FACTORS ASSOCIATED WITH MORBIDITY AND MORTALITY IN CHILDREN UNDER-FIVE YEARS ADMITTED WITH SEVERE ACUTE MALNUTRITION TO A REGIONAL PAEDIATRIC HOSPITAL IN KWAZULU-NATAL

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A mini-thesis submitted in partial fulfilment of the requirements for the degree of Master in Public Health at the School of Public Health,
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KEY WORDS

Severe acute malnutrition (SAM)

Survival

Morbidity

Under-five mortality

Predictive factors

Diarrhoea

Pneumonia

HIV-infection

Tuberculosis

KwaZulu-Natal

ABSTRACT

Background: Malnutrition is a complex condition profoundly impacting child mortality and morbidity, especially in sub-Saharan Africa. Severe acute malnutrition is of growing concern locally where unacceptable mortality rates persist, despite reasonable standards of clinical care.

Aim: To determine factors associated with morbidity and mortality in children under-five years admitted with severe acute malnutrition to a regional paediatric hospital in KwaZulu-Natal.

Methodology: This was a quantitative study. A retrospective observational study design was used. Medical records of all children with severe acute malnutrition, under the age of five years, admitted between April 2015 and December 2016 to the regional paediatric hospital in KwaZulu-Natal were included. Data was obtained from medical records and admission books. A trained research assistant was used to extract and record data with a piloted data extraction tool. Data was entered and cleaned using Microsoft Excel and analysed using SPSS (v 20) and STATA (v 14). Descriptive summary statistics were used to describe the characteristics of the study population and bivariate analysis using t-tests and Chi-square tests to determine significance. Kaplan Meier and Multivariate Cox regression was used to assess the association of variables with morbidity and mortality.

Results: Of the 276 eligible case records included in the study, 54% were male and 90% of all cases were younger than 2 years. Even though associations did not reach significance, teenage pregnancy and unemployment was high amongst the caregivers of the study population. Most of the malnourished children admitted (74%) presented with multiple comorbidities. Diarrhoea (43%), HIV- infection (30%) and respiratory tract infections (30%) were the top three comorbidities found, followed by tuberculosis (27%). The overall mortality rate was 8.7%. Survival probability was significantly reduced in children with pneumonia and those who presented with hypoglycaemia, dehydration, dermatosis, severe pallor, altered consciousness or shock on admission ($p < 0.05$). There was a significantly increased risk of death in males (HR = 0.174, 95%CI = 0.05 - 0.665), and in those who presented with dehydration (HR = 4.1, 95%CI = 1.25 - 13.59), evidence of lethargy or coma (HR = 4.2, 95%CI = 1.04 - 17.12) or multiple clinical signs (HR = 4.4, 95% CI =2.56 - 7.59) on admission ($p < 0.05$). The comorbidities HIV-infection (HR = 9.9, 95%CI = 1.39 - 70.68) and pneumonia (HR = 3.4, 95%CI = 1.56 - 7.43) showed a significantly increased mortality risk ($p < 0.05$).

Conclusion: This study supports the body of evidence that despite reasonable standards of hospital care, it is difficult to obtain the target for severe acute malnutrition mortality (< 5%), likely due to the presence of contextually specific factors. Local interventions at hospital, primary health care and community level is needed, as well as further research to facilitate comprehensive policy-making.

DECLARATION

I declare that FACTORS ASSOCIATED WITH MORBIDITY AND MORTALITY IN CHILDREN UNDER-FIVE YEARS ADMITTED WITH SEVERE ACUTE MALNUTRITION TO A REGIONAL PAEDIATRIC HOSPITAL IN KWAZULU-NATAL, is my own work, that it has not been submitted for any degree or examination at any other university, and that all the sources I have used or quoted have been indicated and acknowledged by complete references.

Tanya van Aswegen

Date: 9 November 2018

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I am profoundly grateful to:

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My family, for your ongoing support and encouragement.

And lastly but most importantly, my husband. My greatest supporter, my pillar of strength.

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ACRONYMS AND ABBREVIATIONS

SAM:	Severe acute malnutrition
WHO:	World Health Organization
UNICEF:	United Nations International Children's Emergency Fund
HIV:	Human immunodeficiency virus
AIDS:	Acquired Immune Deficiency Syndrome
TB:	Tuberculosis
ART:	Antiretroviral treatment
MAM:	Moderate Acute Malnutrition
SADHS:	The South African Health and Demographic Survey
SANHANES:	The South African National Health and Nutrition Examination Survey
MUAC:	Mid-Upper Arm Circumference
CSG:	Child support grant
HR:	Hazard Ratio

OPERATIONAL DEFINITIONS

1. **Previous admission of malnutrition**: An admission to hospital for severe acute malnutrition within a 12-month period of the current admission.

2. **Malnutrition**: Referring to undernutrition.

3. **Nutritional oedema:** Characterized by swelling of extremities and/or the face, caused by severe protein and energy deficiency. Nutritional oedema causes bilateral pitting oedema, with an initial presentation on the feet or legs of the child with severe acute malnutrition (Cloete, 2015). Other terms commonly used is oedematous malnutrition, or Kwashiorkor.

4. **Severe acute malnutrition (SAM)**: The most severe form of undernutrition that is diagnosed on a Mid-Upper-Arm-Circumference measurement < 11.5 cm in children aged 6 months – 5 years and/or a weight-for-height standard deviation scores of less than -3 and/or the presence nutritional oedema (WHO, 2009).

5. **Severe acute malnutrition mortality:** Death due to because of severe acute malnutrition as either a primary or secondary cause.

6. **SAM with complications**: Clinical findings made through physical examination or the measurement of vital signs of the SAM child: Hypothermia, hypoglycaemia, skin lesions (or dermatosis), dehydration, severe pallor, and impaired consciousness and shock. These classifications are based on the local guidelines and policies (Department of Health, 2015b).

   6.1. **Hypothermia**: Child has low body temperature measure by either an axillary temperature ≤ 36.5 ºC or rectal temperature ≤ 35.5 ºC.
   6.2. **Hypoglycaemia:** In children with SAM this is classified as having a blood sugar level < 3.0 mmol/L or having eye-lid retraction if no measurement is possible.
   6.3. **Dehydration**: In children with SAM dehydration diagnosis is made on clinical history of vomiting, diarrhoea, sweating or high fever, or by a recent appearance of clinical signs of dehydration, such as sunken eyes, poor skin turgor (> 2 seconds) or sunken fontanelles. Significant irritability could also signify dehydration.
   6.4. **Skin lesions (or dermatosis):** Child has broken, weeping skin.
   6.5. **Severe pallor:** Significant palmar pallor or unusual paleness of skin compared to other children of the same race.

6.6. **Impaired/altered consciousness**: Referring to either lethargy – child is difficult to wake, very drowsy and unusually sleepy, or comatose – where the child does not respond to any stimuli, even painful stimuli.

6.7. **Shock**: Delayed capillary refill > 3 seconds, cool peripheries and increased pulse.

7. **Under-five mortality**: The probability of dying between birth and the fifth birthday.

8. **Wasting:** Typically characterized by visible wasting of the extremities and buttocks. It is caused by severe energy deficiency due to low food intake and/or infections (WHO, 2009).

9. **World Health Organization severe acute malnutrition (SAM) treatment guidelines**: A standardized practical ten-step treatment protocol used globally to treat children with severe acute malnutrition in hospital to ensure optimized treatment outcomes. Often referred to as the ten steps to manage severe acute malnutrition (WHO, 1999).

CHAPTER 1

INTRODUCTION

1.1. Background

Under-five mortality remains a significant concern in the developing world, with one in twelve children dying before they reach the age of five years (You *et al*., 2015). The South African Health and Demographic Survey in 2016 (SADHS) reported the overall under-five mortality rate to be 38.2 deaths per 1000 live births in the country. Even though there has been substantial progress made in South Africa in terms of child health, the current under-five mortality rate in the country remains far higher than the Sustainable Development Goal (SDG) for the country; which is striving to achieve less than 25 deaths per 1000 live births by 2030 (Massyn *et al*., 2016). Most childhood deaths are related to conditions such as diarrhoea, pneumonia, human immunodeficiency virus (HIV), acquired immune deficiency syndrome (AIDS) and malnutrition (Jones *et al.*, 2003, CoMMiC, 2014). There is continued global emphasis on the importance of strategies to reduce the global burden of childhood mortality by bodies such as the United Nations Children's Fund (UNICEF) and the World Health Organization (WHO).

Malnutrition is one of the most common causes of morbidity and mortality in children globally (WHO, 2013; Gebremichael, 2015) with an estimated 45% of all child deaths linked to malnutrition (WHO, 2016). The most severe form of malnutrition, namely severe acute malnutrition (SAM), is of growing concern nationally (Cloete, 2015), accounting for at least 30% of under-five deaths in South Africa (CoMMiC, 2014). Poor adherence to the World Health Organization's SAM treatment guidelines is often reported to be the cause of poor SAM outcomes (WHO, 2003), but recent studies showed that SAM mortality remains high, despite reasonable standards of clinical care (Maitland *et al*., 2006; De Maayer & Saloojee, 2011). The persistently high mortality rates in children with SAM treated in hospital have also been attributed to various comorbidities (Heikens *et al*., 2008). The link between malnutrition, immunodeficiency, infection and childhood mortality and morbidity is well documented world-wide (Rice *et al.*, 2000; Caulfield *et al*., 2004; Gibbons & Fuchs, 2009), but to a lesser extent in South Africa.

1.2. Problem statement

Severe malnutrition case fatality is graded by the WHO as: > 20% being unacceptable, 11 - 20% poor, 5 - 10% moderate and 1 - 4% is considered good (WHO, 1999). SAM case fatality rates however, only provide information on the outcome of children with SAM, it provides limited information on the contribution of SAM to childhood mortality overall; and should not be used as a single indicator to measure progress (Massyn *et al*., 2016). Since 2012, KwaZulu-Natal has been scaling up various programs to improve case management and early identification of children with SAM, but despite the scaling up of these programs,

under-five mortality linked to severe malnutrition remained high at 30%, and SAM case fatality rates in excess of 10% (CoMMiC, 2014).

King Cetshwayo district (formerly known as uThungulu district) has had some reduction in under-five mortality rates and SAM mortality rates in recent years, however in 2014 the Second Triennial Report published by the Committee on Morbidity and Mortality in Children under 5 years (CoMMiC, 2014), showed that the district ranked twenty-second out of the 52 districts in the country in terms of high under-five deaths. The same report also ranked King Cetshwayo district the second worst performing district in KwaZulu-Natal province in terms of SAM case fatality rates, as shown in Figure 1 (Massyn *et al*., 2015). While only 15.4% of the under-five deaths in the district had underlying SAM (the second lowest in the province), the SAM case fatality rate in 2014 was 16.9%, more than three times the target set by the WHO and almost double the provincial average. These high rates were despite improved clinical care through the implementation of the WHO's SAM treatment guidelines (Department of Health, 2015b). By the end of 2014, King Cetshwayo district was rated amongst the top ten districts in South Africa who had the highest number of children with SAM who died and one of only five districts in the country who has seen a rise in SAM mortality rates (Massyn e*t al*., 2015).

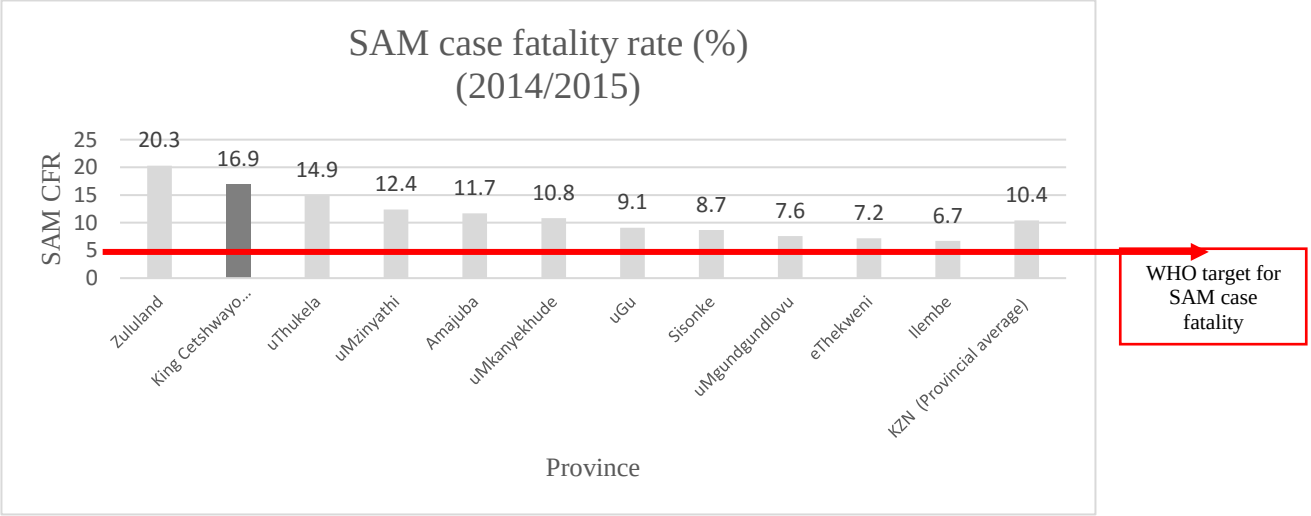


Figure 1: SAM case fatality rates per district in KwaZulu-Natal province (percentage).
(Source: Massyn *et al*., 2015)

The association between malnutrition and all-cause mortality is well established (Adama *et al*., 2016) and the contribution to under-five mortality in South Africa, specifically KwaZulu-Natal, is evident (Massyn *et al.*, 2015, Massyn *et al.,* 2016). Literature shows there is a negative association with SAM mortality and morbidity, certain socio-economic factors, clinical factors and comorbidities (Saloojee *et al.*, 2007; Fergusson & Tomkins, 2009; De Maayer & Saloojee, 2011; Savadogo *et al.*, 2013), but the impact in KwaZulu-Natal is largely unknown.

1.3. Study setting

The study was conducted in a regional paediatric hospital in King Cetshwayo district (formerly known as uThungulu District). King Cetshwayo District is situated in the northern part of KwaZulu-Natal, South Africa. KwaZulu-Natal has 11 provinces; Amajuba, iLembe, eThekwini, King Cetshwayo, Harry Gwala, uMkhanyakude, uGu, uMzinyathi, uMgungundlovu, uThukela and Zululand. Prior to 2017, King Cetshwayo District had 6 subdistricts: Nkandla, Ntambanana, uMfolozi/Mbonambi, uMthlathuze and Mtonjaneni. Ntambanana sub-district was dissolved in 2016 and integrated into the other 5 sub-districts as seen in Figure 2.

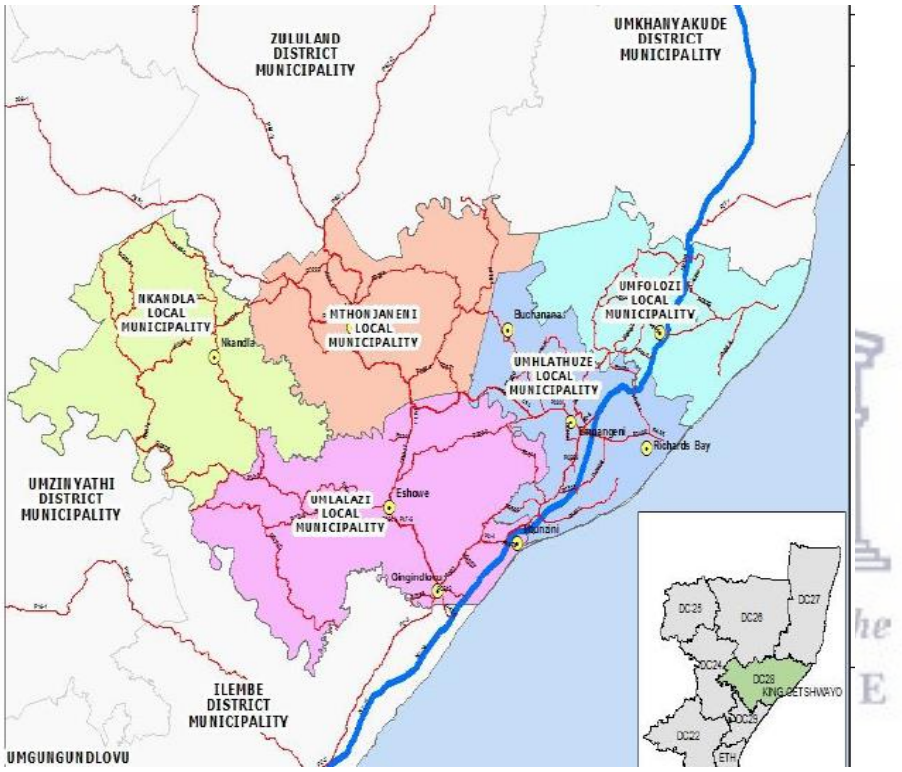


Figure 2: King Cetshwayo district - geographical location.

(Source: http://www.uthungulu.org.za/images/IDP/FINAL%202017_18%20IDP/Section%20A-B%20INTEGRATED%20DEVELOPMENT%20PLAN.pdf)

The district has a mix of peri-urban and rural communities, but the population is considered rural in terms of demographic demarcations. The total population size is 872 505, with children (defined as <15 years) making up 36% of the population. Only 30% of the population have grade 12 and 15.7% have no schooling at all. There is a high prevalence and incidence of malnutrition, tuberculosis, HIV-infection and AIDS. The high burden of disease is compounded by a 35% unemployment rate and significant poverty (Statistics SA, 2011).

The regional hospital (study setting) is exclusively dedicated to obstetrical, gynaecological, neonatal and paediatric patients. It has a ninety-bed paediatric unit, with a dedicated malnutrition sub-unit, admitting the largest volume of malnourished children in the region. Before and during the time of the study, the unit was

well staffed with specialist paediatricians and a multi-sectoral team of health professionals that are all trained on the inpatient management of SAM. Regular internal (facility and district level) and external (Provincial Department of Health) audits are in place as part of the provincial malnutrition policy to monitor the correct implementation of the WHO's SAM treatment guidelines (Department of Health, 2015b). This significantly reduces the chances of clinical mismanagement and improves overall implementation of the treatment guidelines. As the standard of clinical care at this health facility was on par, this study did not include the clinical management of children with SAM as a contributing factor of death. The hospital also serves as referral site for the adjacent districts; Zululand, iLembe, uMzinyathi and uMkhanyakude. Inpatient admissions therefore consist of a range of SAM complications, comorbidities, geographical and socio-economic factors.

1.4. Rationale

Despite reasonable standards of care and significant investment in malnutrition programs, KwaZulu-Natal is failing to reach the WHO target for malnutrition mortality (< 5%). The contribution of malnutrition to under-five morbidity and mortality in the province also remains unacceptably high, according to reports such as the 2014 Second Triennial Report published by the Committee on Morbidity and Mortality in Children under 5 years (CoMMiC, 2014). The purpose of this study was to determine factors that are associated with the morbidity and mortality in children under-five with SAM, who were admitted to an inpatient paediatric hospital in KwaZulu-Natal. All-cause malnutrition is well described in literature, but to a lesser extent in terms of specific factors and comorbidities. There are currently no indicators in the District Health Information System that track comorbidities or clinical conditions of malnutrition in children under-five in terms of admissions and deaths. By identifying socio-demographic factors, clinical conditions and comorbidities associated with the overall morbidity and mortality of SAM children, it could provide contextually specific information to contribute to the reduction of childhood deaths. The study could potentially provide information and motivation to conduct larger epidemiological studies in KwaZulu-Natal.

1.5. Study aim and objectives

Aim:

The aim of this study was to determine factors associated with morbidity and mortality in children under-five years admitted with severe acute malnutrition (SAM) to a regional paediatric hospital in KwaZulu-Natal, between April 2015 and December 2016.

Objectives:

The objectives were:

1. To determine the socio-demographic and socio-economic status of children admitted with SAM and their caregivers;
2. To determine the anthropometric status of children with SAM: at admission; during hospital stay and at discharge; and differences in anthropometric measures between the two types of SAM;
3. To determine clinical signs and symptoms present in children with SAM on admission;
4. To determine the prevalence of comorbidities to SAM identified at admission or discharge/death; and
5. To determine which factors contributed to survival probability and the increased risk of death in children admitted with SAM.

CHAPTER 2

LITERATURE REVIEW

2.1. Introduction

Malnutrition remains one of the biggest contributing factors to under-five mortality rates globally, with an estimated 45% of all child deaths linked to malnutrition (WHO, 2016). The highest burden is carried by developing countries, where 35% of under-five deaths are attributed to various forms of undernutrition (Collins *et al.*, 2006). Severe acute malnutrition (SAM), the most severe form of malnutrition, is estimated to be the cause of two million child deaths globally, each year (Black *et al.*, 2013).

The South African National Development Plan (NDP), in-line with the Sustainable Developmental Goals (SDGs), calls for a reduction of under-five mortality rates to 25 per 1000 live births by 2030 in the country (Massyn *et al.*, 2015; SADHS, 2016). Even though there has been a decline in under-five mortality rates in South Africa from 58 to 38.5 live births per 1000 since 2009, there are still about 100 under-five children dying each day. There is a consensus that the persistently high under-five mortality rates in the country are largely attributed to HIV-infection, which contributes to 33% of under-five deaths; and severe acute malnutrition, contributing to about 30% of these deaths (CoMMiC, 2014).

Malnutrition is a complex, multifaceted disease that presents in different forms, of which SAM carries the highest mortality risk, ranging from 20% - 50% (Collins *et al*., 2006). SAM mortality is often compounded by comorbidities, most commonly infectious disease i.e. diarrhoea, pneumonia, tuberculosis and HIV-infection (Gupta *et al*., 2009; Yohannes *et al*., 2015). Significant strides to reduce SAM case fatality have been made in KwaZulu-Natal, yet despite reasonable standards of care it remains significantly above the WHO target of 1 - 4% (Department of Health, 2015).

2.2. Malnutrition

2.2.1. Types of malnutrition

Malnutrition refers to both under- and overnutrition (Blössner & de Onis, 2005). Undernutrition can present as chronic and acute forms. Chronic malnutrition is the result of long-term macro- or micronutrient deficiencies and is characterized by stunted growth. Acute malnutrition results from the sudden reduction of food intake or diet quality and/or pathological causes such as illness or recurrent infections. Acute malnutrition is characterized by wasting, with or without bilateral pitting oedema and other clinical signs (Collins *et al.*, 2006; Cloete, 2015; Black *et al.*, 2016).

Acute malnutrition is further sub-grouped into severe (SAM) and moderate acute malnutrition (MAM), which is diagnosed based on the measurement of three independent indices as seen below in Table 1.

Table 1: Summary of diagnostic criteria for acute malnutrition.

Indicator	Measure	Severe Acute Malnutrition (SAM)	Moderate Acute Malnutrition (MAM)	No acute malnutrition
Wasting	Weight-for-Height/length SD	< -3 SD	Between -2 and -3 SD	≥ -2 SD
Wasting	MUAC (> 6 months)	< 11.5 cm	Between 11.6 – 12.4 cm	≥ 12.5 cm
Bilateral pitting oedema	Physical assessment	Present	Absent	Absent

(Source: WHO, 2009)

These are: The Mid-Upper-Arm-Circumference (MUAC) cut-offs for children aged 6 months – 5 years; the weight-for-height standard deviation (SD) scores using the WHO weight-for-height growth charts for boys and girls; and the presence of nutritional oedema in children 0 – 5 years (WHO, 2009). The presence of clinical signs (other than oedema) such as sparse hair, dermatosis and eye signs are not independent indicators for a diagnosis of severe acute malnutrition but should carefully be considered during assessment (Cloete, 2015). The degree of wasting is positively correlated with an increase in morbidity and mortality and even though moderate acute malnutrition (MAM) also increases the risk of death compared to well-nourished children, there is currently no standardized approach to the management of MAM (Lenters *et al*., 2013), while SAM is treated according to standardised protocols.

The terms kwashiorkor (SAM with the presence of bilateral pitting oedema) or marasmus (SAM with the presence of severe visible wasting) is commonly used to describe the forms of SAM in literature. The WHO (2013) update on the management of SAM encourages the use of standardized terminology to distinguish between the two forms of acute malnutrition and these terms have been replaced with "SAM with oedema" or "SAM without oedema", respectively (Black *et al.,* 2016, Williams & Berkley, 2016). This updated terminology is also used in the study setting (Department of Health, 2015b).

Literature reports wide differences in the prevalence, morbidity and mortality risk between SAM with oedema and SAM without oedema, within different populations (Jarso *et al*., 2015). Saloojee *et al*. (2007) reported that in African countries, SAM without oedema is more common, while SAM with oedema compromises about 22% - 33% of SAM admissions. Munthali *et al*. (2015) however found that up to 62% of SAM admissions in a Zambian study had oedema, with similar findings in Colombia where 60.8% of the SAM population had oedema (Bernal *et al.* 2008). This is supported by Trehan & Manary (2015) who found that in southern Africa specifically, rates of oedematous malnutrition is very high, making up two-thirds to

three-quarter of the SAM population. In the context of high HIV prevalence, it has also been found that oedematous malnutrition is more prominent (up to 60%) (*Saloojee et al.*, 2007). It is generally reported that SAM with oedema is more common in children older than two years, and SAM without oedema in those younger than two years (Akparibo *et al*., 2016). In some studies, oedematous malnutrition, even in the absence of other medical complications, have been found to be associated with the highest morbidity (Yohannes *et al.*, 2017) and mortality risk (Bernal *et al*., 2008; Teferi *et al*., 2010). Jarso *et al*. (2015) however showed no statistical significance between the two forms of SAM and Munthali *et al*. (2015) found those without oedema have the highest risk of death. These variances found in literature are likely due to the different causes of malnutrition and the prevalence of certain comorbidities in the study populations.

2.2.2. Pathophysiology of malnutrition

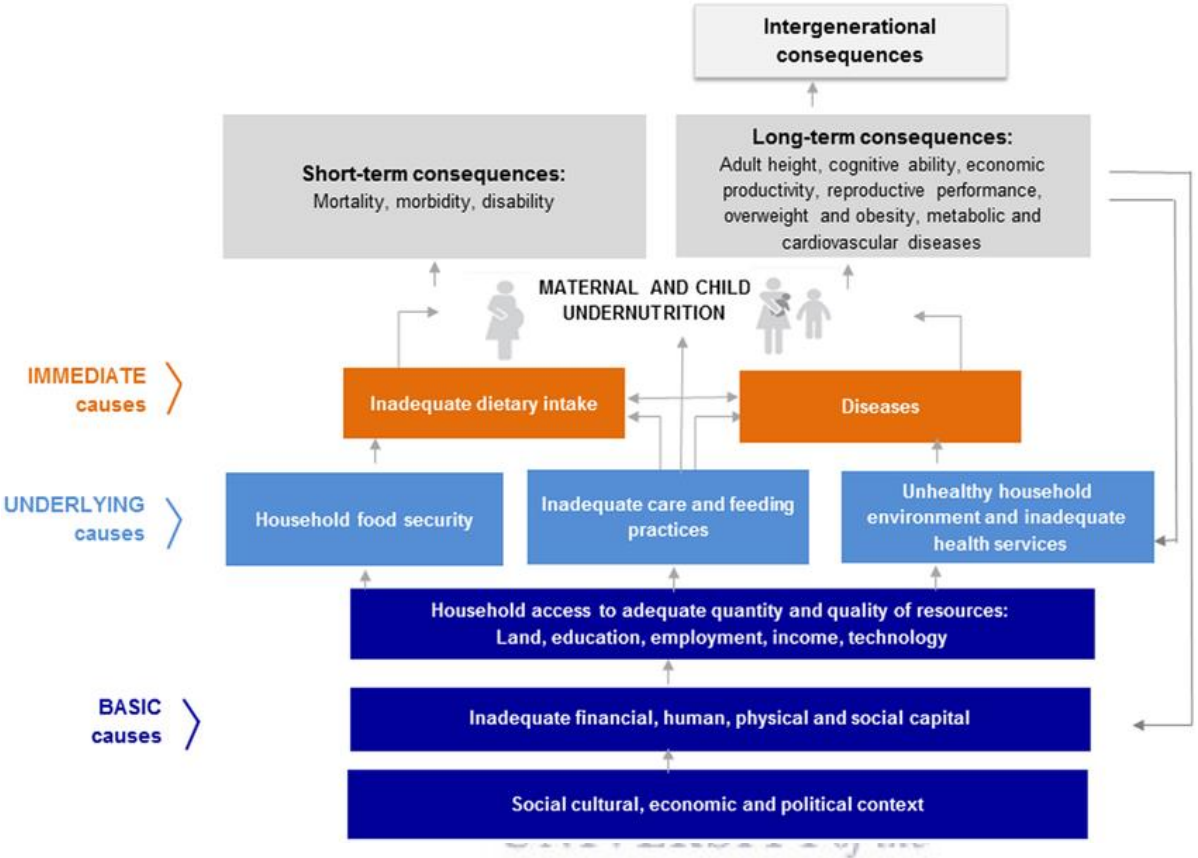
During acute episodes of malnutrition, the body responds to rapid weight loss through a process of reductive adaptation, where energy is saved for critical body functions by reducing other metabolic functions. Most of the body organs and cells are affected in this process, leading to severely disturbed physiological processes and immunosuppression with the consequent risk of concurrent infections and easily overwhelmed body systems (Black *et al*., 2008; Black *et al*., 2016). This process significantly increases the risk of death (Golden, 2000; Heikens *et al*., 2008).

Malnutrition is often compounded by other comorbidities such as diarrhoea, pneumonia and tuberculosis (Yohannes *et al.*, 2015). The adverse relationship between infectious disease and undernutrition is well described (Caulfield *et al.*, 2004). There are various clinical signs and symptoms that are associated with children with SAM. Oedematous malnutrition, hypothermia, hypoglycaemia, dermatosis, severe pallor, dehydration, impaired consciousness and shock are reported to have the most adverse effect on SAM outcomes (Maitland *et al*., 2006; De Maayer & Saloojee, 2011; Munthali *et al.*, 2015; Gebremichael, 2015 Yohannes *et al.*, 2017). Even though the pathophysiology of malnutrition is well known, it has been significantly complicated by the presence HIV-infection (Heikens *et al*., 2008; Savadogo *et al*., 2015) and SAM in the context of HIV have not been well described. Malnutrition cases can be especially difficult to manage if additional medical complications are present (Black *et al*., 2016).

2.2.3. Causes of malnutrition

The UNICEF conceptual framework seen below in Figure 3, explains the multi-factorial causes of malnutrition by grouping causes into immediate, underlying and basic factors (WHO, 1999; UNICEF, 2015). Immediate causes refer to inadequate dietary intake and exposure to diseases, which reduces appetite, increases metabolic requirements and increase nutrient losses (McDonald *et al.*, 2013). Underlying causes

relates to inadequate access to food and health care, which is driven by basic causes such as political and economic factors which are the root cause of malnutrition (WHO, 1999). Collins *et al*. (2006) states that improved SAM outcomes are dependent on individual level care and public health policies.



***The grey arrows above (⟶) show the multi-directionality of malnutrition. The consequences of undernutrition can feed back into the underlying and basic causes of undernutrition, perpetuating the cycle of undernutrition, poverty and inequities.*

Figure 3: The UNICEF conceptual framework for malnutrition.

(Source: UNICEF 2015, Adapted from UNICEF, 1990)

2.3. Malnutrition and disease morbidity and mortality

Malnutrition is a life-threatening condition with severe consequences, most often death. Studies have shown that developmental and cognitive delays are experienced by many children with SAM and emerging evidence also indicate they have a very high risk for developing chronic diseases later in life (Lelijveld *et al*., 2016). The consequences of SAM are perhaps best described by Briend & Berkley (2016) who write that not only do children with SAM fight to survive they also struggle to thrive and reach their full potential.

2.3.1. Global context

Malnutrition remains one of the biggest contributing factors to under-five mortality rates globally, with an estimated 45% of all child deaths linked to malnutrition (WHO, 2016). Both moderate and severe forms of acute malnutrition remain significant global public health concern with 32.8 million and 18.7 million children worldwide being affected by MAM and SAM, respectively (Black *et al.,* 2008). The highest burden is carried by low- and middle-income countries, where 35% of under-five deaths are attributed to various forms of undernutrition (Collins *et al.,* 2006). From 1990 to 2011, the global prevalence rates of moderate and severe malnutrition have declined with an average annual rate of 2.2% per year; from 25% to 16% globally and from 41% to 23% in low- and middle-income countries. Even though there has been a decline in underweight prevalence globally, progress have been slow and inadequate, while the increase in the under-five population have largely counteracted the downward trend, stagnating the progress (De Onis *et al.,* 2012).

Mortality risk is directly related to the severity of malnutrition, with MAM being associated with a mortality rate of 30 - 148 per 1000 children per year. SAM is associated with a mortality rate of 73 – 187 per 1000 children per year (Collins *et al*., 2006), causing two million child deaths globally each year (Black *et al.,* 2013). Children who suffer from SAM are 11.6 times more likely to die, compared to well-nourished children (Akparibo *et al.,* 2016). Death rates of SAM in low- and middle-income countries remain at 20 - 30%, even though evidence show that the correct implementation of the WHO SAM treatment guidelines should reduce SAM death rates to < 5% (Collins *et al*., 2006).

2.3.2. South African context

Overall under-five mortality varies widely amongst provinces in South Africa, with the highest rates seen in the Free State province and the lowest in the Western Cape. Even though there has been a decline in the overall under-five mortality rates in South Africa from 58 to 38.5 per 1000 live births since 2009, the impact of SAM on childhood mortality remains undisputed. Thirty one percent of all under-five deaths in the country are associated with SAM as primary or secondary factors (CoMMiC, 2014; Massyn *et al*., 2015). Figure 4 (CoMMiC, 2014) shows the contribution of SAM to childhood mortality per province for the period

2011 - 2013, clearly indicating that in most provinces, except for Gauteng and the Western Cape, it remains a significant problem.

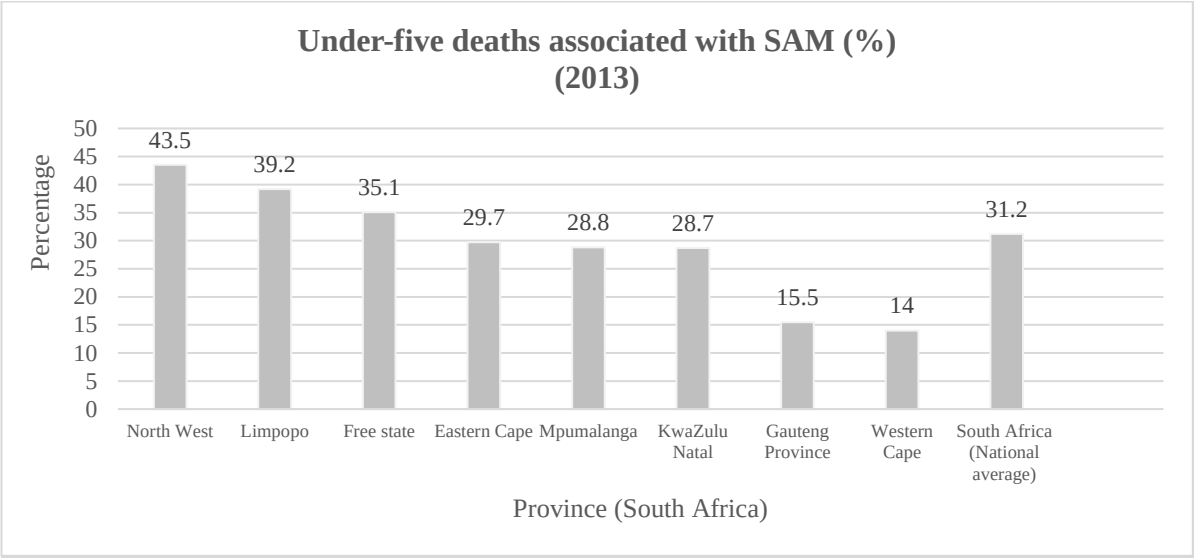


Figure 4: Under-five deaths associated with SAM in South Africa (percentage).

(Source: CoMMiC, 2014)

The South African National Health and Nutrition Examination Survey of 2012 (SANHANES, 2012) reported that children under-three years carries the highest burden of malnutrition, with a wasting and underweight prevalence of 2.2 % and 6% respectively (Shisana *et al.*, 2013). The 2016 SADHS showed that 3% of children under-five in South Africa were wasted; and children younger than 18 months the most affected. The SAM case fatality rate in South Africa declined from 19.3% in 2009 to 11.6% by 2015, but some provinces still had SAM death rates as high as 15% as seen below in Figure 5.

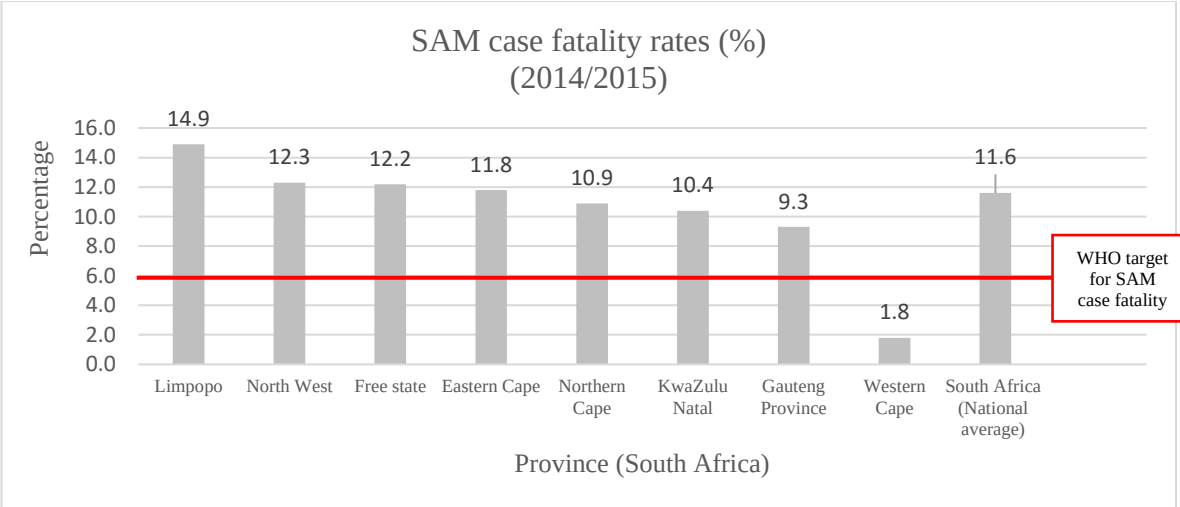


Figure 5: SAM case fatality rate per province in South Africa (percentage).

(Source: CoMMiC 2014)

Except for the Western Cape, all provinces had 2 - 3 times the WHO target for SAM mortality (WHO, 1999). Despite the overall reduction, the proportion that SAM contributes to child mortality remained relatively consistent, while these deaths typically occur in the most disadvantaged districts in the country (Massyn *et al*., 2015). SAM case fatality rates are calculated by looking at the number of children with SAM that died in hospital as the numerator and the total number of SAM children admitted as denominator, which has raised further concern that the improvement seen in South Africa is largely due to an increase in SAM case finding and not a true reflection of a possibly worsening situation of malnutrition (Massyn *et al*., 2016).

2.3.3. Local context (KwaZulu-Natal)

KwaZulu-Natal has an overall under-five mortality rate of 35 per 1000 live births, with almost one third of these deaths being associated with SAM. From 2011 – 2013, under-five mortality associated with SAM modestly declined from 31.2% to 28.7% (CoMMiC, 2014), while SAM case fatality rates in the province increased from 9.2% to 9.7% during the same period (Massyn *et al*., 2014), reaching 10.4% in 2015 (Massyn *et al.*, 2015). In King Cetshwayo district, even though only 15.4% of the under-five deaths in the district had SAM (the second lowest in the province), the SAM case fatality rate in 2014/2015 was 16.9%; more than 3 times the target set by the WHO and the second highest in the province as seen in Figure 1 (Massyn *et al*., 2015; Massyn *et al*., 2016).

2.4. Guidelines for the inpatient treatment of severe acute malnutrition

The WHO's SAM treatment guidelines as seen in Figure 6, is a ten-step protocol used globally to treat children hospitalized with SAM (WHO, 1999; Trehan & Manary, 2015). This protocol has been incorporated into all national paediatric and child health guidelines in South Africa, with a mandate to be implemented in all hospitals and health care facilities (Massyn *et al.*, 2016).

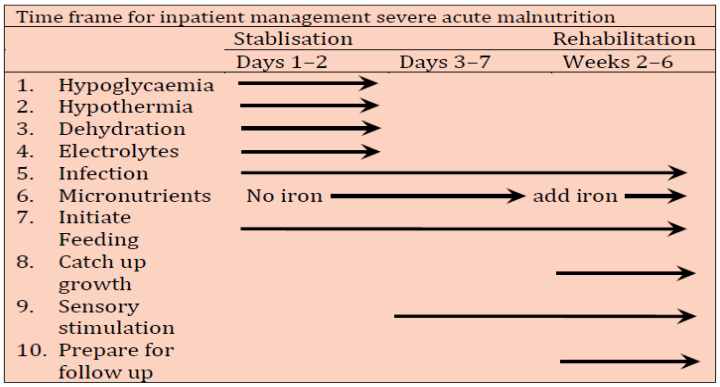


Figure 6: Ten-step inpatient treatment guidelines for severe acute malnutrition.
(Source: Department of Health, 2015b: 16, adapted from WHO, 1999)

The treatment guidelines consist of two phases: Stabilization (initial treatment) and rehabilitation. During stabilization (day 1 to 7) the aim is to restore cellular function and electrolyte imbalances, control infection; prevent and treat hypothermia, hypoglycaemia and dehydration and initiate feeding. If the child is not in shock, feeding is commenced immediately on admission. A cautious approach to feeding is essential due the SAM child's reduced homeostatic capacity. A low protein, low-calorie (75 Kcal and 0.9 g protein per 100 ml) feed, low in lactose and with low osmolarity is used (commonly referred to as starter formula or F-75). Feeding is started at a low volume, usually at 130 ml/kg/day (or 100 ml/kg/day if the child is oedematous), divided into 3 hourly feeds. Episodes of hypothermia and hypoglycaemia should be carefully observed and treated. All children with SAM have excess body sodium, with potassium and magnesium deficiencies being very common. These deficiencies can take up to two weeks to correct. The feeds are therefore fortified with a specific mix of electrolytes. Additional potassium replacement is needed if the serum potassium levels are below 2.5 mmol/L. Dehydration and shock is treated with specific emergency protocols (Department of Health, 2015b, adapted from WHO, 2013).

All children with SAM are treated with a broad-spectrum first line antibiotic, regardless of the presence of medical complications. The rationale behind this is that these children often do not display the overt signs of clinical infections (e.g. fever), while multiple studies have shown improved growth and decreased mortality when treated with antibiotics (Jones & Berkley, 2014). Second line antibiotic use in the SAM child should be guided by local microbiological flora (Williams & Berkley, 2016). Micronutrient deficiencies are corrected with supplements, with a focus on vitamin A, folate and zinc. Iron is only given in the rehabilitation phase when indicated (Department of Health, 2015b). The stabilization phase is a critical time and mortality rates during first 48 hours can be as high as 33% (Maitland *et al*., 2006).

After 3 – 7 days, when appetite is improving and oedema (if present) is resolving, there is a transition to the rehabilitation phase. During this phase, the aim is rebuilding body stores through catch-up feeding, characterized by rapid weight gain of > 5 – 10 g/kg/day. A high calorie and protein feed is used for this phase (100 Kcal and 2.5-3 g protein per 100 ml) and feeds are given at a volume of 150 – 220 ml/kg/day (a catch-up formula or F-100). This phase could continue for two to six weeks, depending on the child's condition and response to treatment. Sensory stimulation should be provided and follow up arrangements made during this phase (Department of Health, 2015b).

2.5. Comorbidities associated with malnutrition

The association between malnutrition and all-cause mortality is well established, but to a lesser extent in terms of comorbidities (Adama *et al*., 2016). SAM children have increased susceptibility to infection and

severe illness compared to well-nourished children and the proportion of children with SAM who have comorbidities are variable (Black *et al*., 2016). The most significant comorbidities reported in children with SAM are infectious disease i.e. diarrhoea, pneumonia, acute respiratory tract infections, tuberculosis and HIV-infection (Gupta *et al*., 2009; Yohannes *et al*., 2015).

2.5.1. Diarrhoea

Diarrhoea accounts for 9% of all under-five deaths in low- and middle-income countries (UNICEF, 2012). In South Africa, the case fatality rate of diarrhoea is 2.2%. While KwaZulu-Natal had the highest number of diarrhoeal admissions and second highest number of deaths in the country, the case fatality rate in 2016 was 2.2%. King Cetshwayo district, had a slightly lower case fatality rate of 1.9% (Massyn *et al.,* 2016). Diarrhoea is defined as the passage of watery stools, usually at least three or more times in a 24-hour period. In acute diarrhoea, watery stools last for several hours or days and chronic (or persistent) diarrhoea lasts for 14 days or more (WHO, 2005). Newer definitions of diarrhoea stress the importance of also defining prolonged diarrhoea, which is watery stools for more than 7 days but less than 14 days (Manary *et al*., 2012).

There is a clearly documented bidirectional relationship between nutritional status and the duration of diarrhoeal disease, where underweight is strongly associated with prolonged diarrhoea and persistent diarrhoea (Moore *et al*., 2010). Diarrhoea affects nutritional status through reduced dietary intake, intestinal malabsorption and increased nutrient requirements due to catabolism (Brown, 2003) and there is mounting evidence to support the adverse short- and long-term outcomes in children with SAM complicated by diarrhoea (Talbert *et al*., 2012). Malnutrition is a predisposing factor for diarrhoea by reducing both immunity and the protective barrier that the skin and mucous membranes usually offer (Brown, 2003), leading to increased frequency and duration of diarrhoea (Guerrant *et al.*, 1992). Chronic (or persistent) diarrhoea is more likely to be present in children with HIV-infection due to an increased prevalence of intestinal parasites and intestinal damage from HIV itself (Jones & Berkley, 2014). There is an emerging body of evidence showing that prolonged acute diarrhoea (more than 7 days but less than 14 days) in the first year of life predicts which children are at increased risk of developing persistent diarrhoea and chromic malnutrition later in life (Guerrant *et al*., 2013). Diarrhoea is said to be the leading cause of malnutrition globally (WHO, 2005) and is associated with an overall 14-fold increase in mortality risk (Roy *et al.,* 2011).

The prevalence of diarrhoea in children with SAM is variable, ranging from 31% to 67.1% (Black *et al*., 2016). A large prospective study conducted in Kenya over four years showed that 49% of SAM cases had diarrhoea on admission with a further 16% developing diarrhoea within 48 hours of admission (Talbert *et*

al., 2012). It is well documented that diarrhoea complicates the treatment of SAM and substantially increase the mortality rate of children with SAM (Heikens *et al*., 2008). Talbert *et al*. (2012) found that the mortality rate for SAM children who had diarrhoea at any time during their admission, was 19% compared to only 9% in those cases without diarrhoea. A child with SAM and diarrhoea is at serious risk of death as they have poor ability to respond to both shock brought on by dehydration, and to fluid overload due to their reduced physiological capacity (Department of Health, 2015b).

2.5.2. Pneumonia

Pneumonia significantly contributes to mortality in children under-five (De Maayer & Saloojee, 2011) and it is considered the largest single cause of child mortality, accounting for 15% of the 6.3 million global child deaths annually. In sub-Saharan Africa, almost half a million children die every year due to pneumonia (Massyn *et al.,* 2016). In South Africa, the case fatality rate of pneumonia is only 2.32%, with KwaZulu-Natal having the highest number of pneumonia cases and deaths, resulting in a case fatality rate of 2.75%. King Cetshwayo district has the highest pneumonia mortality rates in the country of 5.6%. (Massyn *et al.,* 2016). Childhood pneumonia is linked to many poverty related factors such as lack of safe water and sanitation, indoor air pollution and inadequate access to health care, however the association with undernutrition (even if moderately wasted) often proves fatal (Ginsburg *et al.*, 2015).

Up to two thirds of hospitalized malnourished children present with pneumonia (Elsayh *et al*., 2013) which increases their risk of death 15-fold (Ginsburg *et al*., 2015). Rice *et al.* (2000) and Chisti *et al*. (2009) reported a two- to three-fold greater risk of mortality in cases with pneumonia in the presence of malnutrition. The fatal outcome associated with the presence of both these conditions are often most profound in children younger than 24 months (Elsayh *et al.,* 2013). Undernutrition increases the frequency and severity of pneumonia potentially due to a secondary immune deficiency (Rytter *et al.*, 2014) while also reducing the metabolic capacity of children with pneumonia to overcome the increased physical and physiological demands of the illness. A further concern is that the aetiology of pneumonia in children with malnutrition is often different from well-nourished children, making diagnosis and treatment challenging (Ginsburg *et al.*, 2015). Even children with SAM who have radiologically confirmed pneumonia often do not exhibit any of the typical signs or symptoms (Jones & Berkley, 2014).

2.5.3. Tuberculosis

Tuberculosis is both a cause and a consequence of malnutrition, but its role in SAM outcomes has been poorly described, especially in sub-Saharan African countries (De Maayer & Saloojee, 2011; Munthali *et al*.,

2017). A review done by Chisti *et al*. (2013), which included studies from South Africa, Gambia, Ethiopia, and Thailand, found that 21% of SAM children had TB. One study done in Zambia by Munthali *et al*. (2017) showed that only 1.58% of the SAM population had TB, but they were 40% more likely to die than the SAM children without TB. This study showed that TB is a significant contributor to the SAM mortality in hospitalized patients, especially in children younger than 1 year and those who had oedema. Another study in Bangladesh showed no increased in-hospital mortality, but rather high post-discharge mortality in SAM children who had TB (Chisti *et al*., 2014).

Malnutrition causes a secondary immunodeficiency that increases the susceptibility to infection, while tuberculosis leads to decreased food intake due to poor appetite, nutrient malabsorption, nutrient-drug interactions, and increased catabolism that result in weight loss (Gupta *et al.,* 2009). Tuberculosis detection in children with SAM is poor, often due to their inability to produce suitable sputum samples or their delayed hypersensitivity responses to skin tests. This reduce the sensitivity of tests and results, delaying treatment with worsened outcomes. This was also shown by Munthali *et al*. (2017) where only a quarter of the children diagnosed with TB was bacteriologically confirmed cases. It has been suggested that the clinical response such as weight gain and fever should also be used in the diagnosis of TB in children with SAM (Jones & Berkley, 2014).

2.5.4. HIV-infection

HIV-infection and malnutrition is interlinked, creating a cycle of increased needs and decreased immunity and food intake (Cloete, 2015). HIV-infected children with SAM, also present with a complex pathology such as persistent diarrhoea, extensive skin infections and oral thrush (Heikens *et al*., 2008). HIV-infection has dramatically changed the mortality outlook of SAM in sub-Saharan Africa (Jones & Berkley, 2014). Collins *et al*. (2006) report that the prevalence of SAM in children who are HIV positive is very high, particularly in those presenting with marasmus (SAM without oedema). The HIV prevalence in SAM children range from 13.8% - 48.6% (Ndagije *et al.,* 2007; Chinkhumba *et al.,* 2008; Madec, 2011; Benyera & Hyera, 2013; Munthali *et al*., 2015). Mortality risk of SAM associated with HIV-infection can be as high as 80% (Heikens *et al*., 2008) and it is associated with a 3 times higher mortality rate (Jones & Berkley, 2014). A systematic review by Lenters *et al*. (2013) reported that the highest case fatality rates amongst children with SAM were found in those who were HIV-infected. Malnutrition relapse rates amongst children with HIV-infection are five times higher than their non-infected counterparts (Collins *et al*., 2006).

Maitland *et al.* (2006) and Saloojee *et al*. (2007) suggests that failure to reach the WHO target of < 5% could significantly be attributed to HIV-infection. It is proposed that this increased risk of death is related to the pathophysiology and comorbidities of HIV disease and possibly the timing of antiretroviral treatment (Trehan *et al.,* 2012; Rose *et al*., 2014). Furthermore, according to Lenters *et al*. (2013), there remain significant uncertainty about the treatment of HIV-infected children with SAM in low- and middle-income countries. Antiretroviral treatment (ART) is increasingly recognized, improving outcomes in malnourished children as it improves immunity and reduces the risk for infections. However, despite advances in treatment, HIV-infected children on ART still has a 2-fold risk of developing undernutrition (Heikens *et al*., 2008). There remains uncertainty whether ART should be started before or after nutritional rehabilitation (Heikens *et al.*, 2008).

2.5.5. HIV and Tuberculosis co-infection

Tuberculosis, especially pulmonary TB is common in HIV-infected children, possibly due to immunosuppression, which can cause the progression of latent TB to active TB. Coupled with an already compromised immune system in the SAM child, the HIV/TB co-infected SAM child has a significantly increased risk of morbidity and mortality (Chisti *et al.,* 2014). Munthali *et al*. (2017) reported that 46.5% of SAM children with HIV also had TB; and these co-infected children were twice as likely to die, compared to those who had TB, but not HIV.

2.6. Other comorbidities

Cerebral Palsy, cystic fibrosis, renal diseases, liver disease, short bowel syndrome, inflammatory bowel disease, cancer and heart disease are considered other comorbidities of SAM and is often referred to as secondary causes of undernutrition (Chane *et al.,*2014). These are chronic diseases that influence nutritional status indirectly through various pathologies with each disease having different treatment guidelines (Kuperminc & Stevenson, 2008; Gibbons & Fuchs, 2009; Jamro *et al.*, 2012) and is as such out of the scope of this study and these cases were excluded.

2.7. Medical complications associated with malnutrition mortality and morbidity

Due to the physiological changes occurring during a state of starvation, the child with SAM has a significant reduction in their capacity to regulate temperature and water storage and consequently dehydration, hypothermia and hypoglycaemia are more severe and occurs rapidly; while immunosuppression increases the susceptibility to infection (Williams & Berkley, 2017).

Recently, there has been an increase in the body of evidence that sub-group SAM cases as *SAM with medical complications* or *SAM without medical complications* (or uncomplicated SAM) to simplify treatment guidelines. Uncomplicated SAM cases could be managed in an outpatient setting while it is recommended that those with medical complications are treated as inpatients (Williams & Berkley, 2017). Collins *et al*. (2006) estimated that only 15% of children with SAM have medical complications. By international definition the uncomplicated SAM children are those who are clinically well and have no signs of infection, oedema or any disease according to the Integrated Management of childhood Disease guidelines (Collins *et al*., 2006; Williams & Berkley, 2016). The medical complications used for classification in the South African context is shown in Figure 7.

Figure 7 : Medical complications in the child with SAM (South African context).

(Source: Department of Health 2015b)

Hypothermia, hypoglycaemia, dermatosis (or weeping skin lesions), severe pallor (or severe anaemia), dehydration and shock are all associated with poor prognostic outcomes in SAM children (Maitland *et al*., 2006; De Maayer & Saloojee, 2011; Jarso *et al*., 2015). An Ethiopian study found impaired consciousness increased mortality risk by 2.6 times (Jarso *et al*., 2015). Gebremichael (2015) reported that fever, lethargy or coma, dehydration and oedema contribute to poor nutritional recovery and increased morbidity. Maitland *et al*. (2006) found that there was no difference in the frequency of these clinical signs between the types of acute malnutrition (oedema or wasting).

While children with uncomplicated SAM could have mortality rates as low as 5%, those with complicated SAM carry a higher risk (10 - 40%) of mortality during admission as well as an ongoing risk after discharge from hospital (Kerac *et al.*, 2014; Williams & Berkley, 2016). This is supported by similar findings in Kenya

(Maitland *et al*., 2006) where the presence of two or more of these clinical signs were associated with a 9.6 times higher risk of dying in SAM children.

2.8. Nutritional status at discharge

It is recommended that children with SAM reach nutritional recovery before being discharged from inpatient hospital care (WHO, 2013). Early discharge can have benefits in terms of prevention of hospital acquired infections, freeing up bed space and reducing hospital costs, but it carries a significant risk of relapse and eventual death if continuity and quality of care cannot be established in an outpatient setting (Ashworth, 2001). Early discharge of a child with SAM, should therefore be guided by the availability and access to resources, such as nutritional supplements and follow up care (Department of Health, 2015b).

The WHO (2013) defines nutritional recovery as:

- Weight-for-height/length ≥ -2 Z-score and they have had no oedema for at least 2 weeks, or
- MUAC is ≥ 12.5 cm and they have had no oedema for at least 2 weeks.

In KwaZulu-Natal, there is provision for earlier discharge to outpatient supplementation programs, when the child has reached a MUAC of ≥ 11.5 cm, or have reached a weight-for-height/length between -3 and -2 Z-score; and achieved weight gain during the rehabilitation phase of > 5-10 g/kg/day, has a good appetite for food and is clinically well and alert (Department of Health, 2015b).

Long term survival (>1 year) in children with SAM is greater in those who successfully reached nutritional recovery before being discharged (Kerac *et al*., 2014). Somassè *et al.* (2016) found similar results, where a MUAC < 12.5 cm at discharge was associated with higher relapse rates in children with SAM. Relapse rates within 1 year are reported to be up to 10% but is greatly variable between populations due to the complicated aetiology and availability of local resources (Akparibo *et al*., 2016). Kerac *et al.* (2014) found a death rate of 33% in children with SAM who were readmitted within 1 year, within in their study population.

2.9. Socio-demographic and socio-economic risk factors for malnutrition mortality and morbidity

2.9.1. Age

Evidence almost conclusively agree that case fatality rates for children with SAM are significantly higher in younger age groups, with those less than 12 months having the highest risk (Nhampossa *et al*., 2013; Benyera & Hyera, 2013; Ahmed *et al*., 2016). Death rates also remain significant in those younger than 24 months

(Jarso, 2015; Girum *et al*., 2017). A recent study done in Africa showed SAM children younger than 24 months had a 3 times higher risk of death compared to those older than 24 months (Awoke *et al*., 2018). Limited information on mortality rates of SAM infants younger than 6 months is available, as it is a fairly new phenomenon. One study done in Afghanistan highlighted the increased risk of death in SAM children younger than 6 months, where the group 0 - 6 months had a case fatality rate of 17%, compared to 12% in those 7 - 11 months and 8% in children 12 - 18 months (Kerac *et al*., 2010).

2.9.2. Gender

The relationship between gender and malnutrition risk is inconclusive and regional specific, likely due to cultural norms and study limitations such as non-differentiation of types of malnutrition. One study in India, however reported female malnourished children were twice as likely to die as their male counterparts, but this was due to cultural practices (Roy *et al*., 2011).

2.9.3. Maternal education

The link between low maternal education and malnutrition is widely reported, where children born to educated women have a lower risk of developing various forms of malnutrition (Thompson *et al.,* 2017). This is supported by studies in various settings such as Bolivia (Frost *et al.,* 2005) and Kenya (Kabubo-Mariara *et al.,* 2008). It is suggested that improved maternal education is associated with higher income generation and awareness of healthy behaviours, both factors that are determinants of malnutrition (Van de Poel *et al*., 2007).

2.9.4. Employment status of the caregiver and child support grants

The adverse association between low socio-economic status and malnutrition is well documented (van de Poel *et al.,* 2008). Child support grants and the employment status of the principal caregiver is significant economic markers for childhood malnutrition (Soloojee *et al*., 2007). Wondafrash *et al*. (2017) argued that a child is 3 times more likely to be wasted if the mother is unemployed, whereas Eshete *et al.* (2017) found no statistically significant association. South Africa's child support grant (CSG) system constitutes the largest cash transfer program in Africa (Zembe-Mkhaile *et al.,* 2012). There is however disagreement in literature about the impact of child support grants on the nutritional status of children. Globally it is said that these programs have been effective in improving child growth and nutrition. Manley, Gitter and Slavchevska (2011) reported that there is no consistent relationship between cash transfers and nutritional status of children. Agüero, Carter and Woolard (2000) found in a South African study that child support grants do improve childhood nutrition, it was however measured against stunting, a chronic form of malnutrition, and

did not assess weight gain or wasting. There is weak evidence in South Arica that the receipt of a CSG leads to an increased use of growth monitoring services where early signs of malnutrition should be detected, which forms the basis of beliefs why a CSG protects against malnutrition (DSD, SASSA & UNICEF, 2012).

Saloojee *et al*. (2007) suggest child support grants in South Africa could significantly reduce the risk of severe malnutrition, while a Zambian study reported a positive, but not statistically significant impact (Seidenfeld *et al.*, 2014). Child support grant uptake for infants in South Africa is low, with most children only accessing CSGs around 22 months (Zembe-Mkhaile *et al.,* 2012*).* It is widely documented that the age 0 - 24 months is a very vulnerable period for negative health and nutrition outcomes (Pelletier *et al*., 1995). The South African Child Support Grant Impact Assessment conducted in 2012, concluded that access to a CSG in the first year of life and for at least half of the first 36 months of a child's life has significant impact on early childhood development and future health outcomes. The study further found that a mother's education strengthened the impact of the CSG on child development (DSD, SASSA and UNICEF, 2012).

2.9.5. Teenage pregnancies

The South Africa Demographic and Health Survey (SADHS) has found that one in three women will be pregnant by the age of 18 years (Massyn *et al.*, 2016), which is considered an adolescent or teenage pregnancy. Adolescent pregnancy is associated with higher risk during delivery, low birth weight, poor infant growth and early cessation of breastfeeding (Branca *et al*., 2015). Heaton *et al.* (2005) suggests that the risk of malnutrition in children born to younger mothers could also be due to psychological stress of having a child at a young age. Pravana *et al.* (2017) found that maternal age (< 20 years) is an independent determinant of SAM, with 3.21 times higher odds of developing SAM, compared to those who had mothers older than 20 years. This study was done in a very specific setting in Nepal, known for cultural practices such as early marriage. Hien & Kam (2008), found no association between maternal age and malnutrition in a study conducted in Vietnam.

2.10. Conclusion

The prevalence and impact of malnutrition on child mortality and morbidity is profound, especially in sub-Saharan Africa, with little improvement over the last few decades. Malnutrition is a complex medical condition, with a multifactorial aetiology. Research show that high mortality rates from malnutrition persists despite reasonable standards of hospital care, possibly due to certain comorbidities, clinical symptoms and socio-demographic and economic factors. It is widely recognized that further reductions in child mortality will be difficult without addressing undernutrition, evident in the emphasis on child nutrition reflected in the 2030 Sustainable Development Goals.

CHAPTER 3

RESEARCH DESIGN AND METHODOLOGY

3.1. Study design

This was a quantitative study. A retrospective cohort (observational analytical) study design was used. This study design allowed for the investigation of multiple factors and determining possible associations of these factors with morbidity and mortality in the study population. This is a cost and time efficient design as it reduced the duration of the study, while still providing relative strength of association (Song & Chung, 2010).

3.2. Study population

The study population included male and female children under the age of five years, admitted to the regional paediatric hospital in KwaZulu-Natal with severe acute malnutrition (SAM). These cases were admitted between April 2015 and December 2016 and had archived medical records and admissions books.

3.3. Sample size

The sample size was calculated using the Epi Info version 7 computer program, with mortality chosen as the main outcome for the data analysis since an assumption was made that it would give the most significant result. The following other assumptions were applied: Power of 80%, a two-sided confidence level of 95%, the outcome (death) for the uncomplicated SAM group was 10% and complicated SAM group was 25%. The Ratio of unexposed to exposed was chosen as 1:2 (Collins *et al.*, 2006; Jarso *et al.*, 2015; Williams & Berkley, 2016; Girum *et al.*, 2017). An estimation of 10% incomplete medical records was added and a total sample size of 265 was calculated to give statistically significant results.

The hospital admitted on average 15 children with SAM per month with an estimated mortality of 10%. Considering this admission rate and probability of incomplete records, it was calculated that about 20 months of medical records would be needed to reach an adequate sample size; and a timeframe was set from April 2015 – December 2016. It was estimated that this would deliver 300 admissions and 30 deaths.

3.4. Sampling strategy

Medical records were identified from a hospital SAM data base and ward admission books for the period April 2015 – December 2016 prior to data collection. The medical records of all children aged 0 – 60 months that were admitted to the hospital with SAM between April 2015 and December 2016, were included in the study. The following inclusion and exclusion criteria were used:

Inclusion criteria: Records of male and female children aged 0 – 60 months admitted between April 2015 and December 2016, diagnosed with SAM by presenting with a weight for height/length score of < -3 standard deviation and/or a clinical presentation of SAM (oedema or severe visible wasting). In children

older than 6 months a Mid-Upper-Arm-Circumference of < 11.5 cm was also used as an independent indicator for the diagnosis of SAM (WHO, 2009).

Exclusion criteria: Chronic conditions that severely impact feeding and nutritional status; such as children with: Cerebral Palsy, cystic fibrosis, renal diseases, chronic liver disease, short bowel syndrome, inflammatory bowel disease, cancer or heart disease. Rare genetic and chronic disorders were evaluated on a case by case basis.

A final number of 395 cases were identified from the hospital SAM data base and admission books for the period April 2015 – December 2016. Of the 395 reported cases, 276 medical records were included in the study. Seventy-three cases had missing records which could not be located in the archives department. Six records had incomplete information (missing admission pages, incomplete anthropometric or clinical information) and had to be excluded. The researcher cross checked the anthropometric status of each child on admission against the WHO criteria in Table 1 and excluded children who did not meet the criteria; this accounted for 28 participants. Eight participants were excluded based on chronic and/or genetic disorders, one was older than 5 years, one was transferred to another hospital before completing treatment, one was not treated according to the WHO treatment guidelines and one was a duplicate record. Sample selection and reasons for exclusions are shown below in Figure 8.

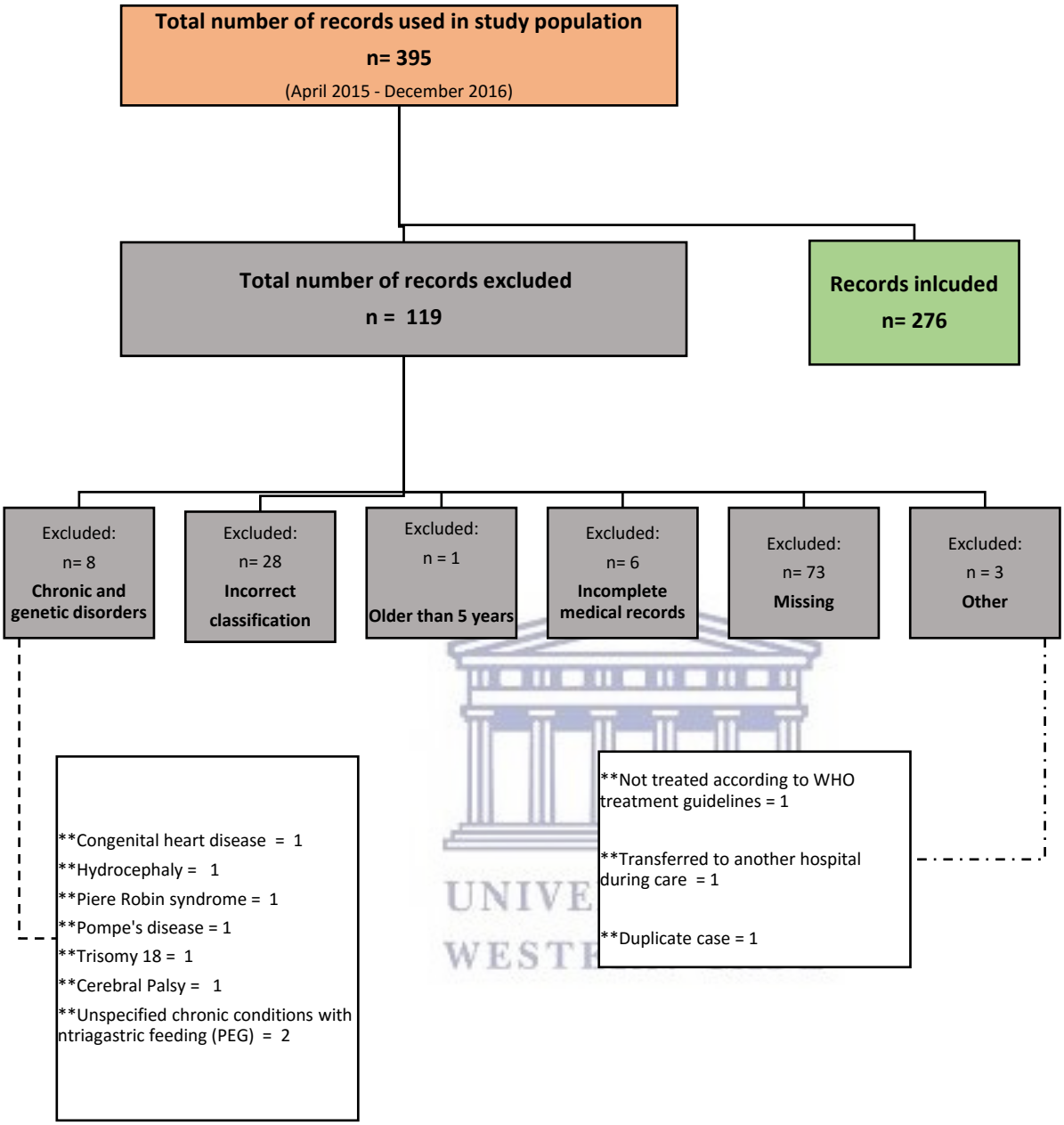


Figure 8: Selection of participants and case records into study population.

3.5. Data collection and management

3.5.1. Data collection tools

A data extraction tool (Appendix 1) was developed and used to record the applicable data from the medical records and admission records. This tool was piloted using 10 hospital records of children admitted to this hospital for SAM before April 2015. The data collected from the pilot was used to gauge validity and ease of use of the extraction tool and relevant changes made prior to data collection.

The variables used in the development of the instrument were mainly obtained from the review of the literature of previous studies on child malnutrition, while also considering time and cost constraints. Definitions of the variables and data collected are described in Appendix 2. The data extraction tool was divided into 4 sections to systematically collect the variables as described below:

Section 1: Socio-demographic and socio-economic variables

This section included; age, gender, place of residence, referral source, access to a child support grant, previous admission for malnutrition in the last 12 months, number of previous admissions, principle caregiver, employment status of the principle caregiver, educational level of the mother, the presence of teenage pregnancy and an open-ended question of social information such as the presence of neglect, abandonment or abuse.

Section 2: Anthropometric variables

The second section included clinical information of the child at admission or during hospital stay. This section was further sub-grouped into anthropometric information; the weight, height and MUAC on admission and discharge from the hospital, the presence of oedema on admission, the nutritional diagnosis on admission and on discharge from the hospital, and weight gained during hospitalization.

Section 3: Comorbidities

The third section of the data extraction tool collected information on comorbidities present on admission including diarrhoea, respiratory tract infections, pneumonia, HIV and TB status. HIV-infection and TB diagnosed during hospital stay, as well as the timing of treatment for these conditions were also collected.

Section 4: Clinical signs and symptoms

The final section looked at the presence of any of the following clinical signs and symptoms on admission: hypothermia, hypoglycaemia, dehydration, dermatosis, pallor, impaired consciousness and shock. Other clinical information collected was the place of admission and length of stay.

3.5.2. Data collection process

One research assistant with a B.Sc. Dietetics degree, experienced in the treatment of SAM and who was knowledgeable about the hospital recording system, was recruited. The research assistant was then trained and standardized to collect data using the data extraction tool. The facility was accessed through standard security procedures of the Department of Health, after approval was received from the district and hospital managers, respectively (Appendix 3). Data was obtained from the hospital records which included patient medical records and ward admission books. The hospital was notified of record review dates in advance, via email correspondence.

3.5.3. Data quality and safety

The names, record numbers, date of birth and month of admission of all the SAM children admitted between April 2015 and December 2016 was obtained from the hospital SAM data base and ward admission books. The researcher compiled a consolidated list of all study participants prior to data collection. Only medical record numbers were submitted to the hospital archives department to obtain medical records. For cases that had missing record numbers, the name, date of birth and admission date had to be used to search for the files, but no identifiable personal information was captured on the data extraction tool. The research assistant cross-checked names, date of birth and record numbers once the medical records were received and then allocated a participant code to the file for anonymity after collection.

Medical records were requested in batches of 20 records for safety reasons and a secure, lockable location on the hospital premises was used for reviewing records. Once reviewed, the files were returned, and the next batch requested. The data and variables were entered and organized in a Microsoft Excel spreadsheet.

3.5.4. Data cleaning

The data was checked and cleaned by the researcher on the same day as the submission by the research assistant and changes made where needed. Data cleaning was done in Microsoft Excel. Obvious errors such as missing information, non-standardized answers, spelling mistakes, ambiguous answers and extreme values were checked and corrected first. The data was then imported into Stata for further exploration. The Stata

commands; “list, describe, codebook and tab” was used for each variable to review data reliability and standardisation and to make further corrections before the final spread sheet was uploaded for analysis.

3.5.5. Data management

During data collection, it was found that there were two cases where medical records indicated the cases were HIV positive based on a rapid HIV test, but Polymer Chain Reaction (PCR) testing was negative. Both these cases were younger than 18 months, and as per the clinical guidelines for the management of HIV in children (Department of health, 2015), rapid HIV tests should not be used in children younger than 18 months for diagnostic purposes as it could give false positive results due to the presence of maternal HIV antibodies (Fergusson & Tomkins, 2009). For both these cases the diagnosis for documentation was recorded as HIV-exposed on admission, but HIV-negative on discharge. Eight cases had no weight recorded on discharge. In this instance, the researcher used the last weight recorded in the medical records within 2 days before discharge, otherwise it was reported as missing values. There were three cases that died within 8 hours after admission and two cases that died between 12-24 hours of admission. Length of stay was recorded in days for all other cases and therefore any admission between 1-24 hours was counted as 1 day. One case was admitted with a weight-for-height SD indicative of MAM (between -2 and -3 SD), but developed oedema on the day of admission and was therefore included. Duration of diarrhoea prior to admission was self-reported by the caregivers and recorded in medical records in a non-standardized way such as “for a month” or “for two weeks”. For these cases, the researcher converted it to the number of days that closest resembled the statement to standardize data collection. The hospital where data was collected has a paediatric outpatient clinic and dietitian outpatient clinic on-site which serves as a referral source for the hospital. Even though these clinics are on the same premises, it delivers primary health care services and should be grouped with other referral sites who offer similar services. These cases were consequently documented as a *referral from a government clinic*.

Recording of the variable “MUAC on discharge” was very poor and 40% of the eligible case records (children > 6 months) had missing values and could not be used for data analysis. Upon data screening for the variable MUAC on admission, 67 cases (representing 24.3% of the sampled data) were identified and excluded during analysis of the MUAC variable because of age (< 6 months). Furthermore, 2 case records with missing values for MUAC were identified. To account for the missing variables, the ages were checked for either inclusion or exclusion during analysis, which indicated they were 19 months and 15 months old. If they were younger than 6 months they would have been excluded. Next, the mean values of MUAC for cases within the same age bracket (above and below 19 months and 15 months) were used to replace the missing values.

3.6. Validity

The study population was clearly defined, and an inclusion and exclusion criteria used to select records into the study population. Human error while recording patient information was anticipated, therefore records were selected using multiple sources (hospital data base and admission books) to ensure no cases were missed. These cases were then reviewed by a research assistant who has clinical experience in the diagnosis and management of SAM, and who was also trained in the operational definitions and the data extraction tool. A standardised and piloted data extraction tool was used to collect information in a systematic and consistent manner. Reasons for exclusions were clearly documented and all missing data was reported. Instrument bias was potentially limited by cross-checking three different independent recorded measures to diagnose SAM (Weight-for-height/length Z- score, MUAC and the presence of oedema or severe wasting).

3.7. Reliability

The data in the source documents are standardized and routinely collected by the hospital. Reliability was improved by following a systematic approach to the research methodology. The extraction tool was piloted and adapted to improve reliability. The researcher verified data captured for each case record for completeness. Any changes made to data during capturing was recorded and described in the data management section.

3.8. Data analysis

Data was entered and cleaned using a pre-developed Microsoft Excel data sheet (Microsoft Corporation, Edmond, Washington). Data was processed and analysed by a qualified statistician, using Statistical Package for the Social Sciences (SPSS, version 25) and STATA (version 14). To maintain the integrity of the data, a missing value analysis for each variable was done to check and account for missing values. Tables and graphs were used to present descriptive statistics.

Categorical variables were described in terms of their frequency distribution by processing them as absolute frequencies (n) and relative frequencies (%). Numerical variables were described through central tendency and dispersion and presented as a mean with standard deviation and median with interquartile range. Univariate analysis was done to measure the contingency of association between variables through t-tests (continuous variables) and Chi square tests (categorical variables) with statistical significance determined by a two-sided p-value < 0.05.

Multi-collinearity among independent variables was checked before logistic regression was applied. The association between SAM and possible exposure variables was investigated by using bivariate and

multivariate logistic regression analysis. During bivariate analysis, the log-rank method was used to test the statistical difference between groups by calculating the Chi-square estimates with the respective *p*-values.

To determine which factors were associated with survival probability and an increased risk of death in children admitted with SAM, the 23 factors were first identified under variable categories of demographic, clinical signs, comorbidities and SAM status. Statistical significance was determined by a two-sided *p*-value < 0.05.

Survival probability:

The mean survival probability and estimated survival times associated with these factors were calculated using the Kaplan-Meier survival analysis. The log-rank method was applied to test the statistical difference between groups by calculating the Chi-square estimates with the respective p-values. The results were summarized in a table and the Kaplan-Meier survival curves was used for graphical representation where applicable.

Factors associated with increased risk of death:

To identify the variables associated with an increased likelihood of death and the strength of association, the Hazard Ratio (HR) with a 95% confidence interval was calculated for the 23 factors. The Cox proportional hazard regression model at a multivariate level was applied. The HR estimates the probability of death at any given point in time, using the Cox regression under the assumption that there are no ties present among the failure times (time to death). It further assumes that data can be uniquely sorted with respect to time, but because time to death in this study was reported to the nearest day, this violated the assumption of the absence of ties. The Efron method (an option for handling tied values within cox regression) was therefore chosen as a more accurate approximation of the exact marginal likelihood.

To determine the most suitable degree of accuracy in the multivariate model, 6 iterations was completed and STATA (version 14) was used to produce the following hazard proportional results: There was no cases of multiple observations as the number of subjects and the number observations were equal (n = 276). Person-time was estimated at 4 761 days while deviance (log likelihood) was estimated at -81.335577. The Prob > Chi2 which is 0.00000 showed that the regression model with 23 covariates was more fitted than the regression model without covariates. The assumption that the hazard ratio is fixed over time, and therefore a time interaction must be non-significant, was tested based on Schoenfeld residuals. The global test results, chi2 = 28.13, df = 23, p = 0.2108, indicated that this assumption was not violated.

3.9. Generalizability

Results could possibly be generalised to children under-five with severe acute malnutrition in the region, as the hospital admits children from various communities throughout the region which shares the same cultural, rural, socio-economic characteristics and disease burden. Findings from this study could also add to the current body of evidence conducted in a similar context.

3.10. Ethical considerations

Ethical approval for the study was obtained from the Biomedical Research Ethics Committee of the University of the Western Cape (Ethics registration number: BM17/9/14) (see Appendix 4). This was followed by obtaining approval from the KwaZulu-Natal Provincial Health Research and Ethics Committee (PHREC) through the National Health Research Database (see Appendix 5). The four principles of Ethics (Wassenaar, 2007) was applied in the following manner:

- ***Principle 1*** - Autonomy was ensured by obtaining approval from the facility, district and KwaZulu-Natal Department of Health as individual patient consent for retrospective data was not possible. There was no direct contact with patients at any time during the record review.
- ***Principle 2*** - Confidentiality was ensured by using codes and not personal identifying information on the data extraction tool and the consolidated list to obtain hospital records. All hard copies were kept in a locked container. All electronic files were password protected and only the researcher and research assistant had the passwords. Patient records was reviewed in a private room and returned to the archives department at the end of the session.
- ***Principle 3*** - Non- maleficence was ensured through the collection of retrospective data where treatment outcomes cannot be changed. There was no direct contact with staff during the record review hence the research assistant could not influence any treatment outcomes of children currently being treated. Sharing initial findings, prior to statistical analysis could lead to false conclusions.
- ***Principle 4*** - Beneficence was achieved by sharing the final results with the Department of Health and therefor providing contextual specific information that could potentially improve future outcomes in SAM children.

CHAPTER 4

RESULTS

4.1. Introduction

This chapter describes the results of the study. The results are presented first as a univariate and bivariate analysis to describe the study population in terms of socio-economic and sociodemographic factors, anthropometric status and the prevalence of various signs, symptoms and comorbidities on admission or during hospital stay. This is followed by a multivariate analysis to determine which factors were associated with survival probability and an increased risk of death.

The study aim was to determine which factors were associated with morbidity and mortality in children under-five years admitted with severe acute malnutrition (SAM) to a regional paediatric hospital in KwaZulu-Natal, between April 2015 and December 2016.

The objectives were:

4.1. To determine the socio-demographic and socio-economic status of children admitted with SAM and their caregivers;

4.2. To determine the anthropometric status of children with SAM: at admission; during hospital stay and at discharge; and differences in anthropometric measures between the two types of SAM;

4.3. To determine clinical signs and symptoms present in children with SAM on admission;

4.4. To determine the prevalence of comorbidities to SAM identified at admission or discharge/death; and

4.5. To determine which factors contributed to survival probability and the increased risk of death in children admitted with SAM.

4.2. Socio-demographic and socio-economic characteristics

The study included 276 medical records of children under the age of five years who were admitted to hospital for severe acute malnutrition. The age and gender categories are shown in Table 2 and the age by gender distribution are shown in Figure 9.

Table 2: Age and gender distribution (number and percentage) of the study population (n = 276).

Age*	Gender[a]					
	Male		*Female*		*Total sample*	
	N	%	N	%	N	%
< 6 months	36	13.0	35	12.7	71	**25.7**
6 - 11 months	48	17.4	27	9.8	75	**27.2**
12 - 23 months	47	17.0	54	19.6	101	**36.6**
24 - 60 months	18	6.5	11	4.0	29	**10.5**

[a] Pearson's chi-squared test

* No association between the age category and gender ($\chi 2$ = 6.356; Cramer's V = 0.152), p = 0.096.

Fifty-four percent of study population were male and 46% female. The age by gender distribution is presented in Figure 9.

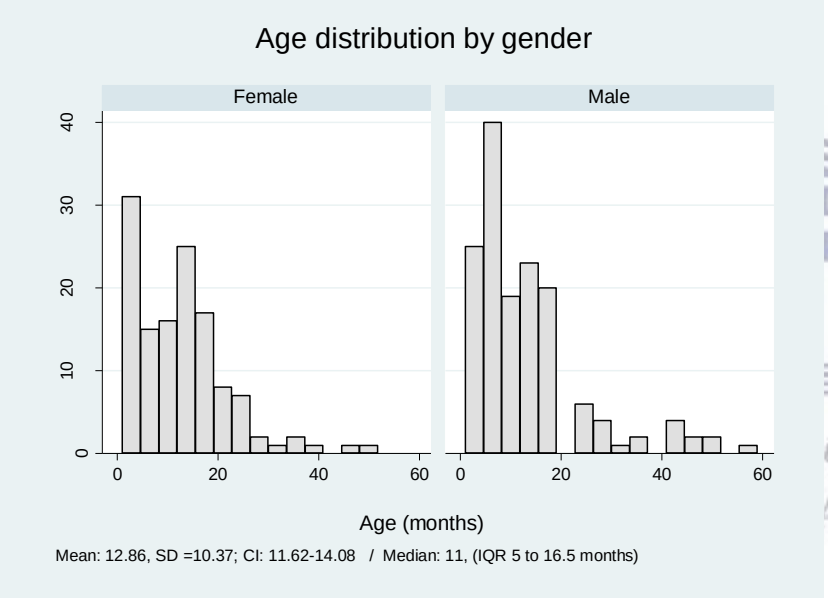


Figure 9: Age distribution by gender.

The mean ± SD age on admission was 12.86 ± 10.37 (95%CI = 11.62 – 14.08) months and the median age 11 months (IQR 5 to 16.5 months). Most of the children were younger than 2 years, and 25.7% had not reach the age of 6 months at the time of admission.

The geographical areas which the study sample originated from at admission, are shown in Figure 10.

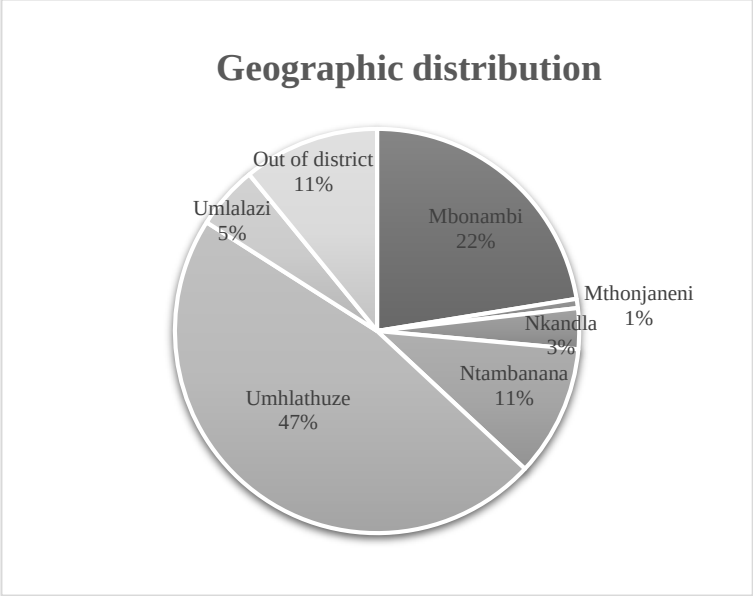


Figure 10: Geographic distribution of study participants (percentage).

Almost half of the participants (47.1%) were from uMhlathuze subdistrict and a further 22.5% originated from Mbonambi subdistrict. Eleven percent of admissions were from areas out of the district. Most of the children admitted were referred from primary health care (PHC) facilities (64%, n = 129), while a further 11% (n = 29) were inter-hospital referrals from local hospitals to the regional specialist hospital. Self-referrals, where patients came directly from home and not any health facility, accounted for 21% (n = 58) of the cases and 4% (n = 10) were referred by physicians. Inter-hospital referrals occurred mostly from Nkandla subdistrict, as well as from out of the district, namely uMkhanyakude district and Zululand district. uMhalthuze as well as Mbonambi subdistricts had the highest number of SAM children referred from PHC clinics, but also the most cases of "self-referrals".

Seventy four percent of the primary caregivers to the children with SAM were mothers; while 18.5% were living with their grandmothers. Only one quarter of the mothers (25%, n = 68) had completed high school, 48% (n = 133) completed up to secondary school and 7% (n = 22) had only primary school education. During data collection, 18% (n = 48) of the cases had no information on the mother's education available in the medical records.

With a large proportion of the caregivers being mothers or grandmothers, the association between the caregivers and their employment status was further explored. Most of the caregivers of the children with SAM in this sample were unemployed (82%, n = 225) and there was insufficient information in the medical records to obtain monthly income of the 15% who were employed. The primary caregivers of the study sample and their employment status is shown in Table 3.

Table 3: Primary caregivers of the study population and their respective employment status.

Caregiver *	Employment Status of Caregiver [a]							
	Employed		*Unemployed*		*Unknown*		**TOTAL**	
	n=43	%	n=225	%	n=8	%	N=276	%
Aunt	4	1.5	5	1.8	1	0.4	10	3.6
Children's home	0	0.0	1	0.4	0	0.0	1	0.4
Father	2	0.7	2	0.7	0	0.0	4	1.4
Grandmother	7	2.5	43	15.6	1	0.4	51	18.5
Mother	29	10.5	172	62.3	3	1.1	204	73.9
Neighbour	0	0.0	1	0.4	1	0.4	2	0.7
Stepmother	1	0.4	1	0.4	0	0.0	2	0.7
Unknown	0	0.0	0	0.0	2	0.7	2	0.7

[a] Pearson's chi-squared test

* Significant association between the type of caregiver and employment status ($\chi 2 = 97.534$, N = 276, and Cramer's V = 0.42), $p < 0.001$.

Almost 16% (n = 43) of the study population had a previous admission for malnutrition (within a 12-month period before their inclusion in the study) and 61% percent (n = 168) of children had access to a child support grant (CSG) as shown in Table 4.

Table 4: Access to a child support grant and malnutrition readmission in the last 12 months.

Access to Child Support Grant *	Malnutrition in the last 12 months [a]					
	No		*Yes*		**TOTAL**	
	n=233	%	n=43	%	N=276	%
No	91	33.0	12	4.4	103	**37.3**
Yes	138	50.0	30	10.9	168	**60.9**
Unknown	4	1.5	1	0.4	5	**1.8**

[a] Pearson's chi-squared test

* No association between access to a child support grand and malnutrition readmission ($\chi 2 = 1.946$, N = 276, Cramer's V = 0.084), $p = 0.378$.

The uptake of child support grants (CSG) by age of the study sample is shown in Figure 11.

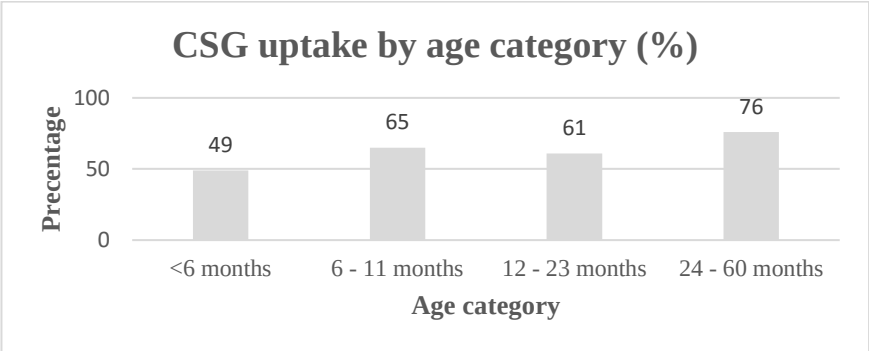


Figure 11: Child support grant uptake by age category of the study population (percentage).

The uptake of CSGs by children with SAM, increased with an increase in age. Only 49% of children < 6 months were receiving a CSG, compared to 76% of children older than 2 years. The uptake of CSGs in children aged 6 - 11 months and those between 12 - 23 months were similar, ranging from 61% - 65%.

Eighteen percent (n = 50) of all the SAM cases in this sample were born to teenage mothers, who were less than 18 years old at the birth of their child, while more than a third (36%, n = 18) of the children with SAM born to teenage mothers did not have access to a CSG at the time the child was admitted to hospital for SAM, as shown below in Table 5.

Table 5: Children with access to child support grants by mother's age at birth of child.

Access to Child Support Grant [a]	**Teenage mother when child was born** [a]					
	YES		*NO*		**TOTAL**	
	n=50	%	n=226	%	N	%
No Access	18	6.5	85	30.8	103	37.32
Access	32	11.6	136	49.3	168	60.87
Unknown	0	0.0	5	1.8	5	1.81

[a] Pearson's chi-squared test used

The number of cases that were born to a teenage mother and had a previous hospital admission for malnutrition within 12 months prior to the episode when they were included in this study, is shown below in Figure 12.

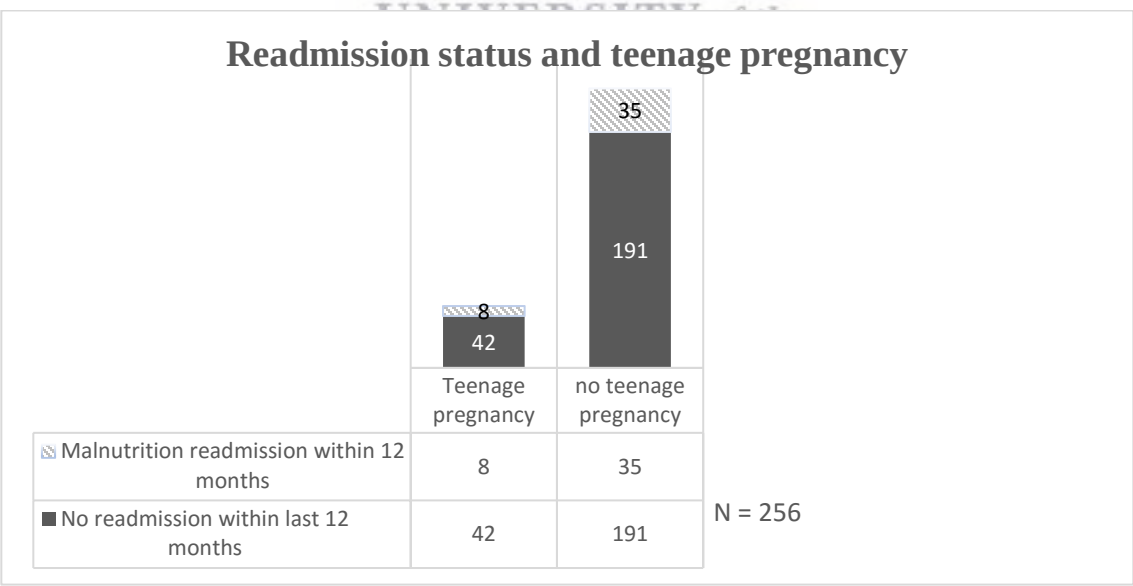


Figure 12: Readmission status and teenage pregnancy.

Sixteen percent (8/50) of the children with SAM who had teenage mothers, had at least one prior episode of malnutrition in the 12 months prior to the admission when they were included in this study.

The association between the various socio-demographic and socio-economic variables were further investigated as shown in Table 6.

Table 6: Association between socio-demographic and socio-economic variables.

Associations between: [a]	*p*-value
Residence & source of referral	<0.001*
Residence & Access to child support grant	0.932
Gender & Access to Child support grant	0.792
Age category & Access to Child support grant	0.732
Teenage pregnancy & Access to child support grant	0.540
Mother's education and access to child support grant	0.218
Mother's education & malnutrition readmission	0.411
Access to child support grant & malnutrition readmission	0.378
Employment status of caregiver & malnutrition readmission	0.08
Teenage pregnancy & malnutrition readmission	0.928
Caregiver & Employment status of caregiver	<0.001*
Age category & Gender	0.096

[a] Pearson chi-square and Cramer's V statistics used

*Statistically significant at $p < 0.05$

It was found that the area of residence was significantly associated with the source of referral that led to hospital admission ($p < 0.001$). There was no statistical significance found between access to a child support grant and the age, residence, gender of the child, mother's education, nor did having a teenage mother show significance, with *p*-values > 0.05. The incidence of malnutrition readmission was not significantly associated with the employment status of the primary caregiver, access to a child support grant, the mother's level of education or having a teenage mother with *p*-values > 0.05. There was also no association between the age and gender of the children admitted with SAM in this study sample with $p > 0.05$.

4.3. Anthropometric status

Anthropometric status was explored on admission, during hospital stay and discharge.

4.3.1. Anthropometric status on admission

Admission weight of the SAM children ranged from 1.72 kg to 13.8 kg, with a mean ± SD admission weight of 6.30 ± 2.46 (95%CI = 6.01 – 6.59) kg. On admission, males were significantly heavier than females with a mean ± SD weight of 6.58 ± 2.67 (95%CI = 6.14 - 7.01) kg compared with 5.98 ± 2.17 (95%CI = 5.59 – 6.36) kg in their female counterparts ($p = 0.04$). Height on admission ranged from 44.5 cm to 106 cm, with

a mean ± SD height of 68.13 ± 11.27 (95%CI = 66.79 – 69.46) cm, with no statistically significant difference in height between males and females (p = 0.35). The MUAC in the children with SAM aged 6 - 60 months on admission ranged from 8.0 – 18.5cm, with a mean ± SD MUAC measurement of 12 ± 1.75 (95%CI = 11.76 – 12.24) cm.

As per the WHO (2013) guidelines, the type of malnutrition on admission was classified as "SAM with oedema" or "SAM without oedema" and the MUAC measurement was grouped into being < 11.5 cm or ≥11.5 cm. Significance in the difference between the anthropometric measures was determined by the p-value, as shown below in Table 7.

Table 7: Anthropometric measures on admission (number and percentage).

Anthropometric measure on admission	N	%	*p*-value
SAM with oedema	108	39.13	
SAM without oedema	168	60.87	
	276	100.00	<0.001*
[a]*MUAC < 11.5 cm*	84	40.19	
MUAC >= 11.5 cm	125	59.81	
	209	100.00	0.005*

[a] < 6 months (67 cases excluded based on age)
* Statistically significant at $p < 0.05$

Thirty-nine percent (n = 108) of the children with SAM had oedema on admission and 61% (n = 168) had no oedema, which was statistically significant with a p-value < 0.001. On admission, 40% (n = 84) had a MUAC < 11.5 cm and 60% had a MUAC ≥ 11.5 cm with a statistically significant difference found between the MUAC categories (p = 0.005).

The prevalence of oedema on admission by the age is shown below in Figure 13.

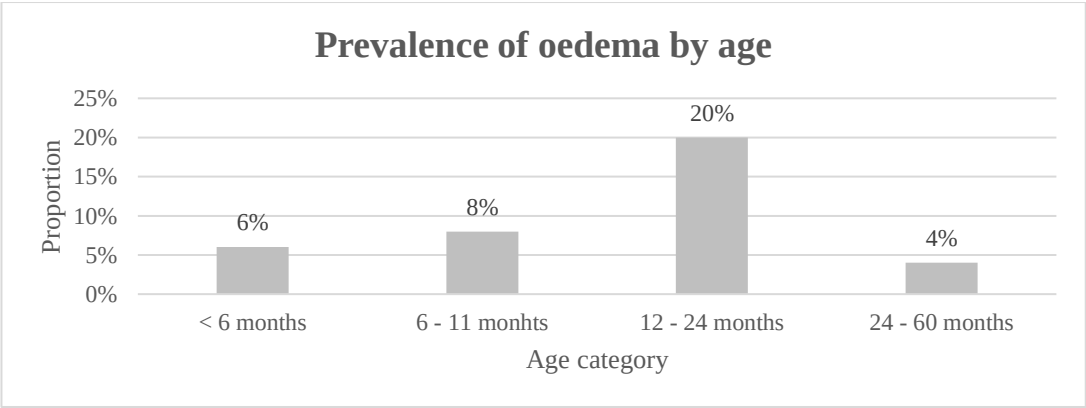


Figure 13: Prevalence of oedema by age (percentage).

The prevalence of oedema was the highest in the children aged 12 - 24 months and the lowest in those older than 24 months**,** however there was no statistically significant association between age categories and oedema.

Anthropometric measures by type of malnutrition at admission, during stay; and length of stay are shown below in Table 8.

Table 8: Anthropometric measures by type of malnutrition on admission and during hospital stay.

Anthropometric Measures [a]	Type of malnutrition	Mean ± SD	*p*-value
Weight on admission (kg)	SAM without oedema	5.42 ± 1.97	0.000*
	SAM with oedema	7.67 ± 2.56	
MUAC on admission (cm)	SAM without oedema	7.76 ± 5.25	0.000*
	SAM with oedema	11.14 ± 4.91	
Height on admission (cm)	SAM without oedema	66.40 ± 11.41	0.001*
	SAM with oedema	70.82 ± 10.55	
Length of stay (in days)	SAM without oedema	18.45 ± 13.88	0.037*
	SAM with oedema	15.39 ± 10.31	
Weight gain during stay (g/kg/day)	SAM without oedema	9.78 ± 9.38	0.000*
	SAM with oedema	1.99 ± 6.45	

[a] Independent sample t-test statistic used, variables measured on ratio scale
*Statistically significant at $p < 0.05$

On admission, the SAM children without oedema had a lower mean ± SD weight of 5.42 ± 1.97 kg and a lower mean ± SD MUAC of 7.76 ± 5.25 cm, compared to 7.67 ± 2.56 kg and 11.14 ± 4.91 cm in those with oedema. The difference in mean weight and MUAC between the two types of malnutrition on admission was statistically significant ($p < 0.001$). Those without oedema were significantly shorter at a mean ± SD height of 66.40 ± 11.41 cm, compared to 70.82 ± 10.54 cm in those with oedema ($p = 0.001$).

4.3.2. Anthropometric status during hospital stay

Length of stay (LOS) is shown below in Figure 14.

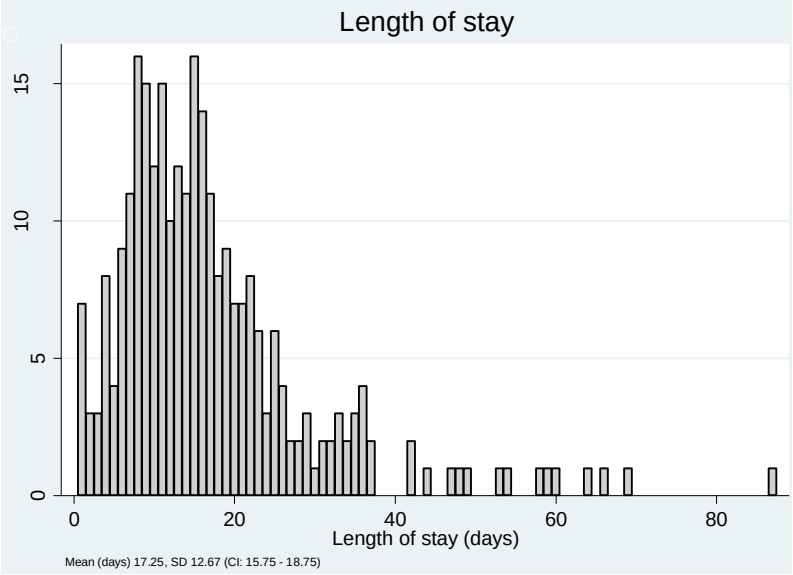


Figure 14: Length of stay (days) to discharge or death.

Length of stay until discharge or death ranged from 1 to 87 days, with a mean ± SD time of 17.25 ± 12.67 (95%CI = 15.75 – 18.75) days. Length of stay by outcome group (discharged or died) is shown below in Table 9.

Table 9: Length of stay by outcome group (discharged or died).

Length of stay			
Group [a]	**Mean ± SD (days)**	**95% CI**	***p*-value**
Discharged	18.18±12.63	16.61-19.74	0.0001*
Died	7.50±8.40	3.95-11.05	

[a] Independent sample t-test statistic used

*Statistically significant at $p < 0.05$

Those who were discharged stayed in hospital on average 18.18 ± 12.63 (95%CI = 16.61 – 19.74) days compared to those who died on average within 7.5 ± 8.40 (95%CI = 3.95 – 11.05) days after admission. The difference in LOS between the outcome groups was statistically significant ($p < 0.001$).

SAM children without oedema stayed a statistically significant longer time in hospital compared to those with no oedema, at 18.45 ± 13.88 days and 15.39 ± 10.31 days, respectively ($p = 0.037$); as seen in Table 8. Weight changes during hospital stay ranged from -2.9 kg to 3.4 kg, indicating some children lost weight. Mean ± SD weight gain was 568 ± 795 (95%CI = 473.93 – 662.46) grams during hospital stay. The WHO

(2013b) guidelines and mathematical formula used by authors Ndzo & Jackson (2018) was applied to calculate weight gain rates (gram/kilogram/day) in children with SAM during hospital stay. The mean weight gain rate for all children with SAM was 6.73 ± 9.17 (95%CI = 5.64 – 7.92) g/kg/day. When comparing weight gain rates between the two types of malnutrition, it was seen that those without oedema had statistically significant higher weight gain rates (9.78 ± 9.38 g/kg/day) compared to those with oedema (1.99 ± 6.45 g/kg/day), at a *p*-value <0.0001.

4.3.3. Anthropometric status on discharge or death

The diagnosis on discharge/death was recorded as either severe acute malnutrition (SAM), moderate acute malnutriton (MAM) or not acutely malnourished; based on the standardised WHO definitions and is displayed below in Figure 15.

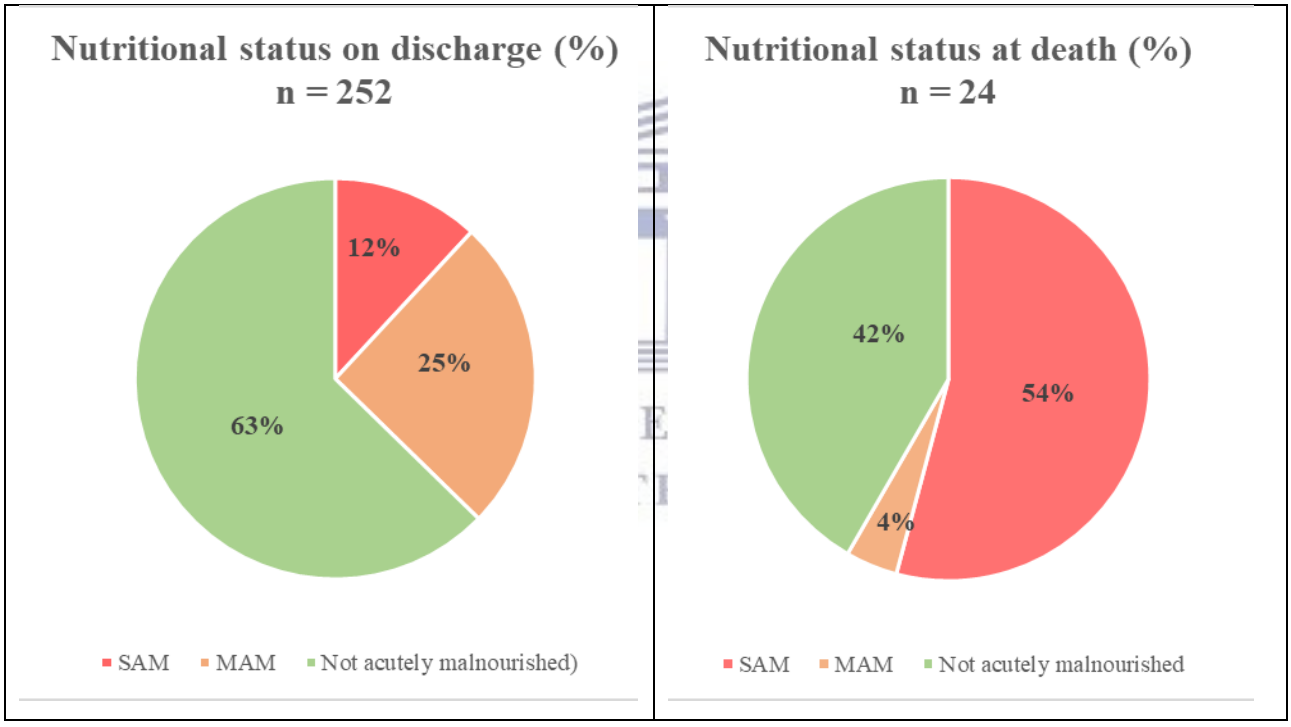


Figure 15: Nutritional status on discharge and death.

Sixty three percent (n = 158) of the children were no longer acutely malnourished by the time they were discharged, reaching a weight-for-height/length ≥ -2 SD or a MUAC ≥ 12.4 cm (if older than 6 months). Twenty five percent (n = 64) were moderately malnourished (MAM) and 12% (n = 30) still qualified for a SAM diagnosis when they were discharged. Most of the children who died were either SAM or not acutely malnourished.

4.4. Clinical signs and symptoms in children with SAM

The clinical signs and symptoms investigated on admission in children with SAM included: Hypothermia, hypoglycaemia, dehydration, skin lesions (or dermatosis), severe pallor, altered consciousness (impaired consciousness or coma) and shock.

The number and proportion of children with SAM that presented with these clinical signs and symptoms are shown below in Table 10.

Table 10: Clinical signs and symptoms (number and percentage) of the study population.

Clinical signs and symptoms	No of cases (N= 276)	Proportion (%)
Dehydration	112	40.6
Hypothermia	79	28.6
Skin lesions or dermatosis	74	26.8
Impaired consciousness or coma	52	18.8
Hypoglycaemia	29	10.5
Shock	18	6.5
Severe pallor	11	4.0

Dehydration (40.6%), hypothermia (28.6%), and dermatosis (26.8%) were the top three clinical symptoms present in children with SAM.

The prevalence of clinical signs and symptoms in the study population was further explored across gender, age, MUAC category and type of malnutrition (oedema or no oedema) and is shown below in Table 11, with the distribution presented in Figure 16.

Table 11: Prevalence of clinical signs and symptoms (number and percentage) by gender, age and type of malnutrition.

Clinical signs and symptoms (N, %)	Dehydration		Hypo-thermia		Skin lesions		Coma or lethargy		Hypo-glycemia		Shock		Severe pallor	
	n=112	%	n=79	%	n=83	%	n=52	%	n=29	%	n=18	%	n=11	%
Male	56	20	43	16	40	14	23	8	16	6	8	3	6	2
Female	56	20	36	13	34	12	29	11	13	5	10	4	5	2
< 6 months	43	16	23	8	13	5	15	5	7	3	8	3	3	1
6 - 11 months	30	11	18	7	16	6	12	4	7	3	4	1	2	1
12 - 23 months	28	10	31	11	34	12	17	6	10	4	3	1	3	1
24 - 60 months	11	4	7	3	11	4	8	3	5	2	3	1	3	1
MUAC < 11.5 cm[a]	29	10.5	52	19	16	6	16	6	8	3	3	1	6	2
MUAC ≥ 11.5 cm	41	15	99	36	45	16	22	8	14	5	7	3	3	1
SAM with oedema	31	11	31	11	53	19	16	6	14	5	5	2	2	1
SAM without oedema	81	29	48	17	21	8	36	13	15	5	13	5	9	3

[a] <6 months excluded due to age

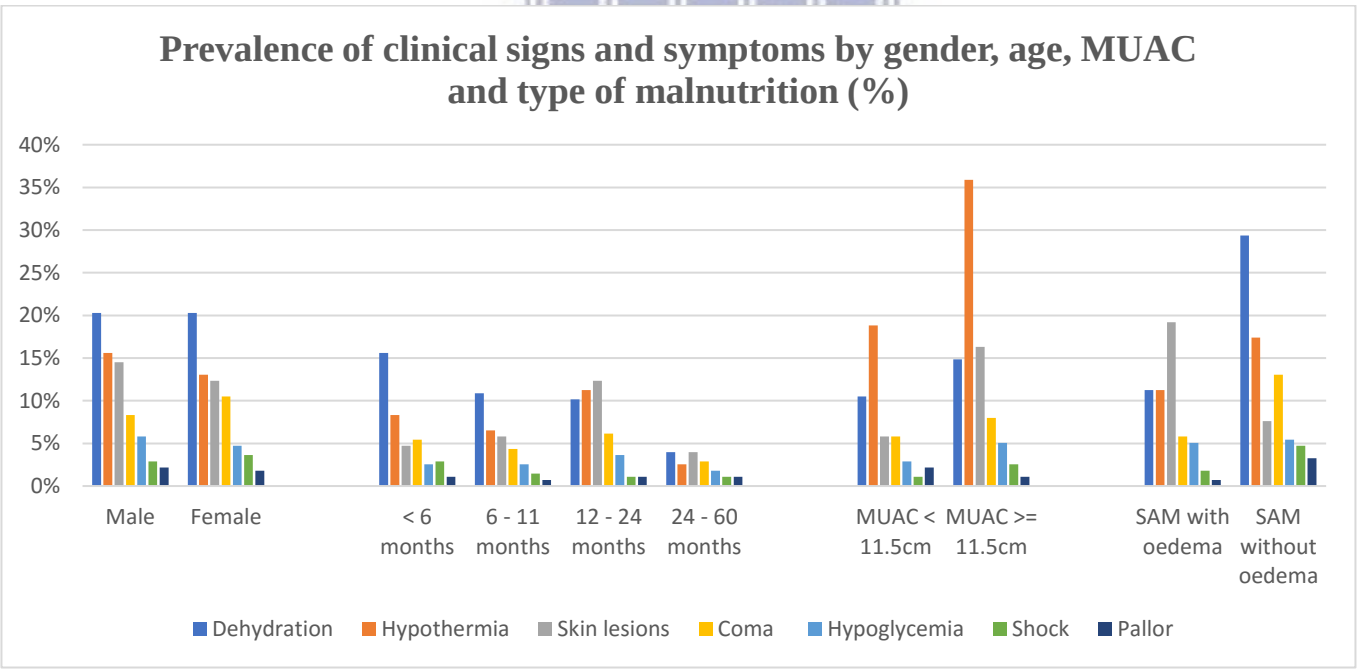


Figure 16: Prevalence of clinical signs and symptoms by gender, age, MUAC and type of malnutrition.

The difference in variability of the clinical signs and symptoms was tested between the different groups and are shown below in Table 12.

Table 12: Prevalence of clinical signs and symptoms variance for gender, age, MUAC and type of malnutrition.

		Gender [b]	*Age* [c]	*MUAC* [d]	Type of malnutrition [e]
Clinical Signs [a]	**N**	***p*-values**			
Dehydration	112	0.274	<0.001*	<0.001*	0.001*
Hypothermia	79	0.926	0.624	0.021*	0.981
Skin lesions/Dermatosis	74	0.989	0.046*	0.007*	<0.001*
Coma	52	0.118	0.506	0.856	0.171
Hypoglycaemia	29	0.893	0.668	0.928	0.288
Shock	18	0.403	0.135	0.101	0.309
Pallor	11	0.970	0.300	0.203	0.147

[a] One-way ANOVA test and F statistic used
[b:] Male or female
[c:] 0 - 6 months, 6 - 11 months, 12 - 23 months, 24 - 60 months
[d] < 11.5 cm or ≥ 11.5 cm, < 6 months excluded
[e] Oedema or no oedema
* Statistically significant at $p < 0.05$

The prevalence of dehydration, hypothermia, skin lesions, coma, hypoglycaemia, shock and pallor; was not significantly different between the male and female children admitted with SAM.

Across age categories, the prevalence of dehydration significantly decreased with an increase in age, showing younger SAM children (< 24 months) have a higher risk of developing dehydration ($p < 0.001$). Children aged 12 – 24 months had the highest prevalence of skin lesions or dermatosis, which was statistically different from the other age groups ($p = 0.046$). There were no statistical differences among the children across the age categories in terms of the other clinical signs present on admission.

Those with a MUAC ≥ 11.5 cm had a significantly higher prevalence of dehydration ($p < 0.001$), hypothermia ($p = 0.021$) and skin lesions ($p = 0.007$). No statistical differences among the children across the MUAC categories in terms of other clinical signs such as coma, hypoglycaemia, shock and pallor were found.

The prevalence of dehydration and skin lesions was significantly different between the types of malnutrition, where SAM children without oedema presented with a higher prevalence of dehydration ($p = 0.001$) and those with oedema a higher prevalence of skin lesions ($p < 0.001$). No other statistical differences among the children admitted with oedema and those without oedema were found in terms of the clinical signs such as hypothermia, coma, hypoglycaemia, shock and pallor.

4.5. Comorbidities in children with SAM

The following comorbid conditions were investigated in the children with SAM: Diarrhoea (acute and chronic), respiratory tract infections (other than pneumonia), pneumonia, HIV status, TB status and the presence of HIV and TB coinfection. The prevalence of comorbidities is presented in Table 13.

Table 13: Prevalence of comorbidities (number and percentage) found in the study population.

Comorbidities	No of cases (N = 276)	Proportion (%)
Presence of one or more comorbidity	205	74
Diarrhoea (acute and chronic)	120	43
Acute diarrhoea	104	38
Respiratory infection	84	30
HIV-infection (at discharge/death)	82	30
TB (at discharge/death)	75	27
HIV-TB Coinfection	46	17
Chronic diarrhoea	16	6
Pneumonia	9	3

Most of the children admitted with SAM (74%) presented with one or more comorbidity. Diarrhoea (43%), HIV infection (30%) and respiratory tract infections (30%) were the top three comorbidities found in the children with SAM. This was closely followed by TB (27%), with 17% of children with HIV, also being coinfected with TB. Acute diarrhoea was almost five times more prevalent than chronic diarrhoea. Pneumonia was the least prevalent comorbidity found (3%).

The prevalence of comorbidities was further examined to determine if variability occurs across gender, age categories and type of malnutrition (oedema/no oedema) of children with SAM. The number and percentages are shown below in Table 14 and the distribution shown in Figure 17.

Table 14: Prevalence of comorbidities (number and percentage) by gender, age and type of malnutrition.

Co-morbidities (N, %)	Diarrhoea		Acute Diarrhoea		Chronic Diarrhoea		Respiratory Infection		Pneu-monia		HIV-Positive		TB		HIV-TB Co-infection	
	n=120	%	n=104	%	n=16	%	n=84	%	n = 9	%	n=82	%	n=75	%	n=46	%
Male	64	23	55	20	9	3	46	17	6	13	35	13	42	15	25	9
Female	56	20	49	18	7	3	38	14	3	17	47	17	33	12	21	8
< 6 months	38	14	36	13	2	1	21	8	5	2	13	5	12	4	7	2
6 - 11 months	31	9	26	9	5	2	27	10	1	0	18	7	21	8	11	4
12 - 23 months	37	12	32	12	5	2	28	10	2	1	34	12	30	11	20	7
24 - 60 months	14	4	10	4	4	1	8	3	1	0	17	6	12	4	8	3
SAM with oedema	43	16	34	12	9	3	28	10	3	1	19	7	20	7	9	3
SAM without oedema	77	28	70	25	7	3	56	20	6	2	63	23	55	20	37	13

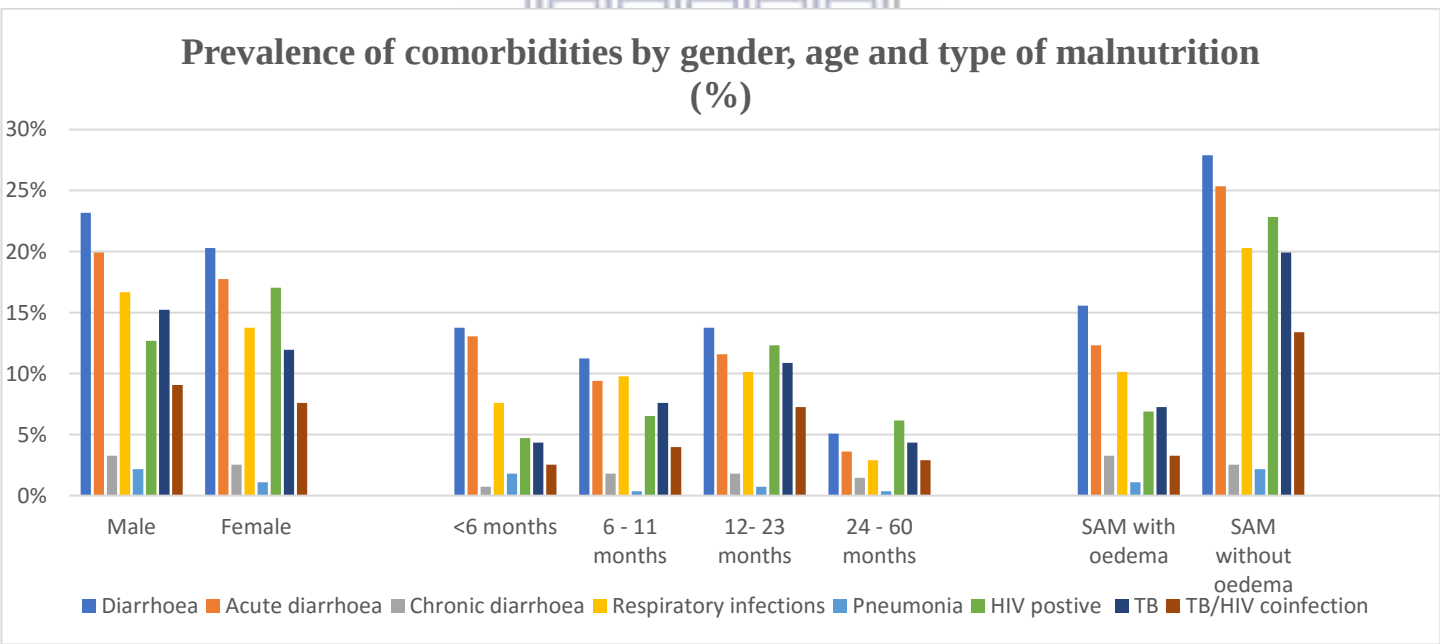


Figure 17: Prevalence of comorbidities by gender, age and type of malnutrition.

The differences in variability of comorbidities found in the children with SAM was tested and shown below in Table 15.

Table 15: Prevalence of comorbidities variance for gender, age and type of malnutrition.

Comorbidities[a]	Gender[b]	Age Category[c]	Type of malnutrition[d]
	p-values		
Diarrhoea	0.849	0.583	0.327
Acute diarrhoea	0.808	0.924	0.169
Chronic diarrhoea	0.808	0.924	0.169
Respiratory infection	0.865	0.726	0.193
Pneumonia	0.178	0.463	0.361
TB	0.588	0.249	0.002*
HIV	0.004*	0.001*	0.001*
HIV-TB Coinfection	0.151	0.003*	<0.001*

[a] One-way ANOVA test and F statistic used
[b:] Male or female
[c:] 0-6 months, 6-11 months, 12-23 months, 24-60 months
[d] Oedema or no oedema
* Statistically significant at $p < 0.05$

The prevalence of HIV-infection was higher in females, with no statistically significant differences of other comorbidities between gender. HIV-infection and HIV/TB coinfection as comorbidities varied significantly in prevalence across age categories with those 12 - 23 months having the highest prevalence of HIV infection and HIV/TB coinfection. For the type of malnutrition; TB, HIV and HIV/TB coinfection as comorbidities varied significantly in prevalence, with those children without oedema having the highest prevalence of all three comorbidities.

4.6. Factors associated with survival probably and increased risk of death

The SAM case fatality rate in this study was 8.7%. To determine which factors contributed to an increased risk of death in the children with SAM, the mean survival probability (in days) was calculated and an estimation of the Hazard Ratio (HR), thus the risk of death over a period of time, was determined.

4.6.1. Survival probability

The estimated mean survival time for the cohort in this study was 76.63 (95%CI = 71.76 – 81.50) days. To determine survival probability, the factors were first identified under the different variable categories i.e. of demographic status, clinical signs, comorbidities and SAM status. The estimated mean survival times of

children with SAM was then calculated based on each of these factors. These results are presented in Table 16.

Table 16: Estimated mean survival times of children with SAM based on various factors.

Variable Category (domain)	Variable	Mean Survival Time (days)	Chi-square	*p*- value [a]
Demographic factors [b]	**Age categories**		2.945	0.086
	< 2 years	78.1		
	2 - 5 years	44.2		
	Gender		4.767	0.029*
	Male	58.7		
	Female	80.2		
	Referral source		17.584	0.001*
	Hospital transfer	32.7		
	PHC Clinic	59.9		
	Private GP	16.7		
	Self	80.3		
	Employment status of caregiver		0.27	0.874
	Employed	30.3		
	Unemployed	77.5		
	Unknown	31.6		
	Teenage pregnancy		1.677	0.195
	Yes	61.2		
	No	75.4		
Clinical Signs and symptoms	**Skin Lesions**		6.733	0.009*
	Yes	49.6		
	No	78.2		
	Hypothermia		5.943	0.015*
	Yes	71.9		
	No	62.9		
	Hypoglycaemia		30.526	<0.001*
	Yes	41.7		
	No	80.3		
	Dehydration		12.361	<0.001*
	Yes	56.7		
	No	80.3		
	Pallor		96.026	<0.001*
	Yes	9.5		
	No	79.2		
	Lethargy/Coma		43.311	<0.001*
	Yes	40.5		
	No	83.5		
	Shocked		54.152	<0.001*
	Yes	30.6		
	No	79.3		

Variable Category (domain)	Variable	Mean Survival Time (days)	Chi-square	*p*- value [a]
Comorbidities	**HIV-infection**		6.191	0.013*
	Negative	60.1		
	Positive	71.7		
	Unknown	2.5		
	Tuberculosis		19.775	<0.001*
	Negative	64.9		
	Positive	74.1		
	Unknown	23.3		
	Diarrhoea		0.873	0.350
	Yes	76.1		
	No	60.5		
	Type of Diarrhoea		1.904	0.386
	Acute	61.0		
	Chronic	48.9		
	Pneumonia		23.110	<0.001*
	Yes	24.7		
	No	49.2		
	Unknown	81.4		
	HIV/TB Coinfection		3.470	0.176
	No	61.8		
	Yes	68.8		
	Respiratory tract infection		0.048	0.827
	Yes	78.3		
	No	60.7		
	One or more Comorbidities		0.728	0.393
	Has comorbidities	75.6		
	No comorbidities	33.1		
SAM status	**Oedema**		0.676	0.411
	Yes	50.6		
	No	78.9		
	MUAC Category [c]		0.010	0.995
	MUAC < 11.5 cm	78.1		
	MUAC >= 11.5 cm	52.6		
	Readmission		0.306	0.580
	No malnutrition admission in last 12 months	77.9		
	Readmitted	54.2		
	Place of Admission		29.322	<0.0001*
	High care	45.7		
	Normal ward	83.5		
	PICU	20.4		

[a] Kaplan Meier survival analysis and log rank method used

[b] Statistics not computed for CSG because all cases were censored

[c] < 6 months excluded

* Statistically significant at $p < 0.05$

4.6.1.1. Survival probability: Demographic factors

Out of the five demographic variables used to estimate the mean survival times across groups, only two of them were statistically significant; namely: gender and referral source. From Table 16, it is seen that female children with SAM are estimated to survive a statistically longer time (80.2 days) compared to 58.7 days in their male counterparts ($p = 0.029$). Similarly, survival time based on the referral source were significantly different. Those who were "self-referred" had the longest estimated survival time (80.3 days), followed by those who were referred from a PHC facility (59.9 days). Children referred from a private GP had the shortest overall survival time of only 16.7 days ($p = 0.001$).

4.6.1.2. Survival probability: Clinical signs and symptoms

The sampled children's survival status was examined based on clinical symptoms identified on admission (hypoglycaemia, hypothermia, dehydration, skin lesions or dermatosis, severe pallor, impaired consciousness or coma and shock). Apart from hypothermia, on average, the survival time for those SAM children without the presence of these signs and symptoms were significantly longer compared to those with the presence of these symptoms at p-values < 0.05. In most cases the average survival time in the absence of these clinical signs were 2 - 3 times longer compared to those with these signs and symptoms. Those without severe pallor however had an average survival time almost 8 times longer than those who had severe pallor on admission ($p < 0.001$). Contrary to the other clinical signs and symptoms, the SAM children who presented with hypothermia on admission, had a significantly longer survival time compared to those who were not hypothermic ($p = 0.015$).

4.6.1.3. Survival probability: Comorbidities

When investigating the impact of comorbidities on the survival probability, the results showed (with p-values < 0.05) that HIV-infection, tuberculosis and pneumonia are comorbid variables that have significantly different mean survival times across the groups examined. Those who were HIV-positive ($p = 0.013$) or had tuberculosis ($p < 0.001$), had a longer mean survival time compared to their non-infected counterparts, however HIV/TB coinfection ($p = 0.176$) showed no significant difference in the survival times. Those children without pneumonia had a survival time almost double that of the SAM children who were diagnosed with pneumonia ($p < 0.001$) at 49.2 days and 24.7 days, respectively.

4.6.1.4. Survival probability: SAM status

The presence of oedema in cases 0 – 60 months, or a MUAC cut-off <11.5 cm in those older than 6 months, did not have a statistically different outcome in terms of mean survival times, neither did a previous

admission of malnutrition within the last 12 months ($p > 0.05$). The place of admission however resulted in significantly different survival times, with those admitted to paediatric intensive care (PICU) having the shortest survival time ($p < 0.0001$).

4.6.2. Factors associated with increased risk of death

The hazard ratio (HR) was estimated for all the 23 factors across the four domains (demography, clinical signs, comorbidities and SAM status). Table 17 below shows the HRs of all the covariates with their respective *p*-values and relevant parameters.

Table 17: Factors associated with increased risk of death (Hazard Ratios).

Domain	Factors	HR	SE	Z	*p*-value [a]	95%CI
Demographic factors	*Age category (< 2 years or 2 - 5 years)*	0.646	0.474	-0.600	0.552	0.154 - 2.717
	Gender	0.174	0.119	-2.560	0.011*	0.046 - 0.665
	Referral Source	0.985	0.341	-0.040	0.964	0.499 - 1.942
	Employment Status of Caregiver	0.586	0.413	-0.760	0.448	0.147 - 2.334
	Teenage mother	2.557	2.301	1.040	0.297	0.438 - 14.916
Clinical signs	*Skin lesions*	3.779	2.625	1.910	0.056	0.968 - 14.747
	Hypothermia	2.007	1.275	1.100	0.273	0.578 - 6.969
	Hypoglycaemia	2.194	1.468	1.170	0.240	0.592 - 8.139
	Dehydration	4.113	2.508	2.320	0.020*	1.245 - 13.591
	Pallor	3.167	2.387	1.530	0.126	0.723 - 13.876
	Lethargy /coma	4.229	3.017	2.020	0.043*	1.045 - 17.115
	Shocked	2.885	2.411	1.270	0.205	0.561 - 14.845
	Presence of multiple clinical signs ((0,1,2 or ≥ 3 clinical signs)	4.40	1.222	5.350	0.000*	2.569 - 7.593
Comorbidities	*Diarrhoea*	2.402	4.069	0.520	0.605	0.087 - 66.466
	Diarrhoea type (acute or chronic)	1.802	1.705	0.620	0.533	0.282 - 11.507
	Tuberculosis	1.634	0.662	1.210	0.226	0.738 - 3.616
	HIV-infection	9.935	9.945	2.290	0.022*	1.397 - 70.676
	HIV-TB coinfected	0.459	0.243	-1.470	0.142	0.162 - 1.297
	Pneumonia	3.400	1.356	3.070	0.002*	1.556 - 7.429
	Respiratory tract infection	2.849	1.947	1.530	0.125	0.747 - 10.873
	Presence of multiple comorbidities (0,1,2 or ≥ 3 comorbidities)	1.463	0.317	1.760	0.078	0.0958 - 2.236
SAM status	*Presence of oedema*	2.858	2.089	1.440	0.151	0.682 - 11.973
	MUAC based on 11.5 cm cut off	1.961	0.869	1.520	0.128	0.823 - 4.674
	Readmission status	1.316	1.016	0.360	0.722	0.290 - 5.974

Abbreviations: Hazard Ratio (HR), Standard Error (SE), Z-statistic (Z), Confidence Interval (CI)

[a] Cox proportional hazard regression at multivariate level (Efron method)

*Statistically significant at $p < 0.05$

Five individual factors showed a significant association with the likelihood of death. These factors were; gender, dehydration, lethargy or coma, HIV-infection and pneumonia. Hazard curves for these factors are presented in Appendix 6. The presence of multiple clinical signs on admission also significantly increased the risk of death.

Gender significantly increased the risk of dying in children with SAM with a HR = 0.174 (95%CI = 0.046 - 0.665) at $p = 0.011$. The HR indicated a decreased risk of death in female children with SAM of 83%.

Dehydration and lethargy or coma significantly increased the risk of death in children with SAM. The risk of death in those children with dehydration were 4.1 times higher compared to those who were not dehydrated, with a *p*-value = 0.02 (HR = 4.113, 95%CI = 1.245 - 13.591). The risk of death in SAM children who were lethargic or comatose on admission were 4.2 times higher compared to those who were not, with a *p*-value = 0.043 (HR = 4.229, 95%CI = 1.045 - 17.115). Children with SAM who had one or more clinical sign/symptom on admission had a 4.4 times higher risk of death (HR = 4.40, 95%CI = 2.560 - 7.593), $p < 0.0001$.

HIV-infection and pneumonia were the only comorbidities that had statistically significant associations with an increased risk of death in children with SAM, at a confidence level of 95%. In HIV-infected SAM children, the risk of dying was almost 10 times higher than those who were HIV negative (HR = 9.935, 95%CI = 1.397 - 70.67) at a *p*-value = 0.022. Those SAM children with pneumonia had a 3 times higher risk of death than those who did not have pneumonia (HR = 3.4, 95%CI = 1.556 - 7.429) at a *p*-value = 0.002.

CHAPTER 5

DISCUSSION AND LIMITATIONS

5.1. DISCUSSION

5.1.1. Introduction

The purpose of this study was to investigate factors associated with morbidity and mortality in children under-five with SAM, who were admitted to an inpatient paediatric hospital in KwaZulu-Natal. The overall case fatality rate amongst the SAM children in this study was 8.7%, which is higher than the WHO recommended target of < 5%. The study however had a lower SAM case fatality rate compared to the KwaZulu-Natal average (10.4%) and the South African national average (11.6%) (Massyn *et al.,* 2015). Person-time at risk for the children was estimated at 4761 days. The estimated mean survival time for the cohort was 76.63 days.

Twenty-three factors across the following domains were investigated to determine the impact on survival probability and mortality risk: Socio-economic, socio demographic, clinical signs and symptoms, SAM status and comorbidities. Survival probability was significantly associated with gender, all the clinical factors, the place of admission as well as HIV-infection, TB and HIV/TB coinfection. Increased mortality risk in the multivariate model was only significantly associated with gender, dehydration, altered consciousness, the presence of multiple clinical signs on admission, HIV-infection and pneumonia. These findings could provide contextually specific information to contribute to improving malnutrition outcomes in children with SAM.

5.1.2. Socio-demographic and socio-economic factors

5.1.2.1. Age

Most of the children with SAM (90%) were younger than 2 years at the time of admission. The mean age of the children were 13 months, which was consistent with similar studies conducted in developing countries (De Maayer & Salojee, 2011; Benyara *et al*., 2013; Gupta *et al*., 2015, Adama *et al*., 2016). This is reflective of the situation in South Africa as shown in the 2016 South African Health and Demographic Survey where it was found that children younger than 18 months are the most affected by wasting (SADHS, 2016). It is widely documented that the first two years of life is a very vulnerable period for negative health and nutrition outcomes (Pelletier *et al*., 1995), raising concern as to longer term impact of malnutrition on this age group.

Twenty five percent of the sample had not reached the age of 6 months at the time of admission with SAM, a period where exclusive breastfeeding should be protecting these children against malnutrition (Bhutta *et*

al., 2013). Hendricks, Goeiman, & Hawkridge (2013) concluded that SAM in children younger than 12 months is increasing in South Africa, the direct result of inadequate breastfeeding. While this study did not investigate infant feeding practices, it highlights the need to further investigate the drivers of poor infant feeding practices in this community, the effectiveness of programs that promote exclusive breastfeeding and the appropriate treatment guidelines for this age group. Kerac *et al.* (2015) shares this concern, arguing that the physiological and pathological differences in this age group demands a very different approach to that used in older children; and while breastfeeding is key, underlying infant diseases and maternal physical and mental health should be also be considered.

Literature almost conclusively agree that case fatality rates for children with SAM are significantly higher in younger age groups, with those younger than 2 years having a 3 times higher risk of death compared to those > 2 years (Nhampossa *et al*., 2013; Jarso, 2015; Ahmed *et al*., 2016; Girum *et al*., 2017; Awoke *et al*., 2018). This was however not supported by findings in this study as there was no statistically significant difference between the ages < 2 years and 2 - 5 years, or between the four age categories (0 - 6 months, 7 - 11 months, 12 - 23 months and > 24 months) in terms of mean survival probability or risk of death. This is possibly due to the small number of deaths that occurred during the study period.

5.1.2.2. Gender

More than half (53%) of the children with SAM in this study were males. Gender was significantly associated with malnutrition outcomes, where female children had a longer survival probability as well as a decreased risk of dying, compared to male children with SAM. This is in contradiction with many other findings (Benyara *et al.,* 2013, Jarso *et al.,* 2015), where results showed females either have a higher overall risk or there were no differences found between gender. The relationship between gender and malnutrition outcomes is inconclusive and possibly regional specific, likely due to cultural and social norms and not because of a biological predisposition (Roy *et al*., 2011). It is well documented that caregiver behaviours are deeply rooted in cultural and social values which impacts on child growth through their effect on dietary practices and decisions made around a child's health (Flax, 2015), but this was outside the scope of this study.

5.1.2.3. Geographical distribution

Most of the children with SAM stemmed from uMlhathuze and Mbonambi subdistricts, which is expected as the study setting is the only paediatric admission facility in the surrounding area. The study could not determine mortality risk based on the traditional geographic demarcations (rural or urban), as some of the subdistricts have a mix between urban and rural areas. This distinction would've only been possible if the

exact residential location of each child with SAM was known. It was however found that the area of residence was associated with the source of referral that led to hospital admission. Inter-hospital referrals occurred mostly from Nkandla subdistrict, as well as from out of the district, namely uMkhanyakude district and Zululand district. This finding could indicate that these hospitals are not sufficiently equipped to deal with complicated cases of SAM. uMhalthuze as well as Mbonambi subdistricts had the highest number of children with SAM referred from primary health care clinics, but also the most cases of "self-referrals", which indicates that a large proportion of these children did not access primary health care services. The reasons for this are likely multifactorial, relating to factors such as poor access to healthcare, lack of quality of health care and health seeking behaviour (Flax, 2013); which was out of the scope of this study. Furthermore, survival time was significantly associated with the referral source, where those who were "self-referred" had the longest estimated mean survival time (80.3 days), followed by those who were referred from a primary health care facility (59.9 days). Children with SAM referred from a private general physician, had the shortest overall survival time of only 16.7 days. With significant poverty levels in the area (Statistics SA, 2011), it is not unexpected that only a small number of caregivers would have been able to access a private physician and by the time they did, the child would have possibly been critically ill. Even though the small number of deaths included in this study might have influenced results, the shorter survival time in children referred from primary health care facilities compared to those who were "self-referred" raises questions about the assessment, care and referral systems in place at primary health care level to manage children with SAM.

5.1.2.4. Socio-economic factors

Sixty one percent of the study population had access to a child support grant (CSG), which is slightly lower than the national average of 76% (Department of Social Development, 2014). There was no statistical significance between gender or area of residence of the children with SAM and their ability to access a CSG. There was no statistical difference between the teenage mothers and non- teenage mothers in terms of access to CSG, even though by law the teenage mother cannot simultaneously be both a caregiver applicant (on behalf of her own children) and a beneficiary (in terms of her own mother's application). This could mean that if these teenage mothers were already beneficiaries of the grant they would have had to forfeit their own CSG to access that of their child's (DSD, SASSA & UNICEF, 2012), which often would lead to them leaving school early to find employment. Child support grant uptake increased with age, where infants (< 1 year) had the lowest CSG uptake, a finding supported by national studies (Department of Social Development, 2014; DSD, SASSA & UNICEF, 2012), but there was no statically significant association between age and CSG uptake in this study. It is uncertain whether access to a CSG would have had an impact on survival

probability or mortality risk as all cases were censored during multivariate analysis. There was no association between malnutrition readmission rates and access to a CSG found in our study, contradicting findings in literature where greater access to CSG lead to a reduction of the incidence of readmissions in malnourished children (Saloojee *et al*., 2007; Wondafrash *et al*., 2017). Most of the mothers of SAM children had reached secondary school education and only 25% completed high school. This is representative of the larger population where statistics show only about 30% have matriculated (Statistics SA, 2011). The mothers who reached secondary school were the most likely to have to access to CSG, although it did not reach statistical significance. Even though the mother's level of education did not significantly associate with the incidence of malnutrition readmission in this study, the combination of higher levels of education and access to a CSG, could possibly improve outcomes, as shown in a study in South Africa where a mother's education can complement the CSG in strengthening important impacts on child health and development (DSD, SASSA & UNICEF, 2012). It should also be mentioned that almost a quarter of the study population did not have the mother as primary caregiver, and there is uncertainty whether these caregivers received the monetary value of the CSG, as this was outside the scope of this study.

Eighteen percent of the cases with SAM in this study were born to teenage mothers, who were younger than 18 years old at the time of birth of the child. The high prevalence of teenage pregnancy found in this study is supported by the South Africa Demographic and Health Survey (SADHS, 2016) reporting that one in three women will be pregnant by the age of 18 years (Massyn *et al.*, 2016). There was no association found between the prevalence of teenage pregnancy and survival probability or risk of death. Teenage pregnancy however has been associated with higher risk during delivery, low birth weight, poor infant growth and early cessation of breastfeeding (Branca *et al*., 2015), which could all be associated with malnutrition and other adverse child outcomes and would warrant further investigation.

Considering the poor socio-economic status of the region, where unemployment rates are higher than 35% (Statistics SA, 2011), it was not unexpected to find that most (82%) of the caregivers in this study were unemployed. Even though 74% of the children who were readmissions for malnutrition had caregivers that were unemployed, malnutrition readmission and the employment status of caregivers did not show a significant association. Employment status of the caregiver showed no statistical significance in reducing survival probability or increasing risk of death in the multivariate analysis. Caregivers often falsely report they are unemployed when they are in receipt of a CSG, out of fear that it could be revoked as there is significant misinformation about the eligibility criteria for CSGs (DSD, SASSA & UNICEF, 2012). Furthermore, given that a large proportion of the caregivers were grandmothers, they could have been

unemployed by virtue of age, but had access to pension or other sources of income from the informal work sector. The adverse association between low socio-economic status and malnutrition is well documented (van de Poel *et al.,* 2008), and the lack of association found in this study is likely due to insufficient information collected on socio-economic variables to control for confounding factors.

5.1.3. Anthropometric factors

On admission, males were significantly heavier than females, similar to other findings in literature (Irena *et al.,* 2011), while there was no statistically significant difference in height between males and females. More than half (60%) of the cases were admitted without oedema (wasting) which was statistically significant. Correct diagnosis of the type of malnutrition is essential as it impacts the management and outcomes of children with SAM (Trehan & Manary, 2015).

Literature reports wide differences in the prevalence of the forms (oedematous or wasting) of SAM within different populations (Jarso *et al*., 2015). In some African countries, Latin America and Asia, wasting is more common, which is supported by findings in our study (Saloojee *et al*., 2007). Trehan & Manary (2015) however found that in southern Africa specifically, rates of oedematous malnutrition are higher, making up two-thirds of the SAM population. In the context of high HIV prevalence, it has also been found that wasting is more prominent (Saloojee *et al.,* 2007). Our study, which had a high overall HIV prevalence of 30%, supports this finding, showing that HIV-infection was prevalent in 23% of cases without oedema (wasting), compared to only 7% in those with oedema. The exact pathophysiology of the clinical presentation of malnutrition have not been clearly described and could be linked to the child's diet, genetics, environment, intestinal microbiome or the presence of certain comorbidities (Subramanian *et al*., 2014; Trehan & Manary, 2015). In this context, it could possibly be linked specifically to HIV, TB and HIV/TB co-infection as it was found that those without oedema not only had a significantly higher prevalence of HIV-infection, but also TB and HIV/TB co-infection.

It is generally reported that oedematous malnutrition is more common in children older than two years (Akparibo *et al*., 2016), which was not shown in this study. Most of the SAM cases with oedema was younger than 2 years and the highest prevalence was amongst those aged 1 - 2 years. There was however no statistically significant difference between the age groups in terms of oedema prevalence. There was also no statistically significant association between the presence of oedema and the survival probability or risk of death in the SAM children in this study. This is contradictory to some studies, where oedematous malnutrition, even in the absence of other medical complications, have been found to be associated with the highest morbidity (Yohannes *et al.,* 2017) and mortality risk (Bernal *et al*., 2008; Teferi *et al*., 2010), while this supports findings by others such as Jarso *et al*. (2015) and Gachaua *et al*. (2018) also showing no

statistical significance between the two forms of malnutrition and mortality risk. It should be considered that the severity of the oedema could have been a confounding factor as children with severe oedema have the highest risk of death (WHO, 2018b), but in the current study the severity of oedema was not graded because the medical records on admission only indicated the presence of oedema and not the degree.

The study further showed that there is a statistically significant difference in all the anthropometric measurements of SAM children based on the presence of oedema. Weight and MUAC on admission were higher in those children with oedema, while weight gain during stay was significantly lower in those with oedema. While it is expected to find an increase in weight and lower weight gain rates in children with oedema due to excess intracellular fluid (Myatt *et al.*, 2006; WHO, 2013b), the impact of oedema on MUAC is not well described. MUAC measurements in children with SAM and oedema show great variations and some studies also show gender specific differences (Tadess *et al*., 2017; Alvarez *et al.*, 2018).

There was a significant difference in the mean height between the two forms of malnutrition, where those with oedema were significantly taller than those without oedema, supported by similar findings from Rytter *et al*. (2015). While wasting is an acute form of malnutrition, stunting (or short stature) is the result of chronic malnutrition and is measured by the child's height-for-age. Although the presence of stunting was not investigated in this study because of the current study's aim and objectives, it is known to have a complex and multifactorial aetiology (Altare *et al*., 2016). It is however well documented that repeated episodes of acute malnutrition can lead to stunting (Saaka & Galaa, 2016). It is also hypothesized that this difference could be because oedematous children had been malnourished for a shorter time or that those without oedema had been affected by more infections, which is known to cause stunting (Prentice *et al*., 2013; Rytter *et al*., 2015). This study however showed that it was the children with oedema who had significantly higher rates of chronic infections such as HIV, TB and HIV/TB-coinfection. This would warrant further investigation.

The mean weight gain rate for all SAM children was 6.73 ± 9.17 (95% CI = 5.64 – 7.92) g/kg/day, which was in line with the recommended guidelines for weight gain rates of > 5 – 10 g/kg/day (Department of Health, 2015b). When comparing weight gain rates between the two types of malnutrition, it was seen that those without oedema had statistically significant higher weight gain rates (9.78 ± 9.38 g/kg/day) compared to those with oedema (1.99 ± 6.45 g/kg/day), at a *p*-value <0.0001. Weight gain during stay is expected to be lower on average in children with oedema, as recovery in malnourished children with oedema is determined by the oedema resolving and therefore fluid loss (Department of Health, 2015b). Similar findings were reported by Oumer *et al.*, (2016).

The mean (SD) length of hospital stay in this study was 17.25(± 12.67) days, which is higher than some studies reporting in-hospital stay on average of 10 - 11 days (Benyera *et al.*, 2013; Oumer *et al.*, 2016;

Yohannes *et al.*, 2017), but similar to studies done in other referral hospitals in Africa reporting average length of stay from 17 - 28 days (Jarso *et al.*, 2015; Tirore *et al.*, 2017). These variances are likely due to local policies with different discharge criteria and the prevalence of comorbidities and complications in various study populations. The average length of stay found in this study is however consistent with the minimum international standard set for length of stay for children with SAM of less than 30 days (Layton, 2001). Children with oedema stayed on average (SD) 15.39 (± 10.31) days and those without oedema a statistically longer time of 18.5(± 13.88) days. The longer stay of non-oedematous children was not unexpected as oedema in children with SAM typically resolve within 2 weeks, which is also the discharge criteria for these cases; whereas children who are severely wasted can take up to 6 weeks to achieve catch up growth (WHO, 2013b; Department of Health, 2015b; Kabalo & Yohannes, 2018).

5.1.4. Nutritional status on discharge

Early discharge can have benefits in terms of prevention of hospital acquired infections and reducing inpatient cost but carries a significant risk of relapse and eventual death, if continuity of care cannot be established in an outpatient setting (Ashworth, 2001). At discharge, a quarter of the children were found to be moderately malnourished and 12% still qualified for a SAM diagnosis. The high number of children discharged as moderately malnourished could be explained by local policy. In KwaZulu-Natal, there is provision for earlier discharge to outpatient supplementation programs, when the child has reached a MUAC of ≥ 11.5 cm, or have reached a weight-for-height/length between -3 and -2 Z-score; and achieved weight gain during the rehabilitation phase of > 5 - 10 g/kg/day, has a good appetite for food and is clinically well and alert (Department of Health, 2015b).

Malnutrition relapse rates within 1 year are reported to be up to 10% (Akparibo *et al.*, 2016), while in this study, 18% of the cases had at least one previous admission for malnutrition in the 12 months preceding their enrolment into the study. In this study, there was no statistical association found between the readmission for malnutrition, survival probability or an increased risk of death, likely due to the small number of deaths reported during the study period. It is however well documented that there is a continued risk for relapse and death long term. Kerac *et al.* (2014) found a death rate of 33% in children with SAM, enrolled in their clinical trial, who were readmitted within 1 year, while long term survival (> 1 year) in children with SAM is greater in those who successfully reached nutritional recovery (i.e. Weight-for-height score of > -2 SD or MUAC > 12.4 cm) before being discharged. Those with comorbidities such as HIV-infection and TB are at highest risk of relapse or death if discharged before nutritional recovery is reached, especially when outpatient care is inadequate (Trehan & Manary, 2015). The large number of children discharged before

reaching nutritional recovery in the context of high HIV and TB prevalence and the high readmission rates raise concerns as to the continuity and quality of care at the primary health care level once a child is discharged from hospital, while mortality rates at a community level is still largely unknown (CoMMiC, 2014).

5.1.5. Clinical signs and symptoms

The sampled children's survival status was examined based on clinical signs and symptoms identified on admission i.e.: Hypoglycaemia, hypothermia, dehydration, skin lesions or dermatosis, severe pallor, impaired consciousness or coma and shock. Almost all the cases (96%, $p < 0.001$) admitted with SAM presented with one or more of these clinical signs or symptoms, which would classify them as having SAM with complications (Department of Health, 2015b; Williams & Berkley, 2017). This is much higher than the estimation of 15% made by Collins *et al*. (2006), indicating that the children in this cohort generally had a complicated presentation on admission. The high rate of complications in this study could be due to the study setting serving as a referral and specialist hospital for other hospitals in the region, while the high prevalence of various comorbidities found in the sample would also play a role in their complicated presentation. It could further be speculated that the children present to hospital at the advanced stages of malnutrition, raising questions about early detection and treatment programs at primary health level, health seeking behaviours of the caregivers and the access to health care.

Apart from hypothermia, the mean survival time for children with SAM without these signs and symptoms were significantly longer compared to those who presented with medical complications ($p < 0.05$). The average survival time in the absence of these clinical signs and symptoms were 2 - 3 times longer, while those without severe pallor however had an average survival time almost 8 times longer than those who had severe pallor on admission ($p < 0.001$). This supports various studies reporting the presence of these clinical symptoms and the association with poor prognostic outcomes in children with SAM (Maitland *et al*., 2006; De Maayer & Saloojee, 2011; Jarso *et al*., 2015; Oumer *et al*., 2016).

After multivariate analysis, dehydration and coma/impaired consciousness were the only clinical signs found to be independently associated with an increased risk of death of up to 4-fold, in children with SAM in this study. It was however found that children with one or more clinical sign/symptoms on admission had a significantly higher risk of death (HR = 4.40, 95%CI = 2.56 - 7.59). This is supported by findings in Kenya where the presence of two or more signs was associated with a 9.6 times higher risk of dying in SAM children (Maitland *et al*., 2006) as well as findings by Kerac *et al.* (2014) showing a 2 - 4 times higher risk. There is

also an ongoing risk after discharge from in children who present with complicated SAM (Williams & Berkley, 2016), but this was outside the scope of this study.

5.1.5.1. Dermatosis

Dermatosis was significantly more prevalent in children aged 12 - 24 months ($p = 0.046$) and those with a MUAC > 11.5 cm ($p < 0.001$), and even though statistically not significant, oedema was also most prevalent in this age group. The co-occurrence of these findings corresponds with literature as the characteristic dermatosis is most often seen in young children suffering from oedematous malnutrition and does not usually occur in children without oedema (Latham, 1991; Ryter *et al.*, 2014). The aetiology of dermatosis is still largely unknown, but it has been shown to be a predictor of mortality in hospitalized children with SAM, depending on the severity (Heilskov *et al.*, 2015). Our study supports the body of evidence that dermatosis does have a significant impact on survival probability, especially in young children (< 24 months), but did not find increased mortality risk. This study did not look at the severity of dermatosis, which could have influenced the outcomes and should be considered for future research.

5.1.5.2. Hypothermia

A contradictory finding to literature was that those children who had hypothermia on admission had a significantly longer estimated survival time compared to those were not hypothermic ($p = 0.015$). It is unknown whether the cases who were considered "non-hypothermic" perhaps presented with fever as the study did not collect information on pyrexia. Gebremichael (2015) reported that fever also contributes to poor nutritional recovery and increased morbidity. Severely malnourished children are however particularly vulnerable to hypothermia due to reductive adaptation, which often coincides with hypoglycaemia suggesting serious infection; increasing the risk of death (WHO, 2013). There is significant focus in local policies and staff training on recognizing and treating hypothermia and hypoglycaemia in children with SAM, such as the Emergency Triage Assessment and Treatment (ETAT) guidelines and Integrated Management of Acute Malnutrition (IMAM) guidelines (Department of Health, 2015b), which could have resulted in these children receiving better care and monitoring and therefore improving the survival probability compared to those who did not have these complications. There is also ambiguity regarding the cut off values used in diagnosing hypothermia in the children with SAM in comparative studies. According to local policies, hypothermia is classified as an axillary temperature of < 36.5 degree Celsius (Department of Health, 2015b), while comparative studies that found survival probability to be negatively associated with hypothermia used an axillary temperature of < 35 degree Celsius (Gachaua *et al.*, 2018). This could have led to an overestimation

of hypothermic cases in this study. The finding of improved survival probability in cases with hypothermia, could thus purely be due to institutional factors or due to the limitations of this study.

5.1.5.3. Dehydration

Dehydration was present in 40.6% of the children admitted with SAM and showed a 4-fold increased risk of death (HR = 4.1, 95%CI = 1.25 – 13.59, $p = 0.02$) while also significantly reducing survival probability compared to children without dehydration ($p < 0.001$). The excess mortality risk associated with dehydration found in our study is supported by literature reporting a 3 – 3.5 -fold increased mortality risk in children with SAM who were dehydrated (Jarso *et al*., 2015; Oumer *et al.,* 2016). The prevalence of dehydration found in this study was significantly higher than similar studies by Jarso *et al*., 2015 (11.8%), Desta *et al.,* 2015 (5.1%) and Oumer *et al*.,2016 (17.8%). The prevalence of dehydration significantly decreased with an increase in age, with those < 6 months having the highest prevalence of dehydration ($p < 0.001$).

Due to the physiological changes occurring during a state of starvation, the child with SAM has a significant reduction in their capacity to regulate water storage and consequently dehydration is more severe and occurs rapidly (Williams & Berkley, 2017; WHO, 2018c). Our study showed that dehydration was significantly more prevalent in children without oedema and those with a MUAC > 11.5 cm ($p = 0.001$). Assessing hydration status in children with SAM is difficult, because many of the signs normally used are unreliable, such as skin turgor (WHO, 2015). In children with severe wasting skin turgor appears to be poor due to the absence of subcutaneous fat and could lead to over diagnosis of dehydration, while a diminished skin turgor in children with oedema can be masked due to swelling (WHO, 2005), which could explain our findings.

Our study further showed that diarrhoea was the most prevalent comorbidity (43%), a well-known cause of dehydration. The high prevalence of diarrhoea found in this cohort of children with SAM is similar to various other studies (Chane *et al*., 2014 (43%); Desta *et al*.,2015 (44.6%); Oumer *et al*., 2016 (41.5%)). Although multivariate analysis showed no statistical significance associated with diarrhoea and survival probability or increased risk of death, 66% of the malnourished children with diarrhoea were classified as dehydrated. The treatment of dehydration is dependent on the severity of dehydration, which is almost impossible to distinguish reliably in children with SAM (Maitland, 2009). This makes fluid management in children with SAM, especially those with diarrhoea very complex (Maharaj *et al.*,2003; WHO, 2005; WHO, 2018c). The management of diarrhoea and dehydration in children with SAM has been subject to controversy over recent years as some studies show that diarrhoea predict poor outcomes (Maitland *et al*., 2006; Brewster, 2006; Talbert *et al*., 2012), while others have shown little impact (Waterlow, 1999). An investigation into the

management of dehydration was outside the scope of this study, but it clearly remains a significant predictor of survival probability and mortality risk in children with SAM, especially in those children younger than 2 years. Little is known about the treatment of dehydration in children with SAM younger than 6 months (Kerac *et al.*, 2012), and considering our study showed this age group had the highest prevalence of dehydration, this could be an important finding.

5.1.5.4. Altered consciousness

Altered consciousness (lethargy, loss of consciousness or coma) was found to significantly reduce the survival probability ($p < 0.001$) in children with SAM, as well as increase the risk of death 4-fold (HR = 4.2, 95%CI = 1.04 – 17.12, $p = 0.043$). This increased mortality risk is supported by various studies that also showed a 2-3-fold increased risk of death (Gebremichael, 2015; Jarso *et al*., 2015; Gachaua *et al*., 2018). Only 50% of the children who presented with altered levels of consciousness were admitted to the high care or intensive care units, while the rest was admitted to the normal ward. While it was not the aim of this study, it should be considered that these children perhaps required a higher level of care, given the high risk of death associated with altered consciousness. Furthermore, there is a need to understand what the barriers are for caregivers to seek help before a child presents with an impaired level of consciousness and a severely complicated state.

5.1.6. Comorbidities

Most of the children with SAM (74%) in this study presented with one or more comorbidity. There are wide differences reported with regards to the prevalence of comorbidities of children with SAM globally, ranging from 31% to 90% (Lenters *et al.*, 2013; Black *et al.*, 2016; Desyibelew *et al*., 2017). Our results showed that diarrhoea (43%), HIV-infection (30%) and respiratory tract infections (30%) were the top three comorbidities present in the children with SAM, closely followed by TB (27%), while pneumonia was the least prevalent at 3%. This is supported by the body of evidence that shows that the most significant comorbidities reported in children with SAM are infectious disease i.e. diarrhoea, pneumonia, acute respiratory tract infections as well as tuberculosis and HIV-infection (Gupta *et al*., 2009; Munthali *et al.*,2011; Chisti *et al.*, 2013; Yohannes *et al*., 2015)

Even though it is well documented that children with SAM are likely to have more severe illnesses and worsened outcomes (Lenters *et al*., 2012; Chisti *et al*., 2014; Jones and Berkley, 2014), neither the survival probability or the risk of death in this study was found to be statistically different in the presence of one or more comorbidity. The lack of statistical significance is possibly due to the large overall prevalence of comorbidities in the cohort and small number of deaths that occurred.

5.1.6.1. Pneumonia

The shortened survival time ($p < 0.001$) and the 3-fold- increased risk of death (HR = 3.4, 95%CI = 1.56 – 7.43, $p = 0.002$) in malnourished children presenting with pneumonia, is supported by similar findings showing a 2 - 3-fold mortality risk (Chisti *et al*.,2009; Benyera *et al*,.2013, Oumer *et al*., 2016), while some studies report a much higher risk of death of up to 15 times (Ginsburg *et al*., 2015). In our study, only 3% of the children with SAM presented with pneumonia, which is much lower than similar studies reporting a prevalence between 22% - 45% (Benyera *et al*., 2013; Oumer *et al.*, 2016; Desyibelew *et al*., 2017). Investigations for pneumonia in this study setting is usually only done in the presence of signs such as fever and chest indrawing (Department of Health, 2015b). Other studies have shown that the aetiology of pneumonia in children with malnutrition is often different from well-nourished children, making diagnosis and treatment very challenging (Adegbola *et al.,* 1994; Chisti *et al*., 2009; Chisti *et al.,* 2013b; Ginsburg *et al.,* 2015). Jones & Berkley (2014) found that even children with SAM who have radiologically confirmed pneumonia often do not exhibit any typical signs or symptoms. The difficulty in diagnosing pneumonia in children with SAM, due to subtle clinical signs, together with the different aetiology and response to treatment, could have contributed to low prevalence and the significant increased risk of death also seen in this study.

5.1.6.2. Tuberculosis

While this study did not find excess risk of death associated with tuberculosis (TB), the estimated mean survival time of children with SAM and TB, was longer than those without TB. Tuberculosis is both a cause and a consequence of malnutrition, but its role in SAM outcomes has been poorly described, especially in sub-Saharan African countries (De Maayer & Saloojee, 2011; Munthali *et al*., 2017). The lack of association found between TB and increased mortality risk in this study is contradictory to results found in Zambia where those children with SAM and TB were 40% more likely to die (Munthali *et al*., 2017). It is however supported by a study done in Bangladesh, that showed no increased in-hospital mortality, but rather high post-discharge mortality in children with SAM (Chisti *et al*., 2014) which was not investigated in this study. It is well documented that TB detection in children with SAM is often poor due to the inability of these children in their weakened state to produce suitable sputum samples or their delayed hypersensitivity responses to skin tests, which reduce the sensitivity of tests, delaying treatment and leading to worsened outcomes (Munthali *et al*.,2017). The lack of association could possibly be explained by the early diagnosis and initiation of treatment in children with SAM within this hospital setting as it is part of local policy to screen every child admitted with SAM for TB, while treatment is readily available (Department of Health, 2015b). Similar to what Jones & Berkley (2014) suggest, it is also reasonable to consider that the clinicians

in this study setting with, where there is a very high TB prevalence, is highly skilled in recognizing the clinical response to treatment, such as weight gain and fever in the diagnosis of TB in children with SAM. The finding of a longer mean survival time in children with malnutrition and TB, possibly also supports this, as these children would receive early, appropriate and possibly more intensive care and monitoring than those who were not considered as complicated. It is however unknown what impact tuberculosis has on the post-discharge mortality rates of these children with SAM.

5.1.6.3. HIV-infection

HIV-infection has dramatically changed the mortality outlook of SAM in sub-Saharan Africa (Jones & Berkley, 2014). This study showed that 30% of the children admitted with SAM, were HIV-infected. The prevalence of HIV-infection was significantly higher in children with SAM who were between 12 - 23 months. The overall prevalence of HIV-infection found in this study is comparable to a study done in South Africa that showed that 33.8% of children with SAM were HIV-infected (Muzigaba *et al*., 2017).

HIV-infection significantly increased the risk of death almost 10 times (HR = 9.9, 95%CI = 1.39 - 70.68, p = 0.022), much more than the 3-fold increase reported by Jones & Berkley (2014) and supported by a systematic review done by Lenters *et al*. (2013) who found the highest SAM case fatality rates in HIV-infected malnourished children. The risk of death in children with SAM who were HIV-infected was at least 40% higher than their uninfected counterparts, which is supported by findings of De Maayer & Salojee (2011) that showed in a high HIV prevalent setting in South Africa, HIV-infection increased the risk of death by at least 30% in malnourished children. It has been proposed that this increased risk of death is related to the pathophysiology and comorbidities of HIV disease and possibly the timing of antiretroviral treatment (Trehan *et al.*, 2012; Rose *et al*., 2014) which was not investigated in this study. The estimated mean survival time was statistically longer for children with SAM who were HIV-infected compared to those who were not HIV-infected. Given the likelihood that the children who were HIV-infected could have had a more complicated SAM presentation as they are prone to having multiple comorbidities (Rose *et al*., 2013), the increased mean survival time could potentially be related to better clinical management and closer monitoring. The pathophysiology of HIV-infected children with malnutrition and response to standard treatment is however poorly described (De Maayer & Salojee, 2011; Binka *et al*., 2015) and would need further investigation. This study supports findings by Salojee *et al*. (2007) that attaining a case fatality rate < 5% in children with SAM is difficult to achieve in settings with a high HIV prevalence and echoes conclusions from Lenters *et al*. (2013) that much is unknown about the appropriate treatment for malnourished children who are HIV-infected and that a contextually specific approach is needed to improve outcomes.

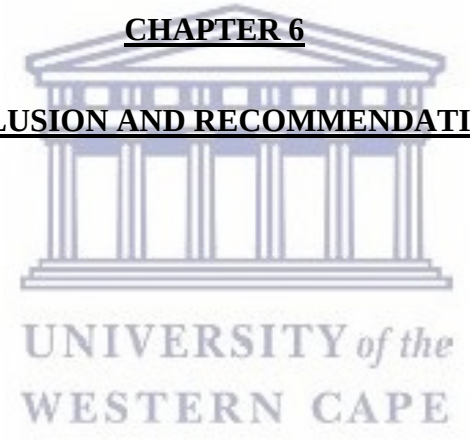
Furthermore, the HIV and TB status of the children in this study were based on their discharge diagnosis as most cases were admitted with "unknown" status. HIV and TB testing is standard as part of the care process for all SAM children admitted to hospitals in KwaZulu-Natal (Department of Health, 2015b). While this strengthened the reliability of the results in terms of the identification of these comorbidities, it should be highlighted that 21% of all the HIV-positive cases and 64% of all TB infected cases in the sample were only diagnosed in hospital and was not known on admission. Seven percent of the HIV-infected children with SAM and 4% of those with TB died before treatment could be initiated. In the South African health system, where there is significant investment in HIV and TB prevention, early diagnosis and care (SAHR, 2016), this finding highlights possible gaps in primary health services, especially with regards to paediatric care.

5.2. LIMITATIONS

- Due to the study design used (retrospective record review) quality control of the diagnostic equipment used for children with SAM and the accuracy of the information captured in the medical records could not be controlled by the researcher. This might have influenced the reliability and validity of data.
- There were a relatively small number of deaths recorded in the study period, which could have underestimated the hazard ratios and confidence intervals associated with them.
- Even though the hospital also serves as a referral site for the adjacent districts; resulting in a wide range of SAM complications, geographical as well as socio-economic factors; selection bias is an inherent problem of hospital-based studies and the general population of children with SAM may not have been well represented.
- Investigating the clinical management and quality of care received by children with SAM was outside the scope of this study. The WHO SAM treatment guidelines have been incorporated into all national paediatric and child health guidelines in South Africa, with a mandate to be implemented in all hospitals and health care facilities (Massyn *et al*., 2016). This study setting regularly undergoes auditing by local stakeholders for compliance of these guidelines and has a team of highly skilled professionals that receive ongoing in-service training on the management of SAM and standards of care. An assumption was thus made that reasonable standards of clinical care is being implemented. It is well documented that the implementation of the WHO SAM treatment guidelines (10 steps) reduces SAM death rates and each step in these treatment guidelines is essential to ensure improved outcomes (Collins *et al.*, 2006; Karaolis *et al*., 2007; WHO, 2013). It should therefore be considered that the outcomes of the children with SAM in this study, regardless of underlying conditions, could have been influenced by clinical case management that could not be controlled by the researcher.

CHAPTER 6

CONCLUSION AND RECOMMENDATIONS



6.1. CONCLUSION

While there has been improvement in the survival of children with SAM in South Africa and KwaZulu-Natal, the mortality rate found in this study remains above the WHO target of < 5% (WHO, 1999). It has been speculated that it is unlikely that SAM will be eliminated in the foreseeable future (Black *et al*., 2013; Tickell & Denno, 2016) and improving outcomes are therefore critical.

The results showed an overall mortality rate of 8.7%. Most of the study population were younger than 2 years, had a complicated presentation; having multiple clinical signs, symptoms and comorbidities on admission. The type of malnutrition (with or without oedema) did not show any significant difference in survival outcomes but did indicate SAM cases without oedema were statistically shorter, which should be further explored. At a 95% confidence interval, five factors showed significant association with the likelihood of death in children with SAM. These factors were; male gender, the presence of dehydration, lethargy or coma on admission, being HIV-infected or having pneumonia. The presence of multiple clinical signs and symptoms on admission also significantly increased the risk of death. Except for male gender increasing mortality risk, these findings are consistent with studies highlighted in the literature review. The higher mortality risk associated with male SAM children is likely due to specific cultural and social norms or the statistical power of the study. Although socio-demographic and socio-economic variables were not found to be statistically significant in terms of morbidity and mortality, the study does highlight certain factors at a health care and community level that would warrant further investigation. These factors were high rates of teenage pregnancy and unemployment amongst caregivers, high malnutrition readmission rates despite access to child support grants, concerns about late identification of HIV-infection and tuberculosis at primary health care level and continuity of care once discharged from the hospital.

This study supports the growing body of evidence that despite reasonable standards of care, it is difficult to meet the WHO target for SAM mortality and it highlights that the presence of multiple clinical signs and symptoms on admission, the presence of dehydration, lethargy or coma on admission, being HIV-infected or having pneumonia, as key contributing factors to poor outcomes in children with SAM. One clear limitation of this study is the relatively small number of subjects who died during the study period, which could have led to the underestimation of hazard ratios and the statistical significance of some variables. While it is evident that further research is needed, the study does support the need for a multi-dimensional and multi-sectoral approach to reduce morbidity and mortality associated with SAM in this study population.

6.2. RECOMMENDATIONS

This study found several factors that could potentially contribute to the persistently high mortality rates amongst children under-five in the district where the study was conducted, and the following recommendations are offered to stakeholders:

- Explorative research should be conducted in this study setting and surrounding communities to investigate social and cultural norms, drivers of poor infant feeding practices (specifically exclusive breastfeeding in those younger 6 months), barriers to accessing health care and caregiver behaviours with regards to the health of their children.
- There is a need for multi-stakeholder engagement to reduce unemployment rates, teenage pregnancy and improve maternal education. Further studies in this field could explore the scope for more comprehensive policy-making.
- The Department of Social Development in collaboration with the Department of Health should conduct research into the effectiveness of child support grants in protecting against malnutrition, especially repeated episodes.
- It is recommended that local policy makers assess the services rendered for children at primary health care level. The process of early diagnosis and referral of children with SAM as well as the continuity and quality of care when discharged from inpatient care need to be critically evaluated. It is well known that post-discharge mortality rates in children with SAM are high, but the extent in KwaZulu-Natal is relatively unknown. Systems need to be put in place to track malnourished cases once discharged from hospital and to monitor the long term outcomes. Further studies are also needed to determine the impact of the type of malnutrition (with oedema or without oedema) on chronic malnutrition (stunting) risk.
- There is a need to investigate the reasons for late identification of HIV-infection and tuberculosis in paediatric cases at primary health care level. Cases with SAM who were only diagnosed with HIV-infection or tuberculosis at hospital level, should be audited and their care traced to identify the gaps in the health care system.
- The Provincial Department of Health should support Nkandla hospital, uMkhanyakude and Zululand district to manage complicated cases of SAM. Conducting a situational analysis to determine the needs and potential concerns in these health settings is recommended.

- While the KwaZulu-Natal malnutrition policy gives clear guidance on the discharge criteria for children with SAM and makes provision for discharge from inpatient care before full nutritional recovery is reached through ongoing nutritional support at a community level, the hospital and district should ensure that there is a locally appropriate system for referral and follow up at outpatient clinics in place, before discharging children who have not reached nutritional recovery.
- In view of the high HIV prevalence and the significantly increased mortality risk associated with HIV found in this study setting, it is recommended more research is done on the effectiveness of the current standard treatment guidelines in a HIV-infected cohort of children with SAM. This is a knowledge gap that needs urgent attention, also highlighted by other studies in the literature review.
- The inpatient management of dehydration in children, especially those younger than 6 months need to be reviewed. Initial clinical audits need to be conducted to determine if these children are being identified and treated appropriately according to current protocols. This should be followed by the necessary training or the need to review policy guidelines in view of the physiological and pathological differences in this age group.
- Proper assessments of SAM children's level of consciousness need to be conducted on admission and higher levels of monitoring and care should be considered for those with impaired consciousness.
- The need for early and correct diagnosis of pneumonia should be emphasised amongst clinicians. Experienced physicians should ensure new entry medical officers understand the presentation of pneumonia in children with SAM is often different to those of other children and educate them to use multiple methods of assessment.
- Future studies investigating factors associated with SAM mortality and morbidity should include the adherence to the SAM treatment guidelines (10 steps) in order control for potential confounding factors relating to clinical care.

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APPENDICES

Appendix 1 : Data extraction tool

DATA EXTRACTION TOOL

Title: Factors associated with morbidity and mortality in children under-five years admitted with severe acute malnutrition to a regional Paediatric hospital in KwaZulu-Natal.
(Ethics approval nr: BM17/9/14)

	Participant code:
Research assistant name:	**Date:**

IF PARTICIPANT IS EXCLUDED INDICATE THE REASON:

- **Chronic condition present (Cerebral Palsy, Liver disease, kidney disease, heart disease, short bowel syndrome, inflammatory bowel disease, cystic fibrosis or cancer**
- **Unable to obtain medical records**
- **Comments:**

IF PARTICIPANT IS EXCLUDED – DO NOT CONTINUE WITH THE REVIEW

Admission date:	**Discharge date:**	**Date of death (if applicable):**

MAIN REASON (S) DOCUMENTED FOR ADMISSION (from admission book)

SOCIO-DEMOGRAPHIC AND SOCIO-ECONOMIC FACTORS					
AGE (months):			**GENDER:**	Male	Female
PLACE OF RESIDENCE	uMthlatuze	uMlalazi	Mfolozi/Mbonambi	Nkandla	Ntambanana
	Zululand	uMkhanyakude	Other		
PRINCIPLE CAREGIVER	Mother	Grandmother	Other (specify):		
CURRENT EMPLOYEMT STATUS OF CAREGIVER	Employed		Unemployed		
HIGHEST LEVEL OF EDUCATION OF MOTHER	Grade :				
IS CHILD RECEIVING CHILD SUPPORT GRANT			Yes	No	Unknown
PREVIOUS ADMISSION FOR MALNUTRITION IN LAST 12 MONTHS?			Yes	No	Unknown
REFERRAL SOURCE	Walk-in	Government clinic/transfer	Private GP	Other:	
CLINICAL INFORMATION (page 1/2)					
PLACE OF ADMISSION ON ARRIVAL	High Care	PICU	Normal Ward		

WEIGHT ON ADMISSION: kg	WEIGHT ON DISCHARGE kg

CLINICAL INFORMATION continued (page 2/2)

WEIGHT GAIN DURING HOSPITAL STAY	**g/day weight gain** **= (Discharge weight – admission weight / days in hospital)** **g/kg weight gain** **= (g/day weight gain / weight at discharge)**

HEIGHT ON ADMISSION: cm		
WHZ ON ADMISSION:	**WHZ ON DISCHARGE:**	
MUAC ON ADMISSION: cm	< 6 months	Not recorded
MUAC ON DISCHARGE: cm	< 6 months	Not recorded

NUTRITIONAL OEDEMA PRESENT ON ADMISSION	Yes	No
NUTRITIONAL OEDEMA DEVELOPED DURING HOSPITALISATION	Yes	No
SKIN LESIONS (DERMATOSIS) PRESENT ON ADMISSION	Yes	No
HYPOTHERMIA (<36.5°C) ON ADMISSION	Yes	No
HYPOGLYCAEMIA (<3mmol/L) ON ADMISSION	Yes	No
DEHYDRATION PRESENT ON ADMISSION	Yes	No
SEVERE PALLOR ON ADMISSION	Yes	No
IMPAIRED CONSCIOUSNESS (LETHARGY/COMA) ON ADMISSION	Yes	No
SHOCKED ON ADMISSION	Yes	No

DIARRHOEA ON ADMISSION	Yes	Duration: days	No
DIARRHOEA DEVELOPED DURING HOSPIAL STAY	Yes	Duration: days	No

PNEUMONIA ON ADMISSION	Yes	No	Unknown
PENUMONIA DEVELOPED DURING HOSPITAL STAY	Yes		No
HIV STATUS AT ADMISSION	Positive	Negative	Unknown
HIV STATUS AT DISCHARGE OR DEATH	Positive	Negative	Unknown

IF HIV POSITIVE: ON ANTIRETROVIRAL TREATMENT	Yes	Start date:	No	N/A
TB STATUS ON ADMISSION	Positive	Negative	Unknown	
TB STATUS ON DISCHARGE OR DEATH	Positive	Negative	Unknown	
IF TB POSTIVE: ON TB TREATMENT	Yes	Start date:	No	N/A

REASEARCH ASSISTANT NOTES:

Date submitted to researcher: **Date reviewed by researcher**

Appendix 2: Variable/data definitions

	Variable	Definition
Socio-demographic and socio-economic factors	Age	The date of birth was used as reference, and the patient's age was recorded (in months). Age was rounded to the nearest month at the time of admission.
	Gender	The patient's gender as indicated on the medical file was recorded (male or female)
	Place of residence	The physical address recorded on the admission tool in the medical records was used as primary residence. The physical address was then linked to the appropriate sub-district. During the study period King Cetshwyao District was grouped into 6 sub-districts: Nkandla, Ntambanana, uMfolozi(Mbonambi), uMthlathuze and Mtonjaneni. Addresses outside the district's demarcations was linked to the appropriate districts and recorded.
	Referral source	The source of referral as noted in the admission records was used. The participants came as either a walk-in (self-referral), referral from a government clinic (including mobile clinics), transfer from another hospital or from a private General Practitioner.
	Access to child support grant (CSG)	Recorded as either currently in receipt of child support grant (yes), no or unknown. An unknown option was added as this is information is not always recorded.
	Previous admission for malnutrition in the last 12 months	A previous admission of severe malnutrition in the last 12 months was recorded as yes or no.
	Number of previous admissions for SAM	Recorded as the number of times the SAM child was admitted for another episode of malnutrition in the last 12 months.
	Principle care giver	The principle care giver was defined as the person who the child resides with most of time. Based on knowledge of the area this was recorded as either the grandmother; mother or other. The research assistant had to specify "other cases".
	Employment status of principle care giver	This was recorded as either employed (earning any income aside from grants) or unemployed. No differentiation was made between formal or informal employment.
	Educational level of the mother	Defined as the highest grade of schooling achieved by the mother. Recorded as grade 1 -12 or post matric (college or university). Data disaggregated as primary school, secondary school or completed high school.
	Teenage pregnancy	Defined as a mother who was less than 18 years old when she delivered. Recorded as yes or no.
	Other social information	This was an open-ended question that included any other social information of relevance that was recorded in the medical records, i.e abuse, abandonment and neglect.

Clinical information	**Anthropometric status at admission and during hospital stay**	
	Weight on admission	The weight recorded by nursing staff once admitted to the ward, rounded to the first decimal (kg).
	Height on admission	The height recorded by nursing staff once admitted to the ward, rounded to the first decimal (cm).
	Mid-Upper-Arm-Circumference (MUAC) on admission	The MUAC measurement recorded by nursing staff once admitted to the ward, rounded to the first decimal (cm). MUAC is not relevant in cases of children < 6 months.
	Weight on discharge/death	The weight recorded by nursing staff at time of discharge or death (or within 2 days), rounded to the first decimal (kg).
	Height on discharge/death	The height recorded by nursing staff at time closest to discharge or death, rounded to the first decimal (cm).
	Mid-Upper-Arm-Circumference on discharge/death	The MUAC measurement recorded by nursing staff at the time closes to discharge or death (or within 2 days), rounded to the first decimal (cm). MUAC is not relevant in cases of children < 6 months.
	SAM sub-group on admission	Defined as SAM with medical complications (where any medical complications as listed in **Error! Reference source not found.** was present) or SAM without medical complications.
	Nutritional diagnosis at discharge	Based on the discharge weight and height Standard-Deviation (SD) as defined in Table 1.
	Presence of nutritional oedema on admission	The presence of bilateral pitting oedema (any grade) at the time of admission (recorded as either yes or no)
	Anthropometric Classification of malnutrition on admission (type of malnutrition)	Captured as SAM with oedema or SAM without oedema.
	Development of nutritional oedema during stay	The onset of oedema any time during the admission if not present on admission.
	Weight gain during hospitalization	Calculated in grams per kg per day.
	Comorbidities on admission and during hospitalization were recorded based on the diagnosis found in the medical records	
	Diarrhoea on admission	Data captured as yes (with duration – number of days of having diarrhoea), or no diarrhoea. Acute diarrhoea: Defined as the passage of watery stools, at least three times in a 24-hour period (lasting for several hours or days). Persistent diarrhoea: Defined as diarrhoea that lasts for 14 days or longer.
	Diarrhoea developed during hospitalization	Data captured as yes (with duration – number of days indicated), or no diarrhoea.
	Respiratory tract infections on admission (other than pneumonia)	Data captured as yes or no Data based on the medical diagnosis found in medical records, as either lower respiratory or upper respiratory infections present on admission, excluding pneumonia
	Pneumonia on admission	Data captured as yes, no or unknown

	Pneumonia developed or diagnosed during hospitalization	Data captured as yes or no.
	HIV status on admission	Data captured as exposed, positive, negative or unknown
	HIV status at discharge	Data captured as positive, negative or unknown
	Timing of antiretroviral treatment	Data captured as on treatment (yes or no) and start date of antiretroviral treatment. To measure the number of days on ART treatment (if applicable) prior to the admission as well to determine if treatment was started before admission, during the hospitalization episode or after discharge (Timing of ART treatment)
	TB status on admission	Data captured as positive, negative or unknown
	TB status at discharge	Data captured as positive, negative or unknown
	TB treatment duration	Captured as on treatment (yes or no) and start date of TB treatment. To measure the number of days on TB treatment (if applicable) prior to the admission as well to determine if treatment was started before admission, during the hospitalization episode or after discharge (Timing of TB treatment)
	HIV and TB coinfection	Using data from those who had confirmed HIV status on discharge, who was also diagnosed with TB
	Clinical signs and symptoms present on admission	
	Hypothermia	Categorized according to the inpatient admission tool used in the hospital (captured as yes or no).
	Hypoglycaemia	
	Dehydration	
	Skin lesions or dermatosis	
	Severe pallor	
	Impaired consciousness or coma	
	Shock	
	Other clinical information	
	Place of admission	Recorded as high care, Paediatric Intensive Care Unit (PICU) or normal ward
	Length of stay	Recorded as date of admission and date of discharge/death. Admission and discharge dates was captured as short dates in Microsoft Excel 3. Length of stay was Auto-calculated in Microsoft Excel using the formula = Length of stay (days) = (date of discharge/death) – (date of admission)
Other	Outcomes	Recorded as Discharged (with nutritional status on discharge) or Death (with nutritional status on death)
	Comments	Open ended section for any comments that the research assistant feel would be of relevance.

Appendix 3: Permission letters from the District and Hospital

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

Physical Address: No. 2 Corner Lloid Avenue & Chlorine Crescent, Empangeni, 3910
Postal Address: Private Bag X20034, Empangeni, 3910
Tel: 035 787 5208/6319 Fax: 035 787 0644 Email: Phakama.diwati@kznhealth.gov.za
www.kznhealth.gov.za

DIRECTORATE:
District Management

Date: 31/10/2017
Enquiries: Ms. PPT Diwati
Ref: 25/1

Mrs. Tanya van Aswegen
Student Number: 3618617
Principal Investigator
University of the Western Cape, Masters of Public Health

CC: 1. Dr. Elizabeth Lugte
Manager: Research Unit KZN DOH
2. Mrs. CNN Mkhwanazi: CEO Lower uMfolozi War Memorial Regional Hospital

RE: PERMISSION TO CONDUCT STUDY AT KING CETSHWAYO DISTRICT- LOWER uMFOLOZI WAR MEMORIAL REGIONAL HOSPITAL

I have pleasure in informing you that permission has been granted to you by the Name of District Office/Facility to conduct research on "Factors associated with morbidity and mortality in children under-five years admitted with severe acute malnutrition to a regional Paediatric hospital in KwaZulu-Natal"

Please note the following:

1. Please ensure that you adhere to all the policies, procedures, protocols and guidelines of the Department of Health with regards to this research.
2. This research will only commence once this office has received approval of your study from the Provincial Health Research and Ethics Committee (PHREC) in the KZN Department of Health.
3. Please ensure this office is informed before you commence your research.
4. The District Office/Facility will not provide any resources for this research.
5. You will be expected to provide feedback on your findings to the District Office/Facility.
6. You are required to contact this office regarding dates for providing feedback when the research has been completed.

Thanking you.

Sincerely

Ms. PPT Diwati
Acting Director: DHO
King Cetshwayo District

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

DIRECTORATE: QUEEN NANDI REGIONAL HOSPITAL

29 Union Street – Empangeni - 3880
Private Bag X20005 - Empangeni - 3880
Tel: 0359077000 Fax: 0866292075 Email: MerithaSamjowan@kznhealth.gov.za

27 March 2018

To: Ms T Van Aswegen

RE: PERMISSION TO CONDUCT RESEARCH AT QUEEN NANDI REGIONAL HOSPITAL

Dear Madam

I have pleasure in informing you that permission has been granted to you by Queen Nandi Regional Hospital Ethics Committee to conduct research on " Factors associated with morbidity and mortality in children under 5 years admitted with severe acute malnutrition to regional paediatric hospital in KZN."

Please note the following:

1. Please ensure that you adhere to all the policies, protocols and guidelines of the Department of Health with regards to this research.
2. Please ensure this office is informed before you commence your research.
3. QNRH will not provide any resources for this research.
4. You will be expected to provide feedback on your findings to our institution.

Sincerely

Dr I Popa
Chairperson
Ethics Committee

Approved by:

Mrs CNN Mkhwanazi
Chief Executive Officer QNRH

Appendix 4 : Ethics clearance letter - University of Western Cape

OFFICE OF THE DIRECTOR: RESEARCH
RESEARCH AND INNOVATION DIVISION

UNIVERSITY of the WESTERN CAPE

Private Bag X17, Bellville 7535
South Africa
T: +27 21 959 2988/2948
F: +27 21 959 3170
E: research-ethics@uwc.ac.za
www.uwc.ac.za

09 November 2017

Ms T van Aswegen
School of Public Health
Faculty of Community and Health Sciences

Ethics Reference Number: BM17/9/14

Project Title: Factors associated with morbidity and mortality in children under five years admitted with severe acute malnutrition to regional paediatric hospital in Kwazulu-Natal.

Approval Period: 27 October 2017 – 27 October 2018

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project.

Any amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

Please remember to submit a progress report in good time for annual renewal.

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms Patricia Josias
Research Ethics Committee Officer
University of the Western Cape

PROVISIONAL REC NUMBER -130416-050

Appendix 5: Ethics clearance letter - KwaZulu Natal Provincial Department of Health Research and Ethics Committee

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

Physical Address: 330 Langalibalele Street, Pietermaritzburg
Postal Address: Private Bag X9051
Tel: 033 395 2805/ 3188/ 3123 Fax: 033 394 3782
Email:
www.kznhealth.gov.za

DIRECTORATE:
Health Research & Knowledge Management

HRKM Ref: 482/17
NHRD Ref: KZ_201711_037
Date: 7 December 2017

Dear Ms T van Aswegen
University of the Western Cape

Approval of research

1. The research proposal titled **'Factors associated with morbidity and mortality in children under-five years admitted with severe acute malnutrition to a regional Paediatric hospital in KwaZulu-Natal'** was reviewed by the KwaZulu-Natal Department of Health.

   The proposal is hereby **approved** for research to be undertaken at Lower Umfolozi War Memorial Hospital.

2. You are requested to take note of the following:
   a. Make the necessary arrangement with the identified facility before commencing with your research project.
   b. Provide an interim progress report and final report (electronic and hard copies) when your research is complete.

3. Your final report must be posted to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za

For any additional information please contact Mr X. Xaba on 033-395 2805.

Yours Sincerely

Dr E Lutge
Chairperson, Health Research Committee
Date: 07/12/17

Fighting Disease, Fighting Poverty, Giving Hope

Appendix 6: Hazard curves: Factors associated with increased risk of death

Figure 18: Hazard curve - Gender

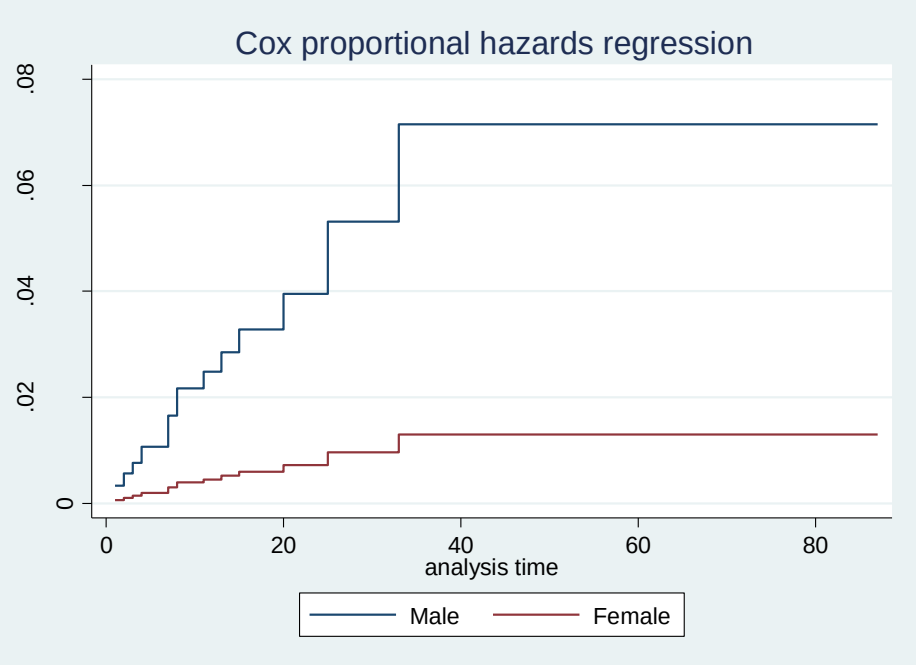

Figure 19: Hazard curve - Dehydration

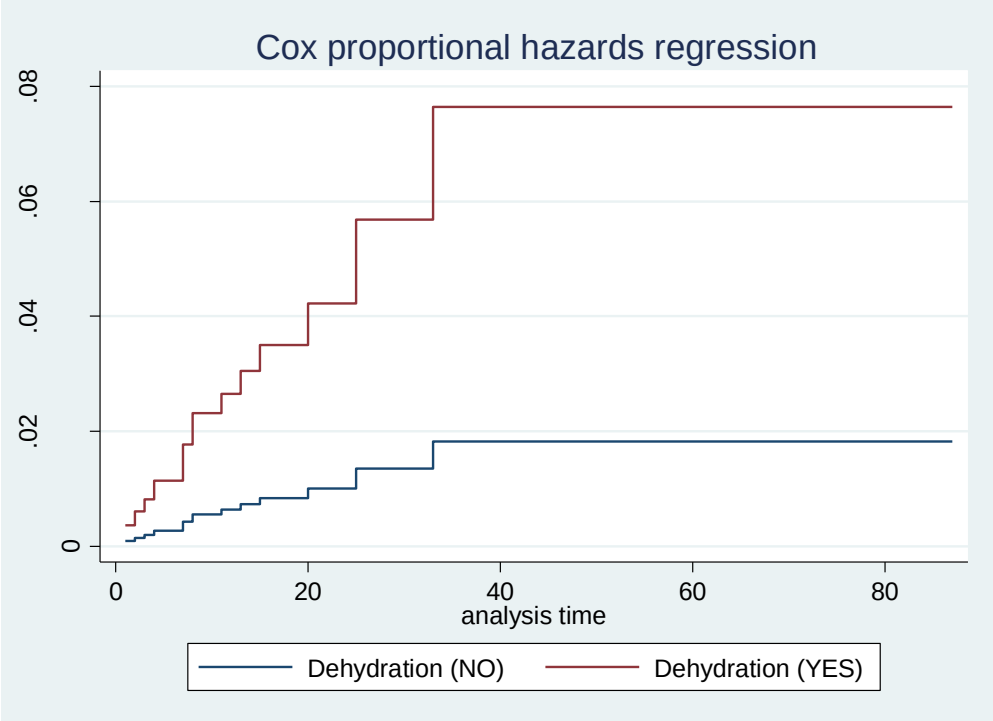

Figure 20: Hazard Curve - Lethargy or coma

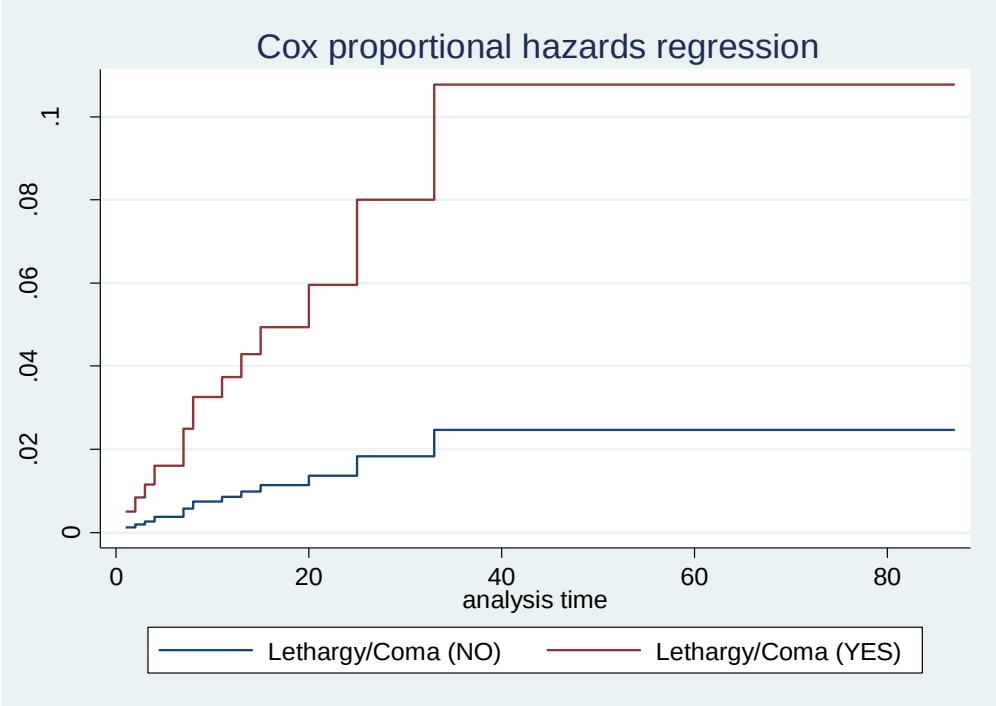

Figure 21: Hazard curve - HIV-infection

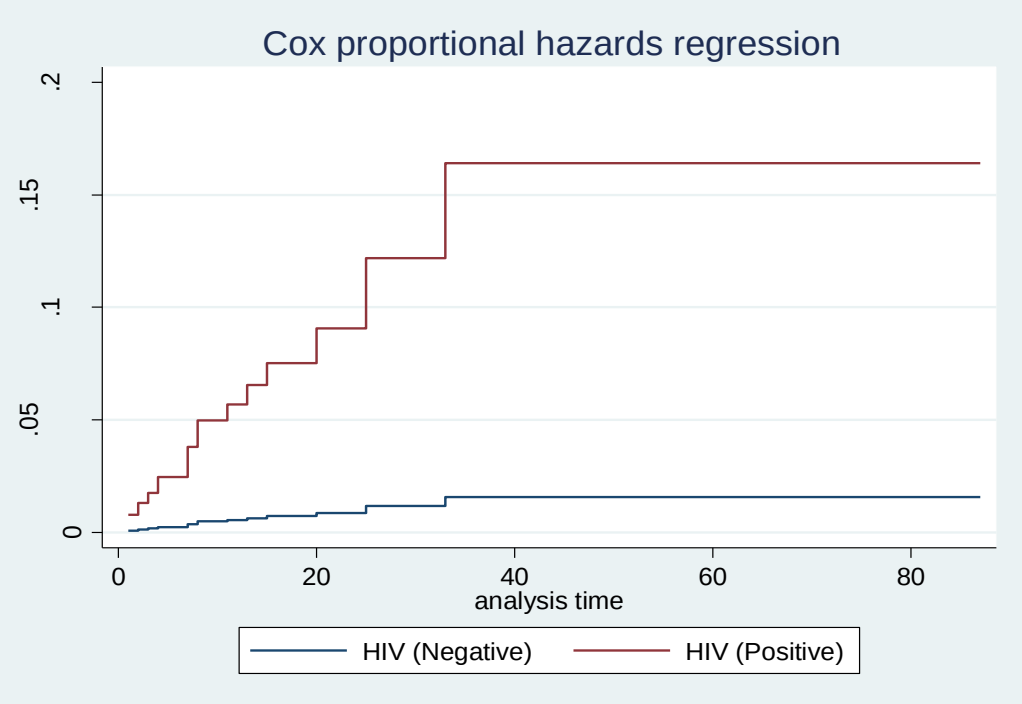

Figure 22: Hazard curve - Pneumonia