may indicate refeeding syndrome (Bandsma *et al.*, 2019; Golden & Grellety, 2011; WHO, 2013).

In infants and children with SAM, poor feed tolerance often results from delayed gastric motility (Tume & Valla, 2018). Causes of delayed gastric motility include the disease process, alterations in hormonal responses, medications, and/or gut tissue alterations (Martinez *et al.*, 2015; Tume & Valla, 2018). A common symptom of feed intolerance observed in children with SAM is osmotic diarrhoea, which refers to an increase in faecal flow volume and frequency because of the ingestion of a poorly absorbable solute, such as carbohydrate or divalent ions, that inhibit normal water and electrolyte absorption (Frothingham & Sethi, 2018). Lactose is the biggest culprit due to the reduction in lactase production from the intestinal brush border, caused by inflammation and or starvation (Bowie *et al.*, 1965; James, 1971). In infants and children with SAM, osmotic diarrhoea is attributable to the inadequate intestinal absorption capacity of nutrients because of villous atrophy and pancreatic insufficiency (Bandsma *et al.*, 2019; Golden & Grellety, 2011).

There are currently no specific feeding guidelines on how to achieve nutritional requirements for the transition phase (WHO, 2013). The WHO suggests two approaches to transition children with complicated SAM from the stabilisation to the rehabilitation phase (**Table 2-3**). However, these feeding approaches are based on indirect evidence and expert opinion of the guideline development group (WHO, 2013). These transitional feeding approaches (summarised in **Table 2-4**) depend on the clinical experience and skills of staff available to supervise feeding and monitor children with complicated SAM during feeding (WHO, 2013).

Table 2-3: Transition feeding approaches from stabilisation to rehabilitation phase for children 6–59 months with complicated SAM

Therapeutic food	RUTF	F-100
Feeding approach	1. Give the prescribed quantity of RUTF for the transition phase. Allow the child to take clean and safe water freely. Top up the RUTF with F-75 if the child fails to consume the prescribed quantity 2. Alternatively, increase the amount of RUTF over 2–3 days until the child takes the diet's full quantity for the transition phase If the child fails to take more than half of the prescribed diet in 12 hours, stop giving RUTF and give F-75 again Retry the same approach after 1–2 days until the child takes 90% of the RUTF	1. Replace F-75 with the same amount of F-100 for 48 hours Increase F-100 with each successive feed by 10 ml until some feed remains undrunk Change F-100 to RUTF if the child achieves a rapid weight gain Observe that the child is tolerating RUTF before being transferred to an outpatient programme
The rationale for the choice of feed	RUTF is the preferable diet for the transition phase, as children with SAM can continue taking the RUTF as a take-home diet after being transferred to the outpatient therapeutic programme	F-100 is used to treat children with SAM if the RUTF is unavailable or the child fails to take it

Note: RUTF = Ready -to-use therapeutic food; SAM = severe acute malnutrition; F-75 = formula 75; F-100 = formula 100

Source: Transition phase feeding (Golden & Grellety, 2011; WHO, 2013).

Infants and children with SAM are described as successfully transitioned if they can eat at least 90% of the RUTF or F-100 prescribed for the transition phase (WHO, 2013). Children with oedematous malnutrition must have a good appetite, and oedema should decrease from more severe to less severe (severe: generalised oedema affecting both feet, legs, hands, arms; moderate: oedema affecting both feet, plus lower legs, hands, or lower arms or mild: oedema affecting both feet) (Golden & Grellety, 2011; WHO, 2013). A failed transition in a child with complicated SAM is shown by poor appetite, development of refeeding syndrome, rapid enlargement of the liver, worsening of osmotic diarrhoea, progressive oedema, tense abdominal distention, and deterioration of a child's condition (Golden & Grellety, 2011). Children with SAM who develop these signs and symptoms should revert to the stabilisation phase, while those who are successful should be transferred to the rehabilitation phase (WHO, 2013).

2.8.3 Rehabilitation phase

Children with SAM who have completed the transition feeding phase should be transferred to the nutritional rehabilitation phase (WHO, 2013). The rehabilitation phase aims to promote weight

gain, emotional and physical development and prepare the child for regular feeding at home (WHO, 1999; WHO, 2013). This phase takes 2 to 6 weeks and is accomplished in two parts: for the first part, which usually takes 2 to 3 days, the child should be treated in the hospital with RUTF or F-100, while a regular diet is re-introduced slowly (WHO, 1999; WHO, 2013). Once the child with SAM completes the first part of the rehabilitation phase, he or she needs transferring to the second part of the rehabilitation phase, known as the outpatient therapeutic programme. Completion of the first part of rehabilitation is by the resolution of medical complications, eating satisfactorily, and gaining weight (usually 2–3 weeks after admission). In this phase, the child with SAM requires 150-220 kcal/kg per day of energy to achieve a catch-up growth of 10 g per kilogram body weight per day (Ashworth *et al.*, 2003; WHO, 2013). During this phase, the child with SAM should be given RUTF alongside the home diet (WHO, 1999; WHO, 2013).

2.9 Nutritional treatment guidelines of children 6–59 months with complicated SAM in Ghana

Ghana adopted the WHO's protocol for the treatment of complicated SAM in 2010 (GHS, 2010). According to the Interim National Guidelines for Community-based Management of Severe Acute Malnutrition in Ghana, children with SAM are classified using WHO guidelines (GHS, 2010). In Ghana, all children with complicated SAM are treated in a health facility with trained staff to manage complicated SAM using the WHO's ten-step guidelines (GHS, 2010). During the stabilisation phase, children with complicated SAM are fed using a cup and saucer every three hours (eight feeds per day) to prevent hypoglycaemia; weak children are fed by spoon, dropper, or syringe. The use of a nasogastric tube is only in the stabilisation phase, when the child cannot consume enough F-75 by mouth. Adequacy of intake is defined as an intake of 80% of the daily F-75 prescribed for the stabilisation phase (GHS, 2010). The calculation of the amount of F-75 for the Ghanaian children with complicated SAM during this phase uses the admission weight. If the child loses or gains weight during the stabilisation phase, the amount of F-75 should not be adjusted (GHS, 2010). The Ghanaian SAM guidelines state the stabilisation phase should last 2 to 3 days for children with a good appetite and no oedema (GHS, 2010), similar to that recommended by the WHO (WHO, 2013).

Similarly to WHO recommendations, infants and children with complicated SAM receive RUTF during the transition phase in Ghana (GHS, 2010; WHO, 2013). The transition phase prepares the child for outpatient care and usually lasts three days (GHS, 2010). The testing of RUTF acceptability occurs at every feed by offering the RUTF to a child. When the child eats at least 75% of the required amount of RUTF, they are ready for discharge to outpatient care (GHS, 2010). The WHO, conversely recommends that children with complicated SAM consume full (100%) daily prescribed feeds during the transition period before being moved to the rehabilitation

phase (WHO, 2013). For children who refuse the RUTF on the first attempt, the recommendation is to offer it at every feed until they eat the full diet. Like the WHO's recommendations, children with complicated SAM, who fail to consume the RUTF, receive F-100 at 130 ml/kg/day (GHS, 2010). Children with complicated SAM who fail to regain appetite between 4–7 days from admission are classified as failure to respond to treatment in Ghana (GHS, 2010).

In contrast with the WHO's recommendation, the rehabilitation phase in Ghana is usually implemented in outpatient care (GHS, 2010). In hospital, rehabilitation is only for children with SAM who struggle with eating RUTF, or were on F-100 during the transition phase. However, before referring the child to outpatient care in Ghanaian hospitals, the child should be observed for at least 24 hours eating RUTF to ensure he/she does not develop complications and is able to meet his/her nutritional needs on RUTF alone (GHS, 2010). After the 24 hours of observation, children progressing to the rehabilitation phase on a RUTF diet are discharged from inpatient care to outpatient care. During the outpatient care, children recovering from SAM are monitored weekly in the outpatient department (GHS, 2010). **Table 2-6** shows the amount of RUTF given to children with complicated SAM during the transition phase and the rehabilitation phase in Ghanaian hospitals (GHS, 2010).

Table 2-4: The amounts of RUTF to give a child per day or week based on 92 g packets containing 500 kcal

Weight of child (kg)	Packets per week	Packets per day (200 kcal/kg body weight/day)
3.5–3.9	11	1.5
4.0–4.9	14	2
5.0–6.9	18	2.5
7.0–8.4	21	3
8.5–9.4	25	3.5
9.5–10.4	28	4
10.5–11.9	32	4.5
≥ 12	35	5

Source: (GHS, 2010)

2.10 Studies reporting feeding practices in children treated for complicated SAM

Table 5 summarises studies reported in-hospital feeding practices for infants and children with complicated SAM and their outcomes. In this table, only two references, Lanyero *et al.*, (2017) and Versloot *et al.*, (2017), reported the feeding approaches during the transition phase in children with complicated SAM and their outcomes. The other references, Teferi *et al.*, (2010) and Ahmed *et al.*, (1999), compared overall outcomes in feeding practices for children with complicated SAM treated using WHO feeding protocols versus non-standard protocols.

In Lanyero *et al.*, (2017), children aged 6–59 months treated for SAM at Mulago hospital, Kampala, Uganda were observed how they tolerated transition feeding approaches as a prospective study nested in a clinical trial. Children received half of the energy required for the transition phase from RUTF and the other half from F-75. Children who successfully transitioned from F-75 to RUTF on the first attempt took between 1 and 2.8 days. RUTF was gradually increased to be the only source of energy. In this study, children had successfully transitioned to RUTF if they could gradually consume up to 135 kcal/kg/day of RUTF in the transition phase on the first attempt. Children who failed the appetite test or developed profuse diarrhoea or vomiting when ingesting RUTF, or those who had progressively reduced RUTF intake during the subsequent days, failed the transition to RUTF. In this study, the transition period's median duration was 4 (3–8) days. This finding is in line with the WHO guidelines that recommend the transition period to last for 3 to 7 days (Ashworth *et al.*, 2003). Out of 341 children with complicated SAM, only 65% successfully transitioned from F-75 to RUTF on the first attempt, and 5% of these children failed to transition from F-75 to RUTF on the second attempt; hence, treatment with F-100. Poor acceptance was noted in younger children (for each month increase in age reflected a 4% lower likelihood of failure to transition), severely wasted children, HIV infected, and those with severe illnesses. Authors attributed poor tolerance to RUTF in younger children to its consistency (semi-solid state) and the delayed introduction of complementary semi-solid food practices among young children in Uganda, as previously reported by Kikafunda *et al.* (2003). Authors attributed poor RUTF tolerance to reductive adaptation for severely wasted children because of long periods of starvation and structural changes in the body organs. Reductive adaptation requires more time to re-adapt when therapeutic feeding is re-introduced (Lanyero *et al.*, 2017). For children with HIV, poor tolerance to RUTF was attributed to malabsorption from chronic diarrhoea and lactase deficiency, as reported by Collins *et al.* (2006) in a previous study.

The second study observed the transition feeding practices among children with complicated SAM treated in Malawi's hospital setting (Versloot *et al.*, 2017). This was an open-label pilot study that recruited 74 Malawian children with complicated SAM aged 6–60 months. These children enrolled in the transition phase only after stabilising, gaining appetite, and resolving oedema for those with oedematous malnutrition (Versloot *et al.*, 2017). The children were assigned to one of the three commercial feeds used during the transition phase: F-100, RUTF, or RUTF + F-75. The prescribed number of feeds for transition phase regimes were to a maximum energy intake of 135 kcal/kg/day, calculated based on WHO guidelines and reference tables. This study's primary endpoint was the low faecal power of hydrogen (pH) ($\text{pH} \leq 5.5$) measured in stool collected three days after the introduction of the transition phase diets. Faecal pH of ≤ 5.5 (acidic stool) was considered suggestive of carbohydrate malabsorption responsible for osmotic diarrhoea in

children with complicated SAM (Schiller *et al.*, 2014). The secondary outcomes observed at the end of treatment were the duration of hospital stay, diarrhoea status, weight gain and mortality.

The mean faecal pH was 5.8 ± 0.7 on admission and 6.1 ± 0.7 on transition day 3, showing that there was continuing carbohydrate malabsorption during hospital admission. Children with acidic stools (pH ≤ 5.5) did not significantly differ between groups before discharge with 30, 33, and 23% for F100, RUTF, and RUTF + F75, respectively. The mean duration of hospital stay after transitioning was 7.0 ± 3.4 days, with no differences between the three feeding strategies. The mean weight gain per day during the transition phase was 27.1 ± 75.4 g in the F75 + RUTF group and 42 ± 33.5 g in the RUTF only group, and the mean weight loss of 6.6 ± 63 g in the F100 group. Although, the weight gain was not significantly different between the groups during the transition phase. Diarrhoea was present upon admission in 33% of patients and was significantly higher (48%) during the transition phase across the three commercial feeding regimens. The authors also noted no significant difference in mortality in children with complicated SAM assigned to different diets during the transition phase. Therefore, this study showed that the transition feeds (F-100, RUTF, or RUTF + F-75) currently used in treating complicated SAM were similar since biochemical and clinical outcomes in children with complicated SAM did not differ. However, the authors in this study noted that the sample size was too small to generalise the results. To date, this is the only study that has compared the transition feeding regimens/approaches (RUTF, F-100, or F-75 + RUTF) with clinical outcomes at the end of hospital treatment for children with complicated SAM (Versloot *et al.*, 2017).

Before the updated WHO guidelines of 2013, Teferi *et al.*, (2010) reviewed reports involving 11,335 patients with complicated SAM from 25 therapeutic feeding centres in Ethiopia. In this study, new management (WHO feeding protocol, which involved three phases: the stabilisation with F-75, the transition with F-100, and the rehabilitation with F-100) was compared with the traditional feeding protocol. The traditional feeding protocol involved administering locally prepared feeds by mixing cow's whole milk, oil, raw egg, sugar, iron, and potassium chloride. The new protocol showed significant improvements in the death rate (3.6%) compared to the 20 to 40% observed in the traditional feeding methods. In the new protocol, the hospital's average length of stay was 25 days for children with severe wasting and 21 days for those with oedematous malnutrition. Severely wasted children gained 14 g/kg/day compared with 13.4 g/kg/day for children with oedematous malnutrition. The death rate decreased with increasing age and the cure rate increased. These results were below the minimum international standard set for the management of complicated SAM, which is a cure rate of at least 75% and death rate less than 10%, the average length of stay of fewer than 30 days, and average weight gain of 8 g/kg/day (Sphere Association, 2018).

In 1999, Ahmed *et al.* conducted a study that did not use WHO feeding guidelines for the treatment of complicated SAM, because back then, the ten-steps guidelines did not exist (Ahmed *et al.*, 1999). The study compared outcomes in children aged 0–5 years with complicated SAM with diarrhoea managed by a standardised (WHO) protocol compared with those with a non-standard protocol. In this study, children treated using standardised protocol begun feeding immediately on admission, with milk given every 2 hours. Children with severe wasting or those with wasting plus oedema received 80 kcal/kg/day on day 1, 96 kcal/kg/day on days 2 and 3. Children with oedematous malnutrition received 72 kcal/kg/day for one to three days. Children with no diarrhoea received 108 kcal/kg/day from day 4 onwards. Non-breast-fed infants younger than four months received cow-milk-based infant formula, for breastfed infants, the mother had to breastfeed every 30 min and children who were anorexic were fed by nasogastric tube. For children treated using a non-standard method, feeding was delayed until rehydration was complete, and nasogastric tube feeding was used only in the very sick children. Liquid feeds were offered every 2 hours, but intake was not ensured, and older infants were offered rice porridge two to three times daily. In this study, children treated using the standardised protocol resulted in weight gain, fewer hypoglycaemia episodes, less need for intravenous fluids, and a 47% reduction in mortality. The authors concluded that all children with diarrhoea and complicated SAM should have the standardised protocol.

Table 2-5: Studies reporting feeding practice for inpatient infants and children with complicated SAM

References	Study type	Sample size	Age months	Country	Methods	Outcome
Lanyero <i>et al.</i> , (2017)	Nested randomised clinical trial	400	6-59	Uganda	Children with complicated SAM - During the transition phase, - Children with SAM received half RUTF plus half F-75 - RTF gradually increased to the full feed - Successful: - The child consumes up to 135 kcal/kg/day or RUTF - Failure: - Failed appetite test OR had progressively reduced RUTF intake in subsequent days, OR developed profuse diarrhoea, OR vomiting after taking RUTF	- Successful; 65% of children with SAM - Failure: 35% - Younger children - Severely wasted - HIV infected - Severe illnesses
Versloot <i>et al.</i> , (2017)	An open-label pilot randomised controlled trial	74	6–60	Malawi	Children with complicated SAM - In the transition phase: - The first group received F-100 - The second group received RUTF - The third group received F-75 + RUTF	- Hospital stay 7.0 days (SD 3.4) no differences between groups - Weight gain: insignificant between treatment groups - For the non-oedema: - F-75 + RUTF: 27.1 g - RUTF: 42 g - Weight loss (Oedema) - F-100: 6.6 g

Table 2-6: Studies reporting feeding practice for inpatient infants and children with complicated SAM, (Continued).

References	Study type	Sample Size	Age months	Country	Methods	• Outcome
Teferi <i>et al.</i> , (2010)	A retrospective review of reports	13,843	6-216	Ethiopia	- Children with complicated SAM - Phase I: given F-75 - Transition phase: given F-100 - Phase II: As much F100 as the children could take, plus family diet	- Length of phase I and transition 2-7 days - Weight gain: 13.4 – 14 g/kg/day
Teferi <i>et al.</i> , (2010)	Non-randomised superiority study	627	0-59	Bangladesh	Children with complicated SAM Standard protocol feeding - Feeding begun immediately on admission, with milk given every 2 hours - Children with severe wasting and wasting plus oedematous malnutrition received 80 kcal/kg/day on day 1.96 kcal/kg/day on days 2 and 3 - Children with oedematous malnutrition were given 72 kcal/kg/day on days 1 to 3, and if no diarrhoea, 108 kcal/kg/day on day 4 onwards - Non-breast-fed infants younger than 4 months received cow-milk-based infant formula - Breastfed infants: mother told to breast-feed every 30 min - Anorexic children: fed by nasogastric tube - Hypoglycaemia: 50 ml 10% glucose orally or by nasogastric tube; if a hypoglycaemic child was unconscious or convulsive, 25% intravenous glucose 2 ml/kg was given followed by oral glucose	- Weight gain; - Standard protocol: 4.4 g/kg/day - Non-protocol: 3.5 g/kg/day - Hospital stay: 4.5 days

Non-protocol management

- Feeding delayed until rehydration was complete
- Only the very sick were fed via nasogastric tubes
- Liquid feeds offered every 2 hours, but intake was unfollowed
- Older infants offered rice porridge two to three times daily
- The total daily dietary energy was 100 kcal/kg for children with severe wasting, 80 kcal/kg for wasting plus oedematous malnutrition, and 60–70 kcal/kg for oedematous malnutrition
- For hypoglycaemia, intravenous glucose was given, but without an oral glucose drink

Note: RUTF = Ready-to-use therapeutic food; HIV = Human immune virus; SAM = Severe acute malnutrition; kcal/kg/day = kilocalories per kilogram per day; g/kg/day = gram per kilogram per day; F-75 = Formula 75 ; F- 100 = Formula 100; ml = millilitre; min = minutes

2.11 Conclusion

This literature review has confirmed that complicated SAM remains a substantial public health concern, especially in children under 5 years of age because of its complexity. This review has summarised the literature on therapeutic feeding for children treated for complicated SAM. It further reveals the research gap in therapeutic feeding, especially during the transition phase, and its outcome needs investigating further.

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CHAPTER 3 ARTICLE

3.1 Title page

Title: Transition phase feeding in infants and children (6–59 months) treated for severe acute malnutrition in Ghanaian referral hospitals.

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Word count:

Abstract (322)

Main body word count (4231)

Number of references (36)

Number of tables and figures (7)

Contributions: Humphrey Chatenga was responsible for the planning and execution of the study, data analysis, interpretation, and writing of the manuscript. Mrs Cornelia Conradie, Miss Sanele Nkomani, and Mrs Philna Neethling supervised and conceptualised the study and reviewed the manuscript. Dr Martani Lombard reviewed the final manuscript, and provided overall guidance of the study to align it with the SAMAC larger study. Mr George Mwenyephiri supervised data analysis and reviewed the interpretation of the results. All authors contributed in drafting, proofreading and approval of the manuscript.

Acknowledgements: We thank Miss Hanna Asare and Miss Janet Carboo, former MSc students at North-West University, for coordinating data collection at the three hospitals in Ghana. Further appreciation goes to the staff of the Records Departments of Komfo Anokye Teaching Hospital, Princess Marie Louis Children's Hospital, and Tamale Teaching Hospital.

Source of funding: This work is based on the research supported in part by the National Research Foundation of South Africa (Grant Numbers: 122483) and the Supporting Nutrition Research in Africa (SuNREA). The funding agencies had no influence on the execution of the research.

3.2 Abstract

Background: Globally, 3 million lives of children under 5 years of age are at risk of death owing the severe acute malnutrition (SAM).

Objectives: This study aimed to determine the associations of the feeding regimens used during the transition phase with vomiting, diarrhoea status, and duration of the transition phase in infants and children (6 to 59 months) treated for complicated SAM in three Ghanaian referral hospitals.

Design: This study was embedded within the Severe Acute Malnutrition in African Children (SAMAC) study. The SAMAC larger study is a multi-country multi-hospital study that is based on a longitudinal study design with a quantitative, descriptive-comparative.

Setting: This study used data collected from Komfo Anokye Teaching Hospital, Princess Marie Louise Children's Hospital, and the Tamale Teaching Hospital.

Data collected: Data collection involved the type of the transition feeding regimens, diarrhoea and vomiting during the transition phase, and length of the transition phase.

Results: The majority (40%) of children treated for complicated SAM from the referral hospitals received F-100, followed by RUTF (32%), RUTF + F-75 (24%), and "other foods" (2%) during the transition phase. Seventy-two percent of 380 children included in this study failed the transition phase on the first attempt; 21% had diarrhoea, and 8% vomited during the transition phase. There were no associations between the transition feeding regimens and diarrhoea status, vomiting, and length of the transition phase. However, oedematous malnutrition, vomiting and diarrhoea during admission, and an HIV positive status were found to be predictors of vomiting and diarrhoea during the transition period, as well as increased length of the transition phase.

Conclusions: The transition feeding regimens used in Ghanaian referral hospitals were not significantly associated with diarrhoea status, vomiting, and length of the transition phase. However, these feeds appear to have a low transition success rate due to overfeeding and poor digestibility as previously reported in literature. We therefore recommend the exploration of actual consumption and better alternative transition feeds or a more cautious transition phase.

Keywords: Severe acute malnutrition; transition phase feeding; diarrhoea; vomiting; length of the transition phase; referral hospitals.

3.3 Introduction

Childhood malnutrition, mostly wasting, is a major public health problem owing to its associated risk for death from infectious diseases such as diarrhoea, pneumonia, and measles¹. The 2020 Levels and Trends of Childhood Malnutrition report shows wasting continues to threaten approximately 47 million lives of children globally². Severe acute malnutrition (SAM), which is a severe form of wasting, affects 14.3 million children globally and contributes nearly half a million deaths of children under 5 years of age annually^{2, 3}. SAM affects 1% of children under five years of age in Ghana⁴. As children with complicated SAM are 11 times more likely to die than their healthy counterparts⁵, Ghana remains committed to eradicating all forms of malnutrition in children under five years of age⁴.

The WHO defines wasting as a child that is too thin when his or her weight-for-height/length z-score (WHZ/WLZ) fall below the -2 standard deviation (SD) of the WHO growth standards⁶. A WHZ/WLZ score of less than -3 SD indicates severe wasting⁶. Wasting often results from an interaction between poor access to food, healthcare, poverty, diarrhoea, inappropriate complementary feeding practices, intrauterine growth restriction, and/or serious infectious diseases, such as malaria and cholera⁷⁻⁹. Children with wasting have weakened immune systems resulting from muscle loss². Poor immunity fuels a vicious cycle of infection and wasting⁵. When wasting becomes severe, which is also known as SAM, a child develops severe health consequences such as bilateral pitting oedema due to the interaction between nutrient deprivation, infection, and the immune response⁵. The WHO defines SAM in infants and children aged 0–59 months by WHZ/WLZ of less than -3 SD of the WHO child growth standards, or a mid-upper arm circumference (MUAC) of less than 115 mm, or by bilateral pitting oedema (WHO, 2013).

The WHO recommends children with complicated SAM to be treated in hospitals or medical facilities¹⁰. Complicated SAM refers to children with SAM who present with medical complications such as generalised pitting oedema, poor appetite, or the presence of one or more of the Integrated Management of Childhood Illness (IMCI) danger signs (pneumonia, diarrhoea, malaria, measles, fever, and severe anaemia)⁶. Complicated SAM alters physiological processes in the body, which signifies reductive adaptation¹¹, which refers to slowing down the bodily systems, enabling survival on limited nutrients and energy¹². Due to these alterations, therapeutic fluid replacement and feeding that are generally lifesaving in a well-nourished child are associated with

high case fatality rates (CFR) among children with SAM^{12, 13}. Therefore, the successful management of children with SAM requires medical treatment of underlying infections and dietary treatment with specially formulated therapeutic foods¹⁴.

To combat poor CFR in health facilities, the WHO, in 1999, developed guidelines for the successful management of SAM with complications¹⁵, which were updated in 2003 to meet the requirements of health facilities and hospitals with limited resources¹⁴. The WHO guidelines, commonly known as the 'ten-steps,' are implemented in a two-phase approach, namely the stabilisation and rehabilitation phases. A gradual transition phase is proposed between these two steps to avoid feeding complications^{6, 14}; however, there are no clear guidelines on ensuring that nutrition requirements are met during the transition phase⁶. Based on expert opinion, due to a lack of data at the time the guidelines were updated, the WHO suggests the use of Formula-100 (F-100) and/or ready-to-use therapeutic food (RUTF) during the transition phase with the number and skills of staff available supervising and monitoring feeds to ensure that nutritional requirements are met⁶. During the transition phase, gradual feeding is important, as a rapid introduction of a large amount of feed may cause, amongst other serious complications, poor feed tolerance (vomiting, persistent diarrhoea, and abdominal distention)³. Poor feed tolerance may increase the length of the transition phase, which indicates the failure to respond to standard treatment¹⁶. A rapid increase in the amount of nutrition given to a child with complicated SAM may also lead to electrolyte disequilibrium referred to as refeeding syndrome, a potentially fatal complication of SAM⁶. Hence, the stabilisation phase and gradual transition phase prevents these complications⁶.

Since the 2013 update of the WHO guidelines, only two studies have investigated transition-feeding practices^{17, 18}. Versloot *et al.* (2017) evaluated the effectiveness of three transition phase feeding regimens (F-100, RUTF, and RUTF +F-75) and clinical outcomes amongst 72 children with complicated SAM in Malawi. Neither the acidity of faeces, diarrhoea status, length of stay, or death were significantly different between the groups¹⁷. Lanyero *et al.* (2017) described the transition from F-75 to RUTF and identified predictors of failed transition in 400 children treated for complicated SAM in Uganda. In this study, children with complicated SAM received half of the nutrient requirements during the transition phase from RUTF and the other half from F-75. The gradual increase of RUTF continued until it was the only source of energy. In this study, 65% of children completed the transition phase within the recommended two to three days on the first attempt⁶. Failure to transition was observed in younger children, severely wasted, HIV-infected children, and those with severe illness. Both these studies were limited in sample size and the type of feeding regimens investigated^{17, 18}.

The limited evidence on the topic warrants more research. As part of the Severe Acute Malnutrition in African Children (SAMAC) study, this study aimed to determine the associations of the transition feeding approaches used to treat infants and children with complicated SAM at three Ghanaian referral hospitals with vomiting diarrhoea status, and length of the transition phase. To our knowledge, this is the first study conducted in Ghana to investigate the associations between transition-feeding practices and clinical outcomes.

3.4 Study methods

3.4.1 Study design and ethical considerations

This study forms part of the SAMAC study, of which the protocol was previously published¹⁹. The SAMAC study is an observational multi-country multi-hospital study coordinated by the Centre of Excellence for Nutrition at the North-West University in South Africa. This article reports on retrospective data collected from medical records of children aged 6 to 59 months in three randomly selected referral hospitals (namely Komfo Anokye Teaching Hospital (KATH), Princess Marie Louise (PML) Children's Hospital, and the Tamale Teaching Hospital (TTH)) in Ghana.

The SAMAC study collected data from medical records of infants and children aged 0 to 59 months treated for complicated SAM in three referral hospitals in Ghana between 2013 and 2018. Medical records from children diagnosed, hospitalised, and treated for complicated SAM after January 2013 in the selected hospitals were included. The study included infants and children admitted primarily for other medical conditions but were diagnosed and treated for complicated SAM during the hospital stay. These diseases and medical conditions included recurring infections, malaria, dehydration, diarrhoea, tuberculosis, parasite infestations, and cholera. The basis for the diagnosis of complicated SAM was on a medical record indicated by the healthcare provider. Medical records for children admitted with any medical problems not related to complicated SAM (unspecified metabolic neurodevelopmental conditions or any other growth disorders) were excluded, as their nutrition needs differed from children with SAM without these other disorders. Excluded were children without documented transition feeding records and multiple admissions.

This study obtained ethical approval from the North-West University Human Research Ethics Committee NWU-HREC (NWU-00063-17-A1) and the Ghana Health Service Ethical Review Committee (GHS-ECR) (GHS-ERC 09/06/2017). Participating hospitals also provided written permission for the study.

3.4.2 Data extraction

Data from eligible medical records were extracted by trained research assistants using a standardised data extraction tool adapted from the WHO SAM admission criteria and treatment guidelines SAM²⁰. The extracted data included demographic information (treatment hospital, gender, age, date of admission), anthropometric measurements (weight, height, and MUAC), clinical information (diarrhoea status, dehydration, vomiting, oedema status and grade, vital signs such as temperature and blood glucose level) and co-morbid infections (HIV, Tuberculosis status and Malaria). Oedema was classified depending on severity as per WHO classification, where children with oedema of 3+ (generalised oedema) were classified as having severe bilateral oedema, those with 2+ (feet and palms) as moderate oedema, and those with 1+ (feet only) as mild oedema⁶. The healthcare provider defined and recorded the collected data in the medical records; the anthropometric measurements were therefore not standardised. To ensure accuracy and completeness of the collected data, the researchers crosschecked all the extracted data against the medical records used.

3.4.3 Outcomes measurements: Vomiting, diarrhoea status, and length of the transition phase

For the purpose of this study, the definition of the transition phase was as a period when a child treated for complicated SAM received F-100, RUTF, or other feed(s), with or without F-75, after the stabilisation phase. As per the WHO recommendation, children treated with SAM were classified as successfully transitioned if they took two to three days to transition from F-75 to RUTF and/or F-100 on the first attempt and did not develop clinical signs of poor feed tolerance⁶. Children who transitioned successfully should not present with any feeding complications (vomiting and/or diarrhoea) or worsening clinical conditions^{6, 16}. The healthcare provider defined and reported vomiting and diarrhoea in the medical record. Diarrhoea was operationally defined by the observance of ≥ 3 and/or watery stools per day from input and output chart²¹. The calculation of the length of transition (LOT) was by subtracting the last day of transition documented in the patient data extraction form from the first day of transition, as indicated by the healthcare provider.

3.4.4 Exposure measurement: transition phase feeding

The basis for the transition feeding regimens was what the healthcare provider documented in the medical record. These feeds were converted from daily prescriptions (usually in millilitres for F-100 or number of sachets or bars for RUTF) into kilocalories (kcal) for easy comparison. The calculation of the total kcal prescribed per day was determined by adding all the feed quantities prescribed on a specific day. The kcal prescribed per kilogram body weight were calculated by dividing the child's total kcal prescribed by its weight for that specific day. We categorised energy

prescribed based on the WHO's recommendation to indicate over-prescription (>135 kcal/kg/day), recommended feeding (100-135 kcal/kg/day), or under-prescription (<100 kcal/kg/day) during the transition phase⁶.

3.4.5 Statistical analysis

The sample size required for hospitals in Ghana was 1000 medical records as described in the SAMAC larger study protocol¹⁹. Extracted from the three Ghanaian referral hospitals were 603 medical records which met the inclusion criteria, and 380 records were available for analysis, 223 records were excluded because they had no transition feeding record or had age of less than 6 months or multiple admissions. All the data was captured into Microsoft Access Database software, then exported to Microsoft Excel (v. 16.0; Microsoft Office Professional Plus 2016, Albuquerque, NY, USA.) for cleaning and data analysis. A final analysis was conducted using SPSS software (v. 26; IBM Corp, Armonk, NY, USA).

Variables were tested for normality using Kolmogorov's and Shapiro Wilks tests. Normally distributed data were reported using means and standard deviations ($\pm$ SD), and non-normally distributed data by medians and interquartile range (IQR) of the 25th and 75th percentiles. Categorical variables were reported using frequencies (n) and percentages (%). According to WHO categorisation (6 to 11 months; 12 to 23 months, and 24 to 59 months), age was stratified since different age groups have different nutrition requirements and different treatment procedures. The calculation of weight-for-age z-score (WAZ), height-for-age z-score (HAZ), and WHZ/WLZ used the WHO's Anthro Survey Analyser, available at <https://worldhealthorg.shinyapps.io/anthro/>.

Logistic regression models determined associations between the feeds and the outcomes. Independent variables (transition feeding regimens) were tested for collinearity against covariates. Collinearity was tested using variance inflation factor (VIF) of 3²². The primary covariates (F-100, RUTF, other foods) were adjusted for non-collinear variables including child age, gender, route of feeding, admission hospital, oedematous malnutrition, HIV and tuberculosis status, Malaria, vomiting, and diarrhoea during admission. All variables were reported as pooled data from the three study sites and stratified according to hospital admission and age groups. Significance was set at a p-value of <0.05 .

3.5 Results

3.5.1 Characteristics of the study population

The collection of data from 603 medical records took place at the three Ghanaian referral hospitals between 2017 and 2018. Medical records of children treated for SAM between 2013 and 2018 were captured. After careful screening, only 380 were eligible for inclusion in the analysis. Excluded were 223 medical records; 159 records had no transition feeding records, 47 had children aged below 6 months, 16 had multiple admissions, and one had a wrongly captured birth date.

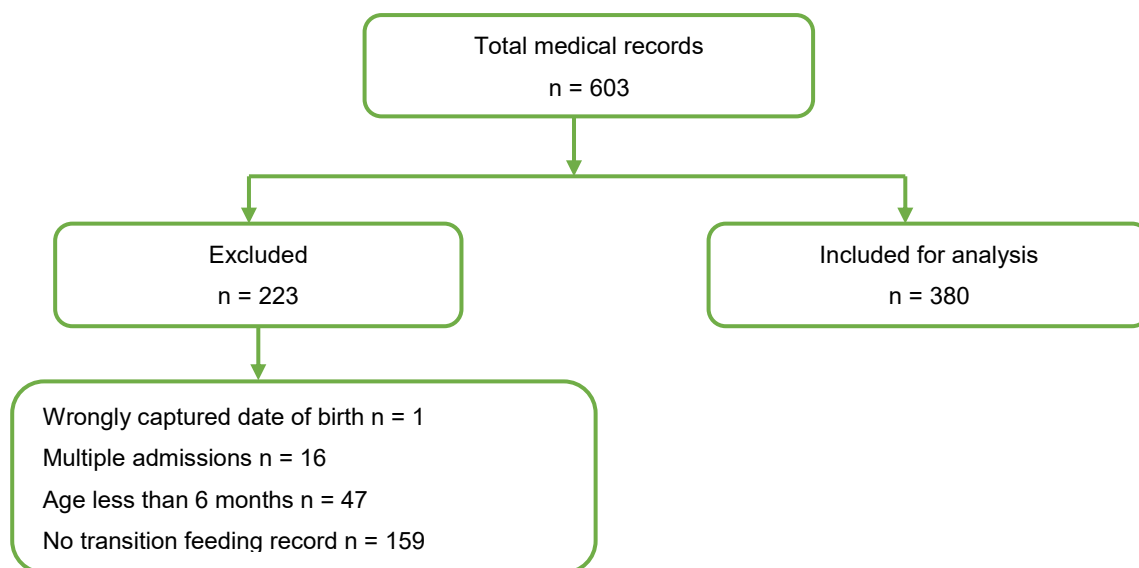


Figure 3-1: Medical records for children with complicated SAM in Ghanaian hospitals included in the study

Table 3-1 depicts the characteristics of the study population. The majority (54%) of children included in this study were boys. Two hundred and twenty (58%) of the study participants were admitted at TTH, 94 (25%) at PML and 66 (17%) at KATH. The median age of children at admission was 15 (IQR: 10.0; 24.0) months, and the majority (41%) of children with SAM were within the 12 to 23 months age group. Thirty-six percent of the children had malaria, 9% were HIV-infected, while 6% had Tuberculosis. Severe wasting (MUAC < 115 mm and/ or WH/LZ) affected 86% of children, while 28% had oedematous malnutrition. Forty-one (37%) children with complicated SAM were severely stunted. Most children (66%) who presented with severe wasting and oedematous malnutrition (70%) were admitted to TTH.

3.5.2 Clinical presentation at admission to the hospital

Of the 380 children included in this study, nearly half (49%) presented with diarrhoea, 48% with vomiting, and 43% with dehydration on admission (**Table 3-1**). Respiratory infections were present in 59% across all hospital admissions.

Table 3-1: Participants characteristics and transition feeding regimens according to admission hospital and age groups, (n = 380)

	Total sample ¹	KATH (n = 66)			PML (n = 94)			TTH (n = 220)		
		Age group (months)			Age group (months)			Age group (months)		
		6 – 11 (n = 21)	12 – 23 (n = 30)	24 – 59 (n = 15)	6 – 11 (n = 47)	12 – 23 (n = 31)	24 – 59 (n = 16)	6 – 11 (n = 59)	12 – 23 (n = 95)	24 – 59 (n = 66)
Participant characteristics	Median (IQR) or n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
A. Demographic characteristics and clinical presentation at admission										
Age in months	15 (10.0; 24.0)	8 (7.0 ; 9.0)	16 (13.5 ; 18.3)	24 (24.0 ; 36.0)	9 (7.0 ; 9.0)	16 (13 ; 20)	31 (24.0 ; 46.7)	9 (8.0 ; 10.0)	16 (13.0 ; 19.0)	28 (24.0 ; 34.3)
Girls	174 (45.8)	9 (42.9)	11 (36.7)	9 (60.0)	29 (61.7)	17 (54.8)	4 (25.0)	24 (40.7)	39 (41.1)	32 (48.5)
HIV positive	34 (8.9)	2 (9.5)	5 (16.7)	4 (26.7)	4 (8.5)	5 (16.1)	7 (43.8)	1 (1.7)	2 (2.1)	4 (6.1)
HIV status unknown	200 (52.6)	1 (4.8)	6 (20.0)	3 (20.0)	14 (29.8)	8 (25.8)	5 (31.3)	50 (84.7)	68 (71.6)	45 (68.2)
TB positive	22 (5.8)	3 (14.3)	4 (13.3)	3 (20.0)	2 (4.3)	3 (9.7)	4 (25.0)	0	1 (1.1)	2 (3.0)
TB status unknown	178 (46.8)	4 (19.0)	8 (26.7)	5 (33.3)	25 (53.2)	18 (58.1)	8 (50.0)	28 (47.5)	45 (47.4)	37 (56.1)
Mild oedema	37 (42.5)	2 (50.0)	3 (60.0)	3 (42.9)	1 (2.1)	2 (33.3)	1 (50.0)	4 (80.0)	12 (46.2)	9 (30.0)
Moderate	26 (29.9)	1 (25.0)	0	2 (28.6)	1 (2.1)	3 (50.0)	0	1 (20.0)	10 (38.5)	8 (26.7)
Severe Oedema	24 (27.6)	1 (25.0)	2 (40.0)	2 (28.6)	0	1 (16.7)	1 (50.0)	0	4 (15.4)	13 (43.3)
Irritable	107 (28.2)	7 (33.3)	13 (43.3)	1 (6.7)	14 (29.8)	9 (29.0)	6 (37.5)	15 (25.4)	28 (29.5)	14 (21.2)
VAD signs	9 (2.4)	2 (5.5)	2 (6.7)	0	0	0	0	3 (5.1)	0	2 (3.0)
Diarrhoea	185 (48.7)	7 (33.3)	21 (70.0)	4 (26.7)	21 (44.7)	13 (41.9)	8 (50.0)	31 (52.5)	44 (46.3)	36 (54.5)
Dermatitis	67 (17.6)	9 (42.9)	9 (30.0)	5 (33.3)	3 (6.4)	0	0	4 (6.8)	13 (13.7)	24 (36.4)
Pallor	56 (14.7)	4 (19.0)	6 (20.0)	8 (53.3)	11 (23.4)	5 (16.1)	1 (6.3)	5 (8.5)	11 (11.6)	5 (7.6)
Shock	8 (2.1)	1 (4.8)	3 (10.0)	1 (6.7)	0	0	0	1 (1.7)	1 (1.1)	1 (1.5)
Vomiting	182 (47.9)	7 (33.8)	18 (60.0)	3 (20.0)	18 (38.3)	14 (45.2)	7 (43.8)	31 (52.5)	52 (54.7)	32 (48.5)
B. SAM medical complications										
Dehydration	130 (42.8)	11 (57.9)	14 (50.0)	6 (42.9)	12 (31.6)	8 (32.0)	5 (45.5)	23 (54.8)	29 (37.2)	22 (44.9)
Respiratory Infections	91 (59.1)	3 (20.0)	8 (44.4)	4 (30.8)	13 (76.5)	14 (77.8)	7 (87.5)	14 (66.7)	15 (55.6)	13 (76.5)
Meningitis	1 (1.8)	1 (8.3)	0	0	0	0	0	0	0	0
Severe anaemia	32 (17.2)	1 (100)	1 (100)	3 (100.0)	2 (66.7)	1 (50.0)	1 (100.0)	7 (14.0)	8 (10.7)	8 (16.0)

Table 3-1: Participants characteristics and transition feeding regimens according to admission hospital and age groups, (n = 380), (Continued).

	Total sample ¹	KATH (n = 66)			PML (n = 94)			TTH (n = 220)		
		Age group (months)			Age group (months)			Age group (months)		
		6 – 11 (n = 21)	12 – 23 (n = 30)	24 – 59 (n = 15)	6 – 11 (n = 47)	12 – 23 (n = 31)	24 – 59 (n = 16)	6 – 11 (n = 59)	12 – 23 (n = 95)	24 – 59 (n = 66)
Hypoglycaemia	9 (8.0)	0	1 (3.6)	4 (28.6)	0	0	1 (20.0)	0	1 (9.1)	2 (15.4)
Malaria	80 (36.0)	5 (25.0)	9 (32.1)	3 (21.4)	2 (9.1)	1 (11.1)	1 (12.5)	20 (60.6)	21 (52.3)	18 (40.9)
Hypothermia	3 (0.8)	0	0	1 (6.7)	0	0	1 (6.3)	1 (1.7)	0	0
C. Admission anthropometric measurements										
MUAC < 115 mm	147 (85.5)	5 (100.0)	3 (60.0)	3 (60.0)	15 (78.9)	17 (85.0)	7 (70.0)	29 (93.5)	48 (96.0)	20 (74.1)
WH/LZ < -3 SD	74 (84.1)	14 (93.3)	23 (92.0)	8 (88.9)	4 (80.0)	5 (100.0)		8 (66.7)	8 (66.7)	4 (80.0)
H/LAZ < -3 SD	41 (37.6)	5 (26.3)	8 (26.7)	5 (33.3)	3 (50.0)	2 (28.6)	1 (100.0)	5 (41.7)	8 (61.5)	5 (83.3)
WAZ < -3 SD	257 (88.9)	15 (93.8)	24 (96.0)	8 (100.0)	42 (93.3)	24 (96.0)	13 (100.0)	44 (81.5)	57 (83.8)	30 (85.7)
D. Transition feeding regimen²										
RUTF	123 (32.4)	1 (4.8)	4 (13.3)	1 (6.7)	4 (8.5)	4 (12.9)	1 (6.3)	37 (62.7)	41 (43.2)	30 (45.5)
F-100	151 (39.7)	20 (95.2)	26 (86.7)	14 (93.3)	3 (6.4)	7 (22.6)	6 (37.5)	15 (25.4)	39 (41.1)	21 (31.8)
RUTF + F-75	93 (24.5)	0	0	0	30 (63.8)	18 (58.1)	8 (50.0)	7 (11.9)	15 (15.8)	15 (22.7)
F-100D	1 (0.3)	0	0	0	1 (2.1)	0	0	0	0	0
F-100D + RUTF	5 (1.3)	0	0	0	5 (10.6)	0	0	0	0	0
Others ³	7 (1.8)	0	0	0	4 (8.5)	2 (6.5)	1 (6.3)	0	0	0
E. Feeding complications in the first three days of transition										
Vomiting	27 (7.9)	5 (33.3)	3 (14.3)	1 (14.3)	5 (13.2)	4 (14.8)	2 (14.3)	2 (3.4)	2 (2.1)	3 (4.6)
Diarrhoea	74 (21.1)	2 (12.5)	4 (17.4)	0	3 (6.7)	8 (28.6)	2 (13.3)	15 (26.3)	23 (24.5)	17 (26.2)
LOT (IQR)	6 (3.0; 10.0)	8 (3.5; 13.5)	5 (3.0; 11.25)	8 (3.0; 13.0)	5 (3.0; 8.0)	6 (3.0; 8.0)	4 (2.0; 8.75)	5 (2.0; 9.0)	6 (3.0; 8.0)	6 (4.0; 11.25)
LOT 2-3 days	108 (28.4)	5 (23.8)	8 (26.7)	4 (26.7)	18 (38.3)	9 (29.0)	6 (37.5)	18 (30.5)	26 (27.4)	14 (25.4)
LOT > 3 days	272 (71.6)	16 (76.2)	22 (73.3)	11 (73.3)	29 (61.7)	22 (71.0)	10 (62.5)	41 (69.5)	69 (72.6)	52 (78.8)

Note: IQR = Interquartile range; LOT = Length of transition; MUAC = Mid upper arm circumference; VAD = Vitamin A deficiency; WH/LZ = Weight-for-height or length z-score; H/LAZ = Height or length-for-age z-score; WAZ = Weight-for-age z-score; RUTF = Ready-to-use therapeutic feed; F-100 = Formula 100; F-75 = Formula 75; F-100D = Diluted F-100; HIV = Human immune virus; SAM = Severe acute malnutrition; NGT = Nasogastric tube; KATH = Komfo Anokye Teaching Hospital; PML = Princess Marie Louise Children's Hospital; TTH = Tamale Teaching Hospital.

¹Missing variables = missing data or data not reported in the medical records: Dehydration (n = 76); Hypoglycaemia (n = 267); Hypothermia (n = 6); Severe anaemia (n = 194); Gastroenteritis (n = 286); Oedema (n = 76); Oedema grade (n = 293); MUAC (n = 219); H/LAZ (n = 299); WAZ (n = 42); WH/LZ (n = 315); Respiratory infection (n = 226); Meningitis (n = 326); Malaria (n = 158); MUAC (n = 208); WH/LZ (n = 292); WAZ (n = 91); H/LAZ (n = 271); Vomit during transition phase (n = 40); Diarrhoea during transition phase (n = 30).

²Feeds given from the first day of transition. ³Other feeds: Include Yomi yogurt, porridge, and infant formula that was prescribed for infants and children treated for complicated SAM in Ghana

3.5.3 Therapeutic feeding during the transition phase

The majority (40%) of children with complicated SAM received F-100 as a transition feed. RUTF was received by 32%, RUTF + F-75 by 25%, and 'other foods' by only 2% of children (**Table 3-2**). Tamale Teaching Hospital mainly used RUTF (88%) and F-100 (49%). Komfo Anokye Teaching Hospital used F-100 mostly (91%), while PML (59%) used RUTF + F-75 as a transition feed for children with complicated SAM. The median energy prescribed per kilogram body weight during the transition phase was 153.2 (IQR: 102.3; 208.3) kcal. This energy intake was higher than the WHO's requirements of 100 to 135 kcal/kg/day for the transition phase⁶. Of the 380 children, 58% had over-prescription of energy, while 26.8% had under-prescription. Approximately three-quarters (73%) of the 209 children who had over-prescription of energy were admitted at TTH, while 41% of children with under-prescription of energy were admitted at PML. Only 14% of the recruited children across all hospitals were prescribed energy within the recommended range (100 kcal/kg/day to 135 kcal/kg/day) during the transition phase. Children aged 6 to 11 months across all the hospitals were prescribed the highest energy quantities, with a median of 172 kcal/kg/day (IQR 110.20; 219.96 kcal/kg/day). Children aged 12 to 23 months and 24 to 59 months of age were prescribed 149.7 kcal/kg/day (IQR: 98.11; 204.08 kcal/kg/day) and 151.4 kcal/kg/day (IQR: 106.91; 199.21 kcal/kg/day) respectively across all hospitals.

Table 3-2: Feeding regimens and clinical outcomes during the transition phase stratified according to age groups, (n = 380)

	6 - 11 months (n = 127)	12 - 23 months (n = 156)	24 - 59 months (n = 97)
A. Transition feeding regimens	n (%)	n (%)	n (%)
RUTF	42 (33.1)	49 (31.4)	32 (33.0)
F-100	38 (29.9)	72 (46.2)	41 (42.3)
RUTF + F-75	37 (29.1)	33 (21.2)	23 (23.7)
F-100D	1 (0.8)	0	0
F-100D + RUTF	5 (3.9)	0	0
Others	4 (3.1)	2 (1.3)	1 (1.0)
B. Energy prescriptions			
Median energy (kcal/ kg/ day) prescribed	172.41 (110.20; 219.96)	149.67 (98.11; 204.08)	151.35 (106.91; 199.21)
Under-prescribed (< 100 kcal/kg/day)	27 (22.1)	43 (30.1)	22 (24.4)
Recommended (100 - 135 kcal/kg/day)	16 (13.1)	22 (15.4)	16 (17.8)
Over-prescribed (> 135 kcal/kg/day)	79 (64.8)	78 (54.5)	52 (57.8)
C. Clinical outcomes during the transition phase			
New diarrhoea during transition phase	8 (22.2)	19 (52.8)	9 (25.0)
Continued diarrhoea from stabilisation phase	12 (32.4)	17 (45.9)	8 (21.6)
New vomiting during transition phase	5 (50.0)	3 (30.0)	2 (20.0)
Continued vomiting from stabilisation phase	7 (41.2)	7 (41.2)	3 (17.6)
LOT 2-3 days (successful)	41 (32.3)	43 (27.6)	24 (24.7)
LOT > 3 days (failed)	86 (67.7)	113 (72.4)	73 (75.3)

Note: F-75 = Formula 75; F-100 = Formula 100; F-100D = Diluted formula 100; LOT = Length of transition; RUTF = Ready-to-use therapeutic food; kcal/kg/day = Kilocalories per kilogramper day; > = Greater than; < = Less than.

3.5.4 Clinical outcomes during the transition phase for children treated for complicated SAM

As depicted in **Table 3-1**, 74 (21%) children had diarrhoea during the transition phase of which 36 (49%) had new onset while 37 continued from stabilisation phase or recurred. Of the 27 (8%) children who vomited during the transition phase 10 (37%) had new onset of vomiting. The median LOT for children admitted at the three referral hospitals in Ghana was 6 (IQR: 3.0; 10.0) days. The majority (72%) of children with complicated SAM failed the transition phase on the first attempt, while 108 (28%) had a successful transition phase. **Figure 3-2** shows that 42% of children with diarrhoea received F-100, followed by RUTF, RUTF + F-75, F-100D + RUTF, and other foods. Diarrhoea was persistently high at TTH across all the age groups with a prevalence of 52.3%, 46.3% and 54.5% for ages 6 to 11 months, 12 to 23 months and 24 to 59 months, respectively. Fifteen of 27 children who vomited and 129 of 227 children who failed the transition on the first attempt received F-100. Diarrhoea was more common in children aged 12 to 23 months, while vomiting was more prevalent in children aged 6 to 11 months. Of the 272 children who failed the first attempt of transition, 59% were admitted at TTH, while 17% were admitted at PML. The majority (41%) of children who failed the transition phase on the first attempt were aged 12 to 24 months, followed by those aged 6 to 11 months (31%) across all hospitals (**Table 3-2**).

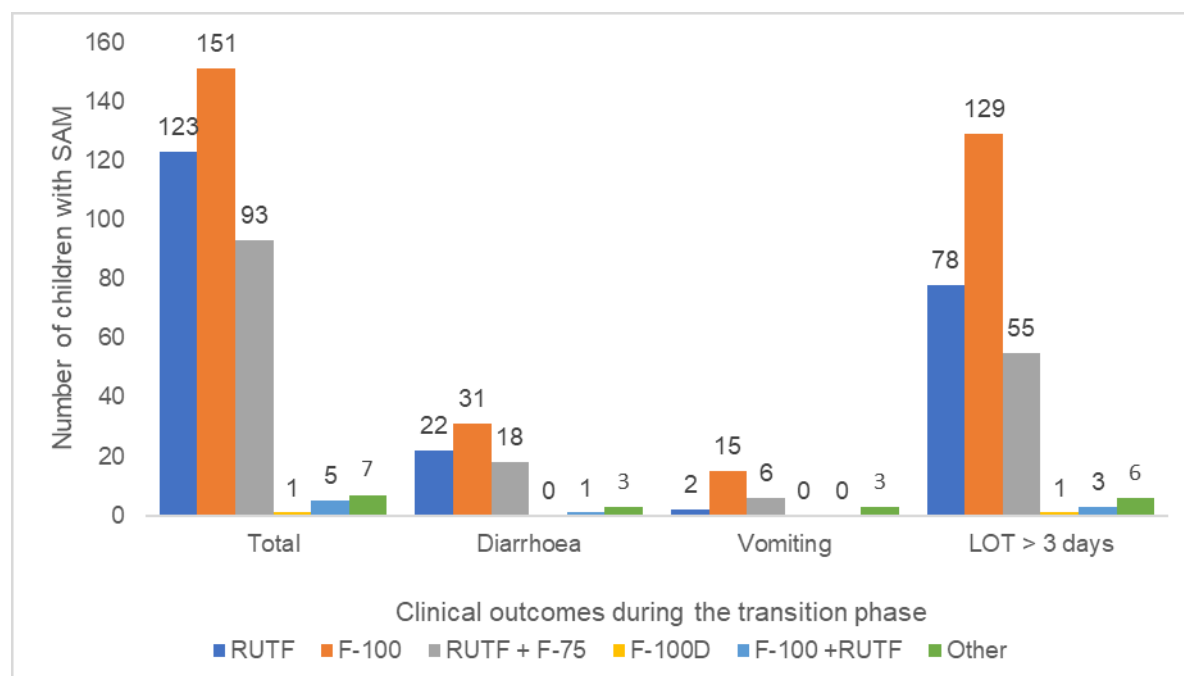


Figure 3-2: The number of children having diarrhoea, vomiting, and failed transition on the first attempt according to the type of transition feeding regimen in Ghana

3.5.5 Association between the transition feeding regimens with clinical outcomes

Logistic regression analyses were performed to investigate if there were relationships between the transition feeding regimens (F-100, RUTF, and RUTF + F-75) with diarrhoea status, vomiting, and LOT (Tables 3-3 to 3-5). We could not make associations between diluted formula-100 (F-100D), other feeds and F-100 + RUTF, because children who received these feeds were too few ($n = 1, 7, 5$, respectively). In **Table 3-3**, the predictor variable, F-100, in the logistic regression analysis did not contribute to the model; hence, there were no significant associations between the F-100 and diarrhoea status during the transition phase. However, vomiting during admission, oedematous malnutrition and HIV positive contributed to the model with an estimated odds ratio (OR) of 2.43 ($p < 0.05$), 3.18 ($p < 0.01$), and 3.12 ($p < 0.05$), respectively. Similarly, RUTF, as a predictor variable, did not contribute to logistic regression models of diarrhoea, vomiting and LOT, as depicted in **Table 3-4**. However, oedematous malnutrition and being HIV positive contributed to logistic regression models with estimated OR of 1.46 ($p < 0.01$), 2.36 ($p < 0.01$) respectively. Ready-to-use therapeutic food plus F-75 did not contribute in the logistic regression models for the response variables of diarrhoea, vomiting and LOT (**Table 3-5**) with estimated OR of 0.48 ($p > 0.05$), -0.56 ($p > 0.05$), -0.55 ($p > 0.05$).

Table 3-3: Logistic regression for F-100 adjusted for covariates against diarrhoea status, vomiting, and length of the transition phase for children treated for complicated SAM in Ghana

	Diarrhoea ¹		Vomiting ²		Length of the transition phase ³	
	OR	95% C.I.	OR	95% C.I.	OR	95% C.I.
F-100	0.698	(0.43, 9.31)	2.465	(0.34, 413.68)	0.98	(0.65, 10.92)
Oral feeding	-2.067	(0.01, 2.49)	-1.409	(0.00, 13.66)	-0.491	(0.05, 7.96)
NGT (referent)						
Age groups (months)						
06-11	1.264	(0.57, 22.00)	0.65	(0.10, 36.39)	0.376	(0.05, 6.11)
2-23	1.379	(0.64, 24.73)	-1.48	(0.01, 8.96)	-0.023	(0.28, 3.47)
24-59 (referent)	-	-	-	-	-	-
Gender						
Girl	-1.18	(0.07, 1.31)	-0.692	(0.06, 39)	0.589	(0.64, 5.11)
Boy (referent)	-	-	-	-	-	-
Admission hospital						
KATH	-2.243	(0.01, 1.22)	0.33	(0.06, 33.49)	-1.002	(0.08, 1.89)
PML	0.288	(0.17, 10.75)	0.186	(0.04, 34.42)	-0.632	(0.13, 2.16)
TTH (referent)	-	-	-	-	-	-
Diarrhoea on admission	-0.706	(0.09, 2.82)	-2.732	(0.00, 1.43)	-1.255*	(0.09, 0.92)
Child dehydrated on admission	0.506	(0.42, 6.55)	1.128	(0.33, 28.76)	1.306*	(1.14, 11.93)
Vomiting on admission	2.426*	(1.47, 86.81)	3.116	(0.51, 1004.92)	1.295*	(1.16, 11.54)
Oedematous SAM	3.176**	(3.39, 174.14)	1.422	(0.13, 129.04)	1.109	(0.87, 10.61)
HIV status of the child						
HIV negative	-0.702	(0.10, 2.46)	-0.879	(0.02, 8.64)	1.205	(0.95, 11.68)
HIV positive	3.12*	(1.61, 316.16)	2.306	(0.29, 510.57)	0.997	(0.42, 17.37)
Unknown (referent)	-	-	-	-	-	-
TB status of the child						
TB negative	2.36*	(1.62, 69.09)	0.621	(0.12, 28.06)	0.326	(0.49, 3.95)
TB positive	†		-0.875	(0.00, 6850.37)	1.197	(0.25, 43.14)
Unknown (referent)	-	-	-	-	-	-
Malaria	-0.967	(0.09, 1.68)	0	0	0.145	(0.38, 3.53)

Note: OR = Odds ratio; CI = Confidence interval; RUTF = Ready-to-use therapeutic food; HIV = Human immune virus; TB = tuberculosis; SAM = Severe acute malnutrition; NGT = Nasogastric tube; KATH = Komfo Anokye Teaching Hospital; PML= Princess Marie Louise Children's Hospital; TTH = Tamale Teaching Hospital.

*** Significance at the $p < 0.001$; ** Significance at the $p < 0.01$; * Significance at the $p < 0.05$; † = insufficient sample

¹Nagelkerke $R^2 = 0.493$; Omnibus Tests $\chi^2 = 40.941$ $p = 0.001$

²Nagelkerke $R^2 = 0.593$; Omnibus Tests $\chi^2 = 35.196$ $p = 0.004$

³Nagelkerke $R^2 = 0.278$; Omnibus Tests $\chi^2 = 26.662$ $p = 0.045$

Table 3-4: Logistic regression analysis for RUTF adjusted for covariates against diarrhoea status, vomiting, and the length of the transition phase for children treated for complicated SAM in Ghana

	Diarrhoea ¹		Vomiting ²		Length of the transition phase ³	
	OR	95% C.I.	OR	95% C.I.	OR	95% C.I.
RUTF	-0.375	(0.28, 1.67)	-0.938	(0.07, 2.16)	-0.542	(0.26, 1.39)
Oral feeding	-1.559	(0.04, 1.09)	-1.235	(0.05, 1.71)	0.499	(0.42, 6.26)
NGT (referent)						
Age groups (months)						
06-11	0.529	(0.52, 5.56)	0.335	(0.30, 6.40)	-0.004	(0.37, 2.65)
2-23	0.638	(0.71, 5.07)	-0.819	(0.10, 1.92)	-0.041	(0.40, 2.30)
24-59 (referent)	-	-	-	-	-	-
Gender						
Girl	-0.184	(0.39, 1.70)	-0.705	(0.16, 1.51)	0.419	(0.78, 2.95)
Boy (referent)	-	-	-	-	-	-
Admission hospital						
KATH	-1.342	(0.06, 1.15)	0.748	(0.42, 10.71)	-0.33	(0.25, 2.06)
PML	0.089	(0.38, 3.16)	1.188	(0.72, 15.02)	-0.863	(0.17, 1.06)
TTH (referent)	-	-	-	-	-	-
Diarrhoea on admission	0.064	(0.46, 2.47)	-1.041	(0.11, 1.17)	-0.442	(0.32, 1.30)
Child dehydrated on admission	0.255	(0.60, 2.79)	0.98	(0.91, 7.80)	0.061	(0.55, 2.06)
Vomiting on admission	0.272	(0.56, 3.05)	1.60*	(1.40, 17.65)	0.5	(0.82, 3.31)
Oedematous SAM	1.456**	(1.77, 10.42)	0.297	(0.35, 5.2)	0.555	(0.78, 3.90)
HIV status of the child						
HIV negative	-0.393	(0.28, 1.66)	-0.007	(0.29, 3.40)	0.57	(0.82, 3.83)
HIV positive	2.363**	(2.03, 55.49)	1.805	(0.88, 42.19)	0.465	(0.41, 6.25)
Unknown (referent)	-	-	-	-	-	-
TB status of the child						
TB negative	0.439	(0.70, 3.45)	0.859	(0.70, 7.91)	0.347	(0.72, 2.89)
TB positive	-2.138	(0.01, 1.85)	-0.549	(0.04, 8.29)	0.43	(0.31, 7.51)
Unknown (referent)	-	-	-	-	-	-

Note: OR = Odds ratio; CI = Confidence interval; RUTF = Ready-to-use therapeutic food; HIV = Human immune virus; TB = tuberculosis; SAM = Severe acute malnutrition; NGT = Nasogastric tube; KATH = Komfo Anokye Teaching Hospital; PML= Princess Marie Louise Children's Hospital; TTH = Tamale Teaching Hospital.

*** Significance at the $p < 0.001$; ** Significance at the $p < 0.01$; * Significance at the $p < 0.05$

¹Nagelkerke $R^2 = 0.214$; Omnibus Tests $\chi^2 = 30.901$, $p = 0.009$

²Nagelkerke $R^2 = 0.311$; Omnibus Tests $\chi^2 = 34.951$, $p = 0.002$

³Nagelkerke $R^2 = 0.104$; Omnibus Tests $\chi^2 = 16.444$, $p = 0.353$

Table 3-5: Logistic regression analysis for RUTF and F-75 adjusted for covariates against diarrhoea status, vomiting, and the length of the transition phase for children treated for complicated SAM in Ghana.

	Diarrhoea ¹		Vomiting ²		Length of the transition phase ³	
	OR	95% C.I.	OR	95% C.I.	OR	95% C.I.
RUTF + F-75	0.48	(0.29, 9.01)	-0.56	(0.02, 14.16)	-0.55	(0.15, 2.22)
Oral feeding	-2.20	(0.01, 2.17)	-2.05	(0.00, 5.95)	-0.53	(0.05, 7.62)
NGT (referent)	-	-	-	-	-	-
Age groups (months)						
06-11	1.08	(0.49, 17.59)	0.24	(0.08, 20.40)	0.21	(0.30, 5.01)
2-23	1.36	(0.64, 23.51)	-1.84	(0.01, 5.61)	-0.12	(0.26, 3.10)
24-59 (referent)	-	-	-	-	-	-
Gender						
Girl	-1.33	(0.06, 1.15)	-0.89	(0.05, 3.55)	0.56	(0.58, 4.29)
Boy (referent)	-	-	-	-	-	-
Admission hospital						
KATH	-1.85	(0.02, 1.69)	1.08	(0.12, 72.66)	-0.52	(0.15, 2.29)
PML	0.08	(0.13, 8.86)	-0.07	(0.03, 31.34)	-0.49	(0.14, 2.75)
TTH (referent)	-	-	-	-	-	-
Diarrhoea on admission	-0.94	(0.07, 2.10)	-3.04	(0.00, 1.02)	-1.43*	(0.08, 0.75)
Child dehydrated on admission	0.38	(0.38, 5.78)	0.99	(0.29, 25.29)	1.28*	(1.13, 11.42)
Vomiting on admission	2.46*	(1.67, 81.37)	3.17	(0.59, 959.47)	1.50*	(1.39, 14.26)
Oedematous SAM	2.92**	(9.94, 116.88)	0.38	(0.08, 27.73)	0.98	(0.78, 9.07)
HIV status of the child						
HIV negative	-0.56	(0.12, 2.77)	-0.34	(0.03, 15.84)	1.27*	(1.03, 12.25)
HIV positive	3.28*	(2.05, 347.07)	2.81	(0.33, 837.37)	1.00	(0.43, 17.06)
Unknown (referent)	-	-	-	-	-	-
TB status of the child						
TB negative	2.42*	(1.80, 70.17)	0.65	(0.15, 24.06)	0.50	(0.60, 4.51)
TB positive	†		-1.91	(0.00, 332.53)	1.25	(0.28, 43.72)
Unknown (referent)	-	-	-	-	-	-

Note: OR = Odds ratio; CI = Confidence interval; RUTF = Ready-to-use therapeutic food; HIV = Human immune virus; SAM = Severe acute malnutrition; NGT = Nasogastric tube; KATH = Komfo Anokye Teaching Hospital; PML= Princess Marie Louise Children's Hospital; TTH = Tamale Teaching Hospital.

*** Significance at the $p < 0.001$; ** Significance at the $p < 0.01$; * Significance at the $p < 0.05$; † = insufficient sample

¹Nagelkerke $R^2 = 0.48$; Omnibus Tests $\chi^2 = 40.414$, $p = 0.001$

²Nagelkerke $R^2 = 0.566$; Omnibus Tests $\chi^2 = 33.344$, $p = 0.007$

³Nagelkerke $R^2 = 0.266$; Omnibus Tests $\chi^2 = 25.345$, $p = 0.064$

3.6 Discussion

In this study, we observed that most children treated for complicated SAM in Ghana received WHO-recommended feeds during the transition phase. Although no significant associations between the transition feeding regimens and diarrhoea status, vomiting, and length of the transition phase were found, oedematous malnutrition, vomiting and diarrhoea during admission, and an HIV positive status were found to be predictors of vomiting and diarrhoea during the transition period, as well as increased length of the transition phase.

The transition feeding regimens used in Ghana were mainly the WHO-recommended feeds, thus, F-100, RUTF, and RUTF + 75^{6, 10}; however, 2% of children admitted at PML were prescribed other feeds such as Yomi yoghurt, a ferment daily product claimed to resolve diarrhoea and porridge. We also noted that some children were fed F-100D, F-100D + RUTF or F-100D + RUTF; the Interim Guidelines for the Management of SAM in Ghana does not mention these feeding regimens. Therefore, the assumption is that they received these at the discretion of the healthcare provider in the referral hospitals. We could not make any associations with these feeds, as the sample sizes were small. The WHO recommends that F-100D be used in infants aged 0 to 6 months of age during the stabilisation and the rehabilitation phases⁶. We observed that five children from PML were prescribed F-100 together with RUTF. According to the WHO guidelines, the F-100 should not be given together with RUTF since both feeds are similar in composition, except RUTF has added iron^{6, 25}. Contrary to Interim Guidelines for Management of SAM in Ghana and WHO guidelines, the use of nasogastric tubes for F-100 during the transition phase was observed in six children^{6, 10}. The guidelines indicate that children who require nasogastric tube feeding are not ready for the transition phase, hence, F-100 should not be given⁶.

In this study, we observed that over half (55%) of the children with SAM had over-prescription of energy, of which 98% were prescribed the RUTF feeding regimen. For this study, over-prescription during the transition phase was defined as prescribing energy above 135 kcal/kg/day⁶. We attribute over-prescription in children receiving RUTF to administration challenges as RUTF formulations come in fixed quantities (sachets and bars), unlike liquid feeds such as F-100²⁵. Over-prescription could be attributable to a combination of feeds without corresponding weaning of F-75. Bandsma *et al.* (2019) reported that overfeeding resulting from over-prescription is associated with feeding complications, including diarrhoea, vomiting, and refeeding syndrome, amongst others²⁶. To prevent these feeding complications, the WHO formulated feeding reference tables to guide health workers in prescribing feeds given for children with complicated SAM¹⁴.

In this study, we found that only 28% of children with complicated SAM completed the transition phase within the recommended two to three days on the first attempt^{6, 14}. However, this success rate was much lower than the 65% success rate reported by Lanyero *et al.* (2017) for children transitioning from F-75 to RUTF¹⁸. We attribute the lower success rate of the transition phase in this study to either over-prescription of feeds during the transition phase, poor documentation of clinical outcomes in the medical records or limited involvement of skilled medical professionals such as dietitians in the management of complicated SAM in Ghanaian hospitals²³. According to Molefi *et al.* (2019), children with complicated SAM in Ghanaian referral hospitals were mostly attended by health workers who had less experience in the management of SAM such as house officers and nutrition officers, unlike dietitians and paediatricians. Molefi *et al.* (2019) observed that in Ghanaian referral hospitals starter feeds were mainly prescribed by nutrition officers (37%) and the house officers (36%) across the hospitals where as the transition feeds were mostly prescribed by nutrition officers (69%) at TTH, by dietitians (69%) at PML and by the house officers (33%) at KATH²³.

The prevalence of new episodes of diarrhoea during the transition phase was lower than on admission, at 9.5% versus 49%. Of the 74 children who had diarrhoea during the transition phase, 50% were already having diarrhoea from the stabilisation phase. Diarrhoea was more prevalent in children who received F-100, RUTF, and RUTF + F-75, respectively; however, this study did not find significant associations in diarrhoea prevalence between the transition feeding regimens. The overall prevalence of diarrhoea was lower than the 50 to 67% reported in the literature^{27, 28}. A possible explanation of the low prevalence of diarrhoea in this study could be variation in the definition of diarrhoea by the medical providers, poor recording, under-reporting, lack of experience by some health professionals, or an enormous shortage of dietitians, as previously reported^{23, 29}. A high prevalence of diarrhoea in children with complicated SAM is generally due to carbohydrate maldigestion and malabsorption resulting from a reduction in enzyme production from the intestinal brush border, caused by inflammation and starvation. Other causes of diarrhoea in children with complicated SAM include use of antibiotics, secondary infections like TB of abdomen or HIV enteropathy^{30, 31}. The insignificant differences in diarrhoea prevalence between the transition feeding regimens are attributable to similarities in carbohydrate content between the three feeding regimens¹⁷.

In this study, we found that diarrhoea predictors in children receiving the three transition feeding regimens were vomiting during admission, oedematous malnutrition, and HIV-positive status; these results support previous studies³²⁻³⁴. For children with HIV among other infectious causes, diarrhoea is attributed to malabsorption caused by lactase deficiency, HIV enteropathy, antibiotic use and secondary infections³³, while for those with oedematous malnutrition, diarrhoea results

from either mucosal injury and lactose intolerance³⁴. We did not find significant differences between the transition feeding regimens on vomiting among children with complicated SAM in the referral hospitals.

The first attempt of the transition phase was successful in 28% of children admitted to the study hospitals. A child was classified to be successfully transitioned on first attempt if he or she took two to three days of transition and had no feeding complications (vomiting and/or diarrhoea) or worsening clinical conditions during the transition phase as recommended by the WHO⁶. Failure to transition on the first attempt – as defined by taking more than three days of transition, presence of feeding complications such as vomiting and diarrhoea and worsening of clinical conditions during the transition phase – appeared to be more prevalent in the F-100 group, followed by RUTF and RUTF + F-75 groups. However, there were no significant associations between the transition feeding regimens against failure to transition. Our findings were similar to what Versloot *et al.* (2017) reported in a prospective study, despite their comparison on transition feeding diets with different content of carbohydrates and their effect on faecal pH, length of stay and other clinical outcomes at the end of treatment²⁰. The predictor variables for a failed transition on the first attempt in our study were the presence of diarrhoea, vomiting, and oedematous malnutrition. Revelas (2012) and Manary *et al.* (2012) reported that diarrhoea, vomiting, and oedematous malnutrition are associated with reduced absorption of nutrients and fluids, increasing the LOT and overall length of hospital stay^{32, 35}.

This study had several strengths, including being among the first studies exploring the transition feeding regimen among children treated for complicated SAM using the WHO's recommended feeding regimens. This study is the first study conducted in Ghana, exploring the transition phase feeding practice among children treated for complicated SAM. The other strength is that the study was not influenced by healthcare providers' practice as the collection of data was from previously recorded information; this represents a real-life situation, guaranteeing no alteration. This study also took place at three randomly selected referral hospitals that provide a better understanding of the health system in Ghana.

Besides the strength alluded, this sub-study had some limitations in that it included a high rate of missing variables that prevented us from making some associations. The exclusion of some participants could also have contributed to selection bias that might have affected the results. In addition, we could not determine associations between actual kilocalories consumed and the clinical outcomes as actual consumption by the children could not be determined due to the poor

recording of intake in the medical records. Finally, the quality of data was a challenge to the study since there was no control of data recorded by the healthcare provider.

3.7 Conclusion

In conclusion, this study's findings show there are no associations between the transition feeding regimens with diarrhoea status, vomiting, and LOT. The actual calorie intake should be considered, as the low success in the transition might be due to the over-prescription of calories. Furthermore, since we can predict that children with complicated SAM are likely to have a longer and more complicated transition phase (i.e. those with diarrhoea, vomiting and HIV at admission), specialised feeds, for example, semi-elemental feeds, might be merited for a more cautious transition phase. Therefore, a large multi-hospital and rigorous controlled prospective study in this specific population is warranted to further develop nutritional guidelines for the successful transitioning from the stabilisation to the rehabilitation phase.

3.8 Reference

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CHAPTER 4 DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

4.1 Introduction

This chapter summarises this sub-study's main findings concerning the aim and objectives and provides general conclusions as well as proposed recommendations. This study forms part of the Severe Acute Malnutrition in African Children (SAMAC) larger study. The SAMAC study is an observational, multi-country, multi-hospital study that collects data from five countries Ghana, Botswana, South Africa, Kenya, and Malawi. This sub-study used data collected from Ghana.

The World Health Organization (WHO) recommends a gradual transition phase in children treated for complicated severe acute malnutrition (SAM) to avoid feeding complications. These feeding complications are associated with the rapid introduction of high-protein and high-energy diets, such as ready-to-use therapeutic food (RUTF) and Formula-100 (F-100) (WHO, 2013). However, the rationale behind the transition phase protocol has been based on clinical experience and the understanding of human physiology because of the absence of trial-based evidence (Manary *et al.*, 2012b). With evidence informing the practice of transition phase feeding being inadequate (WHO, 2013), this SAMAC study explored different transition feeding approaches used in Ghana to establish associations between the feeding approaches and vomiting, diarrhoea status, and length of the transition phase.

4.2 Research aim

The sub-study aimed to determine the associations of the feeding regimens used during the transition phase with vomiting, diarrhoea status, and the duration of the transition phase in infants and children (6–59 months) treated for complicated SAM in three Ghanaian referral hospitals.

4.3 Specific objectives

The objectives of this study were to:

- 4.3.1. Identify the transition feeding regimes used to manage children (6–59 months) with complicated SAM in three Ghanaian referral hospitals.
- 4.3.2 Describe:
 - a. the total energy prescribed per kilogram body weight (kcal/kg/day) by considering the volume and type of transition feed prescribed;
 - b. vomiting and diarrhoea that developed during the transition phase;
 - c. the number of days spent in the transition phase.

CHAPTER 4 DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

- 4.3.3 Determine the transition feeding regimens' associations with vomiting, diarrhoea, and length of the transition phase.

4.4 The transition feeding regimes used for the management of children with complicated SAM in three Ghanaian referral hospitals.

The WHO recommends the use of F-100, RUTF, and RUTF plus F-75 as standard feeds during the transition phase for children with complicated SAM. The transition phase provides an opportunity to change energy intake from a low-calorie diet (F-75) gradually to a high-calorie diet (F-100 or RUTF) that is necessary for catch up growth without necessarily overwhelming the physiological processes of the body in a child with complicated SAM (WHO, 2013). This study shows that 98% of children treated for complicated SAM in Ghana received WHO-recommended feeds, including F-100, RUTF, or RUTF plus F-75; the remaining 2% of the children received non-standardised feeds, such as Yomi yoghurt and porridge.

The standard feeds recommended by WHO are specially designed to treat complicated SAM (Ashworth *et al.*, 2003). Formula-100 provides per 100 ml of feed: 100 kcal of energy, 13 g protein, 26 g fat, and 5.9 mmol potassium (WHO, 2002). The quantities of energy and proteins in this diet are higher compared to 100ml of F-75 (75 kcal of energy, 5.9 g protein, 15.6 of fat and 3.6 mmol potassium) and aims at promoting tissue repair and catch-up growth (Ashworth *et al.*, 2003; Lenters *et al.*, 2016). The alternative transition feed recommended by WHO is RUTF (WHO, 2013). Ready-to-use therapeutic foods are energy-dense micronutrient enriched foods available as pastes, spreads, or biscuits with a nutritional profile similar to F-100 (Manary *et al.*, 2012c; Schoonees *et al.*, 2019). These foods are often made of peanuts, oil, sugar, milk powder, vitamin and mineral supplements (Manary *et al.*, 2012b). Ready-to-use therapeutic food is soft and can be consumed easily by children with complicated SAM from 6 months of age (UNICEF, 2013). The RUTFs provide all the nutrients required for recovery, have a good shelf life, have a limited risk of contamination, and are safe to use without refrigeration (UNICEF, 2013). The use of RUTF in the management of children with SAM has replaced F-100 during the transition phase and the rehabilitation phases in various settings where children with complicated SAM are treated (WHO, 2019).

4.5 Total energy prescribed per kilogram bodyweight

In addition to the transition-feeding regimen, the quantity of feeds given to children with complicated SAM during the transition phase plays an essential role in clinical outcomes. In this study, we observed that over half of children with complicated SAM (58.5%) had over-prescription of energy, of which 98% were prescribed RUTF. We attribute over-prescriptions in children receiving RUTF to administration challenges as RUTF formulations come in fixed quantities

CHAPTER 4 DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

(sachets and bars), unlike liquid feeds such as F-100 (Manary *et al.*, 2012b). Over-prescription was also due to a combination of feeds without weaning of F-75 during the transition phase. Research has shown that overfeeding resulting from over-prescription is associated with feeding complications such as diarrhoea, vomiting, and refeeding syndrome, amongst others (Golden & Grellety, 2011; Bandsma *et al.*, 2019). To prevent these feeding complications, the WHO formulated feeding reference tables to guide health workers in prescribing feeds for children with complicated SAM (Ashworth *et al.*, 2003). From the over-prescription of feeds, it though seems as if these are either not used or not correctly used by the health care workers.

4.6 Vomiting and diarrhoea and length of the transition phase

Despite the high prevalence of energy over-prescription, we observed few diarrhoea and vomiting cases during the transition phase among children treated for complicated SAM in Ghanaian hospitals. Specifically, 21% of children admitted in the Ghanaian referral hospitals developed diarrhoea during the transition phase, while 8% of the children vomited. The prevalence of diarrhoea observed in the current study was lower than the overall 50 to 67% reported in the literature (Irena *et al.*, 2011; Talbert *et al.*, 2012). Though, the definition of diarrhoea often differs depending on perceptions of the attending healthcare provider and setting (Irena *et al.*, 2011). In addition, there were no specific feeding regimens associated with either diarrhoea or vomiting during the transition phase. A possible explanation for the low prevalence of diarrhoea and vomiting observed in the current study could be under-reporting and high missing variables rates (Shihundla *et al.*, 2016). Generally, the high prevalence of diarrhoea and vomiting in children with complicated SAM, as reported in other studies (Lanyero *et al.*, 2017; Versloot *et al.*, 2017) can be due to carbohydrate malabsorption and maldigestion resulting from a reduction in lactase production from the intestinal brush border, caused by inflammation, vomiting, and starvation.

This study also observed that, although not significant, the first attempt of the transition phase (two to three days), as recommended by the WHO, was lower (28%) than previously reported (65%) in the literature (Lanyero *et al.*, 2017). The failure to transition on the first attempt as defined by the development of vomiting and diarrhoea and taking more than 3 days of transition appeared to be more prevalent in the F-100 group, followed by the RUTF and RUTF plus F-75 groups. However, there were no significant differences between the transition feeding regimens against failure to transition on the first attempt. The findings support those of Versloot *et al.* (2017) on similar transition feeding regimens.

CHAPTER 4 DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

4.7 Associations of the transition feeding regimens with vomiting, diarrhoea, and length of the transition phase

In the current study, we did not find any associations between the type of transition feeding regimen with diarrhoea, vomiting, and length of the transition phase. However, predictors of diarrhoea, vomiting, and increased length of transition phase observed in this study were vomiting during admission, oedematous malnutrition, and an HIV positive status. Acute gastroenteritis is the most common cause of vomiting in children (Revelas, 2012). Vomiting is associated with poor digestion and low nutrient absorption (Wharton *et al.*, 1968; Revelas, 2012). Collins *et al.* (2006) attributed diarrhoea in children with HIV to malabsorption caused by lactase deficiency. Diarrhoea results from mucosal injury and lactose intolerance (Wharton *et al.*, 1968). All these variables are associated with reduced absorption of nutrients and fluids, thereby increasing the length of the transition and overall length of stay (Manary *et al.*, 2012a). A limitation to this study was though that we could not study the association between the actual calorie intake and the outcomes as intake was not well recorded in medical records.

4.8 Conclusions and recommendations arising from the study

This study demonstrated that referral hospitals in Ghana use the WHO-recommended feeds (F-100, RUTF, RUTF plus F-75) during the transition phase. The current transition feeding regimens are also not associated with diarrhoea, vomiting, or increased length of the transition phase. These low transition success rates might however be due to over-prescriptions which may result in overfeeding and poor digestibility, as observed from previous studies. More research on this is thus warranted. Furthermore, since we can predict children with complicated SAM who are likely to have a longer and more complicated transition phase from admission (i.e. those with diarrhoea, vomiting and HIV at admission), these populations could benefit from specialised feeds, for example, lactose-free, semi-elemental feeds or a more cautious transition phase. Therefore, a study in this specific population is justified to further develop guidelines for optimal care. At the same time, there is an urgent need to explore better alternative feeds with better digestibility. Therefore, the recommendation is for a large multi-site and rigorous controlled prospective study to explore alternative transition feeding regimens with real-time data collection on consumption. The study also proposes improving monitoring and documentation of children treated for complicated SAM in Ghana's referral hospitals.

4.9 Strength of the study

This study had several strengths, including being amongst the first studies to explore the transition feeding regimen among children treated for complicated SAM using the WHO's recommended feeding regimens. This is the first study conducted in Ghana that has explored the transition phase feeding practice among children treated for complicated SAM.

CHAPTER 4 DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

Another strength is that the study did not influence healthcare providers' practice, as the collection of data was collected from previously recorded information; this represents a real-life situation, guaranteeing no alteration. The sub-study also took place in three randomly selected referral hospitals that provide a better understanding of the health system in Ghana.

4.10 Limitation of the study

Besides the strength alluded, this sub-study had some limitations, including a high rate of missing variables, which failed to make some associations. The high missing variables did not allow us to report the actual consumption of the transition feeds by the children being treated for SAM in Ghana. Due to poor reporting of the actual feed intake within the medical records, we could also not determine associations between the energy consumed and the outcomes studied. The exclusion of some participants may also have contributed to selection bias that could have affected the results.

Finally, the study was challenged by the quality of data, as there was no control over the data recorded by the healthcare providers.

CHAPTER 4 DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

4.11 References

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Talbert Alison, Thuo Nahashon, Karisa Japhet, Chesaro Charles, Ohuma Eric, Ignas James, Berkley James A, Toromo Christopher, Atkinson Sarah & Maitland Kathryn. 2012. Diarrhoea complicating severe acute malnutrition in Kenyan children: a prospective descriptive study of risk factors and outcome. *PloS one*, 7(6):e38321.

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<https://www.who.int/news-room/fact-sheets/detail/children-reducing-mortality> Date of access:
09th July 2020.

ANNEXURES

ANNEXURE 1: NWU HREC Ethical Approval for the SAMAC Study



Private Bag X6001, Potchefstroom,
South Africa, 2520

Tel: (018) 299-4900
Faks: (018) 299-4910
Web: <http://www.nwu.ac.za>

Research Ethics Regulatory Committee

Tel: +27 18 299 4849
Email: Ethics@nwu.ac.za

ETHICS APPROVAL CERTIFICATE OF STUDY

Based on approval by Health Research Ethics Committee (HREC) on 19/01/2018, the North-West University Research Ethics Regulatory Committee (NWU-RERC) hereby approves your study as indicated below. This implies that the NWU-RERC grants its permission that provided the special conditions specified below are met and pending any other authorisation that may be necessary, the study may be initiated, using the ethics number below.

Study title: Evaluation of admission criteria and treatment guidelines of African infants and children (0-59 months) diagnosed with severe acute malnutrition – the SAMAC-study

Study Leader/Supervisor: Dr MJ Lombard

Student:

Ethics number:

N W U - 0 0 0 6 3 - 1 7 - A 1

Institution Study Number Year Status
Status: S = Submission; R = Re-Submission; P = Provisional Authorisation; A = Authorisation

Application Type: Large Study

Commencement date: 2018-01-19

Risk:

Minimal

Approval of the study is initially provided for a year, after which continuation of the study is dependent on receipt of the annual (or as otherwise stipulated) monitoring report and the concomitant issuing of a letter of continuation.

Special conditions of the approval (if applicable):

This approval is provided for the study to be undertaken in Ghana. Before the study can commence in Botswana or South Africa, however, the researchers will have to:

1. Please provide the HREC with copies of the ethical approval letters from the Botswanan Ministry of Health indicating that the study can be conducted.
2. Please provide the HREC with copies of the approval letters from the South African provincial Department of Health for the different provinces to be included, indicating that the study can be conducted.
3. Please provide the HREC with copies of the goodwill permission letters from hospitals to be included in the study indicating that you can utilise their services/facilities.

General conditions:

While this ethics approval is subject to all declarations, undertakings and agreements incorporated and signed in the application form, please note the following:

- The study leader (principle investigator) must report in the prescribed format to the NWU-RERC via HREC:
 - annually (or as otherwise requested) on the monitoring of the study, and upon completion of the study
 - without any delay in case of any adverse event or incident (or any matter that interrupts sound ethical principles) during the course of the study.
- Annually a number of studies may be randomly selected for an external audit.
- The approval applies strictly to the proposal as stipulated in the application form. Should any changes to the proposal be deemed necessary during the course of the study, the study leader must apply for approval of these amendments at the HREC, prior to implementation. Should there be any deviations from the study proposal without the necessary approval of such amendments, the ethics approval is immediately and automatically forfeited.
- The date of approval indicates the first date that the study may be started.
- In the interest of ethical responsibility the NWU-RERC and HREC retains the right to:
 - request access to any information or data at any time during the course or after completion of the study;
 - to ask further questions, seek additional information, require further modification or monitor the conduct of your research or the informed consent process.
 - withdraw or postpone approval if:
 - any unethical principles or practices of the study are revealed or suspected,
 - it becomes apparent that any relevant information was withheld from the HREC or that information has been false or misrepresented,
 - the required amendments, annual (or otherwise stipulated) report and reporting of adverse events or incidents was not done in a timely manner and accurately,
 - new institutional rules, national legislation or international conventions deem it necessary.
- HREC can be contacted for further information or any report templates via Ethics-HREC@nwu.ac.za or 018 299 1200.

The RERC would like to remain at your service as scientist and researcher, and wishes you well with your study. Please do not hesitate to contact the RERC or HREC for any further enquiries or requests for assistance.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Refilwe' followed by a stylized surname.

Prof. Refilwe Phaswana-Mafuya
Chair MWU Research Ethics Regulatory Committee (RERC)

ANNEXURE 2: Sub-Study HREC Approval



Private Bag X1290, Potchefstroom
South Africa 2520

Tel: 086 016 9698
Web: <http://www.nwu.ac.za/>

**North-West University Health Research Ethics
Committee (NWU-HREC)**

Tel: 018 299-1206
Email: Ethics-HRECAppl@nwu.ac.za (for human
studies)

13 November 2020

ETHICS APPROVAL LETTER OF STUDY

Based on approval by the North-West University Health Research Ethics Committee (NWU-HREC) on 13/11/2020, the NWU-HREC hereby approves your study as indicated below. This implies that the NWU-HREC grants its permission that, provided the general conditions specified below are met and pending any other authorisation that may be necessary, the study may be initiated, using the ethics number below.

Study title: Transition phase feeding in infants and children (6-59 months) treated for severe acute malnutrition in Ghanaian referral hospitals: the SAMAC study																																											
Principal Investigator/Study Supervisor/Researcher: Ms C Conradie																																											
Student: H Chatenga - 33471177																																											
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Application Type: Sub-study Commencement date: 13/11/2020 Expiry date: 30/11/2021																																											
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Approval of the study is provided for a year, after which continuation of the study is dependent on receipt and review of an annual monitoring report and the concomitant issuing of a letter of continuation. A monitoring report is due at the end of November annually until completion.																																											

General conditions:

While this ethics approval is subject to all declarations, undertakings and agreements incorporated and signed in the application form, the following general terms and conditions will apply:

- The principal investigator/study supervisor/researcher must report in the prescribed format to the NWU-HREC:
 - Annually on the monitoring of the study, whereby a letter of continuation will be provided annually, and upon completion of the study; and
 - without any delay in case of any adverse event or incident (or any matter that interrupts sound ethical principles) during the course of the study.
- The approval applies strictly to the proposal as stipulated in the application form. Should any amendments to the proposal be deemed necessary during the course of the study, the principal investigator/study supervisor/researcher must apply for approval of these amendments at the NWU-HREC, prior to implementation. Should there be any deviations from the study proposal without the necessary approval of such amendments, the ethics approval is immediately and automatically forfeited.
- Annually a number of studies may be randomly selected for active monitoring.
- The date of approval indicates the first date that the study may be started.
- In the interest of ethical responsibility, the NWU-HREC reserves the right to:
 - request access to any information or data at any time during the course or after completion of the study;
 - to ask further questions, seek additional information, require further modification or monitor the conduct of your research or the informed consent process;

- *withdraw or postpone approval if:*
 - *any unethical principles or practices of the study are revealed or suspected;*
 - *it becomes apparent that any relevant information was withheld from the NWU-HREC or that information has been false or misrepresented;*
 - *submission of the annual monitoring report, the required amendments, or reporting of adverse events or incidents was not done in a timely manner and accurately; and/or*
 - *new institutional rules, national legislation or international conventions deem it necessary.*
- NWU-HREC can be contacted for further information via Ethics-HRECAppl@nwu.ac.za or 018 299 1206

Special conditions of the research approval due to the COVID-19 pandemic:

Please note: Due to the nature of the study i.e. (statistical analyses of previously collected data from the SAMAC study), this study will be able to proceed during the current alert level, following receipt of the approval letter. No additional COVID-19 restrictions have been placed on the study except that the researcher must ensure that before proceeding with the study that all research team members have reviewed the North-West University COVID-19 Occupational Health and Safety Standard Operating Procedure.

The NWU-HREC would like to remain at your service and wishes you well with your study. Please do not hesitate to contact the NWU-HREC for any further enquiries or requests for assistance.

Yours sincerely,

 Digitally signed
by Prof Petra
Bester
Date: 2020.11.15
18:49:28 +02'00'

Chairperson NWU-HREC

Current details: (23239522) G:\My Drive\9. Research and Postgraduate Education\9.1.5.4 Templates\9.1.5.4.2_NWU-HREC_EAL.docm
20 August 2019
File Reference: 9.1.5.4.2

ANNEXURE 3: Ethical Approval from Ghana Health Service**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

MyRef. GHS/RDD/ERC/Admin/App 1-5 611
Your Ref. No.

Janet Adede Carboo
North-West University
South Africa

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

GHS-ERC Number	GHS-ERC: 25/06/17
Project Title	Assessment and Evaluation of In-patient Diagnosis and Discharge Protocols in Ghanaian Infants and Children (0-59 Months) Diagnosed with Severe Acute Malnutrition – The SAMAC – (Ghana Sub-Study)
Approval Date	27 th June, 2017
Expiry Date	26 th June, 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

ANNEXURE 4: Ethical Approval from Ethics Review Committee of KATH



KWAME NKURUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY
COLLEGE OF HEALTH SCIENCES



SCHOOL OF MEDICAL SCIENCES / KOMFO ANOKYE TEACHING HOSPITAL
COMMITTEE ON HUMAN RESEARCH, PUBLICATION AND ETHICS

Ref: CHRPE/AP/374/17

30th June, 2017.

Dr. Matani J. Lombard
Directorate of Child Health
KATH-KUMASI

Dear Sir,

LETTER OF APPROVAL

Protocol Title: *"Evaluation of Admission Criteria and Treatment Guideline of Sub-Saharan Africa and Children (0-59) Diagnosed with Severe Acute Malnutrition – the SAMAC Study."*

Proposed Site: *Chest Clinic, Directorate of Medicine, Komfo Anokye Teaching Hospital.*

Sponsor: *Cfar Grant.*

Your submission to the Committee on Human Research, Publications and Ethics on the above named protocol refers.

The Committee reviewed the following documents:

- A notification letter of 26th April, 2017 from the Komfo Anokye Teaching Hospital (study site) indicating approval for the conduct of the study in the Hospital.
- A Completed CHRPE Application Form.
- Participant Information Leaflet and Consent Form.
- Research Protocol.
- Questionnaire.

The Committee has considered the ethical merit of your submission and approved the protocol. The approval is for a fixed period of one year, beginning 30th June, 2017 to 29th June, 2018 renewable thereafter. The Committee may however, suspend or withdraw ethical approval at any time if your study is found to contravene the approved protocol.

Data gathered for the study should be used for the approved purposes only. Permission should be sought from the Committee if any amendment to the protocol or use, other than submitted, is made of your research data.

The Committee should be notified of the actual start date of the project and would expect a report on your study annually or at the close of the project, whichever one comes first. It should also be informed of any publication arising from the study.

Thank you Sir, for your application.

Yours faithfully,

Rev. Prof. John Appiah-Poku,
Honorary Secretary
FOR: CHAIRMAN

Room 7 Block J, School of Medical Sciences, KNUST, University Post Office, Kumasi, Ghana
Phone: +233 3220 63248 Mobile: +233 20 5453785 Email: chrpe.knust.kath@gmail.com / chrpe@knust.edu.gh

ANNEXURE 5: Letter of Approval from KATH and PML Management

**KOMFO ANOKYE
TEACHING HOSPITAL**

DIRECTORATE OF CHILD HEALTH



P. O. Box 1934
KUMASI - GHANA
Tel: +233 - 3220-22301 - 4
Fax: +233 - 3220 - 24654/24621
Website: www.kathsp.org

Our Ref. No:.....

Your Ref. No:.....

12 MAY 2017

DR. MARTANI LOMBARD

Dear Sir/Madam

LETTER OF APPROVAL

RE: "EVALUATION OF ADMISSION CRITERIA AND TREATMENT GUIDELINES OF SUB-SAHARA AFRICAN INFANTS AND CHILDREN (0-59 MONTHS) DIAGNOSED WITH SEVERE ACUTE MALNUTRITION –THE SAMAC- STUDY AT KOMFO ANOKYE TEACHING HOSPITAL"

Approval is hereby given for you to conduct the study entitled "Evaluation of admission criteria and treatment guidelines of sub-Saharan African infants and children (0-59 months) diagnosed with severe acute malnutrition – the SAMAC- study at Komfo Anokye Teaching Hospital" subject to ethical approval.

It is required that any future revisions or amendments are duly communicated to the directorate.

Thank you.


PROF. E. O. D. ADDO-YOBO
HEAD OF DIRECTORATE

A Centre of Excellence

ANNEXURE 6: Letter of Approval from PML Children's Hospital

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

My Ref. No. GHS/PMLCH/RS/C-43

Your Ref. No.



PML CHILDREN'S HOSPITAL
GHANA HEALTH SERVICE
POST OFFICE BOX GP 122
ACCRA.

TEL. NO. 0302-664137/34673477
FAX #: 0302-673344

E-mail: pmlhosp@ghs.gov.gh
Website: www.pmlhosp.com.gh

September 9, 2017

DR. MARTANI LOMBARDO
CENTRE OF EXCELLENCE FOR NUTRITION
SCHOOL OF PHYSIOLOGY, NUTRITION AND CONSUMER SCIENCES
NORTH-WEST UNIVERSITY, POTCHEFSTROOM CAMPUS

APPROVAL LETTER

This is to officially inform you that approval has been given for Ms. Janet Carboo to carry out her research on the Topic: *Evaluation of Admission Criteria and Treatment Guidelines of African Infants and Children (0-59 Months) Diagnosed with Severe Acute Malnutrition - The SAMAC-Study (Ghana Sub-study)* in the Princess Marie Louise Children's Hospital having seen the Ethical Clearance from the Ghana Health Service.

Thank you

DR. ISAAC KOBINA ABBAN
(MEDICAL SUPERINTENDENT (AG))

ANNEXURE 7: Approval from TTH Management

**Department of Research & Development
Tamale Teaching Hospital**

TTH/R&D/SR/46
28/03/2018

TO WHOM IT MAY CONCERN**CERTIFICATE OF AUTHORIZATION TO CONDUCT RESEARCH IN
TAMALE TEACHING HOSPITAL**

I hereby introduce to you **Dr. Martani Lombard (Primary Investigator), Dr. Robin Dolman, Mrs. Cornelia Conradie, Dr. Cristian Ricci and Prof. Etienne Nel (Co-Primary Investigators)**, A team of researchers from the centre of Excellence for Nutrition (CEN) at North-West University, Potchefstroom, South Africa. They have been duly authorized to conduct a study on **"Evaluation of Admission criteria and treatment guidelines of African infant and children (0-59 months) diagnosed with severe Acute Malnutrition-The SAMAC-Study (Ghana Sub-study)"**.

Please accord them the necessary assistance to enable them complete their study. If in doubt, kindly contact the Research Unit on the second floor of the administration block or on Telephone 0209281020. In addition, kindly report any misconduct of the Researcher to the Research Unit for necessary action.

Please note that this approval is given for a period of four months, beginning from 28th of March, 2018 to 15th of July, 2018.

Thank You.

ALHASSAN MOHAMMED SHAMUDEEN

(HEAD, RESEARCH & DEVELOPMENT)

ANNEXURE 8: Screening Form

SAMAC

Screening form: Ghana

For each file screened, the following questions should be considered to determine inclusion.

INCLUDED: All questions are answer YES (Y).

EXCLUDED: 1 of more questions are answered NO (N)

(Conditions or diseases related to SAM: recurring infections, malaria, dehydration, diarrhoea, TB, parasite infestations, cholera etc.)

(Medical problems NOT related to SAM: metabolic, neurodevelopmental or any other growth disorder)

Date	Hospital	File number	Criteria for inclusion:																	
			Age between 0 – 59 mo?		Diagnosis of SAM?		Diagnosis of condition or disease related to SAM?		Medical problems not related to SAM is <u>NOT</u> present?		Date of file ≥ 2013?		Born full term?		Normal birth weight?		Complete medical information?			
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED
			Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	INCLUDED	EXCLUDED

ANNEXURE 9: Data Extraction Register

SAMAC-Study

PARTICIPANTS- GHANA

Participant Nr	Date	Hospital	File number
GHA-001			
GHA-002			
GHA-003			
GHA-004			
GHA-005			
GHA-006			
GHA-007			
GHA-008			
GHA-009			
GHA-010			
GHA-011			
GHA-012			
GHA-013			
GHA-014			
GHA-015			
GHA-016			
GHA-017			
GHA-018			
GHA-019			
GHA-020			
GHA-021			
GHA-022			
GHA-023			
GHA-024			
GHA-025			
GHA-026			
GHA-027			
GHA-028			
GHA-029			
GHA-030			
GHA-031			
GHA-032			
GHA-033			
GHA-034			
GHA-035			
GHA-036			
GHA-037			
GHA-038			
GHA-039			
GHA-040			

ANNEXURE 10: Data Extraction Form

SAMAC

DATA EXTRACTION FORM

1. DEMOGRAPHIC INFORMATION													
1.1. Participant number						1.2. Country				1.3. Hospital			
1.4. Town						1.5. Province/District							
1.6. Data collected by (Name of field worker):						1.7. Date of data collection							
1.8. Was patient referred from a clinic or hospital?			Yes		No		1.9. If YES, name of hospital or clinic						

2. ADMISSION DATA (Status of child at admission)																					
2.1. Admission information documented by				Paediatrician			GP			House officer/ Intern			Dietitian			Nutrition officer			Nurse		
				Others (Specify)																	
2.2. Date of admission		20	Y	M	D	2.3. Time of admission		2.4. Date of birth		20	Y	M	D	2.5. Current Age (months)							
2.6. Gender		Boy		Girl		2.7. When was SAM diagnosed		At admission				While admitted									
2.8. Date of SAM diagnosis while on admission		20	Y	M	D	2.9. New admission for SAM		Yes		No		2.10. Readmission for SAM		Yes		No					
2.11. Weight on admission (kg)		Kg				2.12. Height/length measurement (cm)		cm													
		Not recorded						Not recorded													
2.13. Which of the following was measured:						Height				Length				Not indicated							
2.14. MUAC (mm)						2.15. Recorded weight for height/ length Z score															
		Not recorded						Not Recorded													
2.16. Oedema grade		0		+ (mild)			++ (moderate)			+++ (severe)											

Participant Number:

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SAMAC

DATA EXTRACTION FORM

2.17. Clinical Signs	Irritability		Wasting		Eye signs		Diarrhoea	
	Dermatitis		Severe pallor		Shock		Vomiting	
	Convulsions		Irregular heart beat		Weak pulse			
	Slow capillary fill (> 3 seconds)		Cold hands / feet		Fast pulse			
2.18. HIV/RVD status at admission	Positive		Negative		Unknown			
2.19. ARV/RVD treatment at admission	No		Yes, Prior to admission		Unknown			
2.20. List ARV/RVD medications at admission	Medication	Dosage	Medication	Dosage	Medication	Dosage		
2.21. TB status at admission	Positive		Negative		Unknown			
2.22. TB treatment at admission	No		Yes, Prior to admission		Unknown			
2.23. List TB medications at admission	Medication	Dosage	Medication	Dosage	Medication	Dosage		
2.24. Other medications at admission	Medication	Dosage	Medication	Dosage	Medication	Dosage		
	Medication	Dosage	Medication	Dosage	Medication	Dosage		
2.25. Medical complication/diagnosis at admission								
Conscious	Not reported	Yes	No	Hypoglycaemia (< 3 mmol/L)	Not reported	Yes	No	
Dehydration	Not reported	Yes	No	Hypothermia (< 35 °C)	Not reported	Yes	No	
Respiratory tract infection	Not reported	Yes	No	Urinary tract infection	Not reported	Yes	No	
Meningitis	Not reported	Yes	No	Malaria	Not reported	Yes	No	

Participant Number:

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SAMAC

DATA EXTRACTION FORM

2.26. List other diagnosis at admission													
2.27. Did the patient receive any IV at admission/Casualty/Emergency								Yes		No			
2.28. If yes, Type of IV fluid received			Rate	___/___hrly	Total volume		Duration (no of hrs):						
If yes, Type of IV fluid received			Rate	___/___hrly	Total volume		Duration (no of hrs):						
If yes, Type of IV fluid received			Rate	___/___hrly	Total volume		Duration (no of hrs):						
2.29. Did patient receive 10% glucose or sucrose solution within 30 minutes of admission								Yes		No			
Route	NGT		Oral		IV		Rate	___/___hrly	Total volume		Duration (no of hrs)		
2.30. Did the patient receive ReSoMal?								Yes		No			
Route	NGT		Oral				Rate	___/___hrly	Total volume		Duration (no of hrs)		
2.31. Did the patient receive other oral rehydration solutions at admission?								Yes		No		Name of ORS given	
Route	NGT		Oral				Rate	___/___hrly	Total volume		Duration (no of hrs)		
2.32 Did patient received any feed (s) within 30 minutes of admission								Yes		No			
2.33. What feed was given at admission													
Route	NGT		Oral				Rate	___/___hrly	Total volume		Duration (no of hrs)		

SAMAC

DATA EXTRACTION FORM

[illegible]

Participant Number:

SAMAC

DATA EXTRACTION FORM

[illegible]

Participant Number:

SAMAC

DATA EXTRACTION FORM

4. BIOCHEMICAL INFORMATION (Information during hospital stay)									
Blood Tests	Unit	Date	Result	Date	Result	Date	Result	Date	Result
S-Na									
S-K									
S-Cl									
S-urea									
S-Creatinine									
S-Albumin									
S-CRP									
Red Blood Count									
Hb									
Haematocrit									
MCV									
MCH									
MCHC									
Platelet Count									
White Blood Count									
S-Fe									

Participant Number:

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SAMAC

DATA EXTRACTION FORM

5. FEEDING (During hospital stay)													
5.1. Feeds prescribed by		Paediatrician		GP		House officer/Intern		Dietitian		Nutrition Officer		Nurse	
		Others (Specify)											
5.2. When were feeds initiated		Date					Time			Not Recorded			
5.3. STARTER FEEDS													
Date	Feed (F75, Infant formula, Breast milk, others.)	Name of Product	Pre-mixed	Self-mixed	Route		Rate	Nr of feeds/day	Total volume prescribed /day (ml)	Total volume consumed/ day(ml)	Ward diet or solids given while on starter feeds		If Yes, which ward diet or solid feed was given
					NGT	Oral					Yes	No	
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						

Participant Number:

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SAMAC

DATA EXTRACTION FORM

5. FEEDING (During hospital stay)													
5.3. STARTER FEEDS Continued													
Date	Feed (F75, Infant formula, Breast milk, others.)	Name of Product	Pre-mixed	Self-mixed	Route		Rate	Nr of feeds/day	Total volume prescribed /day (ml)	Total volume consumed/ day(ml)	Ward diet or solids given while on starter feeds		If Yes, which ward diet or solid feed was given
					NGT	Oral					Yes	No	
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
5.4. For self-mixed recipes feeds record recipe													

SAMAC

DATA EXTRACTION FORM

5. FEEDING (During hospital Stay)														
5.5. Feeds prescribed by		Paediatrician		GP		House officer/Intern			Dietitian		Nutrition Officer		Nurse	
		Others (Specify)												
5.6. When were feeds transitioned		Date			Time			Not Recorded						
5.7. TRANSITION FEEDS														
Date	Feed (FI00, Infant formula, Breast milk, RUTF, others.)	Name of Product	Pre-mixed	Self-mixed	Route		Rate	Nr of feeds/day	Total volume prescribed /day (ml)	Total volume consumed/ day(ml)	Ward diet or solids given while on transition feeds		If Yes, which ward diet or solid feed was given	
					NGT	Oral					Yes	No		
							___/___hrly							
							___/___hrly							
							___/___hrly							
							___/___hrly							
							___/___hrly							
							___/___hrly							
							___/___hrly							
							___/___hrly							
							___/___hrly							

Participant Number:

SAMAC

DATA EXTRACTION FORM

5. FEEDING (During hospital Stay)													
5.7. TRANSITION FEEDS continued													
Date	Feed (FI00, Infant formula, Breast milk, RUTF, others.)	Name of Product	Pre-mixed	Self-mixed	Route		Rate	Nr of feeds/day	Total volume prescribed /day (ml)	Total volume consumed/ day(ml)	Ward diet or solids given while on transition feeds		If Yes, which ward diet or solid feed was given
					NGT	Oral					Yes	No	
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
							___/___hrly						
5.8. For self-mixed recipes feeds record recipe													

SAMAC

DATA EXTRACTION FORM

6. ELECTROLYTE AND TRACE ELEMENTS PRESCRIPTIONS																	
6.1. Prescribed by			Paediatrician		GP		House officer/Intern		Dietician		Nutrition officer		Nurse				
			Others (Specify)														
6.2. Electrolyte and trace elements given during hospital stay																	
Date	Potassium Chloride sol			Trace element mix (MgSO ₄ 280mg, Zn SO ₄ 36mg, CuSO ₄ 0.1mg/1ml oral sol)			Oral Magnesium			MgSO ₄ IM			Zinc (zinc sulphate, gluconate acetate, picolinate)			Others	Others
	Yes	No	Dosage	Yes	No	Dosage	Yes	No	Dosage	Yes	No	Dosage	Yes	No	Dosage	Dosage	Dosage

Participant Number:

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SAMAC

DATA EXTRACTION FORM

[illegible]

SAMAC

DATA EXTRACTION FORM

8. MEDICAL TREATMENT										Did the patient receive any of the following:																			
8.1 Prescribed by				Paediatrician		☐		GP		☐		House officer			☐		Dietitian		☐		Nutrition officer			☐		Nurse		☐	
				Others (Specify)																									
8.2. Medications given during hospital stay																													
Name of medication						Indication						Route				Date started		Date stopped		Dosage		Freq/day							
												IM IV NG Oral																	
												IM IV NG Oral																	
												IM IV NG Oral																	
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												IM IV NG Oral																	

SAMAC

DATA EXTRACTION FORM

[illegible]

SAMAC

DATA EXTRACTION FORM

[illegible]

Participant Number:

SAMAC

DATA EXTRACTION FORM

9A. ADDITIONAL PROGRESS NOTES (Anthropometry and Clinical Signs)															
Date	Anthropometry		Clinical Signs												
	Weight (Kg)	MUAC (mm)	Oedema	Appetite	Dermatitis		Pallor		Convulsion		Irritability		Shock		Others
					Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	

SAMAC

DATA EXTRACTION FORM

9B. ADDITIONAL PROGRESS NOTES (Oral rehydration and IV fluids)												
Date	ReSoMal				Other Oral Rehydration Solutions					IV Fluids		
	Route		Rate	Total	Name of product	Route		Rate	Total	Type	Rate	Total
	NGT	Oral		Vol/day		NGT	Oral		Vol/day			Vol/day
			___/___hrly					___/___hrly			___/___hrly	
			___/___hrly					___/___hrly			___/___hrly	
			___/___hrly					___/___hrly			___/___hrly	
			___/___hrly					___/___hrly			___/___hrly	
			___/___hrly					___/___hrly			___/___hrly	
			___/___hrly					___/___hrly			___/___hrly	
			___/___hrly					___/___hrly			___/___hrly	
			___/___hrly					___/___hrly			___/___hrly	
			___/___hrly					___/___hrly			___/___hrly	
			___/___hrly					___/___hrly			___/___hrly	
			___/___hrly					___/___hrly			___/___hrly	

Participant Number:

SAMAC

DATA EXTRACTION FORM

10. DISCHARGE DATA (Status of child on date of discharge to home)														
10.1. Date of discharge	20	Y	M	D	10.2. Date of Death	20	Y	M	D	10.3. Cause of death				
10.4. Weight (kg)	Kg				10.5. Height/length measurement (cm)	cm				Not indicated				
10.6. Which of the following was measured:					Height					Length				
10.7. MUAC (mm)					10.8. Weight for height Z score									
						Not Reported								
10.9. Oedema grade	0					+	(mild)				++	(moderate)		
										+++	(Severe)			
10.10. Tested for TB	Yes					10.11. Tested for HIV	Yes				10.12. Referred to outpatient clinic / facility	Yes		
	No						No					No		
	Unknown						Unknown					Unknown		
10.13. TB status	Positive					10.14. HIV status	Positive							
	Negative						Negative							
	Unknown						Unknown							
10.15. Good appetite	Yes					10.16. Infections resolved	Yes				10.17. Five day consecutive weight gain	Yes		
	No						No					No		
	Unknown						Unknown					Unknown		
10.18. Other clinical information noted on Discharge														
10.19. Caregiver given nutrition and health education	Yes					No					If Yes, By whom			
10.20. Number of different health professionals who cared for patient during hospital stay	Paediatrician					GP					Dietitian		Nurse	
	House officer/ Intern					Nutrition officer					Others			

ANNEXURE 11: Author Instructions for South African Journal of Clinical Nutrition

ISSN 003-8-2469

S Afr J Clin Nutr 2008 volume 23 number 4 (December)

**Author instructions**

All manuscripts and correspondence to be submitted electronically to: www.sajcn.co.za

Copyright

Material submitted for publication in the South African Journal of Clinical Nutrition (SAJCN) is accepted provided it has not been published elsewhere. Copyright forms will be sent with acknowledgement of receipt and the SAJCN reserves copyright of the material published. The SAJCN does not hold itself responsible for statements made by the authors.

Authorship

All named authors must give consent to publication. Authorship should be based only on substantial contribution to: (i) conception, design, analysis and interpretation of data; (ii) drafting the article or revising it critically for important intellectual content; (iii) final approval of the version to be published. All three of these conditions must be met (Uniform requirements for manuscripts submitted to biomedical journals; www.icmje.org/index.html).

Manuscripts

Short items are more likely to appeal to our readers and therefore to be accepted for publication. **Manuscript should not exceed 4000 words in total all contents inclusive.**

Original articles of 4 000 words or less, with up to 6 tables or illustrations, should normally report observations or research of relevance to the field of nutrition. References should preferably be limited to no more than 25.

Short reports or scientific letters, which include case reports, side effects of nutrient supplements/drugs and brief or negative research findings should be 1000 words or less, with 1 table or illustration and no more than 6 references.

Editorials, Opinions, Issues in the field of nutrition, should be about 1000 words and are welcome, but unless invited, will be subjected to the SAJCN peer review process.

Review articles are rarely accepted unless invited.

Letters to the editor, if intended for the correspondence column, should be marked 'for publication', signed by all authors and presented in triple spacing. Letters should be no longer than 400 words with only one illustration or table.

Obituaries should not exceed 400 words and may be accompanied by a photograph.

Manuscript preparation

- Please submit your manuscript electronically at www.sajcn.co.za. (Register as an author, log in and follow the 5 steps to upload your manuscript.)
- Please submit the manuscript as a MS Windows Word document.
- Please have your manuscript edited by a language expert or colleague proficient in English prior to submission. Articles must be in UK English.
- All manuscripts must include an abstract (50-250 words).
- Research articles should have a structured abstract not exceeding 250 words (50 for short reports) comprising: Objectives, Design, Setting, Subjects, Outcome measures, Results and Conclusions.
- Refer to articles in recent issues for guidance on the presentation of headings and subheadings.
- Abbreviations should be spelt out when first used in the text and thereafter used consistently.
- Scientific measurements should be expressed in SI units except: blood pressure should be given in mmHg and haemoglobin values in g/dl.

If in doubt, refer to www.icmje.org/index.html

Illustrations

1. All illustrations must be submitted electronically. High resolution (300dpi) .jpg or .tiff files are preferred.
2. Figures consist of all material that cannot be set in type, such as photographs and line drawings.
3. Tables and legends for illustrations should appear on separate sheets and should be clearly identified.

4. Line drawings should be arranged to conserve vertical space. Note that reduction to 80 mm for a single column or 170 mm for double columns should not render lettering illegible. Explanations should be included in the legend and not on the figure itself.
5. Figure numbers should be clearly marked on the back of prints and the top of illustrations should be indicated.
6. If any tables or illustrations submitted have been published elsewhere, written consent to republication should be obtained by the author from the copyright holder and the author(s).
7. A limited number of illustrations are free at the discretion of the editor. Colour illustrations are encouraged but are charged to the author.

References

References should be inserted in the text as superior numbers and should be listed at the end of the article in numerical and not in alphabetical order.

Authors are responsible for verification of references from the original sources.

References should be set out in the Vancouver style and approved abbreviations of journal titles used; consult the List of Journals in Index Medicus for these details.

Names and initials of all authors should be given unless there are more than six, in which case the first three names should be given followed by et al. First and last page numbers should be given.

Journal references should appear thus:

1. Price NC. Importance of asking about glaucoma. *BMJ* 1983; 286: 349-350. Book references should be set out as follows:
1. Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975: 96-101.
2. Weinstein L, Swartz MN. Pathogenic properties of invading microorganisms. In: Sodeman WA jun, Sodeman WA, eds. *Pathologic Physiology: Mechanisms of Disease*. Philadelphia: WB Saunders, 1974: 457-472.

Manuscripts accepted but not yet published can be included as references followed by (in press).

Unpublished observations and personal communications may be cited in the text, but not in the reference list.

Manuscript revisions

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