A STUDY ON THE EFFECT OF HIV INFECTION ON THE DURATION OF THE STABILIZATION PHASE OF CHILDREN WITH SEVERE ACUTE MALNUTRITION AT THE UNIVERSITY TEACHING HOSPITAL, DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH, LUSAKA, ZAMBIA

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A dissertation submitted in partial fulfilment of the requirement for the award of the degree of Master of Medicine in Paediatrics and Child Health

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DECLARATION

I hereby declare that this dissertation represents my own work and has not been presented either wholly or in part for a degree at the University of Zambia or any other University

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ABSTRACT

Title: The Effect of HIV Infection on the Duration of the Stabilization Phase in Children with Severe Acute Malnutrition at the University Teaching Hospital, Lusaka, Zambia.

Background: Severe Acute Malnutrition (SAM) is a major cause of under 5 mortality in developing countries. The prevalence of HIV infection in children with SAM is high. HIV infection complicates the clinical presentation and outcome of SAM. The aim of this study was to determine the effect of HIV infection on the duration of the stabilization phase in children with SAM admitted to the malnutrition ward at the University Teaching Hospital, Lusaka. Specifically the study compared the duration of the stabilization phase between HIV-infected and HIV-uninfected children with SAM, mortality between these two groups and determined whether being on Highly Active Antiretroviral Therapy (HAART) had an effect on the duration of the stabilization phase.

Methods: In this analytical observational cohort study, children were recruited from the malnutrition ward at UTH from November 2014 to April 2015. The HIV status of each child was determined using age appropriate methods in order to assign to a corresponding arm of the study depending on the result. Enrolled children were followed up until stabilization was achieved. The number of days to stabilization and mortality in each arm was recorded over this period.

Results: A total of 170 children were recruited. There were 87 males and 83 females. The median age was 19 months (IQR 6, 49). There were 90 patients (52.9%) that were HIV-infected and 80 patients (47.1%) that were HIV-uninfected. There were 84 children (49.4%) with marasmus and 57 children (33.5%) with kwashiorkor. A total of 95 children (55.9%) were severely stunted. The mean number of days to stabilization was 6.7 days in the HIV infected children and 4.9 days in the HIV-uninfected (P-value <0.01). The mortality rate in the HIV-infected children was 17.8% compared to 7.5% in the HIV-uninfected children (P-value= 0.05). The mean number of days to stabilization was 5.8 days in the children on HAART and 6.6 days in the children not on HAART (P-value=0.36).

Conclusion: The study shows that HIV infection prolongs the duration of the stabilization phase and the mortality is higher in the HIV-infected children. It also shows that being on HAART doesn't affect the duration of the stabilization phase.

DEDICATION

I dedicate this study to my amazing wife, Cindy and our wonderful children, Chisola, Chanda and Maria whose support gave me the strength to complete this process.

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LIST OF ACRONYMS AND ABBREVIATIONS

SAM	Severe Acute Malnutrition
MUAC	Mid-Upper Arm Circumference
SD	Standard Deviation
CMAM	Community Management of Acute Malnutrition
RUTF	Ready to Use Therapeutic Food
F75	Formula 75
F100	Formula 100
HEPS	High Energy Protein Supplement
HIV	Human Immunodeficiency Virus
UTH	University Teaching Hospital
WHO	World Health Organization
AIDS	Acquired Immunodeficiency Syndrome
HAART	Highly Active Antiretroviral Therapy
CD4	Cluster of Differentiation
PCOE	Paediatric Centre of Excellence
DNA PCR	Deoxyribonucleic Acid Polymerase Chain Reaction
FBC	Full Blood Count
PTB	Pulmonary Tuberculosis
PDD	Persistent Diarrheal Disease
AGE	Acute Gastroenteritis

OPERATIONAL DEFINITIONS

1. **Marasmus:** Another term used for this condition is severe wasting. Children with marasmus have Wt/ht less than -3SD or MUAC less than 11.5cm but no oedema. A child with severe wasting has lost fat and muscle and appears like “skin and bones”.

2. **Kwashiorkor:** Another term used for this is SAM with oedema. Children with kwashiorkor have bilateral pitting nutritional oedema. Oedema is swelling from excess fluid in the tissues. Oedema is usually seen in the feet and lower legs and arms. In severe cases it may also be seen in the upper limbs and face.

3. **Marasmic-Kwashiorkor:** Another term used for this is SAM with severe wasting and oedema. These children have Wt/ht less than -3SD or MUAC less than 11.5cm and bilateral pitting nutritional oedema.

4. **Grading of Oedema:**
    a. (1+) or mild: both feet
    b. (2+) or moderate: both feet, plus lower legs, hands, or lower arms
    c. (3+) or severe: generalized oedema including both feet, legs, hands, arms and face

1. Background

Severe Acute Malnutrition (SAM) is responsible for 1.5 million of the 10 million child deaths that occur worldwide annually.[1, 2] Millennium Development Goal 4 which aims to reduce child mortality by two thirds by the end of 2015 will not be achieved without adequately tackling the problem of SAM. According to the Zambia Demographic Health Survey 2013-2014, about 40 percent of the under 5 children in Zambia are stunted and 2% are severely wasted.[3] About 2000- 2500 patients are admitted annually with SAM to the University Teaching Hospital (UTH) malnutrition ward in Zambia. The case fatality rate in this ward is 30-40% according to quarterly ward mortality audits. Malnutrition refers to deficiencies, excesses or imbalances in intake of energy, protein and/or other nutrients. Contrary to common usage, the term 'malnutrition' correctly includes both under-nutrition and over-nutrition. For the purpose of this study, malnutrition will be used to refer to under-nutrition. SAM is defined as oedema of both feet or severe wasting. Severe wasting is defined as MUAC <11.5cm or Wt/ht SD < -3. Children with SAM have lowered resistance to infection and are therefore prone to more frequent and severe infections.[4] Infection also contributes to malnutrition hence a vicious cycle is formed. Some of these infections are diarrhoea, pneumonia and pulmonary tuberculosis. Malnutrition is strongly associated with an increased risk of mortality from diarrhea and acute respiratory infection.[5] These children are in danger of death from hypoglycaemia, hypothermia and fluid overload. The children with SAM require specialized treatment because their physiology is abnormal as a result of reductive adaptation.[6] This is a process of slowing down of the body's systems in order to allow survival on limited calories.[6]

The current approach towards the treatment of acute malnutrition is Community Management of Acute Malnutrition (CMAM).[7] Under CMAM, children with Moderate Acute Malnutrition (MAM) and SAM with no medical complications are managed in the community at the local clinic while those with medical complications are admitted for inpatient care. Inpatient care is divided into three phases: stabilization , rehabilitation and follow up. The stabilization phase of treatment ends when the child readily finishes F75 by mouth and oedema has reduced. It indicates that infections are under control, the liver is able to metabolize nutrients, and other metabolic abnormalities are improving. The child may also smile at this stage. When this occurs, it signifies transition from F75 to a higher calorie feed, F100 or RUTF. The stabilization phase takes 2 to 7 days in most children

with SAM however experience from the malnutrition ward at the University Teaching Hospital has shown that it takes longer in HIV-infected children (unpublished data).

The prevalence of HIV infection among children with SAM has been reported to range from 22 to 54%.[8, 9, 10, 11] HIV infection complicates the clinical presentation and outcome of SAM. The case fatality rate for children with SAM in Africa is over 20% and HIV infection is partly responsible for this.[12, 13] Despite reduced mortalities noted with strict compliance to treatment recommendations; the case fatality rate is still well above the expected WHO levels.[14, 15-17] Apart from HIV-infection, other contributing factors to the high case fatality rate seen include over prescription of intravenous fluids and blood transfusion.[8, 18, 19]

The nutritional outcome of HIV-infected patients with SAM is poorer than those that are not infected. This could be explained by recurrent illnesses such as diarrhoea which are common in HIV-infected children due to their lower immunity. A study done in 2004 in Malawi reported that weight gain was significantly slower in the HIV-infected children.[20] This study looked at children that were recruited after a period of hospital stabilization and were being managed in a nutritional rehabilitation unit.

A study in Niger involved children below the age of 5 hospitalised at an intensive therapeutic feeding centre at Niamey National Hospital Pediatric Ward.[21] It was a retrospective study and the children were followed up for the intensive renutrition phase which was defined as the period from admission until the date of death, discharge, transfer to another hospital or date when they left against medical advice. Their findings were that the duration of renutrition was longer in HIV-infected than non-infected children. This study was retrospective and done in a country with a relatively low prevalence of HIV, 0.8% in adults and 9% in the study. The prevalence of HIV infection is much higher in Zambia at about 14.3% in adults.[22] No studies have been done that compare the duration of the stabilization phase in HIV-infected and HIV-uninfected children with SAM.

HIV-infected children with SAM are more likely to die than those that are not HIV infected.[10,23,24-26] Several studies done in Malawi [9,18,23,24,26] showed higher mortality in HIV-infected children with SAM. One study followed up children from admission to the nutritional rehabilitation unit until 4 months post-discharge and discovered a significantly greater mortality among the HIV-infected compared to the uninfected.[23] Another study

reviewed children with SAM admitted to a nutritional rehabilitation unit and compared the clinical presentation and case fatality ratio for HIV- infected against the HIV-uninfected and found mortality to be higher in the HIV-infected children.[10] In South Africa a study done showed that mortality was 6 times more likely in HIV-infected children compared to the non-infected children admitted to malnutrition wards at three tertiary academic hospitals.[25]

Early initiation of HAART in infants and children correlates to decreased mortality and decreased rates of progression to advanced AIDS stages.[27, 28] WHO recommendations are that in children with SAM, HAART should be initiated when they have stabilized and are out of the acute phase of illness.[29, 30] It has been established children initiated on HAART with weight/age <-3 z score(WAZ) at baseline have a higher mortality than those with WAZ >-3 as shown by several studies done in different settings.[31-33] A systematic review done in 2012 on the care of HIV-infected children with SAM concluded that these children are able to respond favorably to HAART but that evidence was insufficient with respect to the optimal timing of initiation.[34]

This study set out to compare the duration of the stabilization phase and mortality between HIV-infected and HIV-uninfected children with SAM. It also looked to determine if being on HAART affected the duration of the stabilization phase.

2. Statement of the Problem

The prevalence of HIV infection is high in children with SAM and mortality usually occurs early during their admission. It has not been determined how HIV infection affects stabilization and overall nutritional recovery. It has been reported that pathogens causing systemic and gastrointestinal infections in HIV-infected and HIV-uninfected children with SAM are similar. However, children infected with HIV present with more severe infections associated with prolonged anorexia resulting in a slower recovery and in some cases with poor response when compared to HIV-uninfected children with SAM.

3. Study Justification

Mortality is as high as 2-6 times more likely in the HIV-infected with SAM when compared to the HIV-uninfected children with SAM hence interventions are necessary in the initial management to reduce this elevated mortality. This will only be possible with improved knowledge of differences that exist between HIV-infected and HIV-uninfected children during the stabilization period. Perhaps HIV-infected children with SAM may require a longer period of stabilization in order to improve their treatment outcome.

4. Research Question

What is the effect of HIV infection on the duration of the stabilization phase in children with SAM at UTH, Lusaka?

5. Hypothesis

HIV infection prolongs the duration of the stabilization phase in children with SAM at UTH, Lusaka.

6. Objectives

6.1 General Objective

To determine the effect of HIV infection on the duration of the stabilization phase in children with SAM.

6.2 **Specific Objectives**

1. Determine the duration of the stabilization phase in HIV- infected and HIV-uninfected children with SAM at UTH, Lusaka.
2. Compare mortality between HIV-infected and HIV-uninfected children with SAM in the stabilization phase at UTH, Lusaka.
3. Determine if HAART affects the duration of the stabilization phase in HIV-infected children with SAM at UTH, Lusaka.

7. **Literature Review**

The prevalence of malnutrition in developing countries remains unacceptably high.[1,2] It is estimated that there are more than 150 million malnourished children under the age of 5 years in developing countries.[4] More than 20 million children suffer from severe malnutrition.[5] The prevalence of severe wasting in children under 5 years in Zambia is 2%.[3] In most developing countries, case fatality rates in hospitals treating SAM remain at 20–30%. CMAM has dramatically reduced case fatality ratios and increased the numbers receiving care.[7] Under CMAM, acute malnutrition is classified as Moderate Acute Malnutrition (MAM), SAM without medical complications and SAM with medical complications. MAM is defined as wasting (Wt/ht < -2SD or MUAC >11.5cm <12.5cm) without oedema. MAM is managed in the community level with the Supplementary Feeding Program (SFP). Under SFP, patients that meet the criteria for MAM are identified and enrolled. They are given food supplements, dewormed, receive Vitamin A and are followed up every 2 weeks to monitor response. The food supplement given is High Energy Protein Supplement (HEPS). HEPS, is an extruded Corn-Soya Blend (CSB), consisting of corn meal, soya and sugar, fortified with vitamins and minerals. It is used mainly to prevent the development of SAM in children with MAM. In SAM with no medical complications, the child is usually clinically well, alert and has a good appetite. SAM without medical complications is also managed in community level through the Outpatient Therapeutic Program (OTP). Under the OTP, children are treated at home with Ready to Use Therapeutic Food (RUTF) with weekly monitoring at designated local clinics. RUTF is an energy dense lipid paste consisting of peanut butter, sugar, milk, vegetable oil and a vitamin/mineral supplement and each 92gm sachet contains 500 kcal of energy. A child with SAM and medical complications is anorexic, lethargic and may present with fever, anaemia, pneumonia, diarrhoea with severe dehydration and other medical complications which require hospital management. This study looks at children admitted for inpatient care.

Inpatient care is divided into three phases:

- **Initial treatment**: This is the stabilization phase in which life-threatening problems are identified and treated as follows:

1. **Prevention and Treatment of Hypoglycemia**: The children are given frequent and small feeds to prevent hypoglycemia and provide nutrients during the initial period of stabilization. If hypoglycemic, 10% dextrose is given orally, by nasogastric tube or intravenously depending on the level of consciousness of the child.[6]
2. **Prevention and Treatment of Hypothermia**: The room temperature is kept between 25-30^{o}C to prevent hypothermia. Other measures include ensuring that the children are fully covered at all times and promptly changing all wet clothes and beddings. If hypothermic, it is advised to actively rewarm with extra blankets, heaters or kangaroo mother care.[6]
3. **Management of Shock**: Shock is an acute, dramatic syndrome, characterized by inadequate circulatory provision of oxygen, so that the metabolic demands of vital organs and tissues are not met. It is characterized by severe weakness, lethargy, or unconsciousness, cold extremities, and fast, weak pulse. It is caused by diarrhoea with severe dehydration, haemorrhage, burns, or sepsis. In SAM, shock is treated using Half-strength Darrow's solution with 5% glucose (dextrose). It is given intravenously over 1 hour at a dose of 15mls/kg/hr. This is repeated after one hour if improvement is noted but stopped if the child is noted to worsen. Pulse and respiratory rates are monitored every 15 minutes. A child with shock who worsens on intravenous fluids is considered to have septic shock and is treated with transfusion of fresh whole blood.[6]
4. **Management of Very Severe Anaemia**: A child with SAM has very severe anaemia when the haemoglobin level is below 4g/dl. This is treated with a blood transfusion of whole blood. If there are signs of congestive cardiac failure then packed cells are given instead.[6]
5. **Emergency Care for Corneal Ulceration**: Corneal ulceration is a break in the surface of the cornea. Corneal ulceration is very dangerous. If there is an opening in the cornea, the lens of the eye can extrude and cause blindness. If a child has corneal ulceration, Vitamin A is given immediately. One drop atropine (1%) is put into the affected eye(s) to relax the eye and prevent the lens from pushing out. Tetracycline eye drops are also given and the affected eye(s) is bandaged.[6]

6. **Management of Watery Diarrhoea**: It is difficult to determine dehydration in a severely malnourished child, as the usual signs of dehydration (such as lethargy, sunken eyes) may be present in these children all of the time, whether or not they are dehydrated. If there is a history of watery diarrhoea or vomiting and weight loss, dehydration is assumed and the child is treated with Rehydration Solution for Malnutrition (ReSoMal). It is a modification of the standard WHO Low Osmolarity Oral Rehydration Solution (ORS). ReSoMal contains less sodium, more sugar and potassium than standard ORS and is intended for rehydration of severely malnourished children with diarrhoea. It should be given by mouth or by nasogastric tube.[6]
7. **Antibiotics**: All children with SAM are given antibiotics for presumed infection. Antibiotic recommendations may vary from place to place based on local patterns of sensitivity. In the malnutrition ward at UTH, Lusaka, isolations and sensitivity patterns from blood cultures led to a combination of Ceftriaxone and Chloramphenicol being used as first line treatment. The most frequent isolates are *Staphylococcus coagulase negative*, *Klebsiella pneumoniae* and *Escherichia coli*. Selection of antibiotics also depends on the presence or not of complications such as septic shock, 3+ dermatosis and urinary tract infections.[6]
8. **Cautious Feeding**: To prevent death, feeding is started as soon as possible with F-75, the "starter" formula used until the child is stabilized. F-75 is specially made to meet the child's needs without overwhelming the body's systems at this early stage of treatment. F-75 contains 75 kcal and 0.9 g protein per 100 ml. F-75 is low in protein and sodium and high in potassium and carbohydrate, which is more easily handled by the child and provides much-needed glucose.[6]

- **Rehabilitation**: Intensive feeding is given to recover most of the lost weight, emotional and physical stimulation are increased, the mother or carer is trained to continue care at home, and preparations are made for discharge of the child. In this phase F-100 or RUTF is given. F-100 and RUTF are higher calorie; higher protein "catch up" feeds intended to rebuild wasted tissues. RUTF is

made from cooked, ground peanuts, oil, sugar, powdered milk and micronutrients. It has a long shelf life of 24 months and provides 500kcal per sachet. F100 is made from dried skimmed milk or dried whole milk with sugar, vegetable oil and complex mineral vitamin mix and provides 100 kcal and 2.9 g protein per 100ml.

- **Follow Up**: after discharge, the child is referred to the OTP centre at their local clinic where they are weighed weekly and RUTF and oral haematinics are given. The aim is to prevent relapse and ensure the continued physical, mental and emotional development of the child.

There is a high prevalence of HIV infection in children with SAM in urban referral hospitals receiving inpatient care.[35] HIV infection has altered the epidemiology, clinical presentation, pathophysiology, case management, and survival of severely malnourished children.[35] The varied clinical presentation of HIV-uninfected children with malnutrition is determined by the complex interactions between specific nutrient deficiencies, infections, and stress within each individual.[36] In the past, nutrition rehabilitation units typically admitted sick severely malnourished children during periods of food insecurity or in the post-weaning period (6–36 months old).[35] With the pandemic of HIV, more and more children outside this age range are being admitted for inpatient care. These are children who come in with multiple pathologies and complications and have higher case fatality rates.

HIV infection and SAM are closely related. HIV-infection can result in SAM due to repeated opportunistic infections which make adequate nutrition impossible.[1] SAM is a marker for severity of HIV-infection. Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy is an AIDS defining condition. A study done in a South African rural district hospital demonstrated that HIV- infected children were more likely to suffer from SAM than the HIV-uninfected children.[37]

HIV-infected children with SAM have high case fatality rates. This is because they are more likely to have complex medical management case issues. Case fatality in severe malnutrition is high because of the concurrence of multiple infections and metabolic

adaptations. When this synergism is compounded by HIV infection the case-fatality rate increases many times.[35]

Marasmus is more common in HIV-infected children with SAM compared to kwashiorkor.[9,10,14,38,40] In a study done in Burkina Faso, 428 HIV-infected children with SAM admitted to the national hospital were reviewed and it was found that 63% had marasmus compared to 13% with Kwashiorkor.[38] In Tanzania of the 102 children studied, it was found that 51% had marasmus versus 28.5% with kwashiorkor.[40] It was however found that Kwashiorkor was more frequent in HIV-infected children than marasmus in another study which surveyed 12 urban and rural nutritional rehabilitation units in Malawi in 2008.[41]

Despite earlier theories that HIV-infected children with SAM were vulnerable to different infections from the HIV-uninfected children, a study done in Zambia showed that they are prone to similar systemic and intestinal infections.[9] Both the seropositive and seronegative children are prone to intestinal infections by organisms such as *Cryptosporidium parvum* and the course of the disease is similar.[42] It was however noted that HIV infection had an influence on the nutritional states of the children. The response to antibiotics in HIV-uninfected children is poor contributing to a higher mortality in these children.[37] It is postulated that this is due to impaired immune function in the HIV-infected children.

SAM is associated with both cell mediated and humoral immunosuppression. HIV infection exacerbates this suppression. A study done in Uganda at Mulago Hospital Pediatric ward compared clinical features, hematological findings and CD4 counts in children with SAM in relation to HIV infection.[43] The HIV-infected children showed a significantly lower immunity. Another study done in Zambia showed that HIV-uninfected children with SAM had normal CD4 counts but that the HIV-infected with SAM had depleted CD4 counts which even declined further despite nutritional recovery.[44]

Nutritional recovery in HIV-infected children with SAM is slower than the non-infected children. One study in 2004 reported that weight gain was significantly slower in the HIV-infected children.[20] This study looked at children that were recruited in a nutritional rehabilitation unit after a period of stabilization in the hospital. In the same year two studies were done concurrently in Malawi on children with SAM discharged from the nutrition unit in Blantyre. These children were put on RUTF and followed up until they

achieved 100% of their weight for height. One study looked at HIV-infected children[45] and the other at non-infected children.[46] The mean time to recovery was much longer in the HIV-infected children.

8. Methodology

8.1 Study Design

It was an analytical observational cohort study.

8.2 Target Population

Children with SAM admitted to the malnutrition ward at UTH, Lusaka.

8.3 Study Population

Children with SAM aged between 6 and 59 months admitted to the malnutrition ward at UTH, Lusaka who met the eligibility criteria.

8.4 Study Site

The study was conducted in the malnutrition ward of the Department of Paediatrics at the University Teaching Hospital. This is a busy ward with a peak period of admission between the months of November and February. In this ward children with SAM undergo stabilization and rehabilitation.

8.5 Eligibility

8.5.1 Inclusion Criteria:

- Children aged between 6 and 59 months admitted to the malnutrition ward at the UTH Department of Paediatrics.
- Children whose parents gave consent
- Children whose parents agreed to HIV testing.

8.5.2 Exclusion Criteria:

- Consent not given to participate in the study.
- Consent not given by parents for HIV testing.
- Children with neurological impairment as it is difficult to assess return of appetite in these children.

8.6 Sample Size

The sample size was 170 and was calculated using Open Epi calculator for cohort studies assuming 95% confidence interval with power of 80%. The ratio of sample size was 1:1 with the percentage of unexposed with outcome put at 80% and those exposed put at 60%.

Two-sided significance level(1-alpha):	95
Power(1-beta, % chance of detecting):	80
Ratio of sample size, Unexposed/Exposed:	1
Percent of Unexposed (no HIV) with Outcome:	80
Percent of Exposed(yes HIV) with Outcome:	60
Risk Ratio detected:	0.75

Kelsey	
Sample Size – Exposed	85
Sample Size-Non exposed	85
Total sample size:	170

8.6.1 Sampling Method

Convenience sampling was used. All children admitted to the malnutrition ward at the UTH in Lusaka between November 2014 and February 2015 were invited to participate in the study.

8.7 Study Procedure

Parents of children with SAM admitted to the malnutrition ward at the UTH were approached and asked to participate in the study.

Upon consent to participate in the study and to have the HIV test done, the HIV status was determined. A drop of blood was collected from the finger of every patient for antibody tests (Determine 1 and 2, Unigold and in case of any discordant results Bioline). DNA PCR was done on all children less than 18 months with positive antibody tests and on those with negative antibody tests but born to HIV-infected mothers.

The HIV-infected children were assigned to one arm of the study and the non-infected to the other arm. Baseline data characteristics were collected from all the participants by way of data extraction sheets and this included: age, sex and area of residence.

A thorough clinical examination of each child recruited to the study was done and weight, height and mid- upper arm circumference were measured. The weight was done using a UNISCALE (mother-infant scale), the length measured using a length board and the height with a stadiometer. The weight for height, weight for age and height for age standard deviation scores were determined using the WHO reference cards based on 2006 WHO child growth standards. The type of malnutrition was also recorded.

The comorbidities were diagnosed based on clinical examination as well as laboratory evidence where possible. Blood was taken for Full Blood Count (FBC) and Liver Function Test, Urea and Electrolytes (LFT/UE) from all the participants. For this 2mls of blood was collected from the medial cubital vein and results processed at Paediatric Centre Of Excellence (PCOE) laboratory. Blood cultures and chest x-rays were done where indicated.

Treatment for malnutrition was commenced according to the WHO guidelines in both the HIV-infected and HIV-uninfected patients.

The duration of the stabilization phase was defined as the period from admission until the point at which the child was transitioned to receive F100 or RUTF. The stabilization phase ended when the child was finishing F75 by mouth and oedema reduced for those who had oedema on admission. Reduction in oedema was determined by a decrease in the grading of the oedema on clinical evaluation for example from 3+ to 2+.

8.8 Ethics Clearance

The research was approved by the University of Zambia Biomedical Research Ethics Committee (UNZABREC). Permission was sought from the UTH management through the Head of Department of Paediatrics and Child Health to carry out the research at the institution.

All guardians to participants were provided an adequately informed consent form and the purpose and nature of the study was explained in the language that they understood best. It was explained that there was no direct benefit of the study to the child but that the mother would benefit because she would know her HIV status and a plan of management could be made if found positive. The community would benefit from the study because the management of HIV-infected children with SAM could be improved. The only risk to the baby was mild pain and discomfort from the prick for HIV status determination and for laboratory investigations. Study information was handled carefully and stored securely to maintain confidentiality. Patients who declined to participate in the study were offered the same standard of care as those who agreed to participate. Further, guardians were allowed to withdraw from the study at any point without giving any reason.

8.9 Data Analysis

Data was entered and stored using Epidata version 3.1 software and analysis was done using SPSS version 21.0. All statistical tests were at 5% significance level. The age and duration of the stabilization phase (continuous variables) were expressed as means. The Pearson's chi-squared test was used for comparison of proportions between groups, and the Fisher's Exact P-value selected where appropriate. The relationship between study variables and mortality was examined using multivariate analysis. The cox proportional hazards regression analysis was used to explore (and adjust for) the effects of several variables such as HIV status and malnutrition type and comorbidities, known to affect stabilization time.

9.0 Results

Variable		n (%)	

9.1 Baseline demographic and clinical characteristics of population studied

A total of 170 children were recruited for the study from October 2014 to April 2015. The median age was 19 months with an interquartile range of (IQR 6, 49).

The sex distribution was almost equal comprising 87 males (51.2%) and 83 females (48.8%). (Table 1)

There were 52.9% (90/170) children who were HIV-infected and 47.1% (80/170) were HIV-uninfected. The 90 HIV-infected includes 31 children less than 18 months confirmed by DNA PCR. (Table 1)

The predominant type of malnutrition was Marasmus at 49.4% (n=84) followed by Kwashiorkor with 33.5% (n=57) and then Marasmic-Kwashiorkor 17.1% (n=29). There were 70.6% (n=120) children that were severely wasted and 77.6% (n=132) that were stunted with 55.9% (n=95) of these being severely stunted. The majority of the children were severely underweight for age accounting for 77.6% (n=132). (Table 1)

A total of 125 children had diarrhoea as a comorbidity; 68% (n=85) of these had acute diarrhea and 32% (n=40) had persistent diarrhoea. The second most common comorbidity after diarrhea was pneumonia accounting for 15.9% (27/170). Sepsis accounted for 5.9% (10/170) while Pulmonary Tuberculosis (PTB) accounted for 4.7% (8/170).

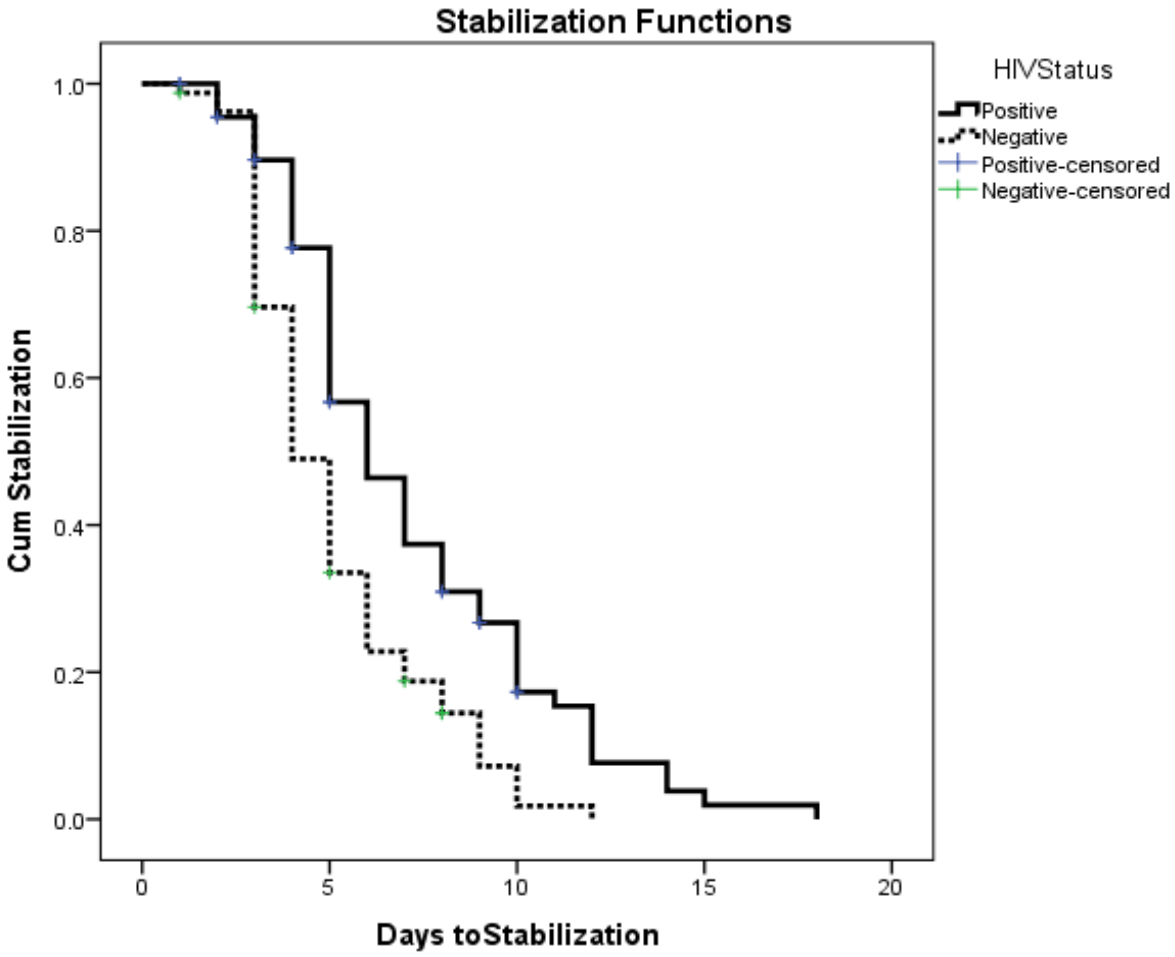
Sex	Male	87(51.2%)		
	Female	83(48.8%)		
HIV Serology	Positive	90(53%)		
	Negative	80(47%)		
Type of Malnutrition			**HIV Status**	
			Positive	**Negative**
	Marasmus	84(49.4%)	57(67.8%)	27(32.2%)
	Kwashiorkor	57(33.5%)	19(33.3)	38(67.7%)
	Marasmic-Kwashiorkor	29(17.1%)	14(48.2%)	15(51.8%)
Weight for Age z score				
	Severely Underweight	132(77.6%)	80(60.6%)	52(39.4%)
	Underweight	23(13.5%)	13(56.5%)	10(43.5)
	Not Underweight	15(8.8%)	6(40%)	9(60%)
Height for Age z score				
	Severely Stunted	95(55.9%)	55(57.9%)	40(42.1%)
	Stunted	37(21.8%)	24(64.9%)	13(35.1%)
	Not Stunted	38(22.3%)	18(47.4%)	20(52.6%)
Comorbidities:				
	Acute Diarrhea	85(50%)	42(49.3%)	43(50.7%)
	PDD	40(23.5%)	31(77.5%)	9(23.5%)
	Pneumonia	27(15.9%)	14(52.4%)	13(47.6%)
	Sepsis	10(5.9%)	6(60%)	4(40%)
	Tuberculosis (Probable)	8(4.7%)	4(50%)	4(50%)
Duration on HAART				
	< 1 month	9(42.8%)		
	1 –to < 6months	6(28.6%)		
	> 6 months	6(28.6%)		

Table 1: Summary of the demographic and clinical characteristics of the population studied.

9.2 Duration to stabilization and mortality.

One hundred and forty eight (87.1%) completed the stabilization phase while 12.9% (22/170) died during stabilization. The mean duration to stabilization was 5.8 days (SD=2.96). The mean duration to stabilization for the children with marasmus was 5.9 days while it was 5.4 days for those with kwashiorkor and 5.6 days for those with marasmic-kwashiorkor. This difference was not statistically significant, P-value = 0.60. The mean number of days to stabilization was 6.7 days for the HIV-infected and 4.9 days for the HIV-uninfected. This was statistically significant, P-value < 0.01. (Table 2). Using the log rank test, there was significant difference in the duration to stabilization between the two groups, P-value < 0.001. (Figure 1) The figure clearly shows the longer duration to stabilization in the HIV-infected children with SAM. When comparing stabilization after 7 days, the HIV-infected took longer to stabilize, Log Rank P-value = 0.025.

Figure 1. Stabilization duration by HIV status (Log rank P-value < 0.001)



It can be seen in figure 1 that the child with the shortest duration to stabilization was HIV-uninfected and took only 2 days. The child with the longest duration to stabilization took 18 days and was HIV-infected.

There was a significant association between the type of malnutrition and the HIV status. The HIV-infected children presented more frequently with marasmus 63.3% (57/90) versus 33.8% (27/80) HIV-uninfected. Among the HIV uninfected children, 47.5% (38/80) had kwashiorkor against 21.1% (19/90) in the HIV-infected group of children, P value < 0.01.

The majority of the HIV-infected children, 77.5% (31/40) had Persistent Diarrheal Disease (PDD) compared to 22.5% (9/40) HIV-uninfected. However this was not statistically significant, P-value=0.10. The number of cases of Acute Gastroenteritis (AGE), Pneumonia, Sepsis and PTB was almost equal between the two groups. The children with PDD took longer to stabilize, 6.4 days compared to those with AGE, 5.4 days and Pneumonia, 5.3 days but this was not statistically significant, P-value=0.41.

Out of the 90 HIV-infected children, 23.3% were on HAART. The duration on HAART ranged from 5 days to 16 months. The mean duration to stabilization for children on HAART was 5.8 days (SD = 4.12) and for those not on HAART it was 6.6 days (SD = 3.08), however, this difference was not significant with a P-value= 0.36.

In the Cox regression model, adjusting for age, sex, type of malnutrition, and coinfections, only HIV status was significantly associated with stabilization duration. The probability of stabilizing was increased by 85% with HIV negative status versus HIV positive status at any given time, and this result was statistically significant [Hazard Ratio (HR) = 1.85, 95% Confidence Interval (CI) = 1.27 – 2.71, P-value = 0.001].

Table 2. Cox regression analysis showed only HIV infection as a significant determinant of duration of stabilization.

Variable	P value
Age(months)	0.417
Sex	0.713
HIV Status	0.001
Comorbidity	0.393
AGE	0.126
PDD	0.151
Pneumonia	0.354
Malnutrition	0.820
Marasmus	0.535
Kwashiorkor	0.639

Mortality was higher in the HIV-infected group, 17.8% (16/90) compared to, 7.5% (6/80) in the HIV-uninfected group and this was marginally significant, P=0.05. The majority of the children who died in the HIV-infected group, 75% (12/16) were not on HAART but this was not statistically significant, P-value=0.86.

Table 3. Association between HAART and Mortality, P-value=0.86

		Died	
		Yes	No
HAART	Yes	4(25%)	17(23%)
	No	12(75%)	57(77%)
Total		16(100%)	74(100%)

		Died	
		Yes	No
HAART	Yes	4(25%)	17(23%)
	No	12(75%)	57(77%)
Total		16(100%)	74(100%) 100.0%

Marasmus was also marginally significantly associated with mortality, 72.7% (16/22), P-value=0.06. When the children with marasmus who were < -4SD were analyzed separately they had a significantly higher risk of dying, P-value <0.01. The weight for age was also associated with mortality. The severely underweight children, 95.5% (21/22) had a higher risk of mortality, P-value=0.03.

Table 4. Biavariate analysis for mortality association

Variable	Died		Survived		P
	N	%	N	%	
HIV status					
Negative	6	27.30%	74	50.00%	0.05
Positive	16	72.70%	74	50.00%	
Type of Malnutrition					
Marasmus	16	72.70%	68	45.90%	0.06
Kwashiorkor	4	18.20%	53	35.80%	
Marasmic-Kwashiorkor	2	9.10%	27	18.20%	
Comorbidity					
AGE	11	50.00%	62	41.90%	0.12
PDD	6	27.30%	28	18.90%	
Pneumonia	4	18.20%	17	11.50%	
Sepsis	1	4.50%	41	27.70%	
Height for age					
Severely stunted	13	59.10%	82	55.40%	0.75
Other	9	40.90%	66	44.60%	
Weight for age					
Severely underweight	21	95.50%	111	75.00%	0.03
Other	1	4.50%	37	25.00%	
Weight for height					
Less than -4SD	16	72.70%	62	41.90%	<0.01
Other	6	27.30%	86	58.10%	

HIV status, type of malnutrition, coinfection, weight for age, and weight for height variables were considered for multiple variable regression analysis predicting death. Using the backward selection method, only weight for height was significantly associated with mortality in the study children (P-value = 0.01).

Table 5. Multivariate analysis showing significant association between Wt/ht and death, P-value= 0.01

Variable	P value
Weight for Height	0.01

10. Discussion

The majority of the children in the study were stunted (77.6%). This means that they had acute exacerbations of already existing chronic malnutrition. Marasmus was the most common type of malnutrition among the HIV-infected children with SAM accounting for 63.3%. Kwashiorkor was more common in the HIV-uninfected children. This is similar to the results of other studies done in Burkina Faso[38] and Tanzania[40]. The study in Burkina Faso also found a predominance of Marasmus at 63% of the HIV-infected with SAM. The

one in Tanzania found that Marasmus accounted for 51% of the HIV-infected with SAM. Other studies done in Zimbabwe[39], Uganda[43], and Malawi[47] have shown similar results. Severe stunting was more common in the HIV-infected children reaffirming the impact that this infection has on the linear growth of these children. They were also significantly more underweight and more wasted than their uninfected counterparts. This was also found in a study in Malawi in 2012 that showed that HIV-infected children were generally more malnourished than HIV-uninfected children.[47] The height and weight for age and weight for height were significantly lower in the HIV-infected children compared to the HIV-uninfected in a study done in South Africa[48] which is similar to the findings in this study.

Diarrhoea was the most common comorbidity accounting for 73.5%. The majority of these, 68% had acute diarrhea and 32% had persistent diarrhea. Similar findings were noted in a study at UTH in 2011 where 67.3% of the 388 children with SAM evaluated presented with diarrhea.[49] The association between diarrhea and SAM is well documented.[50-53] Diarrhea increases the likelihood of mortality in children with SAM. The HIV-infected and uninfected children presented with similar comorbidities. There was no significant difference between the numbers of cases of AGE, Pneumonia, Sepsis or PTB in the two groups. The number of children with PDD was two times higher in the HIV-infected group than in the HIV-uninfected group but this was not statistically significant. This is comparable to the conclusion of a study done in Zambia[9] that systemic infections do not differ between the HIV-infected and HIV-uninfected children with SAM. Another study in South Africa[37] also determined that the HIV-infected children presented with the same disease syndromes as their HIV-uninfected counterparts but did so more frequently and with worse outcome.

There was no statistically significant difference in the duration to stabilization among the different types of malnutrition. A meta-analysis on HIV prevalence and mortality among children with SAM in sub-Saharan also noted that there was no difference in rates of nutritional recovery between patients with marasmus and kwashiorkor regardless of the HIV status.[36]

The mean number of days to stabilization was 6.7 days in the HIV-infected children and 4.9 days in the HIV-uninfected children. This difference was statistically significant. One study in Niger reviewed the duration of nutritional recovery in children with SAM from

admission until discharge from a nutritional rehabilitation unit and showed slower recovery HIV-infected children, 22 days vs 15 days in the HIV-uninfected children. The normal duration of the stabilization phase is 2-7 days however it was noted in this study that several children took longer than 7 days to stabilize particularly those with HIV infection whose mean number of days to stabilization was 11 days vs 9 days in the HIV-uninfected. This was statistically significant. The prolonged duration to stabilization in the HIV-infected children was because that they tended to be more anorexic. The child that took longest to stabilize (18 days) was HIV-infected and eventually diagnosed with PTB which contributed to the prolonged anorexia. Another HIV-infected child with prolonged duration to stabilization (12 days) had PDD with repeated episodes of diarrhea which contributed to the protracted poor general condition of the child.

Of the 90 HIV-infected children, 23% were on HAART prior to admission. These children took 5.8 days to stabilize compared to the children not on HAART who took 6.6 days, however, this difference was not statistically significant. Most of the children were started on HAART 2-4 weeks prior to their admission and they came to the hospital severely malnourished and with medical complications. It is possible that they were started on HAART while they had SAM and medical complications. This would be considered an inappropriate initiation of HAART.[31-33] This is because it is important to address malnutrition and its medical complications before initiation of HAART for better response and outcome. While the systematic review on the care of HIV-infected children with SAM failed to state the exact time when HAART should be commenced, it did state that is should be when all acute illnesses have been treated but this was not the case for the majority of children in the study that were on HAART.[34] This could have contributed to the HAART not significantly affecting the duration of the stabilization phase. Furthermore, the number of children on HAART was too small to make a definitive conclusion. The child with the longest duration on HAART had been on it for 1 year and 4 months and he took 6 days to stabilize. The child with the shortest duration on HAART had been on it for only 5 days prior to admission and she took 11 days to stabilize.

The comorbidities did not have a significant effect on the duration of the stabilization phase. While the patients with PDD took the longest to stabilize (6.4 days), this was not statistically significant. Those with AGE took 5.8 days and the ones with Pneumonia took 5.3 days.

The Cox regression analysis revealed that only HIV-infection was significantly associated with the duration of the stabilization phase. This means that the age, sex, type of malnutrition and comorbidities had no effect on the duration of the stabilization phase.

Twenty two children died during the study giving a case fatality ratio of 12.9%. These are children who died before achieving stabilization; 16 of them were HIV-infected while 6 were not HIV-infected. This case fatality rate is below the median case fatality of 20-30%[12] that is commonly found in most nutritional rehabilitation units but higher than the acceptable WHO case fatality of < 5%. It must be noted that the 20-30% case fatality ratio is overall for stabilization and rehabilitation though the majority of the deaths occur during the first 24-48 hours of admission. Among the HIV-infected children the mortality was 17.8% against 7.5% in the HIV-uninfected children. This was marginally statistically significant. This supports the results of a meta-analysis that was done in 2009 on HIV prevalence and mortality in children undergoing treatment for SAM.[36] It revealed that mortality was higher in the HIV-infected, 30.4% vs 8.4% in the HIV-uninfected. Of note is that the mortality in the HIV-uninfected of 7.5% was closer to the acceptable WHO case fatality and reflects that the burden of HIV plays a major role in the WHO target not being achieved. More HIV-infected children die because their response to antibiotics is affected making recovery very difficult.[48] Contrary to the findings of this study however, a study in Niger found no difference in mortality between the HIV-infected and the HIV-uninfected.[21]

Among the children that died, 73% had marasmus, 4% had kwashiorkor and 2% had marasmic-kwashiorkor. This was marginally statistically significant. Children with marasmus were therefore more likely to die than those with the other types of malnutrition. This contradicts the findings of a study in South Africa which found no association between the type of malnutrition and mortality.[25] Another study done in Malawi by also found no association between mortality and type of malnutrition.[37] A literature review in 1996 of case fatality rates in noted that children with kwashiorkor and marasmic-kwashiorkor had a higher risk of mortality when compared to those with marasmus.[12] Generally it is known that children with kwashiorkor are more likely to die due to dysadaptation but in the face of HIV infection, the children with marasmus have a higher mortality. The higher prevalence of HIV infection among the children with marasmus could explain why in our study they had a higher mortality.

The comorbidities were not significantly associated with mortality. Diarrhoea increases the risk of death in children with SAM.[49, 54] It has further been shown that a child with SAM presenting with diarrhea on admission has a higher risk of dying than one without diarrhea.[49] Of the children that died, 60% presented with diarrhea but this was not statistically significant.

There was no significant association between being on HAART and death. Only 4 of the children who died were on HAART. One of these children had only started medication a month before admission while another had been on HAART for 3 months. The third child had started HAART 6 months prior to admission while the fourth one had defaulted treatment and only recently restarted. All four were very ill children and died within 72 hours of admission. The majority of the children who died were not on HAART. Despite having functioning paediatric HAART centres at the main clinics in Lusaka, most of the confirmed HIV-infected children were not on HAART. We know that early initiation of HAART results in decreased mortality[27, 28] so it should be started in children once diagnosed in order to improve their outcome. In the children with SAM however, commencing HAART while they are acutely ill and severely malnourished is associated with higher mortality.[31-33] HAART should be commenced in children before they deteriorate and develop SAM.

11. Conclusion

1. HIV infection prolongs the duration of the stabilization phase in children with SAM admitted to the malnutrition ward at UTH in Lusaka.
2. Comorbidities are similar between the HIV-infected and HIV-uninfected children with SAM.
3. Mortality is higher in the HIV-infected children when compared to the HIV-uninfected children.
4. HAART doesn't affect the duration of the stabilization phase.

12. Limitations

1. The number of patients on HAART was too small to effectively determine its significance on the duration of the stabilization phase and mortality.
2. CD4 counts were not done on the patients on HAART to give an indication of their immunologic response to treatment. Generally CD4 counts are done when the child is in rehabilitation phase.

13. Recommendations

1. The importance of early detection of HIV infection and commencement of HAART before SAM develops should be emphasized to the local clinics.
2. In the HIV-infected children with SAM, initiation of HAART should be delayed until they are out of the acute phase of illness and in rehabilitation with a weight for height SD score of at least < -2SD.

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APPENDIX 1

DATE EXTRACTION SHEET

Date of presentation to UTH: ……..

Study number:

……

Date of birth:

……..

Age/sex: Age ……Sex……..

Residence:

……...

Guardian and relationship to patient:

Mother, father, brother, sister, aunt, uncle, grandmother, grandfather, neighbour, friend, others

If other specify:

…….

Type of Malnutrition:

……..

Weight for Height SD score:

……

Mid Upper Arm Circumference:

……..

Weight for Age SD score:

……..

Height for Age SD score:

……

HIV Status by Antibody Test:

……

HIV Status by DNA PCR:

…….

On HAART or

Not…….

Date HAART

commenced……

Of days until stabilization:

……

Initial of the Research assistant:

……

APPENDIX 2

INFORMATION SHEET

You are invited to participate in this study that will look at the effect of HIV infection on the duration of the stabilization phase in children with severe acute malnutrition admitted to the malnutrition ward at the University Teaching Hospital.

NATURE AND PURPOSE OF THE STUDY.

In this study we are going to compare the duration of recovery time between children with severe acute malnutrition that are HIV-infected with those that are non-infected. The children will be assigned to one of two arms of the study depending on their HIV status and the duration to recovery will be measured. All the children will receive the standard treatment given to all children with SAM.

PROCEDURES OF THE STUDY.

The child will be pricked on a finger to collect a drop or two of blood to determine their HIV status. For those that are less than 18 months, another prick will be done to get a drop of blood for a special HIV test called DNA PCR. 2 mls of blood will also be drawn from the arm for measurement of FBC and CD4 count. This will be done by specially trained nurses.

POSSIBLE RISKS AND DISCOMFORT.

There are no expected adverse events apart from some pain of a needle prick on one of the fingers pricked.

POSSIBLE BENEFITS.

There will be no immediate direct benefit to the child involved in the study but it will increase our knowledge on the peculiarities of the HIV-infected child with severe acute malnutrition and in this way allow us to make targeted interventions to improve their outcomes.

CONFIDENTIALITY.

All information collected in this study is strictly confidential and data or information that will be collected and reported.

CONSENT.

Your participation in this study is strictly voluntary. With or without participating in the study, the child will get the same quality of care and treatment which we give to all our patients with severe acute malnutrition. You may withdraw from the study at any time and for any reasons and there will be no repercussions.

Thank you for considering your child to participate in this study. If you have any concerns, clarifications or questions please do not hesitate to contact Dr. Chanda Kapoma (Principle Investigator) or the University of Zambia Biomedical Research Ethics committee at the addresses below:

Dr. Chanda Kapoma (Principle Investigator) **Department of Paediatrics and Child Health,** **University Teaching Hospital,** **Private Bag IX RW.** **Cell #: +260 977269305.** **E-mail: drkapoma@yahoo.com**	**The Chairperson,** **Research Ethics Committee,** **Ridgeway Campus,** **Post Box 50110,** **Lusaka,10101. Zambia.** **Cell #: +260-211-256067.** **Fax:+260-211-250753.** **Email:unzarec@zamtel.zm.**

APPENDIX 3

CONSENT FORM

I ……., being a parent/ guardian to the child named…..……..……. aged …… agree to participate in a research on the effect of HIV on the duration of the stabilization phase in children with severe acute malnutrition admitted to the University Teaching Hospital, Lusaka. I have understood that the research will involve the drawing of one to two drops of blood for an HIV test and drawing of blood for FBC and CD4 Count. I also understand that the drawing of blood from the above named child is to be done by medical staff adequately trained at conducting such a procedure. Further, it has been explained to me that the above procedure has minimal risk to the child apart from the pain of a small needle prick to one of the fingers of the hand. In the unlikely event that any advse event arises from the procedure, I understand that all reasonable measures will be taken in accordance with the standard medical practice to mitigate such an event. I also understand that I am free to withdraw from the study at any time and that there will be no repercussions.

PARENT/ GUARDIAN	WITNESS
…… (Signature)	…… (Signature)
…… (Date)	…… (Date)
…… (Relationship to child)	..... (Name and designation)

Thumb Print

APPENDIX 4

ICISHIBISHO

Mwaitwa ukusangwamo mwisambililo ilyakumona nga ubulwele bwa HIV bwalikwatamo amaka mukundapwa kwakubalilapo ukwabana abakwata akashishi ka HIV pamo no bulwele bwansala mubana abo abatekwa muno cipatala ca University Teaching Hospital.

IFILI MWISAMBILILO ILI

Mwisambililo ili, tulefwaya ukumona inshita isendwa mukundapwa kwabana abakwata ubulwele bwa nsala abakwatata nakashishi ka HIV nokulinganya nabana abakwata ubulwele bwa nsala abashakwata HIV. Abana bakabikwa muma bumba yabili necikalekanya kukwata akashishi ka HIV nangula ukushikwata, elyo inshita iyi kapitapo apo bakatekelwa napakupola ikapimwa. Bonse abana bakapoka ukundapwa ukwasuminishiwa mukundapa ubulwele bwansala.

IFIKACITIKWA MWISAMBILILO ILI

Umwana onse akatungwa inshindano pamunwe pakusenda umulopa uwunono pakupima nga alikwata akashishi ka HIV nangula iyo. Abana abashila kwanya imweshi yakufyalwa 18, bena bakatungwa nakabili pakupima ukubomfya icipiminwa nacimbi ico beta DNA PCR. Umulopa naumbi uwunono ukufumya pa kuboko ukasendwa nokupimwa pakumona ifyo umulopa uli mumwana ukubikapofye nokupima amaka yamubili ayetwa CD4 count. Ababonfi bamucipatala abasambilila uwu mulimo ebakalafumya umulopa.

UBWAFYA BWINGASANGWAMO

Ubwafya bwakufumya umulopa kukalipafye panono pamunwe apo batungwa inshindano. Tapalifye naumbi umulandu nakalya.

IFISUMA IFYABAMO

Mukwai tapali ifisuma apopenefye kumwana, nomba ili isambililo likatwafwa ukwishiba ifyo ubu ubulwele bwa HIV bucita mubana abakwata ububulwele pamo nobulwele bwansala pakuti kuntanshi twaishiba ifyakucita pakwafwa abana abaisa naya amalwele pakuti tukalebatangata nokwesha ukubaposha ukucilapofye nefyo twaishiba palilelo.

INKAMA

Fyonse ifyo twasanga mwisambililo ili fyankama, tatwakalumbule amashina nelyo yamo iyo, naponse apo tukalalemba ifi fyonse tatwakabike palwalala nakalya.

UKUSUMINA.

Twatotela sana pakusuminisha ukuti umwana uyu abemo mwisambililo ili. Ngamwakwata amatwishiko nangula amepusho, mukwai tekwikata nakucani nakalya, kuti mwatumina abakalamba baili isambililo ba Dr. Chanda Kapoma nangula icilonganino citwa University of Zambia Biomedical Research Ethics Committee palyaka akeala:

Dr. Chanda Kapoma (Principle Investigator) **Department of Paediatrics and Child Health,** **University Teaching Hospital,** **Private Bag IX RW.** **Musange: +260 977269305.** **E-mail: drkapoma@yahoo.com**	**The Chairperson,** **Research Ethics Committee,** **Ridgeway Campus,** **Post Box 50110,** **Lusaka, 10101. Zambia.** **Lamya: +260-211-256067.** **Fax:+260-211-250753.** **Email: unzarec@zamtel.zm.**

APPENDIX 5

ICAKUSUMININAPO

Ine ……., ne mufyashi/ kasunga wa mwana uweshina…..……..……. imyaka …… nasuminisha ukusangwamo muli ili isambililo ilyakumona nga ubulwele bwa HIV bwalikwatamo amaka mukundapwa kwakubalilapo ukwabana abakwata akashishi ka HIV pamo no bulwele bwansala mubana abo abatekwa muno cipatala ca University Teaching Hospital, muno Lusaka. Ningufwa ukuti muli ili isambililo muli nokufumwa umwana umulopa pakupima nga alikwata akashishi ka HIV nokupima ifyo umulopa uli mumwana ukubikapofye nokupima amaka yamubili ayetwa CD4 count. Ningumfwa nokuti ukufumishiwa kwa mulopa kukalacitwa nababomfi bamu cipatala abasambilila bwino bwino uwu umulimo. Nokukonkanyapo, nabanjeba ukuti uwu umulimo tawakwata amafya iyo, kwabafye uku kalipa panono pakutungwa inshindano pamunwe napakuboko. Nabanjeba ukuti nga fyacitike ukuti kwaba amafya ayali yonse, kuti baesha namaka yonse ukukonkafye nefyalembwa pakundapa ifyo fingakonkapo pakutila umwana aba bwino. Ningishiba ati ninkwata insambu shakufumyamo umwana wandi ngafyacitika ati nshitemenwe iyo elyo umwana bakakonkanyapo uku mutangata nge fya suminishiwa.

ABAFYASHI/KASUNGA KAMBONE

…… (Signature) …….....… (Signature)

…… (Ubushiku) …… (Umwana)

…… (Efyonaba no mwana) ..... (Ishina ne cifulo)

Ukufwantika……..

APPENDIX 6

Recipes for F75 and F100

If you have cereal flour and cooking facilities, use one of the top three recipes for F-75:			
Alternatives	Ingredient	Amount for F-75	
If you have dried skimmed milk	Dried skimmed milk Sugar Cereal flour Vegetable oil Mineral mix* *Water to make 1000 ml*	25 g 70 g 35 g 30 g 20 ml *1000 ml***	
If you have dried whole milk	Dried whole milk Sugar Cereal flour Vegetable oil Mineral mix* *Water to make 1000 ml*	35 g 70 g 35 g 20 g 20 ml *1000 ml***	
If you have fresh cow's milk, or full- cream (whole) long life milk	Fresh cow's milk, or full- cream (whole) long life milk Sugar Cereal flour Vegetable oil Mineral mix* *Water to make 1000 ml*	300 ml 70 g 35 g 20 g 20 ml *1000 ml***	
If you do not have cereal flour, or there are no cooking facilities, use one of the following recipes for F-75:			**No cooking is required for F-100:**
Alternatives	Ingredient	Amount for F-75	Amount for F-100
If you have dried skimmed milk	Dried skimmed milk Sugar Vegetable oil Mineral mix* *Water to make 1000 ml*	25 g 100 g 30 g 20 ml *1000 ml***	80 g 50 g 60 g 20 ml *1000 ml***
If you have dried whole milk	Dried whole milk Sugar Vegetable oil Mineral mix* *Water to make 1000 ml*	35 g 100 g 20 g 20 ml *1000 ml***	110 g 50 g 30 g 20 ml *1000 ml***
If you have fresh cow's milk, or full- cream (whole) long life milk	Fresh cow's milk, or full- cream (whole) long life milk Sugar Vegetable oil Mineral mix* *Water to make 1000 ml*	300 ml 100 g 20 g 20 ml *1000 ml***	880 ml 75 g 20 g 20 ml *1000 ml***

APPENDIX 7

Nutrients and Energy Composition of Ready to Use Therapeutic Food

Nutrient	Per sachet of 92 g	Nutrient	Per sachet of 92 g
Energy	500 kcal	Vitamin A	840 mcg
Proteins	12.5 g	Vitamin D	15 mcg
Lipids	32.86 g	Vitamin E	18.4 mg
Calcium	276 mg	Vitamin C	49 mg
Phosphorus	276 mg	Vitamin B1	0.55 mg
Potassium	1 022 mg	Vitamin B2	1.66 mg
Magnesium	84.6 mg	Vitamin B6	0.55 mg
Zinc	12.9 mg	Vitamin B12	1.7 mcg
Copper	1.6 mg	Vitamin K	19.3 mcg
Iron	10.6 mg	Biotin	60 mcg
Iodine	92 mcg	Folic acid	193 mcg
Selenium	27.6 mcg	Pantothenic acid	2.85 mg
Sodium	< 267 mg	Niacin	4.88 mg

Weight (kg)	**Packets / day**	**Packets / w**
3.5 - 3.9	1.5	11
4.0 - 5.4	2	14
5.5 - 6.9	2.5	18
7.0 - 8.4	3	21
8.5 - 9.4	3.5	25
9.5 - 10.4	4	28
10.5 - 11.9	4.5	32
12.0-13.5	5	35
>13.5	200kcal/kg/day	200kcal/kg/day