OUTCOMES IN MALNOURISHED CHILDREN AT A TERTIARY HOSPITAL IN SWAZILAND: POST IMPLEMENTATION OF THE WHO TREATMENT GUIDELINES

BY

DR OSCAR BENYERA

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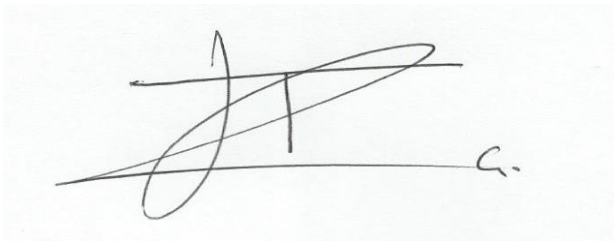
Supervisor: Dr Francis L. M. Hyera

DECLARATION

I, Dr Oscar Benyera, hereby declare that the dissertation which I hereby submit for the degree Master of Science in Clinical Epidemiology at the University of Pretoria is my own work and has not previously been submitted by me for a degree at another university.

Signed  Date 13/03/2013

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ABSTRACT

Background. Swaziland adopted the World Health Organization's (WHO) guidelines for the inpatient treatment of severely malnourished children in 2007 to reduce case -fatality rates for childhood malnutrition. However, no follow-up studies have been conducted to determine the reduction in the case -fatality rate post-implementation of the guidelines.

Objectives. To determine the case -fatality rate for childhood malnutrition post-implementation of the WHO treatment guidelines and determine the level of adherence to the guidelines at Mbabane Government Hospital.

Methods. A retrospective observational study was undertaken. All children under 5 years admitted for inpatient treatment of malnutrition between January 2010 and December 2011 had their demographic-, anthropometric- and clinical characteristics recorded and analysed, as well as the outcome of admission.

Results. Of the 227 children admitted during the study period, 179 (64.6%) were severely malnourished and 98 (35.4%) had moderate malnutrition. One-hundred-and-eleven children died during admission, an overall case -fatality rate of 40.1%. Mortality was significantly higher among severely malnourished children compared to those with moderate malnutrition, (46.9% vs 27.6%, OR 3.0 (95% CI 1.7 to 5.3)). Comorbid pneumonia and gastroenteritis were significant predictors of mortality – , OR 2.0 (95% CI 1.2 to 3.4) and 1.9 (95% CI 1.1 to 3.2) respectively.

Conclusion. Case -fatality rates for childhood malnutrition remain high, despite adoption of the WHO treatment guidelines. A need exists for improved adherence to the WHO guidelines and periodic clinical audits to reduce deaths from childhood malnutrition to meet the WHO mortality target of less than 5% and improve child survival.

Key words: childhood malnutrition, case -fatality rates, WHO guidelines for severe malnutrition.

CONTACT DETAILS

Principal Investigator: Dr Oscar Benyera
MSc Clinical Epidemiology candidate – School of Health Systems and Public Health
University of Pretoria
Faculty of Health Sciences
School of Health Systems and Public Health
5th Floor, HW Snyman Building North
31 Bophelo Road
Gezina
Pretoria
0031
Email: drobenyera@yahoo.com

Supervisor: Dr Francis L M Hyera
Senior Lecturer
University of Pretoria
Faculty of Health Sciences
School of Health Systems and Public Health
5th Floor, HW Snyman Building North
31 Bophelo Road
Gezina
Pretoria
0031
Email: Francis.hyera@up.ac.za

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Abbreviations

<	Less than
>	Greater than
95% CI	95% Confidence Interval
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
Chi2	Chi square test
GE	Gastroenteritis
HIV	Human Immunodeficiency Virus
IMAM	Integrated Management of Acute Malnutrition
IQR	Interquartile Range
NCHS	National Center for Health Statistics
OR	Odds Ratios
P-value:	α value = 0.05. A p-value of 0.05 was used throughout the study
SAM	Severe Acute Malnutrition
SD	Standard Deviation
SDHS	Swaziland Demographic and Health Survey
SNNC	Swaziland National Nutrition Council
TB	Tuberculosis
WHO	World Health Organization

1. BACKGROUND AND LITERATURE REVIEW

1.1 INTRODUCTION

Worldwide an estimated 8.1 million children die each year before they reach their 5th birthday and 99% of these are in the developing world.[1-2] Malnutrition is associated with more than 50% of these deaths.[3-4] Malnutrition is therefore an important risk factor for the burden of disease in developing countries.[5]

1.2 THE EPIDEMIOLOGY OF MALNUTRITION

1.2.1 Global Overview

Nearly a quarter of children under five in the developing world remain undernourished. Southern Asia has the highest prevalence of undernourished children below the age of five, 43% followed by sub Saharan Africa, 22% then South Eastern Asia, Western Asia, Eastern Asia, and North Africa with 18%, 7%, 6% and 6% respectively.[1]

1.2.2 Swaziland Perspective

According to the Swaziland Demographic and Health Survey (SDHS) of 2006, 29% of children under five were stunted, 10% severely. Stunting was highest, 43% among children aged 18 to 23 months and lowest, 12% among children aged 6 to 8 months. Male children, 32% were more stunted compared to females, 26%. Urban children, 23% were less stunted than rural children, 30%. Nationally 3% of children were wasted, with 1% being classified as severely wasted. The wasting level peaked at 7% among children aged 9 to 11 months. About 5% of children were underweight with 1% being severely underweight. The proportion underweight children increased with age, peaking at 8% among children age 9 to 11 months.[6]

In 2009, 1241 patients were admitted for the management of malnutrition under the Integrated Management of Acute Malnutrition (IMAM) program in Swaziland. About 1005 (81%) were children aged less than 24 months (Figure 1). Severe acute malnutrition (SAM) accounted for 39% of the admissions and moderate acute malnutrition (MAM) for the remaining 61%. Of those admitted with SAM, 47% had marasmus, 45% had kwashiorkor and 8% had marasmic-kwashiorkor.[7]

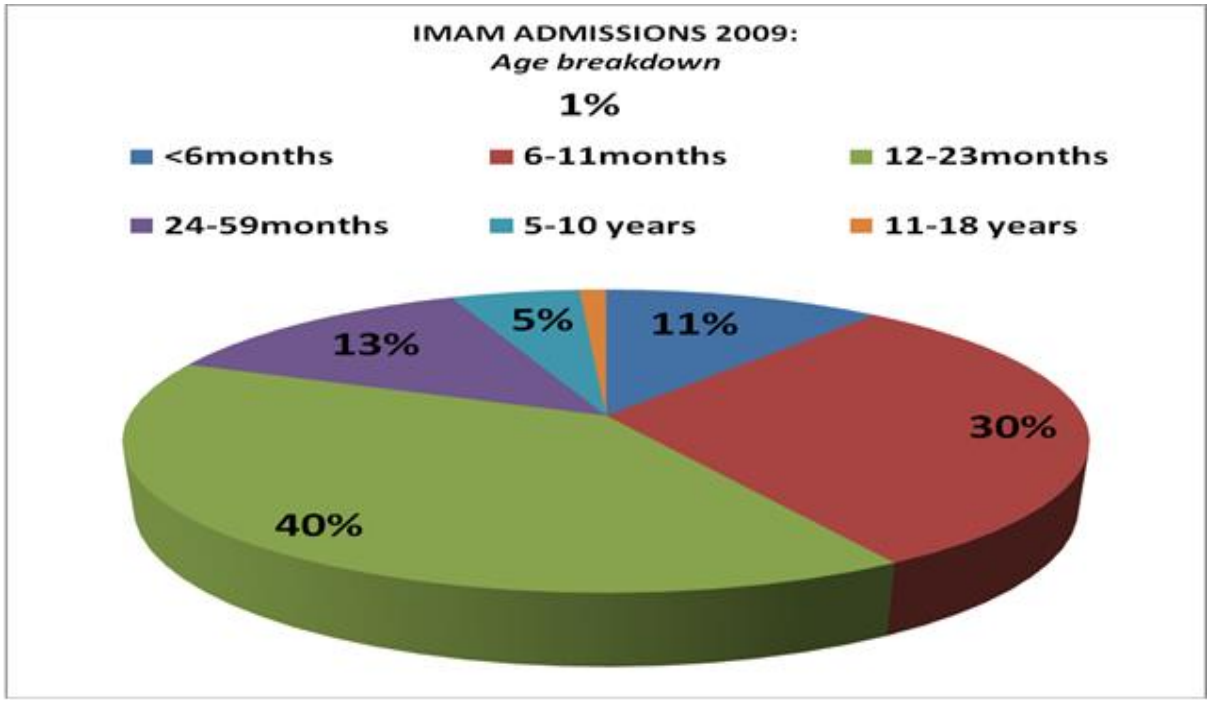

Figure 1: Age distribution of patients admitted for IMAM in 2009. (Source: Swaziland National Nutrition Council Nutrition Bulletin 2009)

1.3 CAUSES OF MALNUTRITION

The basic cause of malnutrition is the intake of nutrients below the minimal requirements for health and growth. Insufficient dietary intake may be due to poor breastfeeding practices, early weaning, delayed introduction of complementary foods and insufficient protein in the diet. Severe or recurrent infections can precipitate malnutrition through the reduction of intake and increasing nutritional requirements because of the infection mediated catabolic state.[8-9]

Poverty is the main underlying cause of malnutrition and its determinants (figure 2).[10-12] The prevalence of poverty in Swaziland, measured by the proportion of people living below the poverty line increased from 66% in 1995 to 69% in 2001 with a projected decline to 64% in 2010.[13] The degree and distribution of malnutrition in a given population depends on factors such as the political and economic situation, the level of education and sanitation, the season and climate conditions, food production, cultural and religious food customs, prevalence of infectious diseases, the existence and effectiveness of nutritional programs and the availability and quality of health services.[10,14-15]

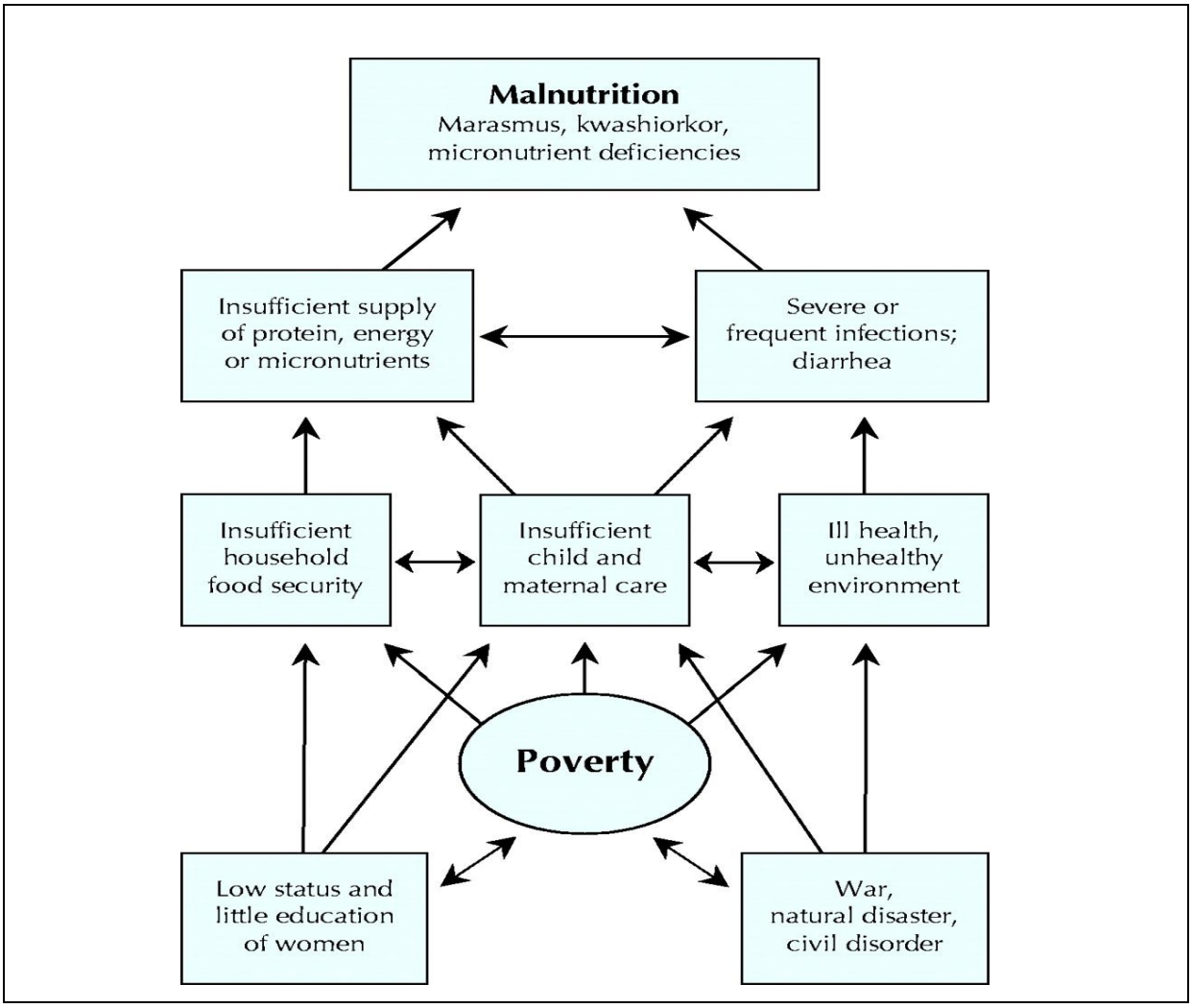

Figure 2: Direct and indirect causes of malnutrition. (Source: Muller and Krawinkel 2005)

1.4 COMMON CO-MORBID CONDITIONS

1.4.1 HIV

In high prevalence settings, HIV is a major contributor to the burden of child malnutrition.[16] Complications of paediatric HIV infection are usually seen in growth failure and finally more serious malnutrition.[17] Furthermore malnutrition exacerbates the effects of HIV by increasing susceptibility to AIDS-related illnesses.[18]The severity of malnutrition in HIV infected children is greater and mortality is three times higher than in uninfected children.[17, 19.]

Swaziland has the highest HIV prevalence in the world of about 26%. Some population subgroups such as women of child bearing age even have higher prevalence rates as high as 49% in the age group 25 to 29 years. HIV prevalence among children aged 2 to 4 years is about 5%.[6]In 2009 between 25% and 48% of children admitted into IMAM program were HIV positive.[7]

1.4.2 TB

Swaziland has a high Tuberculosis (TB) prevalence of about 812/per 100,000 population. TB is the leading cause of morbidity and mortality among adults. It is estimated that TB kills 50% of HIV infected patients and accounts for more than 25% of all hospital admissions.[20] HIV and tuberculosis increase the prevalence of SAM through both the direct effects of infection and the indirect negative effects on livelihoods and food security. HIV and tuberculosis infection decrease skilled human resource capacity in health services and increase case-fatality rates.[21]

1.4.3 Diarrhoea

The prevalence of diarrhoea among children under five in Swaziland is about 13%. Diarrhoeal illness is more common among children age 6 to 11 months, 27% and children age 12 to 23 months, 22% than among younger or older children.[6] Diarrhoea causes about 30-50% of deaths in developing countries. The risk of death due to persistent diarrhoea is related to a lack of breastfeeding, systemic infections, malnutrition and young age.[22]

1.5 THE CLASSIFICATION OF MALNUTRITION

Many classifications have been suggested for the syndromes of malnutrition. The World Health Organization (WHO) classification is the one currently in use at Mbabane Government Hospital and before, the Wellcome classification was in use. According to the WHO classification, severe acute malnutrition (SAM) is defined as a weight-for-height measurement of 70% or more below the median or three standard deviations (SD) or more below the WHO standards.[23] The SD-score is defined as the deviation of the value for an individual from the median value of the reference population, divided by the standard deviation of the reference population.[24] The presence of nutritional oedema is used to further classify the type as either oedematous or non-oedematous (Table 1).

Table 1: The WHO classification of malnutrition

Indicator	**Classification**	
	Moderate	Severe
Oedema	No	Yes (oedematous malnutrition)
Weight-for-height	-3 < SD-score <-2 (70–79%)	SD-score <-3 (<70%) (severe wasting)

Oedematous malnutrition corresponds to kwashiorkor and Marasmic kwashiorkor and severe wasting without oedema to marasmus in the Wellcome classification.[23]

The Wellcome Committee's categorization is based on the presence of oedema and weight-for-age as shown in table 4.[25]

Table 2: The Wellcome Committee categorisation of malnutrition

***Weight**	**Oedema**	
(% of standard)	Present	Absent
80-60	Kwashiorkor	Underweight
< 60	Marasmic Kwashiorkor	Marasmus

Adapted from Wittenberg, * Standard-50th percentile NCHS standard

The severity of malnutrition can be determined by expressing the actual weight as a percentage of the expected weight of a healthy child of the same age using a standard. Children are grouped together according to two criteria: the presence or absence of oedema and the weight-for-age.[25]

1.6 PATHOPHYSIOLOGICAL CHANGES IN MALNITRITION

During malnutrition the physiology of the body changes to conserve nutrients. A malnourished child has reduced digestive, absorptive, hepatic and renal capacity to deal with environmental changes. [26] The loss of subcutaneous fat markedly reduces the body's capacity for temperature regulation and water storage. As a consequence, malnourished children become dehydrated, hypothermic and hypoglycaemic more quickly and severely than others.[10]

During malnutrition the heart shows macroscopic and histological evidence of pathological changes and wasting. In severe cases the cardiac function is altered. There is reduced cardiac output due to a decrease in heart rate and stroke volume and longer circulation time.[26]There often is subclinical or overt cardiac insufficiency, especially when malnutrition is accompanied by oedema. If the myocardial insufficiency is not corrected, iatrogenic fluid and sodium overload quickly escalate into cardiac failure.[10]

Most children with severe malnutrition have asymptomatic infections because their immune system fails to respond with chemotaxis, opsonisation and phagocytosis of bacteria, viruses or fungi. So depressed is the system that the body cannot produce even the fever that is typical of inflammation.[10] Some of the changes associated with malnutrition include decreased helper T-cell counts and reversal of the helper suppressor cell ratio.[27]

Changes in gastrointestinal structure and function that occur in malnutrition lead to malabsorption and worsen nutritional status. Stomach mucosa is often atrophied and gastric acid secretion is reduced leading to bacterial overgrowth.[28]The intestines have reduced peristalsis, motility and transit time.[28] Intestinal villi are shortened and the epithelial cells of the villi with the brush-border disaccharidases become injured and this leads to carbohydrate malabsorption.[25,28] Diarrhoea is almost always present and it further aggravates malabsorption. Repeated and chronic gut infections and infestations worsen nutritional status.[27]

1.7 INPATIENT MANAGEMENT OF SEVERE MALNUTRITION

The hospital management of severe malnutrition is an important component of a comprehensive approach to the problem of undernutrition.[29] A review of case management worldwide has revealed a median case -fatality rate of approximately 25%, with rates in some hospitals as high as 50%.[29-31] Many of these deaths are avoidable and are due to out-dated procedures and protocols, and a lack of familiarity with modern management practices.[29]

1.7.1 The WHO Guidelines for the inpatient treatment of severely malnourished children

Special guidelines are needed for the care of malnourished children because of the profound physiological and metabolic changes that take place when children become malnourished. Because of reductive adaptation, merely increasing the child's food intake is not an effective remedy and furthermore malnourished children do not respond to medical treatment in the same way as if they were well nourished.[32]

The WHO developed consensus treatment guidelines to help improve the quality of hospital care for malnourished children and suggests that, with strict adherence, mortality should be less than 5%.[32-33] Case-fatality rates greater than 20% are considered unacceptable, 11% to

20% is poor, 5% to 10% is moderate, 1% to 4% is good and less than1% is excellent.[23] Implementation studies of the guidelines have shown improvements in case death rates.[30-32]

The management guidelines include a stabilisation phase in which life-threatening problems such as hypoglycaemia, hypothermia and dehydration are identified and treated, followed by a staged introduction of milk-based nutritional rehabilitation, micronutrient plus vitamin supplementation, empiric use of antimicrobial and antihelminthic treatment. This is then followed by sensory stimulation and emotional support. Finally patients are prepared for discharge and follow up.[23]

Table 3 shows a summary of all the elements included in the WHO 10 step management plan. The implementation steps and duration of each of the steps over the period of initial treatment, rehabilitation and discharge and follow-up are given in table 4.

Table 3: Key elements in the management of severe malnutrition

Problem	Management
Hypothermia	Warm patient up; maintain and monitor body temperature
Hypoglycaemia	Monitor blood glucose; provide oral (or intravenous) glucose
Dehydration	Rehydrate carefully with oral solution containing less sodium and more potassium than standard mix
Micronutrients	Provide copper, zinc, iron, folate, multivitamins
Infections	Administer antibiotic and antimalarial therapy, even in the absence of typical symptoms
Electrolytes	Supply plenty of potassium and magnesium
Starter nutrition	Keep protein and volume load low
Tissue-building	Furnish a rich diet dense in energy, protein and all essential nutrients that is easy to swallow and digest
Stimulation	Prevent permanent psychosocial effects of starvation with psychomotor stimulation
Prevention of relapse	Start early to identify causes of protein–energy malnutrition in each case; involve the family and the community in prevention

Source: Adapted from Müller and Krawinkel 2005

Table 4: Time frame for the management of a child with severe malnutrition

ACTIVITY	**INITIAL TREATMENT:** (week 1) days 1 – 2	days 3 – 7	**REHABILITATION:** weeks 2 – 6	**FOLLOW-UP:** weeks 7 – 26
Treat or prevent:				
Hypoglycaemia	→→→→	→→→→		
Hypothermia	→→→→	→→→→		
Dehydration	→→→→	→→→→		
Correct electrolyte imbalance	→→→→	→→→→	→→→→→	→→→→→→→→→
Treat infection	→→→→	→→→→	→→→→→	
Correct micronutrient deficiencies	→→→→	→→→→	→→→→→	→→→→→→→→→
	← without iron	→	← with iron	→
Begin feeding	→→→→	→→→→	→→→→→	
Increase feeding to recover lost weight catch-up growth	→→→→	→→→→	→→→→→	→→
Stimulate emotional and sensorial development	→→	→→→→	→→→→→	→→→→→→→→→
Prepare for discharge			→→→→→	→→→→→→→

Source: Adapted from WHO 1999

2. MOTIVATION FOR THE STUDY

The WHO conducted training in Swaziland on the inpatient treatment of severely malnourished children in 2003. The training was in response to a rising incidence of severe malnutrition. Case -fatality rates at Mbabane Government Hospital at the time were in excess of 50%.[34] During this period there were no special guidelines in use on the treatment of severe malnutrition.

However, it was not until 2007 that the WHO guidelines for the inpatient treatment of severely malnourished children were fully adopted under the IMAM programme. This study was conducted to determine the case -fatality rate post-adoption of the WHO-recommended guidelines and to evaluate the level of adherence to the guidelines at Mbabane Government Hospital.

3. AIM AND OBJECTIVES

3.1. AIM

The aim of the study was to determine if the adoption of the WHO guidelines for the inpatient treatment of severely malnourished children resulted in better outcomes in malnourished children at Mbabane government Hospital

3.2. OBJECTIVES

1) To determine the case fatality-rate for childhood malnutrition post implementation of the WHO treatment guidelines
2) To determine the level of adherence to the WHO treatment guidelines

4. METHODS

4.1. STUDY DESIGN

The study was a retrospective observational study.

4.2. SETTING

The study was conducted in the paediatric unit at Mbabane Government Hospital. The hospital is situated in Mbabane, the capital city of Swaziland in Hhohho region. It is the national referral hospital for a population of about 1,018,449.The hospital serves as a primary care facility for the surrounding population as well as a tertiary care facility receiving referrals from surrounding clinics, rural health centers and district hospitals.

The paediatric unit is housed within the main hospital and consists mainly of the neonatal intensive care unit and the general paediatric ward, which has 56 beds divided into 4 cubicles. The unit admits an average of 1600 patients annually of which about half are medical and the remainder surgical. It also has a busy outpatients department that consults about 18 000 patients per year.

4.3 STUDY POPULATION

4.3.1 Inclusion criteria

Inclusion criteria were all children under 5 years admitted with malnutrition (defined according to the WHO definition)[23] between the months of January 2010 and December 2011.

4.3.2 Exclusion criteria

Children whose parents requested discharge against medical advice were excluded for non-compliance with the treatment guidelines.

4.4 DATA COLLECTION

Individual participant information about presenting history, anthropometrics, clinical findings, co-morbid conditions and the outcome of each admission was abstracted from patients' notes using a structured form (Appendix 1). The following variables determined.

- Demographic variables
- Clinical variables
- Outcome of admission

4.4.1 Demographic variables

1. The age in months.
2. Gender.

4.4.2 Clinical variables

1. Type of malnutrition - edematous or non-edematous malnutrition depending on the presence or absence of nutritional edema.
2. Severity of malnutrition - moderate or severe according to the WHO standards (Appendix 2) and the presence of absence of edema.
3. The HIV status of the patient during the admission as stated in the patient's notes, being classified as positive, negative, exposed (patients born to HIV positive mothers who tested negative at 6 weeks of age who were still at risk of transmission through breast feeding or whose status during admission wasn't ascertained) and unknown in cases where the patient was not tested and the mother, status was unknown.
4. Among HIV positive patients it was also determined if the patient was on antiretroviral therapy (ART) and whether therapy initiated before or during the admission.
5. It was determined if the patient was on concurrent anti Tuberculosis treatment (initiated before or during the admission).
6. It was determined if the patient was diagnosed as having co-morbid pneumonia
7. It was determined if the patient was diagnosed as having diarrhea, defined as three or more loose stools per day.

4.4.3 Clinical Outcomes

1. The outcome of the admission was determined whether the patient died or was discharged.
2. The duration of hospital stay in days from day of admission to day of discharge or death.

4.5 DATA ENTRY

A manual form was developed for initial data collection, backup and for data cleaning purposes (see Appendix 1: Data Collection Tool). Data was then coded and entered into a Microsoft Office Access database with all the variables and limits and normal protocols for data cleaning were used.

4.6 ETHICAL CONSIDERATIONS

Permission to access patient records was obtained from the Senior Medical Officer, Mbabane Government Hospital. The study protocol was approved by the Main Ethics Committee of the University of Pretoria's Faculty of Health Sciences and the Scientific and Research Ethics Committee of Swaziland.Case notes were allocated unique study identification numbers and no patient names were mentioned in the data collection, statistical analysis or report write up. To maintain the confidentiality only the principal investigator had access to the case notes and handled all aspects of data collection and analysis. Data will be stored at the University of Pretoria's School of Health Systems and Public Health.

4.7 DATA ANALYSIS

Stata release 11 (Stata LP, Texas, USA) was used for statistical analysis. Data was described, using standard statistics for continuous and categorical variables. Categorical variables were compared with the Chi2 test and medians were compared using the Wilcoxon rank sum test. Multivariable logistic regression analysis was used to identify risk factors for death. Significant variables in the univariate analyses ($p < 0.30$) were included in a multivariate model. The final model was obtained through the backward-stepwise procedure. The Pearson Chi2 goodness- of-fit test was used to determine the fit of the model. Odds ratios (OR) and their 95% confidence intervals (95% CI) are specified where applicable. A p-value <0.05 was considered statistically significant.

5 RESULTS

5.1 INTRODUCTION

The results of the study were reported in the following sequence:

a) Descriptive statistics

b) Analytical statistics

c) Discussion

d) Limitations of the study

e) Conclusions drawn from the results and recommendations

5.2 DESCRIPTIVE STATISTICS

5.2.1 Patient Demographics and Clinical Characteristics

Of the 337 children initially identified, 277 met the study inclusion criteria. Twenty-three children were excluded from the study because their parents requested discharge against medical advice. A further 37 children were excluded because their case notes did not contain sufficient information for them to be classified accurately in the study. Of the 277 children who were included the study 119 (43.0%) were females. The median age of admission was 12 months (IQR 7 to 17 months) (Table 5).

Table 5: Demographic and clinical characteristics of participants

Characteristics	Overall n = 277
Demographic factors	
Female	119 (43.0)
Median age	12 (IQR 7 to 17)
Nutritional status	
Severe	179 (64.6)
Oedematous	88 (31.8)
HIV profile	
Negative	103 (37.2)
Positive	113 (40.8)
On ART	40 (35.4)*
ART started during admission	8 (20.0) †
Exposed	52 (18.8)
Unknown	9 (3.2)
Co-morbid conditions	
Tuberculosis	87 (31.4)
Diagnosed during admission	66 (75.9) ‡

Pneumonia	124 (44.8)
Gastroenteritis	183 (66.1)
Other	20 (7.2)
Herbal intoxication	3
Kaposi Sarcoma	1
Severe anaemia (transfused Hb<6g/dl)	14
Paralytic ileus	1
Cryptococcal meningitis	1

5.2.1.1 Nutritional Status

Ninety-eight children (35.4%) had moderate malnutrition and 179 (64.6%) had severe acute malnutrition (SAM). Of the 179 who had SAM, 91 (50.8%) were severely wasted and 88 (49.2%) had oedematous SAM.

5.2.1.2 HIV

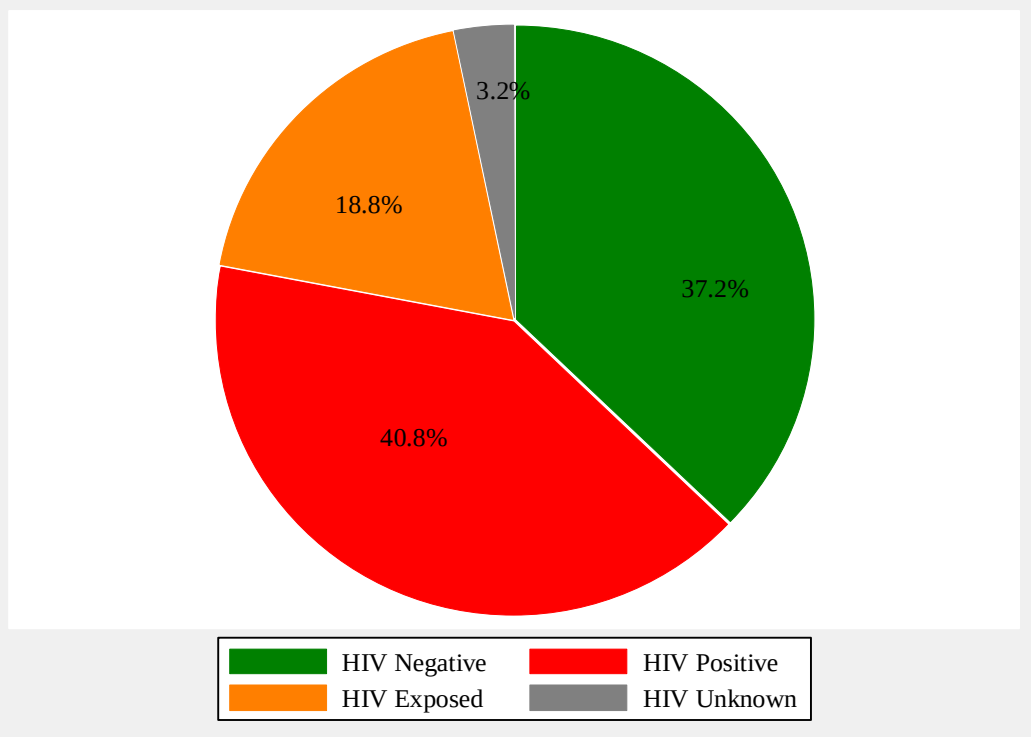

Figure 3: HIV status of study participants

One-hundred-and-three children (37.2%) were HIV -negative, 113 (40.8%) were HIV -positive, 52 (18.8%) were HIV -exposed and 9 (3.2%) were classified as of unknown HIV status. Of the 113 children who were HIV- positive, 40 (35.4%) were on antiretroviral

therapy treatment (ART) and only 8 of them were initiated on ART during the admission period. Among those with SAM, HIV -positive children were significantly more likely to be wasted compared to HIV -negative children (OR 2.2, 95% CI 1.1 to 4.5).

5.2.1.3 TB

Eighty-seven children (31.4%) were treated for Tuberculosis (TB). In 66 of the 87 children, (75.9%) TB was diagnosed during the admission period. Diagnosis was based on clinical suspicion in children with persistent fever despite at least seven days of intravenous antibiotics, failure to gain weight, suspicious chest radiograph or the clinician's discretion. HIV -positive children were more likely to be treated for TB compared to HIV -negative ones (OR 3.1, 95 CI 1.6 to 5.8).

5.2.1.4 Pneumonia

One-hundred-and-twenty-four children (44.8%) were diagnosed with Pneumonia. The diagnosis of Pneumonia was more likely in HIV-positive children compared to HIV-negative children (OR 2.6, 95 CI 1.4 to 4.6)

5.2.1.5 Gastroenteritis

One-hundred-and-eighty-three children (66.1%) had gastroenteritis (GE). There was no statistically significant difference in the occurrence of GE between HIV -positive- and HIV -negative children (OR 1.36, 95 CI 0.75 to 2.47).

5.2.1.6 Other co-morbid conditions

Fourteen children had severe anaemia that necessitated blood transfusion (Haemoglobin < 6g/dl). Four children had concomitant herbal intoxication on admission. One child had cryptococcal meningitis, one had Kaposi Sarcoma and one child developed paralytic ileus during the course of treatment.

5.3 ANALYTICAL STATISTICS

5.3.1 Outcome of admission

One-hundred-and-eleven (40.1%) of the 277 children died in hospital, with 31 deaths (27.9%) occurring within 48 hours of admission. Mortality was significantly higher among patients with SAM compared to those with moderate malnutrition (46.9% vs 27.6%, $p < 0.001$). Among patients with SAM, no significant difference existed in mortality between the two types of malnutrition (oedematous SAM 48.9% vs severe wasting 45.1%, p= 0.61)

Several factors were identified as poor prognostic factors for mortality in the univariate analysis (Table 6).

Table 6: Univariate analysis (crude odds ratios) for prognostic factors for mortality

Variable	Odds ratio (95% CI)	P value
Sex		
Female	Reference	-
Male	1.1(0.7 – 1.8)	0.68
Age (months)		
0 – 6	Reference	-
7 – 12	0.6 (0.3 – 1.1)	0.083
13 – 24	0.4 (0.2 – 0.8)	0.005
25 – 60	0.6 (0.2 – 1.8)	0.35
Type of malnutrition		
Non-oedematous	Reference	-
Oedematous	1.7 (1.0 – 2.8)	0.042
Severity of malnutrition		
Moderate	Reference	-
Severe	2.3 (1.4 – 4.0)	0.002
HIV status		
Negative	Reference	-
Positive	1.8 (1.0 – 3.1)	0.045
Exposed	2.3 (1.2 – 4.6)	0.016
Unknown	2.9 (0.7 – 11.6)	0.130
Tuberculosis	0.8 (0.5 – 1.4)	0.45
Gastroenteritis	1.7 (1.0 – 2.9)	0.048
Pneumonia	1.7 (1.0 – 2.7)	0.041

However, after multivariable logistic regression analysis, 4 factors remained significant predictors of mortality (Table 7). No significant difference existed in mortality between children aged 0 to 6 months compared to those aged 7 to 12 months (OR 0.5, 95 % 0.3 to 1.0). However, children aged 13 to 24 months fared much better compared to those aged six months and below (OR 0.3, 95% CI 0.2 to 0.6).

Table 7: Multivariate analysis odds ratios for factors significantly associated with mortality

Variable	Odds Ratio (95% CI)	P value
Age		
0 – 6	Reference	-
7 – 12	0.5 (0.3 – 1.0)	0.051
13 – 24	0.3 (0.2 – 0.6)	0.001
25 – 60	0.5 (0.1 – 1.4)	0.181
Severe malnutrition	3.0 (1.7 – 5.3)	< 0.001
Gastroenteritis	1.9 (1.07 – 3.2)	0.027
Pneumonia	2.0 (1.2 – 3.4)	0.009

Pneumonia and GE were significant predictors of mortality, (OR 2.0 (95% CI 1.2 to 3.4, p = 0.009) and 1.9 (95% CI 1.1 to 3.2, p = 0.027) respectively).

Mortality was highest among children of HIV -unknown status (55.6%), followed by HIV -exposed (50.0%), then HIV -positive (43.4%), and finally HIV -negative children (30.1%). However, HIV was not a significant predictor of mortality in the multivariate model and neither was TB.

5.3.2 Length of hospital stay

The median length of hospital stay was ten days (IQR 6 to 15 days).

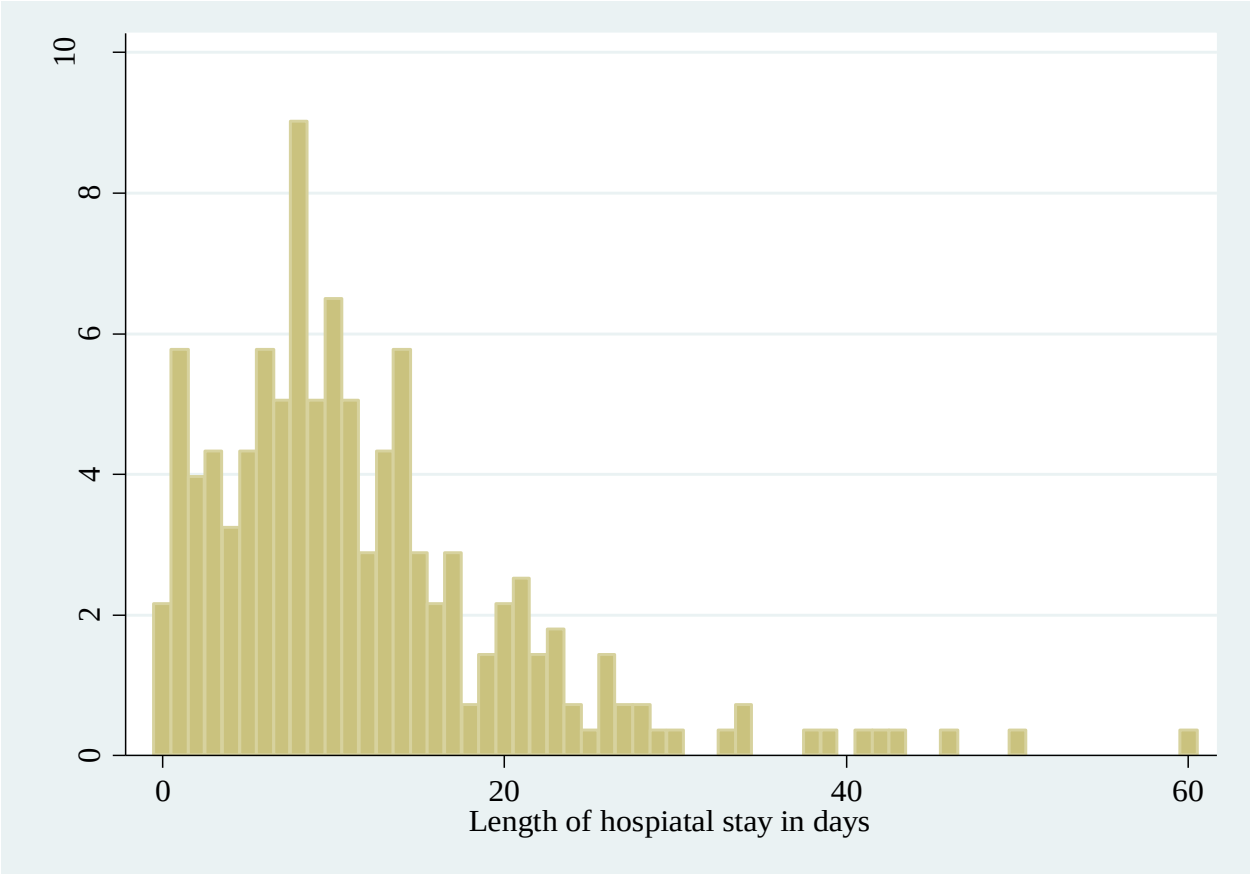

Figure 4: Length of hospital stay of study participants

Children who died had a shorter duration of hospital stay compared to those who were discharged (median 5 vs 12 days, p < 0.001).

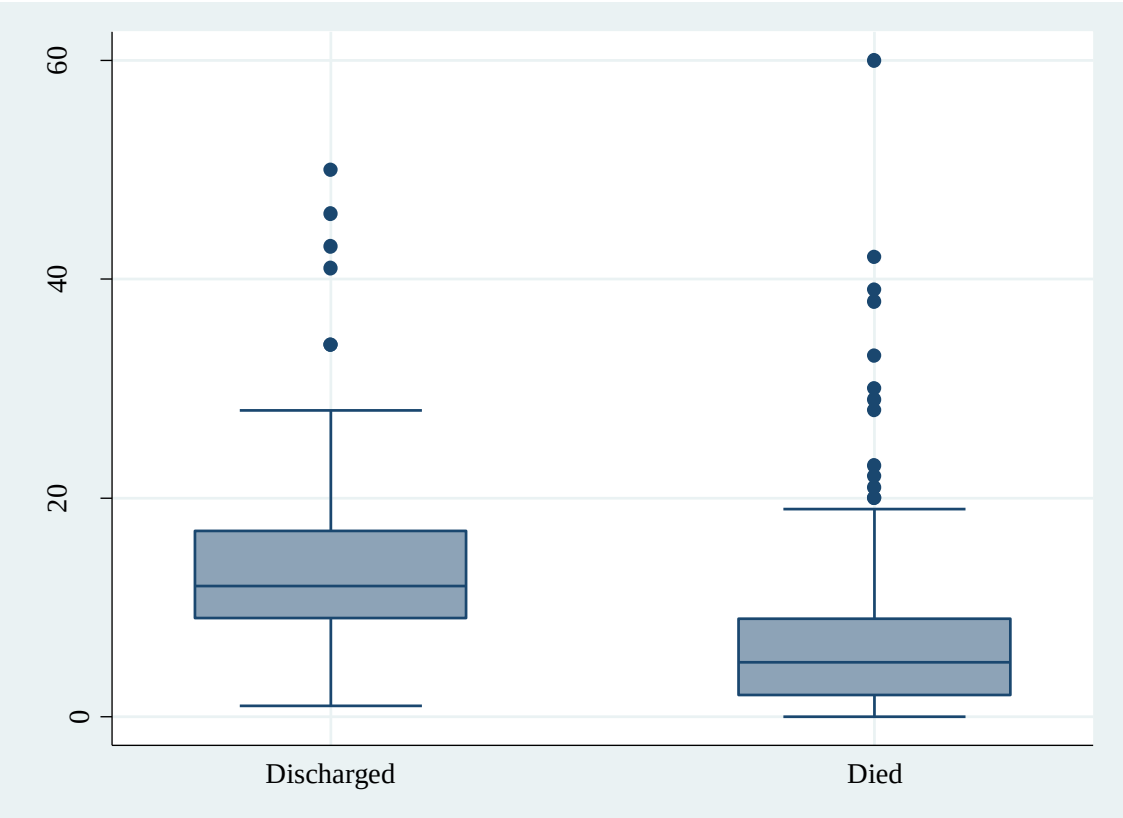

Figure 5: Length of hospital stay (died vs discharged)

5.4 Discussion

This study confirms that the case -fatality rates for childhood malnutrition remain unacceptably high at Mbabane Government Hospital, despite implementation of the WHO treatment guidelines. Even the case -fatality rate for moderate malnutrition was alarmingly high at, 27.55%, almost 6 times the WHO-established targets for severe malnutrition. The high case -fatality rates are indicative of poor adherence to the guidelines during case management.

Critical management principles were not being adhered to during case management. Firstly, hypoglycaemia was not being actively diagnosed or managed. Blood glucose levels were not measured routinely on admission. Furthermore, in cases where blood glucose level was not measured, a presumptive diagnosis of hypoglycaemia was not being made, contrary to what is advised in the guidelines. Children were not being routinely given dextrose water to treat or prevent hypoglycaemia on admission. Some children were not started on therapeutic feeds for up to 24 hours after admission despite doctors' orders. Undiagnosed or poorly managed hypoglycaemia could have resulted in many deaths.

Secondly, hypothermia was not adequately managed. Malnourished children are unable to regulate their body temperature. During the first days of treatment their body temperature is dependent on the ambient temperature.[32] Care is best achieved if the children are nursed in a heated room. There were no heaters in the ward. Blankets were the only means employed to keep the children warm. The kangaroo technique was not being used in younger children. The lack of adequate heating left the children prone to developing hypothermia.

Caution must be exercised when diagnosing and treating dehydration in malnourished children. Appropriately rehydrating the dehydrated malnourished child is critical to survival and recovery.[32] In the study, children with a comorbid diagnosis of GE were almost twice as likely to die as those without. The excess mortality risk for GE could be explained by deaths from dehydration and over hydration due to poor fluid management. Children with severe dehydration were not getting the close and careful monitoring they required during case management.

In severely malnourished children the usual signs of infection are often absent. Routine broad-spectrum antibiotics are therefore recommended.[32] In the study, the outcomes of admission could have been affected negatively by the prescribing practices of medical officers. Children with a co-morbid diagnosis of Pneumonia were almost twice as likely to die as those without. Some children were put on oral antibiotics when their clinical condition warranted intravenous therapy. Second-line antibiotics were not routinely prescribed to children with continued signs of infection after 48 hours of first-line therapy. Furthermore, the prescription choices were often limited by the frequent drug stock-outs that affected the hospital.

They were many causes of the poor adherence to the management principles. The staffing in the paediatric unit was less than adequate. At times there was only one nurse on duty taking care of more than 30 admitted children. The poor staffing levels resulted in the poor monitoring of children, with the nurses failing to identify or appropriately manage critically ill children.

Furthermore, training on the use of the guidelines was not frequent and resulted in a knowledge gap in the care of malnourished children. The lack of knowledge was further worsened by staff attrition and also through the loss of trained staff during the annual staff rotation between the various units in the hospital. The staff morale was also low because of

the poor conditions of service. Low staff morale, poor staffing levels and lack of knowledge due to infrequent training on the use of the guidelines contributed greatly to suboptimal care.

The lack of proper and adequate laboratory support also negatively affected case management. Routine tests ordered during case management were often not available or inaccurate results were provided. The poor laboratory support made the management of children with electrolyte disturbances or severe anaemia difficult, negatively affecting case management.

5.4.1 HIV and TB

The prevalence of HIV among the study participants was 40.8%, which is comparable to that of other African studies reported figures of between 17% and 54%.[35- 36]As described earlier in other studies, HIV -positive children presented more with wasting compared to oedematous malnutrition and were up to six times more likely to die.[35] However, in contrast to these studies, in this study HIV was not a significant predictor of mortality. This lack of significance might be due to fundamental flaws in case management that even rendered the participants' HIV status unimportant.

The diagnosis of TB in children is a challenge and is even more difficult in malnourished and HIV-positive children. Frequently tuberculin skin tests are falsely negative and extrapulmonary TB is more common.[35] In all the 66 children who were started on anti-TB treatment during admission, the diagnosis was based on clinical suspicion. No confirmatory tests to demonstrate the presence of Mycobacterium TB were done, raising the question of how many children actually had TB. The diagnosis of co-morbid TB in this study was not associated with increased mortality.

5.5 Study limitations

The study was retrospective, so analysis of risk factors associated with mortality was limited by the information that could be obtained from the patient charts. Information on various other prognostic factors was either missing or poorly recorded and was of no use to the study.

5.6 Conclusion

Case -fatality rates for childhood malnutrition remain very high at Mbabane Government Hospital despite the implementation of the WHO guidelines. Poor adherence to guidelines during case management is the cause of the persistently high case -fatality rates.

5.7 Recommendations

Reduced case -fatality rates can be achieved through adequate staffing levels, periodical training on the use of WHO recommended guidelines, and refresher courses. The paediatric unit must introduce periodical clinical audits and mortality review meetings to identify and address factors associated with excess mortality. Adoption and implementation of the most affordable Kangaroo method is beneficial for hypothermia. The hospital must fully address operational factors that negatively affect case management such as drug stock-outs and poor laboratory functionality.

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7 APPENDICES

Appendix 1: Data Collection Tool

Study id # _____ Age_____ (months) Sex ☐ Male ☐ Female

DOA ___/___/____ DOD (death/discharge) ___/___/_____ LHS_____days

Nutritional Indices

Weight _____Kg	Height_____cm	Wt/Ht _____%	Oedema ☐Yes ☐ No

Malnutrition Status

Type of malnutrition	Severity
☐ Non-oedematous ☐ Oedematous	☐ Moderate ☐ Severe

HIV Profile

HIV Status	ART Status (If HIV = Positive)
☐ Negative ☐ Positive ☐ Exposed ☐ Unknown	☐ ART initiated before admission ☐ ART initiated during admission ☐ Not on ART

Tuberculosis Profile

Co-morbid TB	When was TB treatment initiated
☐ Yes ☐ No	☐ Treatment initiated before admission ☐ Treatment initiated during admission

Co-morbid Gastroenteritis and Pneumonia

Gastroenteritis	Pneumonia	Other co-morbid conditions (specify)
☐ Yes ☐ No	☐ Yes ☐ No	

Outcome of admission

☐ Discharged ☐ Deceased

Appendix 2: WHO standards for diagnosing malnutrition

Weight for Height Table

Boys and Girls (49.0cm-130.0 cm)

Less than 85 cm should be measured lying down with height board.

WEIGHT-FOR-LENGTH							WEIGHT-FOR-LENGTH						
			Malnutrition							Malnutrition			
			Moderate Wasting 70 to 79%		Severe Wasting <%70					Moderate Wasting 70 to 79%		Severe Wasting <%70	
Height	100%	85%	80%	75%	70%	60%	Height	100%	85%	80%	75%	70%	60%
(cm)	In Kg	in Kg	in Kg	in Kg	in Kg	in Kg	(cm)	in Kg	in Kg	in Kg	in Kg	in Kg	in Kg
49.0	3.2	2.7	2.6	2.4	2.3	1.9	**67.0**	7.6	6.5	6.1	5.7	5.3	4.6
49.5	3.3	2.8	2.6	2.5	2.3	2.0	**67.5**	7.8	6.6	6.2	5.8	5.4	4.7
50.0	3.4	2.9	2.7	2.5	2.4	2.0	**68.0**	7.9	6.7	6.3	5.9	5.5	4.7
50.5	3.4	2.9	2.7	2.6	2.4	2.0	**68.5**	8.0	6.8	6.4	6.0	5.6	4.8
51.0	3.5	3.0	2.8	2.6	2.5	2.1	**69.0**	8.2	7.0	6.6	6.1	5.7	4.9
51.5	3.6	3.1	2.9	2.7	2.5	2.2	**69.5**	8.3	7.1	6.7	6.2	5.8	5.0
52.0	3.7	3.1	3.0	2.8	2.6	2.2	**70.0**	8.5	7.2	6.8	6.3	5.9	5.1
52.5	3.8	3.2	3.0	2.8	2.6	2.3	**70.5**	8.6	7.3	6.9	6.4	6.0	5.2
53.0	3.9	3.3	3.1	2.9	2.7	2.3	**71.0**	8.7	7.4	7.0	6.5	6.1	5.2
53.5	4.0	3.4	3.2	3.0	2.8	2.4	**71.5**	8.9	7.5	7.1	6.6	6.2	5.3
54.0	4.1	3.5	3.3	3.1	2.9	2.5	**72.0**	9.0	7.6	7.2	6.7	6.3	5.4
54.5	4.2	3.6	3.4	3.2	2.9	2.5	**72.5**	9.1	7.7	7.3	6.8	6.4	5.5
55.0	4.3	3.7	3.5	3.2	3.0	2.6	**73.0**	9.2	7.9	7.4	6.9	6.5	5.5
55.5	4.4	3.8	3.5	3.3	3.1	2.6	**73.5**	9.4	8.0	7.5	7.0	6.5	5.6
56.0	4.6	3.9	3.6	3.4	3.2	2.8	**74.0**	9.5	8.1	7.6	7.1	6.6	5.7
56.5	4.7	4.0	3.7	3.5	3.3	2.8	**74.5**	9.6	8.2	7.7	7.2	6.7	5.8
57.0	4.8	4.1	3.8	3.6	3.4	2.9	**75.0**	9.7	8.2	7.8	7.3	6.8	5.8
57.5	4.9	4.2	3.9	3.7	3.4	2.9	**75.5**	9.8	8.3	7.9	7.4	6.9	5.9
58.0	5.1	4.3	4.0	3.8	3.5	3.1	**76.0**	9.9	8.4	7.9	7.4	6.9	5.9
58.5	5.2	4.4	4.2	3.9	3.6	3.1	**76.5**	10.0	8.5	8.0	7.5	7.0	6.0
59.0	5.3	4.5	4.3	4.0	3.7	3.2	**77.0**	10.1	8.6	8.1	7.6	7.1	6.1
59.5	5.5	4.6	4.4	4.1	3.8	3.3	**77.5**	10.2	8.7	8.2	7.7	7.2	6.1
60.0	5.6	4.8	4.5	4.2	3.9	3.4	**78.0**	10.4	8.8	8.3	7.8	7.2	6.2
60.5	5.7	4.9	4.6	4.3	4.0	3.4	**78.5**	10.5	8.9	8.4	7.8	7.3	6.3
61.0	5.9	5.0	4.7	4.4	4.1	3.5	**79.0**	10.6	9.0	8.4	7.9	7.4	6.4
61.5	6.0	5.1	4.8	4.5	4.2	3.6	**79.5**	10.7	9.1	8.5	8.0	7.5	6.4
62.0	6.2	5.2	4.9	4.6	4.3	3.7	**80.0**	10.8	9.1	8.6	8.1	7.5	6.5
62.5	6.3	5.4	5.0	4.7	4.4	3.8	**80.5**	10.9	9.2	8.7	8.1	7.6	6.5
63.0	6.5	5.5	5.2	4.8	4.5	3.9	**81.0**	11.0	9.3	8.8	8.2	7.7	6.6
63.5	6.6	5.6	5.3	5.0	4.6	4.0	**81.5**	11.1	9.4	8.8	8.3	7.7	6.7
64.0	6.7	5.7	5.4	5.1	4.7	4.0	**82.0**	11.2	9.5	8.9	8.4	7.8	6.7
64.5	6.9	5.9	5.5	5.2	4.8	4.1	**82.5**	11.3	9.6	9.0	8.4	7.9	6.8
65.0	7.0	6.0	5.6	5.3	4.9	4.2	**83.0**	11.4	9.6	9.1	8.5	7.9	6.8
65.5	7.2	6.1	5.7	5.4	5.0	4.3	**83.5**	11.5	9.7	9.2	8.6	8.0	6.9
66.0	7.3	6.2	5.9	5.5	5.1	4.4	**84.0**	11.5	9.8	9.2	8.7	8.1	6.9
66.5	7.5	6.4	6.0	5.6	5.2	4.5	**84.5**	11.6	9.9	9.3	8.7	8.2	7.0

Appendix 3: Ethics and Legal Considerations

Approval of study by the relevant departments

The study protocol was approved by the Academic Advisory Committee and Main Ethics Committee of the University of Pretoria's Faculty of Health Sciences (Protocol 25/2012) and the Scientific and Research Ethics Committee of Swaziland.

Permission to access patient records

Permission to access patient records was obtained from the Senior Medical Officer, Mbabane Government Hospital.

Privacy of Information / Confidentiality

Strict confidentiality was maintained for all patients' records that were used in the study. No patient names were used in the data collection, analysis or reporting. The results will be kept at SHSPH for the next 25 years.

Appendix 4 Statistical Analysis

Logistic regression

```
. xi:logistic died i.agegrp  maltype sev i.hiv  tb ge bpn hivtb hivbpn
i.agegrp          _Iagegrp_1-4        (naturally coded; _Iagegrp_1 omitted)
i.hiv             _Ihiv_1-4           (naturally coded; _Ihiv_1 omitted)

Logistic regression                               Number of obs   =        277
                                                  LR chi2(13)     =      43.83
                                                  Prob > chi2     =     0.0000
Log likelihood = -164.59138                       Pseudo R2       =     0.1175
```

died	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
_Iagegrp_2	.4484067	.1641981	-2.19	0.029	.2187651	.9191072
_Iagegrp_3	.3049858	.1163155	-3.11	0.002	.1444269	.6440373
_Iagegrp_4	.3112801	.2003156	-1.81	0.070	.088183	1.098799
maltype	1.564175	.5307597	1.32	0.187	.8043656	3.041705
sev	2.485644	.8333837	2.72	0.007	1.288395	4.795443
_Ihiv_2	1.753814	.6457863	1.53	0.127	.8522272	3.609204
_Ihiv_3	1.406709	.6919458	0.69	0.488	.5364227	3.68894
_Ihiv_4	1.921111	1.569223	0.80	0.424	.3874937	9.52446
tb	.1683925	.1740756	-1.72	0.085	.0222021	1.277178
ge	1.688831	.5021946	1.76	0.078	.9429117	3.024833
bpn	1.445128	1.100271	0.48	0.629	.3249608	6.426611
hivtb	2.116009	1.072701	1.48	0.139	.7834387	5.715182
hivbpn	1.162912	.4240132	0.41	0.679	.5690985	2.376327

```
. est store a

. xi:logistic died i.agegrp  maltype sev i.hiv  tb ge bpn
i.agegrp          _Iagegrp_1-4        (naturally coded; _Iagegrp_1 omitted)
i.hiv             _Ihiv_1-4           (naturally coded; _Ihiv_1 omitted)

Logistic regression                               Number of obs   =        277
                                                  LR chi2(11)     =      40.87
                                                  Prob > chi2     =     0.0000
Log likelihood = -166.07085                       Pseudo R2       =     0.1096
```

died	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
_Iagegrp_2	.441027	.1597698	-2.26	0.024	.2168215	.8970735
_Iagegrp_3	.3039976	.1149107	-3.15	0.002	.1449162	.6377101
_Iagegrp_4	.2997215	.1921283	-1.88	0.060	.0853254	1.052828
maltype	1.583111	.5323596	1.37	0.172	.818982	3.060192
sev	2.527548	.842347	2.78	0.005	1.315293	4.857092
_Ihiv_2	2.128229	.7146143	2.25	0.024	1.102054	4.109924
_Ihiv_3	2.068396	.7988872	1.88	0.060	.9702192	4.409584
_Ihiv_4	2.739451	2.021231	1.37	0.172	.6451	11.63322
tb	.7177855	.2241943	-1.06	0.288	.3891607	1.323916
ge	1.843983	.5364039	2.10	0.035	1.042671	3.261118
bpn	1.987035	.5587884	2.44	0.015	1.145073	3.448086

```
. lrtest a

Likelihood-ratio test                             LR chi2(2)  =      2.96
(Assumption: . nested in a)                       Prob > chi2 =    0.2278
```

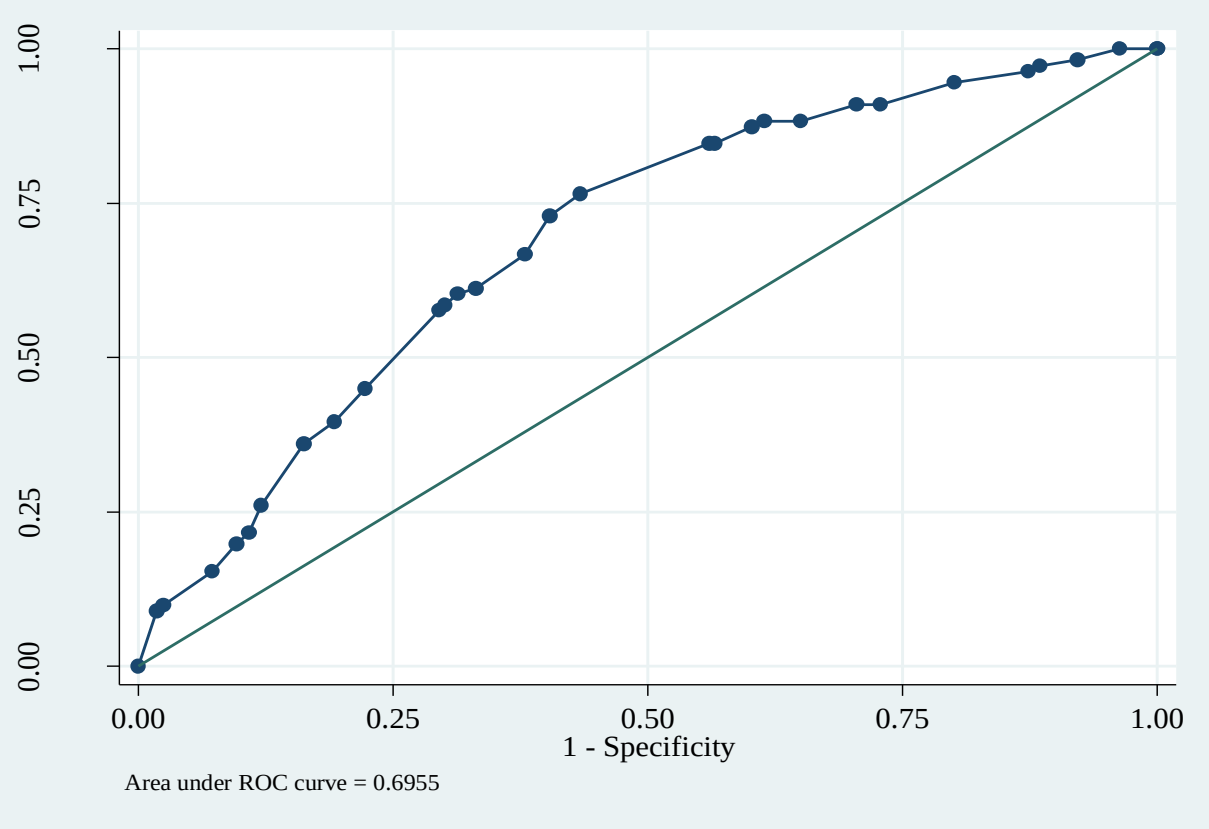
```
. xi:logistic died i.agegrp sev ge bpn
i.agegrp          _Iagegrp_1-4        (naturally coded; _Iagegrp_1 omitted)

Logistic regression                               Number of obs   =        277
                                                  LR chi2(6)      =      31.65
                                                  Prob > chi2     =     0.0000
Log likelihood = -170.68126                       Pseudo R2       =     0.0848

------------------------------------------------------------------------------
        died | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
  _Iagegrp_2 |   .5043788   .1769774    -1.95   0.051     .2535628    1.003294
  _Iagegrp_3 |   .3156768   .1144526    -3.18   0.001     .1551061    .6424754
  _Iagegrp_4 |   .4547757   .2676011    -1.34   0.181     .1435257    1.441003
         sev |   2.968943   .8674026     3.72   0.000     1.674619     5.26366
          ge |   1.860858   .5232203     2.21   0.027     1.072456    3.228843
         bpn |   1.996107   .5306182     2.60   0.009     1.185528    3.360901
------------------------------------------------------------------------------

. est store e

. xi:logistic died sev ge bpn

Logistic regression                               Number of obs   =        277
                                                  LR chi2(3)      =      21.15
                                                  Prob > chi2     =     0.0001
Log likelihood = -175.92959                       Pseudo R2       =     0.0567

------------------------------------------------------------------------------
        died | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         sev |   2.580012   .7207905     3.39   0.001     1.492167    4.460936
          ge |   1.830365   .5039741     2.20   0.028     1.067007    3.139845
         bpn |   1.955361   .5079766     2.58   0.010     1.175158    3.253552
------------------------------------------------------------------------------

. lrtest e

Likelihood-ratio test                             LR chi2(3)  =      10.50
(Assumption: . nested in e)                       Prob > chi2 =     0.0148
```

Goodness of fit test for final logistic regression model

```
. xi:logistic died i.agegrp sev ge bpn
i.agegrp          _Iagegrp_1-4        (naturally coded; _Iagegrp_1 omitted)

Logistic regression                               Number of obs   =        277
                                                  LR chi2(6)      =      31.65
                                                  Prob > chi2     =     0.0000
Log likelihood = -170.68126                       Pseudo R2       =     0.0848

------------------------------------------------------------------------------
        died | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
  _Iagegrp_2 |   .5043788   .1769774    -1.95   0.051     .2535628    1.003294
  _Iagegrp_3 |   .3156768   .1144526    -3.18   0.001     .1551061    .6424754
  _Iagegrp_4 |   .4547757   .2676011    -1.34   0.181     .1435257    1.441003
         sev |   2.968943   .8674026     3.72   0.000     1.674619     5.26366
          ge |   1.860858   .5232203     2.21   0.027     1.072456    3.228843
         bpn |   1.996107   .5306182     2.60   0.009     1.185528    3.360901
------------------------------------------------------------------------------

. estat gof

Logistic model for died, goodness-of-fit test

       number of observations =       277
number of covariate patterns =        29
            Pearson chi2(22) =     15.83
                 Prob > chi2 =     0.8241
```

ROC analysis

```
. lroc

Logistic model for died

number of observations =       277
area under ROC curve   =    0.6955
```



Confusion matrix table for final logistic regression model

```
. estat class

Logistic model for died
```

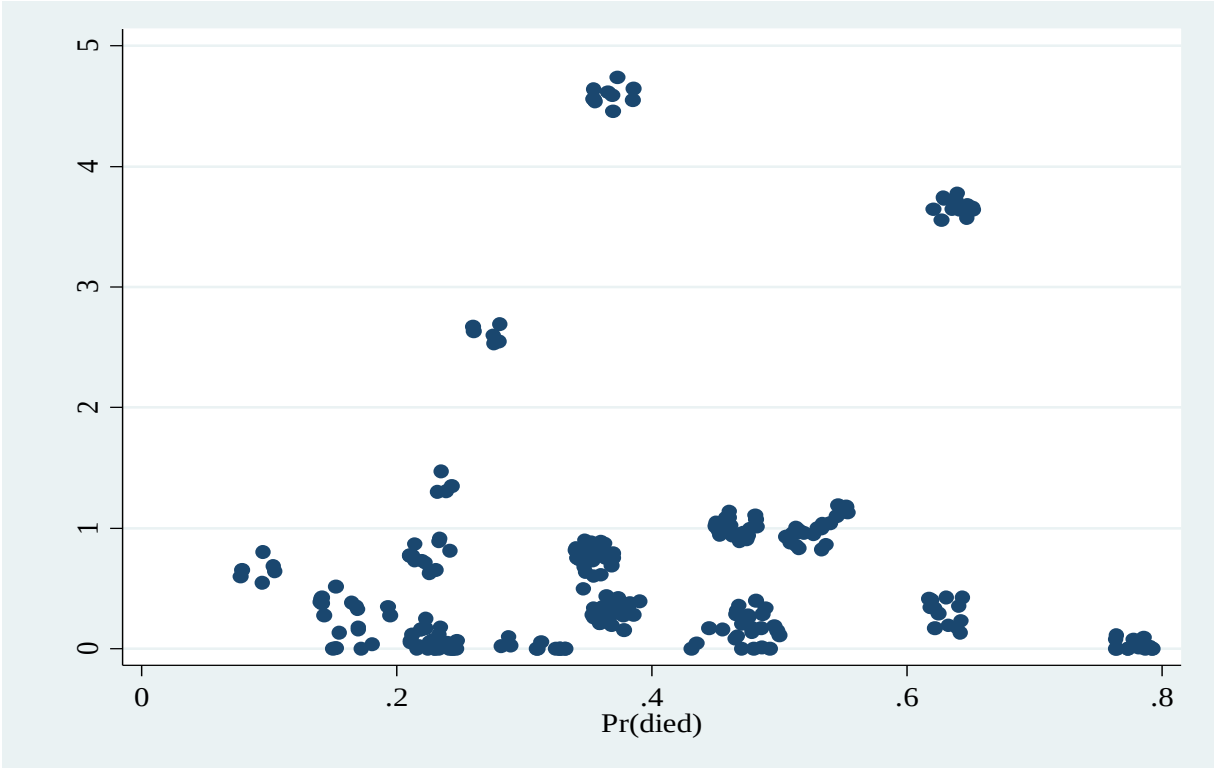
Classified	True D	True ~D	Total
+	40	27	67
-	71	139	210
Total	111	166	277

```
Classified + if predicted Pr(D) >= .5
True D defined as died != 0
```

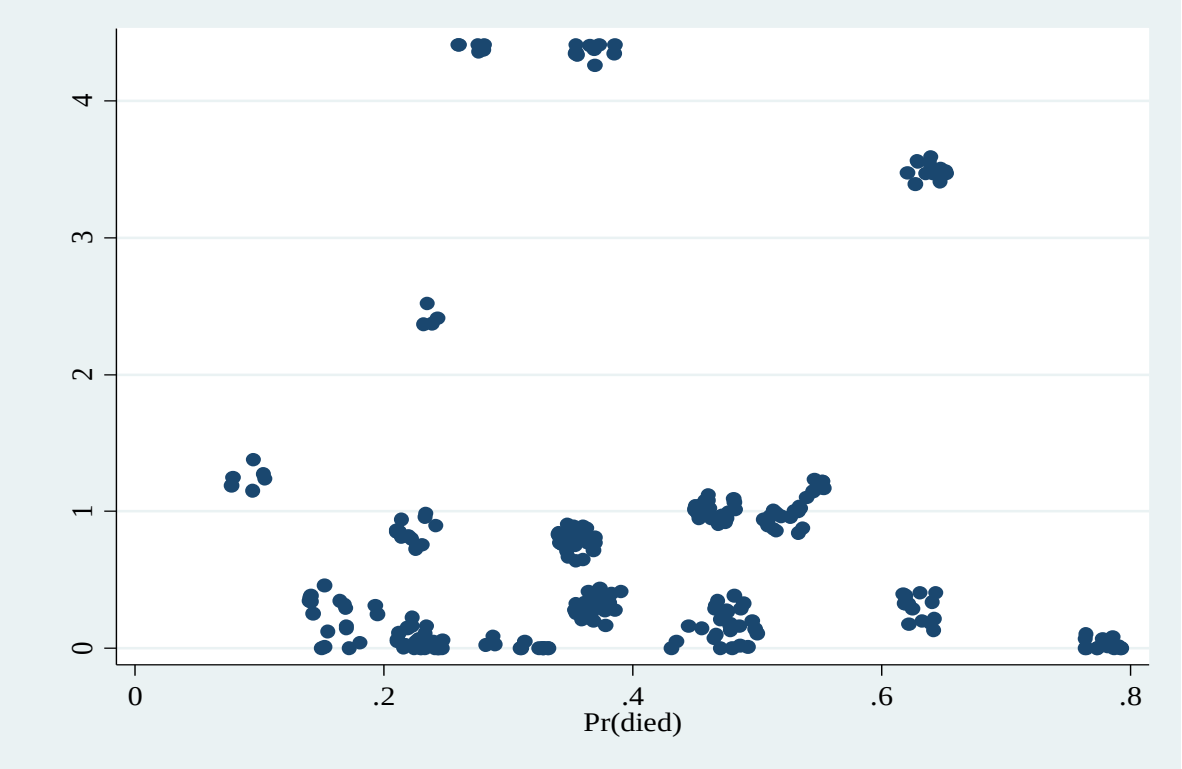
Sensitivity	Pr(+| D)	36.04%
Specificity	Pr(-|~D)	83.73%
Positive predictive value	Pr(D| +)	59.70%
Negative predictive value	Pr(~D| -)	66.19%
False + rate for true ~D	Pr(+|~D)	16.27%
False - rate for true D	Pr(-| D)	63.96%
False + rate for classified +	Pr(~D| +)	40.30%
False - rate for classified -	Pr(D| -)	33.81%
Correctly classified		64.62%

Residual analysis graphs

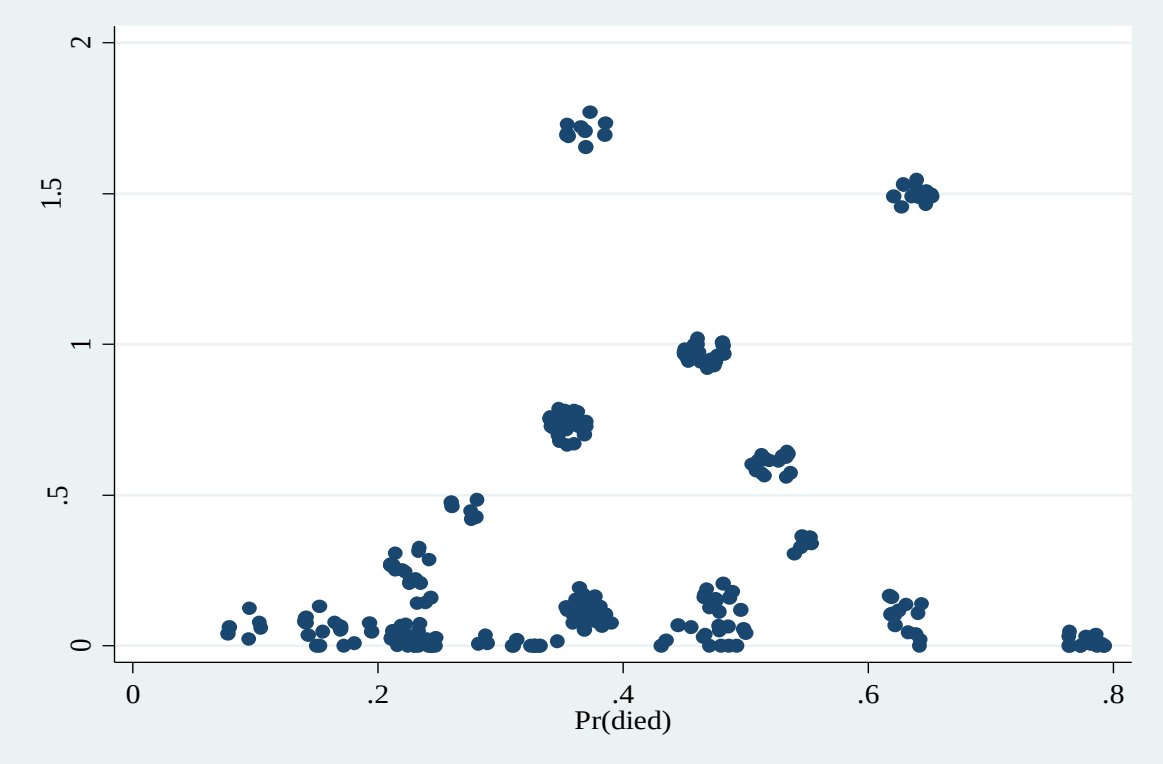
scatter dx2 mu, jitter(5)



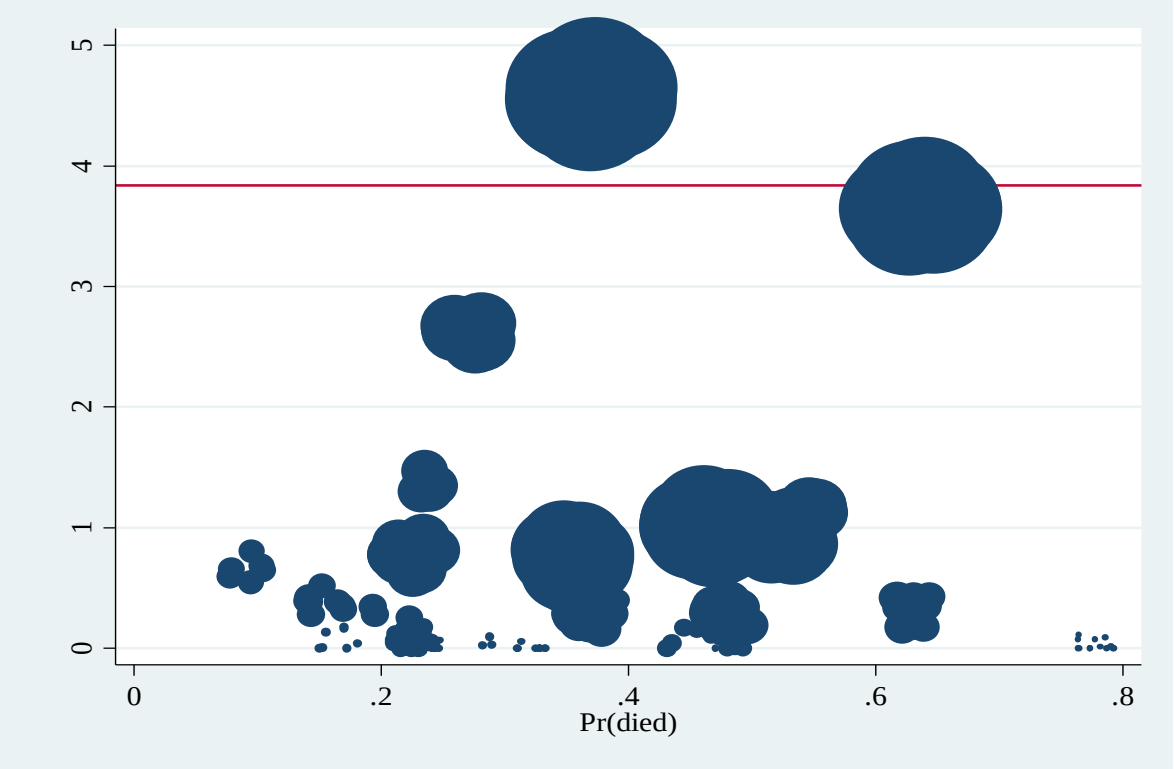
scatter dd mu, jitter(5)



scatter db mu, jitter(5)



scatter dx2 mu [w=db], yline(3.84) jitter(5)



Outcomes in malnourished children at a tertiary hospital in Swaziland: Post implementation of the WHO treatment guidelines

O Benyera, *MBChB (UZ), Dip HIV (CMSA)*
University of Pretoria, School of Health Systems and Public Health and Department of Paediatrics Mbabane Government Hospital

F L M Hyera, *MD (DAR), O&G (Vieena),DTM& H (UP), DOM& H (UP), MSc Comm Health (UP), MMed Comm Health (UP)*
University of Pretoria School of Health Systems and Public Health

Corresponding author: O Benyera (drobenyera@yahoo.com)

Background. Swaziland adopted the World Health Organization's (WHO) guidelines for the inpatient treatment of severely malnourished children in 2007 to reduce case -fatality rates for childhood malnutrition. However, no follow-up studies have been conducted to determine the reduction in the case -fatality rate post-implementation of the guidelines.

Objectives. To determine the case -fatality rate for childhood malnutrition post-implementation of the WHO treatment guidelines and determine the level of adherence to the guidelines at Mbabane Government Hospital.

Methods. A retrospective observational study was undertaken. All children under 5 years admitted for inpatient treatment of malnutrition between January 2010 and December 2011 had their demographic-, anthropometric- and clinical characteristics recorded and analysed, as well as the outcome of admission.

Results. Of the 227 children admitted during the study period, 179 (64.6%) were severely malnourished and 98 (35.4%) had moderate malnutrition. One-hundred-and-eleven children died during admission, an overall case -fatality rate of 40.1%. Mortality was significantly higher among severely malnourished children compared to those with moderate malnutrition, (46.9% vs 27.6%, OR 3.0 (95% CI 1.7 to 5.3)). Comorbid pneumonia and gastroenteritis were significant predictors of mortality – , OR 2.0 (95% CI 1.2 to 3.4) and 1.9 (95% CI 1.1 to 3.2) respectively.

Conclusion. Case -fatality rates for childhood malnutrition remain high, despite adoption of the WHO treatment guidelines. A need exists for improved adherence to the WHO guidelines and periodic clinical audits to reduce deaths from childhood malnutrition to meet the WHO mortality target of less than 5% and improve child survival.

Key words: childhood malnutrition, case -fatality rates, WHO guidelines for severe malnutrition,

Worldwide an estimated 8.1 million children die each year before they reach their 5th birthday and 99% of these are in the developing world.[1-2] Malnutrition is associated with more than 50% of these deaths.[3-4] Malnutrition is therefore an important risk factor for the burden of disease in developing countries.[5]

The hospital management of severe malnutrition is an important component of a comprehensive approach to the problem of undernutrition.[6] A review of case management worldwide has revealed a median case -fatality rate of approximately 25%, with rates in some hospitals as high as 50%.[6-8] Many of these deaths are avoidable and are due to outdated procedures and protocols, and a lack of familiarity with modern management practices.[6]

The World Health Organization (WHO) developed consensus treatment guidelines to help improve the quality of hospital care for malnourished children and suggests that, with strict adherence, mortality should be less than 5%.[9-10] Case-fatality rates greater than 20% are considered unacceptable, 11% to 20% is poor, 5% to 10% is moderate, 1% to 4% is good and less than1% is excellent.[11] Implementation studies of the guidelines have shown improvements in case death rates.[7-9]

The WHO conducted training in Swaziland on the inpatient treatment of severely malnourished children in 2003. The training was in response to a rising incidence of severe malnutrition. Case -fatality rates at Mbabane Government Hospital at the time were in excess of 50%.[12] During this period there were no special guidelines in use on the treatment of severe malnutrition.

However, it was not until 2007 that the WHO guidelines for the inpatient treatment of severely malnourished children were fully adopted under a programme called the Integrated Management of Acute Malnutrition (IMAM). This study was conducted to determine the case -fatality rate post-adoption of the WHO-recommended guidelines and to evaluate the level of adherence to the guidelines at Mbabane Government Hospital.

Aims and objectives

The primary objective was to determine the case -fatality rate for childhood malnutrition post-implementation of the WHO guidelines for the inpatient treatment of severely malnourished children.

The secondary objective was to determine the level of adherence to the WHO treatment guidelines.

Methods

Setting and participants

A retrospective observational study was conducted in the paediatric unit at Mbabane Government Hospital. It is the national referral hospital for Swaziland and also serves as a primary care facility for Mbabane and the surrounding areas.

Inclusion criteria were all children under 5 years admitted with malnutrition (defined according to the WHO definition)[11] between the months of January 2010 and December 2011.

Data collection

Individual participant information about presenting history, anthropometrics, clinical findings, co-morbid conditions and the outcome of each admission was abstracted from patients' notes using a structured form. Data was then entered into a Microsoft Office Access database.

Permission to access patient records was obtained from the Senior Medical Officer, Mbabane Government Hospital. The study protocol was approved by the Main Ethics Committee of the University of Pretoria's Faculty of Health Sciences and the Scientific and Research Ethics Committee of Swaziland.

Analysis

Stata release 11 (Stata LP, Texas, USA) was used for statistical analysis. Data was described, using standard statistics for continuous and categorical variables. Categorical variables were compared with the Chi2 test and medians were compared using the Wilcoxon rank sum test. Multivariable logistic regression analysis was used to identify risk factors for death. Significant variables in the univariate analyses ($p < 0.30$) were included in a multivariate model. The final model was obtained through the backward-stepwise procedure. The Pearson Chi2 goodness- of-fit test was used to determine the fit of the model. OR and their 95% CI are specified where applicable. A p value <0.05 was considered statistically significant.

Results

Two-hundred-and-seventy-seven children were admitted during the period covered by the study. Of these children 119 (43.0%) were females. The median age of admission was 12 months (IQR 7 to 17 months) (Table 1).

Table 1: Demographic and clinical characteristics of participants

Characteristics	Overall n = 277
Demographic factors	
Female	119 (43.0)
Median age	12 (IQR 7 to 17)
Nutritional status	
Severe	179 (64.6)
Oedematous	88 (31.8)
HIV profile	
Negative	103 (37.2)
Positive	113 (40.8)
On ART	40 (35.4)*
ART started during admission	8 (20.0) †
Exposed	52 (18.8)
Unknown	9 (3.2)
Co-morbid conditions	
Tuberculosis	87 (31.4)
Diagnosed during admission	66 (75.9) ‡
Pneumonia	124 (44.8)
Gastroenteritis	183 (66.1)
Other	20 (7.2)
Herbal intoxication	3
Kaposi Sarcoma	1
Severe anaemia (transfused Hb<6g/dl)	14
Paralytic ileus	1
Cryptococcal meningitis	1

*Of those HIV positive; † of those on ART; ‡ of those treated for TB

Ninety-eight children (35.4%) had moderate malnutrition and 179 (64.6%) had severe acute malnutrition (SAM). Of the 179 who had SAM, 91 (50.8%) were severely wasted and 88 (49.2%) had oedematous SAM.

One-hundred-and-three children (37.2%) were HIV -negative, 113 (40.8%) were HIV -positive, 52 (18.8%) were HIV -exposed and 9 (3.2%) were classified as of unknown HIV status. Of the 113 children who were HIV- positive, 40 (35.4%) were on antiretroviral therapy treatment (ART) and only 8 of them were initiated on ART during the admission period. Among those with SAM, HIV -positive children were significantly more likely to be wasted compared to HIV -negative children (OR 2.2, 95% CI 1.1 to 4.5).

Eighty-seven children (31.4%) were treated for Tuberculosis (TB). In 66 of the 87 children, (75.9%) TB was diagnosed during the admission period. Diagnosis was based on clinical

suspicion in children with persistent fever despite at least seven days of intravenous antibiotics, failure to gain weight, suspicious chest radiograph or the clinician's discretion. HIV -positive children were more likely to be treated for TB compared to HIV -negative ones (OR 3.1, 95 CI 1.6 to 5.8).

One-hundred-and-twenty-four children (44.8%) were diagnosed with Pneumonia. The diagnosis of Pneumonia was more likely in HIV-positive children compared to HIV-negative children (OR 2.6, 95 CI 1.4 to 4.6). One-hundred-and-eighty-three children (66.1%) had gastroenteritis (GE). There was no statistically significant difference in the occurrence of GE between HIV -positive- and HIV -negative children.

Fourteen children had severe anaemia that necessitated blood transfusion (Haemoglobin < 6g/dl). Four children had concomitant herbal intoxication on admission. One child had cryptococcal meningitis, one had Kaposi Sarcoma and one child developed paralytic ileus during the course of treatment.

OUTCOMES

One-hundred-and-eleven (40.1%) of the 277 children died in hospital, with 31 deaths (27.9%) occurring within 48 hours of admission. Mortality was significantly higher among patients with SAM compared to those with moderate malnutrition (46.9% vs 27.6%, p < 0.001). Among patients with SAM, no significant difference existed in mortality between the two types of malnutrition (oedematous SAM 48.9% vs severe wasting 45.1%, p= 0.61)

Several factors were identified as poor prognostic factors for mortality in the univariate analysis (Table 2).

Table 2: Univariate analysis (crude odds ratios) for prognostic factors for mortality

Variable	Odds ratio (95% CI)	P value
Sex		
Female	Reference	-
Male	1.1(0.7 – 1.8)	0.68
Age		
0 – 6	Reference	-
7 – 12	0.6 (0.3 – 1.1)	0.083
13 – 24	0.4 (0.2 – 0.8)	0.005
25 – 60	0.6 (0.2 – 1.8)	0.35
Type of malnutrition		
Non-oedematous	Reference	-
Oedematous	1.7 (1.0 – 2.8)	0.042
Severity of malnutrition		
Moderate	Reference	-
Severe	2.3 (1.4 – 4.0)	0.002
HIV status		
Negative	Reference	-
Positive	1.8 (1.0 – 3.1)	0.045
Exposed	2.3 (1.2 – 4.6)	0.016
Unknown	2.9 (0.7 – 11.6)	0.130
Tuberculosis	0.8 (0.5 – 1.4)	0.45

Gastroenteritis	1.7 (1.0 – 2.9)	0.048
Pneumonia	1.7 (1.0 – 2.7)	0.041

However, after multivariable logistic regression analysis, 4 factors remained significant predictors of mortality (Table 3). No significant difference existed in mortality between children aged 0 to 6 months compared to those aged 7 to 12 months (OR 0.5, 95 % 0.3 to 1.0). However, children aged 13 to 24 months fared much better compared to those aged six months and below (OR 0.3, 95% CI 0.2 to 0.6).

Table 3: Multivariate analysis odds ratios for factors significantly associated with mortality

Variable	Odds Ratio (95% CI)	P value
Age		
0 – 6	Reference	-
7 – 12	0.5 (0.3 – 1.0)	0.051
13 – 24	0.3 (0.2 – 0.6)	0.001
25 – 60	0.5 (0.1 – 1.4)	0.181
Severe malnutrition	3.0 (1.7 – 5.3)	< 0.001
Gastroenteritis	1.9 (1.07 – 3.2)	0.027
Pneumonia	2.0 (1.2 – 3.4)	0.009

Pneumonia and GE were significant predictors of mortality, (OR 2.0 (95% CI 1.2 to 3.4, p = 0.009) and 1.9 (95% CI 1.1 to 3.2, p = 0.027) respectively).

Mortality was highest among children of HIV -unknown status (55.6%), followed by HIV -exposed (50.0%), then HIV -positive (43.4%), and finally HIV -negative children (30.1%). However, HIV was not a significant predictor of mortality in the multivariate model and neither was TB.

The median length of hospital stay was ten days (IQR 6 to 15 days). Children who died had a shorter duration of hospital stay compared to those who were discharged (median 5 vs 12 days, p < 0.001).

Discussion

This study confirms that the case -fatality rates for childhood malnutrition remain unacceptably high at Mbabane Government Hospital, despite implementation of the WHO treatment guidelines. Even the case -fatality rate for moderate malnutrition was alarmingly high at, 27.55%, almost 6 times the WHO-established targets for severe malnutrition. The high case -fatality rates are indicative of poor adherence to the guidelines during case management.

Critical management principles were not being adhered to during case management. Firstly, hypoglycaemia was not being actively diagnosed or managed. Blood glucose levels were not measured routinely on admission. Furthermore, in cases where blood glucose level was not measured, a presumptive diagnosis of hypoglycaemia was not being made, contrary to what

is advised in the guidelines. Children were not being routinely given dextrose water to treat or prevent hypoglycaemia on admission. Some children were not started on therapeutic feeds for up to 24 hours after admission despite doctors' orders. Undiagnosed or poorly managed hypoglycaemia could have resulted in many deaths.

Secondly, hypothermia was not adequately managed. Malnourished children are unable to regulate their body temperature. During the first days of treatment their body temperature is dependent on the ambient temperature.[9] Care is best achieved if the children are nursed in a heated room. There were no heaters in the ward. Blankets were the only means employed to keep the children warm. The kangaroo technique was not being used in younger children. The lack of adequate heating left the children prone to developing hypothermia.

Caution must be exercised when diagnosing and treating dehydration in malnourished children. Appropriately rehydrating the dehydrated malnourished child is critical to survival and recovery.[9] In the study, children with a co-morbid diagnosis of GE were almost twice as likely to die as those without. The excess mortality risk for GE could be explained by deaths from dehydration and over hydration due to poor fluid management. Children with severe dehydration were not getting the close and careful monitoring they required during case management.

In severely malnourished children the usual signs of infection are often absent. Routine broad-spectrum antibiotics are therefore recommended.[9] In the study, the outcomes of admission could have been affected negatively by the prescribing practices of medical officers. Children with a co-morbid diagnosis of Pneumonia were almost twice as likely to die as those without. Some children were put on oral antibiotics when their clinical condition warranted intravenous therapy. Second-line antibiotics were not routinely prescribed to children with continued signs of infection after 48 hours of first-line therapy. Furthermore, the prescription choices were often limited by the frequent drug stock-outs that affected the hospital.

There were many causes of poor adherence to the management principles. The staffing in the paediatric unit was less than adequate. At times there was only one nurse on duty taking care of more than 30 admitted children. The poor staffing levels resulted in the poor monitoring of children, with the nurses failing to identify or appropriately manage critically ill children.

Furthermore, training on the use of the guidelines was not frequent and resulted in a knowledge gap in the care of malnourished children. The lack of knowledge on the care of malnourished children was further worsened by staff attrition through the loss of trained staff during the annual staff rotation between the various units in the hospital. The staff morale was low because of the poor conditions of service. Low staff morale, poor staffing levels and lack of knowledge due to infrequent training on the use of the guidelines contributed greatly to suboptimal care.

Lack of proper and adequate laboratory support negatively affected case management. Routine tests ordered during case management were often not available or inaccurate results were provided. Poor laboratory support made the management of children with electrolyte disturbances or severe anaemia difficult, negatively affecting case management.

HIV and TB

The prevalence of HIV among the study participants was 40.8%, which is comparable to that of other African studies that reported figures of between 17% and 54%.[13-14] As described earlier in other studies, HIV -positive children presented more with wasting compared to oedematous malnutrition and were up to six times more likely to die.[13] However, in contrast to these studies, in this study sample HIV was not a significant predictor of mortality. This lack of significance might be due to fundamental flaws in case management that even rendered the participants' HIV status unimportant.

The diagnosis of TB in children is a challenge and is even more difficult in malnourished and HIV-positive children. Frequently tuberculin skin tests are falsely negative and extrapulmonary TB is more common.[13] In all the 66 children who were started on anti-TB treatment during admission, the diagnosis was based on clinical suspicion. No confirmatory tests to demonstrate the presence of Mycobacterium TB were done, raising the question of how many children actually had TB. The diagnosis of co-morbid TB in this study was not associated with increased mortality.

Study limitations

The study was retrospective, so analysis of risk factors associated with mortality was limited by the information that could be obtained from the patient charts. Information on various other prognostic factors was either missing or poorly recorded and was of no use to the study.

Conclusion

Case -fatality rates for childhood malnutrition remain very high at Mbabane Government Hospital despite the implementation of the WHO guidelines. Poor adherence to guidelines during case management is the cause of the persistently high case -fatality rates.

Recommendations

Reduced case -fatality rates can be achieved through adequate staffing levels, periodical training on the use of the guidelines, and refresher courses. The paediatric unit must introduce periodical clinical audits and mortality review meetings to identify and address factors associated with excess mortality. Adoption and implementation of the affordable Kangaroo method is beneficial for hypothermia. The hospital must fully address operational factors that negatively affect case management such as drug stock-outs and poor laboratory functionality

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